Animal Physiology
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Lecture - 11

Welcome back to the NPTEL lectures on animal physiology. In the last class we started with the section 5 where we started with the nervous system. On the first lecture on the nervous system, we dealt with the structure of the neuron, the way action potential is being generated, and we talked about how it is getting transmitted. Because of the voltage gated potassium channels, voltage gated sodium channels, especially the voltage ((Refer Time: 00:46)), the fast activating voltage gated sodium channels and delayed rectifier potassium channel.

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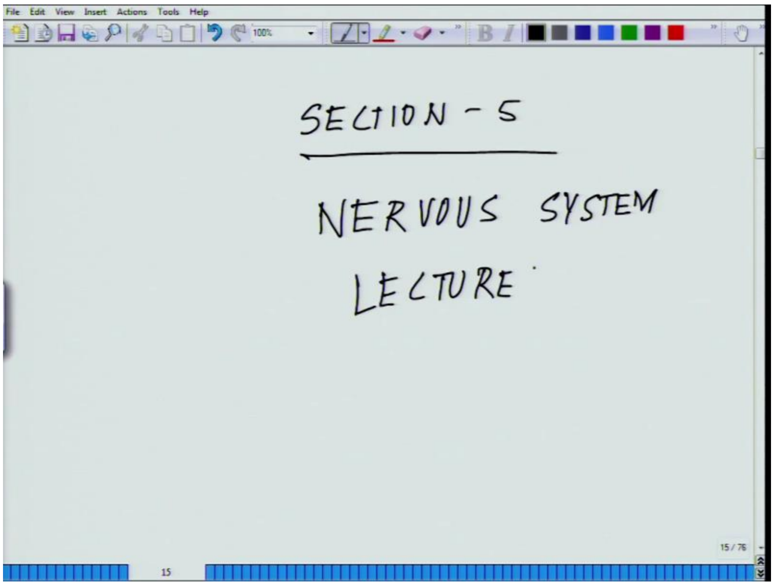

Today, I will just take a slight detour. Coming to section 5, sorry, section 5 is nervous system. This is lecture 2.

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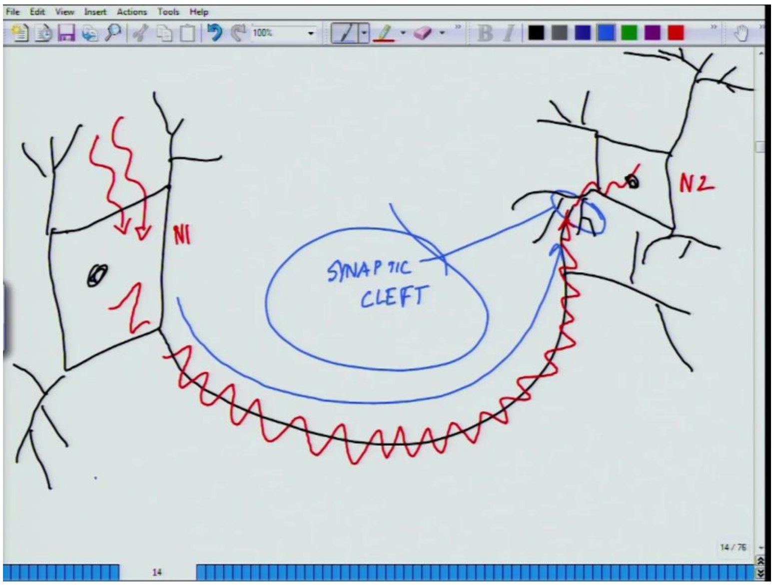

What will do today? If I go back. So, this is what I showed you. The signal comes like, if you see the signal is coming here, signal is coming here, and then this is getting processed, and the signal transmitted and it moves on to this next target, which will be a neuron 2 or neuron 3 or whatsoever. This is how the signal or the messages are being transmitted all along this path way, it moves like this. At this point, I will highlight one more thing.

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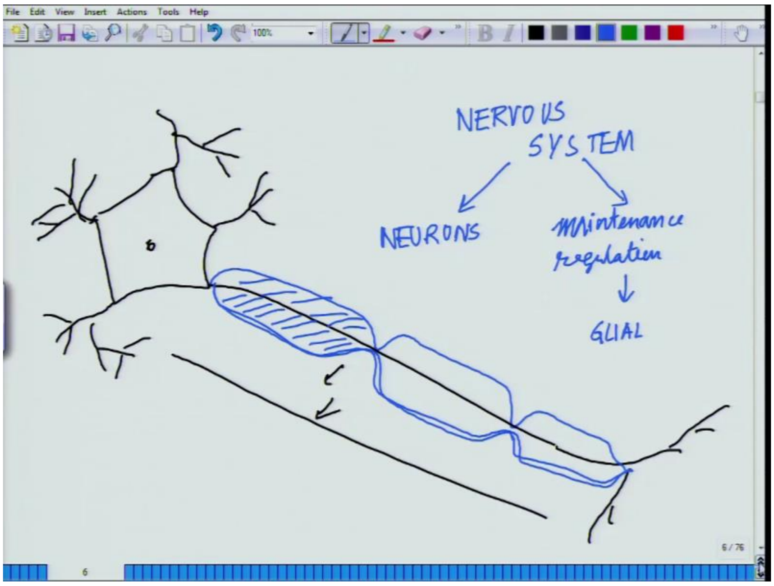

If you remember well, I was drawing the structure of the neuron I told you that there are some neurons, which are like this, if this is the terminal where, the message is being transmitted to the next neuron. This is where the message is being received by the dendrites. We talked about that some of the neurons have an insulated covering like this, which is called myeling sheet. If you go back to the lectures, let me see which one is the one where, I talked about the myeling sheets. Yeah, look at this. This is the myeling sheet what I was telling, what I am trying to tell you. Now, what is this myeling sheet? This is where it comes if I go to one lecture given or the other back.

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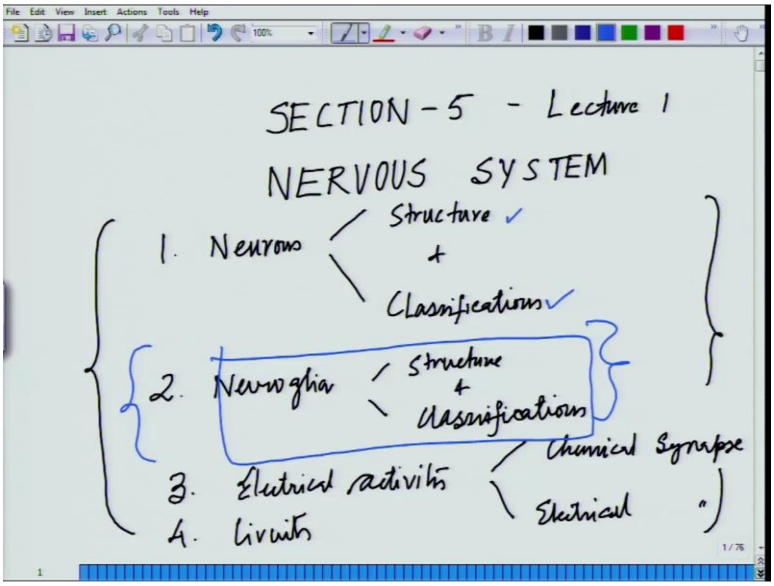

In the classification, we did not talk about as of now, about the neuroglia. So, what I will do before I come back to the nervous transmission- electrical impulse transmission and the synopsis, I will take a slight detour and I will talk about the neuroglia, that how this neuroglial cells are involved information of myeling sheets and all other things. Let us go through and move on to our current lecture, where will be talking about the glial cells.

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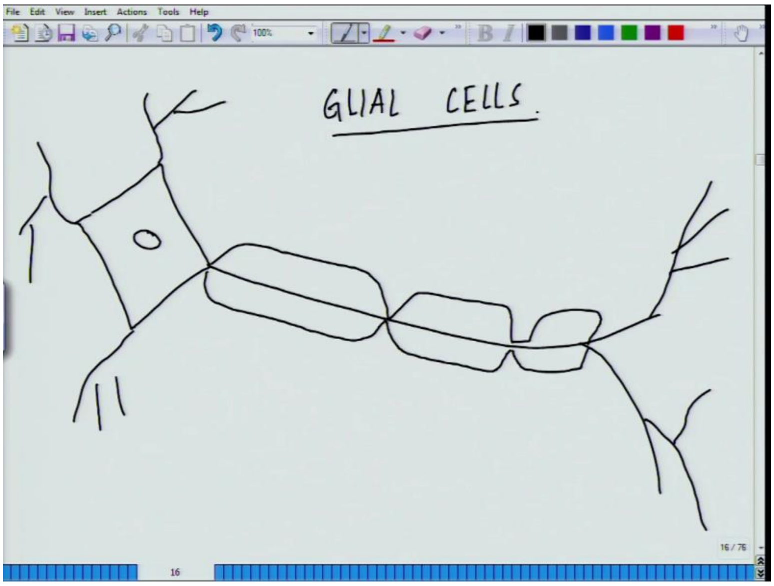

We will start with glial cells . In the nervous system, we started with there are two kinds of cells- the neurons and the glia. Neurons are of different types based on their position. They may be in the peripheral nervous system. They may be in the central nervous system. They may be in the specialized sense organs, whereas the glia 2 has a wide range of classification. They may be in the central nervous system. They may be in the peripheral nervous system. Based on their functions they have wide variations, what we will be going to talk about it.

But broadly speaking, till date, till 2013, when we are at this point, it is as of now, also believed that most of the communication, major electrical signal transfer is taken care by the neurons. In the glial cells are the once, which modulate those signals, but all by itself. Glial cells, as of now haven't been seen, and then could govern a circuit. They are modulators. It is just like say for example, there is a circuit you have certain capacitors which stores charges. You have resistors, which act as a current flow stopper; they create resistance against the current flow.

Likewise, the glial cells are the ones, or you have like heat sinks, which removes the excess heat from the IC chips, the same way the glial cells are very vital supporting structures, but do they involve in direct electrical communication, and do they involve in a information storage, is still a very debatable issue. There is enormous research taking place across the world. There are some well renowned glial biologist across the world, were extensively working to figure this out, that what are the final and may be, in the next fifty or hundred years, we will come to know lot more about the glial cells. But for now let us do the classification of the glial cells.

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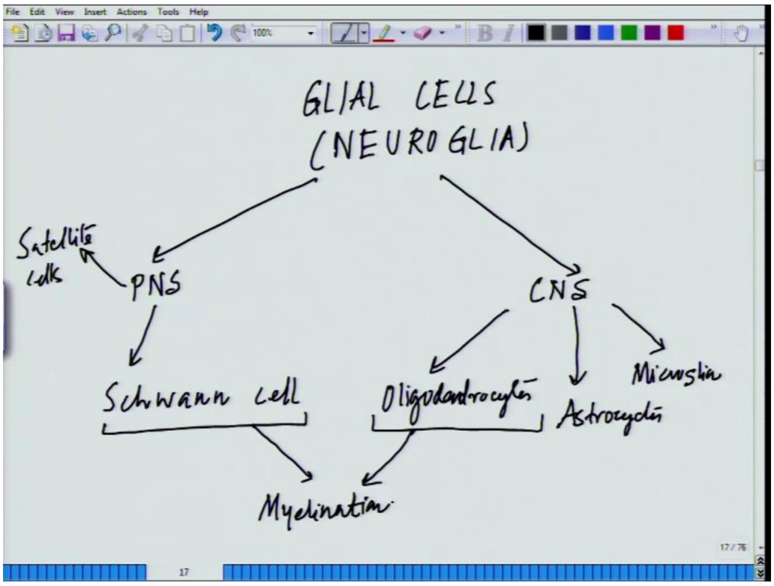

Let us put it like this. Glial cells, and sometimes this is also called neuroglia. Neuroglia is classified into two broad classification, the one which are present in the peripheral nervous system, just the same way as the neurons; the one which are present in central nervous system. Within the peripheral nervous system, you have schwann cells CH, and will come back to this point, just note down all the names here. The schwann cells and and you have the satellite cells. Within the central nervous system, you have oligodendrocytes, astrocytes and you have microglia. Now, what these individual cells have the role to play. We will take up these two cells first; the schwann cells and the oligodendrocytes. Both schwann cells and oligodendrocytes are involved in myelination.

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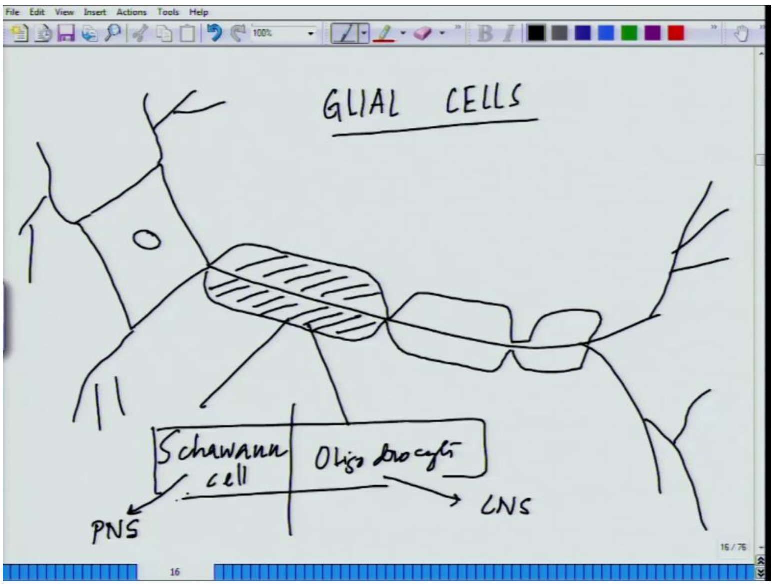

Coming back to the previous slide, this myelination what you see, what I am shading now. This myelination is done by, either it could be schwann cell or it could be an oligodendrocyte. So, if the neuron is present in the central nervous system it is by oligodendrocyte. If the neuron is present in the peripheral nervous system, then it is by schwann cells. Is the pattern of myelination the same? Let us see how exactly it is being taking care.

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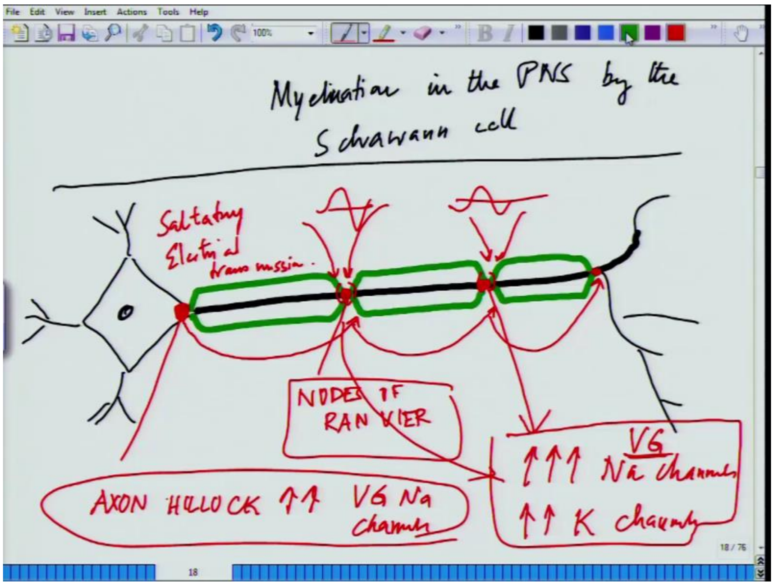

First of all, we will talk about myelination by schwann cells. In other word, we will be talking about myelination in the PNS by the schwann cell. How this looks like? Here is a neuron; a peripheral neuron present outside the central nervous system, dendritic arbor. Here, you have the myeling sheet like this. There is a slight gap here, the way I am drawing it. Let me redraw it. You see there is a slight gap, I am drawing and there is a reason for that, I will come to that.

This is how the basic architecture looks like. Other than this, you have these are called nodes of ran vier. These nodes of ran vier are the places where, maximum electrical signal is transmitted. In other words, when I was trying to draw that, in the previous slide, if you go back to the slide, like this, the transmission.

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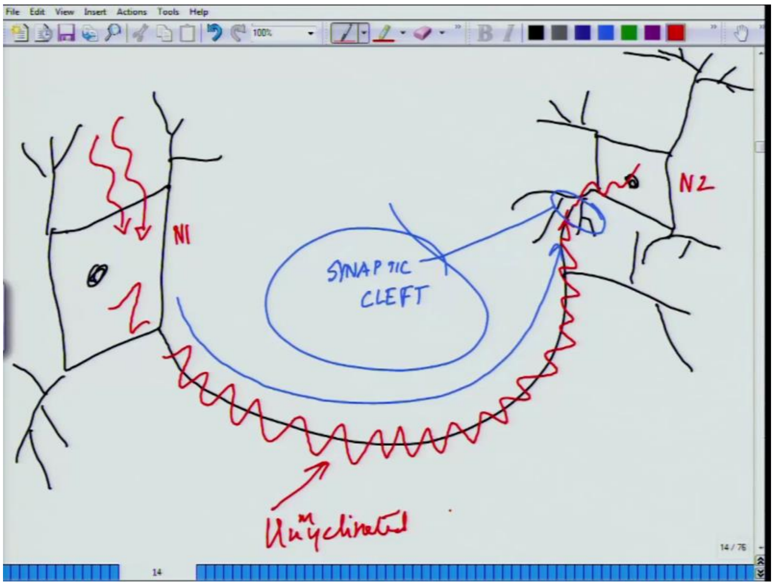

This transmission takes place, this is the kind of transmission in an unmyelinated neuron; there is no myelination. Whereas, in a myelinated neuron like this one or like this one, the signal hopes like this. This is called salutatory transmission of electrical signal and these are the zones, if I have to amplify these zones where, there is gap, these have very rich presence of voltage gated sodium channel.

I am just putting VG as the voltage gated. Voltage gated sodium channels, voltage gated potassium channels; they are very pronounced in these zones. This is where the major transmissions take place. This is the zone, which is called the axon hillock. This is another zone where you will see a very high density of voltage gated sodium channels. If you have some marker that you can locate the special distribution of sodium channels in a myelinated neuron, this is where you will see.

In most of the neurons in axon hillock, you will see a lot of sodium channels out here, out here as well as out here. This is called myelination resulting salutatory or hoping electrical transmission. Now, coming back, this called the nodes of ran vier. How it is structured? This green color structure, what you see, how it is being formed? How it forms, is very important, very interesting. It is something like this.

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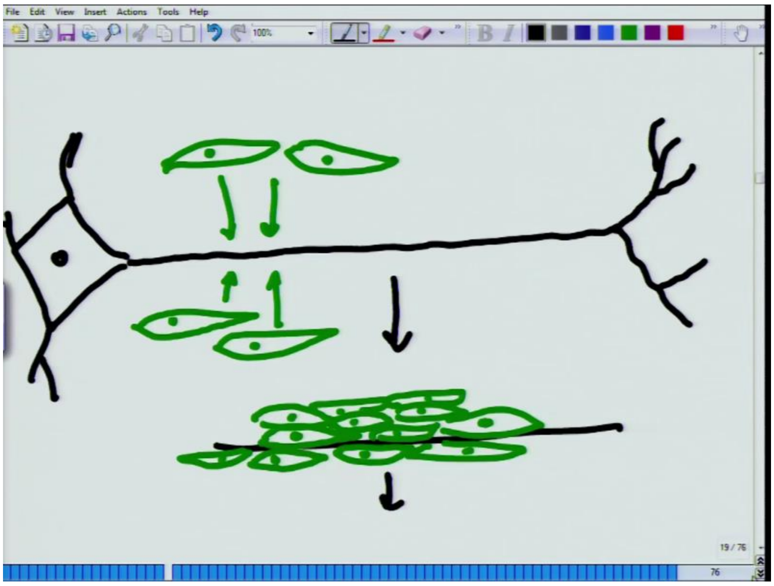

Imagine this is the axonal. What exactly happens in the beginning. Initially, a series of cells called schwann cells, which come close. These are the schwann cells. These are bipolar cells and these are the glial cells. They come close to the axonal body of the neuron. Once they come closer, next thing they do is, these cells come close and get on top of these axon, likewise. At this stage 3, these cells starts dividing on top of each other, likewise. In that process they form all the different gaps and everything. Then, this dividing cell mass, it is kind of what it does; it forms an encapsulation all around it. It goes underneath and it forms a complete cavity something like this.

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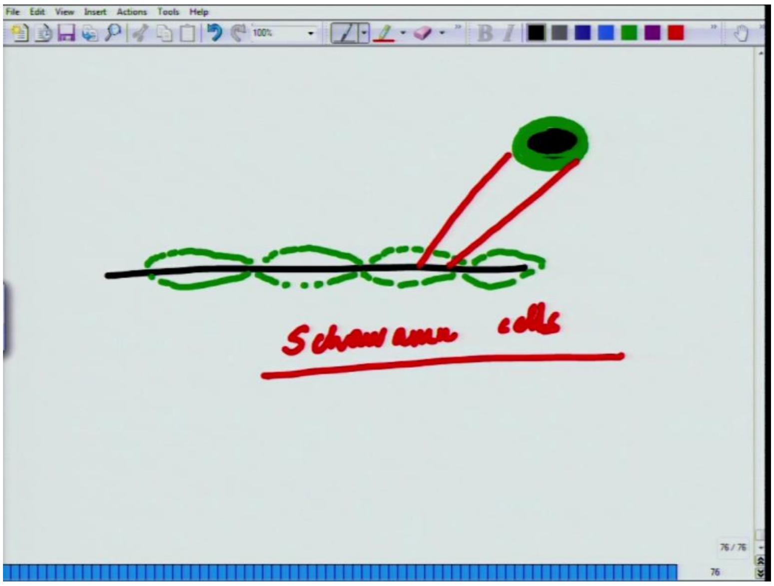

This is the part when, it forms something. These cells eventually starts secreting something called myelin protein and they start forming something like this. This is how the nodes of ran viers are formed. Eventually, what you see, if you look at this, imagine that this is an axon. If this is an axon which is travelling, say for example, this is one end the other end. This is what happens; it forms a wrapping like this. This is the wrapping. So, this is the glial cell, Glial cell mass which forms a wrapping. In other words, if I have to open this up, it looks more like that. These are the individual cells. If you look at this structure, there are pointed ends out here. Then it forms a wrapping on top of it, likewise.

This wrapping is this or this wrapping is something like this. This cover, if you see the cross section of the neuron, it will look like this; the cross section of the neuron will look like this. If you cut the cross section you will see the wrapping, that you can figure this out. The cross section looks something like this. This is the pen which is pointing out is the axon, and this is the wrapping, back you see this is the wrapping. If you draw the cross section, it will look like this. In the center you will see the axon. On the side this is, you will see the wrapping. This is how it looks like. But, is this the same thing which is being followed in the peripheral nervous system?

This is being done by the schwann cells. But, is this the same geometry followed by the oligodendrocytes, which is the second cell? In the case of oligodendrocytes, the formation of the myeling sheet is entirely different. It follows a very different protocol or a very different route modus operandi, while forming the myeling sheet. How it works is this. What I will do; I will make a central nervous system network of neurons and from there, I will try to explain this.

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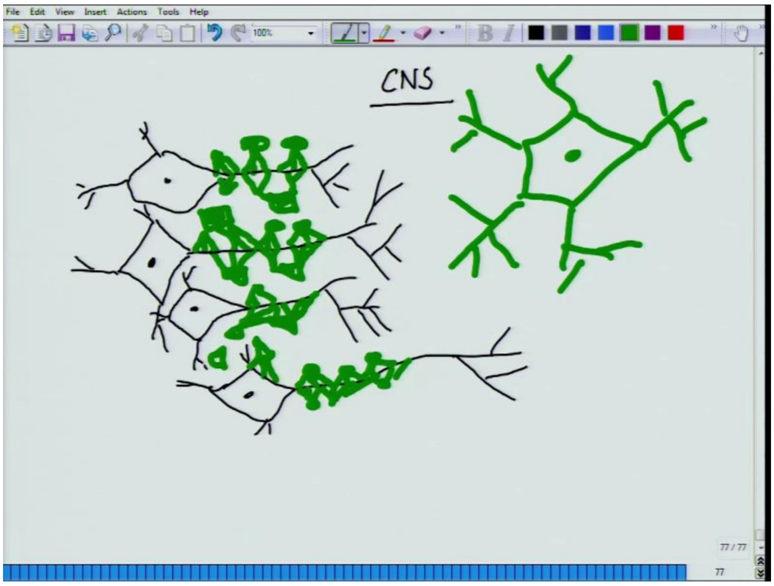

Imagine, this is the central nervous system network of multiple neurons, say for example, these are neurons like this, which is a very dense network of different kind of neurons, likewise. Imagine, just for the simplicity sake, I am keeping three neurons. May be, I will add few more out here. This is in central nervous system which is much more dense network. We will introduce the oligodendrocytes with a different color; here the oligodendrocytes. The oligodendrocytes here, what it does; oligodendrocytes are setting here, much smaller cells out here, likewise. So, these green spots are oligos. If I have a bigger picture for an oligo, oligos are something like this, really different kind of structure, likewise.

They have multiple Imagine a neuron without an axon, almost like that. It is a much more denser structure. This denser structure what it does; see it is making contact and on other side, may be oligos, which instead of wrapping the cell it forms contact likewise, like see, these are making contacts and these contacts actually creates the myeling sheet likewise. So, it is totally different. If you remember while I was trying to explain how the schwann cells are forming a coat; schwann cell coating on top of the axon. Here if you look at it, the cells are in close proximity with the cell body or the axon or something.

But they are all in close proximity. They are sending out their processes with these processes creates that insulated layer, on top of these axons and the cell body, the way you see. Now, the interesting question arises say for example, a cell.

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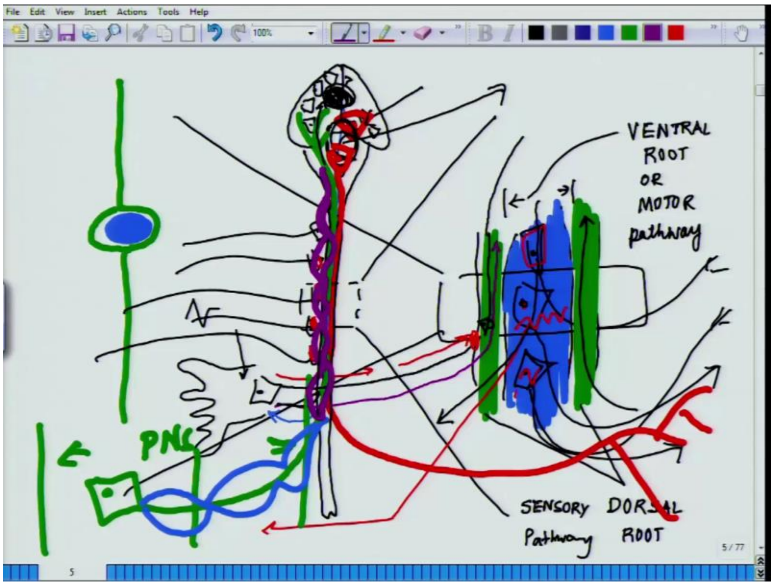

If I go back to one of the pictures which I tried to explain, into this picture. They are all neurons, which from here, say for example, from the peripheries, say for example, they are moving all the way from the peripheral, they move all the way into the spinal cord and they are process may end up into the brain.

What will happen to this neuron? Think of it. Will this neuron have? Because, see, try to understand the situation. This cell is setting in the peripheral nervous system. This is all up to this. This is all in the, sorry, this is all in the peripheral nervous system, whereas, it is entering into the central nervous system. Will it have a complete schwann cell myelination or will it have oligodendrocyte myelination? Interestingly, those cells, which have this kind of long process, is part of which, it is in peripheral nervous system, it is in their cell body, sitting in peripheral, or vice versa even.

Let us think of the reverse situation. Say for example, cell is sitting here or somewhere in the lower part, especially, the motor neurons. These motor neurons are what they are doing; they are coming out all the way, they are reaching to their targets out here. What will happen? Will this neuron have oligodendrocyte myelination or schwann cell myelination? Actually, these kinds of cells have dual myelination. What will happen up to this point; up to this point likewise, they will have the schwann cell myelination. They very moment, they enter into the spinal cord and the brain, they will have oligodendrocyte myelination.

In other word, they are very context dependent, where the cell is located. This is very important for you people to understand, that depending on the situation, even one cell could have two kind of myelination, based on its location and based on its geometry at specific point. This is exceptionally important for you people to understand and appreciate. This is what is happening in the CNS and in the myelination. So, I think that is what I wanted to highlight.

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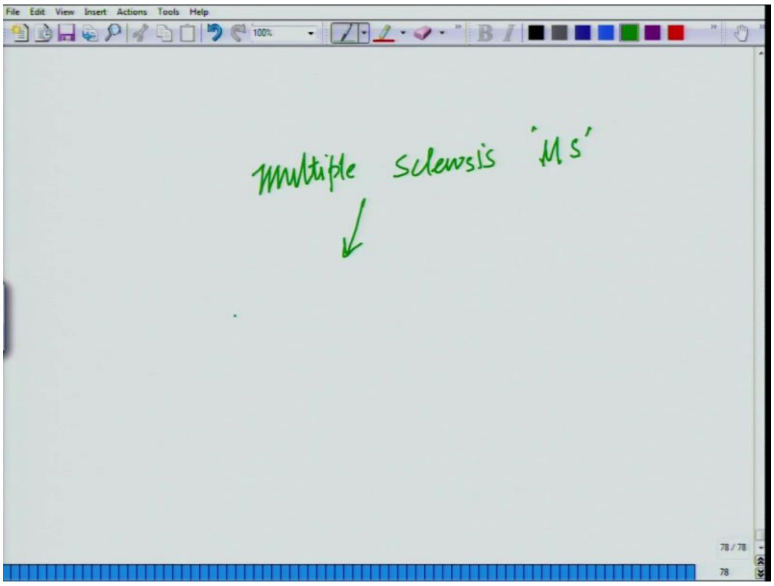

There are diseases like, how many of you heard of these like, multiple sclerosis- MS, sometimes this is being called. These are the diseases where, your insulated insulation layer of the neurons are being compromised. They die out for some x y z reason. These are the people who have enormous problem in there, you know. In other word, what is happening? There are two bear ways like this, like one and likewise, and there is a kind of short circuit between the two, because there is no insulation layer. So, these are the people, who suffers very miserably, who suffers from a multiple sclerosis. As of now, we do not have hardly any cure for these kinds of diseases. These are all diseases of the glial cells. Talking about, let us come back to the classification.

We have talked about two components, the oligodendrocyte from the central nervous system and the schwann cells from the peripheral nervous system. We talked about the geometry by which they are forming the myelination sheet.

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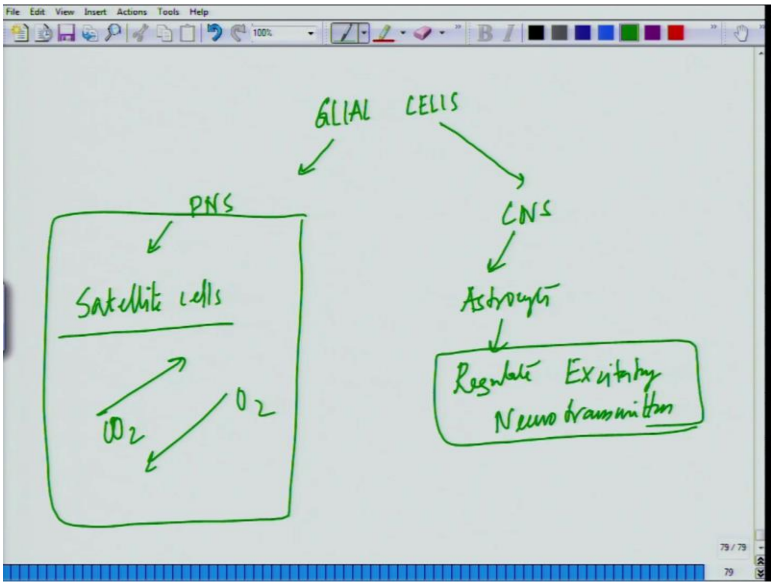

From here, let us move on to the other classification in that category which includes your glial cells. We talked about, within the PNS, we talked about satellites cells. What satellite cells does? The satellite cells are the ones, which ensure oxygen delivery and carbon dioxide removal. This one of the major tasks it does. Then, within the central nervous system, you have the astrocytes. Astrocytes have a wide role to play in, as more and more research is coming up, we are realizing. They regulate excitatory neurotransmitters like glutamate and I will come to that transmission, transmitter classification and all those things.

They regulate excitatory. In other word, let me tell you what that exactly means. Say for example, this is a neuron. This is the cell body, this is axon of the neuron and say, at this end it is transmitting signal to the next neuron. It does using a bunch of specific chemicals, which falls under the broad category of neurotransmitters. Neurotransmitters; from one neuron to another they are transmitting signals. These chemicals have to be regulated very tightly. Excess of those could lead to diseases like epilepsy or other mental disorders whereas, lesser quantity of those could lead to paralysis or something like Parkinson, and all those kind of things.

We will come in depth what that means. So, it has to be very tightly regulated and how it is being tightly regulated. It is being tightly regulated by a series of enzymes and the surrounding cells which are present. Io, if you see a network of neuron, it is something like this.

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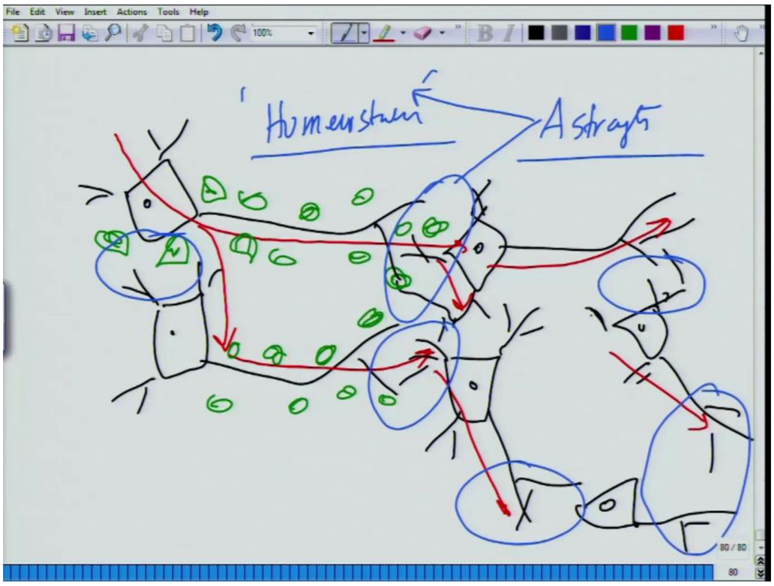

Let us draw a simple network. Here is a network forming. From here, neuron goes like this. They have the dendritic arbor. Even within this, if you look at the complexity of the situation. A signal may start from here, say for example, here it may move like this or it may move like this. It is the connectivity between the two, moves like this, they may come here or it may move like this or it may move like this. Whereas, the glial cells are all sitting in this surrounding. I am just putting them like this out here, out here, out here, out here. Already, we have talked about their role in myelination. These, say for example, this is a zone; this is a very hot zone where basically, all the information transfers are taking place, like here and like here. This is the zone where there is lot of chemicals involved. These chemicals have to be regulated.

One of the key components, which helps in regulating these different chemicals are astrocytes. They help in maintaining the homeostatus of the nervous system and the balance within the nervous system. This is very important and we are learning more and more about astrocyte, as the research is unfurling some of their most vital and beautiful roles in this area.

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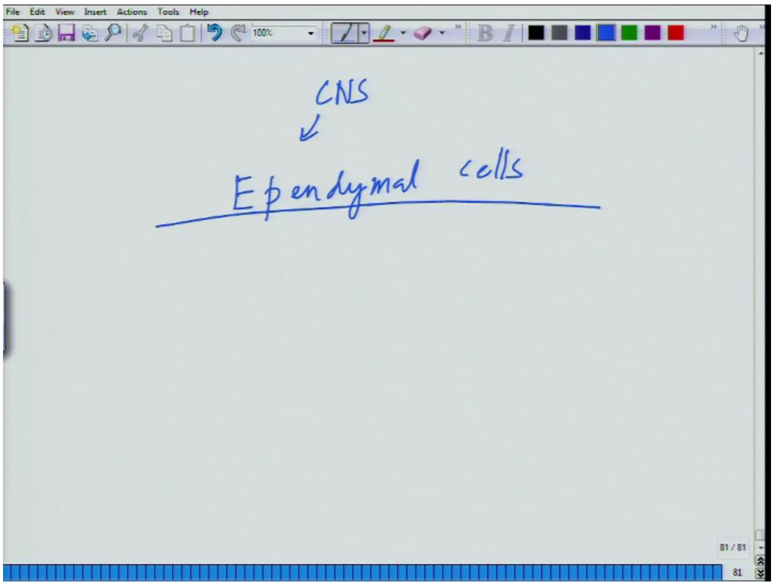

Then, we have another group of cells within the CNS, which are called ependymal cells. What are ependymal cells? These are the cells which lying, that mean, let me again take a slide detour for your understanding. What is so challenging about the central nervous system? In terms of its drug because, there is something called a blood brain barrier, which I may draw it, that will make you to realize.

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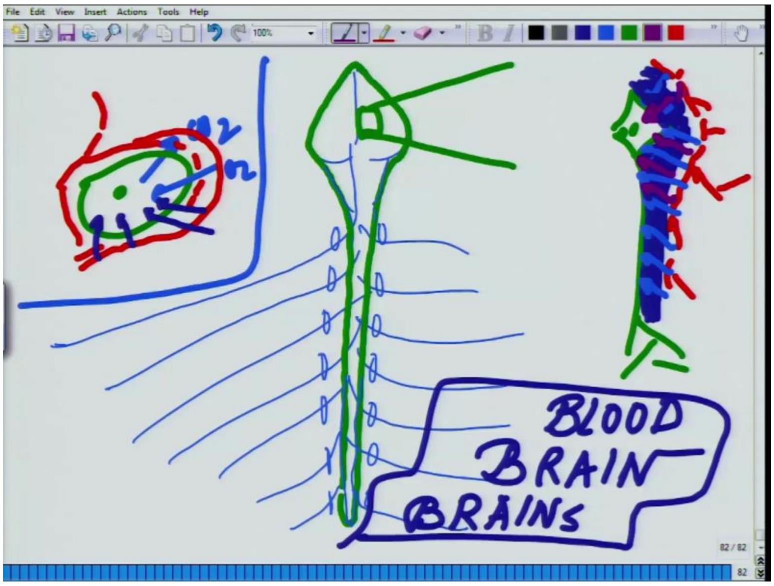

You remember in the first picture, I was drawing that, like, this is the brain. This is the brain stem and this is the spinal cord. These are the ganglions from where, central nervous system and peripheral nervous system, and all this things are happening. This is how the signals are; all the neurons are coming into the central nervous system and it coming out of the central nervous system, likewise and so and so forth.

Now, this part, what you see, this whole thing; this whole cellular structure or architecture, this whole, all the cells out here. They are not in direct contact with the blood vessels. All the blood vessels, which are coming close or coming on top of the brain, something like this. All the blood vessels, which are coming out into the vein or anything, between the brain and between the tissues out here, at the cellular level, if you have to understand. Because this is kind of drawing, say, at the cellular level what is happening? Imagine this is a neuron in the central nervous system.

Most of the time, what we believe is that if there is a cell like this, say for example, here is a cell somewhere else; the blood vessels and the capillaries are all over this, and the capillaries are involved in all kind of the Co2 intake, oxygen downloading and uploading; and we have already studied about this. But in the case of neuron the capillaries are not in the close proximity, likewise. No. this is not how the neuron architecture is, specially, in the central nervous system. What is there instead, is this? Say for example, this nervous system. There is a barrier. The capillaries are somewhere out here, not in direct contact with the neuron.

In between, there is a layer of another tissue, which is filled with a specific kind of fluid, likewise. All the capillaries are on the periphery, likewise, all throughout it. This fluidic barrier is called blood brain barrier. This is very important. This is important for 1001 reasons. The major reason is that, what we do? What a doctor does? You have to see the practical situation. A doctor injects a drug, either you take it orally. If you take it orally, it goes to your gastro intestinal tract. From there, it is being absorbed by the blood vessels. If it has to have a very fast action, the doctor does, they inject the drug directly into your blood vessels, or they inject the drug into substitunous, somewhere in your muscles and from there, the blood vessel picks up the drug.

This is how most of the drugs are being injected. End of the day, every drug, if it has to go at any part of your body, it has to be injected into, finally, it has to travel through the blood vessel, unless, it is some specific on the spot, some muscle or something. Other than that, it has to travel through all the blood vessels. The blood vessels, while delivering oxygen and taking away the carbon dioxide, ensure the drug is delivered at a specific spot. Of course, this is a problem. A drug cannot decide which a specific spot is. It is a kind of gets delivered, and that is why, we see the side effects because, a drug goes all your body.

Say for example, I have pain out here. Technically speaking, I would love all the drug should come here. But, how could you decide that? It is not possible because, it is travelling all over your body. It will keep on downloading and that is why, instead, a drug which could have actually acted with, say 5 microgram or 1 picogram, you need to take a pill of say, 50 milligram. Why because, rest of the 50, out of that 1 picogram or 1 microgram or 10 microgram or 100 microgram, rest of the drug is all over your body and they do some unusual things. That is what, we talk about, why we should avoid too much medication because, and you have other complications. Because, that drug it is not needed rest of the body it is needed by some specific spot.

There is no localized way of telling the drug- hey you know what. You have to go here because, this is where you need it. There is no way. This problem becomes even more complex, while we talk about the brain. Why is it so? Because, as of now, if you see this diagram, that will clarify your situation. In this diagram you see, so the drug is present here. Drug is being taken up by the cell, which is perfectly all right, but think of it. Now, this blood vessel is not in direct contact with this green cell. What will happen whether in situation like this? Think of it.

The drug needs a molecule which ensures, that it reaches the other side, something like a fairy boat, likewise. That is why, there are very few drugs for central nervous system because, the blood brain barrier ensures, that your brain or the spinal cord of the central nervous system is not exposed to other necessary molecules. It is very tightly regulated. It has to be absolutely ensured on that thing. Ensuring is being done by this barrier. This barrier is made of, why I take a detour to blood brain barrier is, that I talked about the ependymal cells. These ependymal cells are forming the lining of the blood brain barrier, apart from other cells; there are endothinal cells and all those things, on the blood side of it. These are formed by the ependymal cells.

That is why, I have to take all the detour, but it is good that I discuss this blood brain barrier with you people, that will help you to realize why a drug because, what happens along this, if you see this diagram. What happens at this zone? There are specific boats; pretty much like molecular boats, which carries the specific molecules. There are glucose carriers. There are, of course, the gases moves through this by the simple diffusion. But there are further for glucose, for fructose, for XYZ molecules. There are specific carriers which helps them to travel to the other end of the brain. Your only other option left is that, if you want to directly deliver, then you have to directly inject something; directly to the neuron or that neuronal mass. There is no other way, a neuron can reach, sorry a drug can reach directly to the neurons, till it crosses the blood brain barrier. So, that is the role of the ependymal cells. Now, as I am progressing through, you must be realizing that how important these glial cells are.

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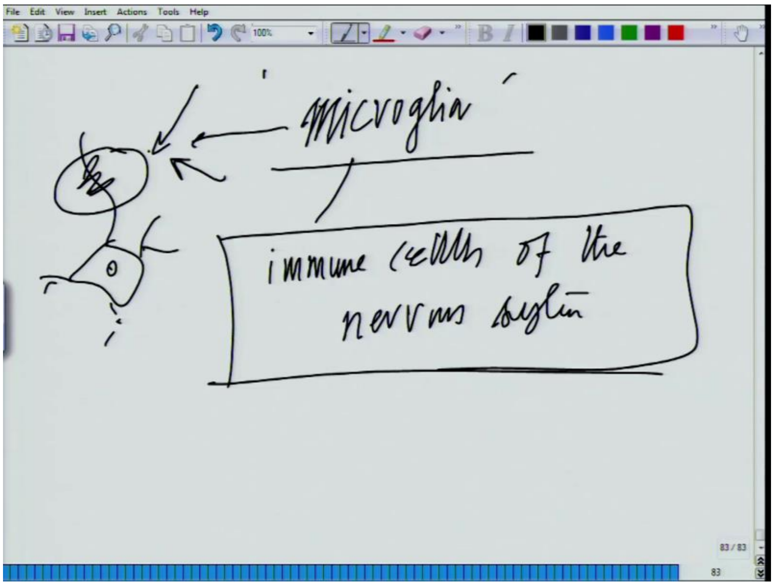

One more in that same line, we have not talked about this. Let me get back to that one, is the microglia. These are some specialized cells and there is lot of controversies. Whether, we should call them; whether, it should be part of the nervous system or they should be part of the immune system, because these are the cells, which can be termed as the immune cells of the nervous system. What they do is whenever, there is a scar or something at some point, say, some point in the circuit, there is a scar or something, see this is the scar. These microglia rushes to that site and ensures to clean it out. It is just like, on the road there is some form of an accident or something. As soon as there is an accident, very soon there are convise, which come, which ensures that clean up all the stuff from there so that the traffic can move on.

It is exactly what microglia does. It is a cell; series of cells, which comes there and clean up all the chemical debris. They eat away everything and ensure, that the traffic is continued and at times, they even form very specialized structure out there, and will come to that in spinal cord injury and all the things. In order to summarize, what we talked about the neuroglia; we talked about neuroglia could be on two sites; in the PNS as well as in the CNS. Within the PNS, they could be satellite cells, which are regulating carbon dioxide and oxygen. There are schwann cells which are forming the myelination sheet. On the CNS side of the oligals, which ensures the myelination process in a totally different fashion, as compared to the schwann cells

You have the astrocytes which regulates neurotransmitters and few and several other things, it helps in (( )) of the nervous system, and they are in huge number. Then, you have microglia, which are the immune cells of the nervous system. Then, you have the ependymal cells, which are forming the lining of the blood brain barrier. So, these are some of the very important aspects of the glial cells. One more thing, glial cells are the dividing cells of the nervous system.

Neurons do not divide, of course, there are some controversies here. You will come back to that, while we are talking out some of the diseases. Do all neurons do not divide or there are some neurons, which has the ability to divide? But, will come to this because, there are some specific type species, where a group of brain neurons do divide, but they are very specialized case studies (( )) and few other biological systems, where they divide and will come back to those, while talking about the different diseases and deviation from what we see normally. There are deviations indeed.

Whenever you hear about brain tumor or something, it is basically, uncontrolled division or brain cancer or something; it is basically, uncontrolled division of the glial cells. Because, the neurons do not divide. It is the unregulated, unchecked division of the glial cells, which leads to any form of brain cancer, brain tumor or any other those kind of diseases, where the cell division control, or the check points are being compromised and we land up with troubles. From here, I will come back. So, this was the detour I wanted to take, before I move on to the next slide, where will be talking about the synaptic activity.

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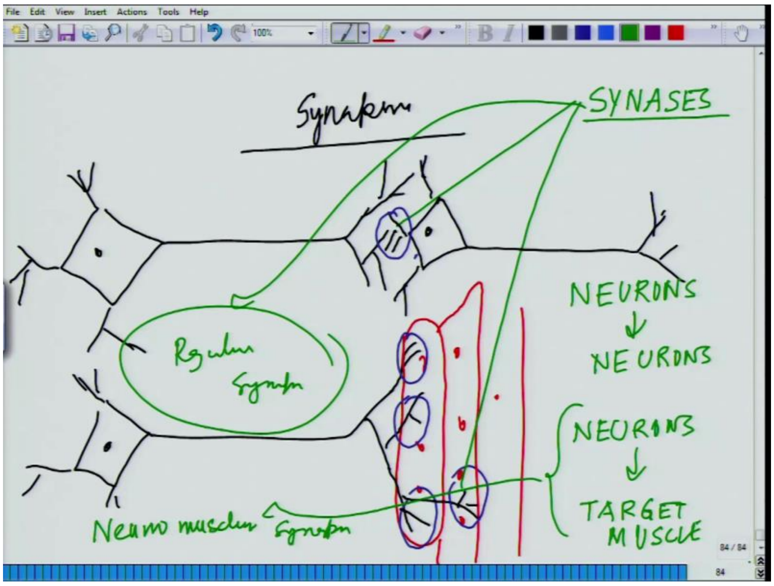

What is the synapse? This is where we are going to concentrate now. If this is a neuron and this is the axonal end, and this is the second neuron out here, sitting here or it could be any other target tissue. It could be a muscle. So, rest of all that also; neuron and here is the muscle. This junction, what you see out here; this junction; these junctions, where the information are been transmitted or this junction, any other such situation; these are called synapses. This could be between neurons to neurons, or neuron to the target tissue; it could be muscle. This contact is called neuromuscular junction or neuromuscular synapse. These are called normal regular synapse. There is no such term called regular synapse, but these are just the synapse.

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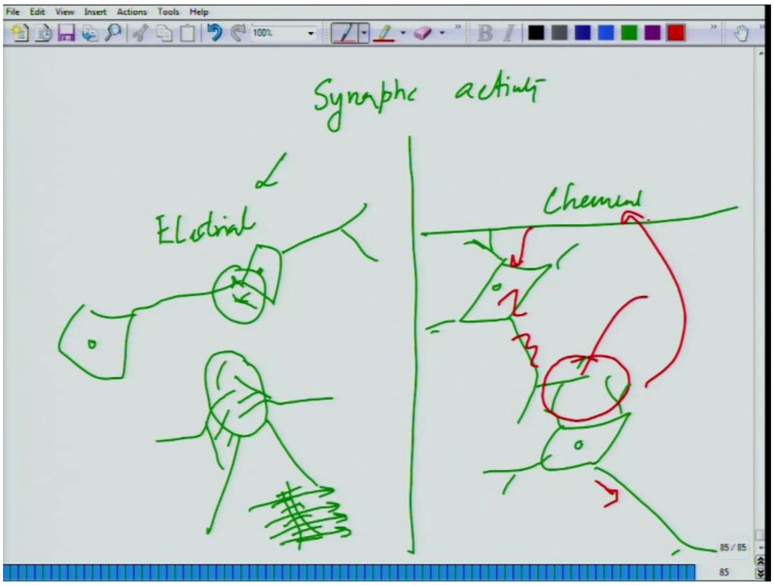

Synaptic activity could be electrical as well as chemical. What we meant by electrical and chemical. Electrical synapses are very rare and very few in the body. Electrical synapses means, say for example, here is the contact point. Between the axon terminal and dendritic part, if I amplify this, this is the axon terminal out here. These are the receiving dendrites out here. This is where the synapse is forming. Between these, if I further flow it up, between two processes, there are gap junctional connection; the electrical connection, which allows the flow of information. But such information flow is a very local information flow, something what you see in cardiac cell. It is in a very enclosed structure, where all the cells are transmitting. But, when we talk about a nervous system which has huge network within our body, these electrical synapses are not very successful.

They are very few and located in very specific areas of the brain, from the basket cells, some of the perking cells. They have those kinds of synapses, but not very many. What is more pronounced is the chemical synapses. What is a chemical synapse? It is something like this. There is a neuron and it receives, and here is another second neuron, which is sitting here, moving on. So, here is a signal coming and moving. This is the zone where this neuron transmits an electrical signal to this neuron, and it does so using specific set of chemicals called neurotransmitters. So, this is what a chemical synapse is all about and will talk more about the chemical synapse in the next lecture. So, I am closing on this lecture at this point.

We will talk about the dimensions of the chemical synapses and what are the neurotransmitter molecules, which are involved in it? How those are being regulated by the surrounding glial cells and all other things? What are enzymes, which are involved in the whole process and how the informations are being collected, converge or diverge and all those things? We are going to talk about those.

Thanks a lot. Thanks for your (( )).