Individual differences in emotion processing
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Recent functional brain imaging studies of the neurobiology of emotion have investigated how individual differences among subjects modulate neural responses during emotion processing. Differences in personality, dispositional affect, biological sex, and genotype can all substantially modulate the neural bases of emotion processing in prefrontal, limbic, and other brain regions, across a variety of domains including emotional reactions, emotional memory, and emotion perception. Analysis of individual differences provides a new window into the neurobiology of emotion processing that complements traditional approaches.

Introduction

Neuroimaging studies in cognitive neuroscience have traditionally relied on group analyses that attempt to characterize common activations across subjects and that usually regard variance among individuals as statistical noise [1]. However, in the domain of emotion processing, individual differences in responses are the rule rather than the exception [2]. A given emotional stimulus can evoke a wide range of emotional responses across individuals, and these individual differences can provide vital cues for elucidating the neural bases of emotion processing. For example, the amygdala is a key region in emotion, and a study of the responses of this area to happy facial expressions found that subjects exhibited highly variable responses, such that the average group response was not statistically significant [3*]. However, the authors found that this variability was strongly corre-

lated with a subjects’ degree of extraversion or outgoingness; the more extraverted the subject was, the more their amygdala responded to the happy faces [3*].

In light of these individual differences, how should affective neuroscientists proceed in their quest to reveal the neural bases of emotion processing? Rather than relying solely on group-averaged brain activations, a growing number of studies have adopted the useful complementary approach of including measures of individual differences in the analysis to uncover brain areas whose activity covaries with these measures [4], for example, personality measures or subjective ratings of emotional responses [5]. Correlations between individual difference measures and regional brain activity can potentially provide a wealth of data regarding the neural bases of emotion.

In this review of recent findings, we focus on studies that have used an individual difference approach to the neurobiological bases of emotion processing. This review highlights the effects of individual differences in genotype (including sex differences), experience, and personality on the neural basis of emotion processes (see Box 1). Specific determinants of individual differences that are covered here include differences in dispositional affect and personality traits, in genotype, and in biological sex.

Individual differences in dispositional affect and personality traits

Individual responses to emotional stimuli vary greatly across individuals: a film scene could bring one viewer to tears and leave another unaffected. Several recent studies have begun to address the neural correlates of these individual differences in emotional reactivity, by associating brain activation differences with specific behavioral determinants, such as affective disposition and personality traits.

The influence of dispositional negative affect on brain activation has been investigated in a study by Schaefer and co-workers [6], who asked participants to regulate their emotional experience in response to negative pictures. When participants were asked to maintain their negative emotional experience after stimulus presentation, prolonged amygdala activation was noted and participants who most strongly expressed a negative trait affect exhibited the greatest amount of activation. One well-known consequence of negative trait affect is a compromised immune response [7]. Using an electroencephalogram (EEG) measure of relatively greater rightsided brain activation as a proxy for negative trait affect, Rosenkranz and co-workers [8*] reported that greater...
Box 1 Emotion processes, representative brain regions, and the individual differences that modulate them

<table>
<thead>
<tr>
<th>Emotion processes</th>
<th>Brain regions</th>
<th>Individual difference factors</th>
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<tbody>
<tr>
<td>Psychological, physiological, and neural emotional responses</td>
<td>Amygdala</td>
<td>Genetics</td>
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<tr>
<td>Emotional memory</td>
<td>Hippocampus</td>
<td>Experience</td>
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<tr>
<td>Emotion recognition</td>
<td>Insula</td>
<td>Personality</td>
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Other studies have focused on dispositions that are more narrowly defined than negative affect, such as specific personality traits. For example, Fischer and co-workers [9] showed film clips of snakes to (non-snake-phobic) individuals and reported that amygdala activation across subjects was correlated with dispositional pessimism as assessed by a questionnaire. Canli and co-workers [3,10,11] have conducted three functional magnetic resonance imaging (fMRI) studies that focused on the personality traits of extraversion (E) and neuroticism (N), which are associated with positive and negative affect, respectively. They reported that E and N were correlated with individual differences in brain activation to positive and negative pictures during a passive viewing task [10], and that E was associated with greater amygdala activation during the processing of happy facial expressions [3] and with greater fusiform activation during a visual attention task [11]. The evidence so far indicates that neural correlates of E and N are represented across a range of emotional processes, including experience, perception, and attention. A major challenge for future work will be to move beyond correlations to construct causal models of brain-personality interactions.

Research on individual differences becomes itself emotionally laden when it deals with social interactions in the context of race relations. To earlier studies on this topic [12–14] we can now add one fMRI study [15] that addressed the intriguing phenomenon that racial interactions reduce some participants’ subsequent ability for executive function [16]. The study found that white participants’ activation in the right dorsolateral prefrontal cortex (DLPFC) to black faces varied as a function of implicit racial bias, as measured by the implicit association test [17], and predicted impairment of executive function after an actual inter-racial interaction. The interpretation was that greater DLPFC activation during inter-racial contact depleted available executive resources in biased individuals, although it must be stressed that the relation between implicit bias measures and overt discriminatory behavior is controversial.

Sex differences in emotional brain activation

The brains of men and women differ in several respects, and several sex differences in emotional processing have been demonstrated, including better episodic emotional memory in women and greater physiological responses to emotional stimuli in women [18]. Consistent with these differences in structure and behavior, functional neuroimaging studies have identified sex differences in the neural processing of emotion in several domains, including responses to emotionally arousing stimuli, responses to emotional facial expressions, and emotional memory.

Sex differences in emotional responses

Neuroimaging studies have frequently examined brain activations elicited by emotional stimuli in either men or women, but have seldom directly compared men and women within the same study, often because the sample sizes for each sex were insufficient. Using meta-analytical techniques, Wager et al. [19] examined 65 neuroimaging studies of responses to emotional stimuli. Surprisingly, women did not show greater activation to emotional stimuli than men, contrary to prior behavioral findings. Men showed greater lateralized activation in response to emotional stimulation, however, consistent with the generally greater hemispheric asymmetry of function that is frequently observed for males. Amygdala activity elicited by emotional stimuli was left-lateralized in both men and women.

Studies that have directly compared male and female responses to emotional stimuli have found largely similar patterns of activation as well as specific sex differences. Canli et al. [20] found largely similar left-lateralized fMRI activations for men and women in response to aversive stimuli, and Wrase et al. [21] also found similar amygdala fMRI responses to aversive pictures in men and women, but primarily in the right hemisphere. In addition, amygdala responses to pleasant pictures were found only for males, in the left hemisphere [21]. However, another fMRI study by Garavan et al. [22] found that pleasant and unpleasant picture stimuli from the same standard stimulus set elicited robust left and right amygdala activation in both males and females, and an fMRI study by Anderson et al. [23] found equivalent amygdala responses to pleasant and unpleasant odors in men and women. A positron emission tomography (PET) study of painful stimulation found that relative to brain activity during a period of rest, during pain women showed greater activation in limbic regions, including ventromedial

right-sided prefrontal EEG activation predicted poorer immune response to an influenza vaccination.
prefrontal cortex, right anterior cingulate cortex, and left amygdala, whereas men showed greater activation of the right dorsolateral prefrontal cortex, insula, and dorsal pons/periaqueductal gray. Interestingly, the anticipation of pain generated the same pattern of sex differences in the same areas [24].

Studies of romantic love and sexual arousal have also identified sex differences in brain activation, consistent with sex differences in these domains. Fischer et al. [25] showed subjects photographs of an individual they loved and a familiar but not loved person, and compared the fMRI responses in each case. When presented with a photograph of an individual they loved reward-related regions were activated in both males and females, but females showed more activity in the caudate, the septum, and the posterior parietal cortex, whereas males showed more activity in visual processing areas. A similar fMRI study of romantic love reported similar reward-related activity but no sex differences, however [26]. Studies of responses to visual sexually arousing stimuli have identified sex differences primarily in limbic regions, including the hypothalamus [27,28] and amygdala [28]. Hamann et al. [28] compared fMRI responses of men and women to sexually arousing and neutral photographs. Men showed greater activation in the amygdala and hypothalamus even when females reported greater arousal, whereas both sexes showed similar activation in ventral striatal regions involved in reward. These findings suggested that the amygdala mediates sex differences in responses to appetitive emotional stimuli and might also be implicated in the greater role of visual stimuli in male sexual behavior. Sex differences in brain activation during male and female sexual orgasm have also been reported recently, with marked activation of the periaqueductal grey and the area linked to the fight-or-flight response observed only during female orgasm [29,30]. Responses to putative human male and female pheromones have also been observed in a PET study [31]. Males showed hypothalamic activation when exposed to female but not male pheromones, and, conversely, females exhibited hypothalamic activation when exposed to male but not female pheromones. Overall, these sex differences in response to emotion-eliciting stimuli appear to be primarily manifested in limbic regions, either as differential lateralization of response or as increased activity in specific regions in one sex.

**Facial emotion processing**

Sex differences in brain activation elicited by emotional facial expressions appear early in development and persist in adulthood. Killgore et al. [32] examined developmental changes in neural responses to fearful faces in children and adolescents. Whereas both males and females showed similar right amygdala activation across ages 9 to 17, left amygdala activation decreased and prefrontal activation increased for females but these developmental changes were not seen in males. This was interpreted as consistent with a differential developmental time course of prefrontal modulation of left amygdala activity. Two other studies compared men and women in neural responses to affective faces and found generally greater activations for males [33,34]. Thus, preliminary evidence points to greater neural responses to affective faces in males.

**Sex differences in emotional memory**

Two studies examined differences in brain activity during memory encoding that predicted subsequent emotional memory. Using PET, Cahill et al. [35] found that amygdala activity at encoding predicted later emotional memory performance for both males and females, but for females this relation was found in the left amygdala, whereas for males it was in the right amygdala. A subsequent fMRI study by Canli et al. [20*] used an event-related paradigm to find that although amygdala activity during encoding was left-lateralized for both males and females, left amygdala activity predicted later memory for emotional items in females, whereas right amygdala activity predicted emotional memory in males, consistent with the findings of Cahill et al. [35]. Canli et al. [20*] suggested that the greater match between the left-sided emotion-elicited amygdala activation and the left-lateralized memory encoding for females might reflect a greater integration of emotional experience and memory for females relative to males. Sex differences have also been found during emotional memory retrieval. During retrieval of emotional word pairs, Bremner et al. [36] reported that women showed greater activation in bilateral posterior hippocampus and cerebellum, and decreased activity in medial prefrontal cortex relative to men.

**Sex hormones and sex-typed personality traits**

In addition to biological sex, two recent studies have suggested that variations in circulating levels of sex hormones and masculine versus feminine personality traits also modulate emotion processing. Krug et al. [37] examined event-related potentials elicited in women by sexually arousing pictures, pictures of infants, and emotional neutral pictures, and found that the late positive component occurring 550-600 ms post-stimulus was increased for sexually arousing stimuli during the ovulatory phase of the menstrual cycle, when levels of estrogen, testosterone, and luteinizing hormone were highest. A behavioral study [38] found that individual differences on a measure of masculinity/femininity predicted retrieval of central versus peripheral information in an emotional memory task, whereas biological sex itself was not predictive. Further investigation is needed to assess the relative contributions of circulating hormones and sex-typed personality traits to the sex differences reviewed here.
Brain activation differences as a function of genotype

Individual differences in emotionality can be characterized in terms of genetic variation. For example, Lesch et al. [39] found that allelic variation in the promoter region of the 5-HT transporter (5-HTT) gene was associated with varying levels of neuroticism, such that individuals who carry one or two copies of the short (‘s’) allele had significantly higher neuroticism scores than those who were homozygous for the long (‘l’) allele. The functional difference between the two variants is that individuals who carry one or two copies of the s-allele have higher levels of synaptic serotonin than those who carry none.

In a pioneering study, Hariri et al. [40**] found that these subtle genetic variations scale up to differences in brain activation in the processing of emotional stimuli. Participants in an fMRI study were genotyped for the 5-HTT polymorphism and engaged in two matching tasks. One involved pictures of emotional (fearful and angry) facial expressions, the other was a control task involving simple shapes. Participants who carried the s-allele exhibited significantly greater amygdala activation in the emotional condition than those who were homozygous for the l-allele (Figure 1). Remarkably, this observation was based on two independent samples of 14 participants each, whereas association studies using behavioral measures often require several dozen or even hundreds of subjects to attain significance. Two independent groups have now replicated the original finding (AR Hariri, pers comm). In addition, Hariri and co-workers have replicated their earlier report with a third and larger sample [41].

Conclusions

Regional brain activity associated with emotion processing can be influenced by a range of individual differences, including differences in personality, dispositional affect, biological sex, and genotype. Studies of correlations between individual differences and brain activity have begun to characterize how individual differences modulate basic mechanisms of emotional response and emotional memory. A common theme across the studies reviewed here is the complementary nature of the group-average and individual-differences approaches. The interpretation of regional correlations between brain activity and specific individual difference measures is guided by studies of group-average characteristics that have laid the groundwork of functional linkages between brain structures and aspects of emotion processing.

Although important insights into the neurobiological basis of individual differences in emotion processing have already been achieved, investigation of such differences is still at an early stage. In several domains of individual differences, only a handful of studies to date have focused on these issues, and conclusions must necessarily be provisional. However, in each domain reviewed, studies have demonstrated that important neurobiological correlates of individual differences on emotion processing can be observed, despite small sample sizes and other factors that would tend to obscure such relationships. A crucial question for future studies will be to determine what aspects of emotion processing are relatively invariant across individuals versus those that are modulated by individual differences. In addition, future studies should explore the potential for interactions between the individual difference factors considered independently here, such as interactions between personality and sex differences. The studies reviewed here demonstrate both the viability and the promise of approaches that acknowledge the importance of human individuality in the domain of emotion, consistent with the growing awareness of the importance of individual differences throughout cognitive neuroscience.

Update

Singer et al. [42**] recently reported a particularly interesting individual difference in brain activation related to empathy for pain experienced by others. Women who were more empathic (as measured by psychological tests) showed greater fMRI activation in brain regions involved in the affective experience of pain than less empathic women when viewing signals indicating that a loved one was in pain.
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References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

• of special interest
•• of outstanding interest


This was the first study to demonstrate that individual variability in amygdala activation to positive facial expressions varies as a function of the personality trait of extraversion (outgoingness).


This study employed a system-level approach to the study of affect-immune system interactions. It related physiological measures of trait affect, brain laterality and immune function to show that greater right-sided prefrontal activation (a measure of negative trait affect) predicted poorer immune response.


The findings of this neuroimaging study suggested that emotional processes engaged during inter-racial contact could reduce neural activity during a subsequent executive function task.


17. Implicit association test. URL: https://implicit.harvard.edu/implicit/demo/.


The authors reviewed several functional neuroimaging studies of emotion that used advanced analysis methods to characterize differences in activations related to sex differences and other factors.


This fMRI study found that although both men and women show a primarily left-sided response in the amygdala to emotionally negative pictures, the sexes differ strikingly in the lateralization of activity during memory encoding that predicts later emotional memory. In women this activity was in the left amygdala, whereas in men this activity was in the right amygdala.


The authors scanned males and females using fMRI while they viewed sexually arousing versus control videos. Sexual arousal elicited widespread activations that were largely similar for males and females. Males showed greater activation in the hypothalamus than females during sexual arousal. However, accounting for individual differences in men and women's arousal using partial regression removed the sex difference, pointing to a central role for arousal in the effect.


This was the first study to compare directly brain activation during sexual arousal between men and women who were carefully selected to be similarly aroused by visual erotica. Sexual arousal elicited widespread activations that were largely similar for males and females. Males showed greater activation in the hypothalamus than females during sexual arousal. However, accounting for individual differences in men and women’s arousal using partial regression removed the sex difference, pointing to a central role for arousal in the effect.


This was the first study to systematically characterize brain responses during male consummatory behavior. Together with more recent conference reports from this group, the findings point to a role for the ventral tegmental area, which is involved in reward and addiction, in both male and female orgasm, but a unique role of the periaqueductal grey region in female orgasm.


This was the first imaging study to characterize group differences in brain activation levels during a cognitive task as a function of genotypic variation, linking systems neuroscience with molecular genetics.


This study used fMRI to characterize brain regions activated by empathy for a pain experienced by a loved one, and compared these regions to those activated by self-experienced pain. Empathy for another’s pain recruited only regions linked to the affective qualities of pain and not the sensory qualities of pain. Importantly, the level of activation in these regions representing the affective qualities of pain (anterior cingulate cortex and insula) was highly correlated with individual differences in empathy, as measured by psychological tests. More empathic individuals showed greater activation in these regions while they viewed a signal indicating that a loved one was experiencing pain.