

The amygdala, emotion and learning

FOR many years the amygdala has been implicated in emotional processing. More recently its importance to our everyday psychology has been highlighted in the popular science press and in books such as *Descartes' Error* by Antonio Damasio (1994) and the *Emotional Brain* by Joe LeDoux (1996). Evidence for its importance comes from a wide variety of sources, including cognitive psychology, neuropsychology and behavioural neuroscience.

In this article I discuss some recent studies combining contemporary animal learning theory with behavioural neuroscience. These complement studies in normal humans and patient populations to increase our understanding of this vital brain structure.

But what exactly is the amygdala?

The amygdala

The amygdala is a small subcortical structure lying deep within the temporal region of the brain. The name amygdala, like many of the seemingly complicated terms in neuroanatomy, is merely a descriptive term related to the appearance of the structure — in this case it is derived from a word meaning 'almond'.

However, this relatively small structure has a complicated neuroanatomy. It receives an enormous range of neural inputs from a wide variety of areas of the brain, both cortical areas and subcortical structures. Much of the information it receives is of a highly processed nature — by which I mean it is information that has undergone a great degree of manipulation,



In the 1999 Spearman Medal Lecture **SIMON KILLCROSS** discussed the complex role of this influential part of the brain.

combination and recombination in other regions of the brain.

It receives highly processed information from the visual system, the auditory cortex, the olfactory and gustatory neocortex and the somatosensory cortex. In short, it is informed about each of our five senses — sight, hearing, smell, taste and touch.

The amygdala also receives projections from areas of so-called association cortex — information of a polymodal nature such as that represented in the frontal cortex. Subcortically it receives information from the thalamus (relaying basic, unprocessed sensory signals), hippocampus (giving more highly processed information about the relationship between different objects and events in the world), and a range of structures important in representing internal bodily states, such as hunger and thirst.

In addition to this vast array of inputs it also projects to a wide variety of areas. It has reciprocal connections to many of the cortical areas just mentioned, as well as projections to subcortical areas involved in motor output, and hypothalamic and brainstem regions involved in the co-ordination of autonomic, endocrine and behavioural responses.

The amygdala and emotion

There is a substantial body of work examining the role of the amygdala that makes use of patients with selective damage to this region. This may occur due to surgery, for example to destroy the epileptic focus in the case of intractable epilepsy, or in some very rare cases due to congenital defects that lead to the progressive calcification of limbic structures sometimes restricted to the amygdala — Urbach–Wiethe disorder.

More recent studies have made excellent use of emerging imaging

technology, employing positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) of healthy participants to examine brain systems underpinning learning and emotion.

One striking finding, which has been replicated a number of times, relates amygdala damage to a deficit in recognising facial expressions of emotion.



Amygdala damage can reduce recognition of fear, anger and disgust in people's faces

This work is typified by studies conducted by Andy Young at the University of York and Andy Calder at the MRC Cognition and Brain Sciences Unit, Cambridge (e.g. Calder *et al.*, 1996). Moreover, this deficit appears to be selective, relating to expressions of fear, anger and disgust, but not to happiness, sadness and surprise.

Similarly, although patients with amygdala damage show surprisingly few deficits across a wide range of neuropsychological tests and can function well in everyday life, recent studies have started to pick out specific problems with social and emotional judgement.

For example, Adolphs *et al.* (1998) took three people with highly selective damage to the amygdala and tested them on their ability to make judgements about the approachability of others from photographs. In comparison to controls

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they were far more likely to rate individual characters as approachable. This finding provides solid empirical evidence to back up anecdotal observations made by families, clinicians, and others working with these groups that their ability to make personal judgements can be abnormal.

Finally, some excellent work has been carried out examining the role of the amygdala in responding to emotionally significant events. These studies have utilised PET and fMRI during Pavlovian conditioning in humans.

In one such study individuals received pairings of pictures of angry faces with an intense and aversive burst of white noise (Morris *et al.*, 1998). Following these pairings, participants were presented with just the pictures of angry faces, whilst undergoing PET analysis of their neural activity. Very brief presentations of an angry face were immediately followed by presentation of a neutral face. This procedure served to 'mask' awareness of the angry face, so that participants were not even conscious they had seen it.

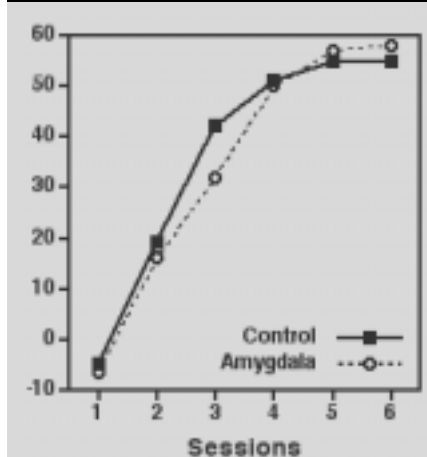
Two important findings emerged from the study. Firstly, participants showed a change in skin conductance response during the subliminal presentations of the angry face, demonstrating that it could generate an emotional response by virtue of previous Pavlovian conditioning, even when subjects were unaware of it.

Secondly, and just as striking, they found a selective activation of the right amygdala following such presentations. This again demonstrates the central role of the amygdala in responding to emotionally significant situations. Morris *et al.* (1998) also found a selective activation of just the left amygdala when the angry face was not masked and participants were aware of the presentations, although discussion of this intriguing result lies beyond the scope of this article.

In summary, there is much evidence to associate the amygdala with emotion, and with learning about emotionally significant events. It is involved in a wide variety of emotional responses, including responding to linguistic threat, facial and vocal expressions of emotion, memory for emotional events, and even simple responding to pleasant and aversive stimuli, including music.

The evidence for the primary involvement of the amygdala in emotion is overwhelming. However, it should be noted that the deficits observed following selective damage to the amygdala are rather subtle, and perhaps not as dramatic as one

FIGURE 1 Acquisition of conditioned responding following selective damage to the amygdala. During a conditioned stimulus that predicts the delivery of food there is no difference in rate of approach to the site of food delivery relative to baseline (per cent) between experimental and control animals



might expect following destruction of a structure that appears to be so critically connected to such a wide variety of other brain regions. Many of the deficits are only fully apparent when a patient is in real-life situations, with all their complex social and emotional interactions, rather than in the more controlled environment of the psychological laboratory.

Nevertheless, the amygdala is implicated in a huge array of mental disorders. These include schizophrenia, depression, generalised anxiety disorders (it has one of the densest collections of benzodiazepine receptors in the brain, receptors that respond selectively to anti-anxiety drugs such as diazepam), obsessive compulsive disorder, and post-traumatic stress disorder. It is also thought to be vitally important in the development and maintenance of drug abuse. All this, and yet deficits following discrete amygdala damage appear to be relatively mild.

In fact these findings reflect earlier

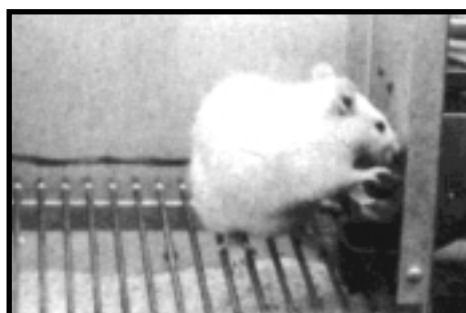
work in animals that similarly revealed the involvement of the amygdala in emotion. Perhaps most well-known are the classic studies by Kluver and Bucy (1939). These studies demonstrated that damage to the temporal lobe in monkeys led to a wide variety of symptoms, which they characterised as disruptions in normal emotional responding.

A classic example of a monkey with Kluver-Bucy syndrome might be an animal that shows little fear of its handlers, a greater propensity to explore new places that are frightening, a decreased ability to recognise objects in the world (visual agnosia), a compulsion to place objects in its mouth to see if they are edible, and an increased tendency to mate inappropriately with cagemates and other monkeys. Monkeys with damage to the temporal lobes may show all or some of these symptoms.

Similar findings have since been reported in humans with gross damage to the temporal lobe (Aggleton, 1992). However, it is now widely recognised that several of the components of this syndrome are not due to damage to the amygdala, but rather to overlying cortical areas, or due to damage to nerve fibre projections through the damaged region.

More recent and more careful studies in primates have revealed that deficits following discrete damage to the amygdala are both subtle and mild (Málková *et al.*, 1997).

Finally, work in laboratory rats has also supported the findings from research examining humans and non-human primates. Deficits following discrete amygdala damage (in many cases to a subnucleus of the amygdala known as the basolateral nucleus) are mild. There is a clear deficit in learning about some aversive events, such as a simple Pavlovian conditioning situation where a signal such as a tone is paired with an aversive event such as mild footshock (Davis, 1992; LeDoux, 1996). But there appears to be little change in the ability



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of animals to learn about pleasant events, such as learning that a signal such as a tone predicts the delivery of food (see Figure 1).

Overall we can see that damage to the amygdala produces some deficits in learning about the emotional significance of events in the world, although these effects are quite subtle and rather varied. We have yet to produce a clear and accurate characterisation of its function in everyday life; given the importance of the amygdala in mental disorders, achieving this would be a valuable goal.

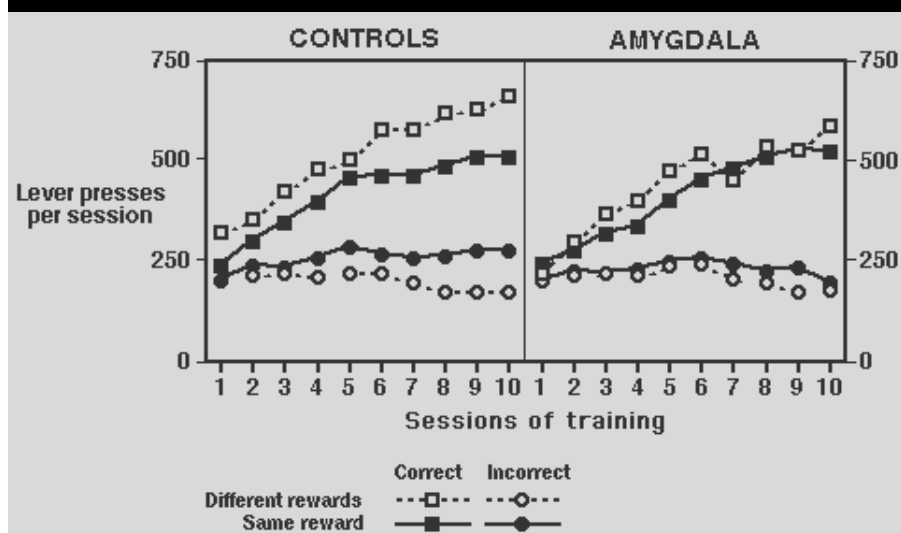
Associative learning

Associative learning theory characterises learning as the formation of an association between mental representations of events in the world. In many cases (but by no means all), this learning is a result of the co-occurrence of the two events. In the psychological laboratory these events might be a simple cue such as a tone, and an emotionally significant event such as presentation of food — a common demonstration of Pavlovian, or classical, conditioning.

Alternatively, the events might be some behavioural response, such as a rat pressing a lever, and an emotionally or motivationally significant event such as presentation of food or water. In this case learning is referred to as instrumental, or operant, conditioning.

It is important to emphasise at this point that we are not merely talking about the formation of stimulus–response habits that are frequently associated with behaviourist theories of learning. We are talking about the formation of associations between mental representations of events, and

FIGURE 3 Increase in presses on a rewarded lever over a non-rewarded lever. In control animals this discrimination is acquired more rapidly if the two levers give different rewards, an effect not found in animals with amygdala damage



contemporary animal learning theory that deals with cognitive issues such as attention and short- and long-term memory, as well as with more traditional topics such as motivation and incentive.

It is from this background that I would like to introduce some studies examining the role of the amygdala in associative learning. Each of these studies makes use of findings drawn from current animal learning theory to try to throw light on the precise function of the amygdala in learning about emotionally significant events. In each case, similar procedures were used, based on simple associations such as those outlined above — a tone predicting presentation of food, and a lever press leading to presentation of food.

Representations for event outcomes and goals

A number of researchers have noted that although animals with damage to the amygdala appear to learn well that a particular signal or response predicts the imminent arrival of rewarding food, they do not seem to retain as much knowledge about this food as normal animals.

Take a specific example of this from recent work (Hatfield *et al.*, 1996). When normal animals have learnt the relationship between a response or stimulus and a reward, researchers can make changes in the value of that reward. For example, they might reduce its value by prefeeding the animal on that reward — a phenomenon known as sensory-specific satiety. This will produce predictable changes in the animal's responses to the predictor of that

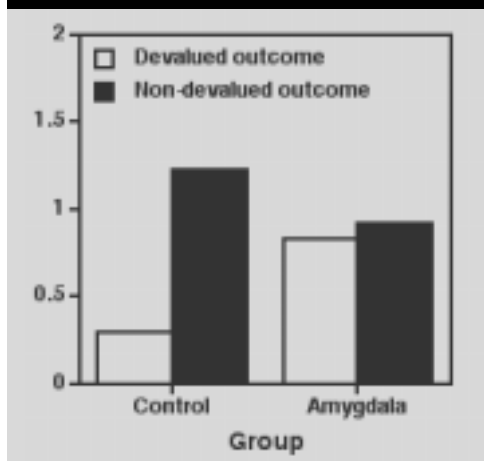
reward: in this example, a reduction in the level of lever pressing for that reward.

This is most clearly demonstrated when animals have a choice of responses to make, one response leading to one type of reward (say, a pellet of food) and a second response leading to another type of reward (delivery of a small amount of sucrose solution). Prefeeding an animal with food pellets preserves responses that lead to sucrose solution, but practically eliminates responses that lead to food pellets. They have already had their fill of food pellets.

This type of result is central to associative learning theory, and demonstrates that responding is governed by an association between a signal or response and a representation of the reward that is predicted. It is generally accepted that satiation is effective as it reduces the value of internal representations of the goal or predicted outcome, and thus reduces the vigour of responding (see Dickinson, 1994).

But animals with amygdala damage fail to show sensitivity to these changes in the value of reward. Figure 2 shows the rate of lever pressing per 10 seconds on two levers during a test of outcome value. Animals had learned that pressing one lever led to food pellets and pressing the other lever led to sucrose solution. Prior to this test, animals were given free access to either food pellets or sucrose solution and allowed to feed to satiety. Responding is split into presses on the lever that led to the food with which the animals had been sated (devalued outcome) and presses on the lever that led to the alternative food (non-devalued outcome). Although control animals assign

FIGURE 2 Lack of sensitivity to changes in reward value following amygdala damage



appropriate value to the outcomes, animals with damage to the amygdala do not.

However, to take the particular example of lever pressing for food, failure of response–reward learning to control behaviour could occur for different reasons. First, animals may fail to discriminate between representations of the two actions. Second, animals may fail to discriminate between representations of the two rewards. Let us address each of these in turn.

Can these animals discriminate between the two actions? Clearly an explicit test of this is required, and is provided most simply by training the animals to perform a simple chain of instrumental responses.

If an animal can distinguish between two responses, then it ought to be able to learn to perform two actions in a particular order to get a food reward. For example, pressing a lever followed by pulling a chain leads to food, but any other order of responding (leverpress-leverpress, chainpull-chainpull, chainpull-leverpress) does not.

Normal animals readily learn this, and in the above example are far more likely to perform a chainpull after a leverpress than any other combination of responses. Our research also indicates that animals with amygdala damage can learn these sequences, thereby ruling out the possibility that their failure to respond appropriately to changes in the value of food rewards is due to an inability to discriminate between the responses that lead to the different rewards.

So can these animals distinguish between different rewards? A similar logic applies in determining this. If animals can learn about the different nature of rewards, they ought to be able to make use of that information to help them get around the world. One way in which knowing about the difference between rewards helps animals is in discriminating between events that lead to those rewards. An animal will more readily learn to tell one frequency of tone from another if the two tones lead to different rewards (say food pellets and sucrose solution) than if they lead to the same reward. This is known as the differential outcomes effect (Trapold, 1970).

We made use of the differential outcomes effect by training rats to press one lever in the presence of one type of auditory signal (a tone), but another lever in the presence of a second auditory signal (a click). In both cases, correct presses were followed by reward, incorrect presses (i.e. those on the opposite lever) by nothing.

Rats readily solved this discrimination, but solved it even more easily if pressing one lever produced sucrose and pressing the other produced food pellets (see Figure 3). In contrast, although rats with amygdala damage learned the discrimination readily enough, they failed to show any benefit of having two different rewards. Hence these rats appear to be unable to represent the food pellets

and sucrose solution as distinct rewards any more.

But what is it about the two rewards they cannot distinguish? Again there are a number of competing alternatives. First, the animals may not represent the reward as an outcome. This might seem to suggest that the animal cannot learn anything at all (and therefore would predict a failure of basic conditioning that is not in fact observed — see Figure 1).

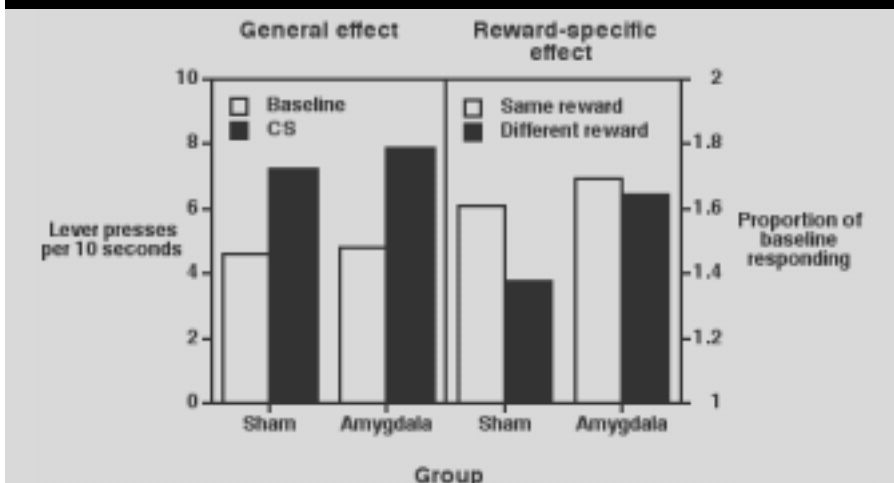
However, there are likely to be several different forms of learning that can occur following the pairing of a stimulus and a reward. At a very basic level the rat might learn some form of stimulus–response (S–R) habit (while associative learning theory does not rely on S–R habits, it does not deny their existence). Here the function of a reward is conceived solely as strengthening the likelihood that a stimulus will elicit a response — it reinforces the association between stimuli present and the response. Responding is therefore not mediated by a representation of the reward, but by a direct connection between stimulus and response.

This S–R interpretation is in contrast to the outcome-based interpretation of responding given above, where performance is held to be mediated by activity in a representation of reward as a consequence of stimulus presentation. The S–R interpretation predicts that animals will not change their behaviour in response to changes in the value of the reward, and further that they will not be sensitive to the exact nature of the reward, but merely to its capacity to reinforce the S–R habit. This is, of course, the pattern of data discussed so far — rats with amygdala damage could be behaving solely on the basis of S–R habits.

A second possible account of the failure of these rats to be sensitive to the nature of rewards might suggest that they are failing to generate a proper associative representation of the rewards. That is, their performance is mediated by a representation of the reward, but this representation is impoverished in some way. More specifically, they may not be able to represent the sensory properties of the reward along with its motivational properties.

By this theory, failure to show an effect of specific satiety occurs because representations of the sensory properties of the reward are no longer available and cannot influence its motivational properties. Similarly, failing to represent the sensory properties of outcomes means that rats

FIGURE 4 Left panel: Rate of lever pressing during the absence (baseline) or presence (CS) of auditory signals that predict reward. Both groups of animals show an increase in lever pressing during signals that predict reward. Right panel: Level of lever pressing during auditory signals that predict reward as a proportion of baseline pressing. Whilst control animals show a greater tendency to press the lever that predicts the same reward as the signal, this selectivity was not observed in animals with damage to the amygdala



cannot make use of this information to help them solve discriminations.

Both of these theories, the S–R interpretation and the failure to represent sensory properties of rewards along with their motivational properties, predict the pattern of results I have discussed to date. So can they be dissociated? Indeed they can, and here we appeal to a third procedure from learning theory — a transfer of control design (Kruse *et al.*, 1983).

Experiments using transfer of control designs combine all the various aspects of Pavlovian and instrumental conditioning I have already discussed. In essence, they look at the way in which Pavlovian conditioned stimuli can influence instrumental responding. For example, if a tone that predicts delivery of food is presented whilst a rat is pressing a lever that also leads to food, an elevation of lever press responding is observed in certain circumstances. In this case, it might be assumed that lever pressing due to the response–reward association is additionally activated by the presence of the tone, which also predicts reward.

Again there are two reasons why this might occur. First, the tone will activate the motivational aspects of the reward representation, producing a general increase in lever pressing due to a non-specific arousing affect, much as any signal for reward will energise action. Second, the tone will also activate the specific sensory aspects of the reward representation, in a sense reminding the animal of what reward it is earning as a result of the response–reward association formed in training. The former relies on the motivational properties of the reward, the latter on its sensory aspects.

So now we can make two predictions about the performance of rats with amygdala damage in this task. If they fail to learn about the motivational properties of reward, and are operating as if they had only S–R associations, then they should not show any general increase in lever pressing, as S–R associations do not rely on any activated representation of reward to produce responding. If they fail to form a correct mental representation of the sensory properties of the reward, they should show a general elevation effect, but it should not be selective to the type of reward signal.

What we found was that animals with selective damage to the amygdala (specifically the basolateral nucleus of the amygdala) showed a general elevation in

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responding during a signal for food, but that this increased responding was not selective to the reward being earned (Figure 4). That is, the animals behaved as if they had failed to properly represent the sensory aspects of the reward in relation to their motivational properties.

Implications

This work reveals that there are likely to be many facets to the function of the amygdala in humans and other animals. Here I have shown that a particular subregion of the amygdala subserves a very specific function in learning about rewarding events in the world. That is, it is responsible for helping to form or maintain a representation of the precise nature of the rewarding event. It facilitates not only the specification of whether a predicted outcome is going to satisfy hunger or thirst, or some other drive, but also access to details of the exact sensory properties of the reward to come.

Further work is needed to determine how this structure and the information it gives access to might be involved in learning about unpleasant or aversive outcomes, although it is likely that a similar story will emerge. Other subregions of the amygdala are likely to play a role in other aspects of emotionally guided behaviour.

In more general terms, an individual with damage to the amygdala may have difficulty in retrieving mental representations of the sensory

characteristics of events in the world. This in turn may lead to subtle alterations in the actions they may take to earn or reject such outcomes, and in their ability to attribute value to them. Similarly, misrepresentation of the nature of outcomes due to malfunction of the amygdala and associated neural structures might change one's response to anxiety-provoking events or might lead to a misjudgement of their likelihood and possible severity. So, although this appears to be a subtle deficit in theoretical terms, it is a deficit that can have very profound consequences in the world.

Summary

Damage to the amygdala selectively impairs the formation or utilisation of mental representations of rewarding outcomes or goals. Other work supports these findings and suggests that the amygdala is involved in the formation of a highly integrated representation of outcomes that is flexible, sensitive to previous and current contingencies, and supports goal-directed, voluntary choice in behaviour (Killcross *et al.*, 1997).

However, whereas the amygdala is clearly involved in modulating the formation of this representation, questions remain as to whether it is the site where information about this representation is stored — other work suggests that storage may be in cortical areas, and perhaps at multiple sites. In humans, for example,

a modulatory role is suggested by the fact that deficits in recognition of emotional expression are found following amygdala damage early, but not late, in life. Imaging studies suggest a cortical representation of outcomes, as presentation of a visual signal that predicts an aversive auditory event produces activity in the auditory cortex.

This combination of associative learning theory and behavioural neuroscience has produced a testable theory of amygdala function that may be examined in humans. In the future I would hope that these areas can continue to be combined to great effect.

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