Microsensors, Implantable Devices and Rodent Surgeries for Biomedical Applications Course Instructor: Dr. Shabari Girishan Department of Electronic Systems Engineering Indian Institute of Science, Bangalore Week - 01 Lecture - 03

Today, we are discussing Neuroanatomy for Neural Engineering. It's an interesting and vital topic in the course for two reasons. Firstly, understanding the gross structure of the brain allows for a better grasp of the anatomical details crucial for rodent experiments we'll explore later. Secondly, comprehending the brain's gross structure helps in framing research questions more effectively. For example, for those planning to delve into neural engineering or considering PhD proposals, a foundational understanding of brain anatomy is essential. Even beginners aiming to formulate research questions will benefit from familiarising themselves with brain anatomy.

So, as I said, you can frame a research question, and once you frame a research question, there are a lot more translational aspects that you can think of when you know the actual structure of the brain. So, that is the brief introduction to today's lecture. Now, we can start looking into the details of the anatomy. Initially, I will deal with the gross anatomy of the human brain, then gradually, we will move on to the rodent's anatomy, comparing it with human anatomy.

So, it is a very fascinating organ, and this is the gross three-dimensional structure of the brain. What I would like to emphasise is the three-dimensional orientation of the brain. As a neurosurgeon, I do not get to see the entire brain in one go. We will be making a very small opening in one part of the skull, and we will be accessing very specific areas of the brain. So, the brain at large is protected, and that is how we sort of give them the benefit of the surgery while protecting their functional outcome.

If I am trying to operate on a motor area, the visual areas and other areas that I am not exposing are protected. So, that is why it is very important to understand the anatomy before we open up the skull. Having said that, I will move to the next slide. This particular lecture is outlined in this manner: with the brief introduction, I will be introducing you to the anatomy of cerebral lobes, deep grey matter nuclei, white matter networks, and imaging of those networks, and of course, I will sum it up with the comparison with rodent anatomy. After this comparison, in subsequent lectures, we will go into detail about rodent neuroanatomy and those experiments.

So, maybe it is a repetition, but what I want to emphasise is that unless we understand the detailed structure of the rodent brain, the rodent experiments that we are considering and thereby the neural data that one is going to collect will be really difficult unless we try to understand the entire structure that is under study. Having said that, why is it essential to know the deep grey

matter nuclei and white matter networks? It's not just the gross anatomy; deep grey matter nuclei are of great interest in research, such as Parkinsonism and disorders like Alzheimer's disease, which are the goldmine of research nowadays. These are all degenerative diseases that demand a lot of translational research. So, unless we are familiar with those nuclei and the various anatomical jargon that are used, it is very difficult to communicate or even write a paper on it. Even if you are a neural engineer, a technology neurotechnologist, or a computational neuroscientist, it is very important to understand the structure that you are going to deal with, whether it's computational data, structural data, or neural signal data. Understanding where this particular data is coming from and how it is going to benefit society at large is crucial.

So, all that is going to be based on the subject's anatomical details. Let us skim through the anatomy briefly—human anatomy briefly—and then I will take you to the rodent part of the anatomy. To begin with, one might wonder what layers are there before we approach the brain. It is very important because unless we plan how to approach the brain, the structure is going to get damaged. So, if we are planning for a craniotomy, then you need to know the layers that we are going to go through surgically.

So, this is important again when we take you into rodent neuroanatomy. There, again, it is very important because the brain is like a pink, soft, jelly-like structure. Unless you handle these layers very carefully, you are going to inflict damage on the underlying brain. Because after we pass through a hard skull, it is immediately the jelly-like brain. So, one plunge deep into the brain is going to cause a lot of damage. As you all can see here, you can make out that these are all the layers from the outside inward.

So, one will start with the skin, which is thick; the human scalp is pretty thick and vascular. You have these various layers of subcutaneous tissue, aponeurotic layer, loose connective tissue, and then only the skull, which is a very protective thick layer of bone. Beneath the skull, it is not directly the brain; between the brain and the skull, you have this potential subarachnoid space, which is made of the arachnoid layer. You can see a cobweb kind of structure which will encase multiple blood vessels supplying the brain. Only after that does the brain come into the picture. So, if I were to show you the structure in the human skull, this is a cadaveric slice where you can see from the top. That is the scalp layer which I just discussed, and that is the bone. You all can appreciate the arachnoid layer there. So, that is the arachnoid membrane. I mean, the name comes from the spider web, which in Latin is "arachnoid." Then this cortex comes into the picture. You can distinctly make out different layers within the cortex: that is white matter, and that is the grey matter.

So, that is the cerebral cortex, which holds information for all our well-being and all our functions. This is like holding this off, this is hardware that has software that is changing throughout our lives. So, that is briefly the different layers until we reach the brain, and you can

see there are blood vessels among different layers there. So, that is the blood vessel within the arachnoid space. Here you can see a blood vessel dipping inside, and then it branches out within the brain substance. So, this is very important to plan the particular surgical trajectory that we would probably be planning.

So, to ensure the vessels are protected and the garden remains safe, only then can we handle the cerebral cortex. After the layers, one needs to observe the different lobar structures. This is the brain as a whole; here, the entire brain is exposed after removing the skull and the protective layers, the dura, and arachnoid, both have been removed to expose the cerebral cortex. This is what is called cortical gyri, and you can see there are spaces in between each cerebral cortical gyri, known as sulci, which are deep depressions between gyri. So, one can fathom if you have to unfold this entire cortical mantle as a huge sheet of the cerebral cortex.

Within the confines of the skull, it is enfolded multiple times, with multiple sulci holding a vast amount of cerebral cortex. Each of these sulci, the major sulci and Sylvian fissure, holds many gyri and a large amount of cerebral cortex within it. That is the beauty of the human brain; it is huge, the largest in the evolution of any species. If you take the human brain, it is pretty large and holds a large amount of cerebral cortex. Grossly, by this Sylvian fissure and these arbitrary lines that you are seeing, it is divided into four major lobes: the frontal lobe, parietal lobe, occipital, and temporal. So, the beauty is that each lobar structure has its detailed functional importance.

For example, the temporal lobe here, on the left side, controls language for a human, which is a very specialised function in the evolutionary hierarchy. The occipital lobe here is in charge of vision, the parietal lobe is in charge of sensation, and the frontal lobe is in charge of the motor cortex, which is the movement of the individual. Apart from that, you still see a large amount of the brain, which are associative areas. There are frontal associative areas where execution takes place, planning takes place, and all major decisions are made by the prefrontal lobes. There are parietal lobe association areas, temporal lobe association areas, and occipital lobe association areas. So, it is these association areas that make a human being a very special species. It is not just seeing a particular object; they associate it with memory, they can associate it with past sensations, and experiences, and then make meaning out of it.

Then the final output can come as visual output itself or for that matter, motor output or sensory output. There are various reasons for this. So, this is grossly how the brain is divided, and these are all the major lobes. Whereas, there is a fifth lobe which is hidden. So, that lobe is called the insular lobe; it is also called the island of rail because it is separated and surrounded by the entirely thick cortical mantle.

In other words, in terms of development, this is called the neocortex, and this is called pallium cortex and archicortex, which are deep within the brain where evolutionally the frontal lobes and temporal lobes are overgrown to cover this particular lobe, and are called the insular lobe, which

is the fifth lobe. And what is being shown here is the hidden gyri within the Sylvian fissure. As I explained earlier, it is a large fissure cleft between the frontal, parietal, and temporal lobes that holds these very important gyri called Heschl's gyri. So, this is of importance because auditory perception ultimately happens here. When an individual hears any sound, the meaning of that particular sound is made out here. I mean, it is not just Heschl's gyri which is a terminal point of the auditory signals that would reach the brain, but from here, the entire perisylvian network is involved in the process of language. So, in other words, this large area here is the sensory perception area, which is called Wernicke's area. And then from there, the fibres are projected anteriorly or into the front to the area called Broca's area, where a person hears a sound, understands it, and then makes meaning of what has been said and then gives a response through Broca's area.

So, that is the functional importance of this particular region. The idea is that there are a large number of hidden structures deep within the brain, and it's very important to understand the anatomical boundaries, structure, and function involved when handling such experiments. Though the experiments are conducted in rodents most of the time, this course is all about how we are going to infer any data that you collect from rodents ultimately for human translation. So, when making meaning out of it or when trying to translate that particular question or hypothesis into humans, this is where it all matters. What is the structure you are dealing with and what is the function you are trying to study in detail?

With that, I will quickly run through the other important surface of the brain, which holds similarly a lot of important structure, that is the basal surface. We have finished with the lateral surface; this is the basal surface, the base of the brain, in other words, the bottom of the brain where you can see that is the hippocampus. I am sure all of you must have heard of the hippocampus in some way or another in various neuroscience experiments, and numerous papers keep coming out concerning the research on the hippocampus. So, this is like a goldmine of any sort of research. So, that is the hippocampus; outwardly, it is called uncus, the middlemost part of the temporal lobe. This whole part is the temporal lobe.

If you all remember the lateral surface when we separated it, it forms the inferior part of the Sylvian fissure; the entire thing is the temporal lobe. So, the medial part of the temporal lobe is the hippocampus which is in charge of our memories; this is where most of the memories are stored. But having said that, memory again is a very sort of higher-order cortical function. You know, in the order of cognition, it's a pretty large area of the network. For example, there are working memories that are stored in the frontal lobe, and there are memories for faces that are stored in what is known as the occipitotemporal gyrus or fusiform gyrus. So, various structures of the brain hold the information, but by and large, our long-term memory comes from the hippocampus as shown here. The lateral part of the temporal lobe again is involved in the process of language and the formation of new memory.

So, that is about the basal surface in general, and you can see here in the centre of the brain, this is called the brain stem. So, what is being shown here is the midbrain, which in other words is called the crus cerebri. Crus in Latin means leg, you know it is the leg of the brain; the entire cortical mandala, the entire cerebral cortex stands on this, and from here onwards it is the pons, medulla, and then it continues downwards as the spinal cord. So, that is, in general, the basal surface of the human brain. That is the hippocampus, which we discussed in the last slide.

The idea of having this particular slide is basically to emphasise how our brain is oriented three-dimensionally. It is very vital to understand the three-dimensional disposition of every single part of the brain. So, you need to understand what is the long axis of that particular structure that is being studied, especially in rodents, since we are dealing with rodents in this particular experiment. So, it is not that the slice or the 2D image that you are seeing is actually what is there in reality.

At the beginning of the introductory slide itself, I said the entire brain is oriented three-dimensionally. So, it is very important to understand, and of course, it is pretty difficult as well to understand initially. But as you start working with it, it is easy to grasp. So, here, what we can see is the hippocampus structure. It starts from the temporal lobe, goes along the middle wall of the atrium, and becomes a fornicial bundle.

So, it gets relayed into the anterior nucleus of the thalamus; from there, it gets into the brainstem and central core of nuclei. As I said, when a person recollects a particular information, it gets processed, and then various outputs can happen. So, that is the importance of having a three-dimensional knowledge of any structure of the brain that we are dealing with. Another system that is of immense research interest is the limbic system. So, the limbic system, as I said, is involved in various mental health disorders, such as Alzheimer's or depression, anxiety, psychosis, you name it; this is one structure where everything ends.

As you can see several nuclei are involved here in the central core of the brain. So, it is not hollow. So, when you see a huge brain, you wonder what is in the centre. It is full of grey matter; this is a different nucleus. I mean, large clusters of millions of neurons are within these structures that you are seeing, and then all these structures are important for our day-to-day living.

Any injury to this central part of the brain is detrimental to life and it is life-threatening. So, what is the research interest, as I said earlier, is a papillary circuit and the various nuclei that are involved in the limbic system as the basis of research in Alzheimer's disease and movement disorders like Parkinsonism. So, to go into the details of this structure a little bit, just to give an example of how intricately arranged various circuits and nuclei are involved in the disease of major depressive disorder. You know what has been shown here is the middle floor brain bundle, which is a very important pathway of the mesolimbic dopamine reward system. It is the

hypoactivity or hyperactivity that will decide whether the person is going for anxiety or OCD, obsessive-compulsive disorder or a depressive disorder.

So, all those are functional disorders where the neurotransmitters involved in this particular reward system go wrong, and then it manifests with various symptoms. There may not be structural problems with it, but then it is the imbalance in the neurochemistry of this particular circuitry that will manifest as various mental health illnesses. I mean, this is just one example. So, another example I can think of in the same circuitry is Parkinsonism and Alzheimer's disease, which are both degenerative diseases. Again, there is an imbalance of neurochemistry, and then it manifests as various functional disorders.

So, it is not just brain tumours that affect the brain; there are various functional disorders like epilepsy movement disorders and mental health illnesses and this kind of translational research has immense importance. So, it is all the more important to understand the various nuclei that are involved and understand the brain and the entire brain anatomy in general. As I said, this kind of research has a lot of translational value, and after many decades of research in this particular field, we now have what is known as deep brain stimulation as a major therapy for movement disorders. Before the invention of this, they used to create lesions, they used to destroy some parts of the brain to alleviate some symptoms of movement disorders. Whereas, now we do not have to do it; we still do it for patients who cannot afford these expensive devices, but by and large, this is the most preferable therapy.

So, deep brain stimulation therapy. So, this is sort of, I would say, an outcome of any of the research that we are going to discuss in detail in the coming part of the lecture series. So, we are trying to look at neural engineering, which is translational research where rodent experiments are going to get translated finally into humans if we are considering this particular line of research, which is very interesting and very important when it comes to alleviating various illnesses affecting the brain. So, deep brain stimulation, as I said, is involved in therapy for movement disorders, mental health illnesses, epilepsy, you name it; there are numerous indications for deep brain stimulation. All that is done is to pass the electrode deep into the brain target that we just discussed, and one of the targets for movement disorder is the subthalamic nucleus. The subthalamic nucleus is involved in Parkinson's disease, as I explained in the last few slides; you saw various circuitries will have an imbalance in neurochemistry where the depletion of dopamine leads to the manifestation of bradykinesia, which is slowness of movement.

A person will have tremors and involuntary movements where unwanted movements are happening. So, the patient, I mean the person, will have difficulty holding a cup of water or even feeding themselves, or dressing themselves; they will have difficulties in major day-to-day activities. So, they do respond initially to drugs, but since it is a degenerative disorder, these

dopaminergic neurons are going to degenerate daily. So, at the end of around 5 to 6 years, the drugs will stop working and they will not help that particular person anymore. They will benefit from these kinds of deep brain stimulation therapies, where we stimulate the end circuitry elements, and they will continue to improve with movement. So, the unwanted movements will be stopped, and the movements that are much needed for daily life activities will be supported by such stimulation therapy. What you're all seeing here is the programmable battery, which will be implanted in the chest wall just below your collarbone in the subcutaneous pocket; none of these devices will be seen outwardly.

So, that is the importance of research in the field of neural engineering. This is the kind of result that we get with this kind of research. So, it is very important to understand the outcome or final translation that is going to happen, so that one can start thinking about the problem or hypothesis in that particular line. So, that is the whole importance of today's lecture.

Having said that briefly, now I will try to cover the white fibres, which are the neural pathways that take information from one area of the brain to the other. It is very important to understand this as well because nowadays, especially in functional disorders like epilepsy or even Parkinson's disease, we depend on white fibres as well. For example, there is functional imaging, which I will be showing in the next few slides, where we can image these white fibres. White fibres are nothing but axonal pathways. So, all of you probably know the structural unit of the brain is the neuron, and the neuron has the axon, dendrites, and the cell body itself.

These axons are the ones that become white fibres. You know, there are millions of axons grouped to form white fibre bundles. So, in the next few slides, I will briefly touch upon the major white fibre pathways which are vital for carrying information from one part of the brain to the other. So, this is like after you make a section of the outermost part of the brain, you will see this white structure, and that is the reason why they are called white fibres in the first place. But in a living patient in surgery, we do not see such white structures.

Obviously, because of the presence of blood and blood vessels, it will be sort of pinkish-white. So, this is a cadaveric brain where the outermost shell of the cortex, which I explained as the frontal and temporal lobe where you see the hidden lobe of this insula. So, at that level, if you remove the outermost layer, this is what one can see. So, what has been shown here is the superior longitudinal fasciculus. So, these are all just Greek and Latin terminologies which only say superior, that is above the upper structure, longitudinal, that is lengthwise from anterior to posterior, from front to back, longitudinal fasciculus, which is a bundle of fibres.

So, this is the one that helps in carrying the auditory information to Broca's area, and of course, when something has been said, you can hear it and understand the meaning of what has been said, which is also important as feedback. So, both to and fro fibres are connecting the temporal lobe to the frontal lobe. In other words, these are called the arcuate fasciculus, okay? And what is

also shown here is the insula, which I already said, has long and short gyri within it. So, as you go a bit deeper and remove the insula, then you will see what is known as the extreme capsule. And what is also important is this uncinate fasciculus, which is very important. I mean, I'm pretty sure that even if you are not directly involved in human brain surgeries or human brain research, even if it is an animal experiment, you do come across such structures in rodents as well or even for that matter, non-human primate models if you guys are considering for research. You will come across these particular structures, very vital structures, which connect the temporal lobe to the frontal lobe involved in memory, which is the uncinate fasciculus.

And then what is known as the extreme external capsule, comes the basal ganglia structure, the putamen, which is an important structure involved in a very important part of the basal ganglia. This is one of the structures we sort of target for various lesioning purposes of movement disorders, and that is the corona radiata. It is a very vital fibre bundle carrying our motor pathway. So, from the motor cortex, first, it becomes the corona radiata; we can see where the radiating fibre bundle approaches the sensory; some amount of sensory information also goes through it, and it becomes the internal capsule, then it goes through the brainstem into the spinal cord and reaches our hands and legs. So, these are the motor fibres, and of course, there are many associative fibres in the parietal lobe and there are in the occipital lobe, and this is the anterior commissure bundle that connects the two temporal lobes, alright?

So, if you go a bit deeper again, you will see what is known as the globus pallidus. This is what I was saying; it is not hollow. As you dissect, you will see various such structures arranged three-dimensionally. So, here they are going from outside inwards and keep removing the structures slice by slice, then you will see all such structures; this is called the globus pallidus.

We do what is known as pallidotomy, which is a lesioning procedure for Parkinson's disease for patients who cannot afford deep brain stimulation or for that matter, if they are not a candidate for deep brain stimulation therapy. We create the radiofrequency thermo-coagulation lesioning in the pallidum, which will alleviate bradykinesia, that is, slowness of movement. Their movement will improve, and their tremors can improve. So, optic radiation is the fibres that carry visual inputs from the eye and optic nerve, then it comes to the geniculate bodies, and then it goes straight into the occipital lobe. So, that is optic radiation, and this is exactly what I said, the internal capsule. As you go in the corona radii from the motor cortex, it goes in as the internal capsule, and then it gets into the brainstem, and these three anterior, posterior, and middle are the different segments of the optic radiations, which are the visual pathways.

Briefly, I would like to touch upon the connectivity matrix or connectivity maps. So, this again is a major research subject nowadays because what you are seeing is the true dataset coming from the Human Connectome Project.

I am pretty sure anybody who is involved in neural research one or the other day will come

across the terminology called connectomes and connectivity functional MRIs and diffusion tensor imaging. So, in the next few slides, I will briefly touch upon imaging because even if it is a rodent experiment and this course deals with rodent experiments there are opportunities where you can image given the rodent brain. Papers are coming out now with functional MRI of the rodent brain where before you implant any sensor into the brain you can look at the functional part of the rodent brain and decide yes this is the motor cortex this is a sensory cortex then you can go ahead and implant as per the coordinates. So, that is the beauty of the research that is happening now. So, briefly, we can imagine these particular white fibres which I showed in the cadaveric brains.

In the structural structure of the brain, you all heard me talking about this arcuate fasciculus and superior longitudinal fasciculus. These are those language fibres which are mapped here where there are frontal sets of you know targets where this fibre ends and then you have temporal lobe fibres and the optic radiation fibres which are seen here. So, all these are interconnected for language. So, but predominantly it involves frontal and temporal lobe areas and these are all arcuate fasciculus with different components. So, you can see here what is known as the dorsal pathway and ventral pathways in the language network itself.

So, it is that complex if you can see that almost two-thirds of the entire brain is involved in language production. It is very important because a person has to talk from memory, use the visual input that a person is getting and that is also conveyed into the language area then there is modulation that happens tone modulation that can happen before something has been said. So, hence the importance of these various language networks, various components of the language network that can be imaged these days. So, having said that, what I am trying to convey is that there is an entity called connectome. You know when there is a cortical area that you can look at using functional MRI and you can look at the various white fibres you know the imaging of white fibre called diffusion tensor imaging DTI. So, when you combine both, what you get is a connectome where you can see the entire structure of the particular circuit that you are studying.

So, this is a curiosity. I am trying to cover this particular subject where imaging is taking very high importance in neural engineering. So, similarly, that is the sensory-motor network and you will see various cognitive networks or apart from the basic structural networks like a sensory-motor or visual and language you have various executive networks like dorsal default mode networks and then you have a salience network where a person's saliency or priority map of the visual environment is taken care of and then of course, you have central executive networks. So, these are of vital importance for human endeavours. You know a person who is working as a professional needs working memory he needs executive decisions to be taken. So, those decisions daily are in charge of you know of these particular targets that we are just discussing and these are available for imaging now. There is an entire group like BrainSite AI which is working to take these imaging to different levels where we can start helping patients with various disorders.

We can imagine this, but we do not have to open up completely and we can plan any sort of surgery and decide which is a part of the brain that needs to be explored. We can preserve the vital functions of the brain and these are the various attention networks that can be imaged before we go in for surgeries. So, after covering various structural and imaging anatomy briefly I will touch upon comparative anatomy because ultimately this course is for rodent experiments, rodent neuroanatomy and various serotactic surgeries that can be performed on rodents to gather vital neural signal data. We need to understand how you know the comparison can be done with the human skull and the human brain so that we understand which part of the brain actually can be translated ultimately into humans when a particular research question is trying to get answers from rodent experiments. So, having said that you can see various parts of the human skull, we have frontal bones, parietal bones and occipital bones. So, similarly, there are colour codings where this is the frontal bones, parietal and occipital bones.

So, it is flattened from front to back and of course, you can see the volume is pretty less. So, the most important landmark in the rodent skull is bregma of course, you have bregma in the human skull as well where the sagittal suture and coronal suture meet to form bregma and the lambdoid suture and sagittal suture meet to form lambda. So, these 2 points are of vital importance which I will be discussing in detail when we discuss rodent stereotactic surgery because every experiment in rodents depends on these particular stereotactic coordinates which are completely based on these 2 anatomical landmarks of bregma and lambda. So, if you were to compare the anatomy the major difference one can easily make out is that the rodent brain does not have a sulci at all.

It is a plain sheet of cortex whereas the human brain has many sulci and of course, it is big in volume and it encumbers a large sheet of the cerebral cortex which I discussed earlier. So, that is a major difference and then there is these deep hemispheric sulci and then there is the central sulcus that is seen in the human brain whereas, here the rodent brain you can make out that there is a cerebral cortex there and that is the cerebellum that is the only major division and of course, there is a very important olfactory bulb which as a species the rodent needs to survive. So, those structures are highly evolved and very obvious whereas, frontal-parietal and occipital lobes are dependent on stereotactic coordinates that you are all going to use in the rodent experiments. So, those must coordinate you know belong to a particular species, a particular age of the rat because that is the one area where the inaccuracy can creep in because though the literature says some coordinate that and that coordinate may not match with your species of rat or your sort of size of the rat. So, it is very very important to understand which part of the brain you are dealing with because most of the time you make a small twistle hole and then deliver a drug or probably implant a sensor.

You might think that you are implanting in the motor cortex, but because of the coordinate

difference between different species you might end up implanting it in the parietal lobe and then your entire neural signal that you are going to read out is different. So, it is exactly the reason why this entire course has been planned so that neural engineering goes. I know that a particular course goes in a particular direction with clear neural data and neural signals that are informative. So, having said that obviously, that is the sagittal orientation of the rodent brain and what I have that has not been shown is this is just a representation, but more or less it is featureless. So, as opposed to the human brain where there are n number of sulci this is easy to divide it into frontal and temporal as I explained earlier whereas, here we need to depend entirely on the stereotactic coordinates. So, that is again the sagittal orientation if you take a midsagittal section where you vertically split into two halves of the brain, that is those are the structures that come into view in the rodent brain.

As I said there is a large olfactory bulb and then there is a cerebral cortex that is a central thalamus which is the midbrain, the mesencephalon is the midbrain pons and medulla oblongata and that is the human brain as I said where this is a midbrain pons medulla which is put together forms a brain stem. If you remember the basal surface I discussed, that is the midbrain which holds the entire cerebral cortex which is then that and that is why it is called crus cerebri. So, briefly the functional divisions in the human brain and the rodent brain. So, it is very important again to understand the different areas that I just discussed, the sensory-motor area of the frontal lobe. This is the sensory area, a motor cortex that is the associative area and of course, this is the speech area Broca's area, Wernicke's area you know.

So, by and large, you can sort of imagine and project it onto the rodent cortex very important to understand where exactly the motor cortex stops and the sensory cortex starts. There are primary sensory areas, secondary motor areas, and secondary sensory areas within these subdivisions and I said that is entirely dependent on the stereotactic coordinates. So, another important feature in the brain that you need to remember is that though the various anatomical images clearly show you all the structures that are needed in reality when you open up the skull of the rodent or the human brain you will see n number of blood vessels. So, this is sort of very important to understand because when you make a small hole as per your stereotactic coordinates and you enter the very next day probably the rodent might die. The reason being one of these vessels might have got ruptured it may be easier to you know sort of avoid these vessels on the surface, but as you go deeper there are n number of vessels which comes in between.

So, it is very important for humans. It is possible to avoid because we have what is known as image guidance where the 3-dimensional volume data is exported onto the image guidance where we can see the images slice by slice and plan a trajectory. Whereas, in rodent experiments, though the research is happening in that direction as well still it is not in vogue. And so, largely we are dependent on the stereotactic coordinates to plan our trajectories, but one has to remember to use these avascular or the area devoid of vessels to enter the brain. And it is very

easy to make out once you open you will see a lot of blood vessels which you can coagulate as long as you are not studying that particular area of the brain to target the deeper structure if your research question deals with the deeper targets. So, before I conclude this particular lecture I would want you all to understand the intricacies and the beauty of the entire neural engineering, what has led to it and how it is making a huge difference in patients' lives.

So, this is one of our patients for whom during the epilepsy surgery we map the data we map the motor area before we begin the surgery. So, that has come out of such research in the neural arena. So, on the right-hand side, you can see where the tungsten microneedle has been implanted into the motor cortex of the rodent which has been anaesthetised and fixed on the stereotactic frame. With the stimulation you can see the left forelimb is getting stimulated and when there is repetitive adduction movement seen. This is akin to this particular patient's brain where one can see when we stimulate the motor cortex he can move his hand and move the thumb area

So, the various areas of the brain will be mapped before we begin. So, that is the awake human surgery that can be performed for both brain tumours and epilepsies. So, such is the translation research that can happen in with neural engineering and that is the importance of having the rodent experiments you know to understand these rodent experiments and then get valuable data out of it and make sense of it as to what you are dealing with and get a very good input for further translational research.