Emotion: Neuroimaging

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Background

Emotions, of which fear is a prime exemplar, are unique among mental states in having in equal measure psychological and somatic referents. The former embody the subjectivity of all psychological states, whereas the latter are evident in stereotyped behavioral patterns of facial expression, comportment, and states of autonomic arousal. Emotional states exert global effects on virtually all aspects of cognition, including attention, perception, and memory. They also exert biasing influences on high-level cognition, including decision-making processes. An informed neurobiological account of emotion must incorporate how these wide-ranging effects are mediated.

Historically, emotional behavior and experience have been attributed to the functions of the limbic system. But an increasing body of evidence suggests that there is widespread propagation of emotional signals within the brain, and this has diminished the general utility of the concept of a limbic-based emotional system. Consequently, contemporary perspectives on emotion emphasize a dynamic brain configuration of emotional states, which to a large extent are determined by an emotion-eliciting context. Within this framework, emotional states are not unique to any single brain region but are expressed in widespread patterns of brain activity, including within early sensory cortices.

Notwithstanding these considerations, the structure most closely affiliated with emotional processing is the amygdala, an anatomically and functional heterogeneous bilateral collection of nuclei in anterior medial temporal cortex. The importance of the amygdala in emotional and behavioral control was first highlighted by reports that rhesus monkeys with bilateral temporal lobe ablations no longer showed appropriate fear or anger responses. The importance of the amygdala derives in part from its extensive anatomical connections with the sensory-processing cortices, hippocampus, basal ganglia, limbic cortex and homeostatic regulatory regions of the hypothalamus and brain stem. This connectivity means that processing within this structure can exert diffuse modulatory influences, including influences on effector autonomic and motor output systems.

Although much of what we can infer about emotional processing in the human brain is derived from the type of studies already described, the advent of high-resolution, noninvasive, functional neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), have greatly expanded this knowledge base.

Imaging Emotional Stimuli

Studies of human emotional processing using functional neuroimaging techniques have invested intensely in an experimental approach that involves presenting to healthy subjects stimuli that represent basic emotions as expressed in facial expressions of fear, anger, sadness, disgust, happiness, and surprise. The key finding from these studies is an enhanced amygdala response to the presentation of fearful faces, as well as enhanced activation in the sensory-processing regions specialized for faces, the fusiform gyrus. A notable observation is that an emotional response to fear in facial expressions is conveyed principally by a specific feature, namely the eyes, such that the presentation of fearful eyes alone can elicit an amygdala response.

The selectivity of amygdala for processing fearful faces, as suggested in neuropsychological studies, is challenged by neuroimaging findings of an amygdala response to a range of emotional faces (**Figure 1(a)**). Thus, although fearful faces provide reliable stimuli for eliciting amygdala responses, other emotional expressions, including sad, anger, and disgust, also evoke increased amygdala activity (**Figure 1(b)**). Indeed, when brain responses to multiple emotions are studies within the same experiment, a reliable amygdala activity is elicited to an entire range of emotions.

A widely held view is that emotion is reducible to dimensions of arousal and valence. A key question arising from this conceptualization is whether amygdala activation due to the presentation of emotional stimuli, seen using functional neuroimaging, reflects a specialization for processing emotional intensity (a surrogate for arousal) or, alternatively, for processing valence. There is good evidence for an amygdala response profile that suggests a more complex profile involving an intensity-by-valence interaction. Consequently, it seems that the amygdala codes neither intensity nor valence *per se* but, instead, an interaction between intensity and valence that reflects the overall emotional value of a stimulus.
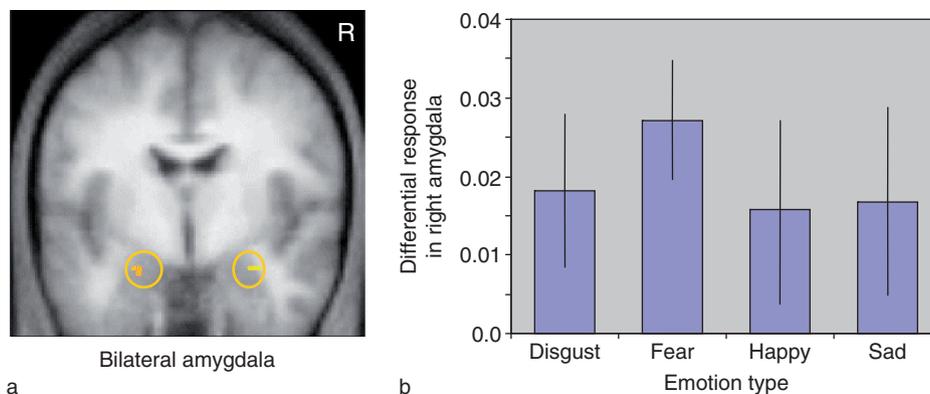
Figure 1 Amygdala responses to emotion: (a) bilateral amygdala activation in response to the presentation of multiple exemplars of emotion; (b) response magnitude for four exemplars of emotion taken from a voxel in the left amygdala.

Imaging the Acquisition of Emotion

In classical or Pavlovian conditioning, a neutral stimulus, through pairing with an emotional stimulus (e.g., an aversive noise in fear conditioning), acquires the ability to predict its future occurrence. Associative learning provides a highly conserved means by which organisms acquire knowledge regarding the causal structure of the environment. Such knowledge endows an organism with the ability to anticipate future events of value, such as the likelihood of food or danger, on the basis of predictive sensory cues. The amygdala plays a central role in this type of causal learning. Thus, amygdala activation is seen when a previously neutral item (the conditioned stimulus (CS+)) acquires predictive significance through its pairing with a biologically salient reinforcer (the unconditioned stimulus (UCS)). This pattern of activation is seen both for aversive and appetitive events. Thus, across a wide range of experiments, an enhanced amygdala response is evident when subjects learn that a neutral stimulus predicts the occurrence of an emotion-inducing event, for example, an aversive event.

Theoretical accounts of associative learning based on the Rescorla–Wagner rule and their real-time extensions, such as temporal difference (TD) reinforcement models, provide plausible descriptions of the computational processes underling associative learning. Crucial to these models is the expression of a teaching signal, referred to as the prediction error. A prediction error is used to direct acquisition and refine expectations relating to predictive cues, and it records a change in expected affective outcomes, being expressed whenever predictions are generated, updated, or violated. Functional neuroimaging studies have demonstrated that such a prediction error is expressed in the human brain in structures such as amygdala, striatum, and orbital-prefrontal cortex (OFC) during aversive and appetitive associative emotional learning.

Imaging Updating of Emotional Value

Predictive contingencies acquired through associative learning are limited in their ability to provide a basis for optimizing future behavior. For example, the value of the states associated with predictive cues can change in the absence of further pairing with these cues. Thus, a cue that predicts that the occurrence of food that is valued when a person is hungry has diminished value when the person is sated with that same food. Consequently, maintaining an updated representation of the current value of a sensory-predictive cue that does not depend on new learning in relation to that cue greatly enhances behavioral flexibility.

In human functional neuroimaging studies, neuronal responses elicited by predictive stimuli (such as a CS+) that have been subject to devaluation are associated with parallel response decrements in the left amygdala and OFC. This response pattern suggests these regions contribute to updating the reward value of predictive stimuli. This pattern of value-related response expressed in these regions may explain why pathologies that impact on the medial temporal and basal orbital-frontal lobes, such as fronto-temporal dementias, are associated with behavioral aberrations such as indiscriminate eating, food cramming, change in food preference, and hyperorality. In these contexts, damage to the OFC and amygdala entails that subjects can no longer recruit motivationally appropriate representations of food-based reward value, either appetitive or aversive, in response to predictive cues.

Imaging Emotion in Social Contexts

The amygdala may be important for social cognition and a functional dysregulation within this structure is often suggested as important in the genesis of disorders of social cognition, such as autism. A role for the amygdala in social cognition is suggested by observations of increased activity to the presentation of faces that subjects rate as untrustworthy. An increased amygdala response in White American subjects viewing pictures of unfamiliar Black (African American) faces has also been reported. Increased amygdala activity was not seen when White Americans viewed familiar positively regarded Black (African American) faces, suggesting that this response pattern reflects a learned, culturally specific phenomenon and not innate processes. Observations such as these have led to a view that increased amygdala responsivity to facial expressions actually indexes the occurrence of potential threat. This idea has gained support from other functional neuroimaging studies which show that threat, as embodied in threatening words, aversive tastes, and aversive odors, all evoke an amygdala response. Thus, a stimulus within any modality perceived as a potential threat evokes increased amygdala activity.

Imaging Modulatory Effects of Emotion on Cognition

The domain in which the modulatory influences of emotion are best characterized is episodic memory. The benefit of emotion to episodic memory function is confirmed across numerous studies which show a mnemonic enhancement for material that encompasses personal autobiographical and picture- and word-based items, an effect best seen in free recall tasks. The critical role played by the amygdala in this modulation is evidenced within functional neuroimaging experiments in which amygdala activity during encoding predicts a benefit in the later recall of emotional material. Thus, enhanced amygdala activity at encoding for both positive and negative stimuli is predictive of later episodic memory function, as determined in free recall tasks.

The role of the amygdala in modulating episodic memory function is not restricted to the encoding of emotional events. This structure is also engaged during the retrieval of emotional items and contexts. Connectivity analysis performed on neuroimaging data indicates that contextual recall of emotional events leads to enhanced amygdalar–hippocampal coupling under a controlling influence from OFC. This finding of enhanced interactions between the amygdala and hippocampus is also supported by observations from patients who have lesions to either the amygdala alone or jointly to the amygdala and hippocampus. During the encoding of emotional items, there are bidirectional interactions between these structures, such that an enhanced amygdala response to emotional items is dependent on an intact hippocampus, whereas, conversely, an enhanced hippocampal response to emotional items is dependent on an intact amygdala.

The neurochemical mediation of emotional memory effects has been a subject of increasing interest. Emotional memory enhancement in human subjects can be blocked by the administration of the β-adrenoreceptor blocker propranolol prior to the study. In subjects who are pretreated with propranolol, functional imaging experiments show an absence of emotion-evoked activation of the amygdala. Intriguingly, the encoding of negative emotional items has anterograde and retrograde amnesic effects such that, for example, in word-list presentations there is a relative amnesia for antecedent and preceding items.

Imaging Emotional Enhancement of Perception

An evolutionary perspective on emotion suggests that environmental events of value should be susceptible to preferential perceptual processing. There appear to be two distinct mechanisms by which emotion influences perception. One of these is through emotion interacting with attention, leading to enhanced deployment of attention, leading to the preferential detection of emotional events. For example, in spatial-orienting tasks there are faster responses to targets appearing on the same side as an emotional cue (e.g., faces, spiders, threat words, or conditioned shapes) and a slower response to those appearing on the opposite side. Neuroimaging data, using spatial-orienting paradigms, indicate that the OFC is the site of the expression of this type of interaction between attention and emotion.

Attention is not the sole means by which emotional stimuli influence perception. There is now evidence for mechanisms that are independent of attention. In visual backward-masking paradigms, a target presented for a brief instance can be rendered invisible if it is immediately followed by a second masking stimulus. In situations in which the hidden target stimulus is an emotional item (e.g., a conditioned angry face or a spider), there is preserved processing indexed by differential skin conductance responses (SCRs) to fear-relevant compared to fear-irrelevant targets. Similar findings are evident using the attentional blink paradigm which refers to a situation in which the detection of an initial target stimulus in a stimulus stream leads to impaired awareness, or

inattentional blindness, for a successive second target. Neuroimaging data show that the processing of emotional stimuli outside the window of awareness is mediated by the amygdala.

Studies of patients with focal brain lesions provide additional evidence for a degree of independence between emotional processing and attentional mechanisms. Following brain damage to the right inferior parietal cortex, patients frequently fail to perceive a stimulus presented in their contralesional hemifield (spatial neglect). This contralesional deficit is greatly attenuated for emotional stimuli (e.g., faces with happy or angry expressions or images of spiders). Nonconscious processing of emotion has also been demonstrated in the blindfield of patients with damage to the primary visual cortex. In terms of the anatomical substrates of these effects, functional neuroimaging evidence implicates the amygdala. In functional neuroimaging experiments, using visual backward-masking paradigms, an amygdala response discriminates between unseen emotional and unseen nonemotional targets. In other experiments that involve overt stimulus presentation but in which attention is systematically manipulated, such that emotional items are presented out of the window of attention, an amygdala response to fearful faces is independent of concurrent attentional focus. Likewise, patient studies of subjects with either blindsight or visual extinction demonstrate an amygdala response to emotional stimuli presented out of awareness in the damaged hemifield. Interestingly, residual processing abilities for the unaware presentation of emotional stimulus are associated with the engagement of a subcortical retino–collicular–pulvinar pathway specific to unaware emotional stimulus processing. The involvement of this pathway is of considerable interest because it is implicated in residual visual processing evident in patients with blindsight. The suggestion here is that certain classes of emotional stimuli, for example fearful faces, can be processed by a non-cortical pathway to allow rapid adaptive responses to danger.

How the pre-attentive processing of emotional events influence, and enhance, perception is a question addressed by studies in normal subjects and patients with discreet lesions. One possibility is that inputs from emotional-processing regions, in particular the amygdala, modulate the very regions involved in object perceptual processing, specifically those related to the emotion-eliciting object. Anatomically the amygdala receives visual inputs from ventral visual pathways and sends feedback projections to all levels of this pathway. Neuroimaging data provide evidence for the enhancement of functional connectivity between the amygdala and extra-striate visual regions, expressed during the processing of an emotional visual input. Crucially, neuropsychological data from patients with amygdala damage indicate that a perceptual enhancement for emotional items is abolished following damage to this structure. Furthermore, in patients with amygdala lesions, the enhancement of activity seen in early extra-striate visual areas during the encoding of emotional items (e.g., faces) is no longer expressed. This type of evidence is consistent with a proposal that early sensory cortex boosting of activity reflects a direct modulatory influence from the amygdala. Indeed, an emotion-induced enhanced connectivity between the amygdala and extra-striate regions associated with boosting of perception has been demonstrated in a visual detection.

Imaging Feeling States

Human emotion research often conflates neurobiological mechanisms that index the perception or occurrence of an emotional event with their subjective experiential counterparts, referred to as feeling states. Feelings can be defined as mental representations of physiological changes that characterize, and are consequent on, processing an emotion-eliciting objects or image. This definition assigns an important causal role in the genesis of subjective feeling states to afferent feedback to the brain, both sensory and neurochemical. At a broader level, feeling states can be subsumed within homeostatic mechanisms that underlie the survival of the organism. In a recent theoretical model, based on neurological observations, prime emphasis is given to the cerebral representation of bodily states as providing the substrate for emotions and conscious awareness.

The key neurobiological question is whether brain systems supporting emotional perception are distinct from those supporting feelings states. Candidate structures that mediate feeling states encompass those that receive inputs regarding the internal milieu and include the brain stem periacqueductal gray (PAG) and parabrachial nuclei, tegmentum, hypothalamus, and insular, somatosensory and cingulate cortices. Functional neuroimaging provides strong evidence that feelings are mediated by neuronal systems distinct from those that support emotional perception. Thus, volunteer studies have shown that the generation and rerepresentation of peripheral autonomic states involve structures such as the anterior cingulate and insular cortex. Recall of subjective feeling states associated with past emotional experiences engages regions encompassing upper brain stem nuclei, hypothalamus, somatosensory, and insular and orbito-frontal cortices. In subjects with pure autonomic failure (PAF), where there is an absence of visceral afferent information regarding the peripheral body state due to selective

peripheral autonomic damage, there is attenuation of subjective emotional feelings and of emotion-elicited neuronal activity in regions implicated in mediating feeling states. A notable feature of these studies is an absence of any deficit in amygdala activity, in keeping with a more critical role for this structure in emotional perception.

Among the regions most strongly implicated in mediating feeling states is the insular cortex. Direct evidence for its role in representing subjective feeling states comes from a study that used a task that taps awareness of internal bodily states, namely a heartbeat detection task. When subjects detect their own heartbeat, there is enhanced activity in the anterior insular cortex. The proposal that this area mediates feelings is also bolstered by evidence that empathetic awareness of the subjective feeling states of others, for example the awareness engendered when we observe another person receiving pain, is reflected in enhanced activity within the anterior insular cortex and anterior cingulate.

Imaging Emotional Influences on Decision Making

Real-life decision making often involves choices between actions which yield rewards with varying probabilities and magnitudes. Decisions that seek to optimize rewards require an estimation of an expected future reward that will follow from choosing a particular action and the subsequent use of these values to guide action selection. In its simplest form, reward prediction based on expected value can be studied through classical conditioning, in which an arbitrary cue (or CS+) takes on predictive value by association with the subsequent delivery of an affectively significant stimulus or UCS (which can be a reward or punishment or, strictly speaking, an appetitive or aversive stimulus). Neuroimaging studies implicate the OFC alongside other structures such as the amygdala and ventral striatum in reward prediction. Enhanced responses to cues predictive of delivery of either a pleasant or aversive odor result in significant orbito-frontal responses suggesting the OFC maintains predictions for negatively valenced as well as positively valenced stimuli. Human neuroimaging studies of classical conditioning for reward report prediction error signals in prominent target areas of the dopamine neurons, including the OFC. The finding that neural prediction error signals are present in the OFC and throughout the reward network is consistent with the possibility that this mechanism is implemented in the human brain to mediate flexible learning and updating of stimulus–reward associations, a function frequently ascribed to the OFC.

Theoretical accounts of human decision making emphasize a rationalistic perspective of utility maximization, which invokes analytic processes mediated by the executive prefrontal cortex. An emotional or value-based contribution to high-level decision making is evident following ventromedial prefrontal cortex damage where, despite the absence of intellectual deficits, patients make real-life decisions that are disadvantageous. The somatic marker hypothesis arising from observations with these type of lesions suggests that this region provides access to feeling states in relation to past decisions during contemplation of future decisions of a similar nature. Thus, the evocation of past feeling states biases the decision-making process toward or away from a particular behavioral option. However, alternative frameworks that might explain the behavioral deficits seen following damage to this region include an inability to represent the value of competing options for action or a discounting of future rewards. Neuroimaging evidence indicates that this region is activated both during anticipatory states in relation to rewards or punishments and by actual outcomes associated with reward or punishment.

To make effective behavioral decisions between different types of reward requires that the rewards be encoded in a common representational space or currency. A distinct representation of value for different rewards can facilitate goals pertaining to specific motivational states. A candidate region that is activated to different types of reward is the anterior sector of the medial OFC, and this region is a potential candidate for mediating a representation of unitary stimulus–reward value.

It is well recognized that human decision making does not always accord with rationalistic perspectives of utility maximization. An influence of prior outcomes on decision processes is captured by regret theory, in which counterfactual thinking involved in comparing an obtained and forgone outcome indicate that the latter, if chosen, would have been more advantageous (**Figure 2(a)**). It is known that subjects who experience regret show a subsequent bias away from the maximization of expected value in their choices. This behavioral bias is associated with engagement of the amygdala and orbito-frontal cortices, regions that are also engaged by the actual experience of regret (**Figure 2(b)**). This pattern is consistent with theories that suggest that the evocation of past emotions in the context of decision making provides a biasing influence on rational decision processes.

A tenet of rational behavior is invariance or extensionality, in which human decisions are held to be consistent regardless of how choices are presented. A deviation from this axiom is described within
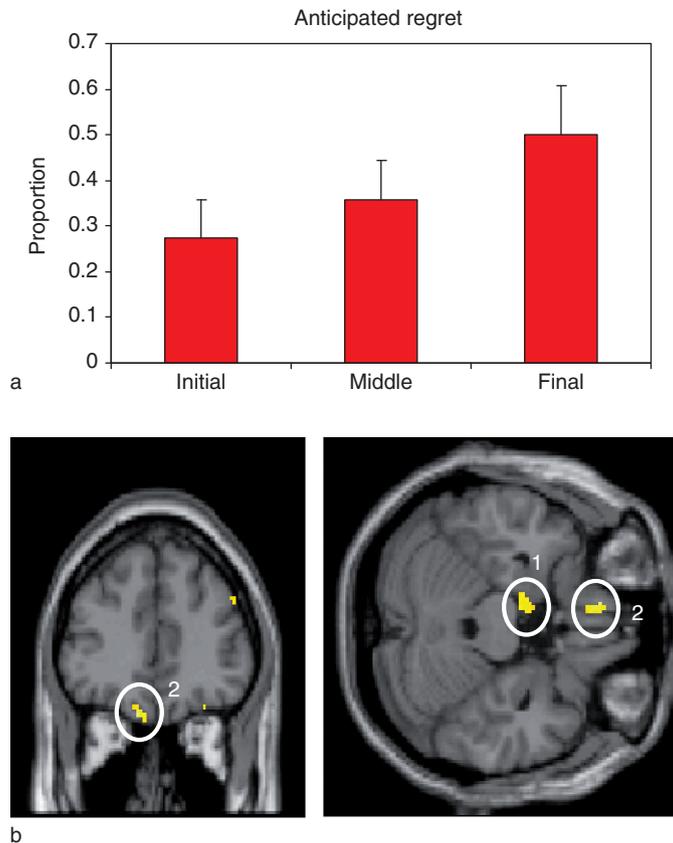
Figure 2 Influence of regret on choices in a gambling task: (a) proportion of subject choices that can be attributed to experiencing regret; (b) brain activity during choice. In (a), the graph shows an increasing attribution of choices to prior experiences of regret; In (b), amygdalar (1) and orbito-prefrontal (2) engagement correlates with the increasing influence of regret on choice.

prospect theory as the framing effect. In simple terms, the framing effect describes a bias in decision making observed when a gamble is presented in terms of gain, leading to choices of a sure option, versus the same gambles presented as a loss leading to risk seeking, when subjects are biased to choose a gamble option. Functional neuroimaging data show that a framing-engendered bias in human decision making, risk aversiveness in the gain frame and risk seeking in the loss frame, is associated with enhanced amygdala activity. The suggestion here is that an emotional heuristic, mediated via key emotion-processing brain regions, is invoked when humans make decisions in situations in which information is incomplete or overly complex.

One common situation that can engender emotion is when an individual makes a decision under risk (the probability distribution of possible outcomes is known) or under ambiguity (where the probability distribution of outcomes is unknown). Subjective utility theory embodies the idea that the outcome probability should influence choice but also that there should no influence on confidence about these probabilities. The Ellsberg paradox shows that subjects behave irrationally when presented with a choice between a risky and ambiguous option, when choices can be shown to depend on subjective probabilities and on ambiguity of events. The possibility that this influence on rational decision making reflects an input from an emotional system is supported in neuroimaging data which show that the level of ambiguity in choices correlates positively with activation of the amygdala.

Conclusion

Neuroimaging has radically altered our conceptualization of emotion. Key observations include evidence that emotion-related activity is expressed across widespread brain regions. A fine distinction between regions that process sensory emotional signals and regions that contribute to the actual experience of emotion has become possible. Furthermore, it has become possible to identify activity in the brain that reflects key computational strategies implemented during emotional learning and emotion-guided decision making.

See also: Aggression: Hormonal Basis; Amygdala: Contributions to Fear; Aversive Emotions: Molecular Basis of Unconditioned Fear; Aversive Emotions: Genetic Mechanisms of Serotonin; Emotion Systems and the Brain; Emotional Hormones and Memory Modulation; Emotional Influences on Memory and Attention; Genetics of Human Anxiety and Its Disorders; Neuroimaging; Social Emotion: Neuroimaging.

Further Reading

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