Lec 06 - Rodent Neuroanatomy

Hello everyone, welcome to the NPTEL series of lectures on Microsensors, Implantable Devices and Rodent Surgeries for Biomedical Applications. So, after the last lecture on human neuroanatomy, I gave a brief introduction as to what are the different divisions of the brain, what are the structure that are usually becomes the part of neural experiments and various neural research that can happen from different structures of human brain. So, with that background, we will start getting into the main the core topic of this module that is the rodent neurosurgeries and rodent neural models. So, as an introduction to the rodent experiment, the first and foremost the foundation is going to be again rodent neuroanatomy. So, unless we are familiar with the various anatomical structures, the names of those different targets, it becomes very difficult for you all to just conduct the experiment based on the available literature or even there are many videos which demonstrate how to do it. But then the structural details are very important to troubleshoot in case if something goes wrong in the middle of your surgeries.

And surgery as again I try to reemphasize that it is very very vital that it goes as per your plan, so that your data is as solid as you expected it to be. So, with that brief introduction, I will start the this particular lecture on rodent neuroanatomy. Today's lecture, we will complete everything about the rodent neuroanatomy. And it is very difficult to get into the every single structure, it is beyond the scope of this particular course, but the whole idea is that how do we approach for the neuroanatomy and what is it that you need to generally know to do any sort of you know rodent surgeries.

So, with a general theme in mind, I will sort of briefly describe the neuroanatomy and I recommend and all those researchers who are involved in the rodent neural experiments to get into the lot more details like microscopic details, cellular details and the network details that needs to be covered which is relevant for your research. So, let us begin the lecture on neuroanatomy. So, this is the outline of today's lecture. So, we are trying to cover the most important aspect of the skull anatomical landmarks which is vital if your study has a craniotomy or for that matter even a twist drill, burr hole, even those requires a specific anatomical landmarks which are based on stereotactic coordinates which will be dealt in the next you know lecture. And along with that skull then we need to know grossly what is the anatomy of the rodent in study.

I am using the word rodent here because more or less the mice and the rat shares lot of anatomical features. And so, what being considered here is mostly the rat anatomy and some of the slides also has mice anatomy. So, overall cerebral structure the various components of the brain is more or less similar. And then I will give you brief examples of the targets and then we will continue with the rodent neurosurgery in the next lecture.

So, first and foremost one need to look into the aspect as to why rodent model in case some of you are still considering which model to really consider.

And if at all your guide or if you yourself considering a rodent model as an animal model for your research, you can question yourself to justify why do you really need to consider rodent model and not a pig model or a rabbit model or any other animal model that are considered. So, I would strongly support the rodent model for a simple reason that over a last few decades we have huge amount of literature mounting on the support of rodent models for various neural experiments. And some of which I have shown here these are all these are all the published literature for DBS targets or even for that matter you know the freezing of gait model in Parkinson disease, D brain stimulation for animal models. For that matter there are n number of neural models I can think of be it epilepsy model or stroke model. Any experimental model that you can think of you do get it in rat or mice.

So, that is the biggest advantage of rodents and it is a small animal model little bit difficult when it comes to the small animal surgeries, but once you crack the learning curve that is involved it becomes immensely helpful because there is a huge amount of data mounting on the various aspects of the rodent model. Be it anatomical details or be it brain atlases that are available or even for that matter stereotactic coordinates. So, I am pretty sure that even other animal model has it, but then there are various many countries which has banned the non-human primate models like monkey. So, those places and those labs are hugely dependent on the rodent models for safety studies and validation of your you know the experimental questions. So, with that brief introduction let us see what we can learn from the rodent neuroanatomy section.

So, to begin with this is the rodent skull and if you all remember what we discussed in the human brain model or human neuroanatomy you can see that there are some similarities when it comes to the skull bones, especially the calvarial bones. Of course, the facial bones and all that is very different, but I am trying to draw a comparison so that it is easy to correlate what is the area that you are dealing with one thing. And of course, what are the brain region that comes right underneath the skull so that you need to make a hole or you can open a part of the skull which is called craniotomy. So, when you look at it this grey area here in front is frontal and many of you are not really familiar with the terminologies that that will be used in many of these lectures. I suggest and strongly suggest all of you to get familiar with all these terminologies that are anatomical terms which are very vital for your surgeries to be successful.

And moreover you need to communicate with any of your colleagues you need to get familiarized. And the best suggestion I can make after having been in this field is that

most of the anatomical terms are Greek and Latin. And if you look into the etymology of those terms they all have basic simple meaning to it. For example, when you say crux of the diaphragm or crux cerebri crux means leg. So, if you look at the structure that you are dealing with maybe it is supporting something or there is a vertebra called atlas.

Atlas supports the globe. So, that is how that name is derived. Frontal for example, here is called frontal bone. Obviously, the bone which is you know placed in front. So, similarly various other terminologies that if you find difficult to remember I strongly suggest go back and look into the literal meaning of it.

And that is an easy way to remember the anatomical terminologies which are very vital to remember. So, with that you know emphasis and introduction this is the frontal bone and this particular landmark here and the corresponding point in the cadaveric picture. This is a cadaveric picture here where the muscles and skin everything has been stripped off with bare skull bone in view. So, that point is very vital for all our rodent experiments that we are going to discuss in next few lectures. So, this is called bregma.

So, where there is a sagittal suture in the center that is the coronal suture. So, these are the new terminologies that I am introducing sagittal suture and the coronal suture this is the lambdoid suture. So, where these two sutures meet that point is called bregma. So, this is a very vital stereotactic point. So, whether you are doing a craniotomy or you are doing a twist drill bar hole for them for implantation of any micro devices or any sort of sensors be it a penetrating electrodes or a surface electrodes or for that matter even a simple lesioning you need to go through certain point in the skull.

Let us say you are you want to target something in the motor cortex. So, they tell you the all the coordinates are in reference to the bregma. So, we will deal with this little more in detail when I discuss stereotactic rodent neurosurgery, but so, this is a very vital point landmark that you all should remember that is called bregma and a similar point posteriorly there is called lambda ok. So, it is a Greek letter lambda the shape including the vertical midline sesital suture and the lambdoid suture it is an inverted y just like lambda. So, that is the lambda point. Bregma and lambda these two points are very vital in order to calculate any coordinates that you are thinking of.

So, it will be in relation to bregma how many millimeters anterior to it anterior is again a sort of anatomical term for front and back and the other terminology that we commonly use is rostral and caudal. Rostral is rostrum means beak structure or the facial structure something towards front or towards the beak is rostrum something towards the tailbone or back or posterior that is caudal. And again the if you want to remember the axis rostrum and caudal means for the obliquity of the structure that is placed whereas,

anterior and posterior is dead front and dead you know back portion. So, where it is a completely perpendicular to the totally perpendicular and horizontal to the vertical plane that is when one would say it is anterior and posterior. If it is an inclined plane maybe around like 45 to you know 90 degree in that position you would generally avoid saying anterior and posterior we would rather use the term rostrum and caudal.

So, that is what so, the anterior posterior medial and lateral medial is closer to the midline lateral is far from the midline that is another anatomical terminology that I would want to introduce at this point because we will be using lot of these terminologies in future and some of you are already familiar with it and those of you are not familiar lateral is away from the midline. If they say 3 centimeter lateral to midline means it is 3 centimeter away from the midline. So, that is the importance of knowing it for the simple reason that when you open up the skull brain has no labelling absolutely and has no morphological features to tell you where you are and especially in rodent neuron at least in human brains there are named sulci named gyri where we have some very specific landmarks to be identified and we can proceed with those landmarks. Whereas in rodent brain as I said earlier it is totally featureless and there are no sulci gyri it is like one shade of isocortex. So, and that is the importance of knowing the skull landmarks.

So, whatever is in front of bregma is the frontal bone behind the bregma are these two parietal bones this brown structure is parietal bone and this green is not occipital in humans behind lambda it would become occipital bone whereas, in rodents this green structure is something called interparietal bone and the blue structure here is the occipital bone which will cover the smaller brain or the hind brain which is cerebellum ok. Cerebrum is the bigger upper part of the brain hind brain which is a smaller brain is a cerebellum and here that green thing which is lateral is the very important bone called temporal bone and then whatever comes anteriorly is all facial bones which is not very important at this point. What you can remember is this is the olfactory part of the bone zygomatic bone and the maxillary process which fuse to form the upper jaw of the rodent. So, this is the lateral side view ok side profile of the rodent bone again that is that is the cadaveric structure this is illustrative picture to show the different components. So, the frontal bone drops vertically from that edge ok.

That is the frontal ridge there that point is again the bregma and this is lambda and is very important when we are doing stereotactic experiments to maintain the bregma and lambda in one horizontal plane and it is very vital and there are techniques how you know explaining how to maintain that we will discuss it in detail later. So, that again is a parietal bone this is inter parietal bone that blue is again is the occipital bone. This entire green structure is temporal bone and if you can see this circle that is the bone which is covering the auditory canal that is the ear of the rat. So, the inter-oral line yeah

somewhere here comes the inter-oral line which is again very vital for stereotactic coordinates. When we discuss it we will look into the incisor line and the inter-oral line and that again a very important relation to maintain the skull in a stereotactic position.

So, that is the auditory canal to which the horizontal bar of the stereotactic apparatus goes in and it is very vital that it goes into this bone so that you will get a rigid fixation when we fix the bone for fix the head of the rodent for surgery. So, this entire green is the temporal bone then comes the zygomatic bone and this is the zygomatic bone this is zygomatic process of the temporal bone. So, that fuse with the maxilla and forms the upper jaw of the rodent and that is the incisor. This incisor is going to sit on the incisor bar which is on the stereotactic apparatus and that is how we actually sort of fix the rodents head for surgery.

Two bars which will go through this I mean to the ear and this incisor here goes and goes and sits on the incisor bar on the stereotactic apparatus. So, that is in brief about the rodent skull. We will come into the details of the various parts of the skull again in the surgery. So, let us look at the entire nervous system in situ. So, again the word in situ means as it is in the rodents body.

So, that is the entire central nervous system. So, again central nervous system refers to the brain here and the spinal cord, brain and this entire spinal cord is considered as central nervous system. And all the nerves goes out laterally that way you know see these nerves goes out from the spinal cord and supply the forelimb and hindlimb of the rodent. So, these nerves are called peripheral nerves again that becomes the peripheral nervous system and this forms constitutes the central nervous system. It is very vital to understand whether your experiment deals with brain and spinal cord which is central nervous system or is it peripheral nervous system which is sort of a conveying cables which runs from the spinal cord to the various aspects of the rodent's body.

And this is a very important aspect of the rodent they have taken a sagittal section you know through the rodent cadaveric body the slice is gone right through the centre of the brain in the midline. And if you all remember the sagittal suture which is in the midline the section is gone through the midline. So, when they split it into two right in the middle this is how the brain would look like it is called medial surface that is inner surface of the rodent brain which will show you all the structures of the brain in relation with the bone which is overlying ok. This is the skull bone which I was talking about and that is the scalp layer. If you all remember the previous lecture where I explained the different layers of the head where there is scalp and there is you know the skull bone comes in and under the skull bone there are different layers which is covering the brain and then the brain comes.

So, there is there is a durameter which is not very clearly seen because it is very very thin, but what I want you all to see is this let me erase this. So, what is important to notice here is that is the bregma that we were discussing so much about and that is the lambda. So, between bregma and lambda you all can see that will house the important part of the cerebral isocortex. So, and that is a cerebellum which I said a smaller brain which sits below the occipital bone here. So, between the bregma and lambda you will have the big parietal bone in front of the bregma is the frontal the large frontal bone which will have the olfactory tubercle which is a large part which is very vital for the rodent to sniff and I am pretty sure many will be dealing with the olfactory system of the rodent.

So, that is the olfactory tubercle there which is which will process the olfaction of the rodent where it sniffs and figures out what is the food and where is it and everything all the vital information that is required for rodent survival comes from the olfactory tubercle which is under the frontal bone. Between bregma and lambda is the most important cortical mantle which will have motor cortex, sensory cortex, visual cortex you name it or most of the structure as here you can see here. So, that much of the brain is under the parietal bone and that is the area of for frontal bone this is for the occipital bone. So, the idea of this slide was to highlight the importance of the bony landmarks in relation to the brain which is right under that bone which is very important when you do a large craniotomy. Of course, you all have the stereotactic landmarks where it is also good to have an idea a gross idea as to what is the isocortex that is below the bone that you are going to handle.

And then you will see this is a large you know the brain matter going down there which is continued as a brain stem here and the spinal cord here. And this is the deep cerebral nuclei I am pretty sure most of you must have come across many terminologies like brain stem nuclei or basal ganglia nuclei all that is housed here. Of course, we will go it in detail, but in relation to the skull this is where it is all right and that is the ventricular system which will house the CSF that is a brain fluid ok. So, you can see that the larger part of the this is the entire head of the rodent it is only around I would say one-fourth of the head has brain. So, this is the reason why I am trying to highlight this particular aspect is that when we extract the brain at the end of surgery it is very vital that you maintain the structure that we are we have implanted.

For example, you must have implanted the sensor on top. So, it is very important that you maintain it. So, the extraction is also becomes very vital. So, for example, we are dealing with an experiment which involves surface electrode we I would rather harvest the brain going from below. So, for which we need I need to sort of take out the lower

jaw and go from the base of the skull there.

So, that is the importance of this particular slide. So, you need to decide are you going to you know extract it from below or extract it from top. So, that is very vital depending on which is a where is a structure that you are dealing with which has to be dealt with at the end of your extraction not in the beginning because the structure is going to get damaged when we handling the skull. So, that is about the over overview of the central nervous system. So, with that we will briefly deal with the various components of the rodent brain.

At this point I would like to you know tell you all that there is an entire huge research lab dedicated to the mouse brain and most of you must have already must be using their atlas it is called Allen Mouse Academy or Allen Mouse Institute, Mouse Brain Institute where they are adding huge data be it a microscopic data or a cytoarchitecture data or various neural circuitry models and there are n number of paper which has been published in nature. And on the right-hand side this structure is basically from the Allen Mouse Brain Atlas which is freely available for you all to access. And I strongly recommend that whoever is involved in the rodent neural experiments please use this models to understand the three-dimensional aspect of the rodent brain and to understand the structure that you are going to operate on or you need to implant on because they have this beautiful reference grid system approximately that would constitutes around 0.5 millimeter. So, and they have this midline and lateral orientation as well and as you see it in future slides they even give us the various subdivision that are involved in the isocortex part of the different cerebellum deep cerebellar nuclei and deep cerebral nuclei.

So, that is the huge repository that is available for the research world. So, having said that on the left-hand side in most of the slides you will have a entire cadaveric picture here and then corresponding illustrative you know picture showing which is the area that you are dealing with or I am explaining and then you will have this three-dimensional orientation model. So, having said that let us see where and how the rodent brain is divided into different areas. So, that leaven corresponds to the center point of bregma there. So, that the large this is the sagittal suture that I was talking to all in the skull this approximately corresponds to the lambda at suture sorry this would be the lambda and that would be the bregma approximately.

It is not very easy to tell after removing the skull where exactly bregma comes that will be completely based on the stereotactic coordinate. Once you identify the bregma you can clear it in the digital acquisition system in the stereotactic apparatus as 0. So, that would be our 0 point this is somewhere comes between this olfactory tubercle and the motor cortex which is somewhere there. So, on in this picture it is very clear what is

motor cortex, what is sensory cortex and that is further broken down in this particular 3D model. So, let me explain first here you can see that entire area this entire area is the motor cortex of the rodent brain.

Again there are various subdivisions and it is important to remember because many of you might deal with primary motor areas and there are experimental model which involves mostly secondary motor areas which are involved in planning the movement. So, the final execution happens in the primary motor strip here and that is the M 2 this is M 1 and that is M 2 areas. So, that is very vital to remember because primary motor cortex lesions leads to a complete paralysis of one-half of the rodent. M 2 will lead to sort of a loss of initiation you know gait abnormalities all sorts of initiation and planning abnormalities not directly paralysis. So, that is the motor cortex and this 7 here is the sensory cortex.

So, the word motor means something going to move. So, that is the motor cortex. Sensory refers to sensation acquiring the information from the surrounding. For example, there is this cortex known as barrel cortex you know. So, that is the whisker I mean rodent is a largely a sensor animal it senses a lot through olfaction and the whiskers because most of the rats does not really have a good vision a stereoscopic vision which human brain has. So, the vision in rodents is mostly through these huge vast tactile apparatus and that is the reason you can see there is a large representation of the sensory cortex.

Again here you have various division like primary sensory cortex, secondary somatosensory areas which deals with the sensation in the opposite half of the body. Its contralateral the wiring goes like that it is always crisscross right half of the brain controls the left half of the body, left half of the brain controls the right half of the body. That is something very vital to remember because any neural experiment that you are dealing with you need to figure out your animal is right-dominant or left-dominant. So, that is called shaping. So, we will deal with it when we discuss the behavioral studies and behavioral setups required for the rodent experiments.

So, it is called shaping of the rodent model to determine which is the dominant hand for that particular rodent. And it is vital because if the rat is right dominant you need to implant on the left side and acquire the data from the left side because the rat will be using mostly the right upper limb. So, that is the importance of knowing the dominant and the side of the hemisphere that you are dealing with. And of course, this is the visual area here and then there is a gustatory area there and then there is medial association cortex various subcortical plates which are very vital to process the information that these primary sensory area and primary motor areas are involved in. So, that is about the axial

orientation and the sense you are looking at the brain from the top and it is in the horizontal plane with respect to the obviously, the floor with reference to the floor it is the axial orientation and lateral orientation is from the side from the sides.

So, from the side view this is how the rodent brain would look like. So, as I said this is the cerebral isocortics, this is the cerebellar part of the brain that is the olfactory tubercle this is important for olfaction that forms the brain stem ok. And that is the part of the midbrain that is seen and then that forms the spinal cord there. So, broadly this is how the rodent brain looks like and these are the major divisions of the rodent brain. Coming to the subdivisions that you are supposed to see on the lateral hemisphere and this is how the coordinates are going to be that much is the motor cortex.

If you all remember the axial orientation from top this would continue laterally or let me raise it for you. So, you all need to understand it is a 3-dimensional structures that we are dealing with. So, in that context it is very very important to orient completely about the structure that you are dealing with. So, this motor cortex here is going to continue sideways and that is what we are seeing here that is continued sideways and it is extending way down there. So, it is a structure which moulds sideways and fits into that skull cavity ok.

So, that is very very important because when you deal with this rostral you know forelimb areas, caudal forelimb areas and then there are hind limb areas. So, it is very vital that you stick to your coordinates and you need to make sure that the model that you are using the rodent species that you are using and the coordinates that you are taken from the literature are the same that is very very important. And of course, the age and weight of the rat should also match for a simple reason that you are depending entirely on coordinates and coordinates are generated by taking serial sections and then putting a reference atlas as I showed that reference grid is your coordinates. So, when you are taking a coordinates from the literature and using it for your experiment it is very vital that you stick to the coordinates so that you identify the area the motor area which is very specific for the action of the forelimb or the forepaw of the rodent and this is the sense this large somatosensory area that you saw.

So, obviously, that is the primary and that is the secondary sensory areas. This part is here is again the most of the neural experiments deals with it is called the hippocampal formation and when you remove the isocortex you will see the remaining part of the hippocampal. It is a big structure in the rodent and that small pinkish structure there is the midbrain of the rodent because the isocortex actually covers that part of the brain and that is the cerebellum which is shown here. This is enlarged here and that is the gustatory cortex and there again is the olfactory tubercle that is the cerebral nuclei again this is

hidden under the larger cap of this isocortex.

So, that is in brief how the brain looks from the sideways. So, this video is again to emphasize the entire three-dimensional orientation of the brain here. So, let me sort of control that and show you all. As I showed that grid is the reference grid where the generally the coordinates are calculated. So, what you need to appreciate is that that is the axial orientation that we discussed and then this is the posterior view. You see the cerebellum though it looks flat on surface it is actually a three-dimensional structure which bends down and goes inferiorly or it goes below the reference plane and then when you look at from the sideways and you can see how that inferior most part of brain again gets rounded and then goes underneath and from.

So, that is the entire structure which goes you know round and round and extending beyond your anatomical planes. So, this sagittal plane that we are discussing is the axial plane that we are discussing is all conventional. So, three-dimensionally this brain model is a globular structure and that is the difficulty that one mode face to understand the structure in detail. So, it is very important to understand this three-dimensional orientation there and you can see the pink structure there that is a midbrain.

So, it is like a multiple layers sitting on top of each other. There is a cap of this isocortex when you remove it the entire brain stem and basally anglia comes into view and when you remove that again then you will see the deeper part of the cerebellum and the spinal cord. That is how the brain is organized and this is something which is common even for human brain which if you all remember from the last lecture that we discussed. So, there are multiple layers that are involved and as you go deeper and deeper the structures are very vital and any injury to that sort of structure will endanger the life of the rodent that you are dealing with. So, invariably there is a lot of learning curve involved in the rodent surgery. So, and then you are dealing when you are doing a rodent neurosurgery you are bound to lose lot many rats if you do not practice it on cadavers.

And if you ask me where do you get cadavers I would say maybe one or two you try the surgery that you are planning to do if in case it dies because of any injuries that that occurs during experiment. I would say use the rat use it put it in the formalin preserve it and study the brain in detail and this entire lecture series that I have developed is keeping in mind that you do get to look at the cadaveric brain. So, cadaveric brain is nothing, but the dead rodents brain which has been kept in formalin to avoid the death of these brain structures. Brain is like a jelly and it undergoes something called liquefactive necrosis it becomes a completely fluid in nature and it loses all the structural details if not put into the formalin.

So, that is the idea. So, if you get a chance to study the cadaveric brain use it to the maximum benefit try out all your approaches and try all the structure that needs to be exposed again and again. So, that you save on the number of rats that you are going to use for experiments and that is something they do expect in any of the animal ethical committee whenever you guys present they would definitely expect to use the least number of rats that are possible ok. So, with that discussion in mind let us look at the medial surface of the brain. As I said you will be able to see this surface of the brain only when you actually divide it in the center you know going in the midline you know if this is the midline center of the skull if you all remember only when you split it in half you will see this surface of the brain as opposed to the lateral surface that you saw that is the common surface which is accessible when you do a crinotomy in the temporal bone you know between the ear and the eye of the rodent when you open you will see the side surface of the brain. Whereas to see this particular medial surface one has to split the skull in the center and then you know divide it completely.

Normally you really do not see the surface in total or completely this surface is never visualized. So, this structure is I mean this surface is purely accessible through stereotactic coordinates and it is totally blind that is the importance of discussing this particular surface little bit in detail because you have lot of these vital structures this is the brain stem and that is the basal ganglia and that is the diencephalon structures where there is thalamus, hypothalamus then you will get a lot of brain stem nuclei that will be discussing. So, and that is the cerebellum again in the half and that is the isocortex. So, it is easy to make out you can see the different layers the idea is that you need to understand that it is arranged in different layers here. So, that is the topmost layer once you remove it you will be accessing the ventricles which is the fluid-filled cavity of the rodent brain with CSF in it and once you deeper to that is the set deep cerebral nuclei which will have thalamus, hypothalamus and all that and then you have this brain stem nuclei hit there then you have cerebellum then there is a pons and medulla oblongata then that come continues as spinal cord.

So, that is very important to remember it is easy to I mean you can see the same diagrammatic illustration there the entire thing is midbrain there, thalamus there this is hypothalamus again as I said hypo means below something thalamus is the center part of the brain below that thalamus is hypothalamus then you have midbrain here which is again the print structure that you saw in the three-dimensional image that you saw then that is the pons that forms the medulla oblongata all this put together it is called brain stem, stem of the brain which will hold the entire cerebral structure. So, that is a brain stem that will continue downwards as spinal cord and that is the cerebellum I am sure many of you will deal with cerebellum in pretty detail and fortunately there are lot of

similarity in the gross anatomy of cerebellum to the human brain though the proportions are much larger in human brain ok. So, that is in brief about the medial surface of the brain. So, the next few slides I will deal with the deep nuclei. So, as I said if at all one need to expose it surgically you need to sort of remove the isocortex there and then remove the cerebellum from posteriorly.

So, that is the whole brain there once you remove this cap of this isocortex that is called cerebrum and then you separate the cerebellum whatever the structure that is remaining here will be the deep nuclei all right. So, that is the brain stem that I just discussed and that is the spinal cord. So, this will be the cervical medullary junction ok, very very vital and any injury to this location will instantly kill the rodent that you are dealing with. So, that is a very vital structure where the brain continues as spinal cord. In humans there is this foramen called foramen magnum through which the spinal cord enters.

So, that is the fourth I mean the ventricle system of the rodent brain and that is the deep nuclei and what are these deep nuclei. So, here is a video to explain which I just you know described in the previous two slides. So, to expose the or to understand the deep nuclei one would need to remove it and this is the huge advantage with the Allen brain explorer and please use this explorer and understand in detail the structures which I just told you in brief and toggle around add more structures remove more structures till you get familiarized with these structure that you are dealing with. It is impossible for any of the PhD scholars or anybody for that matter to master the entire rodent brain. What I suggest is you are dealing with the motor cortex, then you study the entire motor circuitry and definitely some here and there relation that you need to understand the structure that you are dealing with.

May not be very important to understand the hippocampus too much in detail if you are dealing with motor cortex, but you need to really know where the hippocampus comes what is its role in the motor system, but to understand every single structure in detail is really difficult. So, this is how we look at this 3DML structure here. So, once you remove the cerebral isocortex there you will see this blue structure which is actually the deep cerebral nuclei. This will have the thalamus and hypothalamus and various other nuclei there and it also has this caudate and putamen you know.

So, it is called together put together called striatum. So, let us see in detail how it looks in three-dimensionally all right. So, this generally refers to the corpus striatum or the in humans is called basal ganglia. Of course, we do have corpus striatum, but there are many more structures that are involved and that is that as well is very complex anatomy which curves around the ventricular system. This again here is in the inferior portion of the ventricle and of course, you will not be seeing any of these structures in the live brain

because you will be approaching the structures through coordinates. So, really do not have to worry about too much as to how to expose these particular structures because generally it is life-threatening if you end up in exposing it in a you know grossly.

So, we will be dealing with these structures only using stereotactic coordinates. This is just to understand how that structure is you know relation related with other different structures. So, here that green portion is what I said earlier hippocampal formation. So, that is entire structure when we remove that then you will see this structure of brain stem nuclei and I have selected few nuclei to explain you know the relevance the clinical relevance or the research-based relevance. The red target that you are seeing there that is the subthalamic nucleus and which is the what you say the gold mine of any research involved with Parkinson's disease or for that matter movement disorders and that is the first nuclei that was targeted for the deep brain stimulation therapy for Parkinson's disease. So, that again is a gold mine for any research which involves movement disorders and the various other nuclei is the red nuclei and the pars compacta and pars reticulata part of the substantia nigra there.

So, let us look at that little bit in you know detail you can see various sub-nuclei that is coming in that is the part of the substantia nigra there and this is what is known as pediculopontane nucleus which is part of the midbrain. So, all these structures all these nuclei belong to this entire pinky structure belongs to the midbrain this belongs to the striatum part of it where it has a substantia nigra component there and the subthalamic nucleus which comes in the deep nuclei of the brain and that is the substantia nigra that forms the subthalamic nucleus and pediculopontane nucleus there. So, and the posterior eloid structure is the cerebellar part of the structure. So, that is the importance of understanding the 3-dimensional orientation of various nuclei and you have a wonderful opportunity to go through all these you know structures in detail alright.

So, that is in brief the deep nuclei. I just I will briefly mention about cerebellum because we are not dealing too much about it if your research involves a cerebellum just I said as I said earlier please get to know a lot more details about cerebellum by using the same atlas like Allen mouse brain atlas or there are a number of other atlases that are available to know these structures. So, my I would want to draw the attention to the various you know these sulci that are available. So, fortunately at least cerebellum has these deep grooves there. These grooves in cerebrum is absent in mouse brain is present in human brain you understood this groove is known as sulci and the each structure is folia, folia means leaf. So, this is something little bit similar to the human brain where you have various components in the vermis this midline structure is a vermis and then that lateral structure is called cerebellar hemispheres alright.

So, there are different subcomponents and it has you know the function with maintaining the balance of the animal and then it has you know the movement final movement control of the limbs are predominantly by the lateral cerebellar hemispheres. The midline vermis will be involved in the axial movement axial is axial refers to the central anti gravity muscles of the rodent body. So, that is the vermian which controls the midline. So, the beauty is of cerebellum is almost its geometrical with relation to its function. Here right cerebellar hemispheres is involved in the right half of the rodent body, vermis is involved with the midline and the left cerebellar hemispheres is involved with the left half of the brain.

And there you see is the medulla oblongata which continues as spinal cord there. This is from the top view just to emphasize on the cerebellar structure. So, the next few slides I will briefly discuss about the blood supply, venous drainage and little bit of the sectional anatomy. This is very vital to understand for the neural model if it involves a stroke you know there are various studies and it is a very hot topic because in humans the major debilitating disease is stroke is pretty lifestyle-related disease like stroke cardiac arrest. So, when it comes to stroke you need to know the blood supply of the brain inside out if your rodent model involves the creation of stroke models. If your study is relation with Parkinson's you need to know how to create Parkinsonian models by you know creating lesions in various basally angular structure which I just described.

If your study involves epilepsy you are trying to study you are trying to use the various sensors that are important to acquire epileptic form discharges then you need to know how to create epilepsy models by using various agents on surface of the brain or deep to the brain. So, similarly when you are trying to look at stroke model that is when the blood supply of the brain becomes very vital. You need to know how to target particular vessel to create the lesion or to occlude that particular part of the blood supply so that you can recreate the stroke model. I mean there are various models that are available in the literature, but time and again there has been discussed debated and right now the accepted model is I mean when you say accepted model that is the model which is very close to the human stroke. Obviously, rodents are saved from stroke they really do not have stroke in their lifetime unless some injury something else happens.

So, in order to create the model which will replicate the stroke in the humans now we have a model called occlusion models you know vascular occlusion where we surgically occlude the carotid artery, we occlude the middle cerebral artery and we create lesion in the arterial system so that that part of the brain suffers the ischemia. The word ischemia means lack of blood supply to that particular part of the brain. So, you create ischemia and then so that that part of the brain becomes non-functional. So, that is how you create experimentally the stroke models. Maybe we are having another lecture where all these

models will be discussed in detail which is very vital to understand how to do surgeries to create those models.

And as I said your model is what is going to decide what data you are going to interpret with. If your model itself is flawed then obviously, your data and the outcome is going to be flawed. So, with that introduction let me tell you briefly what are the arterial vasculature that is involved. So, as you all can see here they have injected the green latex into the blood vessel of the rodent. So, that it shows up all the blood vessels shows up. Otherwise in reality in a cadaveric brain after rat is dead it is very very difficult to figure out any of these lesions.

So, these pictures are created by injecting a green latex which dries and gets solidified all right. So, and similarly there is some red latex as well injected here. So, what you are seeing here is the middle cerebral artery which is vital this particular one and that is the rostral forebrain artery. In humans it is called anterior cerebral artery. The name the you know the nomenclature is little similar in human brain and rodent brain. And when it comes to that that is the carotid artery internal carotid artery there is external carotid artery and internal carotid artery.

External carotid artery supplies all the different structure facial structures of the head. You know the largely other than brain whatever structures are there in the head are supplied by the external carotid artery. Brain is supplied by the internal carotid artery here which gets divided into one artery which goes in front is called rostral forebrain artery and then it comes laterally to the sideways it goes and then it goes higher to supply the entire cerebral hemisphere. So, that artery is very very vital for the survival of the cerebral hemispheres. Of course, there are deeper arteries which comes in. So, this is again the vertebral artery and the caudal hindbrain arteries which will supply the brain stem and the cerebellum.

So, these are this is the basal surface that is the under surface of the brain this is how it is arranged and this is the arterial circle which is around the ah central part of the brain. So, when you dissected and obviously, as I said unless you are trying to create a stroke model or you are trying to understand the various vascular structures we definitely do not really expose these many vessels ah in an in a live rat all right. So, there are techniques to expose some part of the vessels there and then either you create lesions or you inject some embolic agents to occlude that particular artery. So, from the sideways this is how the venous drainage would look like it is very important to understand the venous system. What you saw earlier was arterial system this arterial system for those of you not familiar with the term artery it takes a blood to the brain of course, it is a common biology and the veins takes away the brain the deoxygenated blood goes away

from the brain.

So, from sideways this is how the venous drainage would look like and that is the ah caudal ah you know vein of the brain and that is the rostral ah brain and believe me there are lot of variations in the nomenclature, but all you need to remember is there is a major vein which runs back this is the front portion again back portion I hope from the last few slide you do remember the gross structure of the brain now. This is important to remember that if you want to create a stroke model from the previous slide when you expose the lateral surface of the brain maybe I have another picture not yet yeah. So, when you really expose this part of the brain you need to differentiate what is artery which comes like that this is the artery there and that is the vein very important that you target only that part of the artery which is going to cause ischemia or destroy the blood supply of that particular area of the brain all right. If by chance you are going to injured this vein then this entire brain is going to get infected and the rodent usually succumbs and again you lose the ah animal that you are dealing with. So, it is that vital it is to understand whether you are going to you are dealing you are creating a lesion in the artery or the vein.

So, it is important to understand that particular surface anatomy and understand how the middle cerebral artery ascends up like that and perpendicular to that is the vein. So, when you expose this area after the crinotomy you will look at artery specifically and create lesions or burn it only on the arterial branches and without damaging the venous system or if your neural experiments involves venous system then you should not touch the arterial system. So, the the simple reason being that it supplies pretty large part of the brain if you are usually dealing with the a truncal part of the or the proximal part of the artery and also it it it does involve larger area of the brain. So, it is more dangerous than the specific lesion that you would create using some toxic agents. If your model stroke model involves creating lesions you know specifically to the artery or to the vein one need to remember what you are dealing with and to understand those anatomy.

So, these these are some of the images to emphasize how the arterial you know tree is arranged within the rodent brain and this is a reason sometimes your rodent dies when you try to target some deeper structures. So, unfortunately not yet we have the I mean we do not have yet the image guidance in the rodent surgery. Almost 90 percent of the rodent experiments involves stereotactic coordinates and those coordinates of course, are planned to avoid these particular vessels. So, for example, you can see that you can target this lesion by choosing this particular coordinate there which goes avoiding these bigger vessels there, but there are many coordinates which will take this trajectory and you might hit these vessels which are deeper and that then the rat dies mainly because they will be bleeding in that particular region and it expands and expands and becomes a

large hematoma inside and the rodent dies.

So, of course, there is a way that you are going to master your trajectories involved in the targets. Best is to replicate exactly what the literature says try and replicate the same similar trajectory try and replicate the exact coordinates that you are dealing with because those coordinates are built upon the experience of various surgeries all right. So, this is the front portion the anterior most slice where you can see the arterial architecture. In the previous slide you saw that artery runs over the surface it does not end there it sends a perpendicular branches to enter the brain substance. These are the cortical branches this is the major vessel that goes on the surface and then it sends the arterial branches there.

So, you need to decide if you are doing a stroke model to tackle this or just this. So, then you need to know which is the area that particular branch is supplying. So, this is the very important structure which artery it called lenticulostriate branches which will supply the lentiform nucleus or the basal ganglia deeper nuclei. So, any damage to this is life threatening for the rodent. So, this is what you need to avoid when you are targeting the deeper nuclei for Parkinsonian models all right for that matter any models which involves the deeper targets.

So, briefly this is the blood supply of the spinal cord. So, of course, when it comes to the structure of the spinal cord you will have this is the anterior that is I would say ventral and dorsal because this is the lie of the rodent there. So, that is a head and then the body comes there and the forep and the hindpaw this is ventral that is dorsal. So, this is dorsal this is ventral that is very very important to remember because obviously, you will be able to access only the dorsal part of the spinal cord when you do rodent spinal surgeries. I mean this entire lecture series is mostly on to the cranium not on the spinal surgeries, but briefly we need to know because many of the neural experiments dealing with the brain will have some relation with the spinal cord. With that in mind I am just briefly introducing the spinal cord anatomy here where you are seeing the tract and fibers which are involving in the touch and proprioception vibrations sensor any sort of sensation from the limbs is carried by this particular fiber and somewhere there comes the motor tract which carries the motor fibers controlling the you know limb movements.

So, that is a sensory tract that is the motor tract there and this is how the supply it is called ventral spinal artery or anterior spinal artery I would say ventral spinal artery in rodent where it the branches enters the spinal cord substance there that is a radicular artery which along the roots. Roots are something which forms the peripheral nerves if you all remember from the spinal cord the peripheral nerve comes like that and then that forms a root. Radical radicular refers to the root of this peripheral nerves and those are the radicular artery. So, briefly about histopathology at the end of your experiment you

will be extracting the brain I mean most of the studies need to know where exactly the sensor were implanted you know which part of the brain it was implanted. So, as a proof not just for the publication even in order to interpret your own results you need to confirm that you have hit the right structure by extracting the brain and subjecting it to the histopathology.

So, extraction I will cover it in the surgical part, but when you take a slice this is a very good stain called mulligan stain where each and every layer is visible. And as I said there are multiple layers which has cerebral isocortex here and then there is a large hippocampal formation I mean this is gone to the posterior portion. The same similar section is going to be very different when you go anteriorly. And another atlas that I would strongly recommend and you will be using as the Paxinos and white atlas this is a stereotactic atlas which has series of coronal side slices which I will call retinal slices and axial slices which will be useful to identify the target, calculate the coordinates and go ahead and do the surgery that is the beauty of that atlas.

So, you will come across various structures in the you know this particular structure in the atlas. This is just to introduce as how it would look like in the slide all right. So, that is the deep cerebral nuclei will be this is these will be the hypothalamic area, thalamic region. So, initially we had seen it you know the sagitally when we see it you know after splitting the brain in the center whereas, this you are dividing it in this is called coronal section. This particular section is called sagittal section when is you know parallel to the midline permitted midline is coronal section, parallel to the floor is the axial section or perpendicular to the coronal plane is axial section.

This particular section is again coronal section. So, where you see this hypothalamus and thalamus and various other structures. So, it is very vital to have an understanding of the histopathology of the brain as well and not just the gross anatomy. So, with that I will conclude the neuroanatomy aspect of it and as I said it is very brief and each and every structure itself is a large series of like you know lecture. So, the idea is to introduce various anatomical terms and various anatomical structures. So, that you all can go and deal with it in detail with relation to the neural experiment that you are dealing with.

So, as I said you know live animal this is how it looks like. I mean if you are doing a crinotomy this is particular area is the crinotomy this is one of the experiment which I was doing where we have we had to implant a surface cortical sensor. We had to do the we needed to do the crinotomy both the sides bilateral crinotomy the sensor shape was like that which is a surface cortical sensor. I am sure Professor Hardik might have discussed in one of his lectures as to the how these cortical sensors developed and how it

will be implanted. And so, from here onwards I will deal with the neurosurgical aspect as to how we are going to do the neurosurgery in rodents. So, here you can see the scalp layer has been reflected and that is how the skull bone would look like and this is exactly the bregma would look like and that is how the lambda would look like.

So, there is a component of blood involved when whenever you do a rodent experiment in a live animal and that makes it little more difficult with because the blood clouds your vision and of course, many of the rodent experiment will require usage of microscope. If it is just a drill then you may not require a microscope. So, we will deal with those equipments in the future slides. So, hopefully you all will join the next lecture as well and we will deal with the rodent neurosurgery in detail in the next few lectures. Thank you.