Introduction to Brain & Behaviour
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Structural Analysis of the Brain
Lecture 09

Hello, and welcome to the course introduction to brain and Behavior. I am Dr. Ark Verma from IIT, Kanpur. As you know, I work at the department of humanities and social sciences, and also the Interdisciplinary program for cognitive sciences at the institute.

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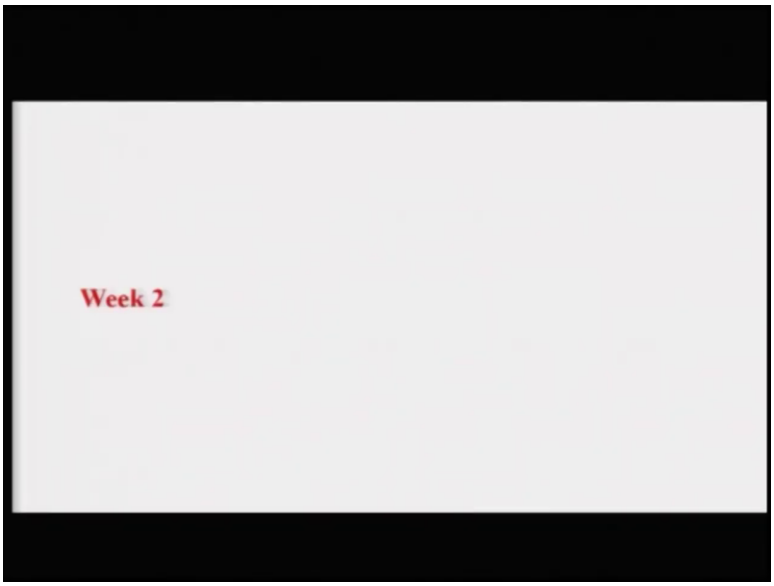

This is the second week of the course. And we are talking about methods to study brain function, normal brain function and so on. Today we will talk about some of the methods which focus on the structural analysis of the brain. Let us begin it.

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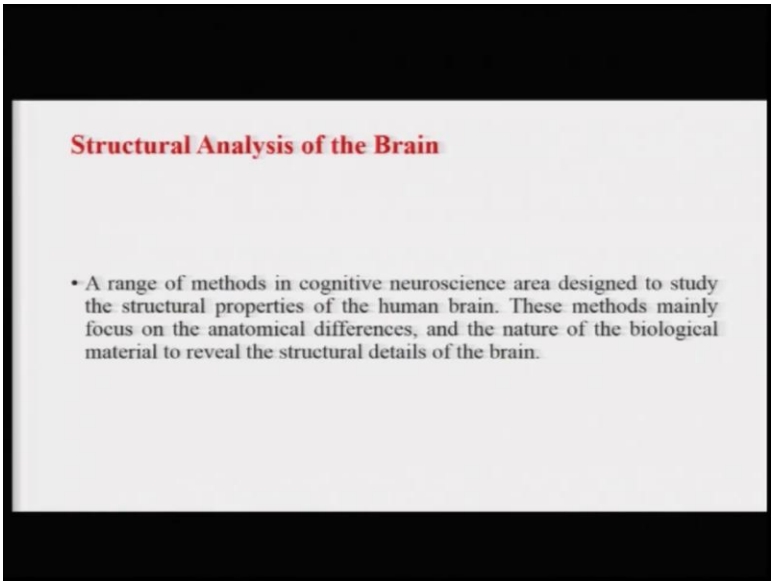

Now, there is a range of methods in cognitive sciences. There have been a range of methods in cognitive science, which have been concerned with basically studying the structural properties of the brain, the anatomical details of the brain. These methods have mainly focused upon the anatomical differences and the nature of the biological tissue, biological material to reveal the structural details of the brain.

Let us look at some of those examples today. The one of the main methods that has been instrumental in getting some kind of a structural overview, some kind of a structural footage of the brain is the computerized tomography.

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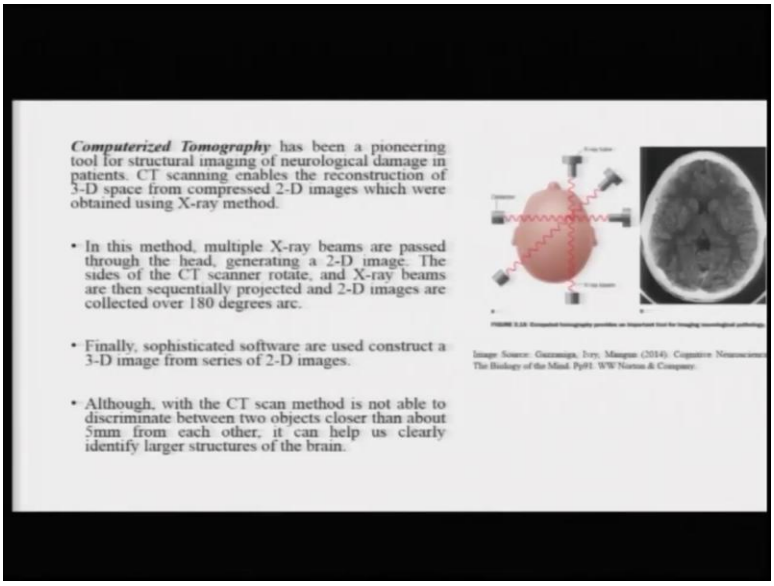

Now, Computerized Tomography or CT, as it is popularly known, has been a pioneering tool for structural imaging of the neurological damages in patients. CT scanning basically enables the reconstruction of 3-D space of the 3-D image of the brain by combining several 2-D images, which have actually been obtained using the X-ray method. In this method, multiple X-ray beams as you can see in the picture on the right, multiple X-ray beams are passed through the head, generating each, generating a separate 2-D image.

The sides of the scanner rotate, and X-ray beams are then sequentially projected and 2-D images are formed through this 180 degree arc. Now finally, what happens is sophisticated software and computer technology is used to reconstruct the 3-D images from the 2-D images that are obtained from the CT scanner.

Although, with the CT scan method we are not able to discriminate areas which are closer than 5 mm, so it does not really have a very high spatial resolution, but it can help us get clear pictures of the larger structures of the brain. So in that sense, it is a fairly useful technique.

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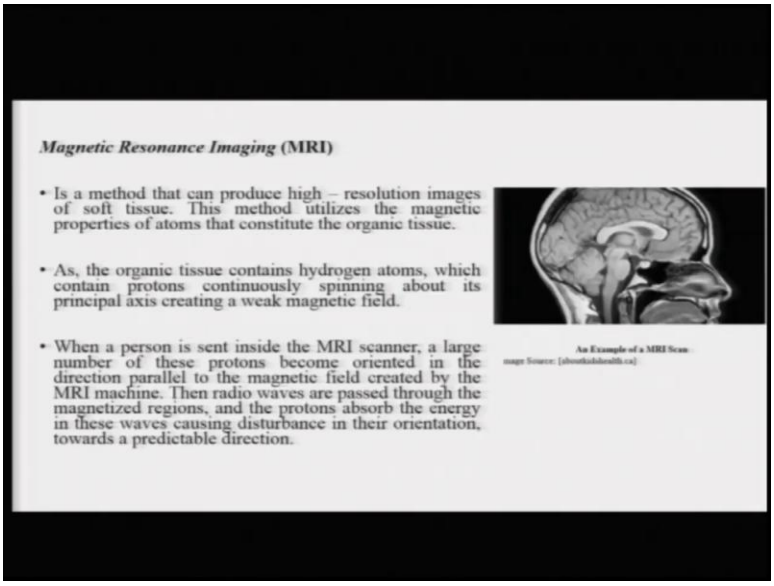

We can now talk about magnetic resonance imaging. Now magnetic resonance imaging is a method that can produce high resolution images of soft tissue of the brain. This method basically utilizes the magnetic properties of the atoms that constitute the organic tissue that makes up the brain.

As the organic tissue contains these hydrogen atoms which contain protons, and these protons are continuously spinning around their principal axis, which creates a little bit of a weak magnetic field. Now when a person is sent inside the MRI scanner, a large number of these protons become oriented in the direction parallel to the magnetic field created by this MRI machine.

Whenever you come across an MRI machine, you will see that it has a magnetic, it has a magnetic power of a few Teslas, 1 Tesla, 0.5 Tesla, 1.5 Tesla. More advanced machines have magnetic, have very high magnetic power up to 3 Tesla.

Now, this magnetic field basically instrumental in getting these images out, so, let us come back. When a person is sent inside the MRI machine, a large number of these protons which are making up this organic tissue become oriented in a direction parallel to the magnetic field that is created by the MRI. Then what happens is the radio waves are passed through this, through the magnetized regions and the protons absorb the energy in these waves, which causes a

disturbance in their orientation towards a particular predictable direction. So you would know that okay, in which direction these are going to get oriented.

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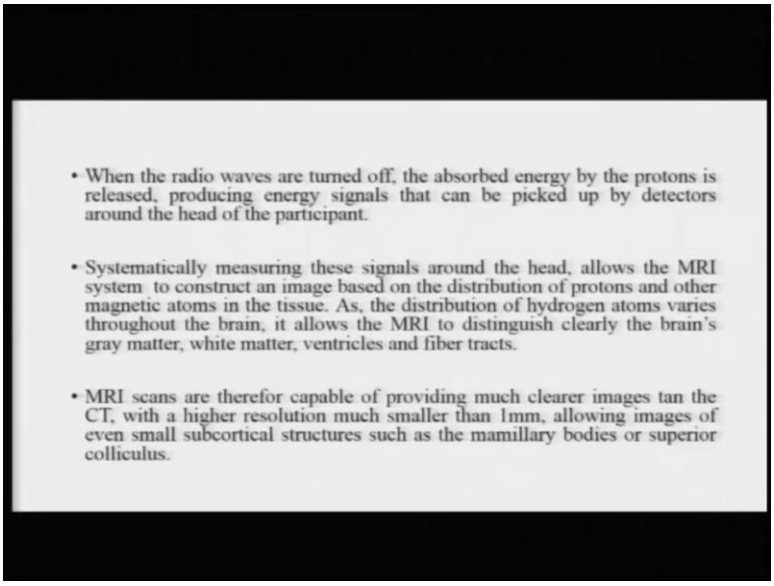

Now, when these radio waves are turned off, the absorbed energy by the protons is released, producing energy signals that can be picked up by the detectors in the MRI scanner.

Systematically measuring these signals around the head, allows the MRI scanner to construct an image based on the distribution of protons and other magnetic atoms in the tissue. As the distribution of hydrogen atoms varies throughout the brain, it allows the MRI to distinguish clearly the brain's gray matter, white matter, ventricles and fiber tracts. So, you can see that it is giving a very clear, a very detailed description of the anatomical parts of the brain.

MRI scans are therefore capable of providing much clearer images than the CT scan, with a much higher resolution of as small as up to 1 mm, allowing images to even capture very, very small subcortical structures such as the mammillary bodies, or the superior colliculi and those nuclei that are in the midbrain.

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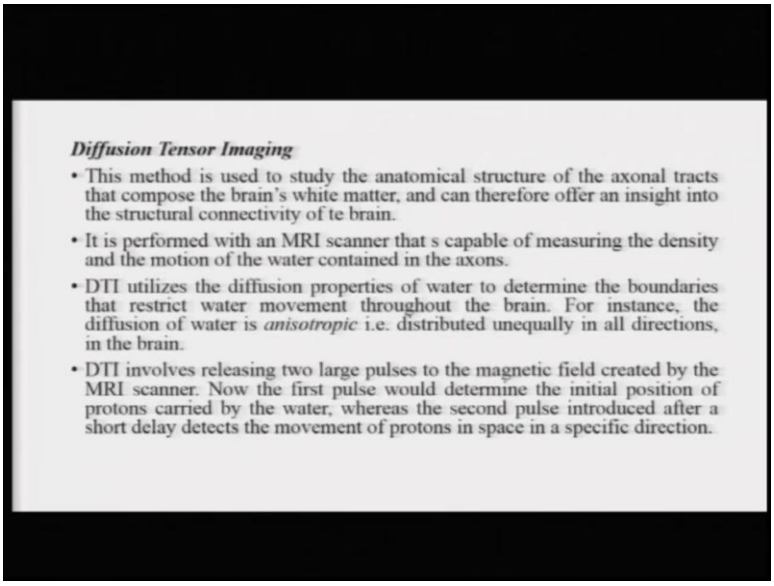

Now, let us talk about another very important method, which is the method of diffusion tensor imaging. Now, diffusion tensor imaging is a very important method, which is basically used to study the anatomical structure of the axonal tracts that compose the brain's white matter. If you remember we have talked about this in the past. The white matter is basically the axons of the millions of neurons, billions of neurons actually matter forming the brain, whereas the top of the surface, which is grayish in color is basically the cell bodies.

Now, the diffusion tensor imaging method is basically more focused at studying the anatomical structure of the brain using these axonal tracts of the neurons that compose the brain's white matter. And therefore, they can offer us a very detailed insight into the structural connectivity of the brain.

The connections between neurons in the brain are basically via these axons. And in case there is a method to actually look at how these axons are connected to each other, how they extend into different areas of the brain, that will and that is bound to provide us with a lot of details about the structural connectivity of the brain, which areas are connected to which areas, which areas project to the other areas and receive projection from some other areas. This information can be very, very useful in basically figuring out what kind of networks of brain areas are involved in doing particular cognitive tasks.

So, this is performed typically with an MRI scanner, that is capable of measuring the density and the motion of water contained in the axons. These axons contain some amount of water. And what this method does is it utilizes the properties of this water that is contained in the axonal tracts to determine the boundaries that restrict water movement. So, if water is there, it will flow to different directions. But there are these boundaries within these axonal tracts that will restrict the movement of the water throughout the brain.

Now, for instance, what could happen is, for instance, a very important property of this water that is contained here is that it is anisotropic and it basically meaning that it distributes unequally in all directions. It does not spread out in all directions, but just spreads out to some directions which are predictable in the brain. Now diffusion tensor imaging basically involves releasing two large pulses to the magnetic field created by the MRI scanner, so two large pulses are created.

Now what happens is that the first pulse basically determines the initial position of the protons carried by the water. Whereas the second pulse introduced after a short delay, detects the movements of protons in a specific direction. So one is in some sense tagging the protons, the other is actually determining where the protons are moving from there.

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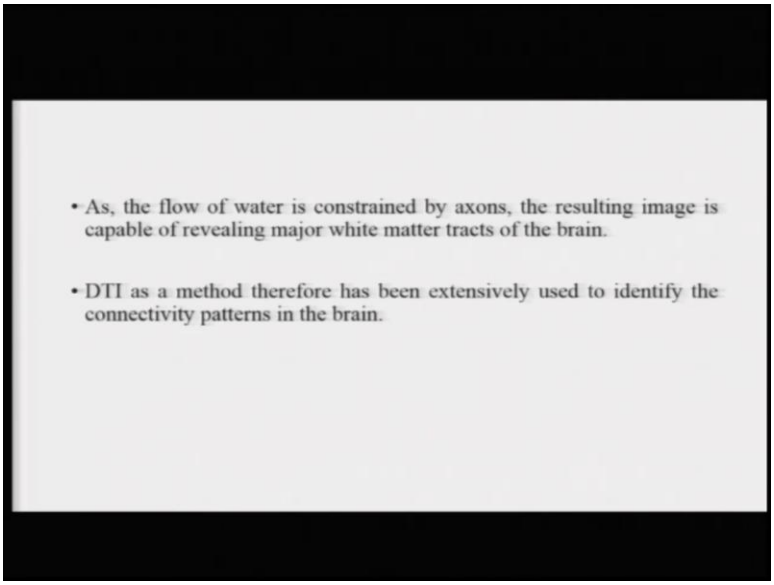

As the flow of water is constrained by the axons, the resulting image that is obtained is capable of revealing major white matter tracts of the brain. DTI therefore, is a very interesting method that has basically been used extensively to identify those connectivity patterns in the brain. So it

is also something that maybe we will come across when you are basically looking at the other chapters. We will come across some of the methods, some of the experiments that are using the diffusion tensor imaging method.

Now let us move our focus to some of the methods that are actually more involved in studying the functioning brain. Okay. So you have seeing some of the methods that do the structural analysis that are more about, you know, what are the structural details of the brain. But we can now move towards some of the methods that are capable of measuring the in vivo functioning of the human brain. Now, the advent of electrodes and systems capable of recording electrical activity from these bunch of electrodes fitted our cap.

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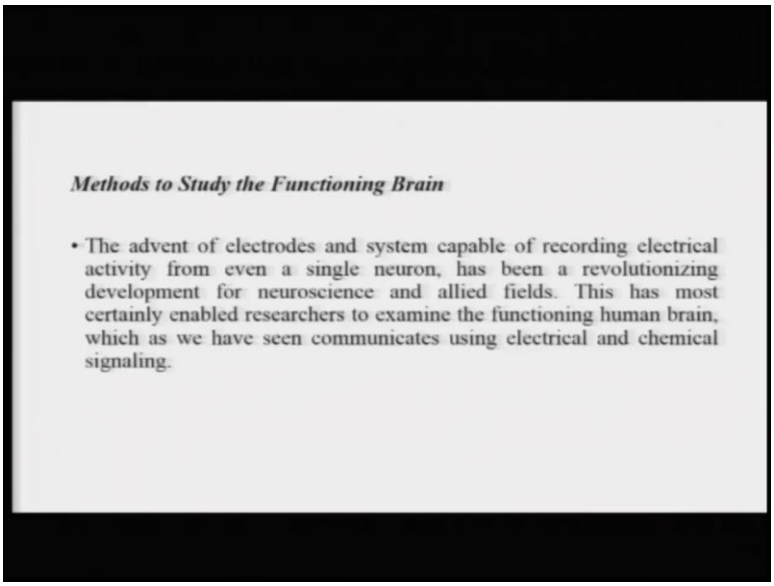

And even say, for example, fitted from a single neuron has been a revolutionizing development for cognitive neuroscience, and its allied fields. This has most certainly enabled researchers to examine the functioning human brain. We know that the human brain functions through electrical and chemical communications, electrical and chemical signaling, and that can be actually measured using some of the methods that I am going to talk about now. First and the foremost method that has been very, very instrumental more or so for animal models, but has been very instrumental to understand the generic functioning of a mammalian brain is that of single cell recordings.

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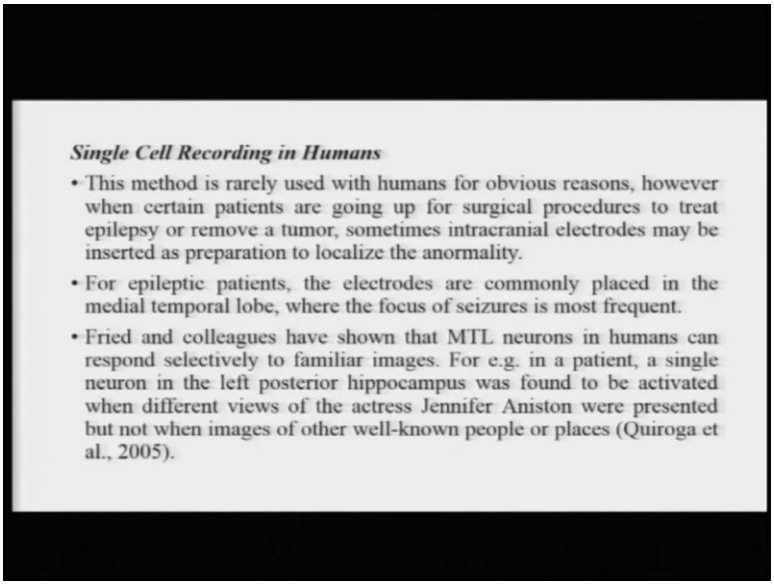

Now single cell recordings, basically have allowed researchers to understand the response patterns of individual neurons in the brain. So, they are basically methods that basically allow you to look at how a single neuron behaves. Okay. Now, what happens in this method is that a thin electrode is inserted inside the animal's brain. And as the electrode reaches in the vicinity of these neuronal membranes, it can measure the changes in the electrical activity surrounding this electrode basically, whatever is happening in the surrounding neurons.

Mostly this is done extra-cellularly because if you sort of impinge or insert the electrode inside the neuronal membrane of a particular neuron, there are more chances that you will damage it. So, typically it is done extra-celluraly, so the electrode is there and some neurons are just around itself. And basically what it does is therefore, it is picking up the electrical activity that is happening around itself.

Interestingly, there is almost no guarantee that whether the electrical activity recorded by the single electrode is from one neuron, or from a bunch of neurons. So, as this is most probably through coming from a bunch of neurons that are surrounding this electrode. So to sort of solve this puzzle, a help is taken from a sophisticated software, which are utilized to basically separate the pooled activity that is recorded on the single electrode to isolate activity of single neurons.

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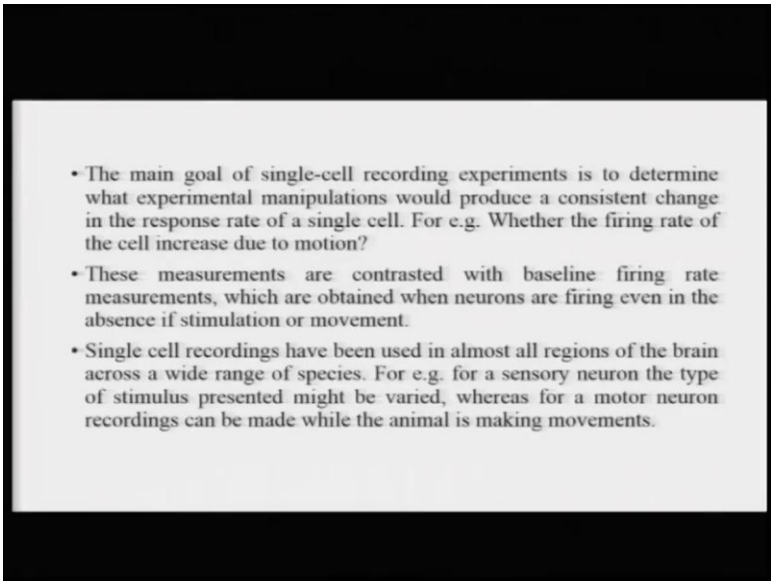

Now, the main goal of these experiments is basically to determine what experimental manipulations produce a consistent change in the response rate of a single cell. You might have seen figures and we will see some of them moving further, is that in single cell recordings with macaques, very, very simple, very, very unidimensional stimuli are used. Say, for example, you can show the monkey one straight line and then you can show them straight vertical line, horizontal line and then the line oriented by 10 degrees to each side and so on or you can show them some very specific picture and see what is actually happening.

So, this kind of studies are typically done with single cell recordings. And basically the dependent variables are whether the neuron is firing or not, if they are firing, what is the firing rate, and how does this firing rate basically change with respect to the stimulus or with respect to different properties of the stimulus like motion, color and so on, orientation for example. Now, these measurements are then contrasted with the baseline firing rate measurements, when there is no stimulus and the baseline firing rate of that neuron is measured.

Single cell recordings therefore have proved to be useful and have been used to determine the behavior of neurons in almost all regions of the brain and across all wide range of species, non-human species mostly. Now, for example, a sensory neuron, the type of stimulus if you want to kind of look at the behavior of the sensory neuron, the type of stimulus that could be presented

might be varied. Whereas for a motor neuron recordings can be made when the animal is viewing motion or making some kind of motion itself.

We can talk a little bit about single cell recording in humans. Now, in humans, for obvious reasons, because you cannot really penetrate the skull and insert an electrode. And because there are these ethical issues, and obviously, you do not want to harm the person. So for obvious reasons, single cell recordings are extremely rare in humans.

However, sometimes, once in a long time, it might happen, that if a certain patient is going for some kind of a neurosurgical procedure, sometimes to treat epilepsy or for some other reason, a stroke or something, sometimes, basically doctors would, with the permission of the patient, insert some of these intracranial electrodes as a preparation to just localize where these abnormal activity is happening that is leading to the epileptic seizures and so on.

For epileptic patients, mostly what happens is that these electrodes are most commonly placed in the medial temporal lobe, where the focus of the seizures is most frequent. Now, Fried and colleagues, Fried and colleagues basically have shown that the medial temporal lobe neurons in human beings can respond selectively to familiar images. Very interestingly in an experiment it was found that a particular patient's neuron in the left posterial hippocampus of a patient, this neuron was specifically activated only by the pictures of the actress Jennifer Aniston, different views of that of the face, but not when the images of other popular or other well-known people or places were shown. So in that sense, that selective response is also found within humans as far as single cell recordings are concerned.

Now, let us move onto another method, electroencephalography. We have talked a little bit about that in the past. Now, electroencephalography is a method where, say for example, a bunch of electrodes embedded in a sort of a plastic cap are placed across the scalp and electrical activity is recorded from the scalp, okay.

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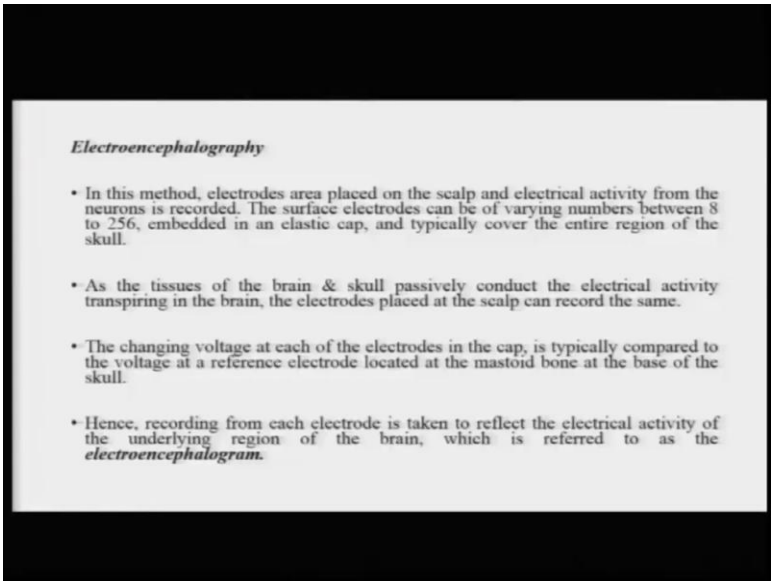

So it is a bit of an indirect method because obviously, between the neurons in the brain there is so much of this cerebral spinal fluid, there is the skull and there is the scalp and everything. So, it is sort of an indirect measure, but it kind of gets the hang of this electrical conductivity and basically gets a decent estimate of what is going on inside the brain.

The assumption is that wherever this electrode is placed, it is basically capturing the electrical activity of the neurons underlying this particular electrode. So, that is one of the reasons why you see that there are a large number of electrodes are used, say for example, anywhere between 8 electrodes, 16 electrodes to up to 256 electrodes, which span the entire skull, and which kind of allow you a very good resolution of as to where in the skull, a particular neuronal activity is recorded with respect to any stimulus that you have presented. So, this is basically how the electroencephalographic method is actually conducted.

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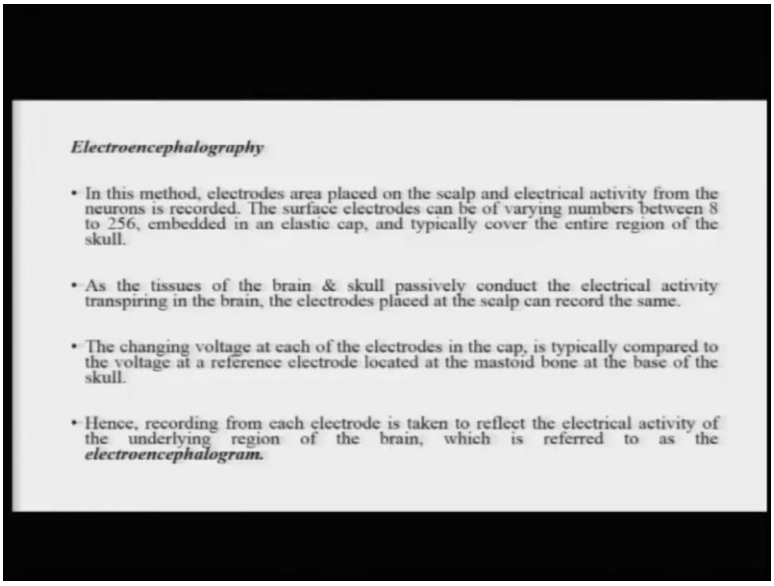

More technically, I mean, just a little bit I will tell you. So, what happens is that when you have place these electrodes there is this recording of changing voltage of the electrodes, which is typically then compared to reference electrode, which is placed along the mastoid bone of the skull, where in no neural activity is happening and then you kind of compare these things. And there it is where you get the actual neural activity that might be happening inside the brain.

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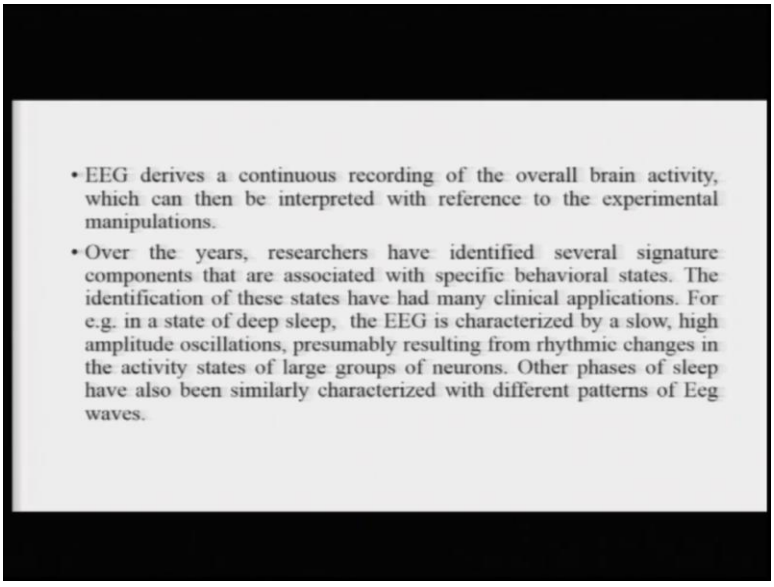

Therefore, what it does is it receives a continuous recording of the overall brain's electrical activity, which can then be interpreted with reference to different kinds of experimental conditions or manipulations. Over the years, researchers have identified several signature components that are associated with behavioral states and are sort of used to predictably, to decently predict what kind of behavioral state a person is in. The identification of these states have had many clinical applications.

For example, in a state of deep sleep, the EEG waves are characterized by slow high amplitude oscillations, presumably resulting from rhythmic changes in the activity of large groups of neurons in the brain. Other phases of similarly say for example, the non-REM sleep, etcetera have also been characterized similarly, by different patterns of EEG waves. So this is one of the ways there.

EEG recording can actually categorize the type of activity that is going on in the brain. A very interesting derivative of the EEG method is the method of extracting what are called event related potentials.

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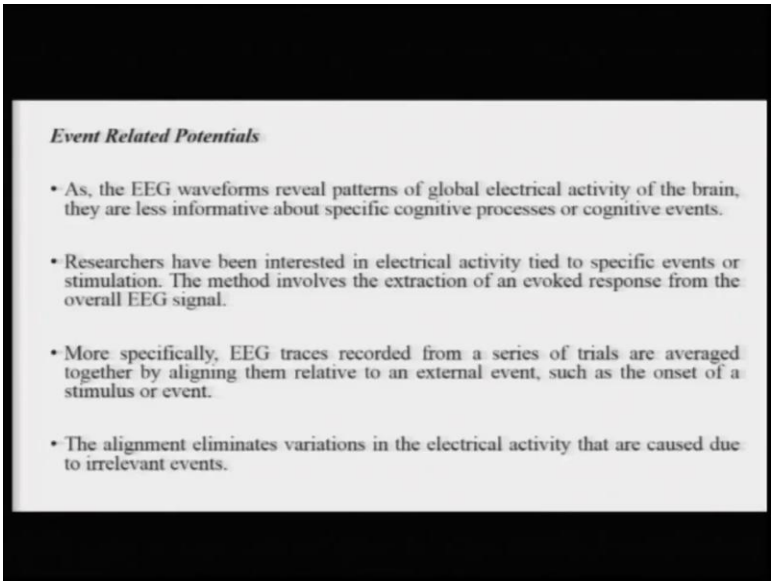

Now as the EEG waveforms reveal patterns of global electrical activity of the brain, they actually tell us less about very specific cognitive processes to which may be very specific areas of the brain might be responding. Now, researchers have obviously been interested in this electrical activity tied to specific events or specific kinds of stimuli of stimulation. The method basically

involves the extraction of an evoked response from the overall EEG signal. So what basically happens here is that EEG traces are recorded from a series of trials. And then they are averaged together by aligning them relative to an external event.

So for example, I am recording EEG waves and I am recording these waves for let us say, 2 minutes or 3 minutes. And within those 2 to 3 minutes, there are let us say 5 times or 10 times a particular event has happened, a particular stimulus has happened.

So what I will do is I will average out waves relative to this particular event or stimulation that I have presented and basically try and lock this electrical activity with respect to this particular stimulus that I have presented. This is basically what is called the event related potential.

Now this alignment that I was talking about, basically what it does is it eliminates variation in the signal that are happening due to random reasons, that are happening due to say for example, sometimes the natural activity of the brain or some time due to some other generic stimuli or environmental stimuli that are present.

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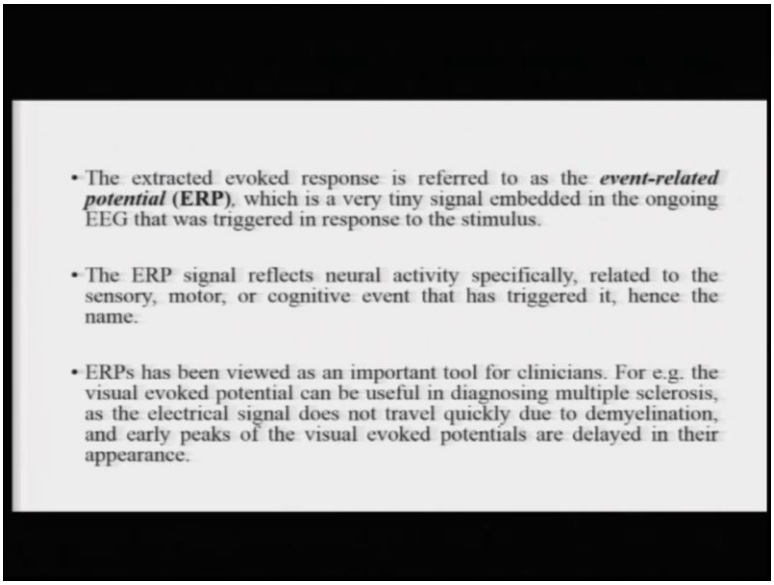

So this extracted response, as I was saying is referred to as the event related potential, which is a very, very tiny signal embedded in the ongoing EEG that was triggered in response to the stimulus.

This ERP signal reflects neural activity specifically related to sensory, motor, or cognitive event that has triggered it. So in that sense, it is a very good, you can make these correlations between the chronology of stimulus presentation, and the chronology of brain events that are unfolding in response to the stimulus presentation.

ERPs therefore have been viewed as a very important tool for clinicians and cognitive psychologists. Say, for example, for clinicians a very good example will be that the visual evoked potential which is gained from the occipital areas of the brain. They are very useful in determining or diagnosing patients with multiple sclerosis.

What happens is that, these electrical, in cases of multiple sclerosis, due to demyelination of the axons, the electrical signals from the neurons do not travel very quickly. And therefore, what you can observe is you can observe a delay in the early peaks of this event related potentials. And therefore, if a neuroscientist is observing that they can come up with a conclusion that there is probably an onset or an ongoing case of multiple sclerosis here.

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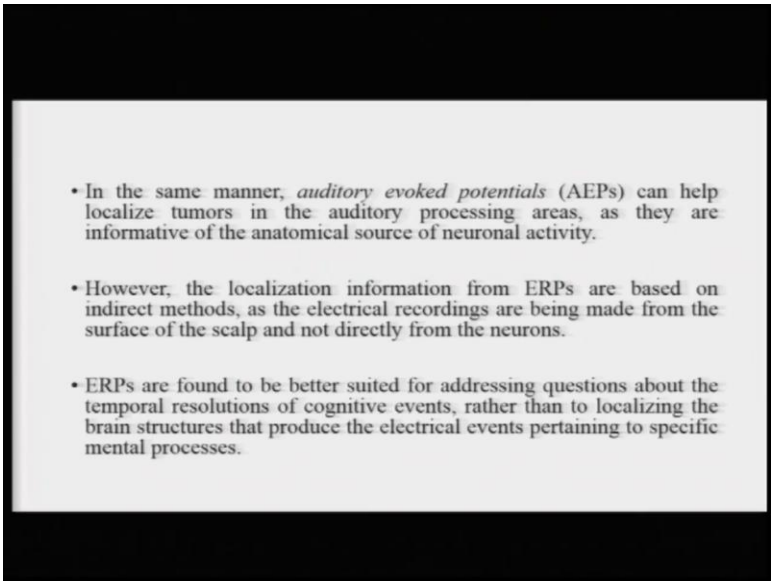

In the same manner, auditory evoked potentials can help localize tumors in the auditory processing areas as they are slightly informative of the anatomical source of these neuronal activity, where is this neuronal activity generating. And in that sense, you can sort of figure out okay, where the tumor might be.

I mean, you have to take this with a pinch of salt, because whatever localization information we are obtaining from ERPs is basically indirect. There is this entire segment of tissue between the origin of these neural signals or electrical signals and what is being recorded at the electrode. So, this is not really a very direct and a very definitive way of spatial localization of neural activity. Although it can say for example, using various ways to be augmented and got a roundabout good estimate of the spatial localization, if there are enough channels and there are enough software methods like functional connectivity analysis, etcetera have been used.

ERPs are found to be better addressed for addressing better suited for addressing questions about the temporal resolutions of cognitive events rather than to localizing brain structures therefore, that reduce these electrical evidence in response to mental processes.

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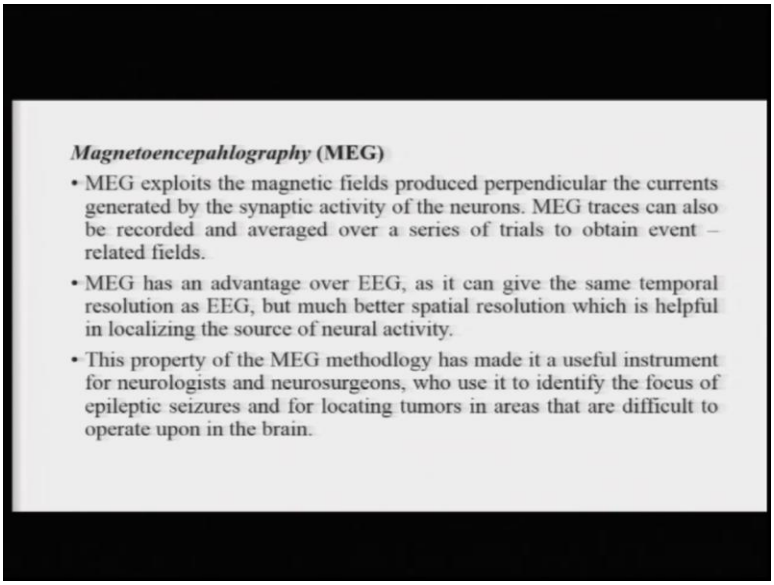

Now, finally, we can talk about magnetoencephalography. So, magnetoencephalography or MEG basically exploits the magnetic fields that are produced perpendicular to the currents generated by the synaptic activity in the neurons. Now, MEG basically, MEG traces and can also be recorded and averaged over a series of trials just like the EEG method. But MEG has a very significant advantage over MEG, because it can give as good as a temporal resolution as the EEG method, but it has ways of it as a method, it provides a much better spatial resolution than EEG or ERP.

This property of the MEG methodology has made it a very useful instrument for neurologists and neurosurgeons who have used it extensively to identify the focus of epileptic seizures for locating tumors in areas that are difficult to operate in the brain. So this is therefore a very useful method.

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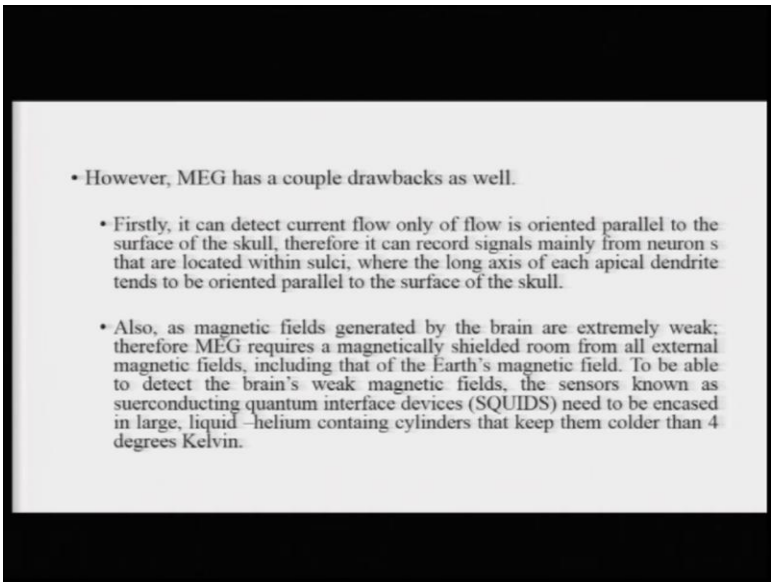

Now MEG, although it is very advantageous, as I said, it has a couple of drawbacks as well. Two very important drawbacks are that basically it can detect current flow only if the flow is oriented parallel to the surface of the skull. So that kind of eliminates a lot of regions, which will generate a current not parallel to the skull.

So mainly for MEG recording the signals can actually be obtained from neurons that are located within the sulci, within these infoldings, where the long axis of these apical dendrites tends to be oriented parallel to the skulls. This is where basically MEG can actually extract most data from.

Also, as magnetic fields that are generated by the brain are extremely weak, MEG requires a lot of expensive equipment to be set up. Say, for example, it requires a magnetically shielded room from all external magnetic fields, including the Earth's magnetic fields, magnetic field generated by other electrical appliances or wirings that might be going around.

These devices which kind of record the signal for MEGs are called SQUIDS, which are superconducting quantum interface devices. They also need to be encase in large, liquid-helium

containing cylinders, so that the temperature is kept around 4 degrees Kelvin and can allow better recording. But then this is a very, very expensive setup as compared to EEGs, of which even mobile versions are being increasingly available now.

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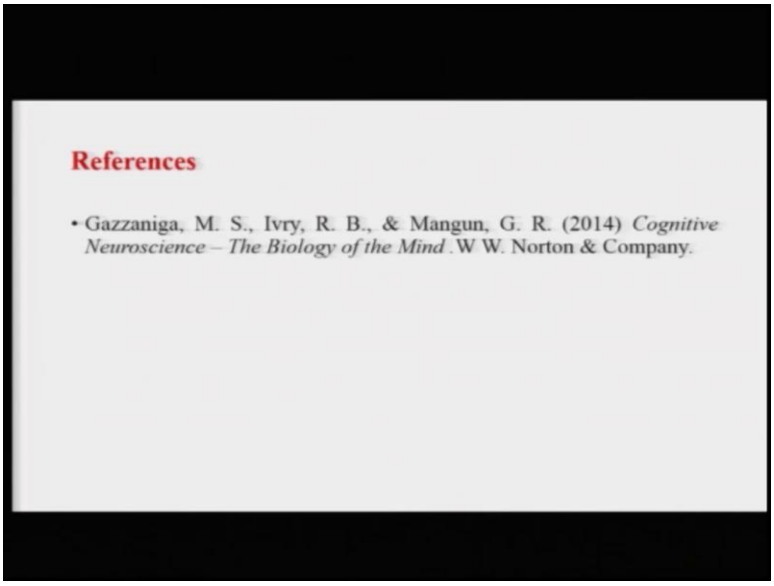

So there is a bit of tradeoff between the cost and the resolution of signal that you might be gaining here. This is all about some of these methods that we are talking about. We will continue this discussion in the next lecture. Thank you.