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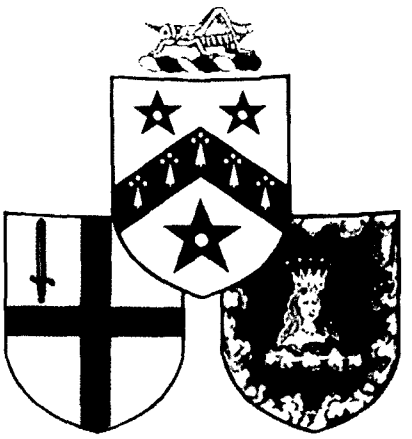

EXPLORING THE BRAIN

Lecture 3

BRAINWAVES

by

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GRESHAM COLLEGE

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GRESHAM LECTURE 3:

BRAINWAVES

This lecture explores ways in which we can study the brain. One of the earliest, purportedly 'scientific' approaches was devised by a doctor from Vienna, Franz Gall, who was born in 1758. Gall was very interested in the human mind, but he considered it was too delicate to probe surgically; given the techniques of the time, he was probably quite right. Instead Gall hit upon another, seemingly more subtle way of studying the brain. He developed the theory that if he studied the skulls of the dead and then saw how these matched up with the alleged characters of those people, then perhaps he could identify a physical trait that corresponded with certain aspects of character. The aspects of the brain that Gall chose to match up were the most easy feature to detect, the bumps on the surface of the skull.

Gall worked out that there were about 27 different character traits. The apparatus that he used to make his analyses was a kind of hat. When placed on the skull, moveable pins were displaced by the bumps on the surface of the skull so that they were pushed upwards to pierce through paper. The particular pattern of perforations in the paper thus gave a somewhat primitive read-out of an individual's character. A colleague of Gall, Johann Caspar Spurzheim, coined the name 'phrenology' to describe the procedure and its underlying philosophy. Phrenology literally means, from the Greek, the study of the mind. Phrenology

became popular because it seemed to present people not only with a more scientific approach, but also with a new basis for morality, something that could be measured and seen and which did not entail difficult and abstract ideas, like soul.

But eventually phrenology was to run into trouble, when clinical observations of brain damage revealed that areas of the brain purportedly associated with one function were in fact more related to some other aspect of human behaviour. Instead, a more promising approach was that started also towards the end of the 19th century, with the development of the Neuron Doctrine, the idea that the basic building block of the brain was the neuron, which functioned as an autonomous entity. Indeed, we now know that neurons can be kept alive in isolation in a dish 'in vitro'. Not only is it possible to grow groups of neurons in isolation, and study factors that can contribute to their growth, but we can also monitor their individual activity, the electrical signals that each neuron generates.

This electrical signal can be monitored via an electrode inserted inside the neuron. However, since the neuron is so small, it is easy for the electrode to fall out. Hence this system is most readily applied in isolated 'in vitro' preparations. If the point of the experiment is, instead, to see how the electrical activity of a single neuron, or indeed group of neurons, is associated with functions or behaviours concerning the holistic brain, then the electrode is kept just outside of the neuron, from where it can monitor the electrical pertubtations caused by the exchange of ions across the membrane wall of the cell.

As long ago as 1875 weak electrical currents were recorded from the brains of rabbits and monkeys but fifty years had to pass before, in 1929, someone first attempted to carry out this procedure in humans. What was found was that if electrodes were placed on the surface of the scalp, it caused no pain whatsoever: the person would be totally conscious and yet the gross activity of many neurons in the cortex could be monitored. This was the start of a technique that is still widely used today in neurology: the encephalogram, (EEG). The EEG records waves of electricity generated from the surface of the brain.

Not only does the EEG show what brain waves look like, it shows how they vary: the pattern can actually change according to the different arousal states a person is in. There are four stages of sleep, distinguished by different patterns of EEG recorded from the scalp. When we fall asleep we descend very rapidly through these four stages, down to the deepest level, Level 4. Throughout the night, we gradually surface and descend again, surface and descend again, through these four stages.

As well as the four stages of sleep, through which we cycle several times a night, there is also another stage of sleep, which is totally different. It is in this stage of sleep that our eyes move rapidly, backwards and forwards, hence its name, Rapid Eye Movement or REM sleep: if people are awakened during REM sleep, they usually report that they have been dreaming. It is easy to imagine that the darting eye movements are a result of us looking at images that move about in our dream world.

What is really interesting is that during this dreaming state of sleep, our EEG is just the same as when we are awake, unlike when we are asleep in dreamless sleep. However in normal sleep, when we are not dreaming, we might be tossing and turning, but in REM sleep our muscles become paralysed: this immobility is important because it stops us acting out our dreams, which could be very dangerous. Imagine, for example, acting out a fall from a tenth storey apartment.

But the EEG can only reveal the electrical activity of the neurons in the cortex, on the surface of the brain. Other methods are needed to probe more deeply. The story of how a deeper exploration of the brain of conscious human subjects is actually becoming possible starts with a familiar procedure, that of using X-rays. X-rays are high frequency, short duration electromagnetic waves. Because X-ray radiation is very high energy, it readily penetrates a test object: the atoms in the test object absorb some of the radiation, leaving the unabsorbed portion to strike a photographic plate, thereby exposing it. So the less radio dense something is, the darker the photographic plate would be, whereas the more dense it is, the whiter it will be.

However, although X-rays are effective for detecting what is happening in most of the body, telling the difference between structures in the brain is very hard because the contrast is not so great between different brain regions. Two solutions to this problem have been developed that tackle the issue from the two different ends: one is to

make the brain more radio opaque, the other to make the technique of X rays more sensitive.

Let's look first at how the inside of the brain itself could be made to resemble the scenario of the gun in a case, how certain components could be made to give greater contrast compared with the rest of the brain. This aim can be achieved by injecting into the brain a dye which is very opaque in that it can absorb a lot of the X-rays. The injection is not directly into the brain through the skull bone. Rather, the dye is introduced into the artery that pumps up blood into the brain all the time. You can locate this artery (the carotid) if you just put your hands to either side of your neck and feel a pulse beating. This artery is taking the blood to the brain. Once the radio-opaque dye enters the blood circulation, it is fed into the brain very quickly. The kind of picture that can then be obtained is called an 'angiogram'. Angiograms give a clear picture of the pattern of branching blood vessels that permeate the brain, going through all the brain regions.

Now imagine there is damage to the cerebral circulation, for example, if someone has a stroke where there is a blockage or a narrowing of the blood vessel walls. This problem will then show up on the 'angiogram'. Similarly, if a patient has a tumour it will sometimes push blood vessels away and the displacement will be detectable to a trained eye. In this way, angiograms are very valuable diagnostic tools which offer a way of circumventing the problem of the insensitivity of X-rays to brain tissue. But what if the blood vessels are functioning

normally? It could be that there are problems with the brain but the blood circulation is not where the problem lies.

The alternative to making the brain more radio-opaque is to make the method of detection more sensitive. With normal X-rays, there are about twenty to thirty variations on the grey scale; but a technique was developed in the 1970s where instead there are over two hundred. This technique has been in operation now for the last fifteen years and it is referred to as 'Computerised Axial Tomography', (CAT). What happens in CAT is that X-rays of the brain are taken in a series of sections or 'scans'. The patient lies with his or her head in a cylinder with an X-ray tube on one side and an X-ray beam on the other, and these two devices are placed around the head. But this time the X-ray does not strike a photographic plate, but rather a sensor that is connected to a computer: this sensor is far more sensitive than the photographic plate used in ordinary X-rays. All the measurements are taken and assembled by computer to give a scan. The tube will move along the axis of the body and this procedure will be repeated some eight or nine times. The kind of pictures that can be seen by CAT scanning give neurologists and brain surgeons a valuable indication of the location and extent of tumours and tissue damage.

Although the inestimable worth of CAT scanning and angiograms is that they are ways of overcoming the problems of X-rays, and are invaluable as diagnostic tools for investigating brain damage, they are still not ideal for studying actual brain function. The problem is that it

takes far too long to see the brain at work over a normal time period. So if you have a CAT scan it will tell you whether you have something physically wrong *and enduring* within your brain, such as a tumour, but it will not be able to tell you what bits of your brain are working or not at particular times during a particular task.

Recently however, other techniques which do not involve X rays at all have overcome this problem. The most widely used of these techniques exploit various features of how brain regions change when they are working particularly hard. When a certain brain region is working, is 'active', compared to less active regions, it uses up a lot more fuel. The fuel for the brain is the glucose in the food that you eat and the oxygen in the air that you breath.

If brain regions are active during a particular task, they are working hard and using more energy, hence they make great demand on oxygen and glucose. It follows that if we could trace the increased demand for oxygen or for glucose by certain parts of the brain, we would be able to say what brain areas were most active or working hardest during any particular task. This is the principle of the two particular techniques we shall briefly consider, which are used to visualise the brain at work.

One technique is known as positron emission tomography, (PET). The basic requirement in PET is for either the oxygen or glucose to be radioactive. Once this 'label' is radioactive it will emit lots of positrons,

hence 'Positron Emission...'. Either radioactive glucose, or water containing radioactive oxygen, is injected intravenously into the circulation. The radioactive label is then carried by the blood into the brain. As soon as positrons are emitted, they will collide with electrons in the brain and the annihilation that results, between positive and negative, creates high energy gamma rays which then bounce off and travel out of the head. Because these gamma rays are very high energy and therefore can travel a long way, they travel right out of the head and strike sensors, the signal from which is then used to build up an image of the brain at work. The glucose or oxygen will accumulate in the brain regions that need them most, namely those which are working the hardest. Using PET it has proved possible to show different areas as active according to different tasks such as saying words compared with reading words.

A second imaging technique, magnetic resonance imaging (MRI) is like PET in that it relies on the differential expenditure of energy by whatever brain regions are working hardest; however this time no injections are involved. Because there is thus no problem with ascertaining exactly when the injected label reaches the brain, MRI has the potential to give an even more faithful reflection of what is going on moment to moment, as a task is being performed. Like PET, MRI also measures changes in blood oxygen concentration serving brain areas that are more active: however the method of detection is different. Oxygen is carried by the protein haemoglobin. MRI exploits the fact that the actual amount of oxygen present affects the magnetic properties of

haemoglobin: these properties can be monitored in the presence of a magnetic field, where the nuclei of the atoms line up as though they were themselves miniature magnets. When bombarded and pushed out of alignment by radio waves, these atoms then emit radio signals as they spin back into line. The radio signal will be unique to the amount of oxygen carried by haemoglobin in the sample and therefore gives a very sensitive measure of the 'activity' of different regions of the brain. This technique can home into an area as small as one to two millimetres and measure events taking place over seconds.

Using these techniques it is becoming ever more apparent that during a single specific task, several different brain regions are working are active simultaneously 'in parallel'. It is not as if there was just one brain area for one function but rather several brain areas appear to contribute to any one particular function. Moreover, if some aspect of the task changes slightly, such as hearing words rather than speaking words, then different regions of the brain appear to predominate.

Techniques such as PET and NMR are offering true windows on to the brain at work. Perhaps the most obvious lesson they have taught us so far is that it really is misleading to think of one brain region having one specific, autonomous function, as in the phrenologists' scenario. Instead, different brain regions will combine in some way to work in parallel for different functions.

The brain is not made up of mini-brains: it is a cohesive and integrated system organised in an albeit highly heterogeneous, and as yet mysterious, way. Rather than studying just one particular brain region at a time and trying to allocate it a specific and complete function, perhaps it might be more informative to travel in the opposite direction. With the new techniques available it will be possible to *start* the other way around, with a specific and familiar function, and see how its processing is parcelled out between multiple areas in the brain.