The functional neuroanatomy of emotion and affective style

Richard J. Davidson and William Irwin

Recently, there has been a convergence in lesion and neuroimaging data in the identification of circuits underlying positive and negative emotion in the human brain. Emphasis is placed on the prefrontal cortex (PFC) and the amygdala as two key components of this circuitry. Emotion guides action and organizes behavior towards salient goals. To accomplish this, it is essential that the organism have a means of representing affect in the absence of immediate elicitors. It is proposed that the PFC plays a crucial role in affective working memory. The ventromedial sector of the PFC is most directly involved in the representation of elementary positive and negative emotional states while the dorsolateral PFC may be involved in the representation of the goal states towards which these elementary positive and negative states are directed. The amygdala has been consistently identified as playing a crucial role in both the perception of emotional cues and the production of emotional responses, with some evidence suggesting that it is particularly involved with fear-related negative affect. Individual differences in amygdala activation are implicated in dispositional affective styles and increased reactivity to negative incentives. The ventral striatum, anterior cingulate and insular cortex also provide unique contributions to emotional processing.

This article presents an overview of recent research on the functional neuroanatomy of human affective processes, focusing on studies using positron emission tomography (PET) or functional magnetic resonance imaging (fMRI). Where relevant, some studies on patients with discrete lesions are also included, as well as animal studies that provide much of the foundation for the modern human work. Research on patients with mood and anxiety disorders is, for the most part, not included as such studies have been extensively reviewed in a number of recent publications.

Over the past 10 years, there has been an enormous increase in animal research that has provided a detailed foundation for understanding the neural circuits of several basic emotional processes. This corpus of literature has helped to make emotion a tractable problem in the neurosciences and has led to the development of affective neuroscience. With recent advances in functional brain imaging, the circuits underlying emotion in the human brain can now be studied with unprecedented precision.
PET and fMRI provide powerful and complementary information that has not been possible to acquire with other methods. These techniques enable scientists to examine regional patterns of activation in normal intact humans with considerable spatial precision and, in the case of fMRI, with temporal resolution on the order of seconds. With PET, in addition to its use as a measure of hemodynamic or metabolic activity, it can also be used to probe components of neurotransmission in vivo in relation to behavioral performance (Ref. a). The application of these methods to the study of emotion has burgeoned over the past several years and has generated a new body of literature on the circuitry associated with selective features of emotional responding and affective traits. There are a number of critical conceptual and methodological issues that are fundamental to neuroimaging studies of emotion:

1. The perception of emotional information must be carefully distinguished from the production of emotion. There are many studies that present as stimuli to subjects, facial expressions of emotion. The presentation of facial expressions of emotion does not necessarily (nor even likely) elicit any emotion. Thus, when investigators use this procedure it is important that it be described as a study of the perception of emotional faces and not a study about emotion per se (Refs b,c).

2. The control conditions against which emotion activation is compared crucially influences the nature of the data obtained. When using subtractive methodology, it is helpful to control for as much of the stimulus content as possible to isolate the effects of emotion itself. For example, the comparison of a condition during which subjects were self-generating emotional expressions involved in retrieving information from memory and voluntarily generating visual imagery. It is good practice to include more than one emotion condition (e.g. both positive and negative), as any effect produced as a consequence of simply generating emotion per se should be common to the two emotions, while differences between conditions can be attributed to the specific nature of the emotional process elicited.

3. Stimuli designed to elicit different emotions must be matched on arousal and on physical characteristics. Arousal can be inferred in several different ways including self-report and skin conductance measures (Ref. a). Differences in patterns of activation observed between two emotion conditions that are not matched on intensity or arousal can obviously result from a failure to match appropriately and might be more a function of the arousal differences rather than the emotion differences between conditions (see Ref. f for more extended discussion). A related issue is the need to match stimuli across emotion and control conditions on physical properties, such as color, the presence of faces, spatial frequency, etc. Some differences found between emotion conditions might conceivably be a function of physical differences between the stimuli that have nothing directly to do with emotion. For example, in our fMRI studies of emotion induced with pictures, we have found (Ref. g) that activation of secondary visual cortex by negative pictures compared with neutral pictures may in part be a function of the color differences between these classes of stimuli.

4. Putatively asymmetric effects must be rigorously statistically interrogated. Many investigators using both PET and fMRI have reported asymmetric changes associated with emotion (Ref. h). In most cases, claims about an activation being asymmetric were made on the basis of trends in one hemisphere that exceeded statistical threshold while homologous trends in the opposite hemisphere did not. However, such an analytic strategy, while typical, was only for the main effects of the condition. To demonstrate an actual difference between the two hemispheres, it is necessary to test the Condition X Hemisphere interaction. The fact that such tests are rarely performed is largely a function of the fact that software is not commercially available to perform such analyses for the entire brain volume. If this interaction was not significant, it is not legitimate to claim that an asymmetric finding was observed since the lack of a significant interaction means that the changes found in one hemisphere were not significantly different from those observed in the other, even if the effects were independently significant in one hemisphere but not in the other. Moreover, it is possible for significant interactions to arise in the absence of any significant main effects. As discussed in the main text, very few investigators who have reported asymmetric effects have properly tested for the Condition X Hemisphere interaction.

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Box 1. Conceptual and methodological complexities in neuroimaging studies of human emotion

levels of detail, the essential characteristics of each system are similar across conceptualizations. The approach system facilitates appetitive behavior and generates certain types of positive affect that are approach-related, for example, enthusiasm, pride, etc. This form of positive affect is usually generated in the context of moving toward a desired goal (see Refs 14,15 for theoretical accounts of emotion that place a premium on goal states). Then appears to be a second
system concerned with the neural implementation of withdrawal. This system facilitates the withdrawal of an individual from sources of incentive stimulation and generates certain forms of negative affect that are withdrawal-related. For example, both fear and disgust are associated with increasing the distance between the organism and a source of incentive stimulation. A variety of evidence drawn from multiple sources suggests the view that the systems that support these forms of positive and negative affect are implemented in partially separable neural circuits. The key elements of the circuitry are reviewed below.

Prefrontal cortex

A large body of neuroimaging, neurosurgery, and electrophysiological data supports the view that the prefrontal cortex (PFC) is an important part of the circuitry that implements both positive and negative affect. There are several important subdivisions of the PFC that are critical to note with respect to affective processing. First are the distinctions among the dorsolateral, ventromedial and orbitofrontal sectors and the second is the distinction between left and right sectors within each of these regions of PFC (see Fig. 1).

A number of early studies that evaluated mood subsequent to brain damage suggested that patients with damage to the left hemisphere, particularly in PFC, were more likely to develop depressive symptoms compared with patients having lesions in homologous regions of the right hemisphere. Most of the lesions in these studies are large and include more than one sector of PFC. However, dorsolateral PFC is affected in the majority of patients represented in these studies. The general finding of left dorsolateral PFC damage increasing the likelihood of depressive symptoms has been interpreted to reflect the contribution of this cortical territory to certain features of positive affect, which, when disrupted, increases the probability of depressive symptomatology. This line of reasoning is consistent with the idea that depression is associated with deficits in positive affect. Recent reviews of the modern literature on this topic have largely supported these earlier studies, though some inconsistencies have been reported (see Ref. 23 for discussion of conceptual issues in this literature).

Bechara and colleagues have amassed considerable evidence over the past several years that patients with bilateral lesions of the ventromedial PFC cannot anticipate future positive or negative consequences of their actions, although immediately available rewards and punishments do influence their behavior. Such patients also fail to show anticipatory electrophysiological responses when confronted by a risky choice whereas normal controls generate such anticipatory autonomic responses even before they explicitly know it was a risky choice. Recently, this group demonstrated a double dissociation whereby patients with anterior ventromedial PFC damage were impaired on a gambling task that assesses anticipation of future positive and negative consequences while performing normally on a working memory task (delayed non-matching to sample). Patients with right dorsolateral PFC damage were impaired on the working memory task while performing normally on the gambling task. Whether separable influences on the anticipation of positive or negative consequences would result from unilateral left-versus right-sided ventromedial damage respectively, has never been studied.

The differential involvement of the left and right PFC in certain forms of positive and negative emotion is supported by electrophysiological measures of regional activation in normal subjects exposed to stimuli that elicit emotion. These studies find increased left anterior activation during negative affect, a pattern of predominantly left-sided activation during positive affect, and increased right-sided anterior activation during negative affect. A major limitation of these studies is the lack of spatial resolution afforded by the electrophysiological measures.

Using an extended-picture-presentation paradigm to induce consistent changes in positive or negative mood, we measured regional glucose metabolism using PET while we independently and objectively verified the presence of the intended emotional states using emotion-modulated startle and facial electromyography. The production of negative affect, we found right-sided increases in metabolic rate in both inferior and superior regions of the PFC including the anterior orbital, inferior frontal, middle frontal and superior frontal gyri. The production of positive affect, a pattern of predominantly left-sided activation was observed with a somewhat more posterior distribution compared with negative affect. During positive affect, left-sided metabolic increases were observed in the region of the pre- and post-central gyri. In addition, increases were observed in the region of the left nucleus accumbens (discussed below).

Relatively few other neuroimaging studies have compared objectively verified positive and negative affect in the same subjects. Some studies have examined patterns of activation that were common across emotions in comparison to Ref. 93.)

Fig. 1. Sectors of human prefrontal cortex. Left: lateral view indicating dorsolateral (blue), ventromedial (red) and orbitofrontal (green) cortical territories. Right: ventral view indicating ventromedial (red) and orbitofrontal (green) cortical territories. Also indicated are the amplitudes located on the medial margin of the temporal lobes, just distal to the sylvian which are identified by the tips of the arrowhead (yellow; see Fig. 2). (Adapted from Ref. 93.)
with a neutral baseline condition. In this latter study, Lance et al. reported that the emotion conditions produced significantly greater activation in the medial PFC compared with the neutral control condition. A very similar finding was obtained in an independent sample of subjects exposed to pleasant, unpleasant and neutral pictures, with the emotional pictures producing increased activation in medial PFC compared with the neutral pictures.

Many other studies that have used PET to measure regional cerebral blood flow or metabolism have observed emotion-related alterations in PFC activation. A common method for the experimental production of aversive emotion has been to use anxiety-disordered patterns exposed to stimuli that provoke anxiety (e.g., pictures of spiders for spider phobics). Pooling across data from three different anxiety-disordered groups (obsessive-compulsive disorder, simple phobia, and post-traumatic stress disorder) Rauch and colleagues found a group of structures commonly activated across these disorders during the experimental provocation of anxiety. Two regions within the PFC were strongly activated across groups: right inferior PFC and right medial orbital PFC. In an fMRI study of symptom provocation among patients with obsessive-compulsive disorder, Breiter and colleagues observed bilateral activation of anterior and posterior orbitofrontal cortex.

Several investigators have used classical aversive conditioning to study the neural substrates of the acquisition and extinction of emotional learning. Most studies have focused on the amygdala and they will be reviewed below. However, in the present context, we note that Hugdahl et al. reported a significant increase in widespread areas of the right PFC including the orbitofrontal and dorsolateral cortices and inferior and superior frontal cortices during extinction compared to habituation.

Various studies have reported significant decreases in PFC blood flow associated with the activation of particular emotional states, with induced happiness resulting in a reduction in activation in the right superior PFC and visually induced recall of an aversive emotional episode being associated with a significant reduction in left-sided PFC activation in the region of Broca's area and the operculum.

In summary, there is growing consistency between the lesion data on the mood consequences of small unilateral lesions and the findings from neuroimaging studies in supporting the view of right-sided activation in several regions within PFC during the experimental arousal of negative emotion. Less evidence is available on the prefrontal changes associated with positive affect, in part because much of the literature on negative affect is derived from the study of patients with anxiety and mood disorders. Systematic study of comparable subjects who are predisposed to positive affect has never been undertaken though certainly could be based upon available evidence. It must be noted that some of the neuroimaging evidence for lateralized changes in PFC activation during emotion is derived from studies that have not rigorously tested the interaction of condition with hemispheric asymmetry, must be regarded with some caution until additional studies using more appropriate analytic procedures have been performed.

Bechara and colleagues' studies on the ventromedial PFC strongly suggest that this neural sector is involved in the anticipation of future affective consequences because patients with damage to this region fail to generate the normal anticipatory electrodermal responses to affectively salient cues. It will be of great interest in the future to carefully examine whether asymmetries in the representation of valence are present in this region. The evidence to date is derived from patients with bilateral lesions.

Many theoretical accounts of emotion assign it an important role in guiding action and organizing behavior in a motivational manner. To accomplish this, it is essential that the organism have some means of representing affect in the absence of immediate elicitors—an affective working memory. It is likely that the PFC plays a crucial role in this process. Damage to specific sectors of the PFC appears to impair a person's ability to sustain emotion and to use it to guide behavior in an adaptive fashion. Note that such damage would not impair immediate reactivity to incentives, but only the capacity to sustain and anticipate such reactions when the immediate elicitors are not present. The ventromedial sector of the PFC is probably more directly involved in the representation of elementary positive and negative states in the absence of immediately present incentives, while the dorsolateral PFC is probably more directly involved in the representation of the goal states toward which these more elementary positive and negative states are directed. This formulation must be tested explicitly in future research.

Amygdala

A growing body of data from a small group of human patients with discrete lesions in the amygdala highlight the importance of this region for both the perception and production of negative affect and associative aversive learning (see Ref. 7 for general review and Ref. 44 for review of animal studies on the amygdala and emotional memory) (see Fig. 2). Adolphs and his colleagues have demonstrated that the recognition of facial signs of fear was impaired in patients with bilateral amygdala damage while recognition...
of other facial expressions was intact. A specific deficit in the recognition of facial expressions of fear in patients with amygdala damage has been demonstrated in two additional studies using a different methodology for the assessment of facial expression recognition (Scott et al. 1998). It is likely that the deficit in the perception of expressive signs of fear in patients with amygdala damage is not specific to facial expressions since Scott et al. (1998) demonstrated a deficit in the recognition of vocalic expressions of fear and anger in a patient with bilateral amygdala damage.

Buchanan and colleagues have demonstrated a crucial double dissociation by comparing a patient with selective bilateral amygdala damage to one with selective bilateral hippocampal damage. During a conditioning task during which electrodermal measures of affective aversive association were obtained, along with measures of declarative knowledge of the conditioning contingencies. It was found that the patient with amygdala damage was impaired in electrodermal conditioning but showed intact declarative knowledge of the task contingencies while the patient with hippocampal damage and an intact amygdala demonstrated reliable electrodermal conditioning but showed no declarative knowledge of the conditioning contingencies. A patient with bilateral damage to both structures was impaired on both sets of measures. Other evidence suggests that declarative memory for complex emotional material is selectively disrupted in patients with bilateral amygdala damage (Scott et al. 1998).

Angrilli and colleagues studied the startle responses of a patient with a benign tumor of the right amygdala in comparison with a group of controls. Among control subjects, they replicated the well-known effect of aversive stimuli potentiating startle magnitude. However, in the patient with the right amygdala lesion, no startle potentiation was observed in response to aversive versus neutral stimuli. These data are consistent with the view that the amygdala is crucial for normal negative-affect potentiated startle in humans. In a very recent study that required subjects to make judgments of the trustworthiness and approachability of unfamiliar individuals from facial photographs, patients with bilateral damage to the amygdala judged the unfamiliar individuals to be more approachable and more trustworthy than did control subjects (Breiter et al. 1997). Collectively, the studies of patients with damage to the amygdala suggest that this structure plays an important role in both the perception and production of certain forms of negative emotion. The extent to which the human amygdala also plays a role in positive affect is unanswered by extant lesion studies. Moreover, the lesion studies need to be complemented by neuroimaging studies that examine activation in the amygdala in intact subjects in response to affective challenges since damage to the amygdala can have functional consequences in territories far removed from the site of the actual lesion.

A growing body of neuromaging literature using both PET and fMRI have reported on changes in the human amygdala in response to emotional stimuli. These studies are helping to clarify the functional role of the amygdala in various components of emotional processing. However, it is necessary to understand the functional heterogeneity of the amygdala. So significant is this heterogeneity that some anatomists have been led to question whether the amygdala should properly be regarded as a discrete, unitary structure (see Ref. 54 for a compelling statement of this position). Unfortunately, because of its relatively coarse spatial resolution, it is not likely that PET will enable investigators to differentiate among different subnuclei of the amygdala. It is more likely that fMRI will have sufficient spatial resolution, particularly at higher field strengths, to resolve different regions within the amygdala, although there have not yet been attempts to manipulate task variables systemathecally in order to determine whether differential activation of regions of the amygdala can be detected.

A number of PET and fMRI studies have been performed with patients having one of several different anxiety disorders and examining cerebral blood flow using the amygdala and other brain regions in response to the experimental provocation of anxiety. For example, using PET measures of blood flow, Rauch et al. (1996) exposed patients with post traumatic stress disorder to imagery scripts that were designed to activate traumatic memories. These were compared to neutral imagery scripts. Activation of the right amygdala was found in this study and remained equally significant when compared to a teeth clenching control condition (Breiter et al. 1995). Birbaumer and colleagues (1995) used fMRI to examine regional patterns of activation in patients with obsessive-compulsive disorder exposed to ideographically tailored stimuli designed to provoke the patient’s symptoms. In response to such stimuli compared with control stimuli, significant bilateral activation of the amygdala was detected. Rehman and colleagues (1998) reported bilateral amygdala activation in response to neutral facial expressions (compared with a resting baseline condition) in a group of male social phobics. The amygdalar activation in this group was comparable in magnitude to that elicited by an aversive odor. In a group of controls, they observed amygdalar activation to the aversive odor but not to the neutral faces.

Consistent with the lesion data are studies that find specific activation of the amygdala in response to faces depicting expressions of fear. Using PET, Morris et al. (1994) demonstrated that fear faces elicit significantly greater blood flow in the amygdala compared with happy faces. Moreover, the intensity of fear displayed in faces was systematically related to increases in blood flow in the left amygdala. In a subsequent re-analysis of these data, Morris and colleagues (1994) found that increased blood flow in the amygdala predicted increased blood flow in extrastriate visual cortex during fear but not during happy presentations. These findings indicate that the pattern of functional connectivity between these regions is altered as a function of emotional expression condition.

Activation of the amygdala in response to fear faces has also been found with fMRI. Because of the better time resolution of fMRI, Birnbaum and colleagues (1997) were able to examine the temporal changes in amygdalar activation and found that the response to fear faces showed rapid habituation. Phillips et al. (1997) replicated this finding and further demonstrated that disgust faces failed to activate the amygdala. Rather, in response to disgust faces, subjects showed activation in a region implicated in processing gustatory stimuli, the anterior insula. Recently, Whalen and colleagues demonstrated activation of the amygdala in response to fear faces that were not consciously perceived. They achieved this by...
masking the fear faces with neutral faces that were presented contiguously with the offset of the fear faces. Happy faces masked in this way showed significantly less amygdala activation compared with masked fear faces.

Using either pleasant and unpleasant pictures or happy and sad faces accompanied by instructions to generate the emotion depicted on faces, while measuring regional blood flow with PET, investigators have found activation in the left amygdala during unpleasant compared to neutral pictures and during sad compared with happy mood generation.

In a conceptual replication of this latter study, the same group used fMRI to detect regional brain activation and again found activation of the left amygdala during contrasting and magnitude of skin conductance responses obtained 1–3 months later.

Fig. 1. Illustration of PET–MRI coregistration and amygdalar ROI delineation. Representative image planes in coronal section are shown for one participant. The PET image plane is presented beside its corresponding coregistered MRI plane. Units of the PET color scale are in mg/100g/min. (Adapted from Ref. 94.)
Using fMRI, we presented pleasant and unpleasant pictures and compared them to neutral pictures and found that only unpleasant pictures activated the amygdala. LaBar et al. found bilateral activation in the amygdala in response to both unpleasant and pleasant stimuli compared to neutral stimuli. Importantly, the LaBar et al. study included erotic nudes in their positive picture set while our studies did not. It may well be that the inclusion of these stimuli made a crucial difference in the activation of the amygdala during the positive condition. We will return to this issue at the end of this section.

Two recent fMRI studies of classical aversive conditioning have reported bilateral amygdala activation during the early phases of acquisition which then habituates.
rapidly. In a recent PET study of conscious and unconscious conditioning, Morris and colleagues\(^1\) compared the responses to backwardly masked angry faces that had been paired with noise to consciously perceived angry faces paired with noise. Masked presentations of the conditioned angry face elicited activation in the right amygdala while unmasked presentations of the same face elicited activation in the left amygdala.

Several other types of manipulations have been found to elicit neural activity in the amygdala. Exposing normal individuals to an unobtainable outcome task of the sort used to induce learned helplessness produced increased blood flow in the amygdala\(^2\). Aversive olfactory stimuli were found to produce asymmetry in the left amygdala\(^3\) compared to a no odorant control condition, while aversive gustatory stimuli produced activation in the right amygdala\(^4\).

Individual differences in amygdala activation have been related to various measures of affective style (see Box 2).

**Issues raised by the amygdala findings**

The data reviewed above clearly implicate the amygdala as an important site for the control of emotion in the human brain. However, the results also raise many questions about the precise nature of the role this region plays in emotion. Here we wish to highlight three major issues.

1. **Affect in general, negative affect in particular, or fear most specifically?** The existing data are equivocal on this issue. Many studies find greater amygdala activation in response to negative elicitors compared with positive elicitors. Some studies find that the greater the reported or autonomic display of negative affect, the greater the activation in the amygdala. Other studies have found amygdala activation in response to both negative and positive emotional challenges. For example, Lalur et al.\(^5\) observed bilateral MR signal increases in the amygdala in response to both negative and positive pictures compared with neutral pictures. As we noted above, this latter study included erotic images among the positive picture set while our study\(^6\), which revealed amygdala activation only in response to negative versus neutral pictures, did not. It is noteworthy that the Breiter et al.\(^7\) MRI study of the effects of cocaine in cocaine addicts (Ref. 75, discussed in more detail below) found significant deactivation of the amygdala during cocaine-induced ‘highs’.

The studies that have compared activation of the amygdala in response to facial expressions depicting different emotions have consistently found the greatest activation of the amygdala in response to fear faces. It is conceivable that these data could be subsumed under a model of amygdala function that assigns a premium role to the detection of ambiguity (see Ref. 76 for a discussion of this theory). On this view, the preferential activation of the amygdala in response to fear compared with angry faces, for example, is explained by the fact that angry faces provide information about the presence of threat as well as the source of threat while fear faces provide information about the former but not the latter. Emotional stimuli may be interpreted as ambiguous for many different reasons (e.g. they might automatically elicit approach, but also could activate avoidance responses because of moral considerations etc.). Inconsistent with this view, however, are the data on the recognition of vocal affect in a patient with bilateral amygdala damage which indicated impaired recognition of both fear and anger\(^8\). What is required is to manipulate the valence of emotion while carefully matching conditions on variables that might be associated with ambiguity. Alternatively, ambiguity can be parametrically varied (e.g. by altering the probability of a shock appearing during the presence of a particular CS) to determine if amygdala activation tracked variations in manipulated ambiguity.

2. **Left, right or both?** During the experimental arousal of negative affect, some studies report changes in left amygdala activation\(^9\), others report changes in right amygdala activation\(^10\), while still others report bilateral changes\(^11\). Adding to this complexity is the recent report by Morris et al.\(^12\) who observed right amygdala activation to unconsciously presented aversively conditioned angry faces and left amygdala activation to conscious presentations of the same face. It is essential to stress the importance of proper statistical analysis of laterality effects in neuroimaging studies (see Box 1 and Ref. 77 for a more in-depth discussion). Until these procedures are followed more rigorously, it will not be possible to sort out whether asymmetric activation in the amygdala is associated with different patterns of affective response.

3. **Can the amygdala be treated as a homogeneous structure?** Of course, the obvious answer to this question is a resounding no, yet most investigators continue to treat this region as if it were a unitary structure. Unfortunately, this state of affairs is not likely to change until studies are completed on MRI scanners with field strengths higher than conventional scanners (i.e. more than 2T). When such studies are performed, it is likely that the region of the amygdala that is activated in response to faces will differ from the region activated during the expression of a negative emotional response. Univariate sampling of the amygdala and partial volume effects with other adjacent structures due to the relatively coarse resolution of most fMRI and all PET studies probably accounts for some of the variability among studies. Future fMRI studies at higher field strength hold great promise in elucidating the functional specialization of different amygdaloid regions.

**Other brain regions**

While most of the extant literature has focused on PFC and amygdala as two critical components of a circuit involved in human emotion processing, many studies have offered evidence of other brain regions participating in affective responding. One key region that has emerged mostly from behavioral, lesion and electrophysiological data is posterior right hemisphere involvement in both the perception of emotional information as well as in the arousal component of emotion. This literature is not reviewed here because it has been recently reviewed elsewhere\(^13\)–\(^15\). In addition, precise anatomical specification of the locus of these effects is not available because the methods that have been used for their study provide only coarse localizing information. Here we briefly review data on three other regions that have been more consistently implicated in emotional processing in recent neuroimaging studies.
Critical role in visceral representation. The insular cortex has been implicated in the autonomic control of visceral function, with activation observed in response to stimuli that elicit visceral responses, such as disgust faces. This activation is consistent with the idea that the insular cortex plays a role in the efferent control of autonomic function.

Activation of the insular cortex has also been reported in studies that manipulated positive affect. For example, Breiter et al. (1999) observed activation in the insular cortex in response to disgusting images, which can be underlined as signifying distasteful stimuli (see recent discussions in Breiter). The insular cortex is topographically organized and includes a major zone dedicated to gustatory processing. This latter fact is probably related to the insular cortex's role in the autonomic control of visceral function.

Research has also focused on the insular cortex's role in the processing of positive affect. For instance, Lane et al. (1997) found that the insular cortex was activated during the condition requiring attention to positive affect. This region might play an important role in mediating the attentional effects of affective arousal. When emotion is evoked it is usually automatically salient. It would be informative in future research to compare emotion evoked non-consciously versus consciously and determine if activation of the ACC occurs during the latter but not the former.

The anterior cingulate cortex (ACC) has also been implicated in the processing of positive affect. Based upon its known inputs and outputs, activation of the insular cortex during emotion is probably associated with the autonomic changes that typically occur when emotion is evoked. However, from the extant evidence, we do not know if the insular activation is primarily a function of visceral afferent feedback or rather is produced by the insular cortex in response to the emotional stimuli.

Conclusions

Just as cognitive neuroscience has taught us the importance of decomposing global cognitive constructs into more elementary constituents whose neural substrates could be identified, so too modern research in affective neuroscience underlines the importance of identifying specific subcomponents of emotion whose anatomic basis may be examined. In this article we have relied on three primary sources of data to make inferences about the circuitry underlying positive and negative emotion in the human brain: lesion, PET and fMRI studies. This corpus of work underlines the importance of several interconnected regions comprising a circuit for human affective responding: the ventromedial prefrontal cortex, the orbitofrontal cortex, the insula, and the anterior cingulate. Each of these regions appears to have a role in a specific aspect of emotion. For example, the ventromedial prefrontal cortex has been implicated in the processing of positive affect, while the orbitofrontal cortex has been implicated in the processing of negative affect.
Review

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Outstanding questions

• To what extent is the amygdala involved in emotion in general, or negative affect or fear in particular? Does the amygdala respond to ambiguity or is its response more selective to specific types of emotion?

• What is the significance of lateralization in the amygdala? Some evidence has implicated the right amygdala more than the left in negative emotion, though inconsistencies exist in the literature on this point. Is there a systematic difference in neurotransmitter function in the left and right amygdala?

• What is the relationship between the cognitive and affective functions of the prefrontal cortex? Is affective working memory subserved by the same or different sectors of the PFC compared with cognitive working memory?

• What are the upstream cortical consequences of amygdala activation? We know that the amygdala projects to many stages of the visual system. Evidence suggests that there is increased activation in secondary visual cortex in response to emotional compared with neutral visual stimuli. Is the increased visual cortex activation a function of amygdala activation? Would patients with amygdala lesions not show this increased visual cortex activation in response to visual emotional stimuli?

• What is the role of visceral afferent feedback in the modulation of activation in the insular cortex? Would peripheral pharmacological blockade of autonomic activation decrease activation in the insular cortex?

processes, these procedures, combined with neuroimaging technologies, will allow us to address questions about brain mechanisms in ways that were previously approachable only through research on non-human species. This new information will provide a compelling foundation for theoretical advances in the basic understanding of the constituents of emotion and for practical advances in the treatment of affective dysfunction.

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