Brain in action: Example of the complex circuit of brain areas involved in emotion processing

- Initial amygdala response → not much conscious processing
- The anterior cingulate rides to the rescue of amygdala and regulates the initial emotional response
- Finally the complex emotion of 'embarrassment' sets in
**THE MAPPING OF EMOTION**

Dr Essi Viding

**Introduction - Professor Raj Persaud**

Welcome ladies and gentlemen to another lecture at Gresham College. My name is Raj Persaud. I am a consultant psychiatrist at the Bethlem Royal and Maudesley Hospitals, and I am attached to the Institute of Psychiatry. This is one of a special series of lectures that have been organised in conjunction between Gresham College and the Institute of Psychiatry. I have been helping to arrange these lectures as part of my role as the Gresham Professor for the Public Understanding of Psychiatry.

I do think this series of lectures on psychiatry for a lay audience is a hugely symbolic series in terms of the history of Gresham College and the history of my institution, the Bethlem Royal Hospital where I work, and the Institute of Psychiatry. Those institutions are all linked together. Gresham is one of the ancient institutions of London and was founded in the 16th Century, and the Bethlem Royal Hospital, where I work, is the second oldest public hospital in London - it was founded in the 13th Century. Actually, my wife, who is a doctor, went to the oldest public hospital in London, St Bart's, as she is often fond of reminding me when I mention how ancient and distinguished the Bethlem Royal is!

Our current lecturer, Essi Viding, is a lecturer both at the Institute of Psychiatry and at University College London. Essi will be talking about the latest research on brain scanning of emotion. She is a very distinguished researcher in this area.

Just before I hand over to her I just want to make one comment about how fascinating and important a field this is, because the new brain scanning technology is allowing us, when we brain scan individuals, to see which parts of the brain light up or are particularly active, so we are able to get more insight into emotion than ever before, and this has some really quite remarkable implications for our society at large. Just to take one example, there is a particular part of the brain called the amygdala. If you are looking at something disgusting or something that you hate or something that really irritates you or makes you very angry, then the amygdala basically lights up in the brain and becomes very active.

Now, they have done some fascinating experiments recently where you take people and you interview them about their views on race, for example. You can use some quite subtle techniques in terms of pencil and paper tests, so that when you ask people about race and their views on the politics of race, most people know the politically correct thing is not to espouse racist views. But with some of the pencil and paper tests, for example using word association and other subconscious techniques, we can often get at the fact that although people verbalise and say they are not racist, a lot of people really secretly are racist and they keep their views to themselves. What is fascinating with the new brain scanning techniques is that if you show these people pictures in the brain scanner of white people or black people or Asian people, no matter what they say about whether they are racist or not racist, with the racists, their amygdala lights up dramatically in the brain scan. This research tells us that we are not far away from a position, and it is quite a unique position in human history, whereby, no matter what you say about how you feel about things, the brain scanners can reveal the truth. I think that is really quite frightening for a lot of us, particularly those of us who are married...!

I would now like to hand over without any further ado to our very distinguished lecturer this evening, Dr Essi Viding.

**Dr Essi Viding, Institute of Psychiatry, King's College London**

The title of the talk is “The Mapping of Emotion”, and I hope that it will give you an adequate whistle-stop overview of the area of emotion research. In addition to the area that Raj mentioned, the brain imaging research on emotion, I will very briefly try and define to you what researchers mean when they talk about emotion, which may be a quite different thing to what people like to think in their everyday lives when they think about emotion. I also will talk about the brain areas involved in emotion processing, from a neurological as well as brain imaging point of view.
Some questions may come to mind when we talk about what is emotion and where is it mapped... Does it, for instance, need to be a conscious experience for us to call it an emotion? Is this a simple or complex phenomenon? Just to give you an example, it may be very simple to perceive that there is threat in the environment, but when we start thinking about guilt and embarrassment, we are actually talking about complex emotions. I am mainly concentrating on the simple phenomena in my talk. Then I want to explore what the purpose of emotions are: why do we have them; is it rational to have emotions; and where they are in the brain?

Emotional responses can be behavioural, the expression of the emotion – smiling for instance – and they can be autonomic. So if we see something that is exciting, we usually get a skin conductance reaction to it. For example, if I go out for a date with my fiancé, my bet is that my heart rate will go up a little bit and my skin conductance reaction will reveal that I am excited to be going on a date with him. We also have hormonal reactions that map the emotion if we are under threat: our hypothalamic pituitary axis goes on overdrive.

In humans and in higher primates, the awareness of body states contribute to the emotion and to the feeling states. However, the bodily state in and of itself is not really specific enough to distinguish an emotional response, so we need an object in the surroundings to create an emotion. In other words, the arousal state does not carry enough specificity in its signal to be distinguished as an emotion in and of its own.

Conscious feelings do not necessarily equate emotion, so basic emotion and affective functions exist in animals with considerably smaller brains than ours, and these are not entities that can articulate emotional experience, yet they act in ways that show that they do some level of emotion processing. We can also learn from emotional experience without explicit awareness that we have done the learning, so we do not necessarily need a conscious experience that we need to be able to articulate in order for us to consider it as an emotion.

Finally, I would like to make the point that, according to the researchers who tried to operationalise emotion, mood does not equate with emotion. So I may wake up in the morning feeling rather depressed, but this is not an emotion I am necessarily having about anyone. It may be just my mood on that particular day – maybe because I slept very poorly.

Is emotion simple or complex phenomena? Well, if you want to study it in the rats, you have to make it simple. Edmund Rolls has done an extraordinary amount of work conceptualising emotion as a response to reinforcement or punishment, as a response to some kind of an object in the surroundings. He maps emotions in a reinforcement space. There are dimensions... For instance, if you have a positive reinforcer, if it is particularly good, you feel ecstatic; if it is mildly good, you feel pleasure. If you have a negative reinforcement, if it is mildly negative, you feel a bit apprehensive; if it is really, really bad, such as electric shock for instance, you will most likely feel terror. You can also feel frustration and anger if you get an omission of a positive reinforcer when you have expected such, or you can feel relief if you get an omission of a negative reinforcer if you have expected such.

What is the purpose of an emotion? Why do we feel emotions? Evolutionary psychologists have argued that the purpose of emotion is to protect us, to enable us to engage in territory defence, and also to tell us when we should engage in approach behaviours.

For instance, most species have species-typical behaviour that warns another animal that they may be attacked if they do not flee or do not show submissive behaviour. So in humans, angry facial expressions could be considered as threat behaviour, and obviously we have a whole lot of bodily postures as well that go with that.

There is also species-typical behaviour. For instance, in dogs, we can see them baring their throats and showing submission cues. In humans, we could consider, for instance, sadness and fear as part of submission cues, that index to the person who is attacking or about to attack us that we are submitting and they should not go on doing that.

What about the mapping of the emotion, how do we map it to the brain? The emotion circuitry in the brain is complex, and I am mainly concentrating on four areas in my talk: amygdala, orbitofrontal cortex, anterior cingulate and insula. As Raj mentioned, amygdala is probably the most prominently researched area in the emotion literature. I also am particularly interested in it because I am interested in a population of individuals who have poorly functioning amygdala, namely psychopaths. So this is the part of the brain that I will spend most time on, purely for selfish reasons. I will also cover the remainder.

All of these brain areas seem to have a slightly different role in emotion processing, but none of these areas acts in isolation. They communicate with each other, and this is generally the story with the brain. When you see an article that says this is where such-and-such a thing is processed in the brain, take it with a pinch of salt because this particular area is never going to act in
isolation.

Amygdala, as most of you probably have figured out, gets its name from the Latin name for almond. It is an almond-shaped structure at the temporal lobe of the brain. It is divided into different parts, which we know more about due to animal research that has tried to dissect the different function of different sub-nuclei of amygdala. I will just briefly run through these nuclei and their functions.

First, if we take a look at the lateral nucleus of the amygdala. This is part of the amygdala that receives rich sensory information from different areas of the brain, and it is the part of the amygdala that starts the quick and dirty response of the brain, a response that can actually proceed without actual conscious awareness to get us on alert and to get us going if there is, for instance, a threat in the environment.

The basal nucleus of the amygdala is a group of sub-nuclei that receives sensory input from the basolateral nuclei and it relays this information to other amygdaloid nuclei and also an area of the brain called periaqueductal grey matter, which initiates the flight, fight and freezing responses that are important in reaction to threat.

The central nucleus of the amygdala is a region that receives information from the basolateral division and it also sends projections to a variety of other regions in the brain that are involved in emotional responses.

The amygdala has an important role in conditioned emotional responses: for instance, Pavlovian conditioning that most of you are probably aware of. So this is where a previously neutral stimulus can take on or come to elicit an emotional response if it is paired with a naturally aversing or naturally reinforcing response. So in Pavlov's case, he rang a bell, and the dogs always heard the bell ring when they were receiving food, and eventually they started salivating to the sound of the bell alone. Or, the other way around, perhaps the dogs thought that they made Pavlov do something…!

You can also get the Pavlovian response to aversive events. For instance, some classic paradigms have given foot shocks to rats, and eventually, if you pair it with a tone, the rats will start the freezing response at the onset of the tone, even prior to receiving the actual foot shock.

So we can think of amygdala as a stimulus reinforcement associator.

The amygdala also has a very important role in perception of emotional expression, particularly negative emotional expressions such as fear. Human brain imaging studies have been very important in discovering this role.

I have got an image of the human face displaying fear. The reason it looks a bit weird, without the actual hair, is that in the task you do not get the people to recognise emotion; you get the people to decide whether the face is male or female. So we mask the hair cues so that they cannot make the judgement based on whether the hair is long or short, and they have to focus on the expression. When you give them fearful faces like that, you see an amygdala response.

What happens if the amygdala is not functioning properly? A research group has studied extensively patients with amygdala damage, and they have found that these individuals have poor emotional conditioned response. They also have poor recognition of fear. Interestingly, they recently gave an eye-tracking device to an individual with amygdala damage, and they discovered that those individuals were not looking at the eyes of the people when they were processing the facial emotion. Eyes are where the cue for the fearful response is; so you can see that your eyes go very wide when you are feeling fearful. If you are not looking at the eyes, presumably you are going to be fairly poor at detecting that somebody is looking fearful.

If we think about psychiatric conditions where we might have amygdala dysfunctioning, psychopaths are one group of individuals where there is now brain imaging data and also neuropsychological data indicating that they have dysfunctioning amygdala. These people are poor at forming stimulus response, reinforcement association and they also are poor at processing fear and sadness. There are brain imaging studies that show structural abnormalities in amygdala in these individuals and also functional abnormalities when they process emotionally significant stimuli.

For instance, one research group has now theorised that these individuals may have this amygdala dysfunctioning online from early childhood, and it may inhibit their socialisation. So, if there is aggression against other people and they don’t process the distress cues efficiently, they will not stop the aggressing, so they won’t have the non-specific response to other people’s submission cues. Also, as they don’t seem to learn from punishment very well, normal socialisation techniques which may give sanctions may not work so well for these individuals.
There is also some data indicating that individuals who have anxiety disorders may have hyper-reactive amygdala, an opposite pattern of responding to psychopaths. These may be individuals who, given threat cues, may react overtly in a way that will impair their functioning in everyday life.

What about orbitofrontal cortex? This is an area of frontal cortex at the lower part of the frontal lobe, so this is the brain turned upside down. It receives input from dorsomedial thalamus, ventral tegmentum and also the now famous amygdala. It also has outputs to cingulate cortex, to hippocampus, temporal lobe, and again, amygdala and hypothalamus. Interestingly, this input to amygdala may mean that orbitofrontal cortex actually regulates amygdala activity, and there are now brain imaging studies that really seem to indicate that. This is a region of the brain that is involved in using emotion to guide actions. So for instance, if we have a situation where Stimulus A is rewarded and Stimulus B is punished, and these reverse in contingency so that A now becomes punished and B now become rewarded, we need orbitofrontal cortex to detect this change in stimulus reinforcement contingencies and to change our behaviour accordingly.

Patients with orbitofrontal damage seem to lack emotion in their decision making, and they do not have the risk aversion that normal people show. In line with this, they show usually very poor social judgement and very poor emotional control, so they may be prone to explosive anger. Perhaps the most famous case of orbitofrontal damage is the Phineas Gage case, who was a rail worker that got a rod through his frontal cortex due to an explosion, and changed from a placid, very reliable man to a man who was prone to rages and prone to all sorts of other anti-social behaviour. His personality seemed to change quite dramatically. A more recent case occurred where a person was a very responsible member of society, had a family, had a very good job; after orbitofrontal cortex damage, this man started making risky investments, had affairs, and basically, although his intellectual functioning seemed unimpared, his personality seemed completely changed.

I will now move to briefly review research into anterior cingulate cortex. This is an area of cortex that is just above the corpus callosum. Most research these days separates the anterior cingulate to the dorsal and cordal regions, and the cordal regions being more responsible with emotional functioning. Cingulate cortex has a role in body representations of emotion: the feeling of pain for instance, and in regulating emotional responses. There is now interesting new research coming out that suggests that amygdala activity couples with the cingulate activity in the brain, so that if you have an amygdala response, the cingulate seems to get recruited to modulate that amygdala response. It is maybe a higher order response that may dampen the initial good response given by the amygdala. Anterior cingulate pathology has been implicated in emotional disorders such as depression and schizophrenia.

Finally, I will briefly look at research on insula. An area of the brain has a role in processing convergent information to produce emotionally relevant contexts for sensory experience, such as disgust or feelings of unease. So it can act as an area that produces a warning mechanism for potentially noxious stimuli. It has an important role in pain experience. It particularly seems to code for affective aspects of pain.

There was a recent study in Science by Tanya Singer that had people attend a scanning session with their loved one. These individuals either received a shock themselves – a very mild shock, I hasten to add – or they had a little signal indicating that their loved one was going to get a shock. You seemed to have a shared representation for your own anticipation of the shock, so for your own anticipatory affective experience, and you seemed to get the same response when you were looking at your partner potentially getting a shock. So it may be an area that is also important in the impactful experience.

It has also been linked to the perception of the disgusted expression, and there was a study by Mary Phillips that was published in Nature in 1997. They showed individuals in the scanner pictures of disgusted faces, and they got right insula activation.

Insula pathology has been implicated in obsessive compulsive disorder. Individuals who have obsessive compulsive disorder seem to get a higher brain activation when you show them stimuli that is relevant to their pathology, as compared with normal controls, and also when you show them pictures of other disgusting stimuli such as rotting food. Their insula just seems to be firing up more than insula of normal control things.

In summary, different parts of the emotional circuitry seem to be selectively affected in different disorders. I think an important message is that these different brain areas seem to have different roles for emotion processing, but nothing in the brain acts in isolation.

So, given this whistle-stop tour, are we to make the conclusion that emotions are rational? I would say yes and no, which seems to be pretty much the stock response to anything in science. The emotions can serve us very well in situations where we need
to react quickly, so the gut reaction can initiate a best response to our survival. They can also give us non-verbal cues about people's trustworthiness and people's intentions, so they can serve us very well in our deciding of whether we engage in social relations with a person. However, they can also go awry and make everyday life difficult. For instance, obsessive compulsive people are not always rational in their compulsions to wash their hands for instance. I think an important message is that different emotional disorders seem to have a different brain signature, as I have briefly overviewed.

I want to talk about exciting future directions for emotion research. There is a lot of research going on at the moment focusing on the nature-nurture interplay of emotional responses: what are the genetic and what might be the environmental influences on emotional responsivity.

A couple of years back, Ahmad Hariri and his colleagues published a landmark paper in science that looked at amygdala reactivity in people with either short or long alleles of the serotonin transporter gene. Those individuals who had short allele showed much higher amygdala reactivity to emotional stimuli than those individuals with long allele. None of these individuals had any psychiatric pathology, none of these individuals had brain damage; they were normal individuals, but their baseline brain reactivity looked different depending on their genotype. This initial study only had 28 subjects. They ran I think 14 in each group. But they have now replicated this finding with nearly 100 subjects and also other groups have reported the same results, so it seems to be a fairly robust finding.

Avshalom Caspi and his colleagues looked at this same serotonin transporter gene in response to depression and an environmental pathogen, a number of stressful life events. What they discovered is that the individuals with the short allele - so this is the same allele that confers higher amygdala reactivity - were far more likely to get depression, but only if they had a significant number of life events.

There was differential amygdala reactivity to threatening or to emotional stimuli in absence of any overt psychiatric pathology. If you coupled this brain reactivity with number of stressful life events, you really start seeing the genotype differences in behaviour as well, but notice that the genotype on its own is not enough to differentiate these people - you need the genotype in conjunction with environmental events to produce psychiatric disorder.

So conclude, emotions can be conceptualised as reactions to reinforcing or punishing object in the surroundings. That is a research conceptualisation; I obviously appreciate that people's everyday conceptualisations of emotions may be quite different. The purpose of the emotions is to warn us and to guide us should we approach something or somebody, should we avoid something or somebody. A large and very varied brain circuitry subserves emotion perception and emotion regulation. Emotion disorders could be seen as malfunctioning on one or several parts of this circuitry. A hot new research topic is to look at the genetic and environmental influences to the functioning of that circuitry.