NEUROPSYCHOLOGY OF FEAR AND LOATHING

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For over 60 years, ideas about emotion in neuroscience and psychology have been dominated by a debate on whether emotion can be encompassed within a single, unifying model. In neuroscience, this approach is epitomized by the limbic system theory and, in psychology, by dimensional models of emotion. Comparative research has gradually eroded the limbic model, and some scientists have proposed that certain individual emotions are represented separately in the brain. Evidence from humans consistent with this approach has recently been obtained by studies indicating that signals of fear and disgust are processed by distinct neural substrates. We review this research and its implications for theories of emotion.

AMYGDALA
A small almond-shaped structure, comprising 13 nuclei, buried in the anterior medial section of each temporal lobe.

BASAL GANGLIA
A group of interconnected subcortical nuclei in the forebrain and midbrain that includes the striatum (putamen and caudate nucleus), globus pallidus, subthalamic nucleus, ventral tegmental area and substantia nigra.

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In recent years, there has been an explosion of interest in the neuroscience of human emotion. Several studies have focused on a debate concerning whether the neural representation of emotion involves individual systems for separate emotions, or an integrated system able to code all emotions. This relates to a more general psychological debate concerning whether emotions are best described in terms of category-based frameworks or unifying dimensional accounts. Exponents of the category-based approach posit that a limited number of emotions (that generally include happiness, sadness, anger, fear and disgust) have a 'basic' status, and that signals of these basic emotions are identified by activating discrete category representations (one for each emotion). The principal support for this model comes from the finding that these basic emotions are pan-cultural and that facial expressions of each emotion are represented by the same distinct facial musculatures across different cultures[1,2]. The main alternative to the category-based account is the view that all emotions can be represented in a single unifying framework; for example, a limited set of dimensions coding specified emotional constructs such as pleasure, arousal, attention/rejection and so on (BOX 1).

In the past seven years, human neuropsychology has begun to make a significant contribution to this debate on two different fronts. First, the discovery that certain types of brain injury and psychiatric disorder can cause selective impairments in the recognition of human signals of fear and disgust. Second, functional imaging research has revealed distinct neural correlates for processing fear and disgust in healthy individuals. In this review, we first address research on humans showing that the AMYGDALA (FIG. 1) has a central role in processing signals of fear. We then discuss the less extensive literature showing that a different neural circuit that primarily involves the insula and the BASAL GANGLIA serves recognition of disgust signals (FIG. 1). Last, we consider the implications of this research for the way we think about human emotion.

Involvement of the amygdala in fear recognition

The amygdala and fear in non-humans. Animal research has clearly shown that the amygdala is important in emotion[3]. This was first indicated by the reduced levels of aggression and fear, and the increased tameness, observed in monkeys with bilateral lesions that included[4], or were restricted to[5], the amygdalae. Until recently, however, the specificity of these effects was unclear, as the ablations made in these studies also destroyed fibres of passage coursing through the amygdala. So, it is important that more recent work using fibre-sparing excitotoxic lesions[6,7] has confirmed that the amygdala has a significant role in the processing of emotions.

Following on from these findings, a significant area of comparative research on emotions has focused on the role of the amygdala in a particular type of emotion processing — FEAR CONDITIONING[8,9]. These studies have shown that lesions of the amygdala and related areas interfere with the acquisition and expression of various indices of conditioned fear, including fear-potentiated startle, freezing and disruption of ongoing behaviour (that is, conditioned suppression).

Amygdala damage in humans. In line with observations from comparative research, the most frequently documented consequence of amygdala damage in humans is a change in emotional behaviour, although the effects are less pronounced than those found in non-human primates[10]. In addition, cognitive impairments after amygdala damage are remarkably limited. Deficits have been found to affect some aspects of face perception[11–18], particularly recognition of facial expression[11–15,17–20], with less consistent evidence showing impaired learning of new faces[16,18,19]. Additional studies have shown that the amygdala is involved in memory for emotional material[21–23]. Overall, these human data concur with non-human primate research in showing that the amygdala is involved in emotion[3,5,24] and face perception[25–27]. These findings are further substantiated by functional imaging and patient-based research that implicates the human amygdala in facial-expression processing[28–35] and in other aspects of social signalling[36,37].

Building on these findings and the role of the amygdala in fear conditioning, Adolphs and colleagues[11–13] addressed the more specific question of whether the human amygdala is preferentially involved in processing facial signals of fear. Their first study included a patient with complete and largely selective bilateral lesions of the amygdala (patient SM), and six patients with unilateral damage to the left or right amygdala[12]. Participants rated examples of six facial expressions of emotion (happiness, sadness, anger, fear, disgust and surprise) plus neutral expressions on several emotional scales. In comparison to controls with or without neurological damage to areas other than the amygdala, SM showed abnormal ratings of facial expressions of fear and, to a lesser extent, anger and surprise. By contrast, patients with damage to the right amygdala showed no significant impairments, whereas patients with lesions of the left amygdala showed some evidence of abnormal performance, but not for fear. However, contrary to these results obtained for the patients with unilateral amygdala damage, Anderson *et al.*[38] have used an adapted version of the task used by Adolphs and colleagues, and found significant impairments in a larger group of patients. These patients had suffered right unilateral anteromedial temporal lobectomies that included the amygdala, and showed abnormal processing of faces expressing sadness, fear, disgust and happiness. Patients with similar damage to the left hemisphere showed no significant impairments.

Adolphs's rating task has also been used in several other investigations[13,20,39–42], including a larger study that involved nine patients with amygdala damage due to various aetiologies[13]. This study found that, when analysed as a group, fear processing was most affected in these nine patients, but not all of them showed obvious impairments for fear. In fact, an earlier study by Hamann and colleagues[42] had reported that two of these patients with complete bilateral damage to the amygdala showed no significant impairment for any emotion on Adolphs's task. In the light of differences between the patients in this study and patient SM[11,12], Hamann *et al.*[42] suggested that a fear-recognition

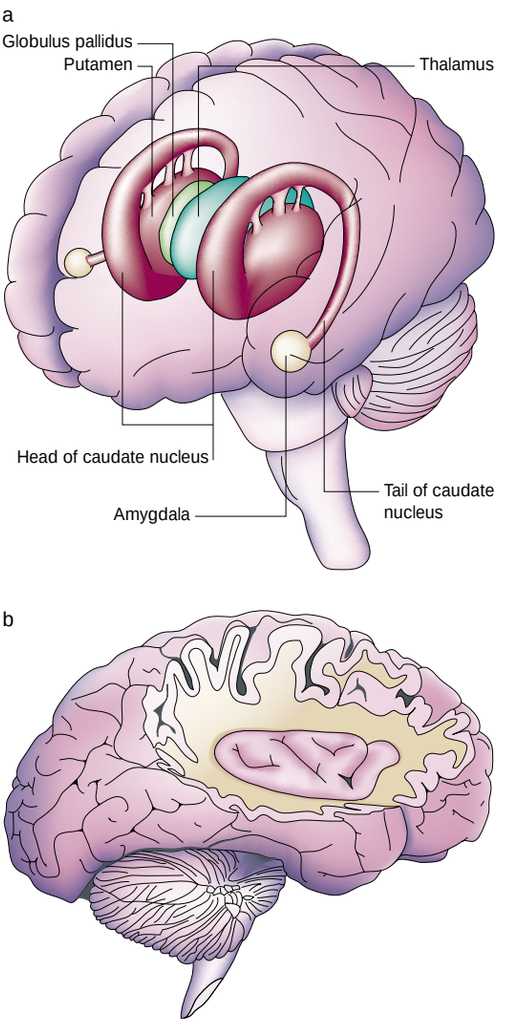


Figure 1 | **The human amygdala, basal ganglia and insula.** **a** | The location of the amygdala and selected nuclei in the basal ganglia (putamen, caudate nucleus and globus pallidus) in the human brain. The amygdala is a small almond-shaped structure buried in the anterior section of the temporal lobe. The putamen and caudate nucleus (striatum) lie beneath the cerebral cortex with the putamen positioned adjacent to the insula. The globus pallidus is positioned on the inner surface of the putamen adjacent to the thalamus. **b** | A view of the right hemisphere of the human brain with the superior temporal lobe and sections of the frontal and parietal lobes removed to reveal the insula. In an intact brain, the insula lies at the base of the lateral (Sylvian) fissure.

FEAR CONDITIONING
A form of Pavlovian (classical) conditioning in which the animal learns that an innocuous stimulus (for example, an auditory tone — the conditioned stimulus or CS), comes to reliably predict the occurrence of a noxious stimulus (for example, foot shock — the unconditioned stimulus or US) following their repeated paired presentation. As a result of this procedure, presentation of the CS alone elicits conditioned fear responses previously associated with the noxious stimulus only.

Box 1 | Unifying accounts of emotion

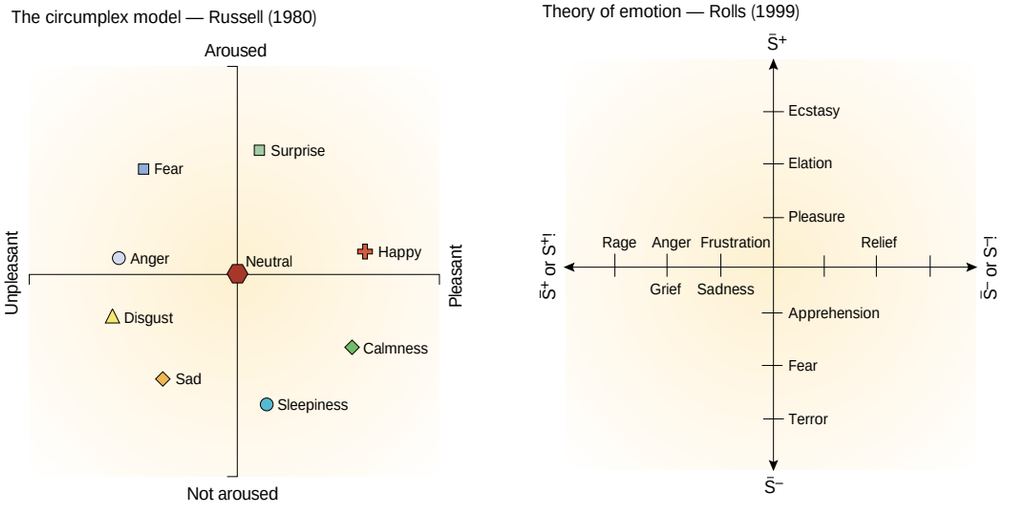
Dimensional models in psychology

Dimensional accounts of emotion were borne out of the observation that human errors in recognizing facial expressions are not random, but instead form consistent, replicable patterns that can be accommodated by a model in which facial expressions are recognized by registering their positions in a continuous two-dimensional space[124]. This approach has survived to the present day, its most recent variant being Russell's circumplex model[111,112], a two-dimensional system coding pleasure–displeasure and arousal–sleepiness.

Several researchers have shown that this type of two-dimensional model can be applied to the recognition of emotion from multiple modalities[111,125–127], and even to emotional experience[112]. The approach therefore reflects a multi-modal level of processing that can be accessed by all of the above modalities.

Dimensional models in neuroscience

A good example is Rolls' theory of emotion[119,120]. In the tradition of animal learning research, Rolls defines emotions in terms of states elicited by positive and negative instrumental reinforcers. Positive reinforcers are rewarding, whereas negative reinforcers are associated with punishment. The vertical axis of the graphic summarises the emotions elicited by the presentation of a reward ($\bar{S}^+$) or punishment ($\bar{S}^-$), whereas the horizontal axis shows emotions produced by the termination (or omission) of a reward ($\bar{S}^+$ or $S^+!$)[1] or punishment ($\bar{S}^-$ or $S^-!$)[1]. Moving away from the midpoint of each axis, the intensity of the emotion increases. A distinction is made between the emotions elicited where an active or passive behavioural response is possible. For example, on termination (or omission) of a positive reinforcer, anger might follow for an active response, but sadness/grief might follow where only a passive response is possible. Rolls[119,120] discusses experimental evidence that links the reward value (positive or negative) of reinforcers to the orbitofrontal cortex and amygdala.



impairment might be contingent on acquiring amygdala damage early in life. However, subsequent evidence of impaired fear recognition from patients that do not satisfy this criterion has made this explanation unlikely[14,15,19]. The puzzle of the contradictory results obtained by Hamann *et al.*[42] has recently been resolved, however, by Schmolck and Squire[41], who found that a different method of analysing these patient ratings revealed impaired performance. Impairments were also found on two additional tests of facial-expression recognition, particularly for fear and sadness. One of these additional tasks used a forced-choice labelling procedure, a format used widely in facial-expression research[43]. This particular forced-choice task was one of two used originally by Calder *et al.*[14] with two additional patients (DR and SE) with bilateral amygdala lesions; the second task involved morphed facial expressions and is illustrated in FIG. 2.

Of the two cases investigated by Calder *et al.*[14], DR's lesions resulted from a series of stereotactic operations for intractable epilepsy, targeted first at the left amygdala and then subsequently at both left and right amygdalae. SE's injury, by contrast, was caused by encephalitis; magnetic resonance imaging (MRI) of his brain shows extensive destruction of the right temporal lobe (including the amygdala) and a small region of abnormality in the left amygdala. Across the two facial-expression recognition tasks, both DR and SE showed impaired identification of fear, and to a lesser extent anger. DR also showed some difficulty in recognizing expressions of disgust. These findings complement the findings of Adolphs *et al.*[12,13] by showing that bilateral amygdala damage affects the recognition of facial expressions of fear and anger on different types of task. Reports of further patients with bilateral amygdala damage have since shown similar fear-recognition impairments on the same forced-choice tasks[15,19].

VOXEL
Volume element. The smallest distinguishable, box-shaped part of a three-dimensional space.

It is important to note that despite their problems in recognizing fear, the patients discussed above can provide plausible situations in which a person might experience fear. In other words, their deficits do not seem to arise from impaired understanding of the concept of fear.

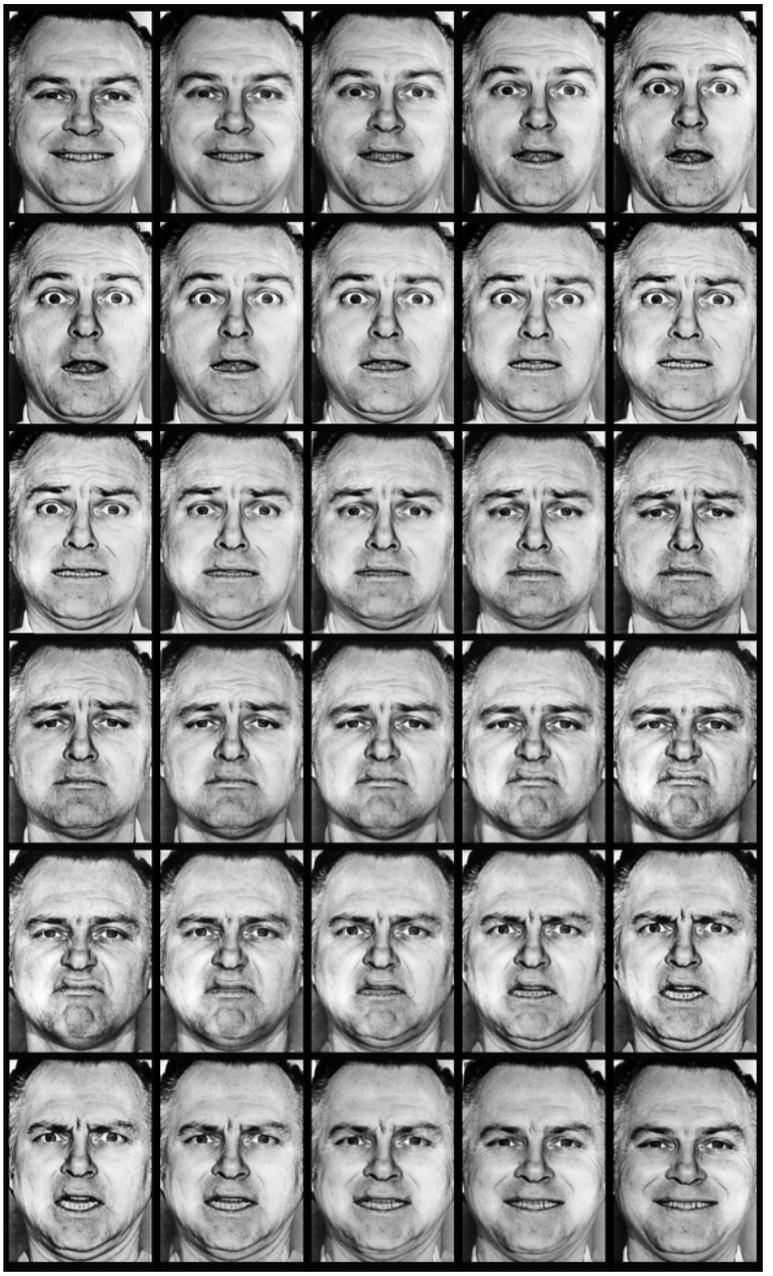


Figure 2 | **The Emotion Hexagon test of facial-expression recognition**[14]**.** The six rows of this illustration contain morphed (blended) continua ranging between the following six expression pairs. From top to bottom, the continua shown in each row are happiness–surprise (top row), surprise–fear (second row), fear–sadness (third row), sadness–disgust (fourth row), disgust–anger (fifth row), anger–happiness (bottom row). Going from left to right, the columns show 90%, 70%, 50%, 30% and 10% morphs along each continuum. For example, from left to right, the top row of images contain the following percentages of the happy and surprised expressions: 90% happy–10% surprise, and then 70%–30%, 50%–50%, 30%–70% and 10%–90% of the same two expressions. Data from neurologically intact participants show that stimuli that contain 90% and 70% of an expression are consistently identified as the intended emotion[14,82,138,139].

Functional imaging studies of fear recognition. The aforementioned patient-based studies clearly show impaired recognition of facial signals of emotion after amygdala damage; the most consistent and severe impairments are seen for fear. Given these observations, it is of considerable interest that functional imaging research has found increased activity in the amygdala for tasks in which participants view facial expressions of fear, relative to control conditions in which the faces convey happiness[28,29,33,34,44], disgust[30,31], anger[45] or no emotion (neutral)[30–33,45,46]. The location of the maximally activated VOXELS in the left and right amygdala found in these studies is summarized in FIG. 3. This figure also shows the maximally activated voxels from several functional imaging studies investigating fear conditioning (see also BOX 2). Functional imaging research has revealed important insights into the nature of the amygdala response to fear stimuli. Four key findings are highlighted below.

Time course of amygdala response. There is debate in the literature as to the temporal properties of amygdala responses to fear-related stimuli[47]. So, it is of interest that several studies, beginning with Breiter *et al.*[33], have shown that the response of the human amygdala to fearful facial expressions diminishes with repeated presentations (that is, the response habituates)[33–35,44]. Phillips *et al.*[35] and Wright *et al.*[44] have addressed this observation in more detail by showing that the habituation rate to facial expressions of fear is more rapid for the right than for the left amygdala. This might explain the larger number of significant left-hemisphere amygdala signals reported in studies using fearful facial expressions (FIG. 3). In addition, Phillips *et al.*[35] found that the haemodynamic response to neutral expressions increased over the course of the experiment in the right, but not the left, amygdala. The authors interpreted this finding as reflecting conditioning of the neutral stimuli to the aversive fear expressions in the right amygdala (see BOX 2 for a summary of fear-conditioning research made in humans).

Non-conscious processing of facial expressions. Öhman and colleagues have investigated non-conscious processing of fear-conditioned facial expressions using a method of presentation in which faces are shown very briefly, followed by an obscuring (neutral facial expression) mask[48]. Although participants are unable to identify the facial expression consciously, an emotional response is elicited. Using the same method of presentation, Morris *et al.*[49] have shown increased relative regional cerebral blood flow (rCBF) in the amygdala to fear-conditioned facial expressions of anger (relative to unconditioned angry expressions) for both masked (non-conscious) and unmasked (conscious) presentation formats. In related work, Whalen *et al.*[34] have shown that briefly presented masked facial presentations of fearful, but not happy, facial expressions increase amygdala activation relative to a neutral fixation-cross condition (see also REF. 50). Together with previous

Box 2 | The human amygdala and conditioned fear

There have now been numerous investigations of fear conditioning in humans using non-invasive imaging techniques such as positron-emission tomography (PET) and functional magnetic resonance imaging (fMRI). Early PET studies showed a remarkable lack of amygdala activation during fear conditioning, possibly due to the poor temporal resolution of the technique, resulting in an inability to disentangle fear conditioning and expression from extinction processes. Notable exceptions were a study[128] showing a positive correlation between conditioned fear, as indexed by heightened electrodermal activity (EDA) and relative regional cerebral blood flow (rCBF) in the right amygdala, and studies by Dolan and colleagues[129] showing amygdala activation using a covert fear-learning paradigm. In fact, some blocked-presentation studies have shown decreased relative rCBF in the amygdala[129,130], although this might relate to the inability to adequately separate extinction from acquisition and expression of fear.

The development of event-related fMRI has allowed investigators to study evoked haemodynamic activity to single stimulus categories, and to separate responses related to acquisition, expression and extinction of conditioned fear. Three of these studies[131–133] have been successful in showing amygdala involvement in conditioned fear. Of note, these studies showed enhanced amygdala activation during initial acquisition and extinction of fear, although how such findings relate to current debates on amygdala involvement in the acquisition and storage of conditioned fear in other species[47] remains unclear.

Although functional imaging studies have shown that the amygdala is involved in fear conditioning in humans, such studies cannot demonstrate that it is necessary. Such evidence has been provided in studies of patients with lesions involving the amygdala[134], who show impaired fear conditioning, as indexed by changes in EDA (see also REF. 135). Of note, damage to the amygdala does not impair explicit memories of the fear-conditioning protocol, only the affective consequences of such conditioning.

The neuroimaging studies are particularly interesting in showing extra-amygdaloid structures involved in fear conditioning. In particular, midbrain/hypothalamic regions and the anterior cingulate cortex are consistently activated[129,130,136]. These regions have been implicated in studies of fear processing in several animal species[137], but their roles in human fear are not fully understood. One concept that might help in this regard is the idea of a hierarchical external defence system, in which progressively higher-level components provide increasingly sophisticated and flexible solutions to the problem of avoiding danger[137].

research[28–33], these findings highlight the involvement of the amygdala in both conscious and non-conscious processing of fear-relevant information[8,9,48].

A neuromodulatory role for the amygdala. Morris and colleagues[28,29] reported that the emotional intensity of fearful facial expressions was positively correlated with changes in rCBF in the left amygdala, whereas the intensity of happy expressions was negatively correlated with rCBF in this area. In addition, regression analyses showed that the rCBF in an area of extrastriate cortex showed a significant positive correlation with left-amygdala rCBF for fear expressions, and a strong trend towards a negative correlation with left-amygdala rCBF for happy expressions. These findings were interpreted as support for the idea that efferent connections from the amygdala have a context-specific role in modulating extrastriate cortical function[51]. A plausible psychological interpretation of these data is that following the presentation of a fearful facial expression, our vigilance is enhanced by amygdala function, which increases the sensitivity of early visual processing. This interpretation concurs with the finding that phobic reactions induced in people with phobias to spiders and snakes also cause increased metabolic activity in the extrastriate cortex[52,53]. Similarly, amygdala and extrastriate activation are observed when subjects view pictures of aversive visual scenes[54–56].

Functional imaging research has also highlighted a neuromodulatory role for the amygdala in memory[57,58]. For example, Hamann *et al.*[57] have shown that recognition memory for both aversive and pleasant emotional scenes was positively correlated with rCBF in certain areas of the amygdala, hippocampus and parahippocampal gyrus at encoding. Moreover, for both positive and negative emotional scenes, rCBF in the identified amygdala areas was positively correlated with rCBF in the identified areas of hippocampus and parahippocampal gyrus, two areas known to be involved in memory. Amygdala involvement in processing positive affect is intriguing and we return to this issue at the end of this section.

Opposite effects of fear and happiness. Some studies have found that, whereas fearful facial expressions produce an increase in amygdala activity, significant decreases in amygdala activity are produced by happy facial expressions[28,29,34] (but see REF. 33). The significance of these findings is currently unclear, especially given the inherent difficulties in interpreting relative deactivations in neuroimaging studies. However, it is nonetheless interesting that levels of fear induced by the local anaesthetic procaine are positively correlated with left-amygdala rCBF, whereas levels of procaine-induced euphoria are negatively correlated with left-amygdala rCBF[59]. Note that the emotional effect of procaine differs between individuals. In relation to the neuromodulatory role of the left amygdala discussed earlier, the procaine study also found that levels of fear were positively correlated with rCBF in the medial occipital cortex, whereas levels of euphoria showed a negative correlation with this brain region.

Together with the observations summarized in the previous section, these findings indicate that the extrastriate cortex is modulated by an amygdala function that is influenced by emotions (that is, fear and happiness) perceived in others, and by emotional states (that is, fear and euphoria) experienced by the self. At a psychological level, these data indicate that seeing someone who is afraid (or happy) might have a similar effect on our level of vigilance towards potential threat of experiencing fear (or happiness) oneself. Clearly, this parallel between perception and experience merits further investigation.

Amygdala and non-facial signals of emotion. In general, functional imaging studies complement the observations of the patient-based research by showing disproportionate amygdala involvement in processing facial signals of fear. In addition, they go substantially further by identifying functions of the intact amygdala in healthy individuals. An important issue, however, concerns whether the role of the amygdala is restricted to facial signals of emotion (in particular, fear), or whether it is involved in processing signals of emotion from other sensory modalities. Anatomical studies of non-human primates show that the amygdala receives inputs from multiple sensory modalities[60]. So, one might expect that the human amygdala would be involved in

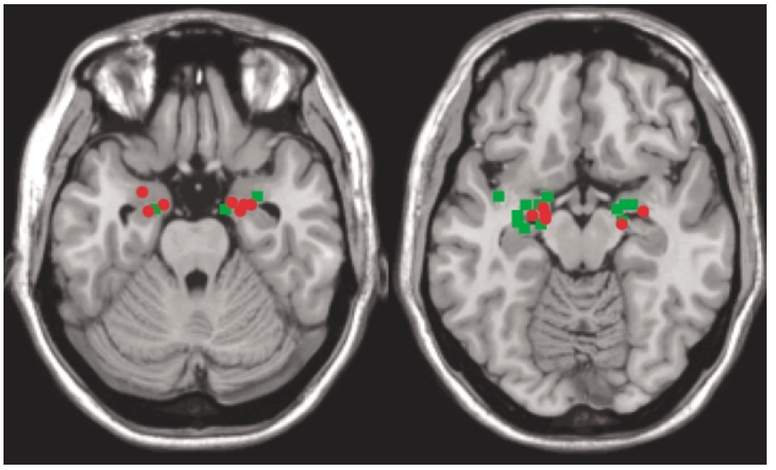


Figure 3 | **Functional imaging studies of fear recognition.** A summary of the maximally activated voxels reported as involving the amygdala from functional imaging studies investigating (i) fearful facial expression processing (green squares)[29-31,33,34,44,46,89], and (ii) conditioned fear (red circles)[49,131–133,140,141]. Different analysis conventions standardize to the brain in the Talairach atlas or the Montreal Neurological Institute (MNI) template. Hence, for display purposes all Talairach coordinates were converted to MNI space[142] and are displayed on a brain standardized to the MNI template. The *x* and *y* coordinates of the maximally significant voxel cluster of each contrast of these studies are plotted on one of two axial slices ($z = -14$ and $z = -24$); these axial slices were chosen because the *z* coordinates from all studies were proximal to one or other slice (mean deviation = 2.04 mm, standard deviation = 1.69 mm). Note that there is a tendency for facial expressions to engage the left amygdala, whereas conditioned fear seems to produce more bilateral activation. It also seems that fearful facial expressions are associated with more dorsal amygdala activity, whereas conditioned fear shows ventral and dorsal involvement. In fact, a Mann–Whitney comparison of the *z* coordinates of all maxima (converted to the MNI template) showed a significant difference between the conditioned fear and facial expression studies; $U = 54.0$, $z = -2.23$, $p<0.025$; no significant effects were found for the *x* and *y* coordinates ($p>0.2$). These images were prepared using MRIcro[143].

coding fear cues regardless of modality. Nonetheless, some have argued that the amygdala is not essential for recognizing emotion from vocal signals, or more specifically, prosodic cues[40,61].

Strong support for the cross-modal hypothesis comes from two bilateral amygdala patients — DR[14,62] and NM[15] — that were tested with largely the same test battery. DR showed impaired recognition of fear and anger from both facial and vocal cues[14,62], whereas NM's deficits with facial, vocal and body posture cues were predominantly restricted to fear[15]. In other words, both patients' impairments in the visual domain were mirrored by their impairments for processing auditory signals of emotion.

By contrast, Adolphs *et al.*[40] found that SM and a second bilateral amygdala patient (RH) showed no significant deficit on a vocal variant (emotional prosody) of Adolphs's facial-expression-rating task, despite both showing impairments on the original facial-expression task[11,40]. However, one method of analysing the vocal data indicated that RH actually experienced limited difficulty with vocal cues of fear and sadness[40]. In related work, Anderson and colleagues[20,61] have reported intact recognition of vocal but not facial signals of fear in an additional patient with bilateral amygdala damage (SP). However, the results obtained with SP need to be interpreted in relation to this patient's impaired recognition of vocal signals other than fear (that is, disgust and surprise)[61]. Hence, at the very least, the results from the analysis of SP are consistent with amygdala involvement in processing emotional signals from both visual and auditory modalities.

So, two patients with bilateral amygdala damage (SM and RH) show no obvious impairments in recognizing vocal signals of emotion, whereas two other patients (DR and NM) with similar damage do. This paradox requires explanation. In light of research on the role of the basal ganglia in the interpretation of prosody[63], some researchers have suggested that the impairment of DR in processing vocal cues might be caused by her limited extra-amygdaloid damage in this area[40,61]. Similarly, NM has additional damage to the thalamus and internal capsule. However, given the manner in which these patients' emotional deficits are mirrored across the visual and auditory processing domains, it seems unlikely that this could arise from damage to separate underlying systems. So, although we agree that extra-amygdala damage might be a necessary prerequisite of cross-modal impairments, the current patient data nonetheless concur with animal research showing that the amygdala is involved in coding fear cues from different domains and sensory modalities[64].

Unfortunately, few functional imaging studies have used fear cues other than facial expressions. One of these studies has shown considerable overlap in the neural correlates of processing facial and vocal signals of fear, which include the amygdala[31]. However, a second study that compared vocal signals of fear, sadness and happiness to a neutral condition, found an interaction between increased rCBF in the anterior insula and decreased rCBF in the right amygdala that was specific to vocal expressions of fear[65]. The reason for the discrepancy between these two studies is unclear, but it might relate to the different control conditions — mild happiness[31] and neutral 'voiced nasals'[65]. A third relevant study to the cross-modal debate used printed words presented in the form of an EMOTIONAL STROOP TASK[66]. The results showed that threat-related words (for example, assault, abuse, torture) resulted in increased rCBF in both amygdalae, and longer naming times relative to a neutral word condition (but see REF. 67). Last, it is worth noting that pictures of aversive visual scenes (for example, human violence, frightening animals and so on) also engage the amygdala[54,57].

Amygdala and the conscious experience of fear. An obvious question is whether the system involved in recognizing fear in others also contributes to the experience of this emotion. At present, there is a paucity of empirical data on this issue; however, at least three pieces of evidence indicate that the answer to this question might be affirmative. First, patient NM, whose case was discussed earlier, showed an abnormal score on a self-assessment questionnaire tapping the experience of fear[15] but normal scores for similar questionnaires assessing his experience of anger and disgust. Second, Halgren[68] has pointed out

EMOTIONAL STROOP TASK
A task in which participants are asked to name the colour of the font in which neutral and threat words are printed. Results show that colour-naming times for the threat words are slower than for neutral words. The generally accepted interpretation is that emotional words involuntarily capture attention, distracting the participants from naming.

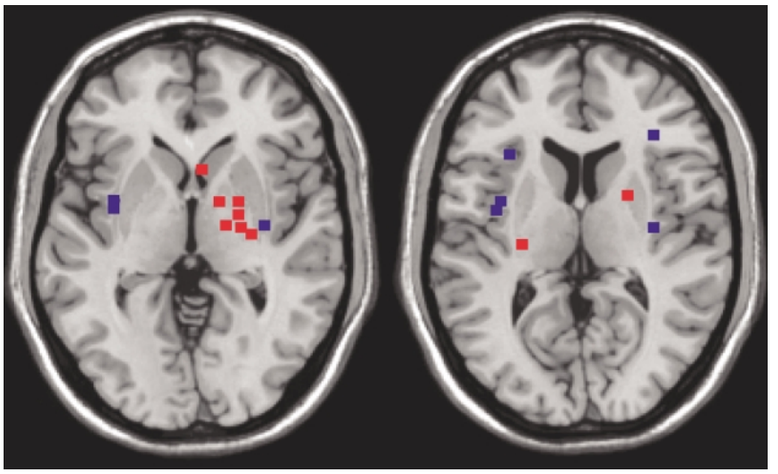


Figure 4 | **Functional imaging studies of disgust recognition.** A summary of the maximally activated voxels reported as involving the insula or basal ganglia from functional imaging studies investigating the processing of facial expressions of disgust[30,31,89]. Different analysis conventions standardize to the brain in the Talairach atlas or the Montreal Neurological Institute (MNI) template. Hence, for display purposes all Talairach coordinates were converted to MNI space[141] and are displayed on a brain standardized to the MNI template. The *x* and *y* coordinates of the maximally significant voxel cluster of each contrast of these studies are plotted on one of two axial slices ($z = 0$ and $z = 10$); these axial slices were chosen because the *z* coordinates from all studies were proximal to one or other slice (mean deviation = 2.75 mm, standard deviation = 2.08 mm). Blue squares indicate maxima reported as insula, red squares indicate maxima reported as basal ganglia. Open squares represent disgust minus neutral contrasts, filled circles represent disgust minus fear contrasts. The figure shows that the basal ganglia signals are largely confined to the right hemisphere, whereas the insula signals are more evenly distributed between the two hemispheres. These images were prepared using MRIcro[143].

that electrical stimulation of the amygdala in human subjects undergoing surgery for epilepsy can induce various reactions, but when an emotion is reported it is invariably fear. Last, anecdotal reports indicate that bilateral amygdala lesions can disrupt the normal response to fear-provoking situations. However, this is not always expressed as a reduction, or even abolition of the response[16,19], implying that the amygdala is not simply a fear generator. For example, the husband of a woman with bilateral amygdala damage described how his wife seemed to misinterpret the actions of youths who tried to mug him as 'larking around', whereas she became terrified on another occasion by a mildly aggressive exchange between characters in a television drama[19]. The same patient also showed inappropriate fear reactions to her carer and to close members of her family (see also REF. 16). These findings might relate to research in monkeys, which posits dissociable types of unconditioned fear responses for the amygdala (acute fear responses such as reaction to a snake) and orbitofrontal cortex (trait-like anxiety/fear responses such as reactions to humans[7]). A potentially promising line of enquiry concerns the extent to which the human amygdala is involved in the appraisal of potential threat.

Summary. The research that we have reviewed so far provides strong support for the disproportionate involvement of the amygdala in processing facial signals of fear and in fear conditioning. Consequently, several authors[13,14,34,61,62] have suggested that these findings might relate to the posited role of the amygdala in the detection, evaluation and coordination of response to signals of danger in the environment[8,9]. At present, the issue of whether the amygdala is also involved in coding fear cues from other sensory modalities (for example, vocal expressions) is less clear-cut, although we feel that, on balance, the current evidence favours the cross-modal hypothesis. However, there is clear need for more research investigating the cross-modal issue and, given the rarity of patients with selective amygdala lesions, additional functional imaging studies would be a good starting point.

At the present time, it is worth pointing out some cautionary notes. First, Rapcsak *et al.*[69] found that in a group of patients with various focal lesions, the recognition of fearful facial expressions was disproportionately impaired relative to other emotions, regardless of whether the damage included the amygdala or not. They attributed these findings to the fact that neurologically intact controls find fear more difficult to recognize than other emotions, and that the marked fear impairments were simply an effect of the difficulty level. We agree that marked fear-recognition impairments in the context of a general emotion-recognition impairment can arise from this kind of effect, and consequently should be interpreted with caution. However, it is important to note that the patients studied by Rapcsak *et al.*[69] differ from the bilateral amygdala patients in several important aspects. First, none of these patients was screened for basic visual defects. Second, some of the cases that we have discussed show highly circumscribed deficits affecting just fear[15], or fear and only one, or two, other emotions[12,14,41], whereas participants studied by Rapcsak *et al.* showed generalized deficits in which fear was the worst affected emotion. Third, the cases we have discussed show replicable fear impairments that are evident on different tests of facial-expression recognition[11–15,18–20,41], and in some cases, vocal-expression recognition[15,62]. The presence of a consistent fear deficit across different tests and different modalities makes it unlikely that an artefact related to task difficulty can explain the overall pattern of performance.

Second, although facial-expression research has indicated that the amygdala is particularly involved in coding facial signals of fear, functional imaging studies have demonstrated amygdala activation in response to positive stimuli such as pleasant pictures and pleasant tastes[57,70]. Similarly, there is currently a debate within the comparative literature concerning whether, in addition to aversive (fear) conditioning, the amygdala is also involved in appetitive conditioning[71–74]. A discussion of this literature goes well beyond the remit of this article, and at present, there are few human data to address this debate. Nonetheless, these findings are intriguing and might provide important clues concerning the nature of the relationship between the amygdala and fear. One possibility suggested in the literature is that different subnuclei of the amygdala might have different roles in processing positive and negative emotions, for example.

However, this seems unlikely given that cell recording in non-human primate amygdala has shown that the same cells can respond to both positive and negative stimuli[75]. Clearly, this is an important topic for future study. Finally, there is also evidence from functional imaging research to indicate that the amygdala might be involved in coding facial expressions of sadness[76]. However, this effect has not been observed in two additional studies[77,78].

As noted, some authors have preferred to interpret fear impairments as level-of-difficulty effects rather than emotion-specific impairments. Clearly, the most convincing way to refute this argument is to show that other types of brain injury can affect a different emotion while leaving fear intact. It is of particular interest, then, that recent studies have demonstrated disproportionate impairments in the recognition of facial expressions of disgust relative to fear.

The neural substrate of disgust

Rozin and his colleagues[79,80] have proposed that disgust evolved from the phylogenetically more primitive sensation of distaste. As such, non-human studies of conditioned taste aversion provide an interesting animal model of some aspects of this emotion[81]. However, Rozin and colleagues also suggest that the full concept of disgust is essentially unique to the humans. It can be a morally as well as a physically based emotion. For example, many people would not like the idea of putting on Adolf Hitler's jacket. In this example, the distaste involves moral rather than physical repugnance. From this perspective, human studies of disgust are not only informative about the neural representation of this emotion, they can also offer a perspective unattainable in animal studies.

Disgust recognition in Huntington's disease. Evidence that disgust might be associated with a particular neural substrate came first from an investigation of people with manifest Huntington's disease (HD)[82], an autosomal-dominant neurogenetic disorder that in its early stages particularly affects a region of the basal ganglia known as the striatum (FIG. 1). Participants in this study were shown the same facial-expression identification tests that were used with several of the bilateral amygdala patients[14,15,19] (FIG. 2). The patients with HD showed problems in recognizing several expressions, but a disproportionately severe impairment was found for facial signals of disgust.

Further evidence that HD particularly affects the recognition of facial signals of disgust has been shown in two additional studies[83,84]. The first provided detailed case studies of two patients. The second was an investigation of face processing (including facial-expression recognition) in people at risk of carrying the mutation associated to HD[84]. Participants that were subsequently identified as gene carriers (AR^+) were compared with each of two control groups — participants that did not carry the gene (AR^-) and neurologically intact controls. A comparison of the scores revealed just one significant difference for recognition of emotion — the AR^+ group made significantly more errors in recognizing facial expressions of disgust than either control group. Furthermore, this finding held for participants from the AR^+ group who showed no overt symptoms of the disease. So, the HD mutation was in itself sufficient to cause a disgust-recognition impairment in the absence of manifest symptomatology.

Other disorders that affect disgust recognition. The initial stages of HD principally affect the basal ganglia. It is therefore particularly informative that two psychiatric disorders associated with abnormal metabolic activity in this brain system[85–87] — OBSESSIVE-COMPULSIVE DISORDER (OCD) and TOURETTE'S SYNDROME — have also been shown to produce marked impairments in recognizing facial expressions of disgust, and to a lesser extent anger[88]. It is important to stress, however, that people with Tourette's syndrome that participated in this study only showed impaired recognition of disgust if they showed co-morbid obsessive-compulsive symptoms. So, the presence of OCD seemed to be a defining feature of the disgust deficit.

We discussed earlier that the most effective means of showing that impaired recognition of fear is not simply attributable to effects of the level of difficulty is to demonstrate that damage to a separate neural region causes a disproportionate impairment in recognizing a second emotion as compared with fear. Clearly, the fear and disgust impairments we have described have important complementary functions in strengthening the case that each constitutes a genuine emotion-specific impairment. It is important to remember, however, that HD, OCD and Tourette's syndrome are not characterized by focal neuropathology. So, although the patient-based studies are consistent with the idea that disgust and fear recognition are served by separate neural structures, the actual brain regions involved for disgust are unclear. In this regard, functional imaging research has been particularly informative.

Insula involvement in recognizing disgust. In contrast to functional imaging studies using fearful facial expressions, the amygdala has rarely been reported as a neural correlate for the processing of facial signals of disgust. Instead, all of the functional imaging studies that have addressed the neural correlates of viewing facial expressions of disgust[30–32,89] have pinpointed two areas — the insula and basal ganglia nuclei (most consistently, the putamen/pallidum) (FIG. 4). Insula involvement is particularly interesting given its identified role in gustatory function[90,91]. This role is illustrated by the observation made by Penfield and Faulk[92] that electrical stimulation of the insula of conscious human patients undergoing surgery produced sensations of nausea, unpleasant tastes and sensations in the stomach[92]. It is also of interest that lesions of the insula or pallidum in rats have been shown to interfere with CONDITIONED TASTE AVERSION[93,94]. Together, these findings concur with the proposal of Rozin and colleagues[79,95] that disgust has developed from a more primitive system involved in distaste.

OBSESSIVE-COMPULSIVE DISORDER
A psychological disorder in which the person is burdened by recurrent, persistent thoughts or ideas, and/or feels compelled to carry out a repetitive, ritualized behaviour. Anxiety is increased by attempts to resist the compulsion and is relieved by giving way to it.

TOURETTE'S SYNDROME
A rare genetic disorder, characterized by facial and vocal tics, and less frequently by verbal profanities.

CONDITIONED TASTE AVERSION
A form of memory in which a taste is associated with digestive malaise, leading to avoidance of the taste in subsequent presentations. This form of memory depends on the integrity of the insula.

Is there a cross-modal system for disgust? As is the case with impairments in recognizing fear, an interesting question is whether impaired recognition of facial expressions of disgust reflects a more general deficit that affects recognition of this emotion in multiple modalities (for example, vocal expressions). A test of vocal-expression recognition included in the study of patients with HD[82] discussed earlier showed some evidence of a cross-modal impairment for disgust. However, more solid evidence of this phenomenon has come recently from patient NK, a person with a focal lesion of the brain areas that have identified by functional imaging as the neural correlates of processing facial expressions of disgust — the insula and basal ganglia[96]. The damage present in NK is lateralized to the left hemisphere and includes the insula, putamen, internal capsule, globus pallidus and, to a lesser extent, the head of the caudate. On tests of facial-expression recognition and vocal-expression recognition, NK showed a highly selective deficit for disgust in the context of predominantly preserved recognition of other emotions. NK also showed abnormal performance on a questionnaire tapping his experience of disgust, whereas his scores for comparable questionnaires assessing his experience of fear and anger were normal. These results are consistent with damage to a system involved in recognizing signals of disgust from both facial and vocal modalities. In addition, they indicate that this system might be significant in the experience of this emotion. It is worth emphasizing that the performance of NK shows a marked double dissociation with the performance of patients with amygdala damage, particularly patient NM[15], who was tested with a similar test battery.

To our knowledge, very few functional imaging studies have addressed whether a single system might underlie the recognition of disgust in different domains or sensory modalities. In the most relevant study, Phillips *et al.*[31] compared activation after viewing facial signals of disgust to activity after listening to vocal signals of the same emotions. As in previous work, facial signals of disgust engaged areas of the insula and striatum. By contrast, vocal cues produced significant signals in several areas, including the superior temporal regions, thalamus, and rostral and dorsolateral prefrontal areas. A second relevant study did not directly compare signals of disgust from different modalities. However, it showed that pictures of disgusting scenes (for example, decaying food, cockroaches and so on) produce a similar pattern of insula activity to that observed for facial expressions of disgust[97]. A third imaging study showed that recall of events associated with the experience of guilt increased insula activity relative to the recall of neutral events[98]. This is interesting, considering that guilt has been characterized as disgust directed towards the self[99].

Insula–basal ganglia in HD, OCD and Tourette's. Studies of neuroimaging and case NK provide direct support for the involvement of the insula and basal ganglia in disgust recognition. It is worth emphasizing that these structures are highly interconnected[100], and that both regions have been implicated in HD[101–104]. With regard to OCD, functional imaging research has shown that, in addition to the basal ganglia dysfunction discussed earlier[86,87], metabolic activity in the insula is correlated with scores in the Yale–Brown obsessive-compulsive scale (Y–BOCS)[105], a recognized measure of OCD severity[106]. In addition, the first two factors extracted from a factor analysis of scores on this scale were found to be correlated with rCBF in the striatum and parietal cortex (factor 1: checking compulsions, and religious, aggressive and sexual obsessions), and the striatum and temporoinsular cortex (factor 2: symmetry and ordering symptoms)[105]. It is also of interest that OCD symptoms represented by these factors are frequently seen in Tourette's syndrome with co-morbid OCD[107–109], particularly a liking for symmetry and order. This might be important because patients with Tourette's syndrome in the study mentioned above[88] only showed a disgust impairment if they showed OCD symptoms. In this regard, it is also relevant that OCD is a recognized psychiatric correlate of HD.

Summary. Overall, studies on patients and functional imaging research show a link between the recognition of facial expressions of disgust and the insula–basal ganglia regions. Whether these same brain areas underlie the coding of disgust signals from multiple sensory modalities is only beginning to be addressed. However, the current data seem largely consistent with a cross-modal hypothesis. The contribution of these regions to the experience of disgust is also underinvestigated at present, but the limited evidence indicates that there might be a significant link[82,96,98]. As with the fear impairments we have discussed, it is important to point out that patients with disgust-recognition impairments are able to provide examples of plausible situations in which a person might feel disgusted and do not show impaired knowledge of the concept of disgust.

Implications for theories of emotion

We chose to focus on the neuropsychology of both fear and disgust recognition for two reasons. First, remarkably similar pictures seem to be emerging for both emotions. Second, fear and disgust provide a striking double dissociation that substantially strengthens the theoretical impact of either area alone. As discussed, patient-based research has shown that damage to the amygdala causes a disproportionate impairment in recognizing facial signals of fear[11–15,19,20,41], whereas abnormalities of the insula–basal ganglia regions primarily affect the recognition of facial signals of disgust[82–84,88,96]. Functional imaging has substantiated this dissociation[28–34,44–46,89] and, in the case of fear research in particular, it has identified important insights into the underlying neural mechanisms. However, although there is general agreement that human amygdala is involved in recognizing fear from facial signals, its role in recognizing vocal signals of this emotion is still being debated[15,40,61,62]. On the basis of the current evidence, however, we feel that the data for both fear and disgust favour the cross-modal hypothesis; a position that concurs with the limited human data indicating that the amygdala and insula–basal ganglia might also contribute to the experience of fear and disgust, respectively.

It is important to clarify that we are not of the opinion that fear and disgust are represented by entirely distinct neural circuits. Nor do we wish to suggest that the amygdala and insula–basal ganglia regions are simply fear and disgust generators. Our conclusions seem warranted by several lines of evidence. First, functional imaging research shows that facial expressions of fear, disgust and anger all engage similar areas of inferior prefrontal cortex[32,76,78]. Second, research on patients[110] shows that damage to this and the surrounding areas impairs recognition of these emotions. Third, work in both humans and monkeys shows that bilateral amygdala lesions do not abolish all fear reactions[7,19]. However, we think that the studies included in this review do indicate that the neural mechanisms underlying fear and disgust might be separate in part, and this clearly has implications for the representation of emotion.

So, to return to our original question, in what way have these studies of the neuroscience and neuropsychology of disgust and fear contributed to our understanding of human emotion? As we discussed in the introduction, contemporary theories of emotion are essentially of two generic forms — category-based accounts and dimensional models (BOX 1). The idea that individual emotions are represented as distinct psychological categories is clearly consistent with observations that fear and disgust have different neural correlates and can be selectively impaired. The issue of whether dimensional models can account for these observations is less straightforward.

There are several two-dimensional models that have been proposed to account for the structure of emotion, including, for example, Russell's circumplex model[111,112] (BOX 1) and Watson and Tellegen's[113] positive-affect/negative-affect model. Most models are based on purely descriptive taxonomies, and they are reasonably successful in describing the measures of self-reported emotion and the relative confusabilities of different facial expressions (and other emotional cues). However, it is unclear that such models can account for the specific deficits in processing fear and disgust for at least two reasons. First, it has been suggested that these dimensions are the product or the expression of several discrete systems that code more basic emotional constructs. If this is correct, then these models do not provide an appropriate psychological level to account for the selective impairments that we have described. Alternatively, if these dimensions are indeed the foundations of human affect, then damage to just one of these broad dimensions (for example, pleasure or arousal in the Russell model) should produce effects on the wide range of emotions. But this does not seem to be the case (but see REF. 114 for an attempt at such an account).

For the latter interpretation, however, a crucial consideration might be the number of dimensions proposed in such a unifying system. The fear versus disgust dissociations show that a system with low (N = 2) dimensionality runs into serious difficulties. However, there are ways in which dimensional models could be revised to account for the present data. For example, a hybrid model, in which discrete emotions are seen as preferred states or 'attractors' in a state-space defined by N (where $N > 2$) higher-order dimensions[115,116] could potentially account for some of the deficits reported here. It is unclear, however, whether the nature of such abstract dimensions could be discovered on the basis of purely descriptive analyses of, for example, self-report data. Indeed, the thrust of an attractor-state account is to bridge the theoretical gap between the between category-based and multidimensional frameworks — such a system will show properties of both.

We suggest that, in the future, it will be more useful for emotion research to focus on causal mechanisms, rather than descriptive taxonomies. This approach is characteristic of 'basic' emotion accounts[117,118], which posit a variable number of discrete emotions that differ from one another in several fundamental ways. However, the same approach is also evident in other emotional theories, such as those provided by Rolls[119,120] (BOX 1), Gray[121] and Davidson[122,123], which relate broad classes of emotions to underlying reinforcement or motivational systems. However, it is unclear whether these models would predict the patterns of deficit reviewed here.

We would argue that an approach seeking to discover evidence for dissociable emotion systems after brain injury might provide a useful model in which to understand the structure of emotion, both in terms of proximate mechanisms (for example, neural structures) and ultimate causation (for example, adaptive significance). So far, this research has described distinct neural pathways that underlie the processing of signals of fear and disgust in humans. This dissociation can be related to the adaptive significance of these emotions as responses to critical forms of threat that are associated with external (fear) and internal (disgust) defence systems[81].

In a recent article, LeDoux[9] highlighted some of the attributes of the comparative neuroscience approach that, he believes, have facilitated this area's substantial contribution to our understanding of emotion in recent years. These included "… focusing on a psychologically well-defined aspect of emotion, … using an experimental approach to emotion that simplified the problem in such a way as to make it tractable, … circumventing vague and poorly defined aspects of emotion, and … removing subjective experience as a roadblock to experimentation". Similarly, the human neuropsychological studies that we have reviewed here share several of these attributes by focusing on what some maintain to be the bedrock of human affect — the basic emotions. By adopting this general approach, the neuropsychology of emotion can be as useful in dissecting and understanding the emotion system as cognitive neuropsychology has been in understanding the cognitive system.

Links

ENCYCLOPEDIA OF LIFE SCIENCES Limbic system
MIT ENCYCLOPEDIA OF COGNITIVE SCIENCE Emotion and the human brain | Emotion and the animal brain | Amygdala | Limbic system | Basal ganglia

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