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Sex differences in the neural correlates of emotional responses and episodic memory encoding for positive and negative emotional stimuli

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Sex differences in the neural correlates of emotional responses and episodic memory encoding for positive and negative emotional stimuli

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M.A., Emory University, 2009

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Abstract

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By Jennifer Strafford Stevens

Evidence from both cognitive and clinical psychology literatures suggests that women and men differ in emotional functioning. Women show greater emotional responses than men in expression and physiological activation, and are more likely than men to be diagnosed with disorders involving emotion, such as depression, anxiety, and PTSD. The goal of the current research was to characterize differences in how women and men respond to emotional stimuli, at the neural level. This issue is critical to understanding basic individual differences in human mental health and in emotion more generally. We conducted three studies: Study 1 was a meta-analysis of neuroimaging studies of emotional processing in women and men, Study 2 was a neuroimaging experiment investigating sex differences in the response to emotionally-arousing visual stimuli, and Study 3 was a neuroimaging experiment investigating how sex differences in emotional brain regions might influence episodic memory. The meta-analysis combined the results of studies which explicitly examined sex differences with the much larger number of studies that examined only women or men, using activation likelihood estimation (ALE). For studies of negative emotion, women showed greater activation of the amygdala than men. For studies of positive emotion, men showed greater activation of the amygdala than women. The findings provided novel evidence that sex differences depend on whether an emotional stimulus is affectively negative or positive. In study 2, we replicated the finding that women showed greater amygdala responses to negative stimuli, and found greater hypothalamus responses to positive stimuli in men than women. In addition, women showed greater functional connectivity than men between the amygdala and anterior cingulate cortex, a circuit involved in emotion regulation. Men showed greater functional connectivity than women between the amygdala and nucleus accumbens, a circuit involved in reinforcement learning and appetitive motivation. In study 3, we found that the amygdala plays a greater role in encoding emotional stimuli in women than men, and that functional connectivity between the amygdala and hippocampus during encoding was predictive of later memory in women but not men. Overall, the findings provide converging evidence for important differences in women's and men's brain processing of emotional stimuli, and highlight the need for greater consideration of gender in the study of emotion.

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Chapter 1

General Introduction

Considerable evidence indicates that women and men behave differently during emotional experiences. For example, women have been reported to express greater facial emotion than men to a wide variety of emotional stimuli, report feeling more emotional arousal, and display heightened physiological arousal responses (Bradley, Codispoti, Sabatinelli, & Lang, 2001; Grossman & Wood, 1993; Hall, Carter, & Horgan, 2000; Kring & Gordon, 1998). A complementary literature provides evidence that women and men also differ in the recognition of emotional social signals, with a clear advantage for women across different types of emotion and different cue modalities (for a review, see Hall, 1978). For example, women are faster (Goos & Silverman, 2002; Hampson, van Anders, & Mullin, 2006; McClure, 2000) and more accurate (Hall & Matsumoto, 2004) in recognizing emotional facial expressions, and display heightened and more selective responses to unattended emotional verbal sounds (Schirmer et al., 2008; Schirmer, Striano, & Friederici, 2005).

Examples of enhanced emotional reactions in women have led some theorists to propose that, on average, women exhibit emotional responses more strongly than men (Grossman & Wood, 1993). Such proposals are consistent with the Western cultural notion of the women as the emotional sex (Fischer & Manstead, 2000). Surveys of women and men's perceptions of typical behavior for each gender consistently find that women are viewed as more likely to display negative emotionality in facial expression than men (Fischer, Rodriguez Mosquera, van Vianen, & Manstead, 2004; Grossman & Wood, 1993; Hess et al., 2000; Kring & Gordon, 1998), and even children as young as three years of age show evidence of gender stereotypes of the emotional facial expressions that are more "female" (sadness, fear) versus those that are more "male" (anger) (Birnbaum, Nosanchuk, & Croll, 1980).

Emotion can be conceptualized using the basic dimensions of arousal (subjective and physiological emotional intensity) and valence (whether the emotion is positive or negative). The prevailing accounts of sex differences in emotion focus on the arousal dimension, positing that women are more sensitive to emotional stimuli and thus have greater arousal responses than men

(e.g., Fujita, Diener, & Sandvik, 1991; Grossman & Wood, 1993). However, it may also be useful to consider the dimension of emotional valence. Some evidence suggests that sex differences in responses to emotionally arousing stimuli may depend on whether the stimuli are affectively positive or negative. Larger emotional responses in women are most often observed in the context of studies presenting negative emotional visual stimuli (e.g. Bradley et al., 2001; McManis, Bradley, Berg, Cuthbert, & Lang, 2001; Thomsen, Mehlsen, Viidik, Sommerlund, & Zachariae, 2005). Greater subjective and physiological responses to negative stimuli in women are consistent with sex differences in the prevalence of mood-related mental health problems—anxiety and depression are diagnosed more frequently among women, beginning in adolescence and continuing across the lifespan (Leach, Christensen, Mackinnon, Windsor, & Butterworth, 2008; Nolen-Hoeksema, 2001).

For the majority of studies of positive stimuli, there has not been an observed sex difference. However, sex differences have been reliably observed in studies of women and men's emotional responses to erotic stimuli. When viewing sexually-arousing photographs, men report higher levels of emotional intensity than women, and exhibit larger skin conductance responses (Bradley et al., 2001; Chivers, Seto, Lalumiere, Laan, & Grimbos, 2009). Although erotic stimuli may be considered a class of highly-arousing affectively positive stimuli, they activate not only emotional arousal but also sexual arousal responses. Further research is needed to distinguish the extent to which enhanced male responses are specific to erotica, or might be characteristic of general affective responses to highly arousing pleasant stimuli.

Behavioral studies have primarily addressed questions about sex differences by examining differences in subjective and psychophysiological emotional responses in women and men. Because emotions ultimately originate in the brain, these sex differences in emotional responses should be reflected in the activity of brain regions involved in emotion processing. Information about neural processing during emotional experiences may be more sensitive to sex differences in emotion, and can provide unique information about how emotional responses

unfold. Emotions involve many components, including physiological changes, subjective feelings, evaluative cognitive processes, and motivated behavior. While behavioral and physiological measures represent surface-level measures of many aggregated processes, neuroimaging can reveal the individual neural and cognitive processes that form the building blocks for the emotional experience. These brain processes may be each be influenced by the factors that differentiate women and men such as hormones, genetics, and experience. Given the potential for information about brain function to clarify our understanding of sex differences in emotion, the current research employed a neuroimaging approach to investigate differences in women's and men's responses to emotional stimuli, in three studies.

Findings from individual functional neuroimaging studies provide suggestive evidence of neural differences contributing to sex differences in emotional behavior, but relatively few neuroimaging studies of sex differences in emotional processing have been reported. The meta-analytic technique provides a unique way to address this issue, by aggregating results across many studies to determine whether there are reliable sex-specific effects in the brain areas active during emotion. In the first study, we conducted a meta-analytic review of functional neuroimaging findings investigating differences between women's and men's emotional neural responses by synthesizing findings from the past 18 years of research. The aggregation approach is especially helpful in functional neuroimaging research because small sample sizes often restrict statistical power. Individual studies may not detect sex differences, especially within the domain of emotional processing, in which individual differences are likely to influence processing within-sex (Hamann & Canli, 2004). The meta-analysis was designed to identify convergent findings across the neuroimaging literature, to build initial expectations about where we might expect differences in function.

The second study was an experimental assessment of whether the sex differences found in the meta-analysis would be replicated within a single experiment. We examined women's and men's neural responses to emotional scenes using functional magnetic resonance imaging (fMRI).

This study provided a test of the hypothesis that sex differences depend on emotional valence, specifically that we would observe female-specific neural responses to negative stimuli, and male-specific responses to positive stimuli. Another goal of this study was to clarify sex differences in functional connectivity with the amygdala during affective responses, as some previous evidence suggests that the amygdala may participate in different sets of interacting brain regions in women and men.

The third study served as an investigation of whether sex differences in the emotional responses of brain regions such as the amygdala would influence cognitive processing. Here we investigated the role of the amygdala in encoding memories of emotional stimuli, in women and men. Emotional material receives preferential processing by the memory system during encoding, leading to better memory for emotional events later on. The effects of emotion on memory encoding have been shown to be produced through amygdala modulation of the encoding of memory traces in the hippocampus and other regions of the medial temporal lobe (Cahill & McGaugh, 1998; Hamann, 2001). We investigated whether these processes differ in women and men, during the encoding of negative and positive scene stimuli. We used fMRI to examine women's and men's responses to the emotional stimuli as a function of whether each scene was later recalled or forgotten.

The emotional brain

Several brain regions have traditionally been implicated in making key contributions to emotional functions such perceiving and orienting to emotional stimuli, creating and assigning hedonic values to emotional stimuli, and producing and regulating emotional behavior. These regions—observed to reliably knock out emotional behaviors when lesioned in animal and human neuropsychiatric lesion studies, or to be reliably active in functional brain imaging of emotion—include the amygdala, ventral striatum, orbitofrontal cortex, anterior cingulate cortex, hypothalamus, anterior insula, and ventromedial prefrontal cortex (for reviews of emotional brain regions, see Dalgleish, 2004; Pessoa, 2008). Many of the brain regions implicated in emotion

also possess a high density of gonadal hormone receptors, and are thus especially sensitive to sex differences in the internal hormonal milieu. Subcortical regions that are especially rich in gonadal hormone receptors include the hypothalamus, amygdala, and hippocampus; cortical regions include the anterior cingulate cortex, orbitofrontal cortex, and ventrolateral prefrontal cortex (Clark, Maclusky, & Goldman-Rakic, 1988; MacLusky, Naftolin, & Goldman-Rakic, 1986).

Although many brain regions contribute to processing an emotional experience, evidence supports the idea that the amygdala plays a central role in emotional functioning. Research on the neural substrates of fear conditioning, primarily conducted in rodents, has illustrated that plasticity in the amygdala directly mediates the acquisition and extinction of conditioned fear responses (for a review, see LeDoux, 2000). In humans, amygdala damage has been shown to impair physiological responses to stimuli that evoke emotional responses in participants with intact amygdalae (Glascher & Adolphs, 2003). Patients with amygdala damage have also shown impairments in acquiring autonomic arousal responses to conditioned fear stimuli (Bechara et al., 1995), and have difficulty recognizing emotional social signals such as facial expressions (Adolphs, 2003; Adolphs & Tranel, 1994). Thus it appears that an intact amygdala is necessary for many aspects of emotional functioning. A major goal of the current research was to characterize sex differences in emotional responses across the brain and, given the support for the amygdala's critical role in emotional processes, we focused on the amygdala in particular.

Sex differences in brain structure

Women's and men's brains exhibit differences in global structure, and in regions which are involved in emotional processing. Although men's brains are greater in overall volume, women possess a higher ratio of gray to white matter in most cortical region, (Allen, Damasio, Grabowski, Bruss, & Zhang, 2003; Good et al., 2001). Some evidence exists to suggest that structural dimorphisms may be present from birth, as male neonates have around 10% more cortical gray matter, white matter, and overall intracranial volume, similar to differences observed

in adults (Gilmore et al., 2007). It is not yet clear whether global differences in neonates contribute to sex differences in emotion seen early in childhood (e.g., Davis & Emory, 1995; McManis et al., 2001). Global structural differences are not often interpreted in relation to specific functions, and may only indirectly inform our knowledge of sex differences in emotional processing.

Region-specific dimorphisms in brain structure have been more clearly linked to sex differences in emotional behavior. For example, the volume of the orbitofrontal cortex is larger in women than men (Gur, Gunning-Dixon, Bilker, & Gur, 2002). Moreover, the size of this region correlates with emotion regulation ability across individuals, and appears to mediate sex differences in emotion regulation (Welborn et al., 2009). Similar links between regional volume and emotional behavior have been demonstrated in the amygdala. Its volume correlates positively with circulating testosterone levels during adolescence (Neufang et al., 2009), and this correlation increases with physical sexual maturity during puberty (Bramen et al., 2011). Accordingly, men have greater gray matter volume than women in the amygdala bilaterally (Good et al., 2003; Neufang et al., 2009). Larger amygdala volumes have been associated with decrements in the ability to recognize fearful facial expressions (Good et al., 2003). Such sex differences in the structure of emotional brain regions are interesting because they suggest that gender substantially shapes the physical organization of the brain. In addition, regions that exhibit sexual dimorphisms in volume or composition, and are linked to emotional behaviors, may function differently in women and men.

Sex differences in emotion-related brain function

Among the few studies that have directly investigated the influence of sex on emotional brain function in humans, differences in brain activity can be observed even when women and men indicate feeling comparable levels of emotion. When emotional arousal levels are matched between women and men, such differences may be attributed to different types of processing or different cognitive styles (Hamann, 2005). Pleasant picture stimuli eliciting sex-matched levels

of subjective or physiological arousal (e.g., skin conductance) evoke greater amygdala responses in men than women (Hamann, Herman, Nolan, & Wallen, 2004; Wrase et al., 2003). Recent evidence suggests that this phenomenon is not specific to the visual modality. When women and men indicated similar levels of subjective emotionality and detail in recalling emotional personal events, men displayed more BOLD activation in left parahippocampal gyrus, whereas women displayed more activation in right insula and right dorsolateral prefrontal cortex (Piefke, Weiss, Markowitsch, & Fink, 2005). Additionally, when smelling pleasant and unpleasant odors, both women and men show activation in bilateral insula and left amygdala, but women also show activation in left orbitofrontal gyrus (Royet, Plailly, Delon-Martin, Kareken, & Segebarth, 2003). Evidence that women and men recruit different sets of brain regions while reporting similar levels of emotion may suggest categorical differences in how the brain processes emotional stimuli, and not simple differences in the degree of arousal for women and men.

Functional brain imaging studies also suggest that sex-differential patterns of brain activity may depend on the emotional valence of stimuli. Women's enhanced sensitivity to unpleasant events appears to co-occur with enhanced brain responses to unpleasant events. In response to aversive stimuli, women evidence greater BOLD responses than men in medial prefrontal and anterior cingulate cortex, primarily in the left hemisphere (Caseras et al., 2007; Domes et al., 2009; Fine, Semrud-Clikeman, & Zhu, 2009; George, Ketter, Parekh, Herscovitch, & Post, 1996; Wrase et al., 2003). Activation in these regions in women has been interpreted to reflect integration of emotional and attentional signals, and / or emotion regulation processes. Electroencephalographic studies also provide support for left-hemisphere lateralization of this effect—women show larger arousal-related responses than men during early processing, 100-200ms, only on left-hemisphere recording sites (Lithari et al., 2010; Proverbio, Adorni, Zani, & Trestianu, 2009). Trait defensiveness in women has been associated with an frontal asymmetry of the EEG signal that is left-lateralized (Kline, Allen, & Schwartz, 1998). Left-lateralized frontal responses may be a consistent feature of women's processing of negative emotional

events. Neuroimaging studies have also identified enhanced negative affective responses in women in a variety of other cortical and subcortical regions including left middle temporal gyrus and right dorsolateral prefrontal cortex (Domes et al., 2009), right brainstem and putamen (George et al., 1996), and left parahippocampal gyrus (Hofer et al., 2007).

Some findings suggest that men show stronger neural activity than women specifically in response to positive emotional stimuli. Men show larger responses than women for pleasant affective stimuli in several emotion-related brain regions including left amygdala, and bilateral inferior and medial frontal gyri (Wrase et al., 2003). Neuroimaging studies also report that core emotional brain regions such as the amygdala and hypothalamus are activated when men view erotic stimuli (Beauregard, Levesque, & Bourgouin, 2001; Meseguer et al., 2007; Sabatinelli, Flaisch, Bradley, Fitzsimmons, & Lang, 2004; Walter, Stadler, Tempelmann, Speck, & Northoff, 2008), and these regions exhibit greater activity in response to erotic stimuli in men than women (Hamann et al., 2004; Sabatinelli et al., 2004). Pleasant stimuli do not, however, uniformly evoke larger responses in men than women, as some findings indicate larger positive affective responses in women than men in right posterior cingulate cortex and putamen (Hofer et al., 2006; Hofer et al., 2007), left prefrontal cortex (George et al., 1996; Hofer et al., 2006), and right superior temporal gyrus (Hofer et al., 2007). Furthermore, a recent meta-analytic review found that men reliably show greater right amygdala activation than women when recognizing negative and positive emotional facial expressions (Fusar-Poli et al., 2009), suggesting that men may show larger responses than women in certain brain regions regardless of whether an emotional stimulus is positive or negative. In summary, neuroimaging evidence supports the broad proposal that sex differences in patterns of emotional behavior mirror sex differences in patterns of brain functioning.

Sex differences in amygdala responses to emotional stimuli

The amygdala, in particular, has been implicated in contributing to differences in women' and men's emotional behavior (Hamann, 2005). In studies of negative emotion, neuroimaging

evidence supports the idea that amygdala responses are enhanced in women relative to men. Several studies using aversive stimuli have demonstrated larger amygdala responses in female than male participants (Domes et al., 2009; Hofer et al., 2006; Wrase et al., 2003).

Although few studies have compared women and men's responses to pleasant stimuli, beginning evidence suggests a possible pattern of greater left amygdala activation in men than women. Men exhibit left-lateralized amygdala responses to positive emotional pictures (Hamann, Ely, Hoffman, & Kilts, 2002) and words (Hamann & Mao, 2002). Wrase and colleagues (2003) compared the amygdala responses of female and male participants and found that only men exhibit increases in amygdala responses for pleasant stimuli relative to neutral, whereas women do not exhibit increases in amygdala responses to pleasant stimuli. This study also observed that the left amygdala response to pleasant stimuli was greater in men than women (Wrase et al., 2003). However, this sex difference in left amygdala activation may not generalize to non-erotic positive emotion as the pleasant stimuli included erotic scenes, and has not been replicated in a more recent study of responses to pleasant scene stimuli (Hofer et al., 2006). Further, a study of sex differences in face processing reported greater right-hemisphere lateralization of amygdala responses in men than women who viewed happy facial expressions (Killgore & Yurgelun-Todd, 2001). Such findings suggest hemispheric laterality of amygdala responses may not be consistent, or may be influenced by stimulus modality (faces versus scenes). One recent study controlled for the effects of erotica using pleasant and unpleasant non-erotic pictures, and found that emotionally arousing scene stimuli, independent of positive or negative valence, elicited greater left amygdala activation in women than men, and greater right amygdala activation in men than women (Aikins, Anticevic, Kiehl, & Krystal, 2010).

Inconsistencies across studies of emotional experience point to a need for further research to resolve the influence of sex on amygdala activity. A recent meta-analysis attempted to resolve this issue by characterizing the pattern of findings across fMRI studies of emotional face processing (Fusar-Poli et al., 2009). Their results suggested that men were more likely than

women to activate right amygdala in response to emotional face stimuli. Such findings leave open questions about what might be found in women's and men's brain responses to emotional stimuli other than faces, and whether sex differences are dependent upon the whether the emotional experience is pleasant or aversive. The meta-analysis described in Study 1 addresses these questions by testing for sex differences across 44 neuroimaging studies of women and 44 studies of men, across a variety of emotion elicitation tasks.

Sex differences in emotional processing networks

Sex differences in regional activation levels appear to be accompanied by sex differences in connectivity within the network of brain regions recruited during an emotional event. It is necessary to consider the activity of individual brain regions within the context of larger interactions among regions, as the many brain processes that contribute to a particular behavior or cognitive computation take place within circuits of interacting regions. Emotional processing and regulation behaviors are often related to a network of connections between medial-prefrontal cortex and the amygdala and other medial temporal regions (Pessoa, 2008). Several studies examining regions that interact with the amygdala during rest have found that in women, the left amygdala exhibits more widespread functional connectivity than the right, whereas in men the right amygdala exhibits more widespread functional connectivity than the left (Ciumas, Hirschberg, & Savic, 2009; Kilpatrick, Zald, Pardo, & Cahill, 2006; Savic & Lindstrom, 2008). The participation of the amygdala in different functional circuits for women and men suggests that this region may perform different computations or serve different functions in each sex, at rest. Although the amygdala forms a critical node of the network of emotional brain regions, no study has yet explored whether similar sex differences in emotion processing circuits connected with the amygdala are observed during the affective response. Study 2 tests this possibility using task-based functional connectivity analyses.

Sex differences in the amygdala contribution to episodic memory encoding

Amygdala activity during encoding correlates with subsequent memory for arousing events, but does not correlate with memory for neutral events (Cahill et al., 1996; Canli, Desmond, Zhao, Glover, & Gabrieli, 1998; Hamann, Ely, Grafton, & Kilts, 1999). Studies of the amygdala's contribution to emotional memory reveal clear sex differences. The correlation between amygdala activity and memory for negative stimuli occurs in the right amygdala in men, and the left amygdala in women (Cahill et al., 2001; Cahill, Uncapher, Kilpatrick, Alkire, & Turner, 2004; Canli, Desmond, Zhao, & Gabrieli, 2002). Sex differences in the amygdala's contribution to memory for positive stimuli have not been examined previously. Study 3 measured the brain activity supporting memory for both positive and negative stimuli. The findings clarify whether the sex-specific hemispheric asymmetries observed previously may be extended more broadly to characterize the effects of both positive and negative emotion on memory formation in women and men.

Hypotheses

In study 1, among regions that support emotion, I predicted that the amygdala, thalamus, hypothalamus, ventral striatum, anterior cingulate, orbitofrontal cortex, and insula would exhibit sex differences, because they are densely populated with gonadal hormone receptors (Clark et al., 1988; MacLusky et al., 1986; Roselli, Klosterman, & Resko, 2001), and exhibited sex differences in functional neuroimaging studies (e.g., Hamann et al., 2004; Schienle, Schäfer, Stark, Walter, & Vaitl, 2005). Further, these regions were identified as more active in one sex than another in a previous meta-analysis that included a subset of the studies entering the current analysis (Wager, Phan, Liberzon, & Taylor, 2003).

The valence of an emotional stimulus may play an important role in determining the nature of sex differences in the brain response. Relative to men, women display stronger behavioral and physiological responses to negative stimuli, and this sex difference appears early in development (Bradley et al., 2001; Davis & Emory, 1995; McManis et al., 2001). We will test

the prediction that women will show larger brain responses than men in response to negative stimuli, but do not have specific expectations about the brain regions involved. Evidence from studies with sexual stimuli gives some suggestion that, relative to women, men may show stronger responses to positive, appetitive stimuli (Bradley et al., 2001; Chivers, Rieger, Latty, & Bailey, 2004; Taylor et al., 2000). We predict that men may show preferential responses to positive stimuli in amygdala and hypothalamus, as has been observed in studies of appetitive responses to erotic stimuli.

In study 2, I anticipated that there would be substantial overlap in the regions in which responses to positive and negative pictures differ for women and men, between the results of the meta-analytic results and the results of the fMRI study. In addition, I predicted that the amygdala would participate in different circuits in women and men during the initial response to an emotional stimulus.

In study 3, I predicted that emotional encoding would depend on different neural substrates in women and men, for both negative and positive items. I predicted that successful encoding of negative items would depend on the left amygdala to a greater degree in women than men, and the right amygdala to a greater degree in men than women, in line with previous findings (Cahill et al., 2001; Cahill et al., 2004; Canli et al., 2002). As sex differences in the brain activity supporting encoding of positive items have not been examined, I had no explicit predictions about the regions whose activity might differ between women and men. The initial hypothesis was that the encoding of positive stimuli would be associated with similar neural activation as the encoding of negative stimuli.

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Chapter 2

Sex differences in brain activation to emotional stimuli: A meta-analysis of neuroimaging studies

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2.1 Abstract

Substantial sex differences in emotional responses and perception have been reported in previous psychological and psychophysiological studies. For example, women have been found to respond more strongly to negative emotional stimuli, a sex difference that has been linked to an increased risk of depression and anxiety disorders. The extent to which such sex differences are reflected in corresponding differences in regional brain activation remains a largely unresolved issue, however, in part because relatively few neuroimaging studies have addressed this issue. Here, by conducting a quantitative meta-analysis of neuroimaging studies, we were able to substantially increase statistical power to detect sex differences relative to prior studies, by combining emotion studies which explicitly examined sex differences with the much larger number of studies that examined only women or men. We used an activation likelihood estimation approach to characterize sex differences in the likelihood of regional brain activation elicited by emotional stimuli relative to non-emotional stimuli. We examined sex differences separately for negative and positive emotions, in addition to examining all emotions combined. Sex differences varied markedly between negative and positive emotion studies. The majority of sex differences favoring women were observed for negative emotion, whereas the majority of the sex differences favoring men were observed for positive emotion. This valence-specificity was particularly evident for the amygdala. For negative emotion, women exhibited greater activation than men in the left amygdala, as well as in other regions including the left thalamus, hypothalamus, mammillary bodies, left caudate, and medial prefrontal cortex. In contrast, for positive emotion, men exhibited greater activation than women in the left amygdala, as well as greater activation in other regions including the bilateral inferior frontal gyrus and right fusiform gyrus. These meta-analysis findings indicate that the amygdala, a key region for emotion processing, exhibits valence-dependent sex differences in activation to emotional stimuli. The greater left amygdala response to negative emotion for women accords with previous reports that women respond more strongly to negative emotional stimuli, as well as with hypothesized links

between increased neurobiological reactivity to negative emotion and increased prevalence of depression and anxiety disorders in women. The finding of greater left amygdala activation for positive emotional stimuli in men suggests that greater amygdala responses reported previously for men for specific types of positive stimuli may also extend to positive stimuli more generally. In summary, this study extends efforts to characterize sex differences in brain activation during emotion processing by providing the largest and most comprehensive quantitative meta-analysis to date, and for the first time examining sex differences as a function of positive vs. negative emotional valence. The current findings highlight the importance of considering sex as a potential factor modulating emotional processing and its underlying neural mechanisms, and more broadly, the need to consider individual differences in understanding the neurobiology of emotion.

2.2 Introduction

Among the many psychological differences between men and women, sex differences in emotion have long held special interest for scientists and laypersons alike. In contrast to popular conceptions of sex differences, for example, of women as being uniformly more emotionally responsive than men, empirical studies of affective behavior and psychophysiology have yielded a more complex and nuanced picture. Empirical studies have reported differences between women and men in their psychological and physiological responses to wide range of emotional stimuli. For example, women have been reported to respond more expressively than men to emotional stimuli, to report feeling more emotion, and to display heightened physiological arousal responses (Bradley et al., 2001; Grossman & Wood, 1993; Kring & Gordon, 1998). However, the empirical literature remains somewhat inconsistent regarding the nature of these affective sex differences, and the magnitude of observed sex differences has varied widely across studies (Bradley et al., 2001).

A key dimension of emotion that may help explain variability in the experimental literature on affective sex differences is valence, that is, whether an emotion is positive (pleasant) or negative (unpleasant). Sex differences for studies involving negative emotions have been demonstrated more consistently and have been larger on average relative to positive emotions (e.g., Bradley et al., 2001; Davis & Emory, 1995; McManis et al., 2001; Sharp et al., 2006; Thomsen et al., 2005). Women's affective responses to negative emotional stimuli have been of particular interest because enhanced responses to negative emotional stimuli and stressors have been theorized to contribute to mechanisms underlying the greater prevalence of depression and anxiety disorders in women (Leach et al., 2008; Nolen-Hoeksema, 2001; Thomsen et al., 2005).

Fewer studies have investigated sex differences in the context of positive emotions. Although there is currently little evidence to suggest the existence of sex differences in affective responses to positive stimuli in general, limited evidence suggests that men are more emotionally

aroused by visual erotica, showing higher subjective ratings of affect and greater skin conductance responses (Bradley et al., 2001; Chivers et al., 2010).

These affective sex differences in behavioral and physiological responses ultimately arise from differences in brain activity, and thus to fully understand these differences it is necessary to investigate their neural basis. The extent to which sex differences in emotional response are reflected in regional brain activation as assessed by neuroimaging methods remains a largely open question, however. This is in part because only a small number of neuroimaging studies to date have investigated sex differences in emotional responses by directly comparing women and men's emotional and neural responses to the same stimuli. Meta-analytic methods can help overcome these limitations, by allowing the much larger emotion neuroimaging literature comprised of studies of only one sex to be combined with and augment the smaller literature of studies that have directly compared men and women within the same experiment.

Accordingly, we conducted a quantitative meta-analysis of neuroimaging studies of emotion, that allowed us to substantially increase statistical power to detect sex differences by combining emotion studies that explicitly examined sex differences with the much larger number of studies that examined only one sex. We used a voxel-based meta-analysis approach (Activation Likelihood Estimation, ALE; Eickhoff et al., 2009) to characterize sex differences in the likelihood of regional brain activation elicited by emotional stimuli relative to non-emotional stimuli. Because we hypothesized that sex differences would differ by valence, we examined sex differences separately for positive and negative emotions, in addition to examining differences across all emotions combined. To our knowledge, all previous neuroimaging meta-analyses examining sex differences in emotion have combined positive and negative stimuli together when contrasting women and men, precluding examination of sex differences that vary by emotional valence.

The current study used ALE to synthesize and analyze neuroimaging results bearing on sex differences in emotional brain responses. Among regions that support emotion, we predicted

that the amygdala, hypothalamus, ventral striatum, anterior cingulate, orbitofrontal cortex, and insula would exhibit sex differences, on the basis of previous neuroimaging studies of sex differences in emotional responses (e.g., Hamann et al., 2004; Schienle et al., 2005; Wrase et al., 2003) and on the distribution of gonadal hormone receptors in the brain (Clark et al., 1988; MacLusky et al., 1986; Roselli et al., 2001). We predicted that sex differences in brain response would differ by emotional valence, with women showing increased activation likelihood in regions associated with emotion, for negative but not for positive emotion. As noted previously, men have been found to be more responsive to specific types of appetitive, positive emotional stimuli and therefore would be expected to show increased activation likelihood for positive emotion. However, because considerably less evidence supports the view that men are more responsive to positive stimuli, our predictions for such increased activations for men were more tentative than our corresponding predictions for women.

2.3 Methods

Study selection

To help ensure a representative sample of emotion studies, we used relatively broad inclusion criteria to select studies for inclusion in the analysis. Neuroimaging contrasts contributing to the analysis spanned a variety of types of stimuli and specific emotions (see Table 1 and Figure 1). For example, several studies included in the analysis examined emotional responses to affectively pleasant or unpleasant stimuli, whereas other studies examined responses to specific emotions such as anger, disgust, fear, happiness or sadness (Table 1 and Figure 2a).

Candidate studies were selected through searches of PubMed and ISI Web of Science, for publication years 1990 – June 2010, to cover the period of investigation from the earliest PET and fMRI studies of healthy emotional brain function in the early 1990's through the present day. The search was restricted to English language studies with human participants. Search terms were applied to all fields: "emotions" OR "emotion" AND ("magnetic resonance imaging" OR

"fMRI" OR “PET”). The search yielded 2473 studies. From among this group of studies, we included only those which reported maximal coordinates from female-only and/or male-only samples, and reported coordinates for whole-brain activation maxima in either Talairach space (Talairach & Tournoux, 1988) or Montreal Neurological Institute (MNI) space. No coordinates from ROI analyses were included. Data from patient groups, and participants under the age of 18 or over the age of 55 were excluded. Studies were included only if the experimental task elicited emotion, and included no significant component of other types of cognition such as reasoning. Data was included from studies that examined negative emotions, positive emotions, or a combination of several emotions. In total, 44 studies of women and 44 studies of men contributed one or more sets of activation maxima to the current meta-analysis (a 147% increase in the number of studies since the most recent comparable meta-analysis; Wager et al., 2003). Data for women and men were extracted from within-groups results (women-only, or men-only) and no data from comparisons between women and men were included in the meta-analyses. Table 2 summarizes the characteristics of the data set.

Emotions evoked in each neuroimaging study were classified as Negative if they were either specific emotions commonly classified in the emotion literature as negative in affective valence, such as anger, fear, disgust, guilt, or sadness, or were reported as having significantly negative valence in the original study from which the emotion contrast was selected. The corresponding classification for the Positive emotion condition included responses to pleasant, emotionally arousing stimuli, including responses to erotic stimuli, as well stimuli eliciting happiness or amusement. Task conditions that were not specifically associated with emotional responses were omitted. In addition studies of fear conditioning or appetitive conditioning were not included, because these tasks include a significant learning component. No studies of reasoning about emotional situations (e.g., moral dilemmas, theory of mind tasks, empathy tasks) were included, because these tasks include a significant reasoning component. Neuroeconomic studies involving gambling tasks or social games were not included, because they involve a

significant decision-making component. Studies of surprise were also omitted, primarily because of the small number of relevant neuroimaging studies. No studies of hunger, thirst, pain, visceral stimulation, were included, because they involved more basic motivational processes. Deactivations associated with emotion were not included, because few relevant studies have reported deactivations and the interpretation of relative deactivations is relatively unclear in comparison with activations. Each set of activation maxima represented a contrast between an emotionally arousing condition versus a non-emotional baseline condition.

Table 1
Studies included in the meta-analysis

		Valence			*N*		
Study	Year	Pos	Neg	Combined	Female	Male	Experimental contrast(s)
George	1995		x		11		autobio recall + faces: sadness > neutral
Breiter	1996	x	x			10	faces: fear > neutral; happy > neutral
Dolan	1996	x				8	faces: happy > neutral
George	1996	x	x		10	10	autobio recall + faces: sadness > neutral; happiness > neutral
Kosslyn	1996		x			7	pictures: negative > neutral; mental imagery: negative > neutral
Baker	1997	x	x			10	moods elicited before scan: negative (script-driven imagery + music + social interaction) > neutral; positive (script-driven imagery + music + social interaction + monetary gift) > neutral
Beauregard	1997			x		10	words: emotional > fixation
Lane	1997	x	x		12		films + autobio recall: disgust > neutral; sadness > neutral; happiness > neutral
Lane	1997	x	x		12		pictures: negative > neutral; positive > neutral
Reiman	1997			x	12		films: emotion > neutral; autobio recall: emotion > neutral
Zald	1997		x		12		odors: negative > no scent
Phillips	1998		x			6	faces: disgust > neutral; fear > neutral; prosody: disgust > neutral; fear > neutral
Taylor	1998		x		8		pictures: negative > neutral
Blair	1999		x			13	faces: anger > neutral; negative > neutral
Dougherty	1999		x			8	autobio recall: anger > neutral
Mayberg	1999		x		8		autobio recall: sadness > fixation
Morris	1999		x	x		6	prosody: emotion > neutral; fear > neutral
Nakamura	1999			x		7	faces: emotion discrim. > background color discrim.
Rauch	1999	x				8	autobio recall: positive erotic > neutral; positive nonerotic > neutral
Buchanan	2000	x	x	x		10	prosody: emotional > fixation; happy > fixation; sad > fixation
Dolan	2000			x		10	picture retrieval: emotional > neutral
Frey	2000		x		11		environmental sounds: negative > neutral
Liberzon	2000		x		10		pictures: negative > neutral
Liotti	2000		x		8		autobio recall: sadness > neutral
Royet	2000			x		12	odors: emotion > neutral; pictures: emotion > neutral; sounds: emotion > neutral
Shin	2000		x			8	autobio recall: guilt > neutral
Beauregard	2001	x				10	films: erotic > neutral
Herpertz	2001		x		6		pictures: negative > neutral
Tabert	2001		x		9		words: negative > neutral
Williams	2001		x			11	faces: fear > neutral
Aalto	2002	x	x		11		films: sad > neutral; amusing > neutral
Canli	2002		x		12	12	pictures: correlation with increasing arousal
Hamann	2002(a)		x	x		14	words: negative > neutral; positive > neutral
Hamann	2002(b)		x	x		9	pictures: negative > neutral; positive > neutral
Schienle	2002		x		12		pictures: disgust > neutral; fear > neutral
Abel	2003		x			8	faces: fear > neutral

Study	Year	Pos	Neg	Combined	Female	Male	Experimental contrast(s)
Lange	2003		x			9	faces: fear > neutral
Levesque	2003		x		20		films: sadness > neutral
Mitterschiffthaler	2003	x			7		pictures: positive > neutral
Mouras	2003	x				8	pictures: erotic > neutral
Royet	2003	x	x		14	14	odors: negative > no scent; positive > no scent
Wicker	2003	x	x			14	odors: disgust > no scent; dynamic faces: disgust > neutral
Wrase	2003	x	x		10	10	pictures: negative > neutral; positive > neutral
Cahill	2004		x		11	12	pictures: correlation with increasing arousal
Herz	2004			x	5		odors: emotion > neutral
Malhi	2004	x	x		10		captioned pictures: negative > neutral; positive > neutral
McClure	2004		x		8	9	faces: anger > fixation; fear > fixation
Ottowitz	2004		x		8		script-driven imagery: sadness > neutral
Phillips	2004		x			8	faces: disgust > neutral; fear > neutral
Stark	2004		x			24	pictures: disgust > neutral; fear > neutral
Goldin	2005	x	x		13		films: sadness > neutral; amusement > neutral
Habel	2005	x	x			26	faces: sadness > gender descrim.; happiness > gender descrim.
Schienle	2005		x		63		pictures: disgust > neutral; fear > neutral
Shirao	2005		x		13		words: negative > neutral
Harenski	2006		x		10		pictures: negative (moral) > fixation; negative (non-moral) > fixation
Hofer	2006	x	x		19	19	pictures: negative > neutral; positive > neutral
Schienle	2006		x		12		pictures: fear > neutral
Siessmeier	2006			x		13	pictures: emotional > neutral
Ashwin	2007		x			13	faces: fear + neutral > scrambled
Cooney	2007		x		14		films: sad > fixation
Hessl	2007		x			13	faces: fear > scrambled
Hofer	2007	x	x		19	19	verbal: negative words > nonwords; positive words > nonwords
Malhi	2007		x		10		faces: disgust > neutral; fear > neutral
Meseguer	2007	x	x			14	pictures: negative > neutral; positive > neutral
Schienle	2007		x		25		pictures: negative > neutral
Benuzzi	2008		x		15		films: disgust > neutral
Deckersbach	2008		x		17		autobio recall: sad > neutral
Deeley	2008		x			40	faces: disgust > neutral; fear > neutral
Goldin	2008		x		17		films: negative > neutral
Herpertz	2008	x	x			22	pictures: negative > neutral; positive > neutral
Montag	2008	x	x		37		pictures: negative > neutral; positive > neutral
Wright	2008			x		15	pictures: emotion rating > frequency rating
McLean	2009	x				9	sports-related films: positive > neutral
Mériau	2009		x		23		pictures: negative > neutral
Nielen	2009	x	x		23		pictures: negative > neutral; positive > neutral
Trautmann	2009	x	x		16		static faces: disgust > neutral; happiness > neutral; dynamic faces: disgust>neutral; happiness > neutral
Botzung	2010	x				23	sports-related films: high > low arousal
Frewen	2010	x	x		20		script-driven imagery: negative, social > neutral;

Reker	2010	x	x		33		negative, non-social > neutral; positive, non-social > neutral; positive, social > neutral faces: sadness > neutral; happiness > neutral
Zink	2010		x			20	negative faces > neutral objects
Total # Studies		31	65	10	44	44	
Total # Participants					656	561	

Analytic approach

All meta-analyses of functional neuroimaging studies of emotion in women and men were conducted using GingerALE 2.1 software; http://brainmap.org/ale (Eickhoff et al., 2009). This software uses random-effects inference to determine regions that exhibit a greater convergence of activations across experiments than would be expected by chance. Individual neuroimaging studies contributed one or more sets of activation peaks or foci (stereotaxic x, y, and z coordinates) representing the locations of maximal activation in either Montreal Neurological Institute (MNI) or Talairach space. ALE analyses require that all activation location data be transformed into a common stereotaxic space. We used the Montreal Neurological Institute (MNI) space as the common anatomical reference space and transformed any coordinates of maximal activation that had been reported in Talairach space to MNI space using icbm2tal, a standard transformation program (Lancaster et al., 2007).

For each set of activation maxima from an individual study, a modeled activation (MA) map was generated by convolving the peak coordinates with a 3D Gaussian kernel with a full width half maximum (FWHM) between 9 mm and 11 mm (FWHM calculation depending upon sample size; empirical validation elaborated in Eickhoff et al., 2009). An ALE map of the convergence of activations across studies was calculated as the union across all MA-maps, taken at each voxel. Significant areas of convergence within the ALE map were determined by statistical comparison at each voxel to a null distribution of convergence based on random spatial distribution between experiments (see Eickhoff et al., 2009). ALE maps were thresholded using a

voxel-level false discovery rate correction for multiple comparisons (Genovese, Lazar, & Nichols, 2002) pID of .05 and a 100 mm^3 minimum cluster size.

Three emotional valence conditions were examined (Negative emotion, Positive emotion, and a combination of all emotional responses irrespective of valence: All emotion). For each, one ALE map was constructed for women, one map was constructed for men, and a pooled map was constructed that summarized results irrespective of sex. Sex differences were assessed by computing the voxel-wise difference between the ALE maps for women and men. All MA-maps for the pooled analysis of both women and men were then randomly divided into two groups of the same size as the sets for women and for men, and the voxel-wise difference between the ALE maps for these two randomly-assigned datasets was calculated. This process was repeated 10,000 times to create a null distribution of difference scores, and the map of sex differences was compared to this randomly-permuted map of differences. Results were thresholded using a false discovery rate (pID) of .05, and a 100 mm^3 minimum cluster size.

ALE meta-analyses summarize regions where activations spatially converge significantly across studies. We use the term “activation” in the current study to refer to regions of significant convergence, to maintain consistency with the terminology used in previous meta-analyses (Friebel, Eickhoff, & Lotze, 2011).

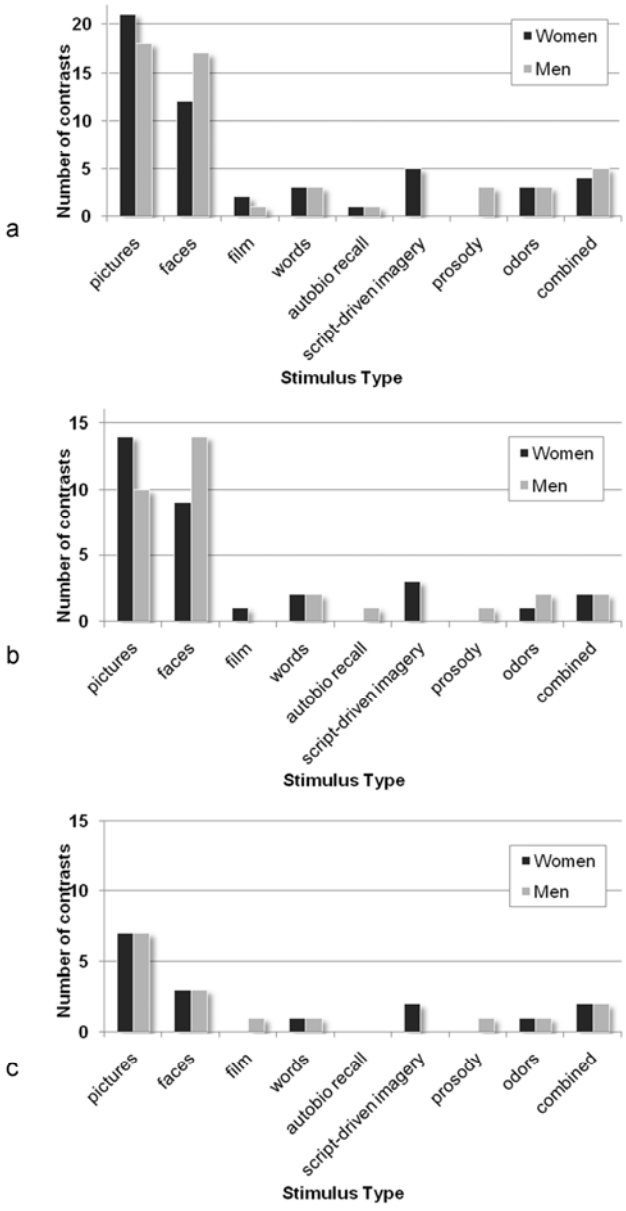

Figure 1. Frequency distribution of stimulus types used for emotion induction, for the studies included in the ALE meta-analyses of the balanced dataset equated for the frequency of specific emotion types across women and men. 1a: All emotion. 1b: Negative emotion. 1c: Positive emotion.

Analyses controlling for specific emotions and stimulus types

In ALE differential activation analyses, conditions associated with more modeled activation maps are more likely to show activation likelihood differences favoring that condition (Laird et al., 2005). For example, in the current study, for the ALE analysis for Negative emotion, if the dataset for women included more MA-maps than the corresponding set for men, then this would introduce an analysis bias towards finding clusters of greater activation likelihood for women, solely because of the imbalance in the number of MA-maps. In addition, because specific emotions (e.g., basic emotions such as happiness and fear) typically recruit partially non-overlapping patterns of brain activation (Vytal & Hamann, 2010), disproportionate inclusion of specific emotion types across groups could also potentially influence the results of an ALE meta-analysis. Though the magnitude of this potential bias is difficult to estimate, it increases with increasingly unbalanced comparisons between conditions or groups. In practice, small imbalances in the number of MA-maps between conditions have typically been viewed in previous ALE meta-analyses as relatively minor potential sources of bias and have been largely ignored. However, in the current study we adopted a conservative approach to this issue and included additional analyses to help establish that our findings were unlikely to be attributable to such imbalances.

Accordingly, to address this potential source of bias, we conducted our ALE analysis in two different ways. We first analyzed the complete set of MA-maps from our selected studies, and then repeated the analysis with a balanced set of MA-maps that controlled for the overrepresentation of specific emotions. This balanced dataset was created by matching comparisons between women and men on emotion type (e.g., sadness, happiness) and stimulus type (e.g., pictures, words). In the few cases for which stimulus matching was not possible, comparisons were matched for sensory modality of stimuli. As a result of this matching procedure, MA-maps from studies of responses to erotic stimuli were excluded from the balanced dataset. Figure 2b shows the distribution of specific emotions in the balanced data set. In

addition, the balanced dataset better equated the number of female versus male participants contributing to each MA-map. The average sample size for MA-maps included in the complete dataset was *M(SD)* = 15.7(10.5) for women and 16.7(11.6) for men. The average sample size for MA-maps included in the balanced dataset was *M(SD)* = 13.0(6.9) for women and 13.6(6.6) for men. The average ages of female and male samples were comparable in both the complete and balanced datasets. 36 of 45 studies of women, and 33 of 44 studies of men reported the mean age of participants. The average age of participants in the complete dataset was *M(SD)* = 28.1(5.6) for women and 30.8(7.0) for men. The average age of participants in the balanced dataset was 28.0(5.7) for women and 31.9(7.5) for men.

As detailed in the Results section, the ALE analysis using the carefully balanced data sets in fact yielded very similar results to those obtained with the complete data set of all MA-maps. In general, the results with the balanced data set constituted a subset of the results obtained with the complete data set, yielding ALE clusters with slightly smaller spatial extent. Because the ALE results with the balanced data set were highly similar to those obtained with the complete data set and were less likely to be affected by bias, in the current report we focus primarily on the ALE results from the balanced data set. For completeness, the results from the analysis of the complete dataset are presented in the Supplemental Tables, and we describe any important differences in findings between the two analyses in the Results.

Table 2
Number of modeled activation (MA) maps contributing to the meta-analysis

	Complete dataset		[a] Balanced dataset	
	Women	Men	Women	Men
Negative Emotion	51	41	32 (.63)	32 (.78)
Positive Emotion	18	22	16 (.89)	16 (.73)
All Emotion	72	71	51 (.71)	51 (.72)

[a] # maps (proportion of complete dataset)

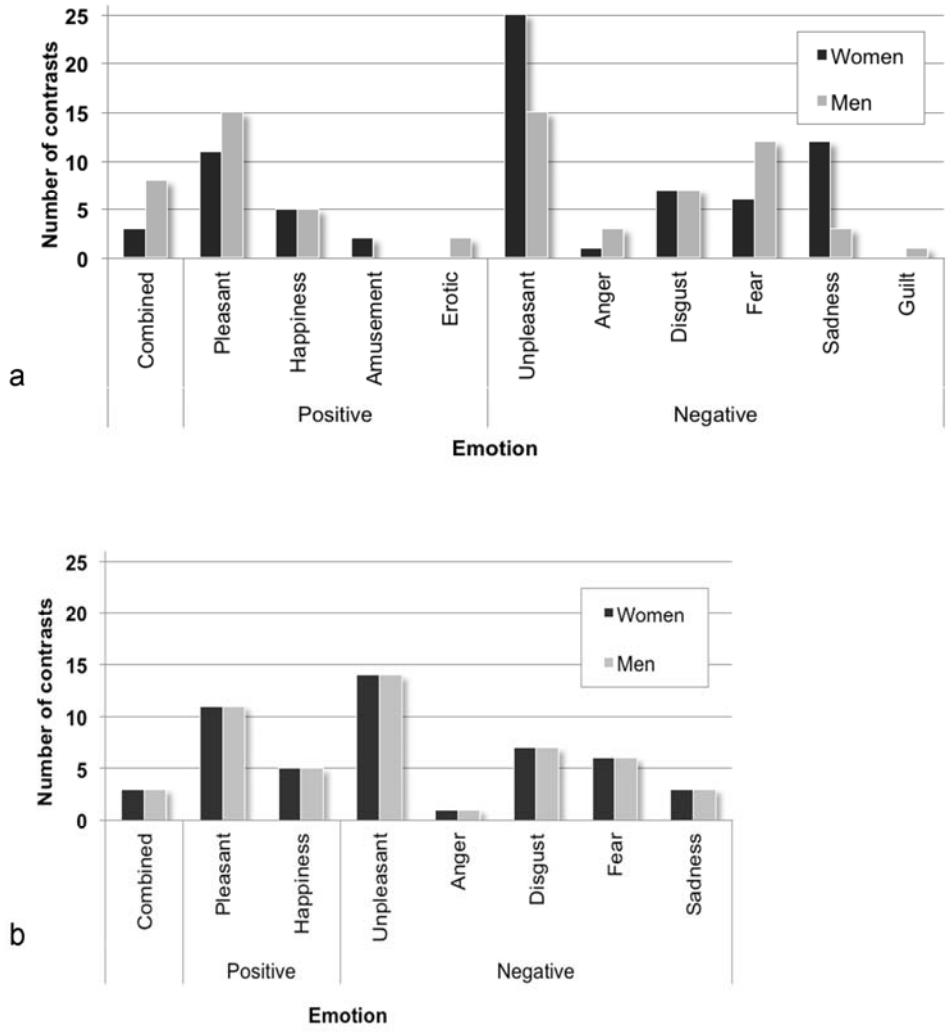

Figure 2. Frequency distributions of specific emotion types included in the meta-analyses, for women and men. "Combined" indicates studies that included both positive and negative emotional stimuli. Negative emotion analyses included activation contrasts from the set of negative emotions. Positive emotion analyses included activation contrasts from the set of positive emotions. All-emotion analyses included all emotion types illustrated here, regardless of emotion category (combined emotion, positive emotion, and negative emotion). 2a: Activation contrasts included in the meta-analyses of the complete dataset. 2b: The subset of activation contrasts included in the meta-analyses of the balanced dataset.

2.4 Results

Negative emotion: Sex differences

Significant differences between women's and men's responses to negative stimuli are shown in Figure 3a and Table 3. Women showed greater activation than men in a cluster that had peaks in the left amygdala and hippocampus (cluster 1). Prominent clusters were also observed in the hypothalamus in the approximate region of the left mammillary body and in the medial dorsal nucleus of the left thalamus (cluster 2), in right middle occipital gyrus, and middle and inferior temporal gyri (BA37, 19, cluster 3), and medial frontal and anterior cingulate gyri (BA10, 32, 9; cluster 4).

Men showed greater activation than women in a large cluster containing peaks in right precentral gyrus, inferior frontal gyrus, and insula (BA6, 9, 13, 44; cluster 1). Prominent clusters were also observed in right superior temporal gyrus and right putamen (BA38, cluster 2), posterior cingulate gyrus (BA23, 29; cluster 3), and left middle temporal gyrus and fusiform gyrus (BA37, 19; cluster 4).

Table 3
Peak coordinates for sex differences in Negative emotion (analysis of balanced dataset)

	Region (>100mm^3)	[a]BA(s)	[b]X	Y	Z	Peak Value	Vol. (mm^3)
	Females > Males						
1	Hippocampus, Amygdala	35	-20	-19	-16	2.64	2112
2	Hypothalamus- Mammillary body, Thalamus- Medial dorsal nucleus	*	-1	-13	-7	2.39	1344
3	Middle Occipital Gyrus, Middle Temporal Gyrus, Inferior Temporal Gyrus	37, 19	52	-69	4	2.59	976
4	Right Medial Frontal Gyrus, Left Medial Frontal Gyrus, Left Anterior Cingulate	10, 32, 9	4	47	8	2.50	648
5	Medial Globus Pallidus, Lateral Globus Pallidus	*	-9	4	-1	2.39	624
6	Middle Frontal Gyrus	9	-50	28	24	2.04	280
7	Cerebellum- Declive	*	26	-62	-19	2.04	208
8	Middle Frontal Gyrus	46	-57	33	18	2.12	112
	Males > Females						
1	Precentral Gyrus, Inferior Frontal Gyrus, Insula	6, 9, 13, 44	44	10	28	2.99	3144
2	Superior Temporal Gyrus, Putamen	38	41	4	-18	2.88	2576
3	Posterior Cingulate	23, 29	-2	-36	24	3.16	2048
4	Middle Temporal Gyrus, Fusiform Gyrus	37, 19	-41	-56	-3	2.40	1328
5	Cuneus, Lingual Gyrus	17, 18	10	-83	14	2.67	1240
6	Inferior Frontal Gyrus	47	-46	36	-16	2.56	752
7	Claustrum	*	-39	-1	-3	2.19	744

8	Thalamus- Pulvinar	*	18	-27	19	3.72	696
9	Fusiform Gyrus	19	41	-72	-11	1.91	360
10	Inferior Frontal Gyrus	10	-36	37	9	2.18	208
11	Inferior Frontal Gyrus	45, 47	51	31	-7	1.96	200
12	Putamen	*	-27	-18	5	2.14	152

Note. Clusters demonstrating significant concordance across studies ($p < .05$, FDR-corrected for multiple comparisons). For each cluster, labels denote regions which contained the peak ALE activation, and regions which contained secondary peaks; clusters may extend across non-labeled regions between peaks and the extent is best characterized in Figure 3.
[a]BA = Brodmann's area, if applicable
[b]X, Y, and Z coordinates represent weighted central activation likelihood focus in MNI space.

Negative emotion: Women

Results are shown in Figure 3b (list of clusters in Table S1). A large cluster contained peaks in both the left and the right amygdala, left hippocampus, left thalamus, right subthalamic nucleus, right superior temporal gyrus (BA38), left mammillary body, left caudate head, and left putamen (cluster 1). Other prominent clusters were observed in left middle and inferior frontal gyri, and insula (BA46, cluster 2; BA47, 13, cluster 5). A major cluster had activation peaks in anterior cingulate gyrus and medial frontal gyrus (BA32, 10, cluster 4).

Negative emotion: Men

Results are shown in Figure 3c and Table S1. This analysis revealed a large cluster with activation maxima in right amygdala, precentral gyrus, superior temporal gyrus, inferior frontal gyrus, claustrum, middle temporal gyrus, and insula (BA 6, 38, 44, 47, 45, 21, 13; cluster 1). A similar cluster in the left hemisphere contained an activation peak in left amygdala with additional peaks in left inferior frontal gyrus and insula, left middle frontal gyrus, superior temporal gyrus, putamen, and hippocampus (BA45, 13, 46, 38, 47; cluster 2). Prominent clusters were also observed in medial cingulate and superior frontal gyri (BA32, 6, 24; cluster 3), left middle temporal gyrus and fusiform gyrus (BA37, 19; cluster 4), left inferior frontal gyrus and precentral gyrus (BA9, 6, 44, cluster 5), and posterior cingulate gyrus (BA23, cluster 6). Two clusters had peaks in right fusiform gyrus (BA19, cluster 7; BA37, cluster 8).

Negative emotion: Women and Men

To investigate the brain regions reliably activated across studies for negatively valenced emotions, regardless of the sex of participants, we conducted an analysis on MA-maps from all studies of negative emotion, collapsing across female and male samples. Results are shown in Figure S1a and Table S1. Peaks were observed in the amygdala bilaterally (right hemisphere: cluster 1, left hemisphere: cluster 2). The largest cluster also included peaks in bilateral thalamus, left caudate body and head, right precentral gyrus (BA6), right inferior frontal gyrus (BA47, 44, 45, 13), right middle frontal gyrus (BA9, 46), right claustrum, right superior temporal gyrus (BA38), left mammillary body and red nucleus, and left medial globus pallidus (cluster 1). A similar but left-lateralized cluster had peaks in left inferior frontal gyrus (BA47, 9, 46), left superior temporal gyrus (BA38), left insula (BA13), the ventral posterior lateral nucleus of the left thalamus, and left putamen (cluster 2). A prominent cluster in frontal cortex had peaks in cingulate gyrus, superior frontal gyrus and anterior cingulate gyrus (BA32, 6, 24; cluster 3).

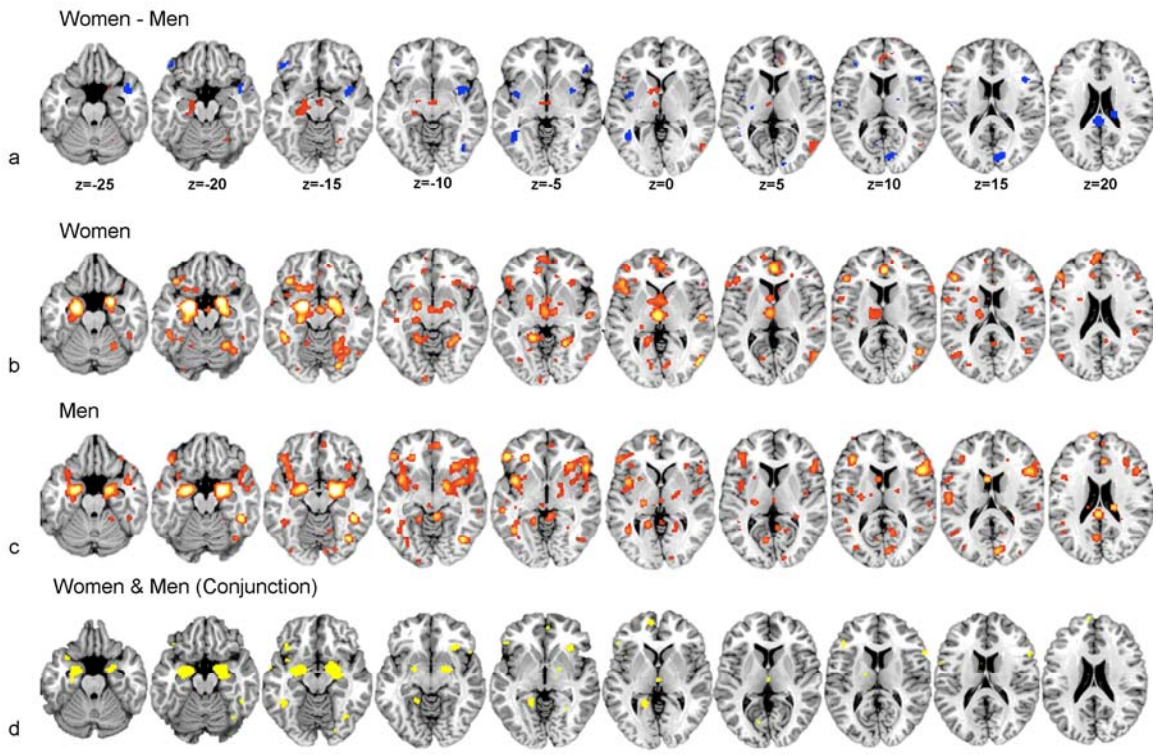

Figure 3. Regions of significant activation ($p < .05$, FDR-corrected for multiple comparisons) for Negative emotion, overlaid on a representative single-subject structural anatomical image template in MNI space. 3a: Significant differences in activation for Negative emotion in women vs. men. 3b: Significant activation clusters for Negative emotion in women. 3c: Significant activation clusters for Negative emotion in men. Red color scale: greater activation for women than men. Blue color scale: greater activation for men than women. Brighter colors indicate greater activation likelihood. Axial slices are shown in neurological orientation (left side of image = left hemisphere; top of image = rostral).

Positive Emotion: Sex differences

Significant differences between women's and men's responses to positive stimuli are shown in Figure 4a (list of clusters in Table 4). Women showed greater activation than men in small clusters in right middle and inferior temporal gyrus (cluster 1), left superior temporal gyrus (cluster 2), and dorsomedial frontal gyrus (BA32, 6, cluster 3).

Men showed greater activation than women in a cluster covering left subcallosal gyrus (BA34), left uncus (BA28), and left amygdala (cluster 1). Prominent clusters contained peaks in inferior frontal gyrus (BA47, 13, right: cluster 4, left: clusters 2, 3), and superior temporal gyrus

(BA38; cluster 2). Other prominent clusters contained peaks in right fusiform gyrus (BA37, cluster 5), and left middle frontal gyrus (BA8, cluster 6).

Table 4
Peak coordinates for sex differences in Positive emotion (analysis of balanced dataset)

	Region (>100mm^3)	[a]BA(s)	[b]X	Y	Z	Peak Value	Vol. (mm^3)
	Females > Males						
1	Middle Temporal Gyrus, Inferior Temporal Gyrus	39, 37	53	-66	10	1.89	1296
2	Superior Temporal Gyrus	39, 22	-55	-56	22	2.08	352
3	Medial Frontal Gyrus, Superior Frontal Gyrus	32, 6	2	16	51	2.05	328
	Males > Females						
1	Subcallosal Gyrus, Entorhinal Cortex, Amygdala	34, 28	-20	3	-24	2.44	792
2	Inferior Frontal Gyrus, Superior Temporal Gyrus	47, 38	-44	25	-25	2.59	752
3	Inferior Frontal Gyrus	47	-23	18	-20	2.22	376
4	Inferior Frontal Gyrus	13	35	6	-21	2.71	360
5	Fusiform Gyrus	37	46	-41	-17	2.04	360
6	Middle Frontal Gyrus	8	-27	35	41	2.08	320
7	Subcallosal Gyrus	34	-13	10	-19	2.50	280
8	Fusiform Gyrus	37	50	-48	-12	1.84	232
9	Claustrum	*	-28	10	-10	2.13	168
10	Lateral Globus Pallidus, Medial Globus Pallidus	*	26	-13	-4	1.86	104

Note. Clusters demonstrating significant concordance across studies ($p < .05$, FDR-corrected for multiple comparisons). For each cluster, labels denote regions which contained the peak ALE activation, and regions which contained secondary peaks; clusters may extend across non-labeled regions between peaks and the extent is best characterized in Figure 4.
[a]BA = Brodmann's area, if applicable
[b]X, Y, and Z coordinates represent weighted central activation likelihood focus in MNI space.

Positive emotion: Women

Results for positive emotion for women are shown in Figure 4b and Table S2. The largest cluster appeared in the ventral anterior nucleus of the left thalamus, and extended into the head of the caudate (cluster 1). Clusters were also observed bilaterally in the amygdala (right: cluster 15, left: cluster 5). Other prominent clusters included right lingual gyrus (BA18; cluster 2), left fusiform gyrus (BA19) and inferior occipital gyrus (BA18; cluster 4), left medial frontal gyrus (BA9; cluster 3), left anterior cingulate gyrus (BA32; cluster 6).

Positive emotion: Men

Results for positive emotion for men are shown in Figure 4c and Table S2. Large clusters appeared in left amygdala extending into left inferior frontal gyrus and the lateral globus pallidus (cluster 1), and in right amygdala extending into right entorhinal cortex (BA34, cluster 3). Prominent clusters were also observed in bilateral inferior frontal gyri / insula (left: BA13, 45, 47 clusters 2, 6; right: BA46, cluster 9), and bilateral fusiform gyri (BA19, right: cluster 5, left: cluster 4). An additional cluster had its maximum in the posterior cingulate gyrus (BA30, cluster 7).

Positive emotion: Women and Men

To investigate the brain regions reliably activated across studies for positive emotions, regardless of sex, we analyzed the MA-maps from all studies of positive emotion, collapsing across the female and male groups. Results are shown in Figure S1b and Table S2. Prominent clusters had peak activations in the bilateral amygdala (right: cluster 5, left: cluster 2), the ventral anterior nucleus of the left thalamus (cluster 1), head of the caudate (cluster 1), medial frontal gyrus (BA9, cluster 4), bilateral inferior frontal gyrus / insula (BA 45, 13, right: cluster 9, left: cluster 3), left anterior cingulate (BA32, cluster 1), and bilateral fusiform gyri (BA19, right: cluster 13, left: cluster 12).

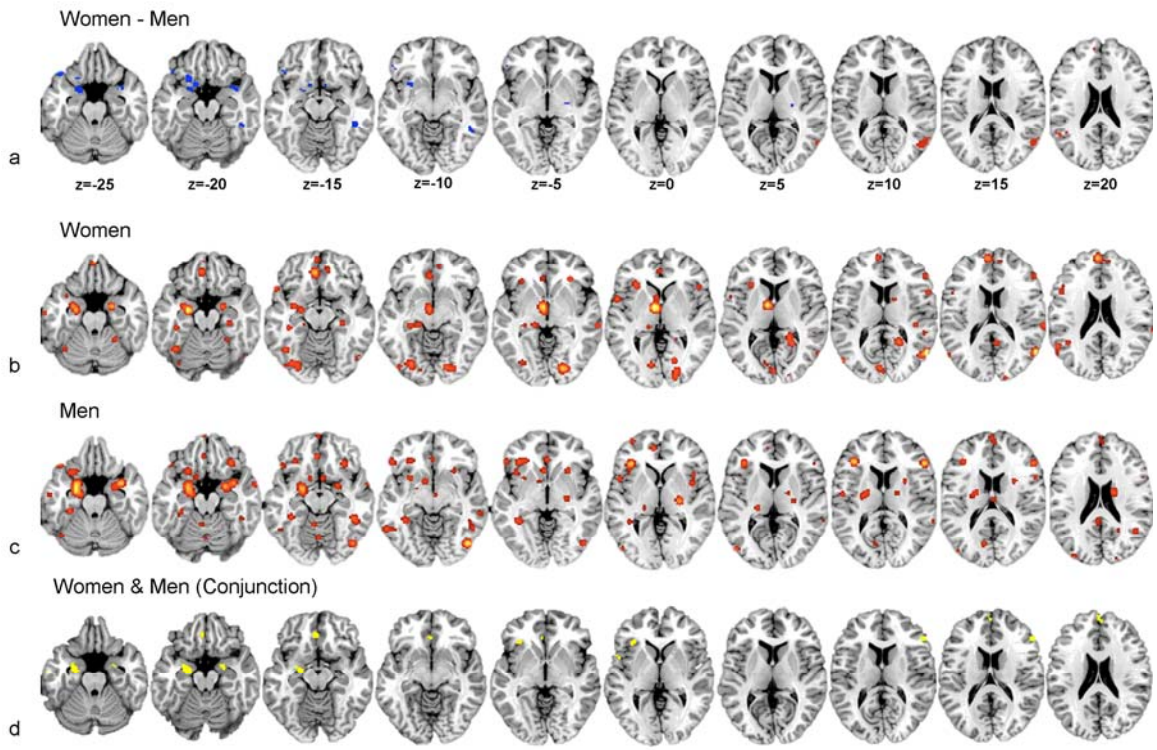

Figure 4. Regions of significant activation ($p < .05$, corrected) for Positive emotion, overlaid on a representative single-subject structural anatomical image template in MNI space. 4a: Significant differences in activation for Positive emotion in women vs. men. 4b: Significant activation clusters for Positive emotion in women. 4c: Significant activation clusters for Positive emotion in men. Red color scale: greater activation for women than men. Blue color scale: greater activation for men than women. Brighter colors indicate greater activation likelihood. Images are presented in neurological orientation.

All emotion: Sex differences

Significant differences between women's and men's responses to all emotional stimuli are shown in Figure 5a and Table 5. Women showed greater activation than men in an extended cluster with peaks in the left thalamus and subthalamic nuclei, lateral globus pallidus, left caudate head, left anterior cingulate (BA25), and the left mammillary body (cluster 1). Prominent clusters were also observed in the left hippocampus (cluster 2), and in right middle occipital gyrus and inferior temporal gyrus (BA37, cluster 3). Women's emotion-related activations also differed from men's in several additional frontal regions, including a cluster in anterior cingulate and

medial frontal gyrus (BA32, 24, 10; cluster 4), in medial and superior frontal gyri (BA9, 10, 6; clusters 5, 7, 8), and in left middle and inferior frontal gyri (BA46, 9; cluster 6).

Men showed greater activation than women in bilateral inferior frontal gyrus (right: BA45, 47, clusters 1, 15, 18; left: BA47, clusters 7, 12, 13, 21). A prominent cluster in posterior cingulate was also more activated in men than women (BA23, 29, 31; cluster 2). A large cluster overlapped right superior temporal gyrus, claustrum, putamen, and right amygdala (BA38, cluster 3). Other prominent clusters appeared in right fusiform gyrus (BA19, 20, cluster 5, 9), and left insula (BA13, cluster 1).

Table 5
Peak coordinates for sex differences for All-emotion condition (analysis of balanced dataset)

	Region (>100mm^3)	[a]BA(s)	[b]X	Y	Z	Peak	Vol. (mm^3)
	Females > Males						
1	Subthalamic Nucleus, Thalamus, Lateral Globus Pallidus, Caudate Head, Anterior Cingulate, Hypothalamus- Mammillary Body	25	-5	-5	-3	3.16	6096
2	Hippocampus	*	-21	-26	-13	2.85	1944
3	Middle Occipital Gyrus, Inferior Temporal Gyrus	37	50	-68	7	3.72	1832
4	Left Anterior Cingulate, Right Anterior Cingulate, Right Medial Frontal Gyrus	32, 24, 10	3	43	6	2.58	1696
5	Left Medial Frontal Gyrus, Right Superior Frontal Gyrus	9	-5	55	19	2.47	1184
6	Middle Frontal Gyrus, Inferior Frontal Gyrus	46, 9	-50	27	23	2.33	1152
7	Medial Frontal Gyrus	10	-10	39	-10	2.00	424
8	Superior Frontal Gyrus	6	4	26	59	2.01	416
9	Cerebellum- Declive, Dentate Gyrus	*	29	-59	-21	2.05	264
10	Uncus	34	19	4	-25	1.88	112
	Males > Females						
1	Insula, Inferior Frontal Gyrus, Precentral Gyrus, Middle Frontal Gyrus	13, 45, 9, 6	45	17	17	3.54	2968
2	Posterior Cingulate	23, 29, 31	-2	-39	24	3.72	2880
3	Superior Temporal Gyrus, Claustrum, Putamen, Amygdala	38	38	2	-17	3.35	2672
4	Middle Occipital Gyrus, Middle Temporal Gyrus	19, 37	-40	-51	-2	3.04	1632
5	Fusiform Gyrus	19	42	-74	-11	2.95	1504
6	Precentral Gyrus, Insula, Claustrum	6, 13	-47	-6	5	2.59	1488
7	Inferior Frontal Gyrus, Middle Frontal Gyrus	47, 11	-47	34	-16	3.35	1360
8	Middle Frontal Gyrus	8	-26	37	38	2.61	1336
9	Fusiform Gyrus	37, 36	44	-41	-15	2.31	1280
10	Cuneus	17	11	-82	14	3.16	824
11	Caudate Body	*	19	-6	22	2.95	776
12	Inferior Frontal Gyrus, Middle Frontal Gyrus	10	-36	36	8	2.49	696
13	Precentral Gyrus, Inferior Frontal Gyrus	6, 9	-38	5	27	2.10	640
14	Putamen	*	-27	-15	7	2.77	632
15	Inferior Frontal Gyrus	47	34	32	-21	2.39	592
16	Thalamus- Pulvinar	*	18	-27	20	3.72	528
17	Supramarginal Gyrus, Superior Temporal Gyrus	40, 39	42	-46	31	2.10	512

18	Inferior Frontal Gyrus	47	55	32	-7	2.43	448
19	Thalamus- Ventral lateral nucleus, Lateral Globus Pallidus	*	22	-10	4	2.54	424
20	Posterior Cingulate	30	-8	-70	14	2.22	320
21	Inferior Frontal Gyrus	47	-44	26	-27	2.04	208

Note. Clusters demonstrating significant concordance across studies ($p < .05$, FDR-corrected for multiple comparisons). For each cluster, labels denote regions which contained the peak ALE activation, and regions which contained secondary peaks; clusters may extend across non-labeled regions between peaks and the extent is best characterized in Figure 5.
[a]BA = Brodmann's area, if applicable
[b]X, Y, and Z coordinates represent weighted central activation likelihood focus in MNI space.

All emotion: Women

Results are shown in Figure 5b and Table S3. For studies of emotional responses in women, ALE analysis revealed a large cluster covering the left thalamus, and extending to the left caudate head, left putamen, bilateral amygdala, bilateral hippocampus, and mammillary bodies (cluster 1). Several large medial frontal clusters contained activation peaks in superior frontal gyrus, anterior cingulate, and medial frontal gyrus (BA9, 32, 10; clusters 2 and 5). Another cluster had peaks left middle frontal gyrus, inferior frontal gyrus, and insula (BA9, 47, 45, 46, 13, 9; cluster 3). A large cluster had peaks in right fusiform gyrus, lingual gyrus, culmen, and the declive of the cerebellar vermis (BA19, 18, 37; cluster 4).

All emotion: Men

Results are shown in Figure 5c (list of clusters in Table S3). For studies of emotional responses in men, ALE analysis revealed an extended cluster covering left amygdala, left inferior frontal gyrus, insula, and postcentral gyrus (BA13, 47, 45, 43; cluster 1). Another prominent cluster peaked in right amygdala, and extended into right inferior frontal gyrus, precentral gyrus, superior temporal gyrus, claustrum, thalamus, precentral gyrus, lateral globus pallidus, and insula (BA45, 6, 38, 47; cluster 2). Substantial clusters were also observed in posterior cingulate and cuneus (BA23, 30, 29; cluster 3), and left middle temporal gyrus and fusiform gyrus (BA19, 37; cluster 4). Other notable clusters were observed in right fusiform gyrus (BA19; clusters 6),

dorsomedial prefrontal cortex (BA32, 6; cluster 5), and in the left thalamus extending into the putamen (cluster 9).

All emotion: Women and Men

To characterize patterns of activation independent of sex differences, primarily for purposes of comparison to previous studies, we conducted an analysis on all MA-maps, collapsing across positive and negative valence, and across female and male groups. Results are shown in Figure S1c and Table S3. In part because of the large number of maps entering into this analysis and attendant increase in statistical power, several activation clusters were relatively large and extended across multiple brain regions. Among these activation clusters, clusters of activation were observed in several regions associated with emotion and reward, including the bilateral amygdala (cluster 1), bilateral thalamus (cluster 1), mammillary bodies (cluster 1), bilateral insula (cluster 1) and left caudate (cluster 1). Activation clusters in prefrontal cortex associated with emotion included bilateral inferior frontal gyri (left: cluster 1, right: cluster 2), anterior cingulate (clusters 4, 14, 26, 39, 44) and left medial frontal gyrus (cluster 4).

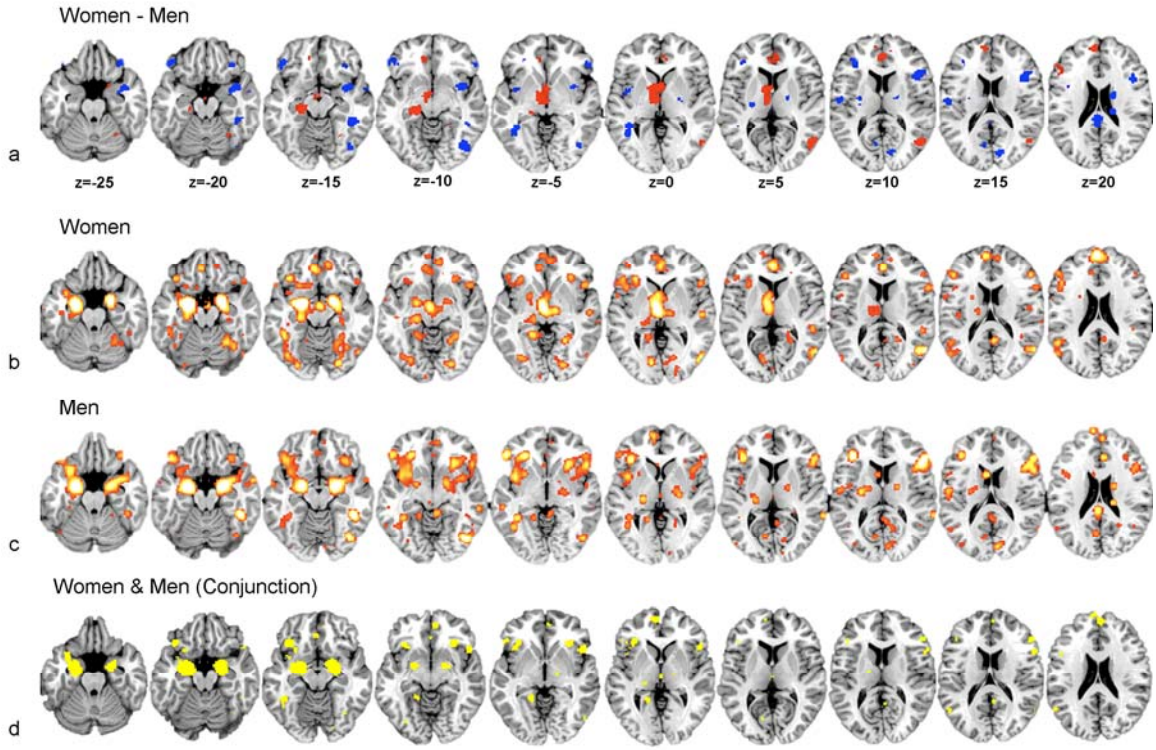

Figure 5. Regions of significant activation ($p < .05$, corrected) for All emotion, collapsed across positive and negative emotion stimuli, overlaid on a representative single-subject structural anatomical image template in MNI space. 5a: Significant differences in activation for All emotion in women vs. men. 5b: Significant activation clusters for All emotion in women. 5c: Significant activation clusters for All emotion in men. Red color scale: greater activation for women than men. Blue color scale: greater activation for men than women. Brighter colors indicate greater activation likelihood. Images are presented in neurological orientation.

Results for the complete dataset

As described in the Methods, to help reduce potential biasing effects of systematic differences in stimuli and emotion type and number of MA-maps between the data sets for women and men, our primary analyses focused on a balanced data set that minimized such effects by matching between women and men on these factors. However, because this procedure necessarily excluded a proportion of studies, it was important to determine whether our primary findings were also observed in the complete dataset comprised of all studies that met our inclusion criteria. This analysis of the complete dataset yielded results that were highly similar to

the findings obtained with the smaller, balanced data set (detailed results for the complete dataset are presented in the Supplemental Tables). In general, highly similar activation clusters were observed in the complete analysis and the balanced dataset, but with greater spatial extent for the complete dataset in many cases, extending across adjacent brain regions.

A few notable additional sex differences were observed in the analysis of the complete dataset. For negative emotion, women showed greater activation than men in the left substantia nigra, left hypothalamus, and left subcallosal gyrus (cluster 1). Men showed greater activation than women for negative emotion in additional clusters in right entorhinal cortex (BA28; cluster 7) and in left insula (BA13, cluster 8). Table S4 and Figure S2a present the full results for the complete analysis of Negative emotion. For positive emotion stimuli, women showed greater activation than men in the following additional brain regions: left thalamus, subthalamic nucleus, hypothalamus, and medial globus pallidus (cluster 1), right superior temporal gyrus (BA42, 13, 22, cluster 4; BA41, cluster 6). No additional clusters of greater activation for men were observed in the complete analysis. Table S5 and Figure S2b present the full results for the complete analysis of Positive emotion. No additional brain regions were activated in the complete analysis relative to the balanced analysis, but as with the examination of Negative and Positive emotion, significant activation clusters were greater in extent. Table S6 and Figure S2c present the full results for the complete analysis of All emotion, combined across positive and negative valence.

2.5 Discussion

The primary goal of this study was to examine and characterize sex differences in brain activation during the processing of positive and negative emotion. We used a quantitative meta-analytic approach, summarizing and analyzing activation findings from the relevant fMRI and PET neuroimaging literature. This analysis characterized differences between women and men in regional activation likelihood for positive and negative emotion separately as well as for both

types of emotion combined. A major finding was that, in line with our predictions, sex differences varied markedly as a function of negative vs. positive emotional valence. The majority of sex differences favoring women were observed for negative emotion, whereas relatively few sex differences favoring men were observed for the analysis of negative emotion. Conversely, the majority of the sex differences favoring men were observed for positive emotion, whereas relatively few sex differences favoring women were observed for positive emotion.

This valence-specificity of sex differences in regional activation was particularly evident for the amygdala, a key region for emotion processing. Women exhibited greater activation than men in the left amygdala for negative emotion, consistent with previous evidence suggesting that women are more psychologically and neurally responsive to stimuli and situations that elicit negative emotion. Conversely, men exhibited greater activation than women in the left amygdala for positive emotion. Notably, this greater amygdala activation for men was found in the balanced dataset that did not include any studies of sexually arousing stimuli, suggesting that this sex difference in amygdala response previously reported for sexually arousing stimuli generalizes to other types of positive emotional stimuli. No sex differences in amygdala activation were observed when all studies were analyzed regardless of valence.

This study extends previous efforts to characterize sex differences in brain activation during emotion processing in several important ways. Our meta-analysis is the most comprehensive such attempt to date, including a substantially larger and more complete set of relevant studies than in previous meta-analyses. This study also represents the first quantitative meta-analytic review to our knowledge that has investigated such sex differences separately for studies of positive and negative emotional valence. A third key feature of our study was that it is the first such neuroimaging meta-analysis to use recently developed whole-brain random-effects statistical meta-analytic methods, as opposed to fixed-effects methods that have been used in previous relevant meta-analyses. Fixed-effects meta-analysis methods are limited because inferences based on them are strictly valid only for the population included in the analysis (i.e.,

the specific neuroimaging studies included), although in practice this limitation has been frequently overlooked. The random-effects meta-analysis method used in the current study allows valid statistical inference about the general population, thereby substantially broadening the scope and generality of our conclusions.

To control for possible bias related to greater representation of specific emotions across groups, as described in the Methods, we conducted our ALE analysis in two different ways and focused our interpretation on results obtained with the more conservative, balanced method that controlled for bias. The results of the two analyses were in fact highly similar, with slightly more extensive activation clusters observed with the less conservative method. Because similar meta-analysis results were obtained with both analysis methods, this suggests that our findings are relatively robust to minor variations in the specific studies sampled.

In the next sections we discuss these sex differences in brain activations in greater detail, focusing on activations in regions involved in emotion and emotion regulation.

Greater activations for women

A primary finding was that women showed greater left amygdala activation for negative emotion, relative to men. This finding supported our prediction that, relative to men, women would show stronger responses to negative emotion in key brain regions associated with emotion processing and parallels findings from the behavioral and psychophysiological literature (Bradley et al., 2001; Fujita et al., 1991; McClure et al., 2004; McManis et al., 2001; Thomsen et al., 2005). These results are also consistent with the findings of some individual neuroimaging studies that have reported greater amygdala activations in women relative to men to negative emotional stimuli, using direct within-experiment comparisons (Domes et al., 2009; Hofer et al., 2006). The activation cluster showing greater activation for women vs. men for negative emotion also contained additional, secondary activation maxima in the anterior hippocampus (Figure 6). Greater activation for women vs. men in the left hippocampus was also observed when all emotion studies (regardless of valence) were analyzed.

These sex differences in amygdala and hippocampal activation are notable in part because interactions between the amygdala and hippocampus are known to be a primary mechanism by which emotion modulates episodic memory (memory for events) (Cahill et al., 1996; Canli et al., 2002; Hamann et al., 1999). These greater amygdala and hippocampal activations for women are consistent with previous findings of enhanced emotional memory for women relative to men (Seidlitz & Diener, 1998). Neuroimaging studies have also identified consistent sex differences in the amygdala's contribution to successful memory encoding for negative stimuli (Cahill et al., 2001; Cahill et al., 2004; Canli et al., 2002), such that right amygdala activation is associated with successful memory encoding in men for negative stimuli, whereas left amygdala activation is associated with successful encoding in women for negative stimuli.

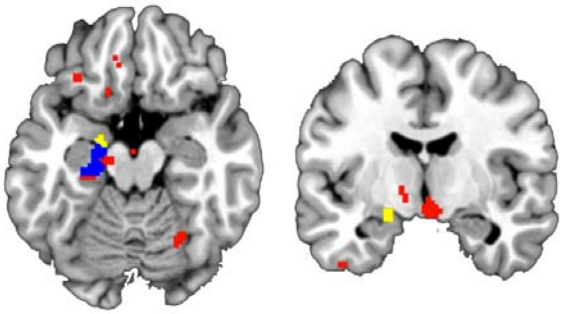

Figure 6. Regions of significantly greater activation for women than for men ($p < 0.05$, corrected) for Negative emotion, highlighting regional overlap with the amygdala and the hippocampus, overlaid on a representative single-subject structural anatomical image template in MNI space. Left panel: axial view at z = -19; right panel: coronal view at y = -7. Yellow regions: overlap with the amygdala; blue regions: overlap with the hippocampus and hippocampal-amygdala transition zone; red: regions where significant ALE voxels were observed outside of the amygdala and hippocampus. Amygdala and hippocampal ROIs were constructed from a digital neuroanatomy atlas based on postmortem brain data, as implemented in the Anatomy Toolbox (Eickhoff et al., 2005). Images are presented in neurological orientation.

In addition to the left amygdala, women also exhibited greater activation to negative stimuli in the anterior cingulate and medial prefrontal cortex, in BAs 9, 32, and 10. Neuroimaging studies of depression and induced sad mood have linked negative affect and

depression to increased subgenual anterior cingulate cortex and medial prefrontal activation (Mayberg et al., 1997; Mayberg et al., 1999) as well as a temporally-prolonged amygdala response (Siegle, Steinhauer, Thase, Stenger, & Carter, 2002). Activity in the medial prefrontal cortex and anterior cingulate has been associated with several cognitive processes linked to depression, including representation of mental states (Abu-Akel, 2003), default-mode resting state activity (Buckner, Andrews-Hanna, & Schacter, 2008), and rumination, the tendency to recollect and focus on negative events and feelings (Denson, Pedersen, Ronquillo, & Nandy, 2009; Ray et al., 2005). Increased rumination in women relative to men has been linked to the higher prevalence of depression in women (Leach et al., 2008; Thomsen et al., 2005). The greater activation we observed in medial prefrontal and anterior cingulate regions is consistent with the higher prevalence of depression and anxiety disorders observed among women relative to men (American Psychiatric Association, 2000; Nolen-Hoeksema, 2001).

Greater responses to negative stimuli in women were also observed in the left medial dorsal nucleus of the thalamus and the hypothalamus, with an activation maximum located near the mammillary bodies. A sex difference in hypothalamic activation is consistent with sex differences in the distribution of hormone receptors in the brain. The hypothalamus and amygdala are densely populated with steroid hormone receptors (Clark et al., 1988; MacLusky et al., 1986), and these regions are thus especially sensitive to hormone levels which differ between women and men. Sex differences in receptor density are greatest in the mammillary bodies relative to other hypothalamic nuclei (Fernández-Guasti, Kruijver, Fodor, & Swaab, 2000). In addition, functional connectivity between the left amygdala and the hypothalamus has been shown be stronger in women than men (Kilpatrick et al., 2006).

For positive stimuli, there were substantially fewer sex differences favoring women, and these differences were observed in regions that have been less specifically associated with emotion processing. Women were more likely than men to exhibit activation in a few clusters in the right temporal gyrus and right medial and superior frontal gyrus. For all emotional stimuli

(see Table 5 and Figure 5c), a number of regions showed clusters of greater activation for women, including the left hippocampus (a region also showing sex differences favoring women for negative stimuli) and the bilateral anterior cingulate cortex. Because these sex differences in activation for all emotional stimuli were a composite of the sex differences observed for negative and positive emotion (together with a small number of studies that combined positive and negative stimuli) and markedly different sex differences were found as a function of negative vs. positive valence, we focus our interpretation on the valence specific sex differences and include the results for the analysis of all emotions primarily for comparison to previous studies. In addition, because there were substantially more studies of negative emotion than of positive emotion in the sampled neuroimaging literature, the overall results for all emotion necessarily reflect the contribution of negative emotion studies significantly more than positive emotion studies, complicating the interpretation of the overall results for all emotions.

Greater activations for men

For studies of positive emotion, men exhibited greater ALE activation than women in the left amygdala. Our predictions regarding possible greater activations for men for positive stimuli were initially more tentative than our corresponding predictions for women and negative stimuli, because of less extant evidence for such a difference from behavioral and neuroimaging studies. The current findings provide further support for this previously suggested sex difference, and are consistent with findings from some individual neuroimaging studies of men's responses to positive stimuli, which have found left-lateralized amygdala activity (Hamann et al., 2002; Hamann & Mao, 2002), and larger left amygdala responses in men than women (Wrase et al., 2003).

These results parallel sex differences previously observed in appetitive responses to a specific type of appetitive stimuli, erotic stimuli, for which men show greater activation relative to women in the bilateral amygdala (Hamann et al., 2004), visual cortex (Sabatinelli et al., 2004), and show stronger emotional physiological responses as indexed by skin conductance responses

(Bradley et al., 2001). Our findings suggest that greater amygdala activation to positive emotional stimuli for men extends beyond sexually arousing stimuli, to other types of positive emotional stimuli. The activation cluster showing greater amygdala activation to positive emotional stimuli for men also overlapped with the entorhinal cortex (Figure 7), a region of the medial temporal lobe which plays an important role in episodic memory supporting successful encoding and retrieval of declarative memory (for reviews, see Eichenbaum, Yonelinas, & Ranganath, 2007; Squire, Wixted, & Clark, 2007).

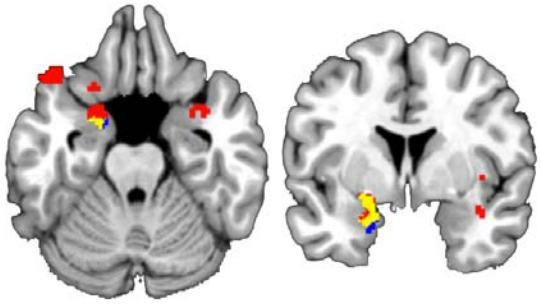

Figure 7. Regions of significantly greater activation likelihood for men than for women ($p < 0.05$, corrected) for Positive emotion, highlighting regional overlap with the amygdala and the hippocampus, overlaid on a representative single-subject structural anatomical image template in MNI space. Left panel: Axial view at z = -25; Right panel: Coronal view at y = 1.Yellow regions: overlap with the amygdala; Blue regions: overlap with the hippocampus and hippocampal-amygdala transition zone; Red: regions where significant ALE voxels were observed outside of the amygdala and hippocampus. Amygdala and hippocampal ROIs were constructed from a digital neuroanatomy atlas based on postmortem brain data, as implemented in the Anatomy Toolbox (Eickhoff et al., 2005). Images are presented in neurological orientation.

Men were also more likely than women to exhibit activation in the insula and lateral prefrontal cortex, in response to both positive and negative stimuli, with activation maxima in bilateral inferior frontal gyrus in BA47 and 45, extending into right anterior insula in BA13. The anterior insula and ventrolateral prefrontal regions have been implicated in representing emotional states (Critchley, Wiens, Rotshtein, Ohman, & Dolan, 2004; Wicker et al., 2003), and

in emotion recognition (Adolphs, Damasio, Tranel, Cooper, & Damasio, 2000; Kringelbach & Rolls, 2003).

For negative emotion, there were substantially fewer sex differences favoring men. Men were more likely than women to exhibit activation in left posterior cingulate, for negative stimuli. This region is preferentially active for emotional stimuli (Damasio et al., 2000; Maddock, Garrett, & Buonocore, 2003) and has been implicated in integrating the emotional value of stimuli with sensory information in memory and spatial orientation tasks (Vogt, Finch, & Olson, 1992). For all emotional stimuli (see Table 5 and Figure 5c), a number of emotion-related regions showed clusters of greater activation for men, including the right insula and right inferior frontal gyrus, posterior cingulate, and right superior temporal gyrus.

Similar activations for women and men

As expected, in addition to these sex differences, we also observed many similarities between women and men in emotion-related brain activation. Sex differences were typically manifested as greater or more extensive activations for one group in regions where both sexes exhibited significant ALE activation clusters. Activations for each group are presented in Table S1 and Figure 3b and 3c for negative emotion, Table S2 and Figure 4b and 4c for positive emotion, and Table S3 and Figure 5b and 5c for all emotions combined. Figures 3d, 4d, and 5d show the conjunction of significant activations for women and men. Some prominent common activations for both sexes for negative emotion and positive emotion included large activation clusters the in the bilateral amygdala, anterior cingulate cortex, and bilateral insula.

Relationships to previous studies

As noted previously, the current meta-analysis represents the most comprehensive such review to date. Three previous quantitative neuroimaging meta-analyses of emotion each considered sex differences, but have some limitations relative to the current study. A major limitation of previous meta-analyses is that they did not analyze sex differences as a function of positive and negative emotional valence. As is evident from the current results, patterns of

observed sex differences differed markedly depending on emotional valence. Previous meta-analyses on this topic have also included a substantially smaller number of studies. Specifically, Fusar-Poli et al. (2009), limited their analysis to only include neuroimaging studies of facial expression, Sergerie et al. (2008) limited their analysis to only include studies that reported significant amygdala activation and examined only the amygdala region, and Wager et al. (2003) only included studies published prior to 2002, thereby including approximately 50% fewer studies than in the current meta-analysis. A third highlight of the current study is its use of a random-effects model, which enabled broader inferences relative to previous whole-brain meta-analyses that have used fixed-effects models.

Although direct comparisons between these previous studies and the current study are complicated by important differences in the number and type of studies included and the methodology, some general comparisons can be made at the level of brain regions implicated in sex differences. For example, previous meta-analyses have implicated the amygdala in sex differences in neural responses to emotion, combining across emotional valence, with greater activation for men than women reported by one study in the right amygdala (Fusar-Poli et al., 2009), and in a region adjacent to the amygdala in another study (Wager et al., 2003). In addition, Wager and colleagues (2003) reported evidence that women were more likely than men to activate the left extended amygdala, but not the amygdala proper. These meta-analysis results are also in line with the findings of individual neuroimaging studies that have reported greater amygdala activations in women relative to men to negative emotional stimuli, in direct within-experiment comparisons (Domes et al., 2009; Hofer et al., 2006).

Potential mechanisms for observed sex differences.

What factors could potentially contribute to the sex differences in brain activation to emotional stimuli observed in the current meta-analytic review? A number of possible relevant factors have been suggested in previous studies. One factor that has received considerable attention and discussion, and has perhaps the most empirical support to date, is the possibility that

systematic differences in emotional reactivity between women and men may contribute to systematic differences in regional brain activation such as those observed here. Greater subjective and physiological responses to negative emotional stimuli have indeed been reported for women relative to men in several previous studies (Bradley et al., 2001; Grossman & Wood, 1993; Hess et al., 2000; Kring & Gordon, 1998; Nolen-Hoeksema, 2001; Sharp, Van Goozen, & Goodyer, 2006), and some limited evidence suggests that this sex difference is reversed for positive emotional stimuli (Bradley et al., 2001; Hess et al., 2000). Systematic differences in intensity or arousal across studies between women and men would be expected to result in corresponding differences in regional brain activation, both in arousal-related regions such as the amygdala, hypothalamus, and brainstem, and regions associated specifically with positive or negative emotion. The general pattern of the sex differences in amygdala activation and other regions observed in the current study is generally in line with this possibility.

The extent to which differences in subjective or physiological emotional responses contributed to the differences observed in the current study is difficult to assess. Individual studies included in the meta-analysis varied widely in whether they included subjective or physiological emotion measures. In addition, for those studies that did include such measures, the size of reported sex differences in emotional responses varied considerably. Further studies of sex differences in emotion-elicited brain activation should include measures of subjective and physiological response, to help determine the role of sex differences in emotional response in contributing to regional brain activation differences.

Other factors in addition to emotional reactivity are also likely to contribute significantly to the sex differences in activation we observed. Individual neuroimaging studies have reported sex differences in regional brain activation in regions associated with emotion such as the anterior cingulate and insula, in the absence of sex differences in emotional responses (Fine et al., 2009; George et al., 1996). Several differences in the neural mechanisms by which women and men process emotion have been proposed that highlight the role of cognitive and other factors. These

have included a variety of proposed differences in the cognitive representation and processing of emotional stimuli, ranging from differences in attentional biases (Schirmer et al., 2008), effects of previous experience on perception and memory (Cahill & van Stegeren, 2003; Seidlitz & Diener, 1998) to differences in emotional executive control processes such as regulation (Domes et al., 2009; McRae, Ochsner, Mauss, Gabrieli, & Gross, 2008) and frequency of rumination about past emotional experiences (Thomsen et al., 2005). Additional sources of sex differences have also been proposed, including differences in lateralization of emotion processing (Canli et al., 2002; Fine et al., 2009; Wager et al., 2003) and temporal characteristics of the emotional response (e.g., prolonged emotional responses; Gard & Kring, 2007). Multiple factors may contribute to particular observed sex differences, and these factors may also interact, for example, sex differences in the effectiveness of emotion regulation (e.g., Domes et al., 2009; McRae et al., 2008) may amplify differences in more basic emotional responsiveness.

Although the ultimate causal factors responsible for sex differences in brain responses to emotional stimuli have yet to be delineated, the categories of likely potential factors are the same as those previously theorized for other sex differences in psychological and brain function: biological mechanisms such as genetic and hormonal influences and associated evolutionary factors, differences between the sexes in socialization and prior experience, and the interaction of these factors. Our results are compatible with any of these potential causal factors. A question for future study is the extent to which each the sex differences in regional activation observed here are valid cross-culturally and can be modified by experience.

Limitations

A number of limitations related to the current study should be noted. The meta-analysis results are based on summary information from individual neuroimaging studies, not the original raw data. Re-analysis of original raw data would be preferable, but this approach is precluded by the fact that such data are generally unavailable for most studies (Salimi-Khorshidi, Smith, Keltner, Wager, & Nichols, 2009). The ALE method retains key aspects of the reported findings

in each study, but like most neuroimaging meta-analysis methods, does not differentially weight information regarding activation statistics beyond requiring that each activation cluster exceeds the significance threshold used in each study. Another limitation concerned the fact that there were substantially fewer studies that could be included that examined positive emotion than examined negative emotion. Thus, there was lower power to detect sex differences for positive emotion studies relative to negative emotion studies.

In addition, the neuroimaging studies contributing to the meta-analysis varied widely in their stimuli, experimental methods, and scanning parameters. Although we took steps to minimize the possible contribution of such factors, it remains possible that systematic differences in such factors may have contributed to some of the observed differences. Future neuroimaging studies examining these issues should include a wider range of stimulus modalities and tasks to enable potential interactions with stimulus and task factors. Another limitation was that, in line with previous meta-analyses, our analysis only considered differences at the level of individual voxels and brain regions. However, meta-analyses that consider functional connectivity and other methods of characterizing distributed networks involved in emotion are a promising avenue for further study, particularly in light of sex differences in amygdala functional connectivity reported in individual neuroimaging studies (Kilpatrick et al., 2006; Savic & Lindstrom, 2008).

In the current study, our analysis focused on examining sex differences as a function of positive and negative emotional valence. This approach was motivated in part by the considerable evidence demonstrating that emotional valence is a key dimension of emotion and the neural representation of emotion (Feldman Barrett & Russell, 1999; Lang, Bradley, & Cuthbert, 1998; Nielen et al., 2009). However, positive and negative valence categories can be further subdivided into more specific emotion types, for example, basic emotions (happiness, fear, etc.; Darwin, 1873; Ekman, 1999) and other classifications such as threat, dominance, and sexual arousal. The extent to which the valence-specific sex differences observed in this study generalize to other emotion categories is an important question for further study.

2.6 Conclusions

In conclusion, the current findings provide new meta-analytic evidence that regional brain activations elicited during emotion differ in several important ways between the sexes. These sex differences in regional activation were substantial and were observed in key regions associated with emotion processing, most strikingly the left amygdala, which showed greater activation for women for negative emotion studies, but greater activation for men for positive emotion studies. Other substantial sex differences were found in additional regions involved in emotion and memory, including the hippocampus, insula, hypothalamus, and medial prefrontal cortex. As expected, these sex differences were found against a background of broad similarities between the sexes in the basic regions recruited during positive and negative emotion processing.

Our findings are consistent the findings of previous individual neuroimaging studies that have directly contrasted women and men in within-experiment comparisons. However, the nature and generality of the findings of these individual studies has remained unclear, in large part because of the small number of studies to date that have examined these differences. The limitations associated with a limited number of studies are particularly prominent for studies of positive emotion (Fine et al., 2009; Hofer et al., 2007; Killgore & Yurgelun-Todd, 2001; Wrase et al., 2003). Here, by taking a meta-analytic approach we were able to make a comprehensive summary assessment of the relevant affective neuroimaging literature. Although the meta-analytic approach has several advantages, it also has significant limitations, highlighting the need to broaden the current neuroimaging literature on affective sex differences with new studies investigating the questions and issues we have examined.

The current findings underscore the importance of considering sex as a potential factor modulating emotional processing and its underlying neural mechanisms, and more broadly, the need to consider individual differences in understanding the neurobiology of emotion. Approaches that integrate knowledge of individual differences will ultimately provide a more complete account than those that regard individual differences as uninteresting or merely as

statistical noise to be filtered out in the search for putative universal psychological and neurobiological mechanisms (Cahill, 2006; Hamann & Canli, 2004). For example, in cases where a regional brain activation effect is present in either women or men, but is either absent or reversed in the other group, examination of results combined across the sexes will produce an incomplete characterization of brain activations. These issues are particularly salient when considering individual differences that are related to depression, anxiety disorders, and other forms of psychopathology. There is growing evidence that women and men differ importantly in psychological and neurobiological mechanisms related to the development of a range of psychopathologies. Understanding the role of these individual differences will foster a better understanding of the neural mechanisms of both healthy and disordered emotional function.

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Chapter 3

Sex differences in neural activity and amygdala connectivity associated with emotion processing

3.1 Abstract

Evidence suggests that women and men differ in emotional expression and physiology. The brain regions that exhibit parallel sex differences in response to emotional stimuli have been investigated in only a small number of studies. The amygdala and hypothalamus in particular might be expected to show sex differences, as these regions are sensitive to sex hormone levels, and have been shown to differ in gross morphometry between women and men. However, previous studies of sex differences in neural responses to emotional stimuli have not consistently found sex differences in the amygdala and hypothalamus, and have primarily used stimuli which evoke a mix of emotional arousal responses and other types of processing, such as faces. Here we investigated women's (n=13) and men's (n=14) neural responses to emotionally arousing scene stimuli using fMRI, and for the first time investigated sex differences in task-related functional connectivity of the amygdala. Women showed greater responses than men to negative stimuli in both the left and right amygdala, and greater functional connectivity between the amygdala and anterior cingulate cortex, perhaps reflective of the engagement of an emotion regulation circuit. Women also showed greater responses to positive stimuli in the right amygdala than men. Men showed greater responses to positive stimuli in the hypothalamus than women, and greater connectivity between the amygdala and nucleus accumbens in response to both positive and negative stimuli. The findings provide support for the idea that women and men engage different neural circuits during emotional responses, and may have relevance for understanding sex differences in the prevalence of mood disorders.

3.2 Introduction

Evidence from both the cognitive and clinical psychology literatures suggests that women and men differ in emotional functioning. Women show greater expressive and physiological emotional responses than men (Bradley, Codispoti, Sabatinelli, & Lang, 2001; Gard & Kring, 2007; Grossman & Wood, 1993; Kring & Gordon, 1998). In addition, women are much more likely than men to be diagnosed with mood-related mental health disorders such as depression (American Psychiatric Association, 2000; Nolen-Hoeksema, 2001; Pratt & Brody, 2008). Increasing evidence demonstrates parallel sex differences in gross structure for brain regions that perform key emotional functions, such as the amygdala and medial prefrontal cortex (Bramen et al., 2011; Good et al., 2001; Good et al., 2003; Gur, Gunning-Dixon, Bilker, & Gur, 2002; Neufang et al., 2009; Welborn et al., 2009). The goal of the current study was to investigate sex differences in brain function that contribute to sex differences in emotional function by examining brain regions in which women and men differ in their responses to emotional stimuli. Such questions are critical to understanding basic individual differences in human mental health, and in emotion more generally.

The proposal that women are generally more expressive of all types of emotion than men has been widely accepted (Hess et al., 2000, Fischer & Manstead, 2000). However, a growing body of findings suggests that women are particularly sensitive to negative or unpleasant emotional events, relative to men. Women show enhanced skin conductance, startle, and heart rate responses to negative stimuli but not positive stimuli (Bradley et al., 2001; Gard & Kring, 2007; Kring & Gordon, 1998; McManis, Bradley, Berg, Cuthbert, & Lang, 2001a). Negative stimuli also evoke greater event-related brain potentials in women than men (Gasbarri et al., 2006; Gasbarri et al., 2007; Kemp, Silberstein, Armstrong, & Nathan, 2004; Lithari et al., 2010). A few studies suggest that men may show greater emotional responses to positive stimuli than women, primarily in response to appetitive erotica (Bradley et al., 2001; Hamann, Herman, Nolan, & Wallen, 2004; McManis, Bradley, Berg, Cuthbert, & Lang, 2001b). Studying whether

and where sex differences exist in neural responses to emotional stimuli can indicate whether differences in behavior are grounded in physiology, and can point to the specific underlying processes which aggregate to create differences in emotional behavior.

The amygdala and hypothalamus play central roles in the production and regulation of emotional responses. Lesions of these regions impair physiological and subjective responses to emotional stimuli, and the acquisition of conditioned fear (LeDoux, 2000). The amygdala and hypothalamus are likely to exhibit sex differences in function because they are densely populated with sex hormone receptors (MacLusky, Naftolin, & Goldman-Rakic, 1986; Roselli, Klosterman, & Resko, 2001; Zuloaga, Puts, Jordan, & Breedlove, 2008), and exhibit sexual dimorphisms in structure. Evidence for differences in women's and men's neural responses to emotional stimuli have been mixed, potentially related to variability in the methods by which emotions are induced, as well as the relatively small sample sizes of typical functional neuroimaging studies. However, a recent meta-analysis of neuroimaging studies found reliable sex differences in amygdala responses to emotional stimuli, as well as in the hypothalamus, and in several additional regions (Stevens & Hamann, 2012). The meta-analysis indicated that for negative stimuli, women consistently showed greater left amygdala and hypothalamus responses than men, and for positive non-erotic stimuli, men consistently showed greater left amygdala responses than women. The findings provided new evidence for sex differences in key regions involved in the production and regulation of emotion. In addition, no sex differences in amygdala activation were observed in an analysis that combined studies of negative and positive emotion, suggesting that sex differences in this region depend upon whether the emotional event is negative or positive.

In the current study, we examined sex differences in neural responses to emotional stimuli by measuring BOLD activation in women and men as they viewed negative and positive emotional scenes, and neutral scenes. Major goals were to investigate men's reactions to positive non-erotic stimuli in an empirical study, and to determine the effects of emotional valence on women's and men's relative responses to emotional stimuli. We predicted that sex would

influence the responses of the amygdala and hypothalamus to emotional stimuli, based on previous neuroimaging studies (Domes et al., 2009; Hamann et al., 2004; Stevens & Hamann, 2012; Wager, Phan, Liberzon, & Taylor, 2003), and the density of gonadal hormone receptors in these regions (e.g., Roselli et al., 2001). Specifically, we predicted that women, relative to men, would show greater responses to negative stimuli in the left amygdala. More tentatively, we predicted that men, relative to women, would show greater responses to positive stimuli in the amygdala and hypothalamus, as has been observed in studies of erotic stimuli (Hamann et al., 2004) , and more generally to non-erotic positive stimuli in the meta-analysis of Stevens and Hamann (Stevens & Hamann, 2012) . In addition, no previous study has investigated sex differences in functional connectivity during an emotional response. Here, we used psychophysiological interaction analyses (PPI) to determine which regions showed functional connectivity with the amygdala in women and men. Information about functional networks engaged with the amygdala will provide novel information about the specific neurocognitive processes that may differ between women and men.

3.3 Methods

Participants

Twenty-eight healthy adults (13 women) were recruited through online advertising and flyers posted on the Emory University campus. Participants were screened in a phone interview to ensure they had no history of severe head injury, drug or alcohol abuse, or psychiatric illness. All participants were right handed, had normal or corrected-to-normal vision, and had high school education or higher. Data from one male participant were excluded due to technical issues with the scanner. Data from the remaining participants were used for behavioral and brain imaging analyses, and included 13 women [age- *M*(*SEM*) = 28.2(1.9) years] and 14 men [age- *M*(*SEM*) = 27.7(1.4) years]. Five women were taking oral contraceptives and two women used a hormonal patch or ring at the time of the experiment. Participants were compensated $75 for completing

the study. All participants gave written informed consent, and gave authorization for the use of their health information for research under HIPAA. Study procedures were approved by the Emory University Institutional Review Board.

Procedure

Participants began the experimental session by practicing the tasks that they would perform in the scanner. To gain familiarity with the timing of stimulus presentation and the response period, they viewed several examples of scene stimuli, and made a like / neutral / dislike judgment following the presentation of each scene. Participants then completed the modified Brief Index of Sexual Function (BISF; Taylor, Rosen, & Leiblum, 1994) and the NEO-FFI (Costa & McCrae, 1992).

During scanning, participants viewed static photographic scene stimuli from the International Affective Picture Series (IAPS; Lang, Bradley, & Cuthbert, 2008), and were instructed to attend to the pictures and feel whatever feelings and think whatever thoughts each picture elicited in them. To verify attention to each picture stimulus, we asked participants to make a simple rating of their emotional reactions, making like / neutral / dislike ratings using a button box. 36 positive, 36 negative, and 36 neutral full-color scenes were presented in a semi-random order such that no more than two pictures of the same valence preceded one another. Each picture was displayed full screen at a resolution of 1024x768 for 1.5 seconds, followed by a screen prompting the participant to make their rating of the picture presented for 1.5 seconds. The rating screen included a black background with “like / neutral / dislike” centered in the middle of the screen in white, 48pt Helvetica font. A white fixation cross centered on a black background followed each trial, comprising a jittered inter-trial interval of 1.5 – 2.5 seconds. This task took 9 minutes in total.

Following the scanning session, participants completed a series of memory tasks designed to assess long-term memory for the emotional and neutral scene stimuli. Results relating to memory for the scenes will be reported in a separate paper. To measure participants’

subjective emotional responses to the scenes, we asked participants to view the 108 pictures from the scanning session and rate each one on a five-point scale of emotional arousal (1- very little or no arousal, 5 – high arousal). The orders of items for the picture viewing and rating tasks were counterbalanced across participants. Psyscope XB53 software (Cohen, MacWhinney, Flatt, & Provost, 1993) was used for stimulus presentation in the encoding and rating tasks.

MRI acquisition and analysis

Scanning took place on a 3.0T Siemens Trio with echo-planar imaging (EPI) (Siemens, Malvern, PA). Whole-brain structural T1 images were acquired with a gradient-echo T1-weighted pulse sequence (TR =2.30s, TE=0.03s, 1x1x1mm voxel size). An EPI scout scan was then used to verify whole-brain coverage. EPI functional images were gathered using 37 3mm slices collected in an interleaved sequence (TR =2.00s, TE=0.03s, 3x3x3 mm voxel size).

Initial data quality checks were performed using ArtRepair software (Mazaika, Whitfield-Gabrieli, & Reiss, 2007), to identify signal spikes and motion artifacts. Slices containing spike artifacts were identified and replaced using linear interpolation, with no more than 4% of slices repaired per participant (mean=0.02%). Volumes affected by motion artifact were repaired using linear interpolation, with no more than 5% of volumes repaired per participant. Additional image preprocessing steps were implemented using statistical parametric mapping software (SPM8, Wellcome Department of Cognitive Neurology). Volumes were slice-timing corrected to the middle slice in time, and spatially realigned to the first image of the run. A 128Hz high-pass filter removed low-frequency noise (Holmes, Josephs, Buchel, & Friston, 1997). Unified segmentation normalization was used to normalize T1s and coregistered functional images to the Montreal Neurological Institute (MNI) template. Functional images were visually examined for signal dropout, to verify that no participant had dropout in any substantial portion of the amygdala or other medial temporal lobe regions. Images were then smoothed with an 8mm Gaussian kernel.

Each participant's BOLD responses to the emotional and neutral pictures were modeled individually in SPM8. Contrast images reflecting increases in activation for the positive and

negative pictures relative to the neutral pictures were created for each individual participant, and individual contrasts then entered group-level random effects analyses. To identify regions in which responses to positive and negative pictures differed for women and men, group-level comparisons were constructed using independent-samples t-tests on each voxel to contrast the responses of women against those of men, for positive > neutral pictures, negative > neutral pictures, and all emotional > neutral pictures. Sex differences were examined within a priori ROIs for the left and right amygdala, defined anatomically using the Anatomy Toolbox (Eickhoff et al., 2005), and the hypothalamus, defined anatomically using the Talairach Atlas. Follow-up analyses tested for differences between women and men across the whole brain. For both the ROI and whole-brain analyses, statistical significance levels were height-extent-corrected to a threshold of $p < .05$, using Alphasim analysis implemented in the REST toolbox (Song et al., 2011). To establish significance thresholds, Monte Carlo simulation was run using 1000 iterations, and an 8mm gaussian FWHM, consistent with smoothing kernel. For the amygdala and hypothalamus ROIs, simulation was run on all of the voxels within each ROI mask, with a single-voxel threshold of $p < .05$. Extent thresholds were $k=20$ for the left amygdala, $k=16$ for the right amygdala, and $k = 9$ for the hypothalamus, to reach corrected thresholds of $p < .05$. For whole-brain analyses, Monte Carlo simulation was run on all of the voxels within the average gray-matter mask. A single-voxel threshold of $p < .01$ was used, resulting in an extent threshold of $k = 59$ to reach a corrected threshold of $p < .05$. This whole-brain threshold was applied to the analyses of regional activation, and of functional connectivity with the amygdala.

To test the hypothesis that the amygdala participates in different emotional circuits in women and men, we conducted task-based functional connectivity analyses using the CONN Toolbox (http://web.mit.edu/swg/software.htm). The right and left amygdala, defined anatomically using the Anatomy Toolbox (Eickhoff et al., 2005), were used as seed regions. Activity in the amygdala was summarized using the mean signal across all voxels within the anatomically-defined volume. Within a gray-matter mask of the whole brain, each voxel's

covariance with the activation of the left and right amygdala was assessed. Potential sources of noise, including movement parameters and main effects of task condition, were modeled as nuisance covariates. Covariance with amygdala activation during responses to positive scenes and negative scenes was contrasted with covariance with amygdala activation during responses to neutral scenes. The resulting contrast images for individual participants then entered group-level analyses comparing women and men.

3.4 Results

Subjective emotional responses

A 3 (emotion: negative, positive, neutral) x 2 (sex: women, men) mixed-effects ANOVA was used to assess the effect of emotion condition on subjective arousal levels, and to test whether this varied by sex. Emotion condition significantly influenced participants' subjective ratings of the scene stimuli, $F(2,50) = 71.17$, $p < .001$. Bonferroni-corrected paired comparisons indicated that negative [$M(SEM) = 3.55(0.13)$] and positive scenes [2.91(0.11)] were more arousing than neutral scenes [1.70(0.08)], positive: $p < .001$, negative: $p < .001$. Negative scenes were more arousing than positive scenes, $p = .005$. Because arousal responses were not balanced for negative versus positive stimuli, we considered negative and positive emotions separately in the brain imaging analyses, and did not compare responses to negative versus positive stimuli. The interaction of emotion by sex was not significant, $F(2,50) = 0.17$, $p = .68$, indicating that women and men did not differ in their arousal responses to the emotional stimuli. Because previous studies found that women reported greater subjective arousal than men for negatively-valenced scene stimuli (Cahill, Uncapher, Kilpatrick, Alkire, & Turner, 2004; Canli, Desmond, Zhao, & Gabrieli, 2002), we conducted a follow-up t-test comparing women's and men's ratings of negative pictures. No significant group difference was observed [$t(25) = 1.10$, $p = .28$; women: $M(SEM) = 3.69(0.22)$, men: 3.40(0.15)]. Women and men also did not differ in their ratings of positive pictures [$t(25) = 0.64$, $p = .53$; women: $M(SEM) = 2.98(0.16)$, men: 2.84(0.15)].

Individual differences: Correlation with NEO

We administered the NEO-FFI (Costa & McCrae, 1992), a five-factor personality questionnaire whose subscales measure neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness. Because the extraversion and neuroticism subscales have been previously related to reactivity to positive and negative stimuli, respectively, we used these subscales to index additional variability in individuals' responses to positive and negative stimuli. Women and men did not differ in their scores for Neuroticism [$t(24) = 0.13$, $p = .90$; $M(SEM)$ = women: 17.92(3.40), men : 18.14(5.26)] or Extraversion [$t(24) = 0.69$, $p = .50$; $M(SEM)$ = women: 26.83(6.79), men: 28.86(7.95)].

Sex differences in the amygdala response to emotional stimuli

All neuroimaging results (for regional activation and functional connectivity) are reported as responses to negative or positive stimuli, relative to neutral stimuli. For negative stimuli, women and men had increased activity in the left and right amygdala (Left: women: k = 82, Z = 4.39, x, y, z = -18, -4, -17; men: k = 58, Z = 3.58, x, y, z = -21, -1, -17), (Right: women: k = 90, Z = 5.52, x, y, z = 18, 2, -20; men: k = 61; Z = 4.01, x, y, z = 21, -1, -11). Women showed greater activation than men in left and right amygdala responses to negative stimuli (Figures 1 and 2). In the left amygdala, a cluster of k = 31 showed greater activation in women than men (Z = 2.44, x, y, z = -21, -7, -20). In the right amygdala, a cluster of k = 32 showed greater activation in women than men (Z = 2.42, x, y, z = 24, -1, -20).

For positive stimuli, women and men also showed increased activity in the left and right amygdala (Left: women: k = 97, Z = 3.47, x, y, z = -18, -7, -14; men: k = 156, Z = 4.47, x, y, z = -21, -4, -20), (Right: women: k = 79, Z = 4.12, x, y, z = 27, -1, -17; men: k = 97; Z = 3.89, x, y, z = 21, -1, -20). Women displayed greater right amygdala responses to positive stimuli than men (Figures 3 & 4). A cluster of k = 22 showed greater activation in women than men (Z = 2.85, x, y, z = 27, -7, -20). No sex differences in responses to positive stimuli were observed in the left

amygdala. Men did not display greater amygdala activation than women, for negative or positive stimuli.

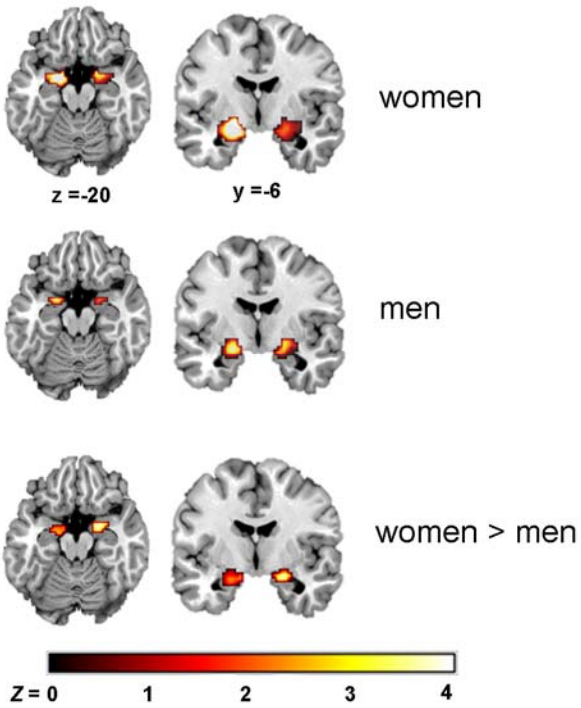

Figure 1. Amygdala responses to negative stimuli in women and men. Shows clusters of significant activation within the left and right amygdala ROIs, $p < .05$, corrected, displayed on the template brain of the Montreal Neurological Institute (MNI), in neurological orientation.

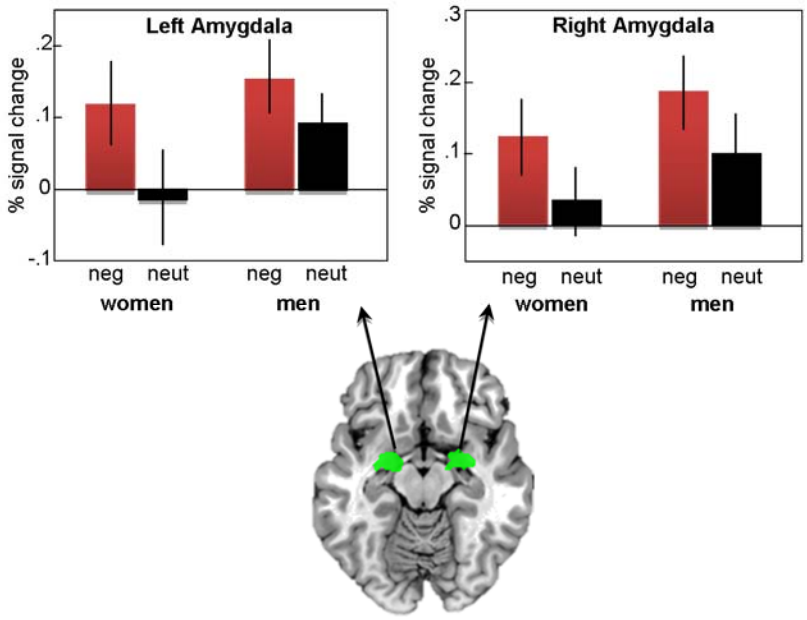

Figure 2. Amygdala responses to negative stimuli, displayed as the average percent signal change across the full anatomical volumes of the left and right amygdala ROIs. Amygdala ROIs displayed in green. Bars show ±1 SEM.

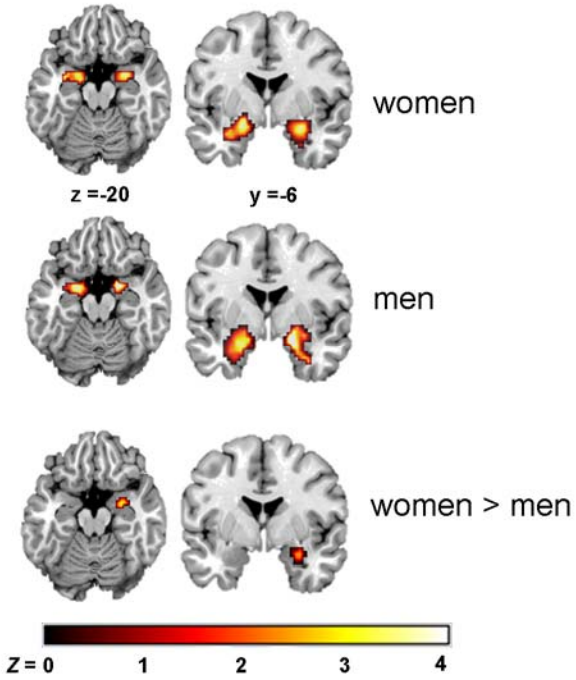

Figure 3. Amygdala responses to positive stimuli in women and men. Shows clusters of significant activation within the left and right amygdala ROIs, $p < .05$, corrected, displayed on the template brain of the Montreal Neurological Institute (MNI), in neurological orientation.

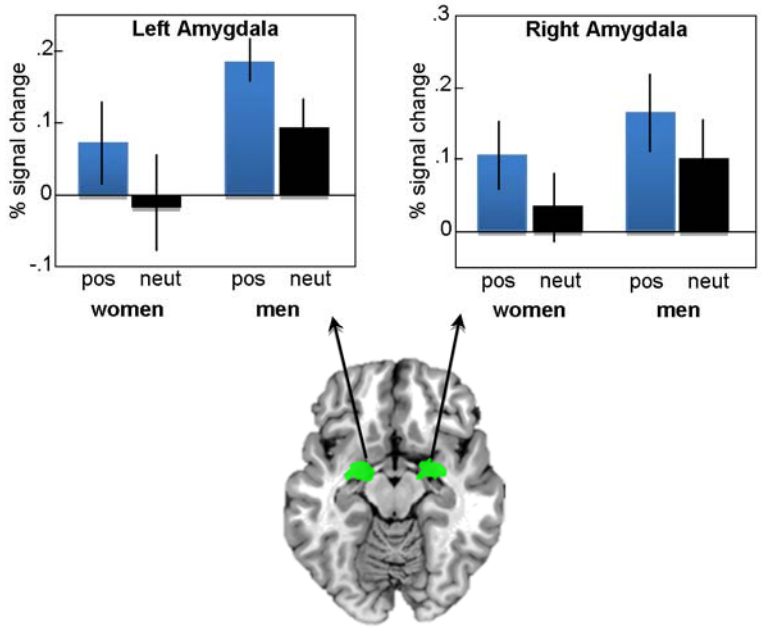

Figure 4. Amygdala responses to positive stimuli, displayed as the average percent signal change across the full anatomical volumes of the left and right amygdala ROIs. Amygdala ROIs displayed in green. Bars show ±1 SEM.

Sex differences in the hypothalamus response to emotional stimuli

For negative stimuli, both women and men showed significant hypothalamus responses (women: k = 72, *Z* = 4.34, x, y, z = 6, -4, -11; men: k = 54, *Z* = 3.42, x, y, z = 6, -1, -5). Women and men did not differ in the hypothalamus response to negative stimuli. For positive stimuli, both women and men showed significant hypothalamus responses (women: k = 30, *Z* = 2.86, x, y, z = -9, -7, -8; men: k = 67, *Z* = 3.79, x, y, z = 6, -1, -5). The group comparison indicated greater hypothalamus activation in men than women (k = 24; Z = 2.67; x, y, z = 3, -7, -11), as illustrated in Figure 5.

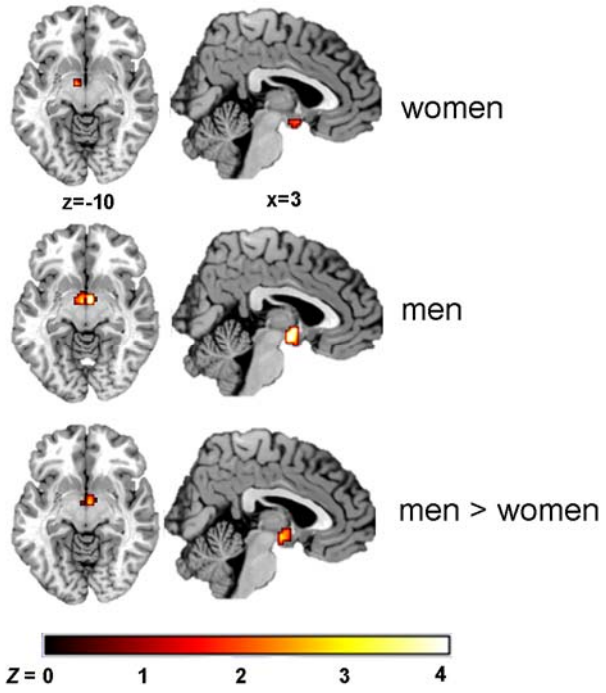

Figure 5. Hypothalamus responses to positive stimuli in women and men. Clusters of significant activation within the left and right amygdala ROIs, $p < .05$, corrected, displayed on the template brain of the Montreal Neurological Institute (MNI), in neurological orientation.

Responses to emotional stimuli in additional regions

For negative stimuli, no significant sex differences were observed in regions outside of the amygdala and hypothalamus ROIs. Within-groups analyses of women and men showed that

each gender group demonstrated enhanced responses to negative stimuli within the amygdala, hypothalamus, insula, striatum, and medial prefrontal cortex (Table 1, Figure S1).

For positive stimuli, men showed greater responses than women in the right superior temporal gyrus, and in posterior cingulate cortex (Table 2). Women did not show greater responses than men in any region. Each group showed greater responses to positive stimuli in the amygdala, hypothalamus, insula, and medial prefrontal cortex (Table 2, Figure S2).

Table 1
Enhanced responses to negative stimuli, relative to neutral stimuli

		MNI Coordinates				
	HEM	x	y	z	Z	k
Women > Men						
No significant clusters						
Men > Women						
No significant clusters						
Women						
Amygdala	R	24	2	-20	5.57	1825
Insula	L	-42	11	-11	4.54	(LM)
Thalamus	L	-3	-13	4	4.45	(LM)
Mid. Temporal G.	L	-60	-61	13	3.82	84
Mid. Temporal G.	L	-57	-67	19	3.17	(LM)
Mid. Temporal G.	L	-48	-55	7	2.85	(LM)
Anterior Cingulate G.	R	3	26	19	3.52	73
Anterior Cingulate G.	L	-3	32	16	3.3	(LM)
Sup. Frontal G.	R	9	41	52	4.2	175
Sup. Frontal G.	R	12	29	64	3.4	(LM)
Supp. Motor Area	R	6	23	55	3.17	(LM)
Sup. Frontal G.	L	-6	50	25	3.69	242
Sup. Frontal G.	R	6	53	31	3.49	(LM)
Anterior Cingulate G.	R	12	50	13	2.75	(LM)
Inf. Frontal G.	L	-48	26	-2	3.34	67
Inf. Frontal G.	L	-39	29	4	2.78	(LM)
Inf. Frontal G.	L	-42	29	-8	2.75	(LM)
Supramarginal G.	R	66	-31	34	4.67	227
Supramarginal G.	R	63	-22	46	4.38	(LM)
Supramarginal G.	R	66	-22	37	4.01	(LM)
Supramarginal G.	L	-66	-28	34	4.02	86
Supramarginal G.	L	-63	-52	31	2.62	(LM)
Fusiform G.	R	45	-40	-26	4.44	466
Inf. Temporal G.	R	54	-70	-8	4.2	(LM)
Mid. Temporal G.	R	60	-61	7	3.79	(LM)
Mid. Occipital G.	L	-51	-79	4	3.66	156
Fusiform G.	L	-39	-46	-20	3.37	(LM)
Fusiform G.	L	-42	-67	-14	3.27	(LM)
Men						
Amygdala	R	21	-1	-11	4.01	161
Thalamus	R	6	-1	-5	3.42	(LM)
Thalamus	L	-3	-19	4	3.34	(LM)
Temporal Pole	R	48	17	-29	4.23	67
Temporal Pole	R	39	17	-26	3.07	(LM)
Temporal Pole	R	48	17	-17	2.63	(LM)
Mid. Temporal G.	R	54	-49	-5	3.58	75
Inf. Temporal G.	R	45	-73	-8	3.12	67
Sup. Frontal G.	R	6	50	28	4.16	135
Sup. Frontal G.	R	6	53	19	4.11	(LM)
Sup. Frontal G.	R	12	38	55	2.97	(LM)
Sup. Frontal G.	L	-3	56	22	3.93	92
Sup. Frontal G.	L	-9	47	31	3.43	(LM)
Inf. Frontal G.	R	51	32	1	3.09	97
Fusiform G.	R	42	-46	-20	3.73	63

Table 2
Enhanced responses to positive stimuli, relative to neutral stimuli

		MNI Coordinates				
	HEM	x	y	z	Z	k
Women > Men						
No significant clusters						
Men > Women						
Sup. Temporal G.	R	57	-4	-5	3.54	64
Temporal Pole	R	60	11	-8	2.74	(LM)
Sup. Temporal G.	R	60	-13	-2	2.68	(LM)
Post. Cingulate G.	R	6	-40	22	3.4	75
Post. Cingulate G.	L	-3	-34	31	3.09	(LM)
Women						
Temporal Pole	L	-33	5	-17	4.5	260
Insula	L	-42	5	-5	4	(LM)
Rolandic Oper.	L	-48	8	1	3.89	(LM)
Temporal Pole	R	36	11	-32	3.67	99
Insula	R	36	14	-14	3.32	(LM)
Temporal Pole	R	30	17	-35	3.15	(LM)
Anterior Cingulate G.	L	-6	41	16	4.37	685
Sup. Frontal G.	R	21	50	25	3.73	(LM)
Anterior Cingulate G.	R	3	47	10	3.43	(LM)
G. Rectus	L	-6	35	-26	3.25	75
G. Rectus	R	3	35	-29	2.44	(LM)
Anterior Cingulate G.	R	0	26	-5	2.38	(LM)
Sup. Frontal G.	L	-15	35	46	3.30	74
Sup. Frontal G.	L	-12	23	55	2.67	(LM)
Sup. Frontal G.	L	-18	26	61	2.57	(LM)
Cuneus	L	-6	-100	16	4.72	122
Calcarine Fissure	L	-9	-88	1	3.31	(LM)
Inf. Occipital G.	R	45	-82	-14	3.96	181
Inf. Occipital G.	R	51	-76	-11	3.82	(LM)
Inf. Occipital G.	R	45	-64	-14	3.30	(LM)
Men						
Amygdala	L	-21	-4	-20	4.47	805
Inf. Frontal G.	L	-33	32	-11	4.20	(LM)
Inf. Frontal G.	L	-30	23	-14	3.98	(LM)
Mid. Cingulate G.	R	6	-1	40	5.28	99
Mid. Cingulate G.	L	-3	11	34	2.57	(LM)
Sup. Frontal G.	L	-12	62	19	4.93	674
Sup. Frontal G.	L	-6	59	-8	4.73	(LM)
Sup. Frontal G.	L	-3	50	-8	4.35	(LM)
Sup. Frontal G.	L	-18	35	49	4.31	122
Mid. Frontal G.	R	45	-7	58	4.33	298
Postcentral G.	R	48	-22	64	3.41	(LM)
Supp. Motor Area	R	15	-7	64	3.23	(LM)
Insula	R	36	11	-8	3.43	135
Inf. Frontal G.	R	45	11	7	3.36	(LM)
Insula	R	42	2	-11	3.31	(LM)
Precentral G.	L	-51	-1	25	3.45	75
Inf. Frontal G.	L	-48	11	22	3.44	(LM)
Inf. Frontal G.	L	-54	14	10	3.05	(LM)
Inf. Occipital G.	R	48	-82	-5	4.32	259
Inf. Temporal G.	R	42	-70	-5	3.69	(LM)
Fusiform G.	R	42	-49	-20	2.77	(LM)
Mid. Occipital G.	L	-45	-85	-2	4.06	127
Fusiform G.	L	-36	-64	-11	3.50	(LM)
Inf. Occipital G.	L	-30	-76	-5	2.70	(LM)
Calcarine Fissure	L	-12	-85	7	4.00	244
Sup. Occipital G.	L	-9	-100	19	3.75	(LM)
Sup. Occipital G.	L	-12	-94	4	3.64	(LM)
Precuneus	L	-9	-55	28	3.07	120
Post. Cingulate G.	R	3	-49	28	2.89	(LM)
Precuneus	L	-3	-61	34	2.87	(LM)

Sex differences in functional connectivity with the amygdala

For negative stimuli, women showed greater functional connectivity than men between the left amygdala and the right inferior temporal gyrus, bilateral thalamus, left insula, and right middle occipital gyrus (Table 3, Figure 6a). Women showed greater functional connectivity than men between the right amygdala and the left pregenual anterior cingulate in BA 32/24, left superior parietal gyrus, and right fusiform gyrus (Table 4, Figure 6a). Men showed greater functional connectivity than women between the left amygdala and the right nucleus accumbens, right superior frontal gyrus, and left paracentral lobule (Table 3, Figure 6b). Men showed greater functional connectivity than women between the right amygdala and the left middle temporal gyrus and left superior and middle occipital gyrus (Table 4, Figure 6b).

For positive stimuli, women showed greater functional connectivity than men between the left amygdala and the left and right middle frontal gyrus (Table 5, Figure 7a). Women showed greater connectivity than men between the right amygdala and the left superior frontal gyrus (Table 6, Figure 7a). Men showed greater functional connectivity than women between the left amygdala and the right nucleus accumbens, left middle frontal gyrus, left superior frontal gyrus, mid-cingulate cortex, left middle occipital gyrus, left paracentral lobule, and right precentral gyrus (Table 5, Figure 7b). Men showed greater connectivity than women between the right amygdala and the middle temporal gyrus bilaterally, the right superior, inferior, and middle frontal gyrus, bilateral occipital cortex, and the left pre- and postcentral gyri (Table 6, Figure 7b).

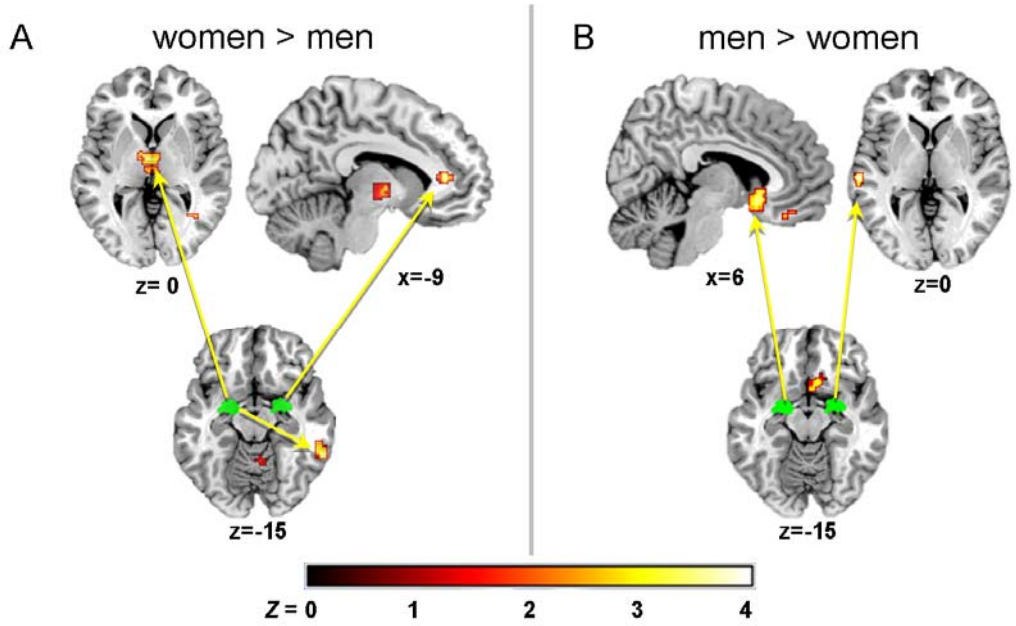

Figure 6. Significant functional connectivity with the left and right amygdala seed regions, in response to negative stimuli. Amygdala seed regions are displayed in green. 6a: Regions that showed greater connectivity with left or right amygdala in women than men. 6b: Regions that showed greater connectivity with left or right amygdala in men than women. Clusters are significant at $p < .05$, corrected, displayed on the template brain of the Montreal Neurological Institute (MNI).

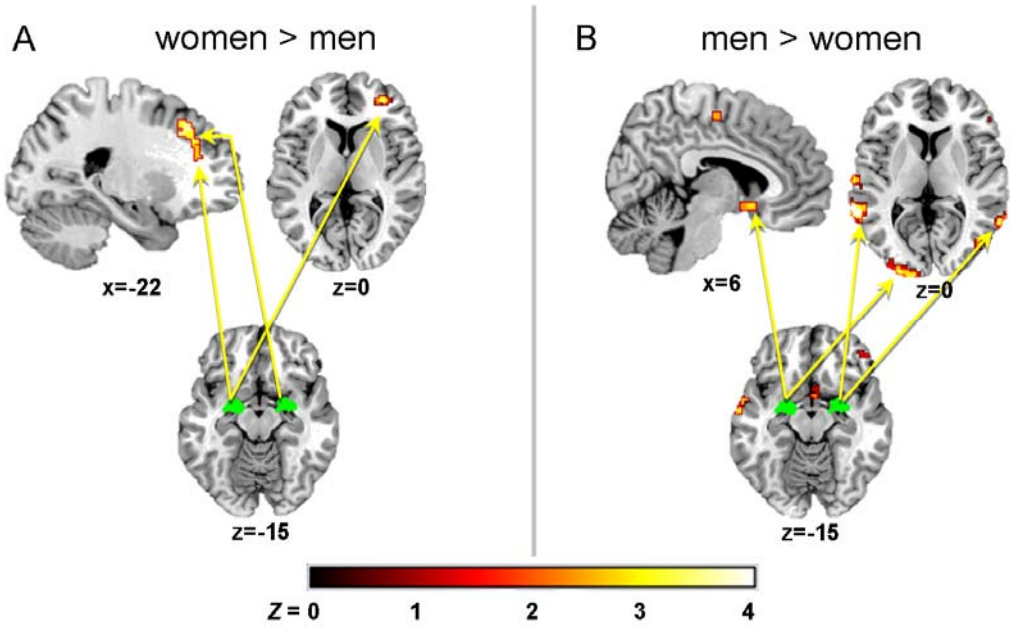

Figure 7. Significant functional connectivity with the left and right amygdala seed regions, in response to positive stimuli. Amygdala seed regions are displayed in green. 7a: Regions that showed greater connectivity with left or right amygdala in women than men. 7b: Regions that showed greater connectivity with left or right amygdala in men than women. Clusters are significant at $p < .05$, corrected, displayed on the template brain of the Montreal Neurological Institute (MNI).

Table 3
Enhanced connectivity with left amygdala for negative relative to neutral stimuli

		MNI Coordinates				
	HEM	x	y	z	Z	k
Women > Men						
Inf. Temporal G.	R	40	-58	-6	3.66	112
Inf. Temporal G.	R	54	-58	-6	2.57	(LM)
Inf. Temporal G.	R	52	-48	-6	2.39	(LM)
Inf. Temporal G.	R	60	-46	-20	3.57	145
Inf. Temporal G.	R	56	-42	-14	2.88	(LM)
Inf. Temporal G.	R	60	-36	-18	2.49	(LM)
Thalamus	L	-6	-8	-2	4.52	256
Thalamus	R	4	-10	-2	2.99	(LM)
Thalamus	L	-2	-14	-6	2.81	(LM)
Insula	L	-38	-16	6	3.23	70
Heschl G.	L	-46	-16	8	2.44	(LM)
Insula	L	-36	-22	14	2.35	(LM)
Mid. Occipital G.	R	42	-80	34	3.22	138
Angular G.	R	54	-72	30	3.01	(LM)
Mid. Occipital G.	R	46	-70	28	2.64	(LM)
Cerebellum- Vermis	R	6	-52	-20	3.31	95
Men > Women						
Nucleus Accumbens	R	6	14	-14	3.58	219
Nucleus Accumbens	R	6	18	-6	3.04	(LM)
Inf. Frontal G.	R	28	22	-24	2.88	(LM)
Sup. Frontal G.	R	10	44	-24	2.71	73
G. Rectus	R	6	34	-24	2.46	(LM)
Paracentral Lobule	L	-6	-22	76	3.13	76
Paracentral Lobule	L	-10	-26	70	2.6	(LM)
Women						
Thalamus	L	-8	-8	-2	4.36	466
Hippocampus	L	-6	-14	-12	3.67	(LM)
Thalamus	L	-2	-10	4	3.6	(LM)
Inf. Temporal G.	L	-48	-44	-20	3.1	63
Sup. Frontal G.	R	10	22	42	3.94	125
Supp. Motor Area	R	6	22	50	3.15	(LM)
Mid. Cingulate G.	R	14	22	30	2.56	(LM)
Insula	R	34	28	6	3.91	480
Inf. Frontal G.	R	40	34	-8	3.64	(LM)
Sup. Frontal G.	R	30	52	12	3.41	(LM)
Inf. Frontal G.	R	30	14	26	3.83	200
Inf. Frontal G.	R	36	14	32	3.42	(LM)
Inf. Frontal G.	R	42	16	24	3.05	(LM)
Cerebellum	L	-14	-76	-32	3.67	501
Cerebellum	L	-12	-64	-20	3.54	(LM)
Cerebellum	R	12	-62	-28	3.39	(LM)
Mid. Temporal G.	L	-56	-70	16	3.63	92
Angular G.	L	-54	-72	26	3.24	(LM)
Mid. Occipital G.	L	-42	-68	24	2.75	(LM)
Cerebellum	L	-32	-38	-32	3.54	89
Cerebellum	L	-32	-30	-30	2.62	(LM)
Cerebellum	L	-40	-40	-32	2.59	(LM)
Mid. Temporal G.	R	60	-38	-14	3.53	360
Inf. Temporal G.	R	64	-44	-18	3.48	(LM)
Inf. Temporal G.	R	40	-58	-6	3.15	(LM)
Cerebellum	R	46	-44	-38	3.52	166
Cerebellum	R	34	-40	-30	2.86	(LM)
Cerebellum	R	26	-38	-26	2.86	(LM)
Rolandic Oper.	R	48	-8	16	3.4	388
Rolandic Oper.	R	52	0	16	3.36	(LM)
Insula	R	34	-14	22	3.31	(LM)
Mid. Temporal G.	L	-60	-16	-14	3.4	103
Mid. Temporal G.	L	-68	-20	-12	2.98	(LM)
Inf. Frontal G.	L	-36	28	4	3.3	217

Inf. Frontal G.	L	-44	22	6	3.19	(LM)
Insula	L	-26	26	4	2.7	(LM)
Parahippocampal G.	L	-26	-34	-14	3.28	107
Hippocampus	L	-30	-28	-10	3.04	(LM)
Putamen	L	-30	-16	-8	2.95	(LM)
Inf. Frontal G.	L	-42	22	-8	3.26	108
Inf. Frontal G.	L	-46	28	-12	2.9	(LM)
Inf. Frontal G.	L	-52	22	-10	2.72	(LM)
Sup. Frontal G.	L	-8	44	22	3.26	85
Ant. Cingulate G.	L	-8	40	12	2.85	(LM)
Ant. Cingulate G.	L	-12	48	10	2.74	(LM)
Angular G.	R	34	-58	34	2.93	61
Angular G.	R	34	-56	44	2.5	(LM)
Cerebellum	R	34	-70	-20	2.82	59
Cerebellum	R	36	-64	-26	2.74	(LM)
Men						
Sup. Frontal G.	L	-14	40	-12	3.53	74
Sup. Frontal G.	L	-18	48	-14	2.69	(LM)
Parahippocampal G.	L	-8	-2	-32	3.46	87
Parahippocampal G.	L	-8	6	-26	3.19	(LM)
Parahippocampal G.	L	-16	4	-32	2.65	(LM)
G. Rectus	R	12	20	-20	2.62	71
Nucleus Accumbens	R	8	16	-14	2.55	(LM)
G. Rectus	R	12	24	-12	2.43	(LM)

Table 4
Enhanced connectivity with right amygdala for negative relative to neutral stimuli

		MNI Coordinates				
	HEM	x	y	z	Z	k
Women > Men						
Ant. Cingulate G.	L	-12	38	8	3.52	88
Ant. Cingulate G.	L	-16	42	14	2.44	(LM)
Sup. Parietal G.	L	-26	-44	72	3.81	147
Sup. Parietal G.	L	-32	-50	70	3.28	(LM)
Postcentral G.	L	-34	-42	70	3.02	(LM)
Fusiform G.	R	34	-58	-6	3.18	79
Lingual G.	R	32	-62	2	2.65	(LM)
Mid. Temporal G.	R	40	-62	-2	2.64	(LM)
Men > Women						
Mid. Temporal G.	L	-62	-26	0	3.33	87
Mid. Temporal G.	L	-62	-32	-6	2.38	(LM)
Sup. Occipital G.	L	-24	-86	24	2.92	103
Mid. Occipital G.	L	-30	-96	16	2.7	(LM)
Mid. Occipital G.	L	-20	-82	18	2.58	(LM)
Women						
Thalamus	L	-18	-16	-6	4.4	249
Thalamus	L	-8	-8	-2	4.17	(LM)
Thalamus	L	-14	-14	2	3.25	(LM)
Postcentral G.	L	-56	-16	28	4.3	268
Postcentral G.	L	-64	-20	28	4.07	(LM)
Postcentral G.	L	-48	-22	30	3.67	(LM)
Insula	R	28	-16	20	4.07	840
Thalamus	R	12	-12	-2	3.96	(LM)
Thalamus	R	10	-8	6	3.72	(LM)
Precuneus	R	18	-68	42	3.8	118
Precuneus	R	18	-60	44	3.41	(LM)
Sup. Occipital G.	R	22	-74	46	2.58	(LM)
Amygdala	L	-26	-2	-18	3.74	161
Hippocampus	L	-26	-14	-18	2.89	(LM)
Hippocampus	L	-20	-4	-24	2.6	(LM)
Inf. Parietal G.	L	-48	-34	42	3.58	81
Postcentral G.	L	-44	-34	50	2.48	(LM)
Angular G.	R	36	-56	36	3.56	94
Inf. Parietal G.	R	40	-52	44	2.9	(LM)
Mid. Temporal G.	L	-32	-60	12	3.5	61
Precuneus	L	-30	-52	14	3.16	(LM)
Mid. Temporal G.	L	-34	-68	12	2.68	(LM)
Cerebellum	R	30	-38	-32	3.48	124
Cerebellum	R	32	-30	-32	3.42	(LM)
Cerebellum	R	34	-44	-28	2.62	(LM)
Mid. Frontal G.	R	42	2	58	3.47	195
Mid. Frontal G.	R	38	-2	64	3.03	(LM)
Sup. Frontal G.	R	32	-8	64	2.92	(LM)
Ant. Cingulate G.	R	12	26	24	3.43	241
Ant. Cingulate G.	R	6	20	18	3.32	(LM)
Mid. Cingulate G.	R	12	22	40	3.24	(LM)
Sup. Temporal G.	R	50	-34	16	3.41	121
Supramarginal G.	R	48	-32	26	2.78	(LM)
Rolandic Oper.	R	46	-26	18	2.59	(LM)
Fusiform G.	R	42	-62	-18	3.39	204
Inf. Temporal G.	R	42	-54	-14	2.65	(LM)
Inf. Temporal G.	R	52	-58	-12	2.59	(LM)
Postcentral G.	L	-26	-34	70	3.33	261
Precentral G.	L	-32	-26	66	3.31	(LM)
Precentral G.	L	-40	-26	64	2.86	(LM)
Inf. Temporal G.	L	-48	-40	-24	3.32	169
Inf. Temporal G.	L	-48	-46	-18	3.13	(LM)
Inf. Temporal G.	L	-52	-36	-30	2.71	(LM)
Supp. Motor Area	R	12	2	64	3.25	96
Supp. Motor Area	R	10	-8	64	2.97	(LM)
Mid. Temporal G.	R	42	-56	16	3.19	100

Mid. Temporal G.	R	52	-52	12	2.61	(LM)
Angular G.	R	40	-52	26	2.41	(LM)
Supp. Motor Area	L	-8	4	54	3.17	146
Sup. Frontal G.	L	-20	2	66	3.1	(LM)
Mid. Frontal G.	L	-20	10	52	2.87	(LM)
Cuneus	R	10	-88	42	3.14	66
Cuneus	R	2	-82	40	2.52	(LM)
Cerebellum	L	-30	-40	-36	3.11	112
Cerebellum	L	-30	-44	-28	3.04	(LM)
Cerebellum	L	-32	-36	-28	2.4	(LM)
Angular G.	R	40	-78	42	2.98	76
Angular G.	R	54	-72	30	2.82	(LM)
Angular G.	R	46	-70	36	2.7	(LM)
Postcentral G.	R	48	-26	48	2.96	94
Postcentral G.	R	48	-18	52	2.45	(LM)
Postcentral G.	R	52	-22	42	2.4	(LM)
Cerebellum	R	12	-46	-18	2.83	69
Cerebellum	R	16	-46	-10	2.5	(LM)
Cerebellum	R	12	-62	-32	3.74	245
Cerebellum	R	24	-76	-36	3.69	(LM)
Cerebellum	R	16	-68	-28	3.14	(LM)
Sup. Parietal G.	R	34	-44	58	2.78	61
Postcentral G.	R	32	-36	58	2.55	(LM)
Men						
Inf. Frontal G.	L	-20	14	-26	4.67	178
Inf. Frontal G.	L	-24	18	-20	3.53	(LM)
Inf. Frontal G.	L	-32	28	-22	2.8	(LM)
Supp. Motor Area	L	-18	-8	64	3.79	118
Paracentral Lobule	L	-12	-14	66	2.99	(LM)
Sup. Frontal G.	L	-24	-2	64	2.93	(LM)
Mid. Occipital G.	L	-20	-80	12	3.68	605
Mid. Occipital G.	L	-26	-82	24	3.33	(LM)
Cuneus	L	-14	-86	36	3.28	(LM)
Cerebellum	R	46	-40	-30	3.67	476
Cerebellum	R	46	-50	-32	3.28	(LM)
Cerebellum	R	36	-46	-30	3.2	(LM)
Sup. Frontal G.	R	22	10	66	3.61	122
Sup. Frontal G.	R	18	4	70	3.06	(LM)
Sup. Frontal G.	R	24	-2	70	2.72	(LM)
Supramarginal G.	R	60	-20	28	3.56	375
Supramarginal G.	R	56	-26	32	3.19	(LM)
Sup. Temporal G.	R	60	-58	22	3.03	(LM)
Mid. Temporal G.	R	46	-68	6	3.55	110
Mid. Temporal G.	R	46	-70	14	3.02	(LM)
Mid. Occipital G.	R	38	-70	10	2.66	(LM)
Mid. Temporal G.	L	-60	-26	0	3.55	88
Sup. Temporal G.	L	-62	-26	8	2.65	(LM)
Sup. Temporal G.	L	-44	-16	-8	3.54	82
Sup. Temporal G.	L	-52	-16	-2	3.04	(LM)
Precentral G.	L	-48	-4	54	3.42	72
Precentral G.	L	-42	-8	58	2.83	(LM)
Precentral G.	L	-52	0	48	2.4	(LM)
Precentral G.	R	60	10	18	3.42	97
Precentral G.	R	64	8	26	2.73	(LM)
Inf. Frontal G.	R	50	10	18	2.66	(LM)
Parahippocampal G.	R	24	8	-24	3.36	77
Sup. Frontal G.	R	16	20	-20	2.63	(LM)
Mid. Temporal G.	R	60	-16	-20	3.32	117
Mid. Temporal G.	R	52	-24	-14	3.26	(LM)
Inf. Temporal G.	R	58	-28	-18	2.41	(LM)
Supp. Motor Area	R	4	2	66	3.32	145
Supp. Motor Area	R	4	-2	74	3.13	(LM)
Supp. Motor Area	R	12	-4	66	2.99	(LM)
Mid. Occipital G.	L	-44	-74	4	3.31	123
Mid. Occipital G.	L	-42	-66	4	2.89	(LM)
Mid. Temporal G.	L	-52	-70	4	2.54	(LM)
Inf. Occipital G.	L	-50	-70	-12	3.29	109
Inf. Occipital G.	L	-50	-60	-14	2.87	(LM)
Inf. Temporal G.	L	-56	-64	-6	2.48	(LM)

Precuneus	R	0	-70	52	3.28	183
Sup. Parietal G.	L	-14	-74	58	2.7	(LM)
Precuneus	L	-2	-56	54	2.69	(LM)
Mid. Occipital G.	L	-36	-92	0	3.24	194
Mid. Occipital G.	L	-38	-82	10	2.99	(LM)
Mid. Occipital G.	L	-44	-88	-8	2.94	(LM)
Inf. Frontal G.	R	40	20	30	3.24	251
Mid. Frontal G.	R	50	12	52	3.06	(LM)
Mid. Frontal G.	R	48	20	36	2.83	(LM)
Supramarginal G.	L	-66	-48	24	3.17	183
Mid. Temporal G.	L	-56	-64	12	3.17	(LM)
Mid. Temporal G.	L	-62	-58	20	2.91	(LM)
Sup. Temporal G.	R	58	-20	-2	3.16	160
Sup. Temporal G.	R	50	-20	0	3.15	(LM)
Heschl G.	R	48	-20	8	2.77	(LM)
Supp. Motor Area	R	14	-22	52	3.16	88
Mid. Cingulate G.	R	8	-26	48	2.89	(LM)
Paracentral Lobule	R	16	-32	48	2.86	(LM)
Cerebellum	L	-6	-68	-18	3.14	82
Cerebellum: Vermis	R	0	-68	-24	2.78	(LM)
Cerebellum	L	-6	-74	-24	2.4	(LM)
Insula	R	48	8	0	3.14	238
Insula	R	36	8	4	3	(LM)
Insula	R	42	-2	0	2.5	(LM)
Precentral G.	R	12	-28	72	3.13	144
Precentral G.	R	24	-20	66	2.85	(LM)
Precentral G.	R	16	-20	72	2.7	(LM)
Sup. Temporal G.	L	-54	4	-6	3.09	82
Temporal Pole	L	-50	12	-8	2.94	(LM)
Calcarine Fissure	R	6	-70	12	3.07	127
Calcarine Fissure	R	16	-86	10	2.78	(LM)
Calcarine Fissure	R	12	-78	12	2.5	(LM)
Cerebellum: Vermis	R	0	-36	0	3.05	77
Post. Cingulate G.	R	4	-38	8	2.85	(LM)
Post. Cingulate G.	L	-4	-36	8	2.67	(LM)
Sup. Occipital G.	R	28	-62	30	3.03	189
Angular G.	R	28	-54	34	2.98	(LM)
Sup. Occipital G.	R	24	-74	36	2.95	(LM)
Fusiform G.	L	-30	-40	-20	3.01	144
Inf. Temporal G.	L	-44	-44	-26	2.67	(LM)
Cerebellum	L	-34	-44	-26	2.39	(LM)

Table 5
Enhanced connectivity with left amygdala for positive relative to neutral stimuli

		MNI Coordinates				
	HEM	x	y	z	Z	k
Women > Men						
Mid. Frontal G.	R	34	46	4	3.65	122
Sup. Frontal G.	R	24	44	14	3.25	(LM)
Ant. Cingulate G.	R	20	38	10	2.64	(LM)
Mid. Frontal G.	L	-24	34	20	3.25	76
Sup. Frontal G.	L	-20	32	30	2.72	(LM)
Cerebellum	R	0	-50	-50	3.57	67
Cerebellum	R	6	-58	-50	2.78	(LM)
Cerebellum	L	-4	-58	-48	2.66	(LM)
Men > Women						
Nucleus Accumbens	R	6	10	-12	2.89	59
Nucleus Accumbens	R	4	4	-18	2.53	(LM)
Mid. Frontal G.	L	-42	8	58	3.71	64
Mid. Frontal G.	L	-38	14	62	2.88	(LM)
Sup. Frontal G.	L	-24	-8	72	3.08	68
Mid. Cingulate G.	R	12	-16	48	3.08	97
Supp. Motor Area	R	8	-10	52	2.77	(LM)
Supp. Motor Area	R	16	-26	52	2.48	(LM)
Calcarine Fissure	L	-18	-104	-6	3.64	193
Mid. Occipital G.	L	-18	-96	-2	2.98	(LM)
Mid. Occipital G.	L	-14	-104	2	2.68	(LM)
Paracentral Lobule	L	-8	-20	72	3.58	111
Paracentral Lobule	L	-16	-22	78	2.62	(LM)
Paracentral Lobule	L	-2	-20	80	2.62	(LM)
Precentral G.	R	48	-20	64	3.24	70
Women						
Inf. Frontal G.	L	-36	32	0	4.29	120
Inf. Frontal G.	L	-40	32	8	2.96	(LM)
Inf. Frontal G.	L	-36	26	-6	2.91	(LM)
Inf. Frontal G.	R	54	26	16	3.86	112
Globus Pallidus	L	-20	-10	-4	3.86	175
Hippocampus	L	-8	-16	-12	3.55	(LM)
Putamen	L	-30	-18	-8	3.52	(LM)
Inf. Frontal G.	R	48	8	24	3.63	61
Inf. Frontal G.	R	40	8	30	2.74	(LM)
Inf. Frontal G.	R	32	8	28	2.71	(LM)
Postcentral G.	L	-62	-2	28	3.57	140
Postcentral G.	L	-60	-8	22	3.28	(LM)
Postcentral G.	L	-60	0	18	2.8	(LM)
Rolandic Oper.	L	-42	-22	16	3.4	159
Sup. Temporal G.	L	-46	-28	12	2.8	(LM)
Sup. Temporal G.	L	-42	-24	6	2.71	(LM)
Thalamus	L	-18	-28	0	3.27	82
Thalamus	L	-22	-32	6	2.66	(LM)
Hippocampus	L	-18	-38	0	2.48	(LM)
Mid. Frontal G.	R	30	38	18	3.26	112
Mid. Frontal G.	R	34	38	26	2.9	(LM)
Mid. Frontal G.	R	42	44	18	2.46	(LM)
Insula	R	40	-8	12	3.22	373
Insula	R	38	-8	20	3.2	(LM)
Putamen	R	36	-4	6	3.11	(LM)
Sup. Frontal G.	R	16	52	24	3.05	138
Sup. Frontal G.	R	22	56	16	2.83	(LM)
Mid. Frontal G.	R	28	62	24	2.62	(LM)
Inf. Frontal G.	R	40	28	-6	3.03	74
Inf. Frontal G.	R	42	38	-2	2.93	(LM)
Inf. Frontal G.	R	38	28	2	2.67	(LM)
Inf. Temporal G.	R	40	-62	-6	2.86	79
Inf. Temporal G.	R	42	-54	-6	2.8	(LM)
Inf. Temporal G.	R	52	-50	-6	2.57	(LM)
Men						

Inf. Frontal G.	L	-60	4	12	3.49	112
Postcentral G.	L	-60	2	20	3.09	(LM)
Postcentral G.	L	-48	-20	24	3.49	94
Postcentral G.	L	-50	-20	32	3.34	(LM)
Postcentral G.	L	-58	-16	34	2.87	(LM)
Rolandic Oper.	R	58	-20	18	3.36	387
Supramarginal G.	R	48	-28	30	3.15	(LM)
Rolandic Oper.	R	50	-20	22	2.85	(LM)
Hippocampus	L	-18	-4	-20	3.28	66
Parahippocampal G.	R	18	-2	-18	3.21	64
Amygdala	R	22	2	-10	2.85	(LM)
Insula	R	46	8	-2	3.09	91
Inf. Frontal G.	R	52	12	2	2.83	(LM)
Sup. Temporal G.	R	54	-2	4	2.43	(LM)
Postcentral G.	R	48	-22	64	3.07	126
Precentral G.	R	44	-18	58	2.67	(LM)
Precentral G.	R	36	-16	54	2.5	(LM)
Paracentral Lobule	L	-8	-26	60	2.89	112
Paracentral Lobule	L	-10	-26	70	2.7	(LM)
Supp. Motor Area	L	-2	-20	58	2.7	(LM)

Table 6
Enhanced connectivity with right amygdala for positive relative to neutral stimuli

		MNI Coordinates				
	HEM	x	y	z	Z	k
Women > Men						
Sup. Frontal G.	L	-18	26	42	3.1	142
Mid. Frontal G.	L	-24	32	30	2.98	(LM)
Mid. Frontal G.	L	-22	22	36	2.75	(LM)
Men > Women						
Mid. Temporal G.	L	-66	-46	6	4.71	208
Mid. Temporal G.	L	-60	-50	0	2.76	(LM)
Mid. Temporal G.	L	-56	-42	4	2.6	(LM)
Mid. Temporal G.	L	-56	4	-30	3.94	97
Temporal Pole	L	-54	14	-24	3.66	(LM)
Temporal Pole	L	-50	10	-30	2.39	(LM)
Mid. Temporal G.	L	-56	-28	0	3.3	129
Sup. Temporal G.	L	-42	-18	-8	3.18	(LM)
Mid. Temporal G.	L	-54	-22	-6	2.68	(LM)
Mid. Temporal G.	R	62	-62	6	3.22	94
Mid. Temporal G.	R	68	-50	12	3.04	(LM)
Mid. Temporal G.	R	64	-54	4	2.95	(LM)
Mid. Temporal G.	L	-60	-10	-8	3.22	91
Mid. Temporal G.	L	-66	-10	-14	3.16	(LM)
Mid. Temporal G.	L	-60	2	-18	3.1	(LM)
Sup. Frontal G.	R	22	4	70	3.24	62
Sup. Frontal G.	R	18	12	70	2.75	(LM)
Sup. Frontal G.	R	14	4	72	2.33	(LM)
Inf. Frontal G.	R	48	16	34	3.15	86
Mid. Frontal G.	R	34	14	40	2.94	120
Mid. Frontal G.	R	48	38	36	2.56	(LM)
Mid. Frontal G.	R	40	20	34	2.52	(LM)
Inf. Frontal G.	R	54	32	-2	2.85	103
Inf. Frontal G.	R	50	38	2	2.65	(LM)
Inf. Frontal G.	R	44	44	-18	2.65	(LM)
Mid. Occipital G.	L	-26	-102	6	3.36	404
Inf. Occipital G.	L	-18	-92	-6	3.15	(LM)
Sup. Occipital G.	L	-12	-104	10	3.07	(LM)
Inf. Occipital G.	R	52	-76	-2	2.94	94
Mid. Occipital G.	R	46	-76	4	2.9	(LM)
Calcarine Fissure	R	26	-102	0	2.94	67
Inf. Occipital G.	R	28	-96	-6	2.68	(LM)
Precentral G.	L	-56	10	40	3.86	118
Precentral G.	L	-56	2	28	3.16	(LM)
Mid. Frontal G.	L	-50	18	40	2.61	(LM)
Postcentral G.	L	-60	-8	42	3.27	78
Postcentral G.	L	-56	-4	48	2.67	(LM)
Postcentral G.	L	-62	-20	18	3.16	171
Sup. Temporal G.	L	-68	-20	6	2.88	(LM)
Sup. Temporal G.	L	-56	-16	12	2.65	(LM)
Women						
Hippocampus	L	-22	-14	-8	4.4	243
Thalamus	L	-10	-4	0	3.25	(LM)
Thalamus	L	-8	-14	0	3.19	(LM)
Thalamus	R	12	-22	18	4.15	90
Thalamus	R	22	-28	18	2.97	(LM)
Thalamus	R	16	-26	12	2.83	(LM)
Rolandic Oper.	R	40	-32	18	3.81	127
Insula	R	32	-30	18	2.7	(LM)
Supramarginal G.	R	46	-38	22	2.46	(LM)
Thalamus	R	12	-16	-6	3.67	174
Hippocampus	R	22	-10	-18	3.02	(LM)
Hippocampus	R	16	-10	-12	3.01	(LM)
Rolandic Oper.	R	46	-4	18	3.48	217
Precentral G.	R	54	4	24	3.22	(LM)
Precentral G.	R	46	4	28	2.89	(LM)
Hippocampus	R	36	-20	-12	3.33	157

Hippocampus	R	34	-32	-6	3.26	(LM)
Parahippocampal G.	R	28	-40	-6	2.94	(LM)
Inf. Frontal G.- Triangular part	R	40	32	6	3.26	69
Insula	R	40	22	6	3	(LM)
Mid. Temporal G.	R	42	-62	0	3.21	193
Inf. Temporal G.	R	46	-58	-6	2.9	(LM)
Inf. Occipital G.	R	36	-62	-6	2.86	(LM)
Supp. Motor Area	R	6	4	70	3.18	76
Supp. Motor Area	R	6	12	66	2.69	(LM)
Supp. Motor Area	R	2	-2	66	2.43	(LM)
Sup. Temporal G.	L	-44	-28	12	2.96	123
Heschl G.	L	-38	-22	12	2.88	(LM)
Heschl G.	L	-30	-26	10	2.69	(LM)
Inf. Parietal G.	R	48	-44	48	2.8	59
Inf. Parietal G.	R	46	-40	56	2.57	(LM)
Inf. Parietal G.	R	52	-36	46	2.5	(LM)
Postcentral G.	L	-60	-2	18	4.5	334
Precentral G.	L	-60	0	26	3.7	(LM)
Rolandic Oper.	L	-62	-2	4	3.25	(LM)
Cuneus	R	10	-76	34	2.6	72
Precuneus	R	6	-82	46	2.56	(LM)
Cuneus	R	2	-80	36	2.55	(LM)
Men						
Sup. Frontal G.	R	6	44	54	4.39	217
Sup. Frontal G.	R	4	50	48	3.92	(LM)
Sup. Frontal G.	L	-2	44	52	3.59	(LM)
Postcentral G.	L	-48	-20	24	4.39	1648
Precentral G.	L	-62	2	28	4.23	(LM)
Postcentral G.	L	-50	-20	32	3.97	(LM)
Sup. Temporal G.	L	-42	-22	-4	4.14	141
Mid. Temporal G.	L	-44	-28	-10	3.27	(LM)
Putamen	L	-32	-16	-8	2.68	(LM)
Supramarginal G.	R	54	-28	30	3.98	611
Heschl G.	R	40	-20	12	3.24	(LM)
Insula	R	42	4	6	3.13	(LM)
Temporal Pole	L	-50	20	-20	3.84	70
Temporal Pole	L	-44	24	-16	2.82	(LM)
Caudate	L	-2	10	-2	3.79	90
Caudate	L	-6	18	-2	2.72	(LM)
Caudate	L	-6	10	-12	2.65	(LM)
Sup. Temporal G.	L	-38	-36	6	3.77	106
Mid. Temporal G.	L	-38	-44	4	3.56	(LM)
Mid. Temporal G.	L	-46	-46	0	2.54	(LM)
Inf. Occipital G.	L	-36	-88	-6	3.56	1109
Mid. Occipital G.	L	-40	-92	0	3.52	(LM)
Sup. Occipital G.	L	-6	-100	18	3.49	(LM)
Sup. Frontal G.	R	0	64	24	3.43	86
Sup. Frontal G.	R	4	68	18	2.73	(LM)
Sup. Frontal G.	L	-12	68	24	2.71	(LM)
Mid. Temporal G.	L	-68	-50	6	3.43	720
Supramarginal G.	L	-40	-46	28	3.4	(LM)
Inf. Occipital G.	L	-50	-74	-12	3.28	(LM)
Sup. Temporal G.	R	64	-2	0	3.42	488
Precentral G.	R	60	4	28	3.35	(LM)
Precentral G.	R	64	8	22	3.18	(LM)
Fusiform G.	L	-38	-44	-26	3.37	289
Cerebellum	L	-38	-36	-30	3.02	(LM)
Fusiform G.	L	-36	-36	-22	2.75	(LM)
Supp. Motor Area	R	12	-24	52	3.37	71
Supp. Motor Area	R	2	-22	54	2.78	(LM)
Supp. Motor Area	R	6	-12	54	2.45	(LM)
Sup. Occipital G.	R	22	-92	6	3.34	272
Inf. Occipital G.	R	26	-102	-6	3.17	(LM)
Calcarine Fissure	R	22	-94	-2	2.92	(LM)
Inf. Frontal G.	L	-18	28	-18	3.26	124
Sup. Frontal G.	L	-18	46	-14	3.17	(LM)
Mid. Frontal G.	L	-18	36	-16	2.74	(LM)
Parahippocampal G.	L	-20	8	-26	3.13	66
Olfactory cortex	L	-18	10	-18	2.79	(LM)

Inf. Frontal G.	L	-20	18	-26	2.36	(LM)
Cerebellum	L	-26	-86	-36	3.11	68
Cerebellum	L	-26	-82	-28	2.68	(LM)
Cerebellum	L	-30	-78	-36	2.46	(LM)
Inf. Occipital G.	R	50	-76	-14	3.1	101
Cerebellum	R	48	-68	-24	2.7	(LM)
Inf. Occipital G.	R	52	-76	-2	2.65	(LM)
Sup. Frontal G.	R	18	-10	66	3.08	66
Sup. Frontal G.	R	24	-14	70	2.71	(LM)
Precentral G.	R	30	-20	72	2.49	(LM)
Inf. Temporal G.	L	-42	-10	-36	3.02	85
Inf. Temporal G.	L	-46	-6	-30	2.8	(LM)
Inf. Temporal G.	L	-46	-6	-42	2.39	(LM)
Mid. Frontal G.	R	28	12	40	3.01	96
Mid. Frontal G.	R	34	18	36	2.75	(LM)
Inf. Frontal G.	R	34	8	24	2.67	(LM)
Supp. Motor Area	R	4	-4	72	3.01	89
Supp. Motor Area	R	12	-14	72	2.86	(LM)
Supp. Motor Area	--	0	4	70	2.43	(LM)
Supp. Motor Area	--	0	20	66	2.9	67
Supp. Motor Area	--	0	8	66	2.64	(LM)
Supp. Motor Area	L	-2	14	60	2.38	(LM)
Cuneus	L	-12	-82	28	2.69	64
Cuneus	L	-8	-92	30	2.35	(LM)

3.5 Discussion

This study examined differences in women's and men's neural responses to negative and positive emotional stimuli, using functional MRI to examine the activation of individual brain regions, as well as patterns of functional connectivity between regions. Women and men did not differ in subjective arousal responses to the negative and positive emotional scene stimuli. However, we did observe sexually dimorphic neural responses to the emotional scenes. Both sexes showed robust amygdala responses to the emotional scene stimuli, but women showed greater amygdala responses than men for both positive and negative scenes. Men showed a greater hypothalamus response to positive stimuli than women. The findings supported our hypothesis that sex differences would vary as a function of emotional valence (negative vs. positive). These findings add to the small literature showing sex differences in neural responses to positive emotional stimuli (Fine, Semrud-Clikeman, & Zhu, 2009; George, Ketter, Parekh, Herscovitch, & Post, 1996; Hofer et al., 2007; Killgore & Yurgelun-Todd, 2001), and represent the first investigation of responses to positive, non-erotic IAPS scene stimuli. Previous studies of positive emotion in women and men primarily used emotional face stimuli, which are more

indicative of responses to non-verbal social cues about others' emotion, rather than emotional arousal responses (Sabatinelli, Fortune, Li, Siddiqui, Krafft et al., 2011). In addition, the current study was the first to examine sex differences in connectivity between brain regions during emotional processing, and identified distinct connections in women and men between the amygdala and other emotion-related regions.

When presented with negative scenes, both women and men exhibited bilateral amygdala activation, but women showed greater amygdala responses than men in both the left and right hemispheres. Previous studies of neural responses to negative stimuli have found enhanced responses to negative stimuli in both the left amygdala and right amygdala in women relative to men (Derntl et al., 2010; Domes et al., 2009; McClure et al., 2004). Although women and men each showed activation across a distributed network of emotion-related regions, no sex differences in negative emotion were observed outside the amygdala.

For positive scenes, both women and men showed activation in the amygdala bilaterally. Although we hypothesized that men would show a greater response than women in the right amygdala, this was not the case. Instead, no region of left or right amygdala was more active in men. In fact, we observed a greater response of the right amygdala in women than men. Men did show a greater response of the hypothalamus than women, consistent with our hypotheses, and with previous studies of sex differences in the neural processing of erotic stimuli (e.g., Hamann et al., 2004). This suggests that enhanced responses to erotic stimuli observed in men in previous studies may generalize to the processing of positive non-erotic stimuli. Studies using the IAPS stimulus set have shown that pictures with erotic content evoke greater emotional arousal and pleasantness responses than other types of positive pictures such as cute animals or appetizing food, and that among the positive pictures, only these highly-arousing erotic pictures evoke stronger brain and physiological responses in males than females (Bradley et al., 2001; McManis et al., 2001a; Sabatinelli, Flaisch, Bradley, Fitzsimmons, & Lang, 2004). The current study provides initial evidence to disentangle effects related to sexual versus emotional arousal

responses. Future studies might observe additional sex differences with more highly arousing, but non-erotic, positive stimuli.

Functional connectivity analyses revealed that the amygdala interacted with this distributed network of regions in both women and men, and differed in its participation with certain regions in each sex. For negative scenes, women showed greater connectivity than men between the amygdala and several regions involved in the regulation of emotional responses, such as the pregenual anterior cingulate cortex, left insula, and bilateral thalamus. These regions of the anterior cingulate and thalamus overlap with the findings of our previous meta-analysis (Stevens & Hamann, 2012), which showed more consistent activation across studies of the amygdala, anterior cingulate, and thalamus in women relative to men. The finding that the anterior cingulate and thalamus show greater functional interaction with the amygdala in women than men is consistent with the idea that a coordinated emotional response involving multiple brain regions underlies the enhanced expressive, subjective, and physiological responses to negative stimuli often observed in women. Women also showed greater connectivity than men between the amygdala and regions of the occipital cortex, fusiform gyrus, posterior parietal cortex, which are involved in processing and attending to visual input cites. For positive stimuli, there were fewer regions in which women showed greater connectivity than men, consistent with the hypothesis that women are especially sensitive to negative stimuli. Women showed enhanced connectivity between the amygdala and left and right superior frontal regions, relative to men.

In contrast, men showed greater connectivity than women between the amygdala and the nucleus accumbens, a region associated with the anticipation of reward and approach-oriented behavior (Knutson, Adams, Fong, & Hommer, 2001; Parkinson, Olmstead, Burns, Robbins, & Everitt, 1999; Salamone, Correa, Mingote, & Weber, 2005). This was observed for both negative and positive stimuli. The preponderance of research links the nucleus accumbens with appetitive responses involving positive stimuli, but has also been observed to be necessary for avoidance responses to aversive stimulation (Salamone, 1994). Men also showed greater connectivity

between the amygdala and regions of lateral temporal cortex, superior frontal cortex, and sensorimotor cortex. Taken together, the functional connectivity findings suggest that the amygdala engages in different neurocognitive processes in women and men, and / or varies in the strength of its involvement in each process.

A key factor in the study of sex differences in emotion is the fact that the same stimuli often elicit different reactions in different individuals (Hamann & Canli, 2004), and different responses in women and men (Bradley et al., 2001; McManis et al., 2001b), along the subjective or physiological dimensions of arousal, or potentially other features of emotion. In the current study, women and men did not differ in their subjective arousal responses to the negative, positive, or neutral stimuli. A lack of sex differences in subjective arousal does not preclude the possibility of sex differences in physiological arousal responses. However, the absence of differences in subjective arousal suggests that women and men engaged different neural and cognitive processes in response to emotional stimuli (Canli et al., 2002). These findings are consistent with those of several studies which balanced subjective and physiological arousal responses in women and men, but still observed sex differences in the activity of the amygdala, hypothalamus, and other emotion-related regions (Hamann et al., 2004; Wrase et al., 2003). Several additional sources of women's enhanced response to negative stimuli have been posited, including a greater propensity to ruminate over negative events (Nolen-Hoeksema, 2001; Thomsen, Mehlsen, Viidik, Sommerlund, & Zachariae, 2005) and greater baseline stress levels (Hammen, 2005), relative to men. Differences in the regulation of negative emotion have also been proposed (Domes et al., 2009; McRae, Ochsner, Mauss, Gabrieli, & Gross, 2008). Fewer explanations have been outlined for men's stronger responses to positive stimuli.

In summary, negative and positive stimuli activated different brain regions in women and men. Women showed stronger amygdala responses to negative stimuli than men, and men showed stronger hypothalamus responses to positive stimuli than women. In addition, the amygdala engaged in different networks in women and men, showing greater connectivity with

regulatory regions such as the prefrontal cortex in women, and with regions mediating appetitive behavior such as the nucleus accumbens in men. These findings highlight the importance of considering gender effects in studies of emotional functioning, and highlight sex differences in brain processes which may inform clinical theory for disorders such as depression and anxiety.

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Chapter 4

Sex influences the role of the amygdala in memory for positive and negative stimuli

4.1 Abstract

The amygdala enhances subsequent episodic memory for emotional stimuli via modulation of hippocampal/parahippocampal activity. Previous studies have reported a sex-related hemispheric asymmetry, such that amygdala activation predicting subsequent memory was left-lateralized in women and right-lateralized in men. However, prior studies examined only negative emotional stimuli. It is not known whether a similar effect extends to positive emotional stimuli. Here we investigated this question, and for the first time examined whether sex differences exist in amygdala-hippocampal interactions previously linked to the emotional enhancement of episodic memory. Women and men viewed emotionally positive, negative, and neutral pictures during event-related fMRI. Subsequent cued recall for positive and negative pictures was enhanced vs. neutral pictures, with similar memory effects in women and men. Women showed greater subsequent-memory-related activation than men for negative vs. neutral stimuli in the left amygdala. In the corresponding analysis for positive stimuli, women showed greater memory-related activation in the right amygdala and at a lower statistical threshold, the left amygdala. Women, relative to men, showed greater functional connectivity related to subsequent memory for negative stimuli between the right amygdala and left hippocampus. In addition, women but not men showed greater functional connectivity related to subsequent memory for positive stimuli between the left and right amygdala and the contralateral hippocampus. Findings suggest that previously observed sex-related hemispheric asymmetries differ according to positive or negative emotional valence of stimuli, and that functional connectivity related to subsequent memory for emotional stimuli differs by sex. Results highlight how emotional memory encoding recruits different brain regions and networks in women and men, differences that may relate to behavioral sex differences in emotional memory.

4.2 Introduction

Memory for emotional stimuli tends to be more accurate, vivid, and long-lasting than memory for neutral stimuli (Cahill & McGaugh, 1998; Hamann, 2001; Talarico, LaBar, & Rubin, 2004). Some evidence suggests that the enhancing effect of emotion on memory is greater in women than men; women recall greater numbers of emotionally evocative autobiographical memories than men (Fujita, Diener, & Sandvik, 1991; Seidlitz & Diener, 1998), report more clarity and emotional intensity when recalling autobiographical memories (Herz & Cupchik, 1992; Hess et al., 2000), and describe past personal experiences in more emotion-laden terms (Bauer, Stennes, & Haight, 2003). These studies reveal mixed findings on whether a sex difference in the effect of emotion on memory is greater for negative stimuli, or is comparable for arousing negative and positive stimuli. The preponderance of evidence suggests the enhancing effect of emotion on memory is driven by emotional arousal/intensity, and does not depend upon valence (whether the stimulus was positive or negative) (Bradley, Greenwald, Petry, & Lang, 1992; Cahill et al., 1996; Hamann, 2001; but see Kensinger, 2004; McGaugh, 2002). However, women have been shown to respond more strongly than men to stimuli or experiences that are negative in valence, whereas fewer sex differences in emotional reactivity have been observed for positive stimuli (Bradley, Codispoti, Sabatinelli, & Lang, 2001; Gard & Kring, 2007; Grossman & Wood, 1993; Thomsen, Mehlsen, Viidik, Sommerlund, & Zachariae, 2005). Greater emotional arousal responses to negative stimuli in women than men might be expected to produce a greater arousal-related enhancement in memory for negative stimuli.

Brain imaging evidence has indicated a parallel sex difference within the amygdala, a brain region implicated in generating and regulating emotional responses (Adolphs & Tranel, 1994; Davis, 1992), as well as modulating the strength of memory traces formed within the hippocampal event memory system (Cahill & McGaugh, 1998; Hamann, 2001). During encoding, or the initial establishment of a memory trace, amygdala activity correlates with subsequent memory for arousing stimuli, but does not correlate with memory for neutral stimuli

(Cahill et al., 1996; Canli, Desmond, Zhao, Glover, & Gabrieli, 1998; Hamann, Ely, Grafton, & Kilts, 1999). Studies of the amygdala's contribution to emotional memory have consistently demonstrated sex differences in hemispheric laterality, finding that subsequent memory for negative stimuli correlated with amygdala activation that was left-lateralized in women, and right-lateralized in men (Cahill et al., 2001; Cahill, Uncapher, Kilpatrick, Alkire, & Turner, 2004; Canli, Desmond, Zhao, & Gabrieli, 2002). However, these studies have focused on the amygdala's contribution to memory for negative stimuli, and have not examined its contribution to memory for positive stimuli.

The primary goal of the current study was to test whether sex differences in the laterality of amygdala activity are observed for the encoding of positive stimuli, as have been observed for the encoding of negative stimuli. Understanding encoding of positive stimuli will help to determine whether sex-specific hemispheric asymmetries in amygdala activity may extend more broadly to characterize the effects of both positive and negative emotion on memory formation in women and men. We used functional magnetic resonance imaging (fMRI) to examine regional brain activation as participants viewed emotionally arousing and neutral picture stimuli (Lang, Bradley, & Cuthbert, 2008). We included both negative and positive emotional stimuli to replicate and extend previous findings showing a sex difference in amygdala laterality for the encoding of negative stimuli. After scanning, participants completed free recall and cued recall tasks, and gave subjective ratings of their emotional reactions to the picture stimuli. We identified brain areas whose activity demonstrated a difference in memory (DM). These were regions that showed greater activity during the encoding of items that were later recalled, relative to items that were later forgotten. To examine the amygdala's contribution to memory for emotionally arousing stimuli, we examined the interaction between emotion and DM activity. We predicted the amygdala would exhibit DM activity for both negative and positive stimuli, but not for neutral stimuli. Based on previous studies that identified sex differences in amygdala laterality for the encoding of negative stimuli (Cahill et al., 2001; Cahill et al., 2004; Canli et al., 2002), we

predicted that the DM for negative stimuli would be greater in the left amygdala for women relative to men, and greater in the right amygdala for men relative to women. A similar pattern of sex differences for positive stimuli would support the idea that sex differences in amygdala laterality are primarily driven by the emotional arousal or intensity of a remembered item, irrespective of its valence (whether it was pleasant or unpleasant).

An additional goal was to examine the network of regions demonstrating functional connectivity during successful emotional encoding in women and men. Amygdala activity has been shown to influence memory in part by modulating activity within the hippocampal memory system during encoding (Cahill & McGaugh, 1998; Dolcos, LaBar, & Cabeza, 2004; McGaugh, 2002). In addition, the amygdala has been shown to participate in networks that may influence memory indirectly (Murty, Ritchey, Adcock, & LaBar, 2010; Robinson, Laird, Glahn, Lovallo, & Fox, 2010; Roy et al., 2009). For example, the amygdala has been shown to modulate activity in ventral visual areas during perception of arousing visual stimuli (Amaral, Behniea, & Kelly, 2003), and this greater perceptual activity may lead to the creation of a more detailed representation in memory. We conducted analyses of whole-brain functional connectivity with the left and right amygdala, to examine sex differences in the networks of regions showing greater encoding-related connectivity for emotional relative to neutral stimuli.

4.3 Methods

Participants

Twenty-eight healthy adults (13 women) were recruited through online advertising and flyers posted on the Emory University campus. Participants were screened in a phone interview to ensure they had no history of severe head injury, drug or alcohol abuse, or psychiatric illness. All were right handed, had normal or corrected-to-normal vision, and had high school education or higher. Data from one male participant were excluded due to technical issues with the scanner. Participants included in behavioral and brain imaging analyses included 13 women [age- *M*(*SEM*)

= 28.2(1.9) years] and 14 men [age- *M*(*SEM*) = 27.7(1.4) years]. Five women were taking oral contraceptives and two women used a hormonal patch or ring at the time of the experiment. Participants were compensated $75 for completing the study. Before beginning the study, participants gave written informed consent, and gave authorization for the use of their health information for research under HIPAA. Study procedures were approved by the Emory University Institutional Review Board.

Procedure

Participants began the experimental session by practicing the tasks that they would perform in the scanner, to gain familiarity with the timing of stimulus presentation and the response period. Participants then completed the modified Brief Index of Sexual Function (BISF; Taylor, Rosen, & Leiblum, 1994) and the NEO-FFI (Costa & McCrae, 1992).

During scanning, participants viewed static photographic scene stimuli from the International Affective Picture Series (IAPS; Lang et al., 2008), and were instructed to attend to the pictures and feel whatever feelings and think whatever thoughts each picture elicited in them. To verify attention to each picture stimulus, we asked participants to make a simple rating of their emotional reactions, making like / neutral / dislike ratings using a button box. Thirty-six positive, 36 negative, and 36 neutral full-color scenes were presented in a semi-random order such that no more than two pictures of the same valence preceded one another. Each picture was displayed full screen at a resolution of 1024 x 768 for 1.5 seconds, followed by a screen prompting the participant to make a rating of the picture, presented for 1.5 seconds. The rating screen included a black background with “like / neutral / dislike” centered in the middle of the screen in white, 48pt Helvetica font. A white fixation cross centered on a black background followed each trial, comprising a jittered inter-trial interval of 1.5 – 2.5 seconds. To minimize primacy and recency effects on participants’ memory for the pictures, black and white buffer images displaying neutral scenes were presented at the beginning and end of the picture viewing task. Memory for these

images was not tested, and participants' BOLD responses to these items were modeled in the error term of the imaging models. This task took about 9 minutes in total.

Immediately following scanning, but before participants exited the scanner, participants were given an unexpected memory test. They were asked to freely recall the pictures in any order, giving brief descriptions out loud. The experimenter allowed a maximum of three minutes for participants to list recalled pictures. Participants then returned to the lab and, after a ten-minute delay, completed a cued recall test of memory for the pictures. Cued recall tasks provide external cues that provide additional support for recollection, relative to un-cued free recall, and have been shown to elicit memory performance levels that are optimal for analyses investigating the neural correlates of successful encoding of emotional scenes (Dolcos et al., 2004). The experimenter cued the participants to recall each picture by giving a simple verbal description of the picture content. Verbal cues ranged from one to three words. Participants indicated whether or not they could recall a picture corresponding with the cue, and described several details of the picture from memory; these details were recorded by the experimenter. Participants then indicated whether they remembered the picture, were familiar with the picture, or it was a new picture. Participants were asked to give a 'remember' response if they saw the picture in the scanner, and could recollect or remember something specific about the picture's presentation that made them confident that it was shown in the scanner. Participants gave a 'familiar' response if the item was familiar but they didn't have a specific recollection of any thought, feeling, or other information about the presentation of the picture. Participants also rated the vividness of their memory of each item, on a scale of 1 (not at all vivid) – 5 (extremely vivid).

Lastly, participants completed an emotion rating task in which they again saw the 108 pictures from the scanning session, and rated their emotional responses to the picture on a 1-5 scale of emotional arousal (1- very little or no arousal, 5 - high arousal). The orders in which items were presented within the encoding, cued recall, and rating tasks were counterbalanced

across participants. Psyscope XB53 software (Cohen, MacWhinney, Flatt, & Provost, 1993) was used for stimulus presentation in the encoding and rating tasks.

Both free and cued recall tasks were included in order to optimize analyses of the neural processes during encoding that lead to successful subsequent memory. Some evidence suggests that participants devote additional processing resources during encoding to items that are later freely recalled, relative to items that are recalled only after cuing (Staresina & Davachi, 2006), because free recall requires a memory trace that is strong or elaborated enough to allow successful memory search in the absence of an external cue. We ordered the tasks under the assumption that a memory trace for a scene that is freely recalled would be of sufficient strength to also allow recall in response to a verbal cue. Additionally, participants did not receive feedback about the accuracy of their responses in the free recall or cued recall tasks, such that memory performance on the cued recall task was minimally contaminated by participation in the earlier free recall task.

FMRI results relating to sex differences in emotional reactions to the scene stimuli will be reported in a separate publication.

Memory task scoring

Free Recall. Free recall performance was scored off-line by two independent raters. Raters attempted to match each of the participant's verbal descriptions with a corresponding scene stimulus. Items were judged to be recalled if the verbal description accurately described the main element(s) of the scene. Disagreements between raters were resolved by a third party. Performance will be summarized using the proportion of items recalled out of the total number of items presented during encoding.

Cued Recall. Cued recall performance was scored off-line by two independent raters who judged whether or not the participant recalled a picture based on the descriptions provided by the participant. A picture was only judged to be correctly recalled if the participant's description included accurate details about the picture's content, and included at least one detail that was not

obvious from the verbal cue provided by the experimenter. Disagreements between raters were resolved by a third party. Performance will be summarized using the proportion of items recalled out of the total number of items presented during encoding.

Analysis of behavioral data

Three (emotion: negative, positive, neutral) x 2 (sex: women, men) mixed-effects ANOVAs were used to assess the effects of emotion condition on subjective arousal levels, performance on the free and cued recall memory tasks, and vividness ratings, and to test whether emotion effects varied by sex. Post-hoc paired comparisons were Bonferroni corrected. Analyses were conducted in SPSS 17 (SPSS, Inc.)

MRI acquisition and analysis

Scanning took place on a 3.0T Siemens Trio with echo-planar imaging (EPI) (Siemens, Malvern, PA). Whole-brain structural T1 images were acquired with a gradient-echo T1-weighted pulse sequence (TR =2.30s, TE=0.03s, 1x1x1mm voxel size). An EPI scout scan was used to verify whole-brain coverage. EPI functional images were gathered using 37 3mm slices collected in an interleaved sequence (TR =2.00s, TE=0.03s, 3x3x3 mm voxel size).
Initial data quality checks were performed using ArtRepair software (Mazaika, Whitfield-Gabrieli, & Reiss, 2007), to identify signal spikes and motion artifacts. Slices containing spike artifacts were identified and replaced using linear interpolation, with no more than 4% of slices repaired per participant (mean=0.02%). Volumes affected by motion artifact were repaired using linear interpolation, with no more than 5% of volumes repaired per participant. Additional image preprocessing steps were implemented using statistical parametric mapping software (SPM8, Wellcome Department of Cognitive Neurology). Volumes were slice-timing corrected to the middle slice in time, and spatially realigned to the first image of the run. A 128Hz high-pass filter removed low-frequency noise (Holmes, Josephs, Buchel, & Friston, 1997). After visually verifying that all participants' T1 images were free of ghosting or smearing artifacts, unified segmentation normalization was used to normalize T1s and coregistered functional images to the

Montreal Neurological Institute (MNI) template. Functional images were visually examined for signal dropout, to verify that no participant had dropout in any substantial portion of the amygdala and / or other medial temporal lobe regions. Images were smoothed with an 8mm Gaussian kernel.

Each participant's BOLD responses to the emotional and neutral pictures were modeled in SPM8. To test the hypothesis that emotional encoding depends on different neural substrates in women and men, we compared encoding-related activation for emotional and neutral scenes in women and men. We isolated brain activity contributing to successful encoding using subsequent memory analyses (Paller, Kutas, & Mayes, 1987; Wagner et al., 1998). For each participant, we constructed contrasts of regions where activation was greater during the initial exposure to scenes that would subsequently be remembered, versus scenes that would subsequently be forgotten. The difference in activation levels for subsequently remembered versus forgotten items is referred to as the difference due to memory (DM), and reflects the brain activity at encoding that is necessary in order for an item to be remembered later. DM activity tends to be larger for emotional relative to neutral items (e.g., Dolcos et al., 2004), and is observed for emotional but not neutral items in emotion-related regions such as the amygdala (Murty et al., 2010). To examine sex differences in DM activity associated with enhanced memory for emotional relative to neutral scenes, contrast images from individual participants entered group-level random effects comparison of emotional versus neutral subsequent memory effects. Independent-samples t-tests were used to compare women's and men's responses for the DM for negative scenes to the DM for neutral scenes, and the DM for positive scenes to the DM for neutral scenes [e.g., (negative recalled – negative not recalled) – (neutral recalled – neutral not recalled)]. Because previous studies have implicated the amygdala and hippocampus in enhanced encoding for emotional stimuli, we conducted ROI analyses for the left amygdala, the right amygdala, and the bilateral hippocampus using anatomical definitions from the SPM Anatomy Toolbox (Eickhoff et al., 2005). Follow-up analyses of whole-brain regional activation for DM activity for negative and

positive scenes were conducted for all voxels within an average gray-matter mask of the whole brain. The gray-matter mask was created by taking the mathematical average of the normalized segmented T1 images from all 27 participants, binarized at a threshold of 0.2.

For both the ROI and whole-brain analyses, statistical significance levels were height-extent-corrected to a threshold of $p < .05$, using Alphasim analysis implemented in the REST toolbox (Song et al., 2011). To establish significance thresholds, Monte Carlo simulation was run using 1000 iterations, and an 8mm gaussian FWHM, consistent with smoothing kernel. For the amygdala and hippocampus ROIs, simulation was run on all of the voxels within each ROI mask, with a single-voxel threshold of $p < .01$. Extent thresholds were k=4 for the left amygdala, k=3 for the right amygdala, and k=11 for the bilateral hippocampus, to reach a corrected threshold of $p < .05$. For whole-brain analyses, simulation was run on all of the voxels within the average gray-matter mask. A single-voxel threshold of $p < .01$ was used, resulting in an extent threshold of $k = 59$ to reach a corrected threshold of $p < .05$. This whole-brain threshold was applied to the analyses of regional activation, and of functional connectivity with the amygdala.

To test the hypothesis that the amygdala participates in different circuits in women and men during emotional encoding, we conducted task-based functional connectivity analyses using the CONN toolbox (http://web.mit.edu/swg/software.htm). The right and left amygdala, defined anatomically using the SPM Anatomy Toolbox (Eickhoff et al., 2005), were used as seed regions. Activity in each the left and right amygdala seeds was summarized using the mean signal across all voxels within the volume. Because our primary interest was in connectivity between the amygdala and hippocampus, we examined the covariance between the timecourse for each amygdala and the individual voxels within the bilateral hippocampal mask. Follow up analyses examined whole-brain connectivity with the amygdala; within the average gray-matter mask of the whole brain, we examined each voxel's covariance with the activation of the left and right amygdala. Individual participants' movement parameters and main effects of task condition were modeled as nuisance covariates. Covariance with amygdala activation during responses to

positive scenes and negative scenes was contrasted with covariance with amygdala activation during responses to neutral scenes. The resulting contrast images for individual participants then entered group-level analyses comparing women and men.

4.4 Results

Emotional responses to scene stimuli

The emotional content of the scene stimuli significantly influenced participants' subjective ratings of the scene stimuli, $F(2,50) = 71.17$, $p < .001$. Negative [$M(SEM)$ = 3.55(0.13)] and positive scenes [2.91(0.11)] were more arousing than neutral scenes [1.70(0.08)], positive: $p < .001$, negative: $p < .001$. Negative scenes were more arousing than positive scenes, $p = .005$. The interaction of emotion by sex was not significant, $F(2,50) = 0.17$, $p = .68$. Because previous studies found that women reported greater subjective arousal than men for negatively-valenced scene stimuli (Cahill et al., 2004; Canli et al., 2002), we conducted a follow-up t-test comparing women's and men's ratings of negative pictures. No significant group difference was observed [$t(25) = 1.10$, $p = .28$; women: $M(SEM)$ = 3.69(0.22), men: 3.40(0.15)].

Memory for scene stimuli

Emotion significantly influenced free recall performance, $F(2,50) = 37.54$, $p < .001$. A greater proportion of negative [$M(SEM)$ = .14(.01)] and positive scenes [.15(.02)] were recalled relative to neutral scenes [.03(.01)], positive: $p < .001$, negative: $p < .001$. No significant difference was observed in free recall of positive versus negative scenes, $p > .99$. The interaction of emotion by sex was not significant, $F(2,50) = 1.26$, $p = .29$. In addition, women and men did not differ in overall free recall performance (combining across emotion conditions), $F(1,25) = 0.29$, $p = .60$. The average proportion recalled for women and men is displayed in Figure 1.

Emotion influenced cued recall performance as well, $F(2,50) = 53.49$, $p < .001$. A greater proportion of negative [$M(SEM)$ = .66(.03)] and positive scenes [.72(.03)] were recalled relative to neutral scenes [.51(.03)], positive: $p < .001$, negative: $p < .001$. Participants also

recalled a greater proportion of positive than negative scenes, $p = .01$. The interaction of emotion by sex was not significant, $F(2,50) = 1.51$, $p = .23$. Women and men did not differ significantly in overall cued recall performance, $F(1,25) = 2.74$, $p = .11$. The average proportion recalled for women and men is displayed in Figure 1.

Similar effects of emotion and sex were observed for free and cued recall. However, the proportion of items recalled in the more challenging free recall task was very low (11%; see previous paragraph), near floor for several individual subjects, which precluded using this task to perform an analysis of subsequent memory of the neuroimaging data. In contrast, performance for cued recall was much higher (63%), in an optimal range for analyses of subsequent memory (Dale & Buckner, 1997).

Participants also rated the subjective vividness of their memories for the scenes, on a scale from 1 (very low vividness) to 5 (very high vividness). Emotion significantly influenced vividness ratings, $F(2,50) = 52.13$, $p < .001$. Negative [$M(SEM) = 3.79(0.11)$] and positive scenes [3.76(0.12)] were recalled with greater vividness than were neutral scenes [3.22(.12)], positive: $p < .001$, negative: $p < .001$. Memories of positive and negative scenes did not differ in vividness, $p = .99$. The interaction of emotion by sex was not significant, $F(2,50) = 0.67$, $p = .52$.

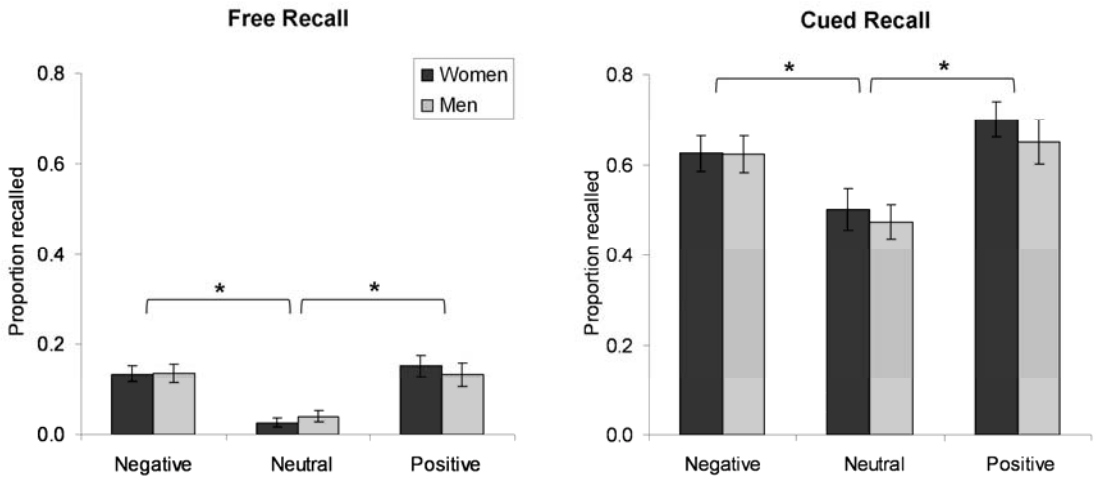

Figure 1. Average levels of performance on the free recall and cued recall tasks, for women and men. The proportion recalled was calculated as the number of items recalled, out of the total number of items presented during the encoding task. Error bars represent 1 standard error of the mean. * $p < .05$.

Sex differences in the amygdala's contribution to subsequent memory for emotional stimuli

The contribution of the amygdala to enhanced memory for emotional relative to neutral stimuli was examined by testing whether DM activity was greater for emotional than neutral scenes, within the left and right amygdala ROIs. For negative scenes, women showed a greater DM effect than men in the left amygdala (k = 5; Z = 3.09; x, y, z = -21, -10, -5), but not the right amygdala (see Figure 1a). Men did not show greater DM effects than women, in either the left or the right amygdala.

For positive scenes, women showed a greater DM effect than men in the right amygdala (k = 6; Z = 2.65; x, y, z = 27, -1, -14), but not the left amygdala (see Figure 1b). At a lower threshold of significance (corrected p < .05 defined by a single-voxel threshold of p < .05 combined with an extent threshold of k = 20 for the left amygdala ROI and k = 16 for the right amygdala ROI), women showed greater DM enhancement than men in both the right and left amygdala ROIs (right: k = 38; Z = 2.65; x, y, z = 27, -1, -14; left: k = 27; Z = 2.39; x, y, z = -21 -

1, -17). Men did not show enhanced DM responses to positive stimuli relative to women, in either the left or the right amygdala.

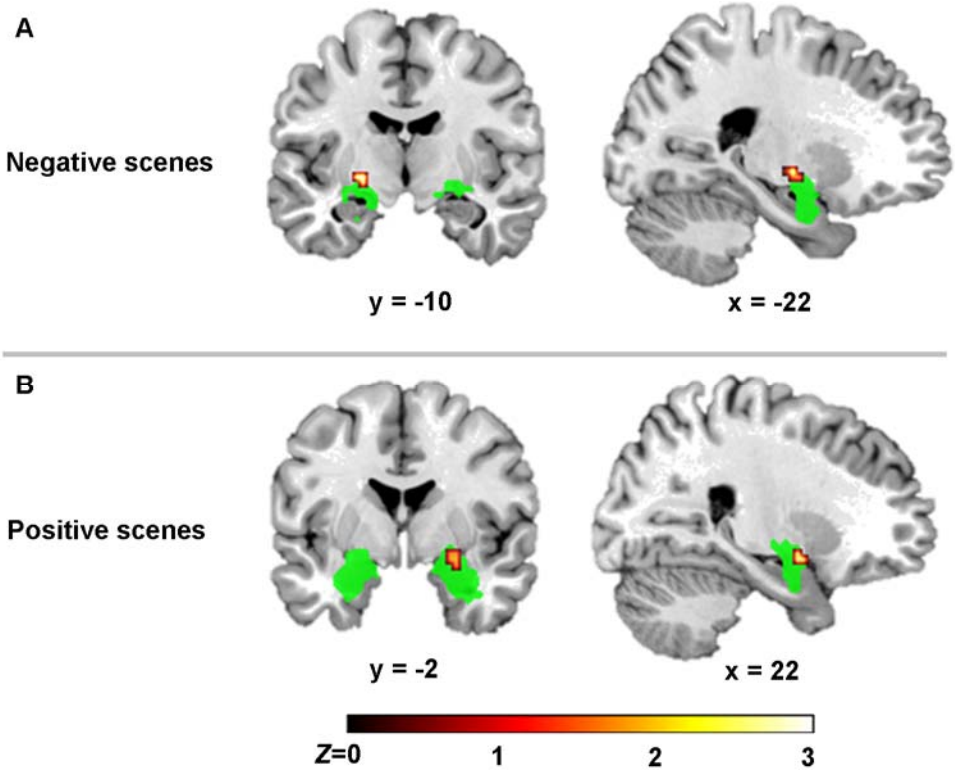

Figure 2. Sex differences in emotional DM activity within the amygdala. 1a: Significantly greater emotional DM in women than men, for negative stimuli. 1b: Significantly greater emotional DM in women than men, for positive stimuli. Left and right amygdala regions of interest displayed in green.

Sex differences in the hippocampal contribution to subsequent memory for emotional stimuli

The contribution of the hippocampus to enhanced memory for negative relative to neutral stimuli was examined by testing whether DM activity was greater for negative than neutral scenes, within a bilateral hippocampus ROI. For negative scenes, women showed a greater DM effect than men in the left hippocampus (k = 26; Z = 3.64; x, y, z = -21, -31, -14). For positive scenes, women showed a greater DM effect than men in a similar cluster in the left hippocampus

(k = 19; Z = 2.78; x, y, z = -21, -28, -11). Men did not show greater DM effects than women in any part of the hippocampus, for either negative or positive scenes.

Sex differences in additional brain regions supporting subsequent memory for emotional stimuli

Additional regions exhibiting increases in DM activation for negative relative to neutral scenes are listed in Table 1. Women showed a greater enhancing effect of negative emotion on DM activation than men in right pregenual anterior cingulate cortex , BA 32, 24, and in right posterior parietal regions including the angular gyrus, supramarginal gyrus, and superior parietal gyrus (see Figure 2). Men did not show greater activation than women in any region. In women, negative emotional scenes were associated with greater DM activity than neutral scenes in the same region of the anterior cingulate that exhibited a sex difference. In men, negative emotional scenes did not produce significant increases in activation in any region.

Additional regions exhibiting increases in DM activation for positive relative to neutral scenes are listed in Table 2. Women showed a greater enhancing effect of positive emotion on DM activation than men in an anterior cingulate cluster which extended into both right and left hemispheres just dorsal to the genu, BA 32, 24; in the right inferior frontal gyrus, BA 45, 47, 48; and the left superior occipital gyrus, BA 17, 18 (see Figure 3). Men did not show greater activation than women in any region. In women, positive emotional scenes were associated with greater DM activity than neutral scenes in the left lingual gyrus, but not in the regions that exhibited sex differences. In men, positive emotional scenes did not produce significant increases in activation in any region.

Table 1
Enhancing effect of negative emotion on encoding-related brain activation (Negative DM > Neutral DM)

		MNI Coordinates				
	HEM	x	y	z	*Z*	k
Women > Men						
Ant. Cingulate G.	R	12	41	4	3.25	61
Ant. Cingulate G.	R	12	50	13	2.73	(LM)
Med. Frontal G.	R	15	47	-5	2.98	(LM)
Angular G.	R	45	-70	46	3.60	93
Sup. Parietal G.	R	30	-73	52	3.06	(LM)
Angular G.	R	42	-55	25	3.30	123
Angular G.	R	48	-40	19	2.91	(LM)
Supramarginal G.	R	54	-46	31	3.11	(LM)
Men > Women						
* No significant clusters						
Women						
Ant. Cingulate G.	R	12	41	13	4.04	111
Ant. Cingulate G.	R	12	44	4	3.43	(LM)
Ant. Cingulate G.	R	6	41	25	2.83	(LM)
Men						
* No significant clusters						

Table 2
Enhancing effect of positive emotion on encoding-related brain activation (Positive DM > Neutral DM)

		MNI Coordinates				
	HEM	x	y	z	Z	k
Women > Men						
Ant. Cingulate G.	R	6	44	19	3.18	65
Ant. Cingulate G.	L	-9	41	16	3.06	(LM)
Inf. Frontal G.	R	42	20	10	3.3	78
Inf. Frontal G.	R	39	26	-14	3.2	(LM)
Inf. Frontal G.	R	30	23	13	2.95	(LM)
Sup. Occipital G.	L	-12	-94	19	3.19	84
Sup. Occipital G.	L	-21	-91	28	2.47	(LM)
Cuneus	L	-6	-79	25	2.37	(LM)
Men > Women						
* No significant clusters						
Women						
Lingual G.	L	-18	-85	-8	3.17	78
Lingual G.	L	-9	-79	-8	3.12	(LM)
Lingual G.	L	-30	-88	-17	2.56	(LM)
Men						
* No significant clusters						

Sex differences in encoding-related functional connectivity between the amygdala and hippocampus

We examined brain regions whose functional connectivity with the amygdala was enhanced during the encoding of scenes that were recalled, relative to scenes that were not recalled, i.e., a DM effect for amygdala connectivity. For negative relative to neutral scenes, women showed greater increases than men in DM-related connectivity between the right amygdala and a posterior region of the left hippocampus (k = 52; Z = 3.09; x = -18, y = -38, z = -6). Men did not show greater DM-related connectivity than women between the amygdala and either the left or right hippocampus. When the female and male groups were examined individually, neither group showed significant increases in DM-related connectivity between the amygdala and hippocampus.

For positive relative to neutral scenes, no significant sex differences were observed in DM-related connectivity between the amygdala and hippocampus. When each group was examined individually, women showed significant connectivity between the left amygdala and an anterior region of the right hippocampus (k = 55; Z = 2.89; x, y, z = 34, -20, -12), and between the right amygdala and an anterior region of the left hippocampus (k = 52; Z = 3.35; x, y, z = -36, -20, -14).

Sex differences in encoding-related functional connectivity between the amygdala and other brain regions

Additional regions which exhibited an increase in DM-related connectivity with the amygdala for negative relative to neutral scenes are listed in Table S1 (left amygdala) and Table S2 (right amygdala). Brain regions that showed stronger DM-related connectivity with the left amygdala in women than men included the right inferior temporal gyrus, right mid-frontal gyrus, right superior frontal gyrus, left posterior thalamus, right caudate and putamen, left insula, left precuneus, sensorimotor areas, and cerebellum (see Table S1). In addition, the left hippocampus showed greater connectivity with the left amygdala in women than men, but this region partially

overlapped with the amygdala seed region. A single cluster showed stronger functional connectivity with the left amygdala in men than women, in the left temporal pole (see Table S1). Brain regions showing stronger functional connectivity with the right amygdala in women than men included the left amygdala and left putamen, the left superior temporal gyrus, the left inferior temporal gyrus, the left anterior cingulate, the left superior frontal gyrus, the right thalamus, sensorimotor regions, and the cerebellum (see Table S2). A single cluster showed stronger functional connectivity with the right amygdala in men than women, in left inferior temporal gyrus and fusiform gyrus (see Table S2).

For positive relative to neutral scenes, regions which exhibited an increase in DM-related connectivity are listed in Table S3 (left amygdala) and Table S4 (right amygdala). Brain regions that showed stronger functional connectivity with the left amygdala in women than men included left temporal regions, middle and anterior cingulate regions, a superior medial frontal region, left posterior thalamus, sensorimotor regions, occipital regions, and the cerebellum (see Table S3). No brain region showed stronger functional connectivity with the left amygdala in men than women. Brain regions that showed stronger functional connectivity with the right amygdala in women than men included the left amygdala, the left hippocampus and superior temporal gyrus, the anterior cingulate, sensorimotor regions, bilateral occipital/ventral visual areas, and the cerebellum (see Table S4). A single cluster showed stronger functional connectivity with the right amygdala in men than women, in the cerebellum (see Table S4).

4.5 Discussion

The goal of the current study was to examine sex differences in brain activity supporting emotional memory encoding. FMRI results supported the hypothesis that women would show greater left amygdala participation than men in encoding negative pictures; no such difference was observed for the right amygdala. In addition, the results provide the first evidence for sex differences in the amygdala's contribution to encoding positive stimuli. Women showed greater

right amygdala (and at a lower threshold, left amygdala) involvement than men in encoding positive pictures. Women, but not men, showed greater functional connectivity related to subsequent memory for positive stimuli between the left and right amygdala and the contralateral hippocampus. Findings suggest that previously observed sex-related hemispheric asymmetries differ according to positive or negative emotional valence of stimuli, and that functional connectivity related to subsequent memory for emotional stimuli differs by sex.

Sex differences in brain activity contributing to emotional encoding

Women showed greater emotional DM activity than men in the amygdala, as well as in several additional brain regions whose functions are related to memory and emotion. Activation in these regions was predictive of whether the emotional items would be subsequently recalled, and is not interpreted as being reflective of emotional arousal responses to the picture stimuli. The findings therefore suggest that these regions were more engaged in women than men in processes contributing to the enhancing effect of emotion on memory.

For negatively-valenced stimuli, the left amygdala showed greater emotional DM activity in women than men. For positively-valenced stimuli, the right and, at a lower threshold, left amygdala showed greater emotional DM activation in women than men. Our findings parallel several previous studies, which similarly observed greater correlations in women than men between left amygdala activation and subsequent memory for negative stimuli (Cahill et al., 2001; Cahill et al., 2004; Canli et al., 2002). Previous studies also identified greater correlations in men than women between right amygdala activation and subsequent memory for negative stimuli (Cahill et al., 2001; Cahill et al., 2004; Canli et al., 2002). In contrast, we did not observe greater emotional DM activity for negative stimuli in the right amygdala for men relative to women. The failure to observe this sex difference may result from smaller emotional memory effects related to the delay between encoding and retrieval. Due to the limited availability of a special participant population (results reported elsewhere), participants in the current study engaged in the cued recall task on the same day as the encoding task, whereas in previous studies

the memory task was delayed by two to three weeks. The enhancing effect of emotion on subsequent memory tends to increase with longer delays (Sharot & Phelps, 2004) as consolidation processes tend to preferentially facilitate memory for emotional relative to neutral stimuli (Hamann, 2001). Work by Canli and colleagues showed that the male-specific right amygdala effect was less reliable than the female-specific left amygdala effect (left amygdala in 72% of women versus right amygdala in 50% of men), and the effect may not have been apparent in our data given the shorter delay.

Sex differences in the contribution of the amygdala to emotional encoding have been observed in several previous studies (Cahill et al., 2001; Cahill et al., 2004; Canli et al., 2002). These findings have been interpreted in the context of two broad ideas about the processes that are influenced by sex: an emotional-arousal based theory positing that women and men tend to differ in the intensity of their emotional responses resulting in corresponding differences in amygdala activation and subsequent memory strength (Fujita et al., 1991), and a theory of cognitive styles positing that women and men differ in the cognitive components engaged during emotional encoding thus engaging the amygdala in different cognitive and processes (Cahill & van Stegeren, 2003).

According to the arousal-based hypothesis, in the absence of sex differences in arousal levels, there would be no difference in amygdala activation during encoding, and thus no sex differences in memory performance. In contrast, the cognitive hypothesis predicts sex differences in the brain activation contributing to emotional encoding, after controlling for sex differences in arousal. Although previous studies have observed sex differences in the effect of emotion on subsequent memory (Fujita et al., 1991; Herz & Cupchik, 1992; Seidlitz & Diener, 1998), we observed no difference in recall performance for women and men. We observed an enhancement of memory performance for emotional relative to neutral stimuli, but women and men did not differ in the size of this enhancing effect of emotion on memory, nor did they differ in subjective arousal responses to the pictures. Sex differences in the brain regions involved in emotional

encoding occurred in the absence of differences in subjective arousal. These findings are consistent with the cognitive hypothesis. By characterizing the brain regions that were co-active with the amygdala and functionally connected with the amygdala during encoding, the current study provides a window on cognitive processes that may differ between women and men.

Women showed greater emotional DM activity than men in several brain regions whose functions are related to memory and emotion. For negatively- and positively-valenced stimuli, women showed greater emotional DM activity than men in the left hippocampus. We also observed that functional connectivity between the amygdala and hippocampus was greater in women than men. Interactions between the amygdala and hippocampus during encoding have been shown to form a major mechanism by which emotion influences memory (Cahill & McGaugh, 1998; Dolcos et al., 2004; Hamann, 2001; Ritchey, Dolcos, & Cabeza, 2008). The current findings illustrate than women differ from men in a central mechanism by which emotion influences memory encoding. The findings agree with previous behavioral studies showing better memory for emotional personal experiences in women than men (Bauer et al., 2003; Seidlitz & Diener, 1998), and suggest that sex differences in autobiographical memory may arise from differences in encoding during the initial experience of an emotional event.

Women also showed greater emotional DM activity than men in the angular and supramarginal gyri of the right posterior parietal cortex for negative stimuli, and in the right inferior frontal gyrus, and left superior occipital gyrus for positive stimuli. Women also showed greater DM activity for both negative and positive stimuli in pregenual anterior cingulate cortex. Men showed no region of greater emotional DM activity relative to women, for either negative or positive stimuli.

Posterior parietal cortex has been hypothesized to participate in memory encoding via its role in attention orienting; Dorsal parietal cortex has been associated with goal-directed attention, and ventral parietal cortex with reflexive attention orienting (Corbetta & Shulman, 2002). Within the context of encoding emotional stimuli, ventral parietal regions are posited to support reflexive

orienting to salient, emotionally-evocative features of a particular stimulus (Murty et al., 2010; Uncapher & Wagner, 2009). We observed greater emotional DM activity in ventral parietal cortex for women than men. Visual attention orienting to salient or evocative features of emotional stimuli has been shown to benefit subsequent memory (Riggs, McQuiggan, Farb, Anderson, & Ryan, 2011; Sharot & Phelps, 2004), and thus forms one mechanism by which emotional responses during encoding can influence later memory. Although women and men did not differ in memory performance in the current study, sex differences in attention orienting may contribute to differences in memory accuracy or vividness for emotional stimuli. Future studies using eye-tracking or visual paired comparison tasks for negative and neutral items would provide further insight into whether sex differences in attention orienting contribute to differences in emotional memory performance.

The anterior cingulate cortex plays a major role in emotion-cognition interactions (Pessoa, 2008). It is involved in emotion evaluation and regulation (Etkin, Egner, & Kalisch, 2010; Goldin, McRae, Ramel, & Gross, 2008; Kim & Hamann, 2007), and participates in emotional processing via interactions with the amygdala (Etkin, Egner, Peraza, Kandel, & Hirsch, 2006). In studies of negative emotion regulation, sex differences have been observed in the region of right anterior cingulate that showed greater emotional DM activity for negative stimuli in women, anterior to the genu in BA 32 and 24 (Domes et al., 2009; McRae, Ochsner, Mauss, Gabrieli, & Gross, 2008). Regulating emotional responses during encoding has been shown to differentially influence memory performance in men and women (Kim & Hamann, in press). A region of the ventrolateral prefrontal cortex, the right inferior frontal gyrus, also showed greater emotional DM activity in women than men for positive stimuli. Functional connectivity between the amygdala and ventrolateral PFC in BA 47 has been shown to increase during emotional encoding (Kilpatrick & Cahill, 2003), and has been interpreted to reflect greater elaboration of subsequently remembered items.

Sex differences in encoding-related functional connectivity with the amygdala

Women also showed greater functional connectivity than men between the left and right amygdala and a distributed network of regions involved in memory, including the ventral parietal cortex, and medial and lateral prefrontal regions. In addition, both positive and negative emotion enhanced encoding-related cross-hemispheric connectivity between the right and left amygdala, and this effect was greater in women than men. In contrast, men showed few regions of greater functional connectivity with the left or right amygdala relative to women. These findings are consistent with previous evidence of baseline differences in amygdala connectivity between women and men; several fMRI studies of the resting state have found that the amygdala participates in more widespread networks in women than men (Kilpatrick, Zald, Pardo, & Cahill, 2006; Savic & Lindstrom, 2008). The current results showed that sex differences in the interaction of the amygdala with a broader network of regions have consequences for behavior, specifically for subsequent memory for emotional items.

Importance of emotional valence

Regardless of whether the stimuli were positive or negative in valence, women showed enhanced emotional DM activity relative to men. In women, emotional regions such as the amygdala and medial prefrontal cortex contributed to subsequent memory for both positive and negative scenes. This is consistent with previous behavioral evidence that women recall more positive and negative life events than men, and their memories are more detailed and vivid (Fujita et al., 1991; Seidlitz & Diener, 1998). These previous findings have been interpreted as reflecting an increased influence of emotion on memory encoding in women than men, irrespective of whether stimuli were positive versus negative.

Conclusions

For women, more than for men, emotional stimuli engaged a memory encoding circuit involving the amygdala, hippocampus, and medial and lateral prefrontal regions. Women engaged this circuit than men for both negative and positive stimuli. These findings suggest that

sex and other individual differences must be taken into account when studying emotional memory.

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Chapter 5

General Discussion

Fewer than 50 years ago, it was generally accepted that the brains of males and females across most mammalian species were similar in structure and function, with only a few differences in regions regulating sexual reproductive behavior, which were mostly investigated at the level of synapses and receptors (Arnold & Gorski, 1984; Cahill, 2012). A change in perspectives has come about as more recent research has firmly established sex differences in systems-level brain structure (e.g., Allen, Damasio, Grabowski, Bruss, & Zhang, 2003; Gilmore et al., 2007; Good et al., 2001). In parallel, research has begun to consistently demonstrate sex differences in cognitive domains such as spatial cognition, child play behaviors, and nonverbal communication (Hines, 2010; McClure, 2000). Findings have less consistently accumulated in the domain of emotion, despite the general cultural sense that women and men differ in their emotional responses, and evidence that brain regions which regulate emotional responses are sensitive to gonadal hormones. The present research adds to the literature on sex differences in emotion by providing converging evidence that women and men differ in their brain responses to emotional stimuli, in the form of a meta-analysis of neuroimaging studies, and two individual neuroimaging studies of emotional processing in women and men.

5.1 Relations between the findings of the meta-analysis and the neuroimaging studies

A primary goal of the fMRI study of differences in women's and men's responses to emotional stimuli (Study 2) was to determine the extent to which the findings of the meta-analysis would be replicated in a laboratory experiment with groups of women and men responding to a single set of stimuli. The meta-analysis found that, relative to men, women had enhanced brain responses to negative stimuli in the left amygdala, anterior cingulate and medial prefrontal cortex, and hypothalamus. Relative to women, men had enhanced brain responses to positive stimuli in the left amygdala, posterior cingulate, and anterior insula / inferior frontal gyrus. Several previous neuroimaging studies have directly investigated sex differences in emotion, but their findings have been mixed. These studies found many commonalities in women's and men's responses to negative stimuli, but often found negligible differences in

regions central to emotional processing such as the amygdala, hypothalamus, or medial prefrontal cortex (Caseras et al., 2007; George, Ketter, Parekh, Herscovitch, & Post, 1996; Hofer et al., 2006; Hofer et al., 2007; Killgore & Yurgelun-Todd, 2001; Royet, Plailly, Delon-Martin, Kareken, & Segebarth, 2003). Studies that used standardized emotionally-arousing visual stimuli from the IAPS tended to find larger sex differences, showing greater amygdala responses to negative scenes in women than men (Domes et al., 2009), and greater amygdala and visual cortex responses to positive scenes in men (Sabatinelli, Flaisch, Bradley, Fitzsimmons, & Lang, 2004; Wrase et al., 2003). Such findings are more consistent with the sex differences identified in the meta-analysis of the broader neuroimaging literature. However, previous studies of positive emotional scenes included erotic scenes along with other scene content, making it difficult to differentiate sexual arousal from emotional arousal responses. To date, very few studies have investigated sex differences in responses to positive stimuli, and none have included positive, non-erotic scene stimuli.

In Study 2, we also used a standardized set of scene stimuli from the IAPS known to elicit moderate levels of emotional arousal for both negative and positive scenes. The findings were broadly consistent with those of the meta-analysis, with some exceptions. We observed that women had greater amygdala responses to negative stimuli than men, in both the left and the right amygdala, consistent with women's enhanced amygdala response to negative stimuli observed in the meta-analysis. Men had greater responses to positive stimuli than women in the hypothalamus, consistent with the neuroimaging literature on male responses to erotic stimuli (Beauregard, Levesque, & Bourgouin, 2001; Hamann, Herman, Nolan, & Wallen, 2004), and broadly consistent with the observation in the meta-analysis of enhanced neural responses to positive stimuli in men. However, we did not observe an enhanced amygdala response to positive stimuli in men as was observed in the meta-analysis. This discrepancy may have been related to a variety of factors, including low power and sample selection issues stemming from the small relative sample size (n=27 for the neuroimaging study, n=1217 for the meta-analysis), and the use

of emotional scene stimuli rather than a mixture of different stimulus types. We conclude that women and men show greater engagement of key emotional brain regions for negative and positive stimuli, respectively. Some effects, such as a greater amygdala response to negative stimuli in women than men, may be observed consistently, whereas other elements of the emotional system may show sex differences in different experimental contexts, depending on the sample of individuals, the nature of the stimuli, and other factors.

We then demonstrated that sex differences in the function of emotional brain regions influences episodic memory encoding. Emotional experiences are better remembered than neutral or non-emotional experiences. Emotional influences on memory for specific events are produced by arousal-related amygdala responses during the initial experience, as well as a modulatory effect of the amygdala on hippocampal encoding. We observed that women show a greater involvement of the amygdala than men in the encoding of both negative and positive stimuli. In addition, the amygdala showed greater encoding-related functional connectivity with the left hippocampus in women than men, as well as with a broader network of regions which have been implicated in the enhancing effects of emotion on memory (Murty, Ritchey, Adcock, & LaBar, 2010). These findings contrasted with findings related to women's and men's initial responses to emotional stimuli. Women showed greater initial responses than men to negative, but not positive stimuli. However, women showed a greater engagement of the amygdala than men in encoding all emotional stimuli, regardless of valence. It must be emphasized that in this case, amygdala activation was not reflective of the size of the response to emotional stimuli, but of the response that predicted whether an emotional item would later be recalled. While men showed greater initial amygdala responses to positive stimuli than women, their amygdala responses were less predictive of later memory.

5.2 Future directions

A major finding of the current study was that the amygdala responds differently to emotional stimuli and participates in different functional networks in women and men. However,

differences in the response of this brain region were not interpreted to index sex differences in emotional arousal, as subjective arousal responses did not differ between women and men. Instead, it is likely that the amygdala engages in different types of processes in women and men. Although the current research provides initial hints about amygdala-linked processes which may differ in women and men, the basic functional implications of sex differences in amygdala responses to emotional stimuli remain to be determined. Future studies might further investigate how the amygdala interacts with different processing paths in women and men by examining the functional connectivity of different amygdala subunits with the rest of the brain. The amygdala can be characterized as a cluster comprised of 12 discrete regions (LeDoux, 2000). The divisions of the amygdala most central to regulating emotion each show functional connectivity with different brain networks, consistent with anatomical connectivity from the non-human animal literature (Roy et al., 2009). Such findings suggest that examining the amygdala in terms of its functional units would provide a more nuanced picture of sex differences in its functional connectivity. For example, Roy and colleagues found that the laterobasal complex of the amygdala showed positive connectivity with the hippocampus and medial prefrontal cortex. It may thus be predicted that this particular subdivision may exert greater modulatory effects on hippocampal activity during encoding in women than men. Similarly, other subdivisions such as the centromedial nuclei may differ in their interactions with output networks through the thalamus, striatum, and brainstem.

In the current research we assumed that the female and male groups differed on average along several dimensions, including their genes, personal experiences, and gonadal hormone levels. In future studies, it would be valuable to measure or hold constant these elements, which each contribute to sexual differentiation, thus facilitating a better characterization of individual and group differences. Hormonal influences, in particular, would be better characterized by assessing menstrual cycle time in the women, and measuring circulating levels of hormones such as estrogen, progesterone, and testosterone.

Questions about sexual differentiation are ultimately developmental questions. It would be valuable to study how sex differences in emotion emerge over the course of early childhood and adolescence, using similar techniques as those employed in the current work. The developmental approach would allow us to follow the timeline of hormonal and external early life events as they unfold, and to isolate developmental change attributable to one source or the other. For example, sexual differentiation emerging in early childhood (pre-school years) would not be attributable to activational hormonal effects as the hypothalamic-pituitary-gonadal system is "off" during this period.

5.3 Implications for mental health

The current findings may have relevance for theories of depression. For example, a major current theory posits that women are disproportionately affected by depression because of how they react to the negative event(s) preceding a depressive episode (Nolen-Hoeksema, 2001). While men distract themselves from thoughts about the negative event, women ruminate and continue to devote attention to memories of the event. We observed greater amygdala involvement in the encoding of emotional events in women, and greater amygdala-hippocampus connectivity predictive of memory for negative events (Study 3). In addition, the meta-analysis provided evidence that women engage the hippocampus more than men during the initial response to an emotional stimulus (Study 1). Such hippocampal activation may reflect increased encoding of negative stimuli, or increased linking between the negative stimuli at hand and memories of previous experiences. Together, these findings support the theory that women use greater memory resources in response to a negative event, and suggest that sex differences in processing such an event begin earlier than previously expected, during the initial response to the negative stimulus.

5.4 Conclusions

Our goal was to characterize the nature of sex differences in emotional function by investigating emotional processes at the neural level, in a meta-analysis of neuroimaging studies,

and in two neuroimaging experiments. The results of all three studies indicated different responses in women and men in brain regions that perform key emotional functions, notably the amygdala, hypothalamus, and anterior cingulate cortex. The current research provided novel evidence that sex differences depend on emotional valence, as both the meta-analysis and the study of responses to emotional stimuli showed that women engage emotional neural systems more strongly than men in response to negative stimuli, whereas men show greater engagement than women in response to positive stimuli. These findings have clear implications for clinical disorders of emotion which disproportionately affect women, such as depression and PTSD, and create predictions for the emotional behavior of women and men in a variety of domains such as motivated behavior (motivation to approach or avoid), mood state, and trait emotionality observable in personality traits such as extroversion / neuroticism. We also showed that sex differences in the function of emotional brain regions not only influence emotional behavior but also influence cognitive processes, finding greater activation in women than men of the brain regions and mechanisms that are responsible for the enhancing effects of emotion on memory for specific events. This research underscores differences between women and men in the field of emotion, and highlights the need for greater consideration of sex and individual differences when studying emotion.

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Appendix A. Supplement to Study 1

Table S1

Peak coordinates for Negative emotion (analysis of balanced dataset)

	Region (>100mm^3)	[a]BA(s)	[b]X	Y	Z	Peak Value	Vol. (mm^3)
	All participants (women and men)						
1	Right Amygdala, Left Thalamus: Ventral Lateral Nucleus, Right Thalamus, Right Precentral Gyrus, Right Inferior Frontal Gyrus, Right Claustrum, Left Caudate Body, Left Caudate Head, Right Superior Temporal Gyrus, Right Middle Frontal Gyrus, Left Mammillary Body, Left Red Nucleus, Left Medial Globus Pallidus	6, 47, 38, 44, 45, 9, 46, 13	27	4	-6	0.052	39016
2	Amygdala, Inferior Frontal Gyrus, Superior Temporal Gyrus, Putamen, Thalamus: Ventral posterior lateral nucleus, Insula	47, 38, 9, 13, 46	-33	8	-10	0.060	35680
3	Right Cingulate Gyrus, Left Cingulate Gyrus, Left Superior Frontal Gyrus, Right Anterior Cingulate	32, 6, 24	1	20	41	0.036	10936
4	Cerebellum: Declive, Fusiform Gyrus, Parahippocampal Cortex, Middle Occipital Gyrus, Culmen, Middle Temporal Gyrus	19, 39, 37	34	-64	-10	0.022	9048
5	Left Medial Frontal Gyrus, Left Anterior Cingulate, Right Anterior Cingulate	10, 32	-1	51	-1	0.022	5360
6	Left Parahippocampal Cortex, Right Cerebellum: Culmen, Left Cerebellum: Culmen	19	-13	-46	-6	0.027	3848
7	Superior Frontal Gyrus	9	-4	60	24	0.031	3280
8	Superior Temporal Gyrus, Middle Temporal Gyrus	39	-48	-60	20	0.014	3056
9	Fusiform Gyrus, Middle Temporal Gyrus, Culmen	37	-43	-49	-13	0.024	2928
10	Cingulate Gyrus	24	-3	-2	33	0.019	1920
11	Fusiform Gyrus	37	46	-44	-19	0.025	1712
12	Posterior Cingulate	23	-2	-36	23	0.018	1048
13	Postcentral Gyrus, Superior Temporal Gyrus	43, 42	-55	-14	15	0.013	976
14	Cuneus, Lingual Gyrus	17, 18	8	-83	9	0.014	960
15	Precentral Gyrus	6	-57	5	15	0.015	928
16	Fusiform Gyrus, Cerebellum: Declive	19	-35	-73	-9	0.013	904
17	Superior Temporal Gyrus	22	55	-18	-2	0.017	816
18	Middle Temporal Gyrus	21	-59	-2	-15	0.017	752
19	Middle Frontal Gyrus, Anterior Cingulate	9, 32	29	28	21	0.012	720
20	Posterior Cingulate	31	-5	-68	22	0.013	688
21	Lingual Gyrus	18	-12	-72	3	0.016	680
22	Cingulate Gyrus	31	5	-22	41	0.016	480
23	Middle Temporal Gyrus	21	-57	-34	-7	0.013	416
24	Posterior Cingulate	30	7	-51	18	0.013	400
25	Thalamus: Pulvinar	*	18	-27	20	0.016	384
26	Sub-Gyral	21	52	-6	-19	0.012	360
27	Anterior Cingulate	24	4	35	-14	0.014	344
28	Superior Temporal Gyrus	39	53	-55	36	0.013	344
29	Insula13	46	-38	21	0.014	336	
30	Supramarginal Gyrus	40	-58	-36	32	0.012	336
31	Middle Occipital Gyrus	19	-33	-81	13	0.012	312
32	Precuneus	7	29	-55	56	0.013	312
33	Posterior Cingulate, Cuneus	30	10	-57	8	0.011	304
34	Middle Frontal Gyrus	9	-27	40	32	0.012	192
35	Superior Temporal Gyrus	22	-48	-23	-8	0.011	184
36	Anterior Cingulate	*	-10	41	-7	0.011	168
37	Postcentral Gyrus, Precentral Gyrus	3, 4	-46	-9	56	0.010	160
38	Insula13	-41	-22	14	0.010	136	
39	Putamen	*	-24	3	16	0.011	136
40	Middle Frontal Gyrus	9	-38	30	30	0.011	136
41	Precentral Gyrus	4	46	-9	58	0.011	112

	Women						
1	Left Amygdala, Right Amygdala, Left Hippocampus Left Thalamus: Ventral lateral nucleus, Left Mammillary Body, Left Caudate Head, Right Caudate Head, Left Putamen, Right Subthalamic Nucleus, Right Superior Temporal Gyrus	34, 38	-5	-8	-14	0.043	27232
2	Middle Frontal Gyrus, Inferior Frontal Gyrus, Insula, Middle Frontal Gyrus	46	-49	25	11	0.015	7080
3	Cerebellum: Declive, Parahippocampal Cortex, Culmen	19, 37	28	-60	-15	0.016	6520
4	Left Anterior Cingulate, Left Medial Frontal Gyrus, Right Medial Frontal Gyrus	32, 10	-1	47	2	0.020	5672
5	Inferior Frontal Gyrus	47, 13	-27	22	-16	0.017	3224
6	Cingulate Gyrus	32	-7	30	31	0.016	3008
7	Parahippocampal Cortex	19	-16	-48	-7	0.016	2984
8	Cingulate Gyrus	32	8	15	39	0.020	2480
9	Superior Frontal Gyrus, Medial Frontal Gyrus	9	-4	59	23	0.021	2472
10	Inferior Temporal Gyrus, Middle Temporal Gyrus	37	50	-69	4	0.017	2136
11	Cingulate Gyrus	24	-4	-2	37	0.011	1792
12	Fusiform Gyrus, Culmen	37	-44	-46	-17	0.016	1736
13	Left Superior Frontal Gyrus, Right Superior Frontal Gyrus	6	1	19	59	0.013	1680
14	Superior Temporal Gyrus	22	55	-18	-2	0.016	1104
15	Superior Temporal Gyrus	38	-37	11	-31	0.013	944
16	Middle Temporal Gyrus	39	-48	-69	16	0.011	840
17	Putamen	*	31	24	-9	0.010	712
18	Precentral Gyrus	6	-57	3	14	0.009	624
19	Superior Temporal Gyrus	39	53	-55	36	0.013	592
20	Inferior Frontal Gyrus	44	61	16	12	0.009	552
21	Putamen	*	-24	3	16	0.011	512
23	Lingual Gyrus	18	9	-78	-1	0.009	464
24	Insula	13	-41	-21	14	0.010	464
25	Insula	13	50	-10	16	0.010	448
26	Posterior Cingulate	30, 29	5	-52	16	0.009	448
27	Middle Frontal Gyrus	46	49	32	17	0.010	448
28	Middle Temporal Gyrus, Angular Gyrus	39	-49	-65	34	0.009	448
29	Lingual Gyrus	18	-13	-76	1	0.009	440
30	Cingulate Gyrus	24	6	-20	41	0.014	416
31	Superior Frontal Gyrus	9	-20	56	28	0.010	400
32	Supramarginal Gyrus	40	-57	-38	36	0.009	400
33	Inferior Frontal Gyrus	46	-44	47	0	0.010	384
34	Medial Frontal Gyrus	6	-7	7	62	0.011	360
36	Extra-Nuclear	13	-39	8	-14	0.008	328
37	Lingual Gyrus	17	-9	-100	-8	0.010	320
38	Culmen	*	47	-45	-23	0.008	288
39	Superior Temporal Gyrus	22	-61	-1	-11	0.009	256
40	Insula	13	45	-39	21	0.009	256
42	Inferior Frontal Gyrus	47	36	21	-21	0.009	192
43	Inferior Frontal Gyrus	47	43	19	-12	0.008	192
44	Superior Frontal Gyrus	10	18	66	12	0.009	168
45	Sub-Gyral	20	-42	-18	-27	0.009	160
46	Cerebellum: Declive	*	-25	-85	-16	0.008	160
47	Anterior Cingulate	24	14	32	-8	0.009	160
48	Thalamus	*	-24	-30	0	0.009	160
49	Inferior Frontal Gyrus	45	-33	30	0	0.009	160
50	Cuneus	18	-6	-73	24	0.008	160
51	Cerebellum: Declive	*	52	-66	-17	0.009	152
52	Superior Temporal Gyrus	22	-46	-24	-10	0.009	152
53	Superior Temporal Gyrus	42	-64	-20	8	0.008	152
54	Superior Temporal Gyrus	22	40	-48	14	0.008	152
55	Middle Temporal Gyrus	39	-39	-70	27	0.008	152
56	Middle Temporal Gyrus	39	42	-68	28	0.008	152
57	Cingulate Gyrus	31	10	-56	30	0.008	152
59	Lingual Gyrus	18	-35	-74	-6	0.008	128

60	Middle Occipital Gyrus	19	42	-84	9	0.008	128
61	Superior Temporal Gyrus	39	-52	-53	24	0.008	128
62	Anterior Cingulate	32	1	36	-14	0.008	120
63	Middle Frontal Gyrus	9	51	21	26	0.008	120
65	Precuneus	7	-11	-64	36	0.008	112
66	Precuneus	7	31	-56	58	0.009	112
67	Precuneus	7	5	-42	60	0.009	112
68	Middle Occipital Gyrus	19	-28	-81	15	0.008	104
69	Precuneus	31	-24	-75	27	0.008	104
70	Precentral Gyrus	6	-51	0	38	0.008	104
	Men						
1	Amygdala, Precentral Gyrus, Superior Temporal Gyrus, Inferior Frontal Gyrus, Claustrum, Middle Temporal Gyrus, Insula	6, 38, 44, 47, 6, 45, 21, 13	37	7	-5	0.035	29768
2	Amygdala, Inferior Frontal Gyrus, Insula, Middle Frontal Gyrus, Superior Temporal Gyrus, Putamen, Hippocampus	45, 13, 46, 38, 47	-35	10	-12	0.023	20576
3	Right Cingulate Gyrus, Left Cingulate Gyrus, Left Superior Frontal Gyrus	32, 6, 24	3	19	39	0.018	5288
4	Middle Temporal Gyrus, Fusiform Gyrus, Cerebellum: Declive	37, 19	-40	-57	-7	0.015	3080
5	Inferior Frontal Gyrus, Precentral Gyrus	9, 6, 44	-47	9	26	0.013	2736
6	Posterior Cingulate	23	-2	-36	23	0.018	2048
7	Fusiform Gyrus	19	40	-71	-13	0.019	1896
8	Fusiform Gyrus	37	46	-43	-18	0.021	1632
9	Middle Temporal Gyrus, Superior Temporal Gyrus	39, 13	-47	-53	25	0.013	1448
10	Posterior Cingulate, Cuneus, Lingual Gyrus	30, 19	13	-56	6	0.010	1440
11	Left Cerebellum: Culmen, Right Cerebellum: Culmen	*	6	-42	-8	0.014	1432
12	Postcentral Gyrus	43	-56	-15	15	0.012	1392
13	Lingual Gyrus, Culmen	19	-17	-47	-5	0.013	1384
14	Cuneus	17	9	-83	13	0.014	1368
15	Thalamus: Ventral posterior lateral nucleus, Putamen	*	-24	-19	3	0.013	1272
16	Anterior Cingulate	32	5	50	-11	0.011	1232
17	Inferior Frontal Gyrus	47	-27	33	-7	0.014	1232
18	Superior Frontal Gyrus	9	-8	64	24	0.018	1144
19	Posterior Cingulate	31	-4	-66	22	0.013	1096
20	Middle Frontal Gyrus	9	34	28	21	0.009	832
21	Caudate Body	*	-6	9	14	0.016	736
22	Thalamus: Pulvinar	*	18	-27	19	0.016	696
23	Anterior Cingulate	24	5	31	20	0.013	672
24	Medial Frontal Gyrus	10	-10	59	-1	0.013	616
25	Cingulate Gyrus	24	-2	-3	29	0.009	616
26	Postcentral Gyrus, Precentral Gyrus	3, 4	-46	-10	56	0.010	616
27	Middle Frontal Gyrus	9	-27	39	32	0.012	608
28	Middle Temporal Gyrus	21	-59	-3	-16	0.011	584
29	Middle Temporal Gyrus	21	-57	-33	-6	0.012	584
30	Medial Frontal Gyrus	9	3	54	24	0.011	568
31	Lingual Gyrus	18	-10	-70	5	0.011	552
32	Middle Frontal Gyrus	9	45	35	28	0.012	504
33	Red Nucleus, Thalamus	*	-6	-25	-6	0.008	344
34	Middle Temporal Gyrus	39	-47	-59	13	0.008	320
35	Postcentral Gyrus	40	60	-24	12	0.007	280
36	Middle Temporal Gyrus	22	-47	-45	8	0.008	264
37	Middle Occipital Gyrus	19	-35	-80	11	0.008	256
38	Thalamus	*	1	-18	2	0.010	232
39	Lingual Gyrus	17	13	-93	2	0.009	224
40	Cuneus	19	14	-78	44	0.010	200
41	Precuneus	7	2	-66	49	0.009	200
42	Superior Frontal Gyrus	6	24	12	64	0.008	192
43	Superior Temporal Gyrus	39	45	-48	30	0.008	184
44	Culmen	*	23	-44	-23	0.008	176

45	Middle Frontal Gyrus	8	-22	30	42	0.009	176
46	Cerebellum	*	9	-86	-16	0.009	160
47	Cerebellum: Declive	*	21	-84	-13	0.008	160
48	Fusiform Gyrus	18	-18	-99	-12	0.008	160
49	Hippocampus		30	-39	3	0.008	160
50	Caudate Tail		28	-42	17	0.008	160
51	Thalamus: Pulvinar	*	-15	-27	18	0.008	160
52	Middle Temporal Gyrus	39	-30	-61	31	0.007	160
53	Inferior Parietal Lobule	40	-58	-33	30	0.008	160
54	Precuneus	7	-24	-54	51	0.008	160
55	Precuneus	7	30	-42	51	0.009	160
56	Precuneus	7	27	-54	54	0.008	160
57	Inferior Frontal Gyrus	47	36	33	-24	0.009	152
58	Inferior Parietal Lobule	40	63	-30	36	0.008	152
59	Precuneus	7	24	-72	54	0.009	152
60	Precuneus	7	0	-48	54	0.009	152
61	Caudate Tail	*	-40	-29	-3	0.009	136
62	Thalamus	*	19	-6	9	0.008	128
63	Superior Parietal Lobule	7	33	-48	66	0.009	128
64	Culmen	*	14	-59	-17	0.008	120
65	Inferior Parietal Lobule	40	50	-33	29	0.007	120
66	Paracentral Lobule	6	-11	-23	52	0.008	120
67	Middle Occipital Gyrus	19	36	-86	17	0.008	112
68	Cerebellum: Tuber	*	-51	-66	-28	0.008	104

Clusters demonstrating significant concordance across studies ($p < .05$, FDR-corrected for multiple comparisons). For each cluster, labels denote regions which contained the peak ALE activation, and regions which contained secondary peaks; clusters may extend across non-labeled regions between peaks and the extent is best characterized in Figure 3a (women), 3b (men), S1a (all participants).

[a]BA = Brodmann's area, if applicable

[b]X, Y, and Z coordinates represent weighted central activation likelihood focus in MNI space.

Table S2

Peak coordinates for Positive emotion (analysis of balanced dataset)

	Region (>100mm^3)	[a]BA(s)	[b]X	Y	Z	Peak Value	Vol. (mm^3)
	All participants (women and men)						
1	Anterior Cingulate, Thalamus: Ventral anterior nucleus, Lateral Globus Pallidus, Caudate Head	32	-5	14	-7	0.020	8392
2	Amygdala, Superior Temporal Gyrus, Inferior Frontal Gyrus	38, 47	-25	-2	-23	0.027	7928
3	Inferior Frontal Gyrus, Insula	45, 13	-35	28	0	0.019	4048
4	Medial Frontal Gyrus	9	-1	57	18	0.017	3368
5	Amygdala, Hippocampus	34	27	-2	-22	0.018	2984
6	Precuneus, Middle Temporal Gyrus, Superior Temporal Gyrus	39, 22	-51	-66	28	0.013	2424
7	Postcentral Gyrus, Inferior Parietal Lobule, Precentral Gyrus, Middle Frontal Gyrus	3, 40, 6	-43	-17	56	0.013	2152
8	Lingual Gyrus	18	21	-86	-5	0.014	2136
9	Inferior Frontal Gyrus, Insula	45, 13	52	28	8	0.020	2112
10	Parahippocampal Cortex	36, 19	-36	-39	-15	0.011	2088
11	Cerebellum: Declive, Fusiform Gyrus, Middle Temporal Gyrus	37	-46	-60	-17	0.011	1968
12	Fusiform Gyrus, Inferior Occipital Gyrus	19, 18	-31	-80	-13	0.011	1840
13	Fusiform Gyrus	19	45	-75	-12	0.016	1528
14	Thalamus, Parahippocampal Cortex, Hippocampus	35	-20	-29	-5	0.010	1296
15	Middle Temporal Gyrus	37	54	-65	11	0.018	1296
16	Precentral Gyrus	6	46	8	30	0.013	1256
17	Parahippocampal Cortex	30	21	-50	7	0.011	1232
18	Inferior Frontal Gyrus, Superior Temporal Gyrus	47, 38	-49	24	-18	0.010	1192
19	Lingual Gyrus, Cuneus	18, 23	-5	-84	9	0.009	944
20	Inferior Frontal Gyrus, Insula	47, 13	31	28	-15	0.009	920
21	Medial Frontal Gyrus	10, 11	-3	57	-18	0.010	896
22	Fusiform Gyrus	20, 37	47	-46	-14	0.010	800
23	Precuneus	7	4	-64	63	0.013	800
24	Superior Temporal Gyrus	22	-54	8	0	0.013	784
25	Inferior Temporal Gyrus	20	-61	-13	-27	0.011	752
26	Superior Frontal Gyrus	6	0	15	53	0.012	752
27	Lateral Globus Pallidus		26	-18	-1	0.012	744
28	Posterior Cingulate	30	-3	-47	24	0.010	744
29	Caudate Body		18	-7	23	0.011	704
30	Middle Frontal Gyrus	6	-37	19	47	0.012	704
31	Inferior Frontal Gyrus	44	57	12	13	0.011	696
32	Cuneus	7, 19	17	-81	38	0.008	640
33	Superior Frontal Gyrus	8	-27	37	40	0.009	608
34	Cingulate Gyrus	31	12	-37	45	0.009	592
35	Middle Occipital Gyrus	19	-50	-78	6	0.010	584
36	Putamen		-23	-9	11	0.009	544
37	Precentral Gyrus	6	-50	4	30	0.008	544
38	Middle Temporal Gyrus	21	64	-32	-8	0.009	520
39	Middle Frontal Gyrus, Inferior Frontal Gyrus	9, 44	-49	17	21	0.009	496
40	Superior Temporal Gyrus	22	66	-32	15	0.009	400
41	Precentral Gyrus	4	45	-10	59	0.014	392
42	Cuneus	18	18	-96	19	0.009	360
43	Precentral Gyrus	6	45	-3	48	0.008	304
44	Precuneus	31	-11	-53	34	0.008	296
45	Cingulate Gyrus	24	-17	4	49	0.008	288
46	Precuneus	7	-24	-44	53	0.009	256
47	Lingual Gyrus	18	-12	-78	0	0.009	248
48	Precuneus	7	19	-40	62	0.009	248
49	Putamen	*	27	19	-7	0.007	240
50	Cingulate Gyrus	32	10	22	33	0.008	240
51	Culmen	*	27	-47	-23	0.008	232

52	Lingual Gyrus	18	18	-72	0	0.009	232
53	Precuneus	31	-16	-42	36	0.008	232
54	Perirhinal Cortex	35	30	-27	-18	0.008	224
55	Middle Frontal Gyrus	8	-45	30	38	0.008	224
56	Medial Frontal Gyrus	10	11	44	-14	0.006	216
57	Superior Temporal Gyrus	41	42	-30	8	0.008	216
58	Postcentral Gyrus	3	30	-30	56	0.009	216
59	Superior Frontal Gyrus	6	-6	16	66	0.008	216
60	Cerebellar Tonsil	*	28	-62	-42	0.008	208
61	Cerebellar Tonsil	*	23	-70	-36	0.008	208
62	Thalamus: Ventral Anterior Nucleus	*	18	-8	7	0.008	200
63	Posterior Cingulate	29	6	-53	14	0.008	192
64	Precuneus	7	8	-64	51	0.007	192
65	Claustrum	*	42	4	0	0.008	184
66	Precentral Gyrus	4	-50	-8	40	0.008	176
67	Middle Frontal Gyrus	6	44	18	48	0.008	176
68	Precuneus	19	-33	-73	44	0.008	168
69	Claustrum	*	-30	10	-10	0.007	160
70	Precentral Gyrus	13	-53	-10	8	0.007	160
71	Putamen	*	28	7	12	0.007	160
72	Middle Temporal Gyrus	22	46	-57	20	0.007	160
73	Precuneus	7	17	-49	46	0.007	160
74	Middle Temporal Gyrus	21	62	2	-19	0.007	152
75	Anterior Cingulate	25	6	9	-14	0.007	152
76	Cerebellar Lingual	*	-6	-50	-18	0.007	144
77	Precentral Gyrus	4	33	-14	46	0.007	144
78	Cerebellum: Declive	*	-1	-68	-17	0.007	136
79	Middle Temporal Gyrus	22	54	-40	7	0.007	136
80	Superior Temporal Gyrus	38	44	18	-39	0.007	128
81	Superior Temporal Gyrus	22	-42	-52	19	0.007	128
82	Caudate Body	*	14	2	8	0.007	120
83	Middle Occipital Gyrus	19	-32	-90	23	0.008	120
84	Superior Temporal Gyrus	22	65	-43	8	0.006	112
85	Inferior Parietal Lobule	40	-58	-49	40	0.007	104
	Women						
1	Thalamus: Ventral Anterior Nucleus, Caudate Head	*	-6	-5	-2	0.018	4032
2	Lingual Gyrus	18	21	-85	-5	0.014	3176
3	Medial Frontal Gyrus	9	-2	57	19	0.013	2640
4	Fusiform Gyrus, Inferior Occipital Gyrus	19, 18	-32	-80	-13	0.011	2624
5	Amygdala	*	-26	-8	-20	0.016	2360
6	Anterior Cingulate	32	-5	37	-14	0.013	1992
7	Superior Temporal Gyrus, Middle Occipital Gyrus, Middle Temporal Gyrus	39, 19, 22	-55	-63	21	0.010	1792
8	Parahippocampal Cortex	30	21	-50	6	0.011	1624
9	Inferior Parietal Lobule, Postcentral Gyrus	40, 3	-45	-22	53	0.010	1536
10	Middle Temporal Gyrus	37	53	-65	11	0.018	1512
11	Lingual Gyrus	18	-6	-84	5	0.009	1424
12	Thalamus, Parahippocampal Cortex, Hippocampus	35	-20	-30	-8	0.009	1392
13	Precentral Gyrus	6	47	6	32	0.012	1048
14	Superior Frontal Gyrus	6	0	15	53	0.012	1032
15	Amygdala	*	22	-5	-24	0.012	1024
16	Insula, Claustrum	13	-31	24	0	0.009	960
17	Cerebellum: Declive	*	-41	-60	-19	0.009	936
18	Cuneus	7, 19	17	-81	38	0.008	928
19	Precuneus	7	4	-64	63	0.013	928
20	Middle Frontal Gyrus, Inferior Frontal Gyrus	9, 44	-49	17	21	0.009	824
21	Cerebellar Tonsil	*	26	-66	-39	0.008	776
22	Medial Frontal Gyrus	10, 11	-3	54	-20	0.008	712
23	Medial Frontal Gyrus	10	10	44	-14	0.006	552
24	Superior Temporal Gyrus	22	66	-33	16	0.009	552
25	Middle Temporal Gyrus, Angular Gyrus	39	-44	-76	31	0.008	464

26	Superior Temporal Gyrus	22	-54	6	0	0.009	456
27	Precentral Gyrus	4	44	-10	59	0.014	432
28	Precuneus	7	-24	-44	53	0.009	408
29	Perirhinal Cortex	36	-39	-31	-18	0.008	384
30	Perirhinal Cortex	35	30	-27	-18	0.008	352
31	Middle Frontal Gyrus	46	54	33	12	0.008	352
32	Culmen	*	27	-47	-23	0.008	328
33	Cingulate Gyrus	31	6	-37	44	0.008	328
34	Cingulate Gyrus	32	10	22	33	0.008	320
35	Precuneus	31	-15	-42	36	0.008	320
36	Superior Temporal Gyrus	38	-55	17	-15	0.008	304
37	Posterior Cingulate	29	6	-53	14	0.008	296
38	Precuneus	19	-33	-73	44	0.008	288
39	Superior Temporal Gyrus	41	42	-30	8	0.008	280
40	Inferior Temporal Gyrus	20	-64	-14	-26	0.008	264
41	Middle Temporal Gyrus	21	66	-30	-4	0.008	264
42	Insula	13	30	30	-6	0.009	264
43	Inferior Frontal Gyrus	45	50	22	0	0.008	264
44	Inferior Frontal Gyrus	44	58	12	10	0.008	264
45	Precentral Gyrus	6	-52	4	34	0.008	264
46	Superior Frontal Gyrus	6	-8	16	66	0.008	264
47	Superior Temporal Gyrus	38	-34	8	-27	0.007	256
48	Superior Temporal Gyrus	22	-42	-52	19	0.007	256
49	Middle Temporal Gyrus	22	53	-40	8	0.007	248
50	Superior Temporal Gyrus	38	44	18	-38	0.007	232
51	Anterior Cingulate	24	-1	42	0	0.006	224
52	Middle Frontal Gyrus	6	44	18	48	0.008	200
53	Caudate Body	*	14	3	8	0.006	192
54	Cuneus	18	17	-98	15	0.008	176
55	Precentral Gyrus	6	-40	-2	63	0.008	176
	Middle Frontal Gyrus	6				0.007	
56	Superior Frontal Gyrus	6	7	30	61	0.008	136
57	Inferior Parietal Lobule	40	-36	-50	64	0.006	136
58	Cerebellum: Declive	*	49	-70	-17	0.007	128
59	Superior Parietal Lobule	7	36	-56	62	0.006	128
60	Lingual Gyrus	18	-16	-87	-10	0.005	120
	Men						
1	Amygdala, Inferior Frontal Gyrus, Lateral Globus Pallidus	47	-23	1	-23	0.015	8048
2	Inferior Frontal Gyrus, Insula, Claustrum	13, 45, 47	-36	29	0	0.014	4160
3	Entorhinal cortex, Amygdala	34	30	1	-22	0.013	2496
4	Perirhinal cortex, Fusiform Gyrus	36, 19, 37	-36	-41	-12	0.009	2152
5	Fusiform Gyrus	19	44	-76	-12	0.016	1616
6	Inferior Frontal Gyrus	47	-47	26	-18	0.010	1568
7	Posterior Cingulate, Precuneus	30, 31	-5	-48	27	0.010	1560
8	Fusiform Gyrus	20, 37	48	-47	-14	0.010	1504
9	Inferior Frontal Gyrus	46	54	29	10	0.014	1104
10	Middle Frontal Gyrus	6	-37	19	47	0.012	1072
11	Lateral Globus Pallidus	*	26	-18	-1	0.012	1040
12	Caudate Body	*	18	-7	23	0.011	1016
13	Superior Frontal Gyrus	8	-27	37	40	0.009	968
14	Inferior Frontal Gyrus	47	32	28	-19	0.009	944
15	Putamen	*	-23	-9	11	0.009	944
16	Anterior Cingulate	32	-2	35	-12	0.009	904
17	Middle Temporal Gyrus, Fusiform Gyrus	37	-56	-56	-12	0.009	896
18	Superior Frontal Gyrus, Medial Frontal Gyrus	9	1	59	17	0.007	840
19	Insula, Claustrum	*	43	10	-1	0.008	672
20	Postcentral Gyrus	3	30	-30	56	0.009	456
21	Middle Frontal Gyrus	8	-45	30	38	0.008	440
22	Cingulate Gyrus	31	17	-37	46	0.009	440
23	Inferior Temporal Gyrus	20	-58	-12	-27	0.009	424
24	Precuneus	7	19	-39	62	0.009	424

25	Precentral Gyrus	4	-41	-14	60	0.008	408
26	Precentral Gyrus	6	-46	4	27	0.008	392
27	Precentral Gyrus	6	45	-3	48	0.008	384
28	Middle Frontal Gyrus	6	-19	4	49	0.008	384
29	Inferior Frontal Gyrus	9	45	13	25	0.008	376
30	Putamen	*	27	19	-7	0.007	368
31	Thalamus: Ventral Anterior Nucleus	*	19	-8	7	0.007	368
32	Claustrum	*	-29	9	-9	0.007	360
33	Precentral Gyrus	4	-50	-7	40	0.008	360
34	Anterior Cingulate	25	5	9	-14	0.007	352
35	Caudate Head	*	-4	19	-5	0.007	352
36	Anterior Cingulate	32	-6	49	0	0.008	352
37	Thalamus: Pulvinar	*	-20	-27	3	0.007	344
38	Precentral Gyrus	4	33	-14	45	0.007	344
39	Cerebellum: Declive	*	-1	-68	-17	0.007	336
40	Precentral Gyrus	13	-53	-9	8	0.007	336
41	Cuneus	23	-11	-75	13	0.007	336
42	Middle Temporal Gyrus	22	46	-57	21	0.007	336
43	Precuneus	7	17	-49	46	0.007	336
44	Precuneus	7	9	-64	51	0.007	336
45	Cerebellar Lingual	*	-7	-50	-17	0.007	328
46	Middle Temporal Gyrus	21	63	1	-19	0.007	320
47	Putamen	*	28	7	12	0.007	312
48	Precuneus	39	-45	-69	41	0.009	296
49	Precuneus	31	23	-56	23	0.006	288
50	Superior Frontal Gyrus	6	-13	33	55	0.006	288
51	Culmen	*	35	-31	-33	0.006	280
52	Superior Temporal Gyrus	22	-52	10	0	0.008	280
53	Inferior Occipital Gyrus	18	-47	-80	3	0.008	280
54	Inferior Frontal Gyrus	44	56	12	16	0.008	280
55	Middle Temporal Gyrus	20	61	-35	-11	0.006	272
56	Superior Temporal Gyrus	22	65	-43	7	0.006	256
57	Supramarginal Gyrus	40	38	-44	30	0.007	256
58	Mammillary Body	*	3	-12	-12	0.006	248
59	Middle Frontal Gyrus	10	-36	58	-1	0.006	248
60	Thalamus	*	1	-16	15	0.006	248
61	Middle Frontal Gyrus	6	28	10	39	0.006	248
62	Middle Frontal Gyrus	6	-24	24	56	0.007	248
63	Superior Temporal Gyrus	38	27	7	-35	0.006	240
64	Superior Frontal Gyrus	9	-16	48	31	0.007	240
65	Cerebellar Tonsil	*	-2	-60	-44	0.006	224
66	Middle Occipital Gyrus	19	-33	-89	22	0.008	224
67	Precentral Gyrus	4	-40	-11	46	0.006	216
68	Uncus	20	-40	-14	-36	0.006	208
69	Medial Frontal Gyrus	10	-2	62	-18	0.006	208
70	Superior Temporal Gyrus	38	-51	16	-32	0.006	200
71	Cerebellum: Tuber	*	-42	-63	-24	0.006	192
72	Cingulate Gyrus	32	6	28	24	0.006	184
73	Cingulate Gyrus	32	-12	32	24	0.006	184
74	Middle Temporal Gyrus	39	-52	-70	26	0.007	168
75	Supramarginal Gyrus, Inferior Parietal Lobule	40	-58	-48	40	0.007	144
76	Middle Occipital Gyrus	19	-43	-84	16	0.006	128
77	Cuneus	18	21	-93	22	0.006	112

Clusters demonstrating significant concordance across studies ($p < .05$, FDR-corrected for multiple comparisons). For each cluster, labels denote regions which contained the peak ALE activation, and regions which contained secondary peaks; clusters may extend across non-labeled regions between peaks and the extent is best characterized in Figure 4a (women), 4b (men), S1b (all participants).

[a]BA = Brodmann's area, if applicable

[b]X, Y, and Z coordinates represent weighted central activation likelihood focus in MNI space.

Table S3

Peak coordinates for All-emotion (analysis of balanced dataset)

	Region (>100mm^3)	[a]BA(s)	[b]X	Y	Z	Peak Value	Vol. (mm^3)
	All participants (women and men)						
1	Left Amygdala, Right Amygdala, Left Inferior Frontal Gyrus, Left Thalamus: Ventral posterior lateral nucleus, ventral lateral nucleus, Right Thalamus: Ventral anterior nucleus, Left Middle Frontal Gyrus, Right Mammillary Body, Left Mammillary Body, Right Superior Temporal Gyrus, Left Caudate Body, Left Caudate Head, Left Insula, Left Putamen, Left Precentral Gyrus, Left Red Nucleus, Right Claustrum	47, 45, 46, 9, 38, 13, 4, 6, 22	-15	2	-11	0.085	71632
2	Inferior Frontal Gyrus, Precentral Gyrus, Claustrum, Middle Frontal Gyrus	45, 6, 47, 44, 46, 9	46	20	5	0.035	19752
3	Fusiform Gyrus, Middle Temporal Gyrus, Middle Occipital Gyrus, Culmen, Cerebellum: Declive	19, 37, 30	39	-63	-7	0.028	10104
4	Anterior Cingulate, Medial Frontal Gyrus	32, 10	1	48	-7	0.025	5360
5	Superior Frontal Gyrus	9	-2	60	22	0.039	3080
6	Superior Temporal Gyrus	22	-49	-57	20	0.023	2936
7	Parahippocampal Cortex, Middle Temporal Gyrus	19, 37	-40	-50	-12	0.017	2360
8	Fusiform Gyrus	37	46	-43	-18	0.034	2192
9	Cingulate Gyrus, Superior Frontal Gyrus	32, 6	-2	20	48	0.024	2104
10	Middle Temporal Gyrus, Angular Gyrus	39	-48	-69	27	0.018	1688
11	Cingulate Gyrus	32	10	21	38	0.038	1112
12	Cerebellum: Declive	*	-36	-72	-12	0.019	1048
13	Fusiform Gyrus, Lingual Gyrus	19, 18	25	-83	-12	0.024	1040
14	Anterior Cingulate	32	-6	32	28	0.020	1016
15	Lingual Gyrus	18	-12	-75	3	0.018	936
16	Fusiform Gyrus, Cerebellum: Declive	19	-28	-81	-12	0.019	832
17	Fusiform Gyrus	37	-42	-52	-14	0.024	632
18	Middle Temporal Gyrus	39	-55	-63	21	0.018	616
19	Medial Frontal Gyrus, Anterior Cingulate	10	-8	50	-4	0.024	528
20	Superior Frontal Gyrus	6	-1	16	49	0.032	496
21	Lingual Gyrus	18	16	-74	0	0.016	472
22	Cingulate Gyrus	24	-2	0	31	0.019	472
23	Posterior Cingulate	23	-1	-36	23	0.021	416
24	Superior Frontal Gyrus	6	-6	20	59	0.015	416
25	Superior Temporal Gyrus	22	66	-43	8	0.020	368
26	Postcentral Gyrus	43	-53	-11	14	0.014	320
27	Precentral Gyrus	4	-41	-13	60	0.017	312
28	Anterior Cingulate	32	1	42	5	0.022	304
29	Cuneus	17	8	-84	13	0.014	296
30	Superior Temporal Gyrus	22	56	-17	-3	0.017	256
31	Superior Temporal Gyrus	41	53	-40	7	0.015	256
32	Anterior Cingulate	24	6	31	21	0.017	256
33	Posterior Cingulate	29	4	-51	14	0.022	248
34	Caudate Body	*	20	-6	23	0.016	232
35	Posterior Cingulate	31	-5	-68	22	0.013	224
36	Parahippocampal Cortex	19	-18	-44	-6	0.027	216
37	Middle Frontal Gyrus	9	-27	39	33	0.015	216
38	Middle Temporal Gyrus	21	-59	-1	-16	0.017	192
39	Middle Temporal Gyrus	21	62	-34	-10	0.014	192
40	Cingulate Gyrus	31	5	-21	41	0.016	192
41	Middle Temporal Gyrus	21	62	2	-19	0.015	176
42	Culmen	*	6	-40	-9	0.014	176
43	Fusiform Gyrus	20	-42	-18	-27	0.013	136
44	Posterior Cingulate	30	23	-57	19	0.013	136
45	Middle Temporal Gyrus	21	-57	-34	-6	0.013	128
46	Thalamus: Pulvinar	*	19	-27	19	0.016	128

47	Precentral Gyrus	4	47	-9	57	0.025	128
48	Lingual Gyrus	18	11	-79	1	0.012	120
49	Superior Temporal Gyrus	39	53	-55	36	0.014	120
50	Precuneus	7	29	-55	57	0.013	120
51	Precuneus	7	3	-64	63	0.013	120
52	Supramarginal Gyrus	40	45	-45	32	0.015	112
	Women						
1	Left Amygdala, Right Amygdala, Right Hippocampus, Left Hippocampus, Left Thalamus: Ventral lateral nucleus, Left Superior Temporal Gyrus, Right Superior Temporal Gyrus, Left Mammillary Body, Right Mammillary Body, Left Caudate Head, Left Medial Geniculate Body, Left Putamen	28, 38, 35, 13	-6	-8	-14	0.054	36640
2	Left Superior Frontal Gyrus, Left Anterior Cingulate, Right Anterior Cingulate, Left Medial Frontal Gyrus, Right Medial Frontal Gyrus	9, 32, 10	-1	50	6	0.032	15040
3	Middle Frontal Gyrus, Inferior Frontal Gyrus, Insula	9, 47, 45, 46, 13, 9	-42	23	5	0.019	11240
4	Fusiform Gyrus, Lingual Gyrus, Culmen, Cerebellum: Declive	19, 18, 37	26	-66	-13	0.020	8440
5	Left Superior Frontal Gyrus, Right Superior Frontal Gyrus, Right Cingulate Gyrus, Right Medial Frontal Gyrus	6, 32	2	17	51	0.023	7152
6	Fusiform Gyrus, Cerebellum: Declive, Lingual Gyrus	37, 19, 18	-37	-68	-14	0.016	5152
7	Superior Temporal Gyrus, Middle Temporal Gyrus, Middle Occipital Gyrus, Angular Gyrus	22, 39, 19	-52	-62	21	0.015	4072
8	Middle Temporal Gyrus, Inferior Temporal Gyrus	37	51	-67	7	0.022	3064
9	Cingulate Gyrus	32	-7	30	31	0.016	2336
10	Inferior Frontal Gyrus	47	50	20	-8	0.014	2096
11	Parahippocampal Cortex	19	-16	-47	-6	0.016	1896
12	Lingual Gyrus	18	-11	-80	2	0.017	1256
13	Cingulate Gyrus	24	-4	-2	36	0.011	1232
14	Insula	13	31	27	-8	0.013	1056
15	Posterior Cingulate	30	5	-52	15	0.015	880
16	Superior Temporal Gyrus	22	55	-18	-2	0.016	864
17	Superior Temporal Gyrus	41	52	-39	6	0.015	824
18	Inferior Frontal Gyrus	44	60	15	11	0.013	824
19	Middle Frontal Gyrus	46	52	32	15	0.014	752
20	Parahippocampal Cortex	30	21	-51	7	0.012	712
21	Precentral Gyrus	6	48	5	33	0.012	536
22	Precentral Gyrus	6	-53	1	36	0.012	536
23	Inferior Parietal Lobule, Postcentral Gyrus	40, 3	-44	-21	53	0.010	480
24	Cingulate Gyrus	24	5	-19	41	0.014	464
25	Precentral Gyrus	4	44	-10	59	0.022	456
26	Precuneus	7	4	-64	63	0.013	456
27	Superior Temporal Gyrus	39	53	-55	36	0.013	424
28	Fusiform Gyrus	20	-42	-17	-27	0.012	392
29	Precentral Gyrus	6	-56	3	13	0.009	368
30	Middle Temporal Gyrus	39	-42	-75	27	0.010	368
31	Cerebellum: Declive	*	50	-68	-17	0.014	336
32	Putamen	*	-25	3	16	0.011	320
33	Cuneus	19	12	-85	39	0.012	288
34	Insula	13	50	-12	15	0.010	280
35	Superior Temporal Gyrus	38	-56	17	-14	0.012	224
36	Insula	13	-42	-20	14	0.010	216
37	Superior Frontal Gyrus	9	-20	56	29	0.010	208
38	Supramarginal Gyrus	40	-56	-39	36	0.009	192
39	Inferior Frontal Gyrus	46	-43	46	0	0.010	184
40	Precuneus	7	32	-56	59	0.010	184
41	Superior Temporal Gyrus	22	-56	6	0	0.010	168
42	Lingual Gyrus	17	-9	-100	-8	0.010	152
43	Superior Temporal Gyrus	22	-61	-1	-11	0.009	144

44	Culmen	*	47	-45	-23	0.008	128
45	Inferior Frontal Gyrus	47	36	21	-21	0.009	104
	Men						
1	Amygdala, Inferior Frontal Gyrus, Insula, Claustrum, Postcentral Gyrus	13, 47, 45, 43	-34	11	-13	0.036	32776
2	Amygdala, Inferior Frontal Gyrus, Precentral Gyrus, Superior Temporal Gyrus, Claustrum, Thalamus: Ventral anterior nucleus, Precentral Gyrus, Lateral Globus Pallidus, Insula	45, 6, 38, 47	37	9	-4	0.038	32704
3	Posterior Cingulate, Cuneus	23, 30, 29	0	-43	20	0.021	4368
4	Middle Temporal Gyrus, Fusiform Gyrus	19, 37	-41	-51	-8	0.017	4000
5	Cingulate Gyrus, Superior Frontal Gyrus	32, 6	4	19	40	0.018	3624
6	Fusiform Gyrus	19	43	-72	-12	0.027	3056
7	Inferior Frontal Gyrus	9	-44	8	27	0.022	2752
8	Fusiform Gyrus	20, 37	45	-43	-17	0.031	2584
9	Thalamus: Ventral posterior lateral nucleus, Putamen	*	-24	-17	6	0.015	2512
10	Superior Frontal Gyrus, Medial Frontal Gyrus	9	-3	60	22	0.019	2128
11	Posterior Cingulate, Lingual Gyrus	31, 18	-7	-69	15	0.013	1624
12	Middle Frontal Gyrus, Superior Frontal Gyrus	9, 8	-26	37	36	0.015	1576
13	Middle Temporal Gyrus, Superior Temporal Gyrus	39, 13	-49	-56	23	0.013	1416
14	Cuneus, Lingual Gyrus	17, 18	10	-82	12	0.014	1368
15	Medial Frontal Gyrus	10	-8	57	0	0.014	1088
16	Anterior Cingulate, Cingulate Gyrus	24, 32	4	30	22	0.017	1088
17	Supramarginal Gyrus, Superior Temporal Gyrus	40, 22	43	-47	31	0.015	1024
18	Lingual Gyrus, Culmen	19	-17	-47	-5	0.013	992
19	Culmen	*	5	-42	-8	0.014	976
20	Caudate Body	*	-7	9	15	0.018	872
21	Precentral Gyrus, Postcentral Gyrus	4, 3	-43	-11	58	0.015	864
22	Caudate Body	*	19	-6	22	0.016	832
23	Anterior Cingulate	32	5	49	-11	0.011	816
24	Middle Temporal Gyrus	21	60	0	-20	0.015	752
25	Superior Temporal Gyrus	22	65	-43	7	0.018	712
26	Thalamus: Pulvinar	*	18	-27	20	0.016	528
27	Middle Temporal Gyrus	20	61	-35	-11	0.013	432
28	Anterior Cingulate	32, 24	1	35	-13	0.009	424
29	Precuneus	7	5	-65	49	0.012	424
30	Middle Frontal Gyrus	9	34	28	21	0.009	408
31	Middle Temporal Gyrus	21	-57	-33	-6	0.012	384
32	Middle Frontal Gyrus	9	45	35	28	0.012	384
33	Middle Frontal Gyrus	6	-37	19	47	0.012	360
34	Middle Temporal Gyrus	21	-59	-3	-16	0.011	344
35	Precuneus	31	-11	-50	34	0.010	336
36	Posterior Cingulate	30	25	-56	21	0.009	328
37	Superior Temporal Gyrus, Insula	22, 13	50	-6	-3	0.009	312
38	Angular Gyrus, Middle Temporal Gyrus	39	-47	-71	35	0.010	296
39	Caudate Head		-4	20	-3	0.010	240
40	Middle Occipital Gyrus	19	-38	-81	12	0.009	208
41	Cingulate Gyrus	24	-3	-4	29	0.009	192
42	Superior Frontal Gyrus	10	-5	63	-16	0.009	184
43	Lingual Gyrus, Parahippocampal Cortex	19, 30	20	-54	1	0.008	152
44	Middle Frontal Gyrus	8	-44	30	37	0.010	152
45	Thalamus	*	1	-18	2	0.010	136
46	Precentral Gyrus, Inferior Frontal Gyrus	6, 44	-57	8	15	0.008	128
47	Lingual Gyrus	17	13	-93	2	0.009	120
48	Superior Temporal Gyrus	38	51	20	-20	0.009	112
49	Cuneus	19	14	-77	44	0.010	104

Clusters demonstrating significant concordance across studies ($p < .05$, FDR-corrected for multiple comparisons). For each cluster, labels denote regions which contained the peak ALE activation, and regions which contained secondary peaks; clusters may extend across non-labeled

regions between peaks and the extent is best characterized in Figure 5a (women), 5b (men), S1c (all participants).

[a]BA = Brodmann's area, if applicable

[b]X, Y, and Z coordinates represent weighted central activation likelihood focus in MNI space.

Table S4

Peak coordinates for sex differences in Negative emotion (analysis of complete dataset)

	Region (>100mm^3)	[a]BA(s)	[b]X	Y	Z	Peak Value	Vol. (mm^3)
	Women > Men						
1	Amygdala, Hippocampus, Substantia Nigra, Hypothalamus: Mammillary body, Subcallosal Gyrus, Thalamus: Medial dorsal nucleus	35, 34	-10	-16	-13	3.036	5416
2	Superior Frontal Gyrus	6	1	27	57	2.357	1584
3	Lateral Globus Pallidus	*	-10	3	1	2.989	1488
4	Putamen	*	-14	18	-16	2.727	1264
5	Middle Occipital Gyrus	37	52	-70	4	2.848	1056
6	Superior Frontal Gyrus, Medial Frontal Gyrus	10, 9	7	63	16	2.290	1048
7	Anterior Cingulate, Medial Frontal Gyrus	32, 9, 10	6	47	8	2.181	936
8	Middle Frontal Gyrus, Inferior Frontal Gyrus	46	-53	30	21	2.135	432
9	Middle Temporal Gyrus, Superior Temporal Gyrus	21, 38	-42	7	-34	2.007	384
10	Anterior Cingulate	32	-10	37	-8	2.251	224
11	Subcallosal Gyrus, Uncus	34	20	5	-24	1.957	200
12	Inferior Temporal Gyrus	20	-44	-8	-43	2.636	168
13	Inferior Frontal Gyrus	45	-50	21	2	2.079	168
	Men > Women						
1	Superior Temporal Gyrus, Claustrum, Precentral Gyrus	38, 13, 22, 6	44	4	-16	3.719	4136
2	Posterior Cingulate	29, 23	-2	-36	24	3.719	1872
3	Precentral Gyrus, Inferior Frontal Gyrus	6, 9	43	8	32	2.820	1680
4	Middle Temporal Gyrus, Superior Temporal Gyrus	39, 22	-37	-60	29	2.848	1552
5	Middle Temporal Gyrus, Fusiform Gyrus	37	-41	-57	-4	2.605	1368
6	Culmen, Posterior Cingulate, Lingual Gyrus	30, 18	10	-51	3	2.400	1368
7	Brainstem, Substantia Nigra	*	16	-18	-17	2.457	1088
8	Insula	13	-41	-1	-3	2.512	1056
9	Cuneus	17	10	-83	14	3.090	992
10	Putamen	*	-26	-17	3	2.794	976
11	Fusiform Gyrus, Cerebellum: Declive, Lingual Gyrus	19, 18	40	-72	-12	2.428	720
12	Postcentral Gyrus, Transverse Temporal Gyrus	40, 41	-56	-19	15	2.197	688
13	Anterior Cingulate	32	3	50	-12	2.748	528
14	Posterior Cingulate	30, 23	-6	-66	20	2.284	472
15	Inferior Frontal Gyrus, Precentral Gyrus	45, 44	48	20	6	2.238	440
16	Inferior Frontal Gyrus	47, 45	50	31	-6	2.106	416
17	Thalamus	*	18	-29	21	2.948	400
18	Middle Frontal Gyrus	47	-46	37	-12	2.382	368
19	Inferior Frontal Gyrus	46	-37	37	8	2.512	368
21	Fusiform Gyrus	20	46	-40	-14	1.946	192
22	Precentral Gyrus	4	-42	-11	58	2.366	128
23	Cerebellum: Declive	*	-37	-81	-13	2.010	120
24	Cuneus	18	14	-77	32	2.590	104

Clusters demonstrating significant concordance across studies ($p < .05$, FDR-corrected for multiple comparisons). For each cluster, labels denote regions which contained the peak ALE activation, and regions which contained secondary peaks; clusters may extend across non-labeled regions between peaks and the extent is best characterized in Figure S2a.

[a]BA = Brodmann's area, if applicable

[b]X, Y, and Z coordinates represent weighted central activation likelihood focus in MNI space.

Table S5

Peak coordinates for sex differences in Positive emotion (analysis of complete dataset)

	Region (>100mm^3)	[a]BA(s)	[b]X	Y	Z	Peak Value	Vol. (mm^3)
	Women > Men						
1	Thalamus, Subthalamic Nucleus, Hypothalamus, Medial Globus Pallidus	*	-9	-5	1	2.079	1912
2	Medial Frontal Gyrus, Superior Frontal Gyrus	32, 6	-2	17	56	2.687	1824
3	Middle Temporal Gyrus, Middle Occipital Gyrus	39, 37	53	-66	10	2.366	1480
4	Superior Temporal Gyrus	42, 13, 22	64	-35	16	2.501	1248
5	Lingual Gyrus, Cerebellum: Declive	18	-29	-78	-9	1.893	856
6	Superior Temporal Gyrus	41	43	-31	8	2.226	168
7	Superior Temporal Gyrus	39, 22	-59	-56	24	1.914	152
8	Superior Frontal Gyrus	6	6	30	61	2.284	128
	Men > Women						
1	Middle Frontal Gyrus, Superior Frontal Gyrus	6, 8, 9	-31	27	43	2.391	2168
2	Inferior Frontal Gyrus, Superior Temporal Gyrus	47, 38	-45	22	-26	2.687	1808
3	Inferior Frontal Gyrus, Entorhinal Cortex	13, 47, 34	32	6	-25	2.770	1504
4	Subcallosal Gyrus, Uncus, Amygdala	34, 28	-19	2	-27	2.312	896
5	Inferior Frontal Gyrus	47	-23	18	-20	2.357	344
6	Precuneus	7	19	-39	62	1.833	304
7	Claustrum	*	39	1	-2	2.590	296
8	Medial Frontal Gyrus	25	-14	11	-20	2.357	168
9	Medial Frontal Gyrus, Angerior Cingulate	9, 32	-12	32	24	2.054	120

Clusters demonstrating significant concordance across studies ($p < .05$, FDR-corrected for multiple comparisons). For each cluster, labels denote regions which contained the peak ALE activation, and regions which contained secondary peaks; clusters may extend across non-labeled regions between peaks and the extent is best characterized in Figure S2b.

[a]BA = Brodmann's area, if applicable

[b]X, Y, and Z coordinates represent weighted central activation likelihood focus in MNI space.

Table S6

Peak coordinates for sex differences in All-emotion (analysis of complete dataset)

	Region (>100mm^3)	[a]BA(s)	[b]X	Y	Z	Peak Value	Vol. (mm^3)
	Women > Men						
1	Hippocampus, Thalamus: Ventral lateral nucleus, medial dorsal nucleus, pulvinar, Subthalamic Nucleus, Hypothalamus	35	-9	-12	-6	3.719	11128
2	Superior Frontal Gyrus, Medial Frontal Gyrus	6	0	22	59	3.239	3600
3	Inferior Temporal Gyrus	37	50	-68	7	3.719	2064
4	Anterior Cingulate, Medial Frontal Gyrus	32, 10, 24	5	45	6	2.727	1920
5	Left Medial Frontal Gyrus, Right Superior Frontal Gyrus	9	-4	56	19	3.036	1360
6	Superior Temporal Gyrus	41, 13	55	-42	10	2.636	1296
7	Middle Frontal Gyrus	46	-49	25	24	2.457	1008
8	Anterior Cingulate	32	-10	37	-9	2.489	840
9	Superior Frontal Gyrus	10	15	64	14	2.312	416
10	Middle Occipital Gyrus	19	-51	-73	13	2.232	352
11	Middle Temporal Gyrus	21	-40	7	-33	2.170	344
12	Superior Temporal Gyrus, Supramarginal Gyrus	39, 40	-57	-57	28	2.106	312
13	Uncus	34	18	1	-25	1.985	184
14	Lingual Gyrus	17	-6	-95	-8	2.357	168
15	Culmen	*	32	-59	-21	1.988	128
	Men > Women						
1	Claustrum, Amygdala, Superior Temporal Gyrus, Fusiform Gyrus	13, 38, 20	43	2	-11	3.540	4000
2	Posterior Cingulate	23, 29	-2	-40	22	3.719	3040
3	Putamen	*	-28	-14	2	3.239	1560
4	Middle Frontal Gyrus	47, 11	-44	34	-16	2.652	1456
5	Fusiform Gyrus	19	41	-73	-11	3.090	1424
6	Parahippocampal Cortex, Fusiform Gyrus	36, 37	45	-43	-14	2.669	1416
7	Inferior Frontal Gyrus	47	37	33	-21	2.590	1224
8	Lateral Globus Pallidus, Thalamus	*	25	-12	-1	2.447	1056
9	Middle Temporal Gyrus	37	-41	-53	-3	2.636	1040
10	Precentral Gyrus, Inferior Frontal Gyrus	44, 45	49	21	9	2.342	1024
11	Middle Frontal Gyrus	8	-26	37	38	2.605	968
12	Right Anterior Cingulate, Left Anterior Cingulate	32, 24	9	34	19	2.748	864
13	Inferior Frontal Gyrus	47	52	32	-8	2.911	832
14	Inferior Frontal Gyrus	47	-34	21	-26	2.576	768
15	Inferior Frontal Gyrus	46	-37	36	8	2.605	728
16	Superior Temporal Gyrus, Middle Temporal Gyrus	39	-38	-61	29	2.549	712
17	Superior Temporal Gyrus, Transverse Temporal Gyrus, Postcentral Gyrus	22, 42, 41, 43, 40	-56	-14	13	2.706	664
18	Caudate Body	*	19	-6	22	2.524	592
19	Precentral Gyrus	6	-38	5	27	2.106	496
20	Culmen	*	7	-47	0	2.186	472
21	Claustrum, Insula	13	-42	1	-4	2.447	368
22	Cuneus	17	12	-81	14	3.239	368
23	Uncus, Amygdala	28	-21	-1	-31	2.418	336
24	Cerebral Peduncle	*	15	-18	-19	2.135	336
25	Supramarginal Gyrus, Superior Temporal Gyrus, Supramarginal Gyrus	40, 39	42	-45	31	2.022	328
26	Inferior Frontal Gyrus	9	40	11	31	2.304	232
27	Posterior Cingulate	30	-7	-69	17	2.066	144
28	Thalamus	*	18	-28	22	2.727	144

Clusters demonstrating significant concordance across studies ($p < .05$, FDR-corrected for multiple comparisons). For each cluster, labels denote regions which contained the peak ALE

activation, and regions which contained secondary peaks; clusters may extend across non-labeled regions between peaks and the extent is best characterized in Figure S2c.
[a]BA = Brodmann's area, if applicable
[b]X, Y, and Z coordinates represent weighted central activation likelihood focus in MNI space.

Table S7

Peak coordinates for Negative emotion (analysis of complete dataset)

	Region (>100mm^3)	[a]BA(s)	[b]X	Y	Z	Peak Value	Vol. (mm^3)
	All Participants (Women and Men)						
1	Left Amygdala, Right Amygdala, Left Inferior Frontal Gyrus, Right Inferior Frontal Gyrus, Left Hippocampus, Right Hippocampus, Left Superior Temporal Gyrus, Right Precentral Gyrus, Left Thalamus: Ventral lateral nucleus, ventral posterior lateral nucleus, Right Thalamus: Pulvinar, Left Caudate Body, Left Insula, Left Middle Frontal Gyrus, Right Middle Frontal Gyrus, Right Hypothalamus: Mammillary Body, Left Caudate Head, Right Cerebellum: Culmen, Left Cerebellum: Culmen, Left Putamen, Right Putamen, Right Claustrum, Left Uncus	47, 19, 38, 6, 13, 46, 44, 11, 45, 9, 28	-2	3	-9	0.076	93136
2	Right Cingulate Gyrus, Left Cingulate Gyrus, Superior Frontal Gyrus	32, 6	0	20	45	0.036	10432
3	Anterior Cingulate, Medial Frontal Gyrus	32, 10	1	51	-1	0.024	5552
4	Superior Frontal Gyrus, Medial Frontal Gyrus	9	-3	58	22	0.032	5384
5	Inferior Temporal Gyrus, Cerebellum: Declive, Middle Temporal Gyrus	37, 39	40	-71	-8	0.023	4552
6	Parahippocampal Cortex, Culmen	19	25	-54	-14	0.024	4232
7	Superior Temporal Gyrus	38	43	10	-32	0.027	4000
8	Precentral Gyrus, Inferior Frontal Gyrus	6, 9	-49	8	32	0.021	3696
9	Middle Temporal Gyrus, Inferior Parietal Lobule, Middle Occipital Gyrus	39, 40, 19	-48	-60	22	0.016	3424
10	Fusiform Gyrus, Culmen	37	46	-47	-21	0.025	2136
11	Middle Temporal Gyrus, Superior Temporal Gyrus	21, 22	-52	-10	-10	0.017	1640
12	Fusiform Gyrus, Inferior Occipital Gyrus	19	-40	-76	-9	0.019	1512
13	Fusiform Gyrus	37	-44	-47	-16	0.024	1464
14	Cingulate Gyrus	24	-4	-2	33	0.019	1288
15	Superior Temporal Gyrus	22	55	-13	-2	0.018	1280
16	Precuneus	31	-4	-68	24	0.017	1136
17	Lingual Gyrus	*	-11	-71	3	0.020	856
18	Middle Temporal Gyrus, Superior Temporal Gyrus	22	58	-36	6	0.018	832
19	Anterior Cingulate	24	3	32	-12	0.017	792
20	Posterior Cingulate	30	12	-57	9	0.016	744
21	Posterior Cingulate	23	-2	-36	23	0.019	744
22	Middle Temporal Gyrus	21	50	-6	-17	0.018	696
23	Anterior Cingulate	32	21	34	16	0.015	608
24	Precentral Gyrus	6	-58	5	15	0.015	432
25	Middle Temporal Gyrus	37	-42	-58	-4	0.015	368
26	Cuneus	17	8	-84	13	0.014	328
27	Thalamus	*	18	-27	19	0.016	328
28	Cingulate Gyrus	31	5	-22	41	0.016	312
29	Postcentral Gyrus	43	-54	-13	16	0.013	296
30	Anterior Cingulate	*	-13	37	-8	0.013	288
31	Insula	13	37	-21	17	0.014	280
32	Middle Temporal Gyrus	21	60	4	-22	0.014	264
33	Posterior Cingulate	30, 29	7	-51	18	0.013	192
34	Superior Temporal Gyrus	39	53	-55	36	0.014	192
35	Precuneus	7	29	-55	57	0.013	192
36	Middle Temporal Gyrus	21	-57	-34	-6	0.014	184
37	Anterior Cingulate	24	6	31	20	0.014	184
38	Insula	13	46	-38	21	0.014	160
39	Precentral Gyrus	4	46	-10	58	0.017	152
40	Inferior Parietal Lobule	40	-59	-36	31	0.012	104
	Women						
1	Left Amygdala, Left Hippocampus,	34, 47,	-9	-3	-10	0.057	60000

	Right Hippocampus, Left Inferior Frontal Gyrus, Left Thalamus: Ventral lateral nucleus, pulvinar, Left Middle Frontal Gyrus, Right Superior Temporal Gyrus, Left Caudate Body, Right Mammillary Body, Right Subthalamic Nucleus, Left Putamen, Right Putamen, Left Caudate Head, Left Lingual Gyrus, Left Red Nucleus, Left Cerebellum: Culmen, Left Insula	46, 38, 19, 9, 18, 13					
2	Superior Frontal Gyrus, Medial Frontal Gyrus	6	-2	20	58	0.022	5696
3	Culmen, Cerebellum: Declive, Parahippocampal Cortex	19, 37	27	-59	-16	0.017	5616
4	Left Superior Frontal Gyrus, Right Superior Frontal Gyrus, Left Medial Frontal Gyrus	9, 10	-1	58	20	0.022	5472
5	Left Anterior Cingulate, Left Medial Frontal Gyrus, Right Medial Frontal Gyrus	32, 10	2	48	4	0.021	4968
6	Insula, Inferior Frontal Gyrus, Putamen	47, 45	43	24	-9	0.016	4472
7	Superior Temporal Gyrus	38	-38	10	-32	0.022	2656
8	Cingulate Gyrus	32	-7	30	31	0.016	2280
9	Inferior Temporal Gyrus, Middle Temporal Gyrus	37, 39	50	-68	5	0.022	2264
10	Cingulate Gyrus	32	8	15	39	0.020	2008
11	Precentral Gyrus	6	-51	-1	41	0.021	1736
12	Inferior Frontal Gyrus	9, 44	53	16	20	0.017	1440
13	Middle Occipital Gyrus, Middle Temporal Gyrus, Inferior Temporal Gyrus	19, 39	-48	-73	14	0.012	1280
14	Cingulate Gyrus	24	-4	-2	36	0.011	1216
15	Fusiform Gyrus	37	-45	-45	-17	0.016	1104
16	Culmen	*	47	-54	-25	0.014	848
17	Superior Temporal Gyrus	22	55	-18	-2	0.016	848
18	Anterior Cingulate	*	-12	38	-7	0.013	832
19	Middle Temporal Gyrus	22	57	-37	6	0.014	808
20	Putamen	*	-25	3	13	0.012	768
21	Anterior Cingulate	24	0	31	-12	0.011	736
22	Middle Frontal Gyrus	46	51	32	16	0.015	736
23	Superior Temporal Gyrus, Middle Temporal Gyrus	39, 37	-54	-55	23	0.012	696
24	Lingual Gyrus	18	-7	-96	-9	0.011	656
25	Precentral Gyrus, Middle Frontal Gyrus	6	56	0	41	0.014	544
26	Insula	13	-41	-18	16	0.011	520
27	Superior Temporal Gyrus	39	54	-55	36	0.013	512
28	Cingulate Gyrus	24	5	-19	41	0.014	464
29	Superior Temporal Gyrus	21	49	-7	-16	0.014	456
30	Culmen	*	2	-60	-21	0.010	384
31	Superior Temporal Gyrus	22	-47	-12	-9	0.012	376
32	Posterior Cingulate	29, 30	4	-55	16	0.009	360
33	Caudate Body	*	10	3	14	0.011	352
34	Insula	13	37	-20	18	0.011	328
35	Precuneus	31	-9	-64	34	0.010	296
36	Insula	13	50	-12	15	0.010	280
37	Superior Frontal Gyrus	9	-19	56	29	0.010	272
38	Lingual Gyrus	18	9	-78	-1	0.009	264
39	Middle Temporal Gyrus, Angular Gyrus	39	-49	-65	33	0.009	256
40	Supramarginal Gyrus, Inferior Parietal Lobule	40	-57	-40	34	0.009	248
41	Precentral Gyrus	6	-58	2	14	0.009	240
42	Precentral Gyrus	4	45	-10	59	0.014	216
43	Middle Temporal Gyrus	21	60	6	-25	0.010	208
44	Thalamus	*	17	-25	5	0.009	200
45	Precuneus	7	32	-56	59	0.010	184
46	Superior Temporal Gyrus	22	-61	0	-11	0.009	176
47	Inferior Frontal Gyrus	46	-43	47	0	0.010	176
48	Inferior Temporal Gyrus	20	-44	-8	-43	0.010	168
49	Precentral Gyrus	6	64	3	13	0.009	168
50	Insula13	40	12	2	0.009	128	
51	Superior Temporal Gyrus	22	-46	-25	-9	0.009	104
52	Superior Temporal Gyrus	22	-58	9	-10	0.009	104

53	Precuneus	7	3	-64	64	0.009	104
	Men						
1	Amygdala, Precentral Gyrus, Superior Temporal Gyrus, Inferior Frontal Gyrus, Entorhinal Cortex, Claustrum, Insula, Middle Temporal Gyrus	6, 38, 47, 44, 35, 13, 22, 45, 21	37	6	-7	0.039	34072
2	Amygdala, Inferior Frontal Gyrus, Insula, Middle Frontal Gyrus, Thalamus: Ventral posterior lateral nucleus, Middle Temporal Gyrus, Uncus, Putamen	13, 47, 46, 11, 21, 28	-35	8	-12	0.027	26328
3	Posterior Cingulate, Culmen, Parahippocampal Cortex	30, 19	12	-50	0	0.016	5064
4	Cingulate Gyrus, Superior Frontal Gyrus	32, 6, 24	3	19	40	0.018	4368
5	Fusiform Gyrus, Middle Temporal Gyrus, Inferior Occipital Gyrus, Parahippocampal Cortex, Cerebellum: Declive	19, 37	-41	-66	-7	0.017	4296
6	Middle Temporal Gyrus, Superior Temporal Gyrus	39, 13	-42	-58	28	0.014	2776
7	Anterior Cingulate	32	5	50	-9	0.016	2120
8	Inferior Frontal Gyrus	9	-45	9	27	0.013	1952
9	Posterior Cingulate	23	-2	-36	23	0.018	1872
10	Anterior Cingulate	32	25	32	17	0.012	1736
11	Fusiform Gyrus	19	40	-70	-13	0.019	1728
12	Lingual Gyrus	19	-17	-48	-4	0.017	1664
13	Fusiform Gyrus	37	46	-43	-18	0.022	1600
14	Posterior Cingulate	31	-4	-67	22	0.015	1496
15	Postcentral Gyrus	43	-56	-17	15	0.012	1344
16	Cuneus	17	9	-83	13	0.014	1168
17	Inferior Frontal Gyrus	47	-27	34	-7	0.014	1088
18	Medial Frontal Gyrus	9	4	53	22	0.016	1032
19	Superior Frontal Gyrus	9	-8	64	24	0.018	1032
20	Thalamus: Pulvinar	*	18	-27	19	0.016	840
21	Caudate Body	*	-6	9	13	0.016	696
22	Anterior Cingulate	24	6	31	20	0.014	624
23	Cerebellum: Declive	*	34	-84	-17	0.014	600
24	Superior Temporal Gyrus	41	59	-28	10	0.009	560
25	Medial Frontal Gyrus	10	-11	59	-1	0.013	528
26	Postcentral Gyrus, Precentral Gyrus	3, 4	-46	-10	56	0.010	504
27	Middle Frontal Gyrus	9	-27	40	32	0.012	472
28	Middle Temporal Gyrus	21	-57	-33	-6	0.012	456
29	Middle Frontal Gyrus	9	45	35	28	0.012	440
30	Lingual Gyrus	18	-10	-70	5	0.011	432
31	Cingulate Gyrus	24	-3	-3	29	0.009	376
32	Middle Temporal Gyrus	20	60	-33	-9	0.010	368
33	Precentral Gyrus	6	-35	-8	46	0.010	304
34	Anterior Cingulate	24	6	32	-13	0.009	264
35	Precentral Gyrus, Inferior Frontal Gyrus	6, 44	-56	9	15	0.008	256
36	Inferior Parietal Lobule	40	-30	-28	39	0.008	208
37	Thalamus	*	1	-18	2	0.010	200
38	Middle Occipital Gyrus	19	-36	-80	11	0.008	200
39	Cuneus	19	14	-78	44	0.010	184
40	Red Nucleus, Thalamus	*	-5	-26	-6	0.008	168
41	Superior Frontal Gyrus	10	-4	63	-15	0.008	144
42	Lingual Gyrus	17	14	-93	2	0.009	144
43	Precentral Gyrus	4	-37	-20	58	0.009	144
44	Cerebellar Tonsil	*	40	-57	-39	0.009	128
45	Cerebellum	*	9	-86	-16	0.009	128
46	Superior Occipital Gyrus	19	33	-74	31	0.009	128
47	Precuneus	7	2	-65	49	0.009	128
48	Caudate Tail		-38	-29	-3	0.009	120
49	Middle Temporal Gyrus	39	-45	-58	12	0.008	120
50	Culmen	*	23	-44	-23	0.008	112
51	Cerebellum: Declive	*	21	-84	-15	0.008	112
52	Middle Temporal Gyrus	22	-47	-45	8	0.008	112
53	Caudate Tail	*	28	-41	17	0.009	112

54	Thalamus	*	-15	-27	18	0.009	112
55	Middle Frontal Gyrus	8	-22	29	42	0.009	112
56	Superior Frontal Gyrus	6	25	12	64	0.008	112
57	Cuneus	18	14	-77	32	0.008	104

Clusters demonstrating significant concordance across studies ($p < .05$, FDR-corrected for multiple comparisons). For each cluster, labels denote regions which contained the peak ALE activation, and regions which contained secondary peaks..

[a]BA = Brodmann's area, if applicable

[b]X, Y, and Z coordinates represent weighted central activation likelihood focus in MNI space.

Table S8

Peak coordinates for Positive emotion (analysis of complete dataset)

	Region (>100mm^3)	[a]BA(s)	[b]X	Y	Z	Peak Value	Vol. (mm^3)
	All Participants (Women and Men)						
1	Amygdala, Superior Temporal Gyrus, Inferior Frontal Gyrus	38, 47	-29	2	-23	0.027	10912
2	Parahippocampal Cortex, Fusiform Gyrus, Thalamus, Middle Temporal Gyrus, Hippocampus	36, 37, 19	-36	-44	-14	0.017	6176
3	Thalamus: Ventral anterior nucleus, Medial Globus Pallidus, Caudate Head	*	-7	-4	-3	0.020	4816
4	Amygdala, Superior Temporal Gyrus	38	27	0	-24	0.021	4088
5	Inferior Frontal Gyrus, Insula	45, 13	-35	28	0	0.019	3696
6	Superior Temporal Gyrus, Middle Temporal Gyrus	22, 39	-53	-61	22	0.015	3232
7	Medial Frontal Gyrus	9	-1	57	18	0.017	3064
8	Precentral Gyrus, Inferior Frontal Gyrus	6, 44, 9	51	10	24	0.013	2896
9	Anterior Cingulate	32	-4	36	-13	0.020	2744
10	Postcentral Gyrus, Inferior Parietal Lobule, Precentral Gyrus, Middle Frontal Gyrus	3, 40, 6	-42	-18	56	0.015	2496
11	Superior Temporal Gyrus, Middle Temporal Gyrus	22, 21	63	-39	13	0.017	2232
12	Inferior Frontal Gyrus, Insula	45, 13	52	28	8	0.020	1960
13	Lingual Gyrus	18	21	-86	-5	0.014	1920
14	Fusiform Gyrus, Cerebellum: Declive, Inferior Occipital Gyrus	19, 18	-30	-82	-13	0.011	1872
15	Insula, Inferior Frontal Gyrus	13, 47	32	30	-13	0.011	1760
16	Middle Frontal Gyrus	6, 8	-31	27	44	0.012	1656
17	Fusiform Gyrus	19	45	-75	-12	0.016	1624
18	Middle Occipital Gyrus	19	-48	-79	6	0.015	1488
19	Lateral Globus Pallidus	*	26	-17	-2	0.017	1232
20	Middle Temporal Gyrus	37	54	-65	11	0.018	1184
21	Superior Frontal Gyrus	6	-2	18	54	0.012	1152
22	Parahippocampal Cortex	30	21	-50	7	0.011	1120
23	Posterior Cingulate	30, 29	-2	-44	22	0.011	1112
24	Fusiform Gyrus	37	48	-45	-16	0.010	1104
25	Cuneus	7, 19	19	-81	40	0.011	992
26	Precentral Gyrus	6	-52	5	33	0.010	864
27	Medial Frontal Gyrus	10, 11	-3	57	-18	0.010	784
28	Superior Parietal Lobule	7	-30	-51	66	0.011	728
29	Superior Temporal Gyrus	22	-54	8	0	0.013	712
30	Precuneus	7	4	-64	63	0.013	712
31	Lingual Gyrus	18	-3	-87	8	0.009	688
32	Inferior Temporal Gyrus	20	-61	-13	-27	0.011	680
33	Claustrum	*	42	2	-2	0.012	664
34	Caudate Body	*	18	-7	23	0.011	592
35	Culmen	*	25	-52	-22	0.009	536
36	Putamen	*	-23	-9	11	0.009	512
37	Middle Temporal Gyrus	21	64	-32	-8	0.009	496
38	Anterior Cingulate	32	-5	46	0	0.009	488
39	Cingulate Gyrus	31	12	-37	45	0.009	480
40	Precuneus	39	-45	-71	39	0.013	448
41	Middle Frontal Gyrus, Inferior Frontal Gyrus	9, 44	-49	16	21	0.009	400
42	Precuneus	7	-25	-44	51	0.010	400
43	Superior Parietal Lobule	7	34	-55	63	0.010	376
44	Precentral Gyrus	4	45	-10	59	0.014	360
45	Cuneus	18	18	-96	19	0.009	288
46	Precuneus	19	-30	-75	44	0.008	272
47	Middle Occipital Gyrus, Cuneus	19, 18	-29	-88	25	0.008	248
48	Lingual Gyrus	18	-12	-78	0	0.009	224
49	Lingual Gyrus	18	18	-72	0	0.009	216
50	Precuneus	31	-11	-53	34	0.008	216
51	Postcentral Gyrus	3	30	-30	56	0.009	216

52	Cingulate Gyrus	32	10	22	33	0.008	208
53	Superior Frontal Gyrus	6	-8	16	66	0.009	208
54	Cerebellar Tonsil	*	22	-70	-36	0.008	192
55	Precuneus	7	20	-40	62	0.009	192
56	Perirhinal Cortex	35	30	-27	-18	0.008	176
57	Precuneus	31	-16	-42	36	0.008	176
58	Precentral Gyrus	6	45	-3	48	0.008	176
59	Cerebellar Lingual	*	-6	-49	-18	0.008	168
60	Superior Temporal Gyrus	41	42	-30	8	0.008	168
61	Cuneus	23	-10	-75	13	0.007	160
62	Middle Frontal Gyrus	8	-43	30	38	0.008	160
63	Cingulate Gyrus	24	-17	4	49	0.008	160
64	Posterior Cingulate	29	6	-52	14	0.008	152
65	Cerebellar Tonsil	*	28	-62	-41	0.008	144
66	Claustrum	*	-30	10	-10	0.007	144
67	Thalamus	*	18	-8	7	0.008	144
68	Precuneus	7	8	-64	51	0.007	144
69	Middle Frontal Gyrus	46	-48	40	15	0.007	136
70	Precentral Gyrus	4	-50	-8	40	0.008	136
71	Medial Frontal Gyrus	10	10	44	-14	0.006	128
72	Middle Frontal Gyrus	46	45	36	20	0.008	128
73	Caudate Tail	*	38	-19	-11	0.007	120
74	Putamen	*	28	7	12	0.007	120
75	Middle Temporal Gyrus	22	46	-57	21	0.007	120
76	Precuneus	7	17	-49	46	0.007	120
77	Precentral Gyrus	4	33	-14	45	0.007	120
78	Middle Frontal Gyrus	6	44	18	48	0.008	120
79	Middle Temporal Gyrus	21	62	2	-19	0.007	112
80	Putamen	*	27	19	-7	0.007	112
81	Culmen	*	-1	-43	-4	0.007	112
82	Precentral Gyrus	13	-53	-10	8	0.007	112
83	Superior Frontal Gyrus	8	-3	43	46	0.007	112
85	Cerebellum: Declive	*	-12	-77	-17	0.007	104
	Women						
1	Thalamus: Ventral anterior nucleus, Caudate Head	*	-7	-5	-2	0.020	4512
2	Lingual Gyrus	18	21	-85	-5	0.014	3096
3	Superior Temporal Gyrus, Middle Occipital Gyrus, Middle Temporal Gyrus	22, 39, 19	-53	-62	19	0.013	3080
4	Left Medial Frontal Gyrus, Right Medial Frontal Gyrus	9	-2	57	19	0.013	2560
5	Fusiform Gyrus, Inferior Occipital Gyrus	19, 18	-28	-80	-12	0.0113	2536
6	Superior Temporal Gyrus, Middle Temporal Gyrus	22, 21	62	-38	14	0.017	2408
7	Amygdala	*	-26	-8	-20	0.016	2304
8	Superior Frontal Gyrus	6	-3	17	56	0.012	2032
9	Anterior Cingulate	32	-5	37	-14	0.013	1968
10	Parahippocampal Cortex	30	21	-50	7	0.011	1592
11	Fusiform Gyrus	37	-42	-58	-17	0.010	1512
12	Middle Temporal Gyrus	37	54	-65	11	0.018	1512
13	Inferior Parietal Lobule, Postcentral Gyrus	40, 3	-45	-22	53	0.010	1456
14	Thalamus, Hippocampus, Perirhinal Cortex	35	-20	-30	-8	0.009	1376
15	Lingual Gyrus	18	-6	-84	6	0.009	1344
16	Cerebellar Tonsil, Cerebellum: Uvula	*	23	-69	-38	0.008	1064
17	Amygdala	*	22	-5	-24	0.012	1008
18	Precentral Gyrus	6	47	6	32	0.012	1008
19	Insula, Claustrum	13	-31	25	0	0.009	936
20	Precuneus	7	4	-64	63	0.013	912
21	Cuneus	7, 19	17	-81	38	0.008	896
22	Middle Frontal Gyrus, Inferior Frontal Gyrus	9, 44	-49	17	21	0.009	816
23	Medial Frontal Gyrus	10, 11	-3	54	-20	0.008	704
24	Medial Frontal Gyrus	10	10	44	-14	0.006	504
25	Middle Temporal Gyrus, Angular Gyrus	39	-44	-76	30	0.008	448
26	Precentral Gyrus	4	44	-10	59	0.014	416

27	Precuneus	7	-24	-44	53	0.009	408
28	Perirhinal Cortex	36	-39	-31	-18	0.008	384
29	Perirhinal Cortex	35	30	-27	-18	0.008	368
30	Middle Frontal Gyrus	46	54	33	12	0.008	352
31	Culmen	*	27	-47	-23	0.008	320
32	Cingulate Gyrus	31	6	-37	44	0.008	320
33	Superior Temporal Gyrus	22	-56	6	0	0.009	312
34	Superior Temporal Gyrus	38	-55	17	-15	0.008	304
35	Posterior Cingulate	29	6	-53	14	0.008	296
36	Cingulate Gyrus	32	10	22	33	0.008	296
37	Precuneus	31	-16	-42	36	0.008	288
38	Caudate Tail	*	38	-19	-11	0.007	280
39	Precuneus	19	-33	-73	44	0.008	280
40	Inferior Temporal Gyrus	20	-64	-14	-26	0.008	264
41	Cerebellum: Declive	*	-12	-77	-17	0.007	264
42	Middle Temporal Gyrus	21	66	-30	-4	0.008	264
43	Insula	13	30	30	-6	0.009	264
44	Inferior Frontal Gyrus	45	50	22	0	0.008	264
45	Superior Temporal Gyrus	41	42	-30	8	0.008	264
46	Inferior Frontal Gyrus	44	58	12	10	0.008	264
47	Precentral Gyrus	6	-52	4	34	0.008	264
48	Superior Frontal Gyrus	8	-3	43	46	0.007	248
49	Superior Temporal Gyrus	38	-34	8	-27	0.007	232
50	Superior Temporal Gyrus	38	44	18	-38	0.007	224
51	Culmen	*	51	-45	-23	0.007	224
52	Anterior Cingulate	24	-1	42	0	0.006	208
53	Middle Frontal Gyrus	6	44	18	48	0.008	200
54	Caudate Body	*	14	3	8	0.006	184
55	Cuneus	18	16	-98	15	0.008	160
56	Precentral Gyrus, Middle Frontal Gyrus	6	-40	-2	63	0.008	160
57	Lingual Gyrus	18	-15	-86	-10	0.006	152
58	Superior Frontal Gyrus	6	6	30	61	0.008	136
59	Cerebellum: Declive	*	49	-70	-17	0.007	128
60	Superior Parietal Lobule	7	36	-56	62	0.006	128
61	Inferior Parietal Lobule	40	-36	-50	64	0.006	128
	Men						
1	Amygdala, Inferior Frontal Gyrus	47	-29	5	-24	0.018	10216
2	Inferior Frontal Gyrus, Insula, Claustrum	13, 45, 47	-37	30	1	0.014	4152
3	Hippocampus, Superior Temporal Gyrus	34, 38	29	2	-24	0.016	4040
4	Parahippocampal Cortex	36, 19	-35	-39	-15	0.013	2752
5	Middle Frontal Gyrus	6, 8	-31	27	44	0.012	2712
6	Fusiform Gyrus	19	45	-75	-11	0.016	1736
7	Lateral Globus Pallidus	*	26	-17	-2	0.017	1672
8	Posterior Cingulate	30, 29	-2	-44	22	0.011	1608
9	Inferior Frontal Gyrus	9	50	13	21	0.010	1600
10	Inferior Frontal Gyrus	47	34	30	-20	0.010	1504
11	Claustrum, Insula	*	42	5	-2	0.012	1376
12	Fusiform Gyrus	20, 37	48	-47	-14	0.010	1368
13	Precentral Gyrus	4	-39	-16	56	0.010	1264
14	Inferior Frontal Gyrus	46	54	29	10	0.014	1072
15	Caudate Body	*	18	-7	23	0.011	928
16	Putamen	*	-23	-9	11	0.009	848
17	Inferior Temporal Gyrus	19	-49	-78	3	0.011	816
18	Middle Temporal Gyrus, Fusiform Gyrus	37	-54	-56	-12	0.009	776
19	Anterior Cingulate	32	-2	35	-13	0.009	768
20	Superior Frontal Gyrus, Medial Frontal Gyrus	9	1	59	17	0.007	728
21	Lateral Globus Pallidus	*	-11	8	-14	0.008	720
22	Middle Temporal Gyrus	19, 39	-51	-64	22	0.008	664
23	Superior Parietal Lobule	7	-28	-52	66	0.010	664
24	Cerebellar Lingual	*	-5	-47	-18	0.008	632
25	Cingulate Gyrus	32	2	32	21	0.006	568

26	Middle Occipital Gyrus, Cuneus	19, 18	-28	-88	25	0.008	560
27	Cingulate Gyrus	31	17	-37	46	0.009	408
28	Precuneus	31	-11	-53	34	0.008	400
29	Precentral Gyrus	6	45	-3	48	0.008	384
30	Middle Frontal Gyrus	6	-19	4	49	0.008	384
31	Precuneus	7	19	-39	62	0.009	368
32	Inferior Temporal Gyrus	20	-57	-12	-27	0.009	352
33	Anterior Cingulate	32	-6	49	-1	0.008	352
34	Precentral Gyrus	6	-46	4	27	0.008	352
35	Middle Frontal Gyrus	8	-45	30	38	0.008	352
36	Cerebellum: Declive	*	-21	-94	-17	0.008	328
37	Claustrum	*	-29	9	-10	0.007	328
38	Caudate Head	*	-5	19	-5	0.007	320
39	Thalamus	*	-20	-27	3	0.007	320
40	Thalamus	*	19	-8	7	0.007	312
41	Precuneus	7	17	-49	46	0.007	312
42	Culmen	*	23	-56	-22	0.008	304
43	Middle Temporal Gyrus	21	63	1	-19	0.007	304
44	Culmen	*	-1	-43	-4	0.007	304
45	Insula	45	29	32	1	0.007	304
46	Anterior Cingulate	25	5	9	-15	0.007	296
47	Precentral Gyrus	13	-53	-9	9	0.007	296
48	Putamen	*	27	19	-7	0.007	288
49	Cuneus	23	-10	-74	13	0.007	280
50	Middle Temporal Gyrus	22	46	-57	20	0.007	280
51	Middle Frontal Gyrus	46	45	36	20	0.007	280
52	Precentral Gyrus	4	-50	-8	40	0.008	280
53	Precuneus	7	8	-64	51	0.007	280
54	Cerebellum: Anterior Lobe	*	-21	-49	-25	0.007	272
55	Brainstem- Red Nucleus	*	3	-22	-24	0.007	272
56	Precuneus	39	-45	-69	41	0.009	272
57	Precentral Gyrus	4	33	-14	46	0.007	272
58	Cerebellum: Declive	*	-1	-67	-17	0.007	264
59	Superior Temporal Gyrus	22	-52	10	0	0.008	264
60	Putamen	*	28	8	12	0.007	264
61	Postcentral Gyrus	3	30	-30	56	0.009	264
62	Superior Frontal Gyrus	6	-14	33	55	0.006	232
63	Middle Frontal Gyrus	6	-24	24	56	0.007	216
64	Middle Frontal Gyrus	10	-36	58	-1	0.006	208
65	Thalamus	*	2	-16	15	0.006	208
66	Precuneus	19	34	-70	39	0.006	208
67	Culmen	*	35	-31	-34	0.006	200
68	Mammillary Body	*	3	-12	-12	0.006	200
69	Middle Temporal Gyrus	20	62	-35	-11	0.006	200
70	Supramarginal Gyrus	40	38	-44	30	0.007	200
71	Middle Frontal Gyrus	6	28	10	39	0.006	200
72	Superior Temporal Gyrus	38	-42	6	-22	0.006	192
73	Superior Temporal Gyrus	38	-57	16	-14	0.006	192
74	Cingulate Gyrus	32	-11	32	24	0.006	192
75	Superior Frontal Gyrus	9	-16	48	31	0.007	192
76	Cerebellum: Tuber	*	-42	-65	-24	0.006	184
77	Superior Temporal Gyrus	22	65	-43	8	0.006	184
78	Precuneus	31	23	-56	23	0.006	184
79	Anterior Cingulate	32	14	38	18	0.006	176
80	Uncus	20	-40	-14	-36	0.006	168
81	Precuneus	7	24	-57	57	0.006	168
82	Cerebellar Tonsil	*	-2	-60	-44	0.006	160
83	Superior Temporal Gyrus	38	46	17	-23	0.006	160
84	Medial Frontal Gyrus	10	-2	62	-18	0.006	160
85	Inferior Parietal Lobule	40	-52	-22	33	0.006	160
86	Precentral Gyrus	6	-55	9	36	0.006	160
87	Precuneus	7	-30	-45	45	0.006	160

88	Superior Parietal Lobule	7	31	-53	66	0.006	160
89	Putamen	*	-32	-12	-3	0.006	152
90	Postcentral Gyrus	2	63	-18	33	0.006	152
91	Precuneus	19	-24	-78	42	0.006	152
92	Supramarginal Gyrus	40	-58	-48	40	0.007	144
93	Inferior Frontal Gyrus	9	56	9	32	0.006	112
94	Middle Occipital Gyrus	19	-43	-84	16	0.006	104

Clusters demonstrating significant concordance across studies ($p < .05$, FDR-corrected for multiple comparisons). For each cluster, labels denote regions which contained the peak ALE activation, and regions which contained secondary peaks.

[a]BA = Brodmann's area, if applicable

[b]X, Y, and Z coordinates represent weighted central activation likelihood focus in MNI space.

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Table S9

Peak coordinates for All-emotion (analysis of complete dataset)

	Region (>100mm^3)	[a]BA(s)	[b]X	Y	Z	Peak Value	Vol. (mm^3)
	All Participants (Women and Men)						
1	Left Amygdala, Right Amygdala, Left Superior Temporal Gyrus, Right Superior Temporal Gyrus, Right Inferior Frontal Gyrus, Left Inferior Frontal Gyrus, Left Thalamus: Ventral lateral nucleus, ventral posterior lateral nucleus, Right Precentral Gyrus, Left Middle Frontal Gyrus, Right Middle Frontal Gyrus, Left Insula, Right Claustrum, Left Hypothalamus: Mammillary Body, Right Hypothalamus: Mammillary Body, Left Caudate Body, Right Lateral Globus Pallidus, Right Putamen	38, 45, 1 47, 6, 9, 46, 13	0	7	-10	0.098	105448
2	Fusiform Gyrus, Culmen, Middle Temporal Gyrus, Inferior Temporal Gyrus, Parahippocampal Cortex, Culmen, Posterior Cingulate	37, 19, 29, 23, 30	32	-56	-5	0.036	16008
3	Superior Temporal Gyrus, Fusiform Gyrus, Inferior Temporal Gyrus, Middle Temporal Gyrus, Angular Gyrus, Cerebellum: Declive	22, 19, 39	-46	-68	9	0.031	10344
4	Superior Frontal Gyrus, Cingulate Gyrus, Anterior Cingulate	6, 32	0	20	47	0.041	9568
5	Medial Frontal Gyrus, Anterior Cingulate	10, 32	0	46	-5	0.028	8576
6	Medial Frontal Gyrus	9	-2	57	21	0.048	6992
7	Inferior Frontal Gyrus, Precentral Gyrus, Middle Frontal Gyrus	9, 6	-50	8	29	0.029	5144
8	Parahippocampal Cortex, Culmen	19	-12	-47	-5	0.030	3472
9	Fusiform Gyrus, Inferior Temporal Gyrus	37, 19, 36	-42	-49	-14	0.027	3176
10	Superior Temporal Gyrus	22	60	-40	9	0.025	2704
11	Fusiform Gyrus, Lingual Gyrus	19, 18	25	-84	-12	0.024	1336
12	Lingual Gyrus	*	-12	-74	2	0.022	1080
13	Precentral Gyrus	3	-40	-17	58	0.021	904
14	Superior Temporal Gyrus	22	-49	-10	-8	0.021	768
15	Superior Parietal Lobule, Precuneus	7	32	-55	60	0.020	632
16	Middle Temporal Gyrus	21	61	3	-21	0.020	504
17	Cingulate Gyrus	24	-3	-1	31	0.019	480
18	Precuneus	31	-4	-69	23	0.017	448
19	Precuneus	7	3	-64	64	0.022	448
20	Superior Temporal Gyrus	22	56	-17	-2	0.018	416
21	Anterior Cingulate	32	19	36	16	0.016	376
22	Anterior Cingulate	24	5	31	21	0.018	368
23	Precentral Gyrus	4	45	-10	58	0.031	368
24	Sub-Gyral	21	51	-6	-18	0.018	328
25	Medial Frontal Gyrus	10	-3	60	-15	0.016	320
26	Middle Temporal Gyrus	21	-60	-2	-15	0.017	280
27	Inferior Temporal Gyrus	20	-62	-13	-26	0.018	272
28	Middle Temporal Gyrus	21	62	-33	-8	0.017	272
29	Lingual Gyrus	18	16	-74	0	0.016	184
30	Caudate Body	*	12	3	10	0.015	136
31	Caudate Body	*	18	-6	23	0.016	136
32	Precuneus	7	-24	-42	54	0.017	128
33	Thalamus	*	18	-27	19	0.016	112
	Women						
1	Left Amygdala, Left Hippocampus, Right Hippocampus, Left Thalamus: Ventral lateral nucleus, Left Superior Temporal Gyrus, Right Superior Temporal Gyrus, Left Precentral Gyrus, Left Inferior Frontal Gyrus, Left Insula, Left Middle Frontal Gyrus, Right Subthalamic Nucleus,	28, 38, 6, 47, 13, 46, 9, 35, 19	-11	-2	-10	0.066	67400

	Left Putamen, Right Putamen, Left Cerebellum: Culmen						
2	Left Superior Frontal Gyrus, Right Superior Frontal Gyrus, Left Anterior Cingulate, Right Anterior Cingulate, Left Medial Frontal Gyrus, Right Medial Frontal Gyrus	9, 32, 24, 10	0	50	8	0.038	16136
3	Left Superior Frontal Gyrus, Right Cingulate Gyrus, Left Medial Frontal Gyrus	6, 32	0	19	54	0.033	8304
4	Culmen, Parahippocampal Cortex, Inferior Temporal Gyrus, Cerebellum: Declive	19, 37	32	-54	-19	0.018	5640
5	Inferior Frontal Gyrus, Insula	47, 45	45	23	-9	0.019	5640
6	Superior Temporal Gyrus, Middle Occipital Gyrus, Middle Temporal Gyrus, Angular Gyrus	22, 19, 39	-50	-63	19	0.022	5008
7	Fusiform Gyrus, Cerebellum: Declive, Lingual Gyrus	37, 19, 18	-37	-66	-14	0.019	4136
8	Inferior Temporal Gyrus, Middle Temporal Gyrus	37	51	-67	7	0.023	3120
9	Superior Temporal Gyrus	22	59	-40	10	0.023	2968
10	Fusiform Gyrus, Lingual Gyrus, Cerebellum: Declive	19, 18	24	-81	-10	0.020	1872
11	Cingulate Gyrus	32	-7	30	31	0.016	1688
12	Inferior Frontal Gyrus	9, 44	55	15	18	0.017	1576
13	Lingual Gyrus	18	-10	-78	2	0.018	1544
14	Precentral Gyrus	6	51	3	37	0.014	1048
15	Middle Frontal Gyrus	46	52	32	15	0.020	968
16	Precuneus, Superior Parietal Lobule	7	3	-63	63	0.022	944
17	Posterior Cingulate	30	5	-53	15	0.016	768
18	Cingulate Gyrus	24	-4	-2	37	0.011	768
19	Superior Temporal Gyrus	22	55	-18	-2	0.016	672
20	Caudate Body	*	12	3	11	0.014	560
21	Precentral Gyrus	4	44	-10	59	0.028	480
22	Putamen	*	-25	3	13	0.012	416
23	Parahippocampal Cortex	30	21	-51	7	0.012	400
24	Precuneus	7	-24	-42	54	0.017	392
25	Lingual Gyrus	18	-7	-96	-9	0.012	368
26	Superior Parietal Lobule	7	34	-56	61	0.014	368
27	Superior Temporal Gyrus	39	54	-55	36	0.013	360
28	Cingulate Gyrus	24	5	-19	41	0.014	352
29	Superior Temporal Gyrus	38, 22	-57	16	-13	0.013	344
30	Lingual Gyrus	18	13	-75	-2	0.011	344
31	Insula	13	-41	-18	16	0.011	320
32	Sub-Gyral	21	49	-7	-17	0.014	304
33	Middle Frontal Gyrus	6	43	17	51	0.014	264
34	Superior Temporal Gyrus	22	-48	-12	-9	0.012	248
35	Cerebellum: Uvula	*	14	-80	-35	0.013	240
36	Sub-Gyral	20	-42	-17	-27	0.012	232
37	Cerebellum: Declive	*	50	-68	-17	0.014	224
38	Inferior Parietal Lobule, Postcentral Gyrus	40, 3	-45	-23	51	0.010	184
39	Inferior Parietal Lobule	40	-36	-50	63	0.013	176
40	Middle Temporal Gyrus	39	-43	-75	27	0.010	168
41	Cuneus	19	12	-85	39	0.013	168
42	Insula	13	37	-20	18	0.011	160
43	Precuneus	31	-9	-62	34	0.010	144
44	Culmen	*	2	-60	-22	0.010	136
45	Thalamus	*	18	-24	4	0.010	104
46	Insula	13	50	-12	15	0.010	104
	Men						
1	Amygdala, Inferior Frontal Gyrus, Precentral Gyrus, Insula, Middle Frontal Gyrus, Superior Temporal Gyrus, Lateral Globus Pallidus, Claustrum, Perirhinal Cortex, Thalamus: Ventral anterior nucleus	45, 6, 11, 38, 35, 44, 13, 47, 9	37	9	-6	0.043	40136
2	Amygdala, Inferior Frontal Gyrus, Insula, Putamen, Thalamus: Ventral Posterior Lateral Nucleus, Insula	47, 13, 45	-33	11	-14	0.038	38856
3	Posterior Cingulate, Cerebellum: Culmen	23, 30, 29	4	-45	13	0.023	7656
4	Parahippocampal Cortex, Middle Temporal Gyrus,	19, 37, 36	-39	-49	-9	0.017	3432

	Fusiform Gyrus						
5	Fusiform Gyrus, Cerebellum: Declive	19	42	-73	-12	0.027	3312
6	Left Medial Frontal Gyrus, Right Medial Frontal Gyrus, Left Superior Frontal Gyrus	9	-2	58	24	0.020	3144
7	Right Cingulate Gyrus, Left Superior Frontal Gyrus	32, 6	5	19	39	0.018	2696
8	Fusiform Gyrus	20	46	-44	-17	0.031	2688
9	Middle Temporal Gyrus, Superior Temporal Gyrus	39, 22, 13	-46	-59	24	0.016	2616
10	Fusiform Gyrus, Inferior Temporal Gyrus	19	-44	-79	-6	0.022	2520
11	Inferior Frontal Gyrus	9	-45	8	28	0.022	2408
12	Anterior Cingulate	24, 32	11	34	18	0.018	2232
13	Anterior Cingulate	32	5	50	-8	0.016	1496
14	Posterior Cingulate, Lingual Gyrus	31, 18	-6	-69	18	0.015	1448
15	Medial Frontal Gyrus	10	-7	58	0	0.018	1368
16	Middle Frontal Gyrus	9, 8	-26	35	38	0.015	1368
17	Precentral Gyrus, Postcentral Gyrus	4, 3	-40	-15	58	0.018	1320
18	Postcentral Gyrus	43	-55	-14	14	0.013	1096
19	Superior Temporal Gyrus, Middle Temporal Gyrus	22, 21	-53	-6	-9	0.013	1080
20	Lingual Gyrus	19	-16	-48	-4	0.017	1040
21	Cuneus, Lingual Gyrus	17, 18	9	-83	13	0.014	760
22	Caudate Body	*	-7	9	14	0.018	712
23	Supramarginal Gyrus	40	43	-46	32	0.015	672
24	Caudate Body	*	19	-6	22	0.016	640
25	Middle Temporal Gyrus	20	60	-34	-10	0.015	584
26	Superior Temporal Gyrus	22	65	-43	7	0.018	576
27	Middle Frontal Gyrus	9	45	35	25	0.013	576
28	Middle Temporal Gyrus	21	60	1	-20	0.015	552
29	Thalamus	*	18	-27	19	0.016	512
30	Precentral Gyrus	6	-36	-9	47	0.013	488
31	Medial Frontal Gyrus	10	-2	63	-16	0.013	472
32	Fusiform Gyrus	18	-21	-97	-14	0.013	464
33	Middle Temporal Gyrus	21	-58	-34	-6	0.013	424
34	Fusiform Gyrus, Inferior Temporal Gyrus	19, 37	28	-53	-8	0.011	408
35	Middle Occipital Gyrus	19	-26	-86	26	0.013	400
36	Anterior Cingulate	24, 32	2	33	-12	0.010	368
37	Inferior Temporal Gyrus	20	-60	-12	-27	0.012	328
38	Culmen	*	23	-55	-23	0.012	328
39	Precuneus	7	4	-65	50	0.012	248
40	Middle Frontal Gyrus	6	-37	19	47	0.012	232
41	Precuneus	7	26	-55	55	0.012	232
42	Superior Parietal Lobule	7	32	-50	66	0.012	192
43	Medial Frontal Gyrus	9	-11	47	16	0.010	168
44	Caudate Head	*	-4	20	-3	0.010	152
45	Precuneus	31	-11	-50	34	0.010	152
46	No gray matter	*	34	29	21	0.009	144
47	Cuneus	19	15	-78	44	0.011	144
48	Middle Temporal Gyrus	21	-63	-16	-18	0.010	112
49	Precuneus	31	33	-74	32	0.010	112

Clusters demonstrating significant concordance across studies ($p < .05$, FDR-corrected for multiple comparisons). For each cluster, labels denote regions which contained the peak ALE activation, and regions which contained secondary peaks.

[a]BA = Brodmann's area, if applicable

[b]X, Y, and Z coordinates represent weighted central activation likelihood focus in MNI space.

Figure S1. ALE maps for analyses of emotion across all participants (analysis of the balanced dataset)

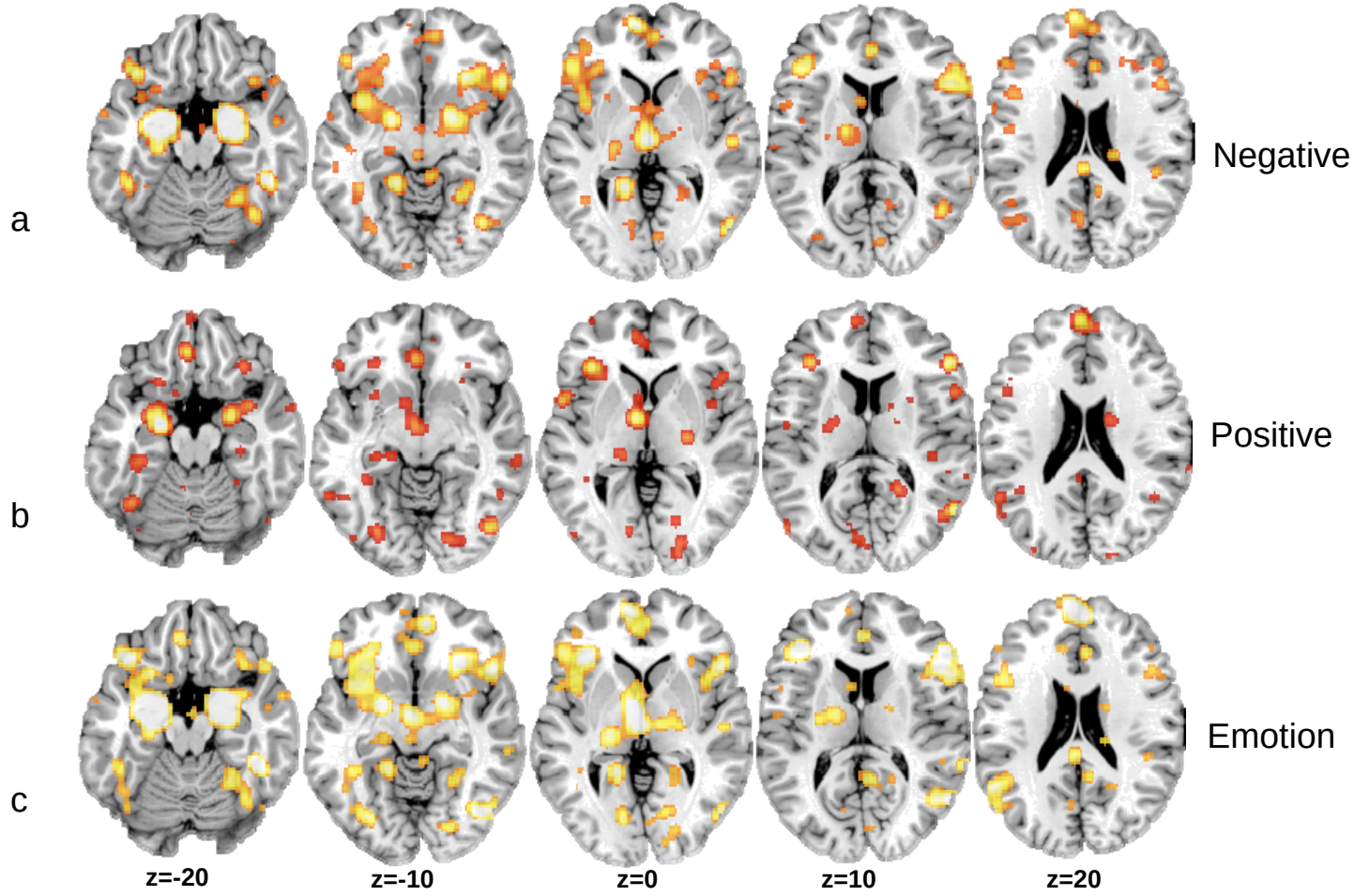

Figure S1. Regions of significant activation likelihood ($p < 0.05$, FDR-corrected for multiple comparisons) for contrasts collapsed across studies of women and men, overlaid on a representative single-subject structural anatomical image template in MNI space. S1a: Significant ALE clusters for negative emotional contrasts. S1b: Significant ALE clusters for positive emotional contrasts. S1c:

Significant ALE clusters for all emotional contrasts (positive and negative emotion stimuli). Images are presented in neurological orientation. Brighter colors indicate greater activation likelihood.

Figure S2. ALE maps of sex differences (analysis of the complete dataset)

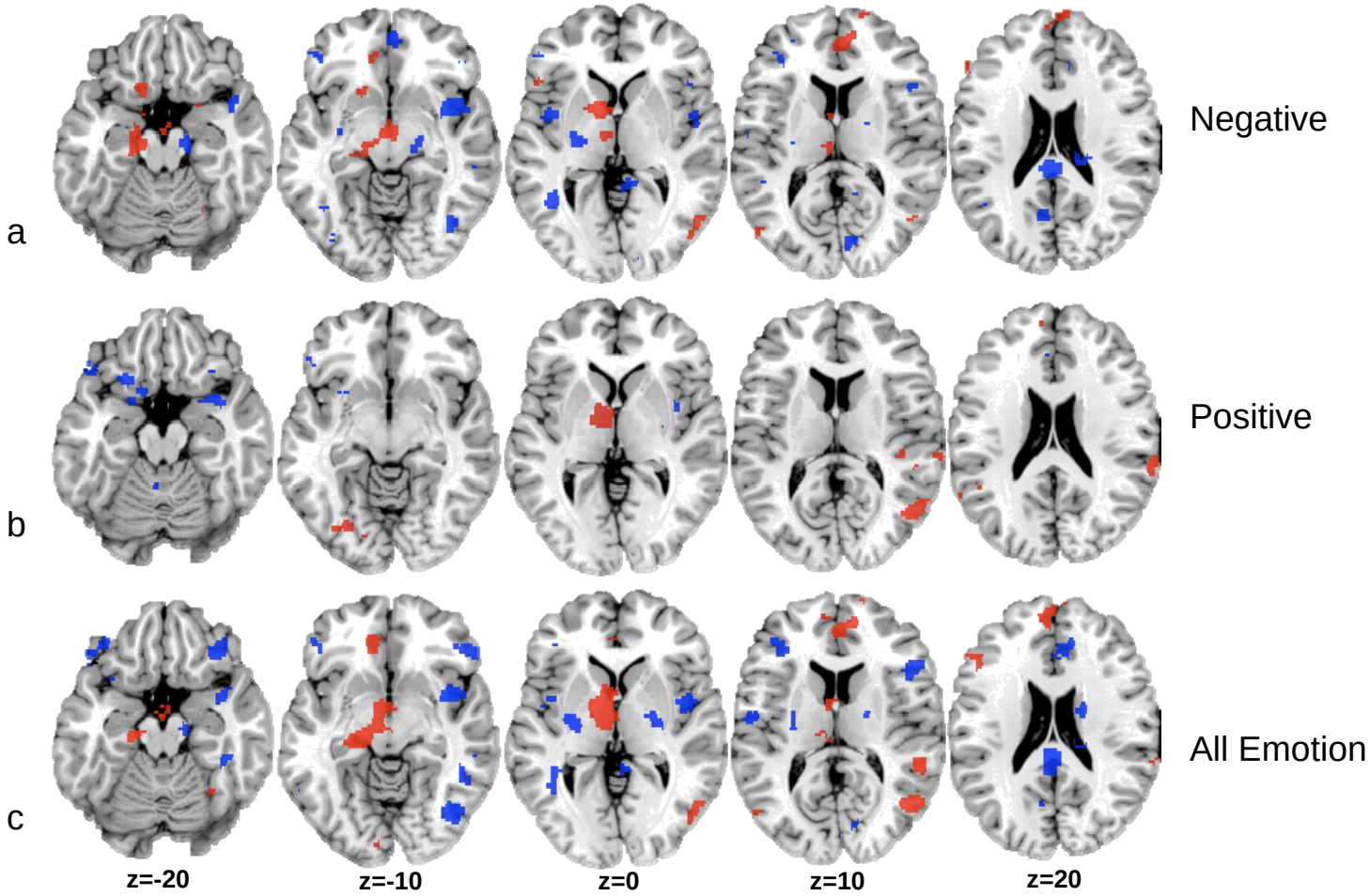

Figure S2. Regions of significant differences in activation likelihood for women vs. men ($p < 0.05$, corrected). S2a: Sex differences in activation likelihood for contrasts of negative emotion. Red color scale: greater activation for women than men. S2c: Sex differences in activation likelihood for all emotional contrasts, collapsed across positive and negative valences. S2b: Sex differences

in activation likelihood for contrasts of positive emotion. Blue color scale: greater activation for men than women. Images presented in neurological orientation. Brighter colors indicate greater activation likelihood.

Appendix B. Supplement to Study 2

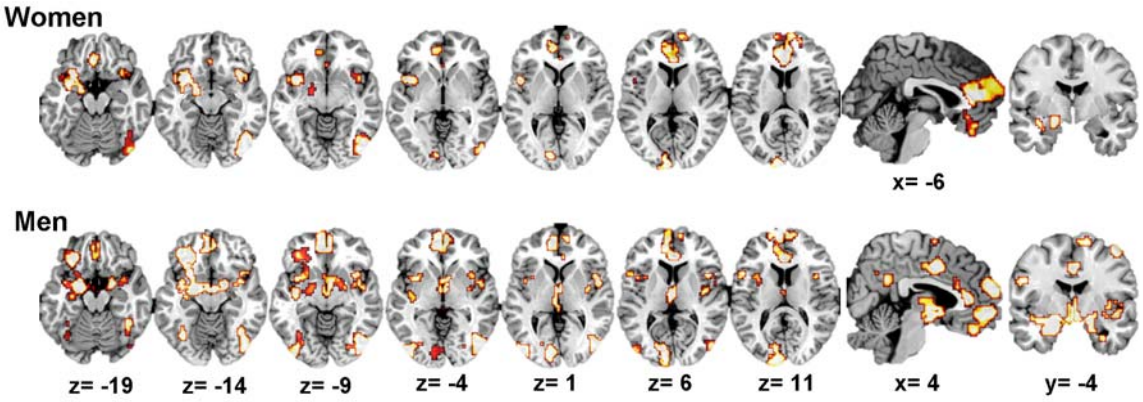

Figure S1. Responses to negative emotional stimuli in women and men, across all gray-matter voxels.

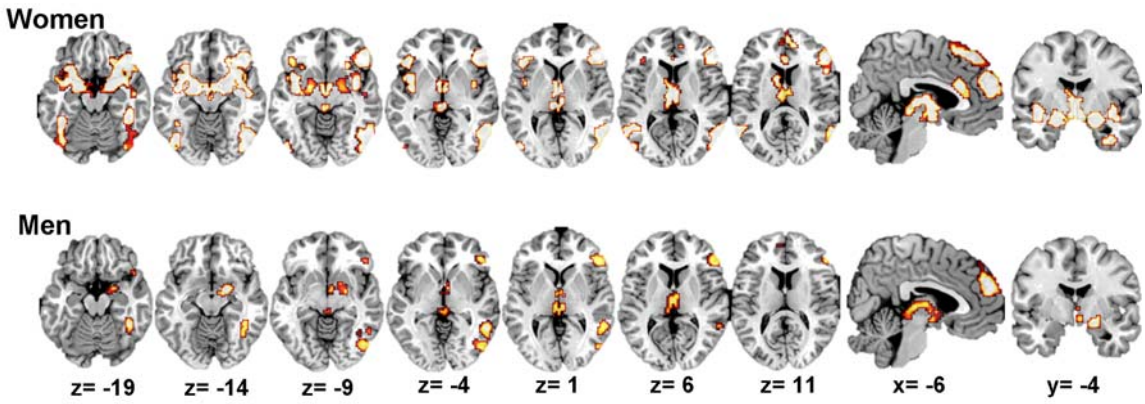

Figure S2. Responses to positive emotional stimuli in women and men, across all gray-matter voxels.

Appendix C. Supplement to Study 3

Table S1
Enhanced encoding-related connectivity with left amygdala for negative relative to neutral stimuli

	HEM	MNI Coord. x	y	z	Z	k
Women > Men						
*Amygdala	L	-18	-8	-14	3.3	61
Hippocampus	L	-14	-14	-10	2.6	(LM)
Inf. Temporal G.	R	54	-44	-12	3.2	139
Inf. Temporal G.	R	46	-50	-8	2.9	(LM)
Mid. Temporal G.	R	58	-44	-4	2.6	(LM)
Mid. Frontal G.	R	34	32	22	4.4	362
Mid. Frontal G.	R	36	32	32	3.2	(LM)
Mid. Frontal G.	R	40	38	16	3.0	(LM)
Mid. Frontal G.	R	28	20	54	3.4	212
Mid. Frontal G.	R	34	26	52	3.1	(LM)
Mid. Frontal G.	R	22	14	54	3.1	(LM)
Sup. Frontal G.	R	6	46	34	3.7	175
Sup. Frontal G.	R	6	54	36	3.6	(LM)
Sup. Frontal G.	R	10	52	44	3.0	(LM)
Thalamus	L	-14	-34	6	4.0	278
Post. Cingulate G.	L	-6	-38	16	3.6	(LM)
Thalamus	L	-24	-28	12	3.4	(LM)
Mid. Cingulate G.	R	4	-4	28	2.9	78
Thalamus	L	-4	-8	24	2.5	(LM)
Putamen	R	26	0	12	4.0	188
Putamen	R	36	-8	6	3.3	(LM)
Caudate	R	26	-2	20	3.2	(LM)
Insula	L	-32	-2	12	3.4	109
Insula	L	-38	-8	12	3.1	(LM)
Insula	L	-30	2	20	3.0	(LM)
Precuneus	L	-12	-68	58	3.0	150
Sup. Parietal G.	L	-30	-64	54	2.8	(LM)
Sup. Parietal G.	L	-22	-70	54	2.7	(LM)
Precuneus	L	-8	-56	40	3.0	62
Precuneus	L	-6	-48	46	2.4	(LM)
Supramarginal G.	R	40	-36	34	3.0	63
Angular G.	R	42	-44	32	2.6	(LM)
Angular G.	R	48	-50	28	2.6	(LM)
Sup. Frontal G.	L	-32	-8	66	3.3	70
Precentral G.	L	-26	-14	64	2.4	(LM)
Paracentral Lobule	L	-12	-20	78	3.2	63
Precentral G.	L	-20	-22	76	2.7	(LM)
Supp. Motor Area	L	-8	-12	76	2.6	(LM)
Postcentral G.	L	-38	-32	52	3.3	199
Inf. Parietal G.	L	-38	-28	36	2.8	(LM)
Postcentral G.	L	-32	-40	52	2.5	(LM)
Sup. Frontal G.	L	-24	-10	74	2.4	(LM)
Postcentral G.	R	36	-38	54	3.1	74
Postcentral G.	R	30	-32	46	2.6	(LM)
Postcentral G.	L	-50	-20	24	2.7	69
Postcentral G.	L	-56	-16	34	2.7	(LM)
Inf. Parietal G.	L	-54	-26	36	2.5	(LM)
Inf. Occipital G.	L	-38	-56	-6	3.5	142
Fusiform G.	L	-32	-52	-14	2.9	(LM)
Cerebellum	L	-24	-56	-24	2.8	(LM)
Cerebellum	--	0	-58	0	3.6	102
Cerebellum	R	6	-48	4	2.6	(LM)
Lingual G.	R	4	-62	8	2.4	(LM)
Cerebellum	R	4	-86	-38	3.5	87
Cerebellum	L	-6	-80	-42	2.9	(LM)
Cerebellum	R	4	-78	-42	2.5	(LM)
Men > Women						
Temporal Pole	L	-44	10	-24	3.3	117
Temporal Pole	L	-46	18	-24	2.9	(LM)
Mid. Temporal G.	L	-56	-2	-20	2.8	(LM)

	HEM	MNI Coord. x	y	z	Z	k
Women						
Sup. Frontal G.	L	-12	44	-28	4.0	89
G. Rectus	L	-2	44	-30	3.0	(LM)
Sup. Frontal G.	L	-8	52	-26	3.0	(LM)
Inf. Frontal G.	R	36	26	28	3.7	59
Mid. Frontal G.	R	34	28	18	2.5	(LM)
Sup. Frontal G.	R	18	10	50	3.5	70
Mid. Frontal G.	R	28	16	54	2.4	(LM)
Sup. Frontal G.	R	6	46	34	3.4	144
Sup. Frontal G.	R	10	46	46	3.2	(LM)
Sup. Frontal G.	R	6	54	36	2.9	(LM)
Sup. Frontal G.	R	18	68	-2	3.1	118
Sup. Frontal G.	R	14	72	4	3.0	(LM)
Mid. Frontal G.	R	22	64	-12	2.5	(LM)
Thalamus	L	-6	-22	16	3.1	73
Thalamus	--	0	-18	22	2.8	(LM)
Putamen	R	22	2	14	3.7	107
Putamen	R	28	-2	18	3.4	(LM)
Putamen	R	30	-8	12	3.0	(LM)
Post. Cingulate G.	L	-6	-38	12	3.6	653
Precuneus	R	12	-50	12	3.6	(LM)
Thalamus	L	-14	-34	6	3.5	(LM)
Precuneus	R	4	-52	66	4.3	918
Precuneus	L	-4	-56	66	3.7	(LM)
Precuneus	R	6	-64	48	3.2	(LM)
Supramarginal G.	L	-54	-26	28	3.6	145
Postcentral G.	L	-56	-18	30	3.3	(LM)
Supramarginal G.	L	-44	-28	34	2.9	(LM)
Inf. Parietal G.	L	-38	-38	52	3.0	133
Postcentral G.	L	-44	-38	58	3.0	(LM)
Postcentral G.	L	-36	-30	54	2.6	(LM)
Supramarginal G.	R	58	-26	36	3.0	115
Supramarginal G.	R	54	-32	24	2.7	(LM)
Supramarginal G.	R	58	-22	28	2.7	(LM)
Postcentral G.	R	30	-38	52	3.6	584
Sup. Parietal G.	R	40	-46	60	3.4	(LM)
Supramarginal G.	R	46	-38	40	3.1	(LM)
Supp. Motor Area	R	4	-10	70	3.5	89
Paracentral Lobule	--	0	-16	64	2.6	(LM)
Supp. Motor Area	L	-4	-12	70	2.5	(LM)
Inf. Occipital G.	L	-44	-68	-12	3.2	247
Mid. Temporal G.	L	-50	-62	0	3.0	(LM)
Mid. Temporal G.	L	-50	-52	6	2.9	(LM)
Inf. Occipital G.	R	48	-62	-14	3.0	177
Inf. Temporal G.	R	48	-54	-12	3.0	(LM)
Inf. Temporal G.	R	54	-62	-20	2.8	(LM)
Cerebellum	L	-20	-96	-26	3.7	98
Cerebellum	L	-24	-90	-30	3.3	(LM)
Lingual G.	L	-28	-94	-22	2.5	(LM)
Cerebellum	L	-56	-64	-30	3.6	68
Inf. Temporal G.	L	-54	-62	-22	3.4	(LM)
Cerebellum	L	-56	-60	-38	2.5	(LM)
Cerebellum	L	-32	-62	-24	3.3	219
Cerebellum	L	-18	-70	-26	3.0	(LM)
Cerebellum	L	-20	-62	-20	2.8	(LM)
Men						
G. Rectus	L	-12	38	-18	3.3	90
Sup. Frontal G.	L	-8	40	-26	3.0	(LM)

Table S2
Enhanced encoding-related connectivity with right amygdala for negative relative to neutral stimuli

	HEM	MNI Coordinates x	y	z	Z	k
Women > Men						
Putamen	L	-20	4	-6	3.7	300
Amygdala	L	-20	2	-18	3.2	(LM)
Amygdala	L	-26	-2	-12	3.1	(LM)
Sup. Temporal G.	L	-36	-40	8	3.9	309
Mid. Occipital G.	L	-36	-70	0	3.4	(LM)
Mid. Temporal G.	L	-42	-52	8	3.1	(LM)
Inf. Temporal G.	L	-62	-46	-14	3.3	83
Mid. Temporal G.	L	-54	-44	-6	2.5	(LM)
Mid. Temporal G.	L	-62	-50	-4	2.4	(LM)
Inf. Temporal G.	R	46	-58	-8	3.2	77
Inf. Temporal G.	R	44	-50	-8	2.8	(LM)
Ant. Cingulate G.	L	-6	30	12	3.3	77
Ant. Cingulate G.	L	-6	40	12	2.9	(LM)
Ant. Cingulate G.	L	-8	26	20	2.6	(LM)
G. Rectus	L	-2	22	-28	3.7	104
Sup. Frontal G.	L	-10	20	-28	3.2	(LM)
G. Rectus	--	0	14	-30	3.1	(LM)
Olfactory cortex	R	6	14	-14	3.6	158
Olfactory cortex	R	2	10	-20	2.7	(LM)
Sup. Frontal G.	R	12	12	-26	2.7	(LM)
Sup. Frontal G.	L	-16	14	52	3.4	188
Sup. Frontal G.	L	-14	24	52	3.1	(LM)
Sup. Frontal G.	L	-22	22	54	2.9	(LM)
Inf. Frontal G.	R	46	34	6	3.2	65
Inf. Frontal G.	R	58	34	10	2.8	(LM)
Thalamus	R	18	-28	4	3.5	96
Thalamus	R	8	-20	0	2.6	(LM)
Thalamus	R	22	-14	0	2.8	75
Thalamus	R	18	-10	8	2.8	(LM)
Putamen	R	30	-16	-2	2.8	(LM)
Angular G.	R	42	-50	28	4.1	619
Mid. Occipital G.	R	40	-68	28	4.0	(LM)
Angular G.	R	42	-62	22	3.5	(LM)
Precentral G.	R	18	-16	76	3.1	59
Sup. Frontal G.	R	18	-6	72	2.6	(LM)
Postcentral G.	R	30	-38	54	3.5	113
Precentral G.	R	36	-28	58	3.1	(LM)
Inf. Occipital G.	L	-26	-82	-8	2.9	62
Fusiform G.	L	-30	-38	-24	3.1	65
Cerebellum	L	-20	-38	-24	2.5	(LM)
Lingual G.	R	16	-82	-8	3.0	210
Cerebellum	R	12	-70	-14	3.0	(LM)
Lingual G.	R	6	-70	-8	2.8	(LM)
Cerebellum	R	12	-86	-36	3.9	124
Cerebellum	R	2	-86	-36	3.1	(LM)
Cerebellum	R	6	-78	-36	2.3	(LM)
Cerebellum	R	36	-46	-38	3.4	76
Cerebellum	R	34	-38	-38	3.0	(LM)
Cerebellum	L	-24	-64	-44	3.0	67
Men > Women						
Inf. Temporal G.	L	-38	-8	-48	3.2	59
Fusiform G.	L	-38	-10	-40	2.9	(LM)

	HEM	MNI Coordinates x	y	z	Z	k
Women						
Mid. Temporal G.	L	-38	-44	4	3.6	104
Mid. Temporal G.	L	-38	-56	-2	3.1	(LM)
Mid. Temporal G.	L	-40	-50	10	2.7	(LM)
Mid. Temporal G.	R	48	-56	-2	3.2	84
Inf. Temporal G.	R	46	-56	-12	2.9	(LM)
Inf. Temporal G.	R	46	-48	-8	2.4	(LM)
G. Rectus	L	-2	22	-32	4.3	102
G. Rectus	--	0	30	-28	3.2	(LM)
Sup. Frontal G.	L	-10	26	-28	3.0	(LM)
Olfactory cortex	R	10	16	-18	4.2	228
Inf. Frontal G.	R	18	20	-20	3.5	(LM)
G. Rectus	R	10	10	-24	3.1	(LM)
Precuneus	L	-6	-58	34	3.6	112
Precuneus	L	-12	-54	38	3.2	(LM)
Angular G.	R	40	-50	24	3.1	63
Sup. Temporal G.	R	48	-58	22	2.6	(LM)
Cerebellum	R	6	-86	-36	2.9	60
Cerebellum	R	16	-86	-32	2.5	(LM)
Cerebellum	R	4	-82	-28	2.4	(LM)
Precuneus	R	4	-56	64	2.7	59
Precuneus	L	-4	-56	66	2.5	(LM)
Precuneus	--	0	-48	68	2.5	(LM)
Cerebellum	L	-26	-62	-48	4.3	195
Cerebellum	L	-28	-64	-40	3.4	(LM)
Cerebellum	L	-20	-68	-44	3.1	(LM)
Cerebellum	L	-56	-62	-36	3.8	68
Cerebellum	L	-54	-66	-26	3.3	(LM)
Men						
G. Rectus	L	-8	40	-20	3.2	69
Sup. Frontal G.	L	-16	42	-20	2.6	(LM)

Table S3
Enhanced encoding-related connectivity with left amygdala for positive relative to neutral stimuli

	HEM	MNI Coordinates x	y	z	Z	k
Women > Men						
Heschl G.	L	-36	-26	6	3.37	256
Mid. Temporal G.	L	-44	-26	-2	3.21	(LM)
Insula	L	-32	-10	12	3.06	(LM)
Sup. Temporal G.	R	52	-10	-6	2.97	114
Inf. Temporal G.	R	52	-16	-18	2.86	(LM)
Mid. Temporal G.	R	52	-20	-10	2.7	(LM)
Mid. Cingulate G.	R	4	-16	30	3.4	283
Ant. Cingulate G.	R	0	-2	26	3.3	(LM)
Ant. Cingulate G.	R	0	6	24	3.01	(LM)
Mid. Cingulate G.	L	-14	-30	34	3.74	110
Mid. Cingulate G.	L	-16	-38	28	2.92	(LM)
Sup. Frontal G.	L	-6	62	4	3.6	152
Sup. Frontal G.	R	4	64	4	2.47	(LM)
Sup. Frontal G.	L	-10	68	8	2.4	(LM)
Inf. Frontal G.	R	24	20	-24	3.51	75
Insula	R	28	22	-16	2.38	(LM)
Sup. Frontal G.	L	-20	58	22	2.92	60
Sup. Frontal G.	L	-14	62	18	2.48	(LM)
Sup. Frontal G.	L	-20	56	12	2.36	(LM)
Thalamus	L	-22	-26	4	3.16	81
Thalamus	L	-14	-34	4	3.02	(LM)
Thalamus	L	-14	-24	4	3.02	(LM)
Postcentral G.	L	-38	-28	52	2.9	147
Inf. Parietal G.	L	-32	-40	36	2.81	(LM)
Precentral G.	L	-32	-20	54	2.78	(LM)
Mid. Cingulate G.	R	10	-2	42	2.89	71
Supp. Motor Area	R	2	-4	48	2.47	(LM)
Supp. Motor Area	R	10	-4	50	2.45	(LM)
Lingual G.	R	18	-80	-6	3.78	359
Lingual G.	R	10	-76	-12	3.22	(LM)
Inf. Occipital G.	R	30	-86	-12	3.09	(LM)
Mid. Occipital G.	L	-36	-62	-4	3.68	71
Mid. Occipital G.	L	-38	-70	-2	3.25	(LM)
Cuneus	R	10	-102	10	2.84	61
Sup. Occipital G.	R	18	-100	16	2.83	(LM)
Lingual G.	R	10	-44	0	3.05	83
Cerebellum: Vermis	R	6	-52	-2	2.67	(LM)
Cerebellum	R	40	-68	-36	4.3	553
Cerebellum	R	42	-76	-38	3.69	(LM)
Cerebellum	R	38	-82	-42	3.37	(LM)
Cerebellum	L	-6	-86	-38	4.27	542
Cerebellum	R	4	-86	-36	3.99	(LM)
Cerebellum	L	-12	-82	-34	3.3	(LM)
Cerebellum	L	-42	-68	-44	3.55	251
Cerebellum	L	-42	-62	-50	3.15	(LM)
Cerebellum	L	-36	-74	-42	3.1	(LM)
Cerebellum	L	-32	-46	-26	3.2	171
Cerebellum	L	-32	-40	-44	3.15	(LM)
Cerebellum	L	-30	-32	-38	2.83	(LM)
Men > Women						
*No significant clusters						

	HEM	MNI Coordinates x	y	z	Z	k
Women						
Hippocampus	R	34	-20	-12	2.89	66
Parahipp. G.	R	22	-20	-18	2.62	(LM)
Hippocampus	R	30	-12	-14	2.38	(LM)
Sup. Temporal G.	L	-42	-32	4	4.56	1275
Insula	L	-32	-10	16	4	(LM)
Insula	L	-32	-20	10	3.99	(LM)
Sup. Temporal G.	R	60	-10	0	3.56	148
Sup. Temporal G.	R	54	-20	0	2.83	(LM)
Sup. Temporal G.	R	66	-8	8	2.65	(LM)
Mid. Frontal G.	L	-22	44	16	4.59	1031
Mid. Frontal G.	L	-30	38	28	4.38	(LM)
Inf. Frontal G.	L	-38	26	24	3.69	(LM)
Mid. Frontal G.	R	40	40	18	4.24	1170
Mid. Frontal G.	R	32	40	22	4.08	(LM)
Mid. Frontal G.	R	28	44	30	3.66	(LM)
Mid. Frontal G.	L	-26	26	36	4.11	348
Mid. Frontal G.	L	-30	10	38	3.39	(LM)
Mid. Frontal G.	L	-26	14	60	3.22	(LM)
Mid. Frontal G.	R	30	16	52	3.53	102
Sup. Frontal G.	R	20	14	58	2.82	(LM)
Mid. Frontal G.	R	28	10	58	2.6	(LM)
Mid. Frontal G.	R	40	56	-8	2.72	67
Inf. Frontal G.	R	36	44	-18	2.66	(LM)
Mid. Frontal G.	R	42	50	-14	2.59	(LM)
Inf. Frontal G.	R	24	20	-24	3.9	81
Sup. Frontal G.	R	22	20	-14	2.66	(LM)
Sup. Frontal G.	R	4	68	0	3.75	119
Sup. Frontal G.	--	0	64	8	2.71	(LM)
Med. Frontal G.	R	6	62	-6	2.7	(LM)
Sup. Frontal G.	R	10	64	18	2.98	59
Sup. Frontal G.	R	2	64	24	2.57	(LM)
Insula	L	-36	16	6	4.33	500
Inf. Frontal G.	L	-46	16	6	3.68	(LM)
Mid. Cingulate G.	L	-14	-32	36	3.79	152
Mid. Cingulate G.	L	-14	-38	42	3.03	(LM)
Mid. Cingulate G.	L	-12	-30	44	2.68	(LM)
Insula	L	-32	24	10	3.42	(LM)
Insula	R	34	-8	10	4.1	1123
Insula	R	36	4	-8	4.06	(LM)
Insula	R	40	2	0	3.96	(LM)
Insula	L	-36	2	-14	3.85	253
Mid. Temporal G.	L	-38	2	-26	3.56	(LM)
Mid. Temporal G.	L	-48	-2	-30	3.25	(LM)
Thalamus	R	12	-16	12	3.84	311
Thalamus	R	8	-20	6	3.32	(LM)
Thalamus	R	10	-26	-6	3.2	(LM)
Thalamus	L	-16	-22	4	3.62	329
Thalamus	L	-10	-8	4	3.38	(LM)
Thalamus	L	-6	-26	10	3.12	(LM)
Mid. Occipital G.	L	-50	-74	0	4.45	572
Mid. Occipital G.	L	-48	-74	8	3.91	(LM)
Mid. Temporal G.	L	-42	-70	14	3.54	(LM)
Sup. Frontal G.	R	16	2	58	4.09	4923
Postcentral G.	R	36	-26	46	4.08	(LM)
Supp. Motor Area	R	4	-4	48	3.97	(LM)
Post. Cingulate G.	R	6	-44	10	3.96	433
Lingual G.	R	10	-44	0	3.35	(LM)
Post. Cingulate G.	R	16	-44	18	3.17	(LM)
Postcentral G.	L	-42	-44	64	3.77	2373
Inf. Parietal G.	L	-32	-40	48	3.71	(LM)

	HEM	MNI Coordinates x	y	z	Z	k
Women (continued)						
Sup. Parietal G.	L	-32	-52	58	3.67	(LM)
Mid. Occipital G.	L	-38	-88	-2	3.53	156
Inf. Occipital G.	L	-32	-86	-12	3.25	(LM)
Mid. Occipital G.	L	-36	-92	8	2.93	(LM)
Sup. Occipital G.	R	30	-68	22	3.35	245
Angular G.	R	40	-70	36	2.83	(LM)
Mid. Occipital G.	R	30	-74	34	2.79	(LM)
Cuneus	R	10	-102	6	3.25	69
Cuneus	R	8	-100	14	2.7	(LM)
Sup. Occipital G.	R	16	-100	16	2.63	(LM)
Supramarginal G.	R	60	-26	24	3.09	91
Supramarginal G.	R	54	-32	30	2.74	(LM)
Supramarginal G.	R	64	-22	18	2.55	(LM)
Sup. Temporal G.	L	-48	-40	16	3.06	59
Mid. Temporal G.	L	-50	-50	16	2.45	(LM)
Supramarginal G.	L	-56	-28	36	2.94	163
Supramarginal G.	L	-62	-34	30	2.71	(LM)
Inf. Parietal G.	L	-56	-26	44	2.67	(LM)
Cuneus	L	-4	-92	34	2.94	64
Cuneus	R	0	-80	28	2.57	(LM)
Cerebellum	L	-20	-62	-20	4.61	2165
Cerebellum	L	-32	-50	-26	3.95	(LM)
Cerebellum	R	0	-84	-36	3.94	(LM)
Cerebellum	R	46	-70	-32	4.17	2152
Cerebellum	R	52	-64	-32	4.03	(LM)
Lingual G.	R	16	-88	-12	3.84	(LM)
Cerebellum	L	-38	-46	-50	3.5	103
Cerebellum	L	-32	-38	-42	3.16	(LM)
Cerebellum	L	-26	-42	-38	2.77	(LM)
Cerebellum	R	40	-46	-32	3.5	413
Cerebellum	R	34	-38	-44	3.28	(LM)
Cerebellum	R	34	-46	-48	3.21	(LM)

	HEM	MNI Coordinates x	y	z	Z	k
Men						
Inf. Temporal G.	R	58	-56	-18	3.05	123
Inf. Temporal G.	R	58	-64	-20	3.04	(LM)
Inf. Temporal G.	R	64	-52	-14	2.57	(LM)
Inf. Frontal G.	R	54	40	4	4.56	486
Inf. Frontal G.	R	46	34	10	3.61	(LM)
Inf. Frontal G.	R	40	26	12	3.48	(LM)
Putamen	R	28	22	4	4.21	806
Inf. Frontal G.	R	52	10	16	3.87	(LM)
Ant. Cingulate G.	R	22	34	10	3.58	(LM)
Mid. Frontal G.	R	24	8	46	3.01	100
Sup. Frontal G.	R	28	2	54	2.97	(LM)
Sup. Frontal G.	R	30	-2	64	2.87	(LM)
Sup. Frontal G.	L	-12	16	40	3.63	105
Mid. Cingulate G.	L	-14	4	40	2.88	(LM)
Supp. Motor Area	L	-6	20	46	2.75	(LM)
G. Rectus	L	-6	28	-26	3.36	90
Sup. Frontal G.	L	-12	32	-22	3.32	(LM)
Angular G.	R	30	-64	46	4.18	423
Inf. Parietal G.	R	36	-52	48	3.5	(LM)
Precuneus	R	10	-62	52	2.93	(LM)
Sup. Parietal G.	L	-18	-70	42	3.42	59
Paracentral Lobule	R	6	-34	52	3.27	109
Mid. Cingulate G.	L	-2	-38	48	2.91	(LM)
Precuneus	R	10	-40	56	2.63	(LM)
Supramarginal G.	L	-66	-38	30	3.07	119
Supramarginal G.	L	-62	-22	28	3.06	(LM)
Supramarginal G.	L	-66	-30	28	2.63	(LM)
Rolandic Oper.	L	-62	4	6	3.55	106
Postcentral G.	L	-60	4	16	2.97	(LM)
Precentral G.	L	-50	2	18	2.7	(LM)
Precentral G.	R	58	-4	42	3.35	412
Supramarginal G.	R	70	-22	18	2.94	(LM)
Postcentral G.	R	68	-14	30	2.93	(LM)
Thalamus	R	0	-22	-6	2.91	66
Cerebellum: Vermis	R	4	-32	-2	2.42	(LM)
Mid. Occipital G.	L	-26	-94	-2	2.77	75
Mid. Occipital G.	L	-36	-96	-8	2.73	(LM)
Mid. Occipital G.	L	-32	-98	2	2.43	(LM)

Table S4
Enhanced encoding-related connectivity with right amygdala for positive relative to neutral stimuli

	HEM	MNI Coord. x	y	z	Z	k
Women > Men						
Amygdala	L	-20	-4	-18	2.88	83
Amygdala	L	-14	0	-14	2.62	(LM)
Olfactory cortex	L	-22	4	-12	2.48	(LM)
Sup. Temporal G.	L	-36	-40	8	3.31	76
Rolandic Oper.	L	-32	-36	14	2.68	(LM)
Hippocampus	L	-26	-40	6	2.48	(LM)
Ant. Cingulate G.	R	4	2	24	3.66	176
Mid. Cingulate G.	R	12	-2	40	3.05	(LM)
Ant. Cingulate G.	L	-4	6	24	3.01	(LM)
Postcentral G.	R	12	-50	72	3.27	70
Sup. Parietal G.	R	10	-58	72	2.83	(LM)
Postcentral G.	L	-48	-22	30	3.23	104
Supramarginal G.	L	-44	-26	24	2.98	(LM)
Postcentral G.	L	-52	-18	24	2.67	(LM)
Mid. Occipital G.	L	-36	-70	0	3.43	114
Fusiform G.	L	-32	-64	-6	3.24	(LM)
Inf. Temporal G.	L	-40	-60	-6	2.35	(LM)
Fusiform G.	R	28	-86	-12	3.38	82
Lingual G.	R	24	-88	-4	2.38	(LM)
Inf. Occipital G.	R	34	-92	-12	2.37	(LM)
Lingual G.	R	40	-82	-18	3.66	83
Cerebellum	L	-32	-44	-26	3.16	137
Fusiform G.	L	-40	-42	-26	3.13	(LM)
Fusiform G.	L	-30	-36	-24	2.72	(LM)
Cerebellum	L	-6	-82	-42	3.47	324
Cerebellum	R	6	-88	-36	3.36	(LM)
Cerebellum	L	-6	-86	-34	3.25	(LM)
Cerebellum: Vermis	R	6	-74	-12	3.4	75
Cerebellum: Vermis	R	6	-66	-8	2.45	(LM)
Cerebellum	R	34	-40	-48	3.29	240
Cerebellum	R	42	-40	-30	3.05	(LM)
Cerebellum	R	36	-44	-36	2.95	(LM)
Cerebellum	L	-26	-76	-30	2.82	85
Cerebellum	L	-28	-76	-22	2.54	(LM)
Cerebellum	L	-26	-68	-24	2.41	(LM)
Men > Women						
Cerebellum	R	6	-24	-42	3.8	88
Cerebellum	R	14	-32	-44	3.48	(LM)
Cerebellum	L	-8	-22	-44	3.19	(LM)

	HEM	MNI Coord. x	y	z	Z	k
Women						
Hippocampus	L	-36	-20	-14	3.35	133
Hippocampus	L	-24	-14	-18	2.95	(LM)
Hippocampus	L	-26	-16	-10	2.86	(LM)
Inf. Temporal G.	R	46	-16	-20	3.69	122
Parahipp. G.	R	38	-16	-24	3.02	(LM)
Inf. Temporal G.	R	52	-20	-30	2.75	(LM)
Temporal Pole	R	46	14	-30	3.62	71
Temporal Pole	R	38	10	-30	2.7	(LM)
Inf. Temporal G.	L	-56	-20	-26	3.42	143
Inf. Temporal G.	L	-56	-14	-32	3.33	(LM)
Inf. Temporal G.	L	-64	-14	-28	2.86	(LM)
Mid. Temporal G.	L	-60	-38	4	3.31	65
Mid. Temporal G.	L	-64	-44	8	2.48	(LM)
Inf. Frontal G.	R	52	38	-2	3.36	418
Mid. Frontal G.	R	48	40	16	3.34	(LM)
Mid. Frontal G.	R	34	38	18	3.14	(LM)
Inf. Frontal G.	L	-56	32	10	3.01	161
Inf. Frontal G.	L	-56	22	4	2.95	(LM)
Inf. Frontal G.	L	-44	26	0	2.76	(LM)
Mid. Frontal G.	L	-26	**10**	60	4.32	689
Mid. Frontal G.	L	-36	4	52	4.22	(LM)
Precentral G.	L	-32	8	40	3.22	(LM)
Sup. Frontal G.	R	6	70	0	4.3	2324
Sup. Frontal G.	R	4	68	12	3.97	(LM)
Inf. Frontal G.	L	-44	18	-8	3.85	(LM)
Sup. Frontal G.	R	18	38	46	3.4	186
Sup. Frontal G.	R	12	42	40	3.32	(LM)
Mid. Frontal G.	R	22	32	42	2.59	(LM)
Sup. Frontal G.	R	16	46	-14	3.02	176
Mid. Frontal G.	R	30	44	-18	3.01	(LM)
Inf. Frontal G.	R	28	34	-20	2.94	(LM)
Putamen	R	28	10	-6	4.16	186
Insula	R	36	14	-8	3.72	(LM)
Insula	R	40	8	-4	2.71	(LM)
Putamen	L	-24	8	-2	3.6	443
Caudate	L	-6	14	-2	3.46	(LM)
Ant. Cingulate G.	L	-8	30	10	3.46	(LM)
Caudate	R	18	26	-2	3.47	63
Caudate	R	14	22	-8	3.29	(LM)
Ant. Cingulate G.	R	20	32	8	2.36	(LM)
Rolandic Oper.	R	46	-16	12	3.55	261
Insula	R	36	-16	12	3.48	(LM)
Sup. Temporal G.	R	46	-26	12	3.4	(LM)
Precentral G.	L	-60	10	30	3.05	97
Inf. Frontal G	L	-54	8	24	2.97	(LM)
Inf. Frontal G.	L	-38	8	24	2.59	(LM)
Postcentral G.	R	58	-20	52	4.54	8250
Postcentral G.	R	54	-28	54	4.45	(LM)
Postcentral G.	R	36	-32	58	4.34	(LM)
Supp. Motor Area	R	12	2	58	3.93	1858
Sup. Frontal G.	R	18	-10	72	3.91	(LM)
Mid. Cingulate G.	R	4	-2	28	3.87	(LM)
Mid. Occipital G.	L	-50	-80	0	4.44	10072
Cerebellum	L	-2	-86	-36	4.35	(LM)
Mid. Occipital G.	L	-38	-76	6	4.23	(LM)
Men						
Mid. Temporal G.	R	54	-8	-26	3.44	79
Mid. Temporal G.	R	58	0	-26	2.42	(LM)

		MNI Coord.				
	HEM	x	y	z	Z	k
Men (continued)						
Inf. Temporal G.	R	58	-56	-20	3.31	189
Inf. Temporal G.	R	54	-62	-24	3.03	(LM)
Inf. Temporal G.	R	56	-68	-18	2.84	(LM)
Sup. Temporal G.	R	48	2	-12	2.96	86
Insula	R	40	-2	-18	2.56	(LM)
Insula	R	42	-4	-8	2.36	(LM)
Mid. Cingulate G.	R	12	0	28	3.47	64
Mid. Cingulate G.	R	8	-8	28	3.08	(LM)
Caudate	R	22	-4	32	2.51	(LM)
Sup. Frontal G.	R	24	44	36	3.19	280
Mid. Cingulate G.	R	12	38	34	3.18	(LM)
Mid. Cingulate G.	R	16	28	30	2.7	(LM)
Sup. Frontal G.	L	-8	64	28	3.82	348
Sup. Frontal G.	L	-2	44	34	3.21	(LM)
Sup. Frontal G.	L	-2	58	28	3.12	(LM)
Mid. Frontal G.	L	-24	2	54	2.92	131
Sup. Frontal G.	L	-24	4	64	2.89	(LM)
Mid. Frontal G.	L	-26	14	60	2.65	(LM)
Inf. Frontal G.	R	48	34	16	2.67	61
Inf. Frontal G.	R	48	38	6	2.58	(LM)
Insula	R	42	-8	6	3.37	146
Insula	R	42	-14	12	3.27	(LM)
Putamen	R	36	-4	0	2.48	(LM)
Supramarginal G.	R	64	-44	28	4.13	218
Supramarginal G.	R	62	-36	28	3	(LM)
Inf. Parietal G.	R	56	-58	46	2.66	(LM)
Inf. Parietal G.	L	-36	-52	48	3.18	224
Inf. Parietal G.	L	-48	-46	42	3.01	(LM)
Sup. Parietal G.	L	-32	-52	56	2.86	(LM)
Inf. Parietal G.	R	36	-46	48	2.96	75
Postcentral G.	R	28	-44	42	2.9	(LM)
Sup. Parietal G.	R	36	-50	56	2.55	(LM)
Calcarine Fissure	R	22	-76	12	3.3	110
Calcarine Fissure	R	14	-80	16	2.85	(LM)
Cuneus	R	22	-86	12	2.5	(LM)
Cuneus	R	24	-58	40	3.23	94
Mid. Cingulate G.	R	22	-48	34	2.8	(LM)
Angular G.	R	30	-64	46	2.76	(LM)
Paracentral Lobule	R	0	-34	64	3.17	95
Paracentral Lobule	R	6	-26	66	2.65	(LM)
Paracentral Lobule	R	0	-32	72	2.44	(LM)
Cerebellum	R	12	-34	-42	3.46	79
Cerebellum: Vermis	R	4	-24	-44	2.97	(LM)
Cerebellum: Vermis	R	0	-32	-48	2.83	(LM)
Cerebellum: Vermis	L	-2	-28	-40	3.28	98
Parahipp. G.	L	-10	-20	-32	2.93	(LM)
Parahipp. G.	L	-2	-14	-36	2.92	(LM)