Prefrontal Contributions to Reward Encoding

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The (primate and human) orbitofrontal cortex receives taste, olfactory, visual, somatosensory, and auditory inputs from cortical regions which are toward the end of the unimodal cortical processing streams that build representations of what stimulus is present in each of these sensory modalities. In this article, I review evidence from human functional neuroimaging and neuropsychology showing that the orbitofrontal cortex and a region to which it projects, the anterior cingulate cortex (ACC), are involved not only in rewards produced by olfactory and taste stimuli but also in much more abstract types of reward, such as monetary reward, and in altering behavior when rewards change. This indicates that the orbitofrontal and cingulate cortices are involved in emotion, and this is confirmed by many changes in emotion described here that can result from damage to the human orbitofrontal or ACC.

Functional Neuroimaging of the Human Orbitofrontal Cortex: Reward and Nonreward

Investigations with functional magnetic resonance imaging (fMRI) show that taste and olfactory stimuli can activate the orbitofrontal cortex and that the activation is related to the pleasantness or unpleasantness of the stimuli, that is, to their reward value. For example, activation of a part of the human orbitofrontal cortex is related to the pleasantness of food odor, in that the activation measured with fMRI produced by one food odor, banana, decreased after banana was eaten for lunch to satiety but remained strong to another food odor, vanilla, not eaten in the meal. Further evidence that pleasant odors are represented in the orbitofrontal cortex is that three pleasant odors (linalyl acetate (floral, sweet), geranyl acetate (floral), and alpha-ionone (woody, slightly food-related)) had overlapping activations in the medial orbitofrontal cortex in a region not activated by three unpleasant odors (hexanoic acid, octanol, and isovaleric acid). Moreover, activation of the medial orbitofrontal cortex was correlated with the subjective pleasantness ratings of the odors, and activation of the lateral orbitofrontal cortex was correlated with the subjective unpleasantness of the odors. Pleasant touch has also been shown to activate the medial orbitofrontal cortex, and pain has been shown to activate the lateral orbitofrontal cortex.

Visual stimuli that activate the human orbitofrontal cortex include those associated with pleasant taste. But it has been possible to extend the types of visual conditioned reinforcers to quite abstract reinforcers, such as monetary reward. In an fMRI study, we used a visual discrimination task in which one stimulus was associated with monetary reward and a different visual stimulus with monetary loss (punishment). The actual amounts of money won on reward trials and lost on punishment trials were probabilistic. This part of the design, and the fact that unexpected visual discrimination reversals occurred so that there were trials on which money was lost, enabled us to show that the magnitude of the activation of the medial orbitofrontal cortex was correlated with the amount of money won on each trial and that the magnitude of the activation of the lateral orbitofrontal cortex was correlated with the amount of money lost on each trial. Activation of the medial orbitofrontal cortex is also correlated with face attractiveness. Auditory stimuli may have similar representations in the orbitofrontal cortex related to their affective value. For example, a correlation has been found between subjective ratings of dissonance and consonance of musical chords and the activations produced in the orbitofrontal cortex. Another type of reward, the administration of amphetamine to naive human subjects, also activates the medial prefrontal cortex.

Cognition can reach down into the orbitofrontal cortex to influence affect, as shown by the effects that word descriptors (such as cheese vs. body odor) have on the activations produced by olfactory stimuli in the medial orbitofrontal cortex. Related to the orbitofrontal cortex error neurons, we have also been able to obtain evidence that nonreward used as a signal to reverse behavioral choice is represented in the human orbitofrontal cortex. Kringelbach and Rolls used the faces of two different people; if one face was selected, then that face smiled, and if the other was selected, the face showed an angry expression. After good performance was acquired, there were repeated reversals of the visual discrimination task. It was found that activation of a lateral part of the orbitofrontal cortex in the fMRI study was produced on the error trials, that is, when the human chose a face and did not obtain the expected reward. Control tasks showed that the response was related to the error and the mismatch between what was expected and what was obtained, in that just showing an angry
face expression did not selectively activate this part of the lateral orbitofrontal cortex. An interesting aspect of this study that makes it relevant to human social behavior is that the conditioned stimuli were faces of particular individuals and the unconditioned stimuli were face expressions. Moreover, the study reveals that the human orbitofrontal cortex is very sensitive to social feedback when it must be used to change behavior.

The activations found in functional neuroimaging studies by many types of reward appear to involve relatively medial parts of the human orbitofrontal cortex and unpleasant stimuli or nonreward appear to involve more lateral parts of the human orbitofrontal cortex. Single-neuron recording studies in macaques show that neurons can be exquisitely tuned differently not only to reinforcers in different sensory modalities (taste, smell, touch, etc.) but also to combinations of these, and even within any one modality (e.g., with neurons tuned to different tastes). Nevertheless, what account might we give for why so many different types of reward are represented in the human medial orbitofrontal cortex? I suggested in _Emotion Explained_ that part of the functional utility of this is that there can be a comparison of the magnitudes of what may be quite different types of reward, implemented by the local lateral inhibition mediated via inhibitory interneurons. The result of the mutual inhibition is that the relative magnitude of the different rewards available can be compared and that the most strongly firing neurons after the competition reflect the strongest reward.

**Neuropsychology of the Human Orbitofrontal Cortex**

Having considered evidence from neuroimaging on the functions of the human orbitofrontal cortex in emotion and motivation, we now consider complementary evidence from the effects of damage to the human orbitofrontal cortex.

**Reward Reversal and Its Relation to Other Changes in Behavior**

It is of interest that a number of the symptoms of frontal lobe damage in humans appear to be related to the functions of representing primary (unlearned) reinforcers and of altering behavior when stimulus–reinforcement associations alter. Thus, humans with frontal lobe damage can show impairments in a number of tasks in which an alteration of behavioral strategy is required in response to a change in environmental reinforcement contingencies. It is of interest that frontal patients may be able to verbalize the correct rules yet be unable to correct their behavioral sets or strategies appropriately.

Some of the personality changes that can follow frontal lobe damage may be related to a similar type of dysfunction in processing rewards and punishers. For example, the euphoria, irresponsibility, lack of affect, and lack of concern for the present or future that can follow frontal lobe damage may be related to a dysfunction in altering behavior appropriately in response to a change in reinforcement contingencies. Indeed, in so far as the orbitofrontal cortex is involved in the disconnection of stimulus–reinforcer associations, and such associations are important in learned emotional responses, it follows that the orbitofrontal cortex is involved in emotional responses by correcting stimulus–reinforcer associations when they become inappropriate.

The hypotheses about the role of the orbitofrontal cortex in the rapid alteration of stimulus–reinforcer associations and the functions more generally of the orbitofrontal cortex in human behavior have been investigated in recent studies in humans with damage to the ventral parts of the frontal lobe. (The description ventral is given to indicate that there was pathology in the orbitofrontal or related parts of the frontal lobe, and not in the more dorsolateral parts of the frontal lobe.) A task that was directed at assessing the rapid alteration of stimulus–reinforcer associations was used because the findings indicated that the orbitofrontal cortex is involved in this type of learning. The task used was visual discrimination reversal, in which patients could learn to obtain points by touching one stimulus when it appeared on a video monitor but had to withhold a response when a different visual stimulus appeared, otherwise a point was lost. After the subjects had acquired the visual discrimination, the reinforcement contingencies unexpectedly reversed. The patients with ventral frontal lesions made more errors in the reversal (or in a similar extinction) task, and completed fewer reversals, than control patients with damage elsewhere in the frontal lobes or in other brain regions (see Figure 1).

An important aspect of the findings was that the reversal learning impairment correlated highly with the socially inappropriate or disinhibited behavior of the patients (see Figure 1), and also with their subjective evaluation of the changes in their emotional state since the brain damage. The patients were not impaired at other types of memory task, such as paired associate learning. It is of interest that the patients can often verbalize the correct response yet commit the incorrect action. This is consistent with the hypothesis that the orbitofrontal cortex is normally involved in executing behavior when the behavior is performed by evaluating the
reinforcement associations of environmental stimuli. The orbitofrontal cortex seems to be involved in this in both humans and nonhuman primates when the learning must be performed rapidly, for example, in acquisition and during reversal.

To seek positive confirmation that effects on stimulus–reinforcer association learning and reversal were related to orbitofrontal cortex damage rather than to any other associated pathology, a new reversal-learning task was used with a group of patients with discrete, surgically produced lesions of the orbitofrontal cortex. In the new visual discrimination task (the same as that used in the O’Doherty et al. in 2001 monetary-reward functional neuroimaging task, two stimuli are always present on the video monitor and the patient obtains monetary reward by touching the correct stimulus and loses money by touching the incorrect stimulus. This design controls for an effect of the lesion in simply increasing the probability that any response will be made. The new task also uses probabilistic amounts of reward and punishment on each trial to make it harder to use a verbal strategy with an explicit rule. The task also had the advantage that it was the same as that used in our human functional neuroimaging study that showed the activation of the orbitofrontal cortex by monetary gain or loss. It was found that a group of patients with bilateral orbitofrontal cortex lesions were severely impaired at the reversal task, in that they accumulated less money. The investigation showed that the impairment was only obtained with bilateral orbitofrontal cortex damage, in that patients with unilateral orbitofrontal cortex (or medial prefrontal cortex) lesions were not impaired in the reversal task. These patients often failed to switch their choice of stimulus after a large loss; and often did switch their choice even though they had just received a reward; this was quantified in a more recent study.

It is of interest that the patients with bilateral orbitofrontal cortex damage who were impaired at the visual discrimination reversal task had high scores on parts of a social behavior questionnaire in which the patients were rated on behaviors such as emotion recognition in others (e.g., their sad, angry, or disgusted mood), in interpersonal relationships (e.g., not caring what others think and not being close to the family), emotional empathy (e.g., when others are happy, they are not happy for them), interpersonal relationships (e.g., does not care what others think and are not close to the family), public behavior (is uncooperative), antisocial behavior (is critical of and impatient with others), impulsivity (does things without thinking), and sociability (is not sociable, and has difficulty making or maintaining close relationships)—all of which could reflect less behavioral sensitivity to different types of punishment and reward. Further, in a subjective emotional change questionnaire, in which the patients reported on any changes in the intensity and/or frequency of their own experience of emotions, patients with bilateral orbitofrontal cortex lesions with deficits in the visual discrimination reversal task reported a number of changes, including changes in sadness, anger, fear, and happiness.

These results on the effects of brain damage to the orbitofrontal cortex and the complementary neuroimaging results already described provide evidence that at least part of the function of the orbitofrontal cortex in emotion, social behavior, and decision making is related to representing reinforcers, detecting changes in the reinforcers being received, using these changes to rapidly reset stimulus–reinforcer associations, and rapidly changing behavior as a result.
An idea of how such stimulus–reinforcer learning may play an important role in normal human behavior, and may be related to the behavioral changes seen clinically in patients with ventral-frontal lobe damage, can be provided by summarizing the behavioral ratings given by the carers of these patients. The patients were rated high on at least some of the following: disinhibition or socially inappropriate behavior, violence, verbal abusiveness, lack of initiative, misinterpretation of other people’s behavior, anger or irritability, and lack of concern for their own condition. Such behavioral changes correlated with the stimulus–reinforcer reversal and extinction learning impairment. The suggestion, thus, is that the insensitivity to reinforcement changes in the learning task may be at least part of what produces the changes in behavior found in these patients with ventral-frontal lobe damage.

The more general impact on the behavior of these patients is that their irresponsibility tended to affect their everyday lives. For example, if such patients had received their brain damage in a road traffic accident and compensation had been awarded, the patients often tended to spend their money without appropriate concern for the future, sometimes, for example, buying a very expensive car. Such patients often find it difficult to invest in relationships, too, and are sometimes described by their family as having changed personalities, in that they care less about a wide range of factors than before the brain damage. The suggestion that follows from this is that the orbitofrontal cortex may normally be involved in much social behavior and the ability to respond rapidly and appropriately to social reinforcers which is, of course, an important aspect of primate social behavior.

Bechara and colleagues also have findings in patients with frontal lobe damage when they performed a gambling task that are consistent with those already described. In the Iowa gambling task, subjects were asked to select cards from four decks of cards and maximize their winnings. During the task, the electrodermal activity (skin conductance responses (SCR)) of the subject was measured as an index of somatic activation. After each selection of a card, facsimile money was lost or won. Two of the four decks produced large payouts with larger penalties (and can thus be considered high risk), whereas the other two decks produced small payouts but smaller penalties (low risk). The most profitable strategy was, therefore, to consistently select cards from the two low-risk decks, which is the strategy adopted by normal control subjects. Patients with damage to the ventromedial part of the orbitofrontal cortex, but not the dorsolateral prefrontal cortex, persisted in drawing cards from the high-risk packs and lacked anticipatory SCRs while they pondered risky choices.

The task was designed to mimic aspects of real-life decision making that patients with orbitofrontal cortex lesions find difficult. Such decisions typically involve choices between actions associated with differing magnitudes of reward and punishment in which the underlying contingencies relating actions to relevant outcomes remain hidden.

Most known cases of human orbitofrontal damage occurred in adulthood, but two cases of damage acquired in early life have been reported. The two patients showed life-long behavioral problems, which were resistant to corrective influences. But more importantly, the patients appeared completely to lack knowledge about moral and societal conventions. Interestingly, other patients with late acquired orbitofrontal lesions retained knowledge of such matters, even if they did not always act in accordance with this explicit knowledge. The lack of this moral knowledge and subsequent reckless behavior in the two patients with early life damage to the orbitofrontal cortex is consistent with the hypothesis that the orbitofrontal cortex is crucial for stimulus–reinforcer association learning. The implication seems to be that the orbitofrontal cortex is necessary for the development of personal moral-based knowledge based on the processing of rewards and punishers.

### Face and Voice Expression

To investigate the possible significance of face-related inputs to the orbitofrontal visual neurons, we also tested the responses of these patients to faces. We included tests of face (and also voice) expression decoding because these are ways in which the reinforcing quality of individuals is often indicated. Impairments in the identification of facial and vocal emotional expression were demonstrated in a group of patients with ventral-frontal lobe damage who had socially inappropriate behavior. The expression identification impairments occurred independently of perceptual impairments in facial recognition, voice discrimination, or environmental sound recognition. The face and voice expression problems did not necessarily occur together in the same patients, providing an indication of separate processing. Poor performance on both expression tests was correlated with the degree of alteration of emotional experience reported by the patients. There was also a strong positive correlation between the degree of altered emotional experience and the severity of the behavioral problems (e.g., disinhibition) found in these patients. A comparison group of patients with brain damage outside the ventral-frontal lobe region, and without these behavioral problems, was unimpaired on the face expression identification test, was significantly less impaired at vocal expression decoding.
identification, and reported little subjective emotional change.

These findings were extended, and it was found that patients with face expression-decoding problems do not necessarily have impairments of visual discrimination reversal, and vice versa. This is consistent with some topography in the orbitofrontal cortex.

To obtain clear evidence that the changes in face and voice expression identification, emotional behavior, and subjective emotional state were related to orbitofrontal cortex damage itself, and not to damage to surrounding areas which is present in many closed-head injury patients, we performed these assessments in patients with circumscribed lesions made surgically in the course of treatment. This study also enabled us to determine whether there was functional specialization within the orbitofrontal cortex and whether damage to nearby and connected areas (such as the ACC), in which some of the patients had lesions, could produce similar effects. We found that some patients with bilateral lesions of the orbitofrontal cortex had deficits in voice and face expression identification and that the group had impairments in social behavior and significant changes in their subjective emotional state. The same group of patients had deficits on the probabilistic monetary reward task. Some patients with unilateral damage restricted to the orbitofrontal cortex also had deficits in voice expression identification, and the group did not have significant changes in social behavior or in their subjective emotional state. Patients with unilateral lesions of the anteroventral part of the ACC and/or medial prefrontal cortex area BA9 were in some cases impaired on voice and face expression identification, had some change in social behavior, and had significant changes in their subjective emotional state. Patients with dorsolateral prefrontal cortex lesions or with medial lesions outside the ACC and medial prefrontal BA9 areas were unimpaired on any of these measures of emotion. In all cases in which voice expression identification was impaired, there were no deficits in the control tests of the discrimination of unfamiliar voices and the recognition of environmental sounds.

Relation to Psychiatric Symptoms

It is also becoming possible to relate the functions of the orbitofrontal cortex to some psychiatric symptoms. Berlin et al. compared the symptoms of patients with a personality disorder syndrome, borderline personality disorder (BPD), with those of patients with lesions of the orbitofrontal cortex. The symptoms of the self-harming BPD patients include high impulsivity, high affective instability, high emotionality, and low extraversion. It was found that orbitofrontal cortex and BPD patients performed similarly in that they were more impulsive; reported more inappropriate behaviors in the frontal behavior questionnaire; and had more BPD characteristics, more anger, and less happiness than control groups (either normals or patients with lesions outside the orbitofrontal cortex).

Both the orbitofrontal and BPD groups also had a faster perception of time (i.e., they underproduced time) than normal controls. This may be one factor underlying their increased impulsiveness; they feel that sufficient time has elapsed to initiate action. It was of considerable interest that the BPD group, as well as the orbitofrontal group, scored highly on the frontal behavior questionnaire, which assessed inappropriate behaviors typical of orbitofrontal cortex patients including disinhibition, social inappropriateness, perseverance, and uncooperativeness. Both groups were also less open to experience (i.e., less open-minded), a personality characteristic.

The orbitofrontal and BPD patients performed differently on other tasks. BPD patients were less extraverted and conscientious, and were more neurotic and emotional, than all other groups. Patients with orbitofrontal cortex lesions had more severe deficits in reversing stimulus–reinforcer associations than all other groups and had a faster perception of time (overestimated time) than normal controls. These deficits were not related to spatial working-memory functions, which are impaired by dorsolateral prefrontal cortex damage.

Thus, some but not other symptoms of self-harming BPD patients are similar to those of patients with orbitofrontal cortex damage. The symptoms the groups have in common include impulsiveness and the inappropriate behaviors typical of frontal patients. This could imply that in BPD patients some aspects of the operation of the orbitofrontal cortex are occurring (whatever their etiology, which could include innate or acquired changes and might involve different expression or operation of neurotransmitters) differently from the way they operate in normal control subjects. Part of our interest in this is that it may help to point toward new concepts that may be useful in the treatment of some of the symptoms of patients with BPD. On the other hand, other aspects of BPD do not appear to be related to orbitofrontal cortex functions, including the more neurotic and more emotional personality characteristics of the BPD group, together with their lower extraversion and conscientious.

Frontotemporal Dementia

Another case in which it is possible to relate psychiatric types of symptom to orbitofrontal cortex function...
is frontotemporal dementia, which is a progressive neurodegenerative disorder attacking the frontal lobes and producing major and pervasive behavioral changes in personality and social conduct resembling those produced by orbitofrontal lesions. Patients appear either socially disinhibited, with facetiousness and inappropriate jocularity, or apathetic and withdrawn. Many patients show mental rigidity and an inability to appreciate irony or other subtle aspects of language. They tend to engage in ritualistic and stereotypical behavior, and their planning skills are invariably impaired. The dementia is accompanied by gradual withdrawal from all social interactions. Memory is usually intact but patients have difficulties with working memory and concentration. Interestingly, given the anatomy and physiology of the orbitofrontal cortex, frontotemporal dementia causes profound changes in eating habits, with escalating desire for sweet food coupled with reduced satiety, which is often followed by enormous weight gain.

The ACC and Affect

The perigenual cingulate area occupies approximately the anterior one-third of the cingulate cortex (see Figure 2) and is involved in emotion; it may be distinguished from a midcingulate area (i.e., further back than the perigenual cingulate region and occupying approximately the middle third of the cingulate cortex), which has been termed the cingulate motor area and may be involved in response selection. Both the perigenual and midcingulate areas are part of what anatomically is frequently termed the ACC; but, for convenience, when using the term anterior cingulate cortex I refer here to the perigenual cingulate cortex and distinguish this from the midcingulate cortex described elsewhere.

Vogt and colleagues showed that pain produced an increase in regional cerebral blood flow (rCBF, measured with positron emission tomography (PET)) in an area of perigenual cingulate cortex which included parts of areas 25, 32, 24a, 24b, and/or 24c. Vogt et al. suggested that the activation of the anterior part of the cingulate area is related to the affective aspect of pain. There are direct projections to the cingulate cortex from medial thalamic areas that relay pain inputs, including the parafascicular nucleus. In terms of other connections, the ACC is connected to the medial orbitofrontal areas, parts of lateral orbitofrontal area 12, the amygdala (which projects strongly to cingulate subgenual area 25), and the temporal pole cortex; it also receives somatosensory inputs from the insula and other somatosensory cortical areas (see Figure 2). The ACC has output projections to the periaqueductal gray in the midbrain (which is implicated in pain processing), to the nucleus of the solitary tract and dorsal motor nucleus of the vagus (through which autonomic effects can be elicited), and to the ventral striatum and caudate nucleus (through which behavioral responses could be produced).

Consistent with the anterior cingulate region being involved in affect, it is close to (just above) the area activated by the induction of a sad mood in studies made by Mayberg and colleagues. Also consistent with this region being involved in affect, Lane and colleagues found increased regional blood flow in a 1997 PET study in a far anterior part of the cingulate cortex, where it adjoins the prefrontal cortex, when humans paid attention to the affective aspects of pictures they were being shown which contained pleasant images (e.g., flowers) and unpleasant pictures (e.g., a mangled face and a snake). The perigenual ACC (approximately the anterior one-third of the cingulate cortex and including parts of areas 32, 24, and 25) is thus related to affect.

The perigenual cingulate cortex may be part of an executive output response-selection system for some emotional states, in which the responses can include autonomic responses. Part of the basis for this suggestion is its inputs from somatosensory cortical areas, including the insula, the orbitofrontal cortex, and the amygdala (see Figure 2), and its outputs to brain stem areas such as the periaqueductal (or central) gray in the midbrain, the ventral striatum, and the autonomic brain stem nuclei. Anterior cingulate lesions in humans can produce apathy, autonomic dysregulation, and emotional instability. We have shown that patients with circumscribed, even unilateral, surgical lesions of the ACC/perigenual cingulate cortex may be impaired for voice and face expression identification; have impaired subjective emotional states; and have some changes in social behavior, including being less likely to notice when other people were angry, not being close to his or her family, and doing things without thinking.

Functional neuroimaging studies showed that there appear to be separate representations of aversive and positively affective stimuli in the ACC/perigenual cingulate cortex. The area activated by pain is typically 10–30 mm behind and above the most anterior (i.e., pre- or perigenual) part of the ACC. Pleasant touch was found to activate the most anterior part of the ACC, just in front of the (genu, or knee, of the) corpus callosum (i.e., the pregenual cingulate cortex). Oral somatosensory stimuli such as viscosity and fat texture also activate this most anterior part of the ACC. More than just somatosensory stimuli are represented, however, in that (pleasant) sweet taste also activates the most anterior part of the

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ACC, as do pleasant odors and cognitive inputs that influence the pleasantness of odors. Unpleasant odors activate further back in the ACC. Activations in the anterior/perigenual cingulate cortex are also produced by the taste of water when it is rewarding because of thirst, by the flavor of food, and by monetary reward. The locations of some of these activations are shown in Figure 3, from which it is clear that many positively affective stimuli are represented in the most anterior part of the perigenual cingulate cortex, with some less positively affective or negatively affective stimuli activating a region of the cingulate cortex which is just posterior to this, above the corpus callosum.

In addition to the pregenual cingulate sites which are activated in many of our studies of affective stimuli, it was also frequently found that activation in a region at the intersection of the medial prefrontal cortex, the subgenual cingulate cortex, and the orbitofrontal cortex is activated by positively affective...
stimuli. The facts that this anterior cingulate region is activated by many rewarding stimuli (as just summarized), affects emotion if lesioned, and is connected with the orbitofrontal cortex indicate that it is important in emotion, perhaps as a region linking the orbitofrontal cortex to outputs. It is in this context very interesting that chronic electrical stimulation in or close to this region (in the subgenual cingulate cortex) relieved symptoms of treatment-resistant depression in some patients. This provides a close link between evidence from neuroscience about the functions of this medial region and the therapeutic potential of these concepts for helping to understand and treat depression.

Overall, it is thus notable that what can be termed an affective part of the ACC, the perigenual cingulate cortex, appears to have a most anterior part where activations are produced by a number of different pleasant stimuli. But further back toward the junction with the midcingulate area and perhaps sometimes including parts of the midcingulate area several affectively negative stimuli produce activations.

An investigation in patients with selective surgical lesions showed that patients with unilateral lesions of the anteroventral part of the ACC and/or medial BA9 were in some cases impaired for voice and face expression identification; had some change in social behavior, such as inappropriateness; and had significant changes in their subjective emotional state. Unilateral lesions were sufficient to produce these effects, and there were no strong laterality effects. Consistent with the effects of the anterior cingulate lesions in humans on recognizing vocal (and, in some cases, facial) emotional expression, neuroimaging studies concerned with vocal expression identification have reported orbital and medial activation. For example nonverbal sounds expressing fear, sadness, and happiness, when compared to a neutral condition, activated BA11 (orbital cortex) bilaterally and the medial BA9 on the left. Fear-related increases in activity were also found on the right only in BA11. In another study, it was found that fearful sounds activated the medial BA32 and BA24 (the anterior cingulate at/below the level of the genu of the corpus callosum), again on the right side only.

There is also neuroimaging evidence that complements the effects of lesions in suggesting a role for certain medial regions in the subjective experience of emotion. In neuroimaging studies by Lane and colleagues with normal human subjects, bilateral activations in the medial BA9 were found as subjects viewed emotion-laden stimuli, and in both the medial BA9 and ventral ACC during self-generated emotional experience (i.e., in the absence of a stimulus) as subjects recalled emotions of sadness or happiness. On the basis of a review of imaging studies which consistently emphasize the importance of anterior and ventral regions of the ACC for emotion, Bush et al. argued that the ACC can be divided into a ventral affective division (which includes the subcallosal region and the part anterior to the corpus callosum) and a dorsal cognitive division, a view strengthened by the demonstration of reciprocally inhibitory interactions between these two regions.

The subgenual part (area 25) of the anterior cingulate cortex is, via its outputs to the hypothalamus and brain stem autonomic regions, involved in the autonomic component of emotion. The ACC is also activated in relation to autonomic events, and Critchley and colleagues showed that there is a correlation with skin conductance, a measure of autonomic activity related to sympathetic activation, in the ACC and related areas.

A current working hypothesis is that the affective part of the ACC receives inputs about expected rewards and punishers, and about the rewards and punishers received, from the orbitofrontal cortex and amygdala. There is some segregation of the areas that receive these inputs. The ACC may compare these signals, and use them in functions such as affective decision making and in producing autonomic

Figure 3  Activations of the most anterior part of the perigenual cingulate cortex by different positively affective stimuli, with less positively affective or negatively affective stimuli producing activations centered just behind this area. Touch: 3 pleasant, 14 unpleasant/pain, 5 unpleasant/pain; Odor: 7 pleasant, 2 correlation with pleasantness ratings, 9 unpleasant; monetary loss: 8; Water: 6 correlation with pleasantness, 15 correlation with pleasantness; Taste: 10 glucose, 11 salt, 4 salt; sucrose and fat: 1; nonreward in a social reversal task: 13, 12. Reproduced from Rolls ET (2005) Emotion Explained, figure 4.61, p. 183. Oxford: Oxford University Press by permission of Oxford University Press.
responses. As such, the perigenual cingulate cortex may act as an output system for emotional responses and actions.

See also: Connectivity of Primate Reward Centers; Cortical Processing of the Reward Value of Food; Flavor Physiology; Orbitofrontal Cortex: Visual Functions; Reward and Learning; Reward Neurophysiology and Primate Cerebral Cortex; Reward Neurophysiology and Orbitofrontal Cortex.

Further Reading

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