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Emotion, Feelings and Hedonics in the Human Brain

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Introduction

Emotions are ubiquitous, and many will agree that it is difficult to imagine our lives without them. Every experienced event—whether current, remembered or imagined—seems to have an emotional tone. We cannot help but attach emotional significance to the events that shape our lives—for better and sometimes for worse. Yet, exactly this subjective quality of the emotions is also what for many years made scientific investigation difficult. For if emotions are highly subjective and private experiences, how can we study them with objective means? Does the subjective quality of emotions mean that they are different for each of us, and does this mean that they are not to be found in other animals? Are emotions different cross-culturally?

This chapter reports on the ongoing scientific struggle with emotion on the edge of our uncertainty and ignorance. While we have been able to gain some important scientific insights into the nature of emotion from both other animals and humans, much remains to be discovered. Neuroimaging methods are now allowing us to begin to start probing the subjective aspects of emotion, including its hedonic aspects, but we are only beginning to understand how brains deal with the intricate social and emotional fabric of human societies.

Of Emotional States and Feelings

Emotion and motivation remained for many years elusive scientific topics and were generally defined, in opposition to cognition, as that which move us in some way, as implied by the Latin root (*movere,* to move). Owing primarily to its perceived subjective nature, the scientific study of emotion was stunted despite ideas put forward by pioneering individuals such as Charles Darwin, who examined the evolution of emotional responses and facial expressions and suggested that emotions allow an organism to make adaptive responses to salient stimuli in the environment, thus enhancing its chances of survival (Darwin 1872).

A highly successful scientific strategy has been to divide the concept of emotion into two parts: the *emotional state* that can be measured through physiological changes such as visceral and endocrine responses, and *feelings,* seen as the subjective experience of emotion (Kringelbach 2004a). This allows emotional states to be measured in animals using, for example, conditioning, and most subsequent research has regarded emotions as states elicited by rewards and punishments (which, of course, is a rather circular definition) (Weiskrantz 1968). Emotional stimuli (primary and secondary reinforcers) are represented by brain structures, depending on the kind of reinforcer. Reinforcers are defined such that positive reinforcers (rewards) increase the frequency of behaviour leading to their acquisition, while negative reinforcers (punishers) decrease the frequency of behaviour leading to their encounter and increase the frequency of behaviour leading to their avoidance.

The subsequent emotional processing is a multistage process mediated by networks of brain structures. The results of this processing influence which behaviour is selected, which autonomic responses are elicited and which conscious feelings are produced (at least in humans).

An early, contrasting, but still influential theory of emotion was proposed in the 1880s independently by William James and Carl Lange, who proposed that rather than emotional experience being a response to a stimulus, it is the perception of the ensuing physiological bodily changes (James 1890; Lange 1887). The James-Lange theory of emotion suggests that contrary to popular perception we do not run from the bear because we are afraid, but that we *become* afraid because we run.

Several scientists have remained sceptical of such bodily theories of emotion. One of the initial main proponents, William Cannon, offered a detailed critique of the James-Lange theory. He showed that surgical disruption of the peripheral nervous system in dogs did not eliminate emotional responses as would have been predicted by the theory (Cannon 1927). Further investigations by Schachter and Singer suggested that bodily states must be accompanied by cognitive appraisal for an emotion to occur (Schachter and Singer 1962). However, this research did not fully resolve the basic question of the extent to which bodily states influence emotion and feelings.

More recently, the James-Lange theory was resurrected, first by Walla Nauta with his ‘interoceptive’ markers (Nauta 1971), and since—to far more popular acclaim—by Antonio Damasio in the form of his somatic marker hypothesis, in which feedback from the peripheral nervous system controls the *decision* about the correct behavioural response rather than the *emotional feelings* as postulated in the James-Lange theory (Damasio 1994).

Among the objections to these and other bodily theories of emotion are that they are underspecified with regard to what constitute emotional stimuli; that signals from the body are noisy and it is not clear whether they can distinguish the different emotions; and that animals and humans with severe spinal cord damage appear to have normal emotions. Some of these objections are addressed in the ‘somatic marker’ theory, which includes an ‘as-if’ loop for those decision-making situations with relatively low uncertainty that allows the brain to bypass the role of body (Damasio 1996). It has also been argued that emotions are constituted in large measure by visceral and endocrine responses rather than through the spinal cord. The orbitofrontal cortex certainly has the connectivity to receive and integrate visceral sensory signals to influence ongoing behaviour, and although it is not clear how this information is integrated, it remains possible that these signals have a significant role in decision making and emotion (Craig 2002). It should also be noted that most primary reinforcers are signaled via an interoceptive route and that this is likely to be essential for hedonic experience.

At the same time it is clear from the evidence of e.g. successful use of various beta blockers in alleviating stage fright, anxiety and panic attacks in stage musicians and other world-class performers that the body clearly must play a role in the regulation of emotions. Some observers have therefore suggested that the role of the body in emotion is perhaps more akin to an amplifier than to a generator.

There are of course close links between body and brain, as was fully clear to even Descartes, who is otherwise widely seen as one of the main proponents for the mind-body split. It is at best misleading to give Descartes such a simple-minded dualistic position (Descartes 1649; Sutton 2001)—although he was clearly on the wrong track when he named the pineal gland as the seat of the soul. Later research has shown that this brain structure is a key structure in the control of hormones and thus an unlikely contributor to the metaphysical construction of the soul.

Investigating Emotional States

Although the theoretical debates over the conceptual framework for emotion research have been very important, the development of experimental paradigms for the reliable testing of emotion in animals and humans has had just as much influence on the field of emotion research. Given that consciousness in animals remains controversial, the presence of feelings in animals is also a contentious issue. Animals do, however, show the characteristic behavioural, autonomic and hormonal responses associated with emotional states when confronted with emotionally salient stimuli.

Neuroscientists have concentrated on understanding the brain structures mediating rewards and punishments elicited by operationally defined reinforcers. Positive primary reinforcers are naturally occurring stimuli (such as sugar) that animals will work to obtain. Negative primary reinforcers are stimuli that animals will work to avoid (such as salt—although only when not salt-deprived). These primary reinforcers can be associated with arbitrary secondary reinforcers, which can be anything from the sound of Pavlov’s bell to abstract paper representations such as banknotes. The learning process is called *conditioning*, and much psychological research has been dedicated to understanding the underlying principles (Skinner 1938; Thorndike 1911).

For many years behaviourism as led by Burrhus Skinner saw the brain as an uninteresting black box where the behaviour of animals was the only interesting feature; where responses slavishly follow stimuli; where subjective experience can ultimately be described solely as patterns of stimuli and responses and where all behaviour is completely flexible given the right reward schedule. Much later research has shown that the main tenets of behaviourism were oversimplified if not plain wrong. The species-specific features of the brain do matter very much and are decisive for its learning potential. Subjective experience does not depend in any simple way on stimuli and responses, and there are species-specific behaviours that even the most cunning reward schedules cannot change. In addition, there are many behaviours where the motivating reward is very seldom external, and often natural as in children's play (Lepper and Greene 1978; Lepper, Greene and Nisbett 1973; McGraw 1978).

Conditioning experiments are nevertheless important as they offer insights into some of the fundamental forms of learning. Neuroscientists have learned a great deal by studying brain activity using experimental paradigms adapted from behaviourism. One of the most successful paradigms in emotion research has been fear conditioning, in which an auditory conditioned stimulus is paired with a foot shock. In other words, when the animal hears a tone, it is given a foot shock and it subsequently learns this association.

LeDoux and others have shown that for rats to learn the appropriate fear response depends crucially on the amygdala, which is a brain structure in the temporal lobes (LeDoux, Cicchetti, Xagoraris and Romanski 1990). Subsequently, much neuroscientific research has concentrated on elucidating the full role of the amygdala in fear, so that it has become popularly known as the fear centre in the brain. However, the amygdala is not a homogeneous brain structure, but rather a collection of at least 13 anatomically distinct nuclei (Swanson and Petrovich 1998). In addition, other research using appetitive conditioning has also implicated the amygdala, indicating that it can be activated by both positive and negative stimuli (Holland and Gallagher 2004). It is therefore unlikely that the amygdala is only concerned with fear. Nevertheless, the fear conditioning paradigm has been very successful in creating an adequate scientific model of emotion and firmly establishing the field of emotion research. It has also become clear that the amygdala might be very important for rodents, but much has happened to the structure of the brain on the evolutionary path to higher primates such as humans.

As an interesting aside, it has been proposed that the amygdala obtains information about significant stimuli in the environment earlier than other brain areas in the cortex (LeDoux 1996). This gives the brain the possibility to quickly send early warning signals via the amygdala to the rest of the brain and the body. If we were to suddenly notice something which at first glance looked like a snake, our brain and body would be able to react quickly but essentially nonconsciously. The emotional fear reactions are able to commence immediately via the quick route of the amygdala, and we become aware that we are fearful before we are aware of what made us fearful. Throughout evolution this has likely conferred an evolutionary advantage to have very fast reactions to certain dangerous stimuli. These essentially nonconscious reactions could be a possible explanation of why James and Lange fashioned the idea that it is the body that controls emotions. But note that this cannot be true in the above example with the snake, as the information is first processed in the brain with the amygdala alerting the body. The example is, however, a good illustration of how little insight we have into our own brain processing.

Emotion and Feelings in Humans

Initially most scientific research thus mostly investigated emotions in experimental animals using conditioning paradigms with negative reinforcers such as fear. However, it was not clear if and how this research transfers to humans, especially given the subjective nature of conscious feelings, which are not necessarily present in other animals. Until quite recently, human research was limited to patients with lesion sites established post-mortem. The recent advent of neuroimaging has afforded a unique window on the living human brain and has also allowed for investigations into positive emotions such as joy.

It was clear, however, even from early behavioural cross-cultural studies, that there might be an innate, biological basis for emotional experience. Paul Ekman demonstrated that facial emotions are universally recognized across cultures (Ekman and Friesen 1971). Furthermore, analyses of emotion terms in all of the world's major languages have led to discussions on the existence and enumeration of the fundamental emotions that can act as basic building blocks of our entire emotional repertoire. Based on such research, up to seven emotions have been proposed: anger, disgust, fear, sadness, joy, shame and guilt. It remains an open question whether these emotions are really distinct or whether they are found on a continuum produced by shared brain mechanisms.

The case of Phineas Gage was one of the first neurological cases to indicate some possible neural correlates of emotions in human (Harlow 1848). Gage was a young railway engineer who suffered a tragic accident in which his brain and more specifically his medial parts of the frontal lobes, including the orbitofrontal cortex, were penetrated by a tampering iron. Miraculously Gage survived, but his personality and emotional processing were changed completely (although care should be taken when extrapolating from this case as our information is rather sparse) (Macmillan 2000).

Later cases of damage to the frontal parts of the brain and in particular the orbitofrontal cortex have been shown to cause major changes in emotion, personality, behaviour, and social conduct. Patients often show lack of affect, social inappropriateness and irresponsibility. It has been shown that patients are impaired at correctly identifying social signals, including for example face and voice expression identification (Hornak, Bramham, Rolls, Morris, O'Doherty, Bullock and Polkey 2003; Hornak, Rolls and Wade 1996). There are even cases of patients who retain their high intellectual abilities but show a complete change in personality and general irresponsibility (Eslinger and Damasio 1985).

Analyses of the effects of lesions to the human orbitofrontal cortex show that lesions impair the patients in a variety of important ways related to emotion, reversal learning and decision making. The severity of these changes can be measured by the patients' performance on neuropsychological tests including gambling (Bechara, Damasio, Damasio and Anderson 1994), reversal learning (Hornak et al. 2003; Rolls, Hornak, Wade and McGrath 1994), and decision making (Rogers et al. 1999).

In summary, animal studies and lesion studies in humans have allowed scientists to outline some of the brain structures involved in emotion. The three key regions in the human brain are the orbitofrontal cortex, amygdala and cingulate cortex (see Figure 3.1). Other important brain structures for emotion include the hypothalamus, insula/operculum, nucleus accumbens, and various brainstem nuclei such as the periaqueductal grey.

However, until the advent of neuroimaging of the normal human brain, almost nothing was known about the neural correlates of the subjective and social aspects of emotion. The following will concentrate on describing some of the recent advances in understanding the neural correlates of subjective hedonic experience. In addition, some of the recent research on representing of the social aspects of emotions will be described.

Hedonic Experience

Part and parcel of all sensory stimuli is our hedonic experience of their pleasant and unpleasant aspects. These hedonic experiences help us decide on the best possible actions for navigating complex physical and social environments. Neuroscience has been successful in elucidating some of the neural correlates of hedonic experience by studying food intake (Kringelbach 2005).

To put hedonic behaviour in a historical context, early drive theories of motivation proposed that hedonic behaviour is controlled by need states (Hull 1951). But these early theories do not, for example, explain why people still continue to eat nice food when they feel full. This was addressed by incentive motivation theories, in which hedonic behaviour is mostly determined by the incentive value of a stimulus or its capacity to function as a reward (Bindra 1978). Need states such as hunger are still important but only work indirectly on the stimulus's incentive value. The principle of modulation of the hedonic value of a consummatory sensory stimulus by homeostatic factors was coined *alliesthesia* (from *allios,* changed, and *esthesia,*

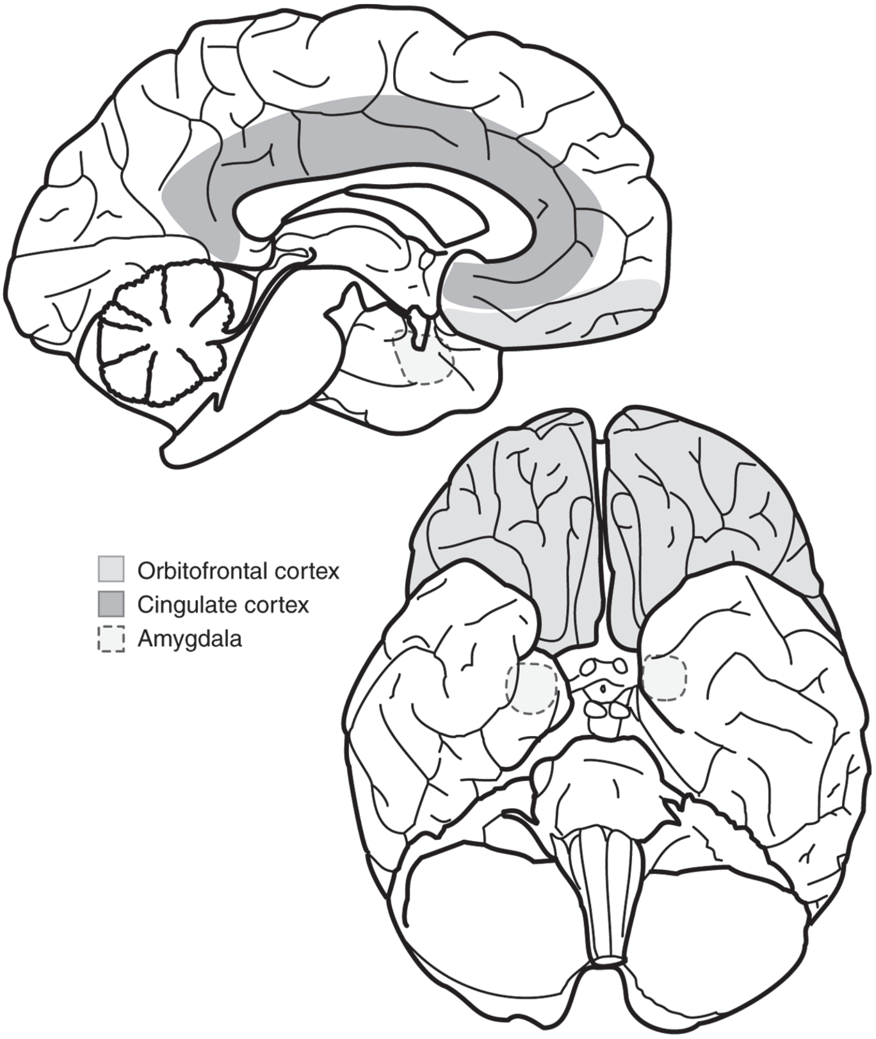

Figure 3.1 Emotion-related brain regions. The figure shows the approximate location of three key brain regions involved in emotion: the orbitofrontal cortex, cingulate cortex and amygdala. At the top is shown a mid-section of the human brain with the front of the brain facing right. At the bottom is shown the brain seen from below with the front facing upwards.

sensation) (Cabanac 1971). A useful distinction has been proposed between two aspects of reward: hedonic impact and incentive salience, in which the former refers to the liking or pleasure related to the reward, and the latter to the wanting or desire for the reward (Berridge 1996; Berridge and Robinson 1998).

Food intake is such a common act that most people rarely think about the complexities involved. Foremost, food intake is a precisely controlled act that can potentially be fatal if the wrong decision is taken to swallow toxins, microorganisms or nonfood objects on the basis of erroneously determining the sensory properties of the food. Humans and other animals have therefore developed elaborate food behaviours which are aimed at balancing conservative risk-minimizing and life-preserving strategies with occasional novelty seeking in the hope of discovering new sources of nutrients (Rozin 2001).

Importantly, food intake must also provide the right balance of carbohydrates, fats, amino acids, vitamins and minerals (apart from sodium) to sustain life. The neural mechanisms regulating food intake are complicated and must, like any regulatory system, include at least four features: system variables, detectors for the system variables, set points for these system variables and correctional mechanisms. A simple regulatory feedback system operates best with immediate changes, and it becomes significantly more complex when the feedback is not immediate. In the case of controlling food intake, there are significant delays in system changes caused by the relatively slow metabolic processes, and therefore the regulatory neural systems controlling food intake must include sophisticated mechanisms to learn to predict in advance when a meal should be initiated and terminated. Many of the basic components and principles of food intake have been elucidated in great detail and have been described in reviews elsewhere (LeMagnen 1985; Woods and Stricker 1999). Simple behaviours linked to food intake are controlled by homeostatic systems in the brainstem, as shown by the fact that even decerebrate animals are able to survive (Grill and Norgren 1978).

However, most of this research has been carried out in other animals, which has not helped to inform about the strong hedonic component of human food intake. Much complex human behaviour related to food intake must be linked to neural activity in the cerebral cortex, integrating the complex multitude of stimuli and situational variables. Important examples of complex behaviour include the decrease of the rated pleasantness of sweet tastes when subjects are sated relative to when they are hungry (alliesthesia) (Cabanac 1971) and satiation signals that selectively suppress further food intake of previously ingested foods, while other foods can still be readily ingested (selective satiety) (Rolls, Rolls, Rowe and Sweeney 1981).

In an aside, it should be noted that the relative sophistication of foraging in higher primates compared to other mammals indicates that significant parts of our large brains are dedicated to the required motivational, emotional and cognitive processing, and that mental processes related to food intake may indeed underlie other higher functions. The special importance of food in human life is underlined by the predominance of food symbols and metaphors in human expressions across cultures (Lévi-Strauss 1964) and the elaborate social constructions regarding purity and taboo of foods (Douglas 1966). Food intake and food choice constitute a fundamental and frequent part of human life and have played a major role in the cultural evolution of nonfood systems such as ritual, religion and social exchange as well as in the advancement of technology, development of cities, illnesses and warfare through agriculture and domestication (Diamond 1999).

Selective Satiety

Everyone is familiar with the important mechanisms for ‘selective satiety’ from the ability to still desire and have plenty of room for the dessert after feeling completely full from the main course. From an evolutionary perspective this has the clear advantage of allowing us and other animals to obtain a sufficiently wide variety of nutrients.

Selective satiety (or ‘sensory-specific satiety’ as it is also known) is a particularly useful phenomenon for studying affective representation in the brain, as it provides a means of altering the affective value of a stimulus, without modifying its physical attributes. As a consequence, any differences observed between the representation of a particular food stimulus in the brain before and after satiety can be attributed to the change in the impact of the reward, or the reward value. This controls for possible confounds such as increases in thirst, gastric distension and changes in blood glucose levels after feeding, by virtue of the fact that the neural response to another food which is not eaten in the meal is also measured. Selective satiety effects are strongest when using quite different foods such as e.g. tomato juice (savoury) and chocolate milk (sweet).

We investigated the neural mechanisms related to selective satiety with functional magnetic resonance imaging (fMRI), which in turn allowed us to identify the neural correlates of subjective pleasantness (Kringelbach, O’Doherty, Rolls and Andrews 2003). For those unfamiliar with neuroimaging I have included a detailed description of the experiment to provide a flavour for the steps involved.

The subjects refrained from eating for at least six hours prior to arriving at the imaging center on the day of the experiment in the late afternoon. Prior to participation in the experiment, the subjects were prescreened to ensure that they found both tomato juice and chocolate milk to be pleasant, and to ensure that they were not overweight or on a diet or planning to go on a diet. Both liquid foods are administrable in liquid form and palatable at room temperature, and the clear difference in their flavour and texture helps to facilitate sensory-specific satiety effects and minimizes the likelihood of the subjects developing a generalized satiety to both liquid foods.

Before feeding, the subjects were placed in the scanner, and scanned while being presented with each of the two liquid food stimuli, as well as a tasteless control solution which was delivered to the subject’s mouth through three polythene tubes that were held between the lips. Each tube of approximately 1 meter in length was connected to a separate reservoir via a syringe and a one-way syringe valve. One reservoir contained the chocolate milk, another contained the tomato juice and a third reservoir contained a tasteless control solution (with the main ionic components of saliva). Note that water is not an appropriate control solution since it is rewarding to hungry subjects.

We used a block design with each epoch lasting 16 seconds. At the beginning of each epoch, 0.75 ml of one of the liquid foods (or the control solution) was delivered to the subject's mouth in under 0.5 seconds on average. The subject was then instructed to roll the stimulus around on the tongue and was then cued to swallow the stimulus (using a visual cue) after 10 seconds. The stimuli were delivered in an interleaved manner for each epoch, such that the subjects received tomato juice in one epoch, followed by the tasteless control solution, followed by the chocolate milk, and then followed again by the tasteless control solution. This cycle was repeated 16 times. At three points during the imaging run, there was an additional 16-second period following the presentation of each stimulus (at cycles 4, 8 and 12), during which no taste stimulus was delivered. Instead, subjects were presented with a visual rating scale ranging from +2 (very pleasant) to –2 (very unpleasant) in 0.25 increments, and had to rate the subjective pleasantness of the preceding liquid food stimulus by moving a vertical bar to the appropriate point on the scale through the use of a button box.

After the initial scanning run, the subjects were taken out of the scanner and fed to satiety on one of the liquid foods. The subjects were instructed to consume the liquid foods for their lunch and were asked to drink as much as they could until they absolutely did not want to have any more. The liquid food was poured into a 150 ml cup and offered to the subject. Once the subject had consumed the contents of the cup, it was then refilled. This was repeated a number of times until the subject was completely satiated and refused the offer of an additional cup. To achieve a balanced design, five subjects were fed to satiety on tomato juice and five subjects were fed to satiety on the chocolate milk. Each subject was randomly allocated one of the two liquid foods for their meal and the subjects were not informed in advance (until after the first imaging run) which liquid food they would be invited to consume.

Once the subjects had finished their meal, the most important part of the experiment took place. We put the subjects back into the scanner and repeated the exact same scanning procedure as before. Now, whether the subjects had been fed on chocolate milk or tomato juice, they reported not liking this stimulus and gave negative scores. But the same subjects still liked the other stimulus which they had not been fed. Importantly, it was only the subjects' subjective *pleasantness* ratings that had changed and not their intensity ratings.

We were then able to correlate the changes in brain activity over the course of the experiment with the subjective pleasantness ratings for all subjects. The statistical analysis found that a part of the anterior orbitofrontal cortex was correlated with the subjects' subjective pleasantness (see Figure 3.2). Since only the subjective pleasantness ratings had changed and not the intensity ratings, and since the experiment was counterbalanced in terms of stimuli, this means that the brain activity is not only related

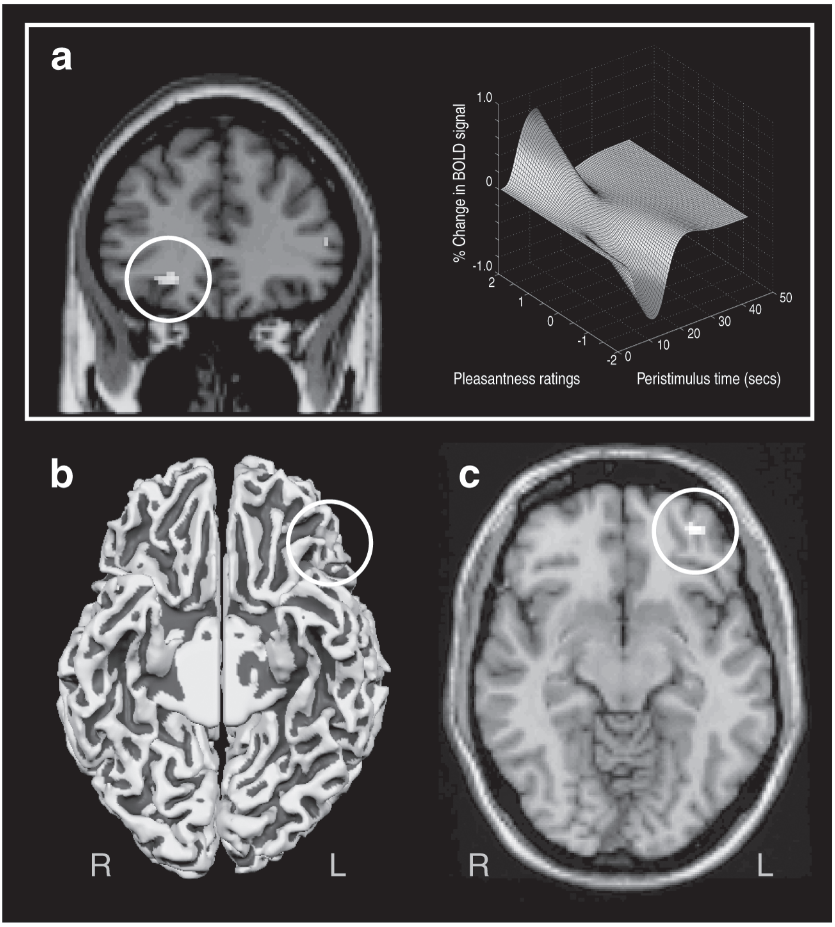

Figure 3.2 Hedonic experience. a) A neuroimaging study using selective satiation found that mid-anterior parts of the orbitofrontal cortex are correlated with the subjects' subjective pleasantness ratings of the foods throughout the experiment (Kringelbach et al. 2003). On the right is shown a plot of the magnitude of the fitted haemodynamic response from a representative single subject against the subjective pleasantness ratings (on a scale from –2 to +2) and peristimulus time in seconds. **b)** Additional evidence for the role of the orbitofrontal cortex in subjective experience comes from another neuroimaging experiment investigating the supra-additive effects of combining the umami tastants monosodium glutamate and inosine monophosphate (De Araujo et al. 2003a). The figure shows the region of mid-anterior orbitofrontal cortex showing synergistic effects (rendered on the ventral surface of human cortical areas with the cerebellum removed). The perceived synergy is unlikely to be expressed in the taste receptors themselves, and the activity in the orbitofrontal cortex may thus reflect the subjective enhancement of umami taste which must be closely linked to subjective experience. **c**) Adding strawberry odour to a sucrose taste solution makes the combination significantly more pleasant than the sum of each of the individual components. The supra-linear effects reflecting the subjective enhancement were found to significantly activate a lateral region of the left anterior orbitofrontal cortex, which is remarkably similar to that found in the other experiments (De Araujo et al. 2003b).

to the pleasantness of chocolate milk or to tomato juice but to both, and therefore to the pleasantness of the combination of taste, smell and structure of these foods.

Other subsequent neuroimaging experiments have also found that the orbitofrontal cortex appears to represent the subjective experience of pleasantness (De Araujo, Kringelbach, Rolls and Hobden 2003a; De Araujo, Rolls, Kringelbach, McGlone and Phillips 2003b; Gottfried, O'Doherty and Dolan 2003; Rolls, Kringelbach and de Araujo 2003a; Rolls et al. 2003b). More evidence to support this comes from studies that show the orbitofrontal cortex and other brain regions are active when representing the subjective effects of drugs such as amphetamine (Völlm et al. 2004) and cocaine (Breiter et al. 1997) as well as sex (Holstege et al. 2003). In addition, activation of the orbitofrontal cortex correlates with the negative dissonance (i.e. pleasantness) of musical chords (Blood, Zatorre, Bermudez and Evans 1999), and intensely pleasurable responses, or 'chills', that are elicited by music are correlated with activity in the orbitofrontal cortex, ventral striatum, cingulate and insula cortex (Blood and Zatorre 2001).

These potentially exciting findings from neuroimaging extend previous findings in nonhuman primates of reinforcer representations to representations of the *subjective affective value* of these reinforcers. One has to be careful not to overinterpret mere correlations with the elusive qualities of subjective experience, and it is unlikely that hedonic experience would depend on only one cortical region. Even so, it would be interesting to obtain more evidence on this issue by investigating patients with selective lesions to these areas to investigate whether their subjective affective experiences have changed. Some evidence has already been obtained to suggest that this is the case (Hornak et al. 2003).

Social Interactions

Humans are intensely sociable creatures and we spend an inordinate amount of time engaged in social interactions with others. The quest to understand intelligent social behaviour has taken many forms, and at least two distinct approaches with slightly different emphasis have led to interesting insights. One approach has emphasized the continuity with social behaviour in other animals, as studied for example by ethologists and zoologists, which points to the importance of environmental interactions in the development and exercise of intelligent behaviour. Other approaches traditionally taken by researchers in the social sciences have tended to emphasize the uniqueness of human behaviour and the uniqueness of the individual person, their environment and their social surroundings. These approaches are not mutually exclusive but complementary.

Most recently, the advances in neuroimaging have made it possible to forge a truce between these approaches and investigate the neural architecture underlying various forms of social behaviour by directly studying the brain mechanisms.

Although still in its innovative phase, these new experimental technologies are already providing insights into the brain activity which allows an individual to interact with others and how that behaviour becomes coordinated in an adaptive fashion over time.

One key aspect of human social interactions, and perhaps even a hallmark of human nature, is our remarkably flexible behaviour, especially in the social domain, which is perhaps also a major reason for our relative evolutionary success. Our social skills are already being honed as children and young adolescents, where we quickly become very adept at forming and breaking alliances within and between groups, and spend much of our time engaged in complex social interactions. At best these interactions enrich our society, at worst they become 'Machiavellian' and exploitative. In fact, while science might appear removed from such politics, many scientists would probably agree that science is in fact a social enterprise which shares many characteristics with other human pursuits, and that any claim to greater scientific truth can only be accorded over decades and even centuries.

Constituting flexible behaviour is the concept of *reversal learning.* While it is obviously important that we can learn arbitrary associations between stimuli and actions, it is also extremely important that we can relatively easily break these associations and relearn others. If we learn that choosing a certain object leads to a reward, it would be rather maladaptive to keep choosing this object when it was no longer associated with a reward but, say, instead a punishment. We need to be able to adapt or *reverse* the learning patterns when things change in order to accommodate complex behaviour.

For a long time it was thought that complex behaviour depends crucially on the prefrontal cortex, but it was not clear which parts were important for reversal learning. This was investigated in a classic paper (Iversen and Mishkin 1970). The authors lesioned discrete parts of the prefrontal cortex in different monkeys and showed convincingly that these lesions had differential effects on the ability of these animals to reverse rewarding associations in an object-reversal task. When the inferior prefrontal convexity and parts of the lateral orbitofrontal cortex were lesioned, these monkeys became significantly impaired on object-reversal learning. Specifically, the monkeys would continue to respond much longer than controls to the object that is no longer rewarded on the first reversal trial. This was not the case for monkeys who had the medial parts of the orbitofrontal cortex lesioned. These monkeys were not completely unaffected by the lesion but showed moderate impairment on all but the first of the object discrimination reversals and furthermore had moderate problems withholding response between trials on an auditory differentation task. This strongly suggested a differential role for the lateral and medial parts of the orbitofrontal cortex.

Iversen and Mishkin persuasively demonstrated the importance of the orbitofrontal cortex in reversal learning, and other studies have since extended this result in nonhuman primates. One study demonstrated that single neurons in the macaque orbitofrontal cortex change their responses to a visual cue after a single trial in which the reward association of the visual cue is reversed (Thorpe, Rolls and Maddison 1983). Another lesion study in marmosets by Dias, Robbins and Roberts (1996) found that the orbitofrontal cortex is essential for performing an emotion-related reversal learning task.

There is also some evidence that humans with lesions to the orbitofrontal cortex have problems with reversal learning, but in the experiments concerned, the lesions, caused by diffuse brain damage, were not very clean or focal (Rolls et al. 1994). In addition, lesions to the orbitofrontal cortex are associated with impairments in emotional and social behaviour characterized by disinhibition, social inappropriateness and irresponsibility (Anderson, Bechara, Damasio, Tranel and Damasio 1999).

However, it is not clear that these results necessarily transfer to humans, and we therefore decided to use neuroimaging of a probabilistic reversal-learning task. The subjects' task was, by trial and error, to determine which of two stimuli is the more profitable to choose, and to keep track of this—and reverse their choice when a reversal occurred. By design, the actual reversal event was not easy to determine since 'money' can be won or lost on both stimuli, but a choice of the rewarding stimulus would in general give larger rewards and smaller punishments, whereas the converse was true of the punishing stimulus, such that losing a large amount of money would often (but not always) signal that a reversal had occurred.

We used fMRI to show that dissociable activity in the medial orbitofrontal cortex was correlated with the magnitude of the monetary gains received, while activity in the lateral orbitofrontal cortex was correlated with the monetary losses received (O'Doherty, Kringelbach, Rolls, Hornak and Andrews 2001). This dissociation between the functions of medial and lateral orbitofrontal cortex mirrors Iversen and Mishkin's initial dissociation in monkeys, where the lateral orbitofrontal cortex in both cases is linked to the reversal trials.

However, our initial imaging study did not reveal the cortical localization of reversal trials due to the probabilistic nature of the task, where receiving a monetary punishment did not always signal reversal. In addition, our task used money as the secondary reinforcer that might be powerful in humans but have little biological relevance for other animals, and may not be linked directly to the interesting social domain.

Social Rewards from Faces

One way to solve these problems with localizing the neural correlates of reversal learning is to instead use facial expressions as the reinforcing stimuli. This makes sense given that the key to social intelligence is the ability to detect subtle changes in communication and act upon these changes rapidly as they occur. Such changes in social behaviour are often based on facial expression and come so naturally to humans (and are in place so early in child development) that some might argue that this functionality is essentially innate. However, human social behaviour is sufficiently flexible that we can easily learn to adapt our behaviour to most face expressions. For example, other people's neutral expressions do not normally indicate that our behaviour should change, but it is easy to think of social contexts where a neutral expression does indeed imply that our current behaviour is inappropriate and should change.

We designed a reversal task where the overall goal was for the subject to keep track of the mood of two people presented in a pair and as much as possible to select the image of a 'happy' person (who will then smile). Over time the person with the 'happy' mood (who will smile when selected), changes her mood to 'angry'. This person will thus no longer be smiling when selected but instead change to a facial expression that signals that this person should no longer be selected. In the main reversal task the facial expression used to cue reversal was an angry expression (the most natural facial expression to cue reversal), while in the second, control version of the reversal task, a neutral expression was used instead. By using two different reversal tasks where different facial expressions are signalling that behaviour must change, we were able to determine which brain areas are specific to general reversal learning rather than just to reversal following a particular expression such as anger.

We used fMRI to show that the ability to change behaviour based on someone else's facial expression is not reflected in the activity in the fusiform cortex (which invariantly appears to reflect only identity and not valence of faces), but that general reversal learning is specifically correlated with activity in the lateral orbitofrontal and anterior cingulate/paracingulate cortices (as well as other brain areas including the ventral striatum and the inferior precentral sulcus) (Kringelbach and Rolls 2003) (see Figure 3.3).

This result confirms and extends the results from the original Iversen and Mishkin paper. Further confirmation came from the neuropsychological testing carried out by Julia Hornak on human patients with surgical lesions to the orbitofrontal cortex, which showed that bilateral (but not unilateral) lesions to the lateral orbitofrontal cortex produce significant impairments in reversal learning (Hornak et al. 2004). Yet, as always, these results are not conclusive and raise many new issues. It is for instance unclear what other areas are necessary and sufficient for reversal learning. Among the other brain areas we found relating to general reversal learning in our study, the ventral striatum is an obvious candidate (Cools, Clark, Owen and Robbins 2002).

In addition, fMRI is essentially a correlative technique with poor temporal information, which makes it very difficult to infer causal relations between brain regions. It thus still awaits further investigations with e.g. magnetoencephalography (MEG) to gain temporal information on the milliseconds scale.

In his original masterpiece *The Prince,* Machiavelli offers a rather pessimistic view on human nature in which '... love is held by a chain of obligation which, since men are bad, is broken at every opportunity for personal gain'. Some of the

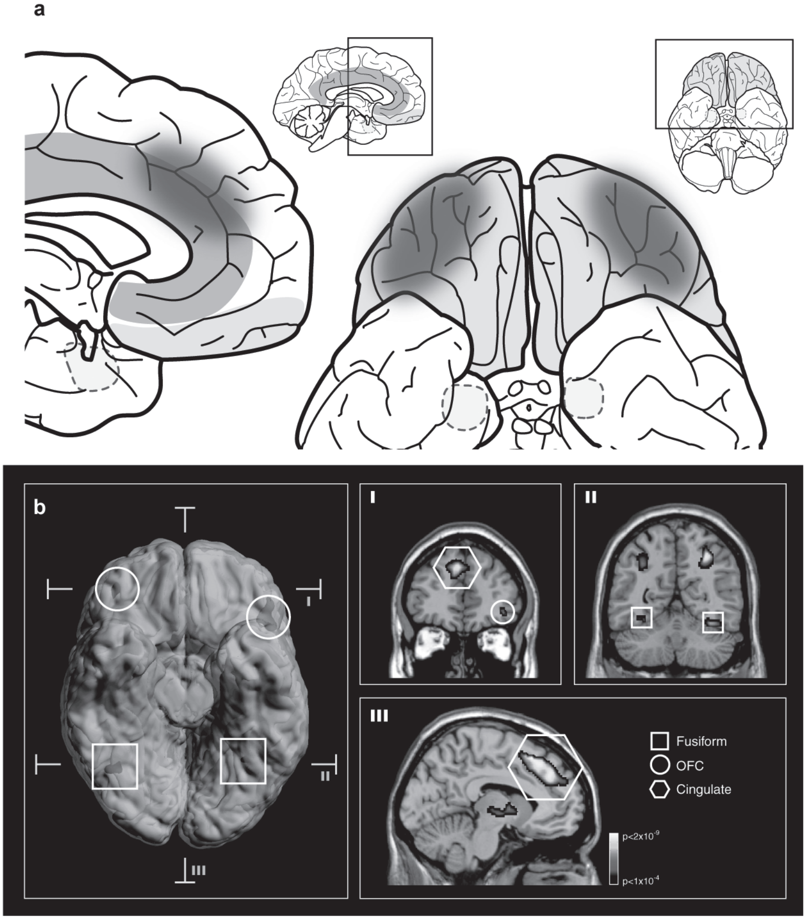

Figure 3.3 Social interactions and the case of reversal learning. a) The lateral orbitofrontal and parts of the anterior cingulate cortices in the rostral cingulate zone are often found to be coactivated in neuroimaging studies (with the regions superimposed in red). Most often this is found in tasks where the subjects have to evaluate negative stimuli which when detected may lead to a change in current behaviour. **b)** A recent neuroimaging study found that the lateral orbitofrontal and the anterior cingulate/paracingulate cortices are together responsible for changing behaviour in an object-reversal task (Kringelbach and Rolls 2003). This task was set up to model aspects of human social interactions (see text for full description of the task). Subjects were required to keep track of the faces of two people and to select the 'happy' person, who would change mood after some time, and subjects had to learn to change, reverse, their behaviour to choose the other person. The most significant activity during the reversal phase was found in the lateral orbitofrontal and cingulate cortices (red and green circles), while the main effects of faces were found to elicit activity in the fusiform gyrus and intraparietal sulcus (blue circles).

challenges that await social neuroscience are to investigate how social interactions allow individuals to operate within a society. It may be that our ability for rapid reversal learning is sometimes used for less noble pursuits in both science and in interpersonal relations in general, but we would be in real trouble if we were not able to learn how to change.

Conclusions

The scientific study of emotion remains in its infancy, especially when it comes to understanding its hedonic aspects and the links to wider societal structures. Some progress has been made in understanding the putative brain structures involved in emotion, mostly based on animal models of emotion. This research has implicated the orbitofrontal cortex, amygdala and cingulate cortex as important for emotional processing. Other important brain structures include the hypothalamus, insula/operculum, nucleus accumbens and various brainstem nuclei such as the periaqueductal grey. These brain regions provide some of the necessary input and output systems for multimodal association regions such as the orbitofrontal cortex that are involved in representing and learning about the reinforcers that elicit emotions and conscious feelings (Kringelbach 2005).

This chapter has provided some of the novel findings from neuroimaging which have foremost demonstrated the importance of the orbitofrontal cortex in emotional processing. In particular, the recent convergence of findings from neuroimaging, neuropsychology and neurophysiology has demonstrated that the human orbitofrontal cortex is best thought of as an important nexus for sensory integration, emotional processing and hedonic experience. In terms of emotional processing, it has become clear that the orbitofrontal cortex plays an important role in emotional disorders such as depression (Drevets 2001) and addiction (Volkow and Li 2004), and it is now possible to offer a tentative model of the functional neuroanatomy of the orbitofrontal cortex (shown in Figure 3.4).

The posterior parts of the orbitofrontal cortex process the sensory information for further multimodal integration. The reward value of the reinforcer is assigned in more anterior parts of the orbitofrontal cortex, from where it can be modulated by hunger and other internal states and can be used to influence subsequent behaviour (in lateral parts of the anterior orbitofrontal cortex with connections to anterior cingulate cortex), stored for monitoring, learning and memory (in medial parts of the anterior orbitofrontal cortex) and made available for subjective hedonic experience (in mid-anterior orbitofrontal cortex). At all times, there is important reciprocal information flowing between the various regions of the orbitofrontal cortex and other brain regions including the anterior cingulate cortex and the amygdala.

At the present time, significant differences in terms of laterality have not been demonstrated in the orbitofrontal cortex (Kringelbach and Rolls 2004). However,

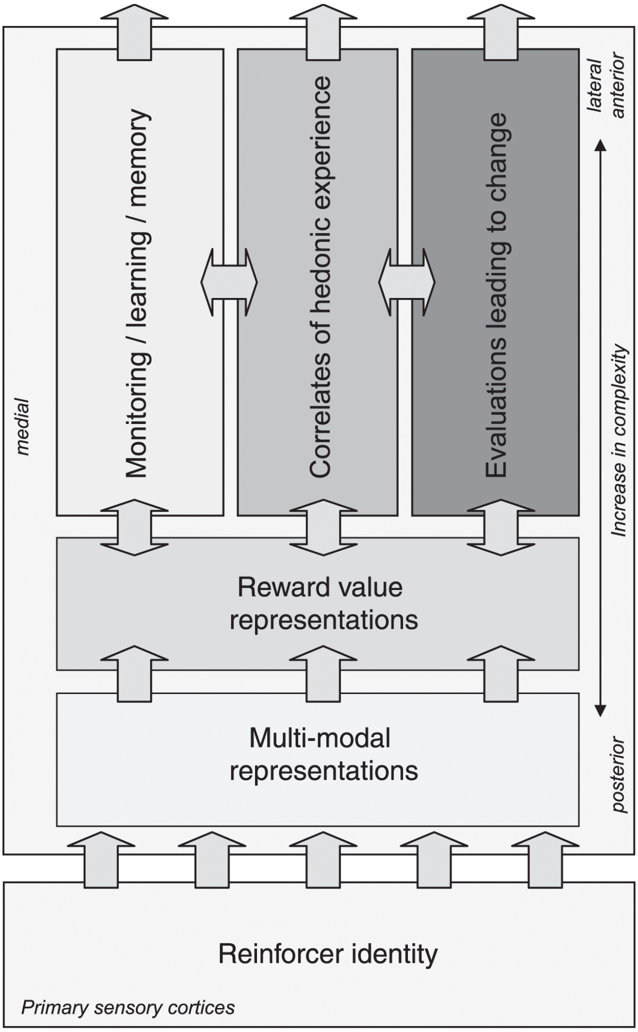

Figure 3.4 Model of the functions of the orbitofrontal cortex. The proposed model shows the interactions between sensory and hedonic systems in the orbitofrontal cortex using as an example one hemisphere of the orbitofrontal cortex (Kringelbach 2004b). Information is flowing from bottom to top on the figure. Sensory information arrives from the periphery to the primary sensory cortices, where the stimulus identity is decoded into stable cortical representations. This information is then conveyed for further multimodal integration in brain structures in the posterior parts of the orbitofrontal cortex. The reward value of the reinforcer is assigned in more anterior parts of the orbitofrontal cortex, from where it can then be used to influence subsequent behaviour (in lateral parts of the anterior orbitofrontal cortex with connections to anterior cingulate cortex), stored for learning/memory (in medial parts of the anterior orbitofrontal cortex) and made available for subjective hedonic experience (in mid-anterior orbitofrontal cortex). The reward value and the subjective hedonic experience can be modulated by hunger and other internal states. In addition, there is important reciprocal information flowing between the various regions of the orbitofrontal cortex and other brain regions.

in terms of neuroanatomy, the orbitofrontal cortex is a highly heterogeneous brain region, and future neuroimaging and neuropsychology studies are likely to find many more functional distinctions between its constituent parts.

The proposed link to subjective hedonic processing places the orbitofrontal cortex as an important gateway to subjective conscious experience. One possible way to conceptualize the role of the orbitofrontal and anterior cingulate cortices would be as part of a global workspace for access to consciousness with the specific role of evaluating the affective valence of stimuli (Dehaene, Kerszberg, and Changeux 1998). In this context it is interesting that the medial parts of the orbitofrontal cortex are part of a proposed network for the baseline activity of the human brain at rest (Gusnard and Raichle 2001), as this would place the orbitofrontal cortex as a key node in the network subserving consciousness. This could potentially explain why all experiences have an emotional tone.

There are many interesting and important issues in emotion research which are not yet fully understood. It is clear that personality and society play a significant role in shaping emotions, but we are a long way from understanding personality in neural terms. Studies in split-brain patients seem to suggest a hemispheric specialization of emotional processing, but the issue of lateralization is still much debated among researchers. It also clear that although conscious appraisal of emotion is important for emotional expression, many emotional stimuli appear to be processed on a non-conscious level, only later to become available for conscious introspection (or, as in the case of blindsight, not at all) (Naccache et al. 2005). Emotion helps to facilitate learning and memory adaptively, and so there are strong links between emotion, learning and memory, but their exact relationships are not yet fully understood.

The most difficult question facing emotion research remains the subjective experience of emotion, and while some progress has been made as described in this article, it is important not to overinterpret mere correlations from neuroimaging with the elusive qualities of subjective experience.

In summary, emotions are evolutionarily important for animals (including humans) in preparing for appropriate actions, and the evolution of conscious feelings in humans could be adaptive, because they allow us to consciously appraise our emotions and actions and subsequently to learn to manipulate these appropriately. Emotion may be one of evolution's most productive breakthroughs, constantly reminding us that we are still animals at heart, but endowed with the possibility of conscious appraisal and the enhanced control of our subjective experience that comes with it.

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