Bioelectricity
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Lecture - 23

Welcome back to the lecture series on Bioelectricity. So, this will be twenty third lecture. So in the last class, we talked about long-term potentiation one of the models of the memory and further I very briefly highlighted the situation of Alzheimer or Parkinson amyotrophic lateral silicosis and all other neuro degenerated disorders. And we made a comparison that what happens in the case of Alzheimer, where you have the loss of memory the loss of identity. Whereas, in the case of Parkinson, we talked about there is a loss of motor coordination or the motor activities. So, there is another form of memory which I highlighted in the last class, but I have not gone in depth that is called long term depression.

So, in the case of long-term potentiation, what happens, there is a very high frequency stimulus, very very high frequency stimulus, and that high frequency stimulus leads to a change in the network properties, so that a network remain it gets potentiated and remains active for a long period of time. And during which there is permanent, it is believed that there are permanent changes within the system. But apart from it, there are situations where you do not get very high frequency stimulus. I was trying to tell you certain situations like you know go walking, you are learning certain things in a much more you know day to day setting which is you are not very intense into it. It will learn eventually. So, this is something like you are getting low frequency stimulus. You are not really very like very much into it or there are situations like you know fear where you see a very small impulse for a very limited period of time, but that is good enough to resulting in a fear psychosis in your brain or some kind of anxiety.

So, these things fall under the second model which is called a long-term depression – LTD. And it was around nineteen eighties a Japanese called Eto was involved was pioneer in starting the work on long term depression, and eventually the resembled people who picked up this model one of them is terrace (( )). And in Indian context, there is Sumantra Chatterjee in NCBS, these are people who have explored it further with long term depression. So, essentially if you have to compare that what exactly happened in

long term depression with respect to long-term potentiation. So, I will be giving you a handout at the end of the course, where you will have a comparative picture of both long term depression and long-term potentiation, but just for your understanding sake, I will kind of draw the situation which will give you an idea what essential is happening.

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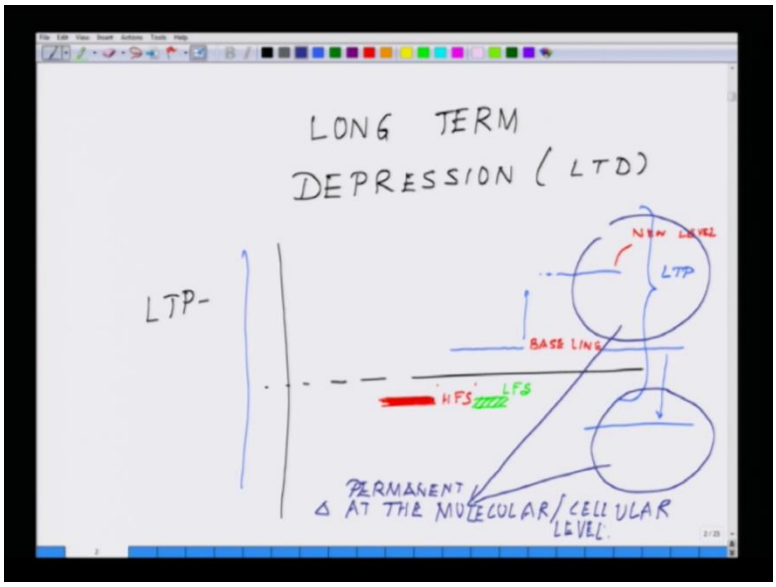

So, coming back, so now you are into lecture twenty third; in twenty third, we are talking about the long term depression or LTD. So, before we talked about long term depression let us see what happened in long-term potentiation - LTP. In the long-term potentiation, there is very say for example, something like this. So, there is very high frequency stimulus and because of the very high frequency stimulus, some point or other, the neural activity of a network if this is the excitable y-axis is talking about the excitability from this baseline value, because of the high frequency stimulus is shifted and it reaches here. This is what is happening in long-term potentiation – LTP. And this is your high frequency stimulus – HFS, and this is the baseline excitation. And after a point, this is the new level attained when both the systems are active. This is how you can show it graphically, I will be giving you the handout which will explain it further.

But in the case of long-term depression, what is happening is slightly different. In the case of long-term depression, what you give is essentially a something like a low frequency stimulus. In the case of long-term depression, you have low frequency stimulation. So, basically, a circuit or a network is receiving a smaller smaller smaller

smaller inputs that is not receiving a huge input as I was kind of highlighting in the case of long-term potentiation. And these smaller units adds up in such a way that the network becomes active at a much more lesser threshold. Say for example, if this is the threshold what the network functions for example, this this is the threshold the baseline threshold. This network will start functioning at a lower threshold than this; it is going to come down.

So, essentially what does that mean; that means, that the circuit becomes active at a very smaller threshold. Unlike a situation, say for example, let us take a practical situation, you are riding a bicycle you hardly need to recall anything you know how to ride a bicycle once you have learnt it. Or you are walking on the street, you do not have to decide that you are going to put which leg first leg and which leg second. So, this is essentially is a situation of long term depression, where the circuits involved in this kind of motor coordination gets activated with a very smaller threshold which you do not even appreciate or understand at that point. That you are actually being a memory recall, but it is fairly inbuilt almost at a very lesser threshold same thing happens in a fear psychosis

Say for example, you have seen a kind of a snake at some point and fraction of a moment, but that fear has activated a circuit, which gets or kind of you know modulated a circuit which gets activated at a very lower threshold of a electrical activity that is exactly is a long term depression. So, there are areas in the brain like medulla which is involved in the fear psychosis that follows the long term depression model is believed that is following a long term depression model.

Similarly, all your motor activity cerebellum and further down, they follow long term depression. It is interesting that the hippocampus too follow both long term depression as well as long term potentiation. But all these different electrical phenomenon what we are discussing are they really happening inside the brain or not, is a different question. Most of these studies have been done out inside the system where in a controlled slice or a network of neurons this phenomenon has been observed.

So, in summary, if you have to say the difference between long potentiation and long term depression is that long term potentiation is a process where there is a high frequency stimulus and that high frequency stimulus leads to make that particular network hyperactive and the output of that network is higher than the baseline. Whereas,

in the case of a long term depression, what is happening is that from the baseline this also becomes hyperactive, but at a much more lesser threshold. It does not need any further I mean at a much more lesser threshold, it becomes more active; just fraction of a moment it will become active.

So, these are the two key models which ensures our, at least it is believed are the major model for memory acquisition. And during this process there are certain permanent changes which are taking place out here, certain permanent changes taking place here, certain permanent changes taking place here, and these changes are taking place at the molecular level or at the cellular level, changes at the molecular slash cellular level. Essentially these changes ensure that our information gets stored.

Now, from here what I will do I will move on to the basic waves which are generated by the brain and their significance. So, in order to just save it, now by this time we have realized, it is a dense network of neurons and there are continuously involved in transferring information or consolidating information or storing information. So, your brain remains electrically active throughout your life. So, during this phase, depending on what is your physiological status at specific time of the day or night, brain generates a series of waves alpha waves, beta waves likewise. And these waves could be detected by placing electrodes on top of your head by which you could have multiple electrodes you know you could have sixty four electrodes sets all over your brain and based on those frequencies one can figure out that what activity you are doing or how much your brain is active and likewise. And this whole thing falls under electroencephalogram.

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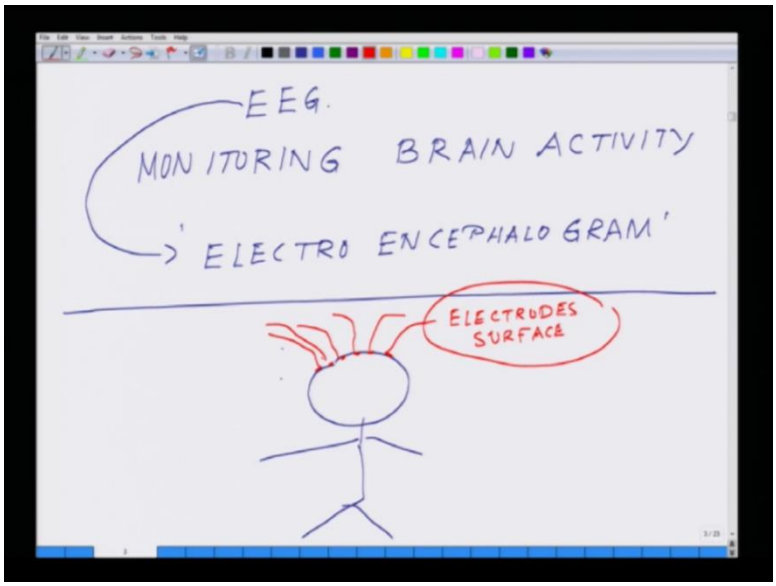

So, let us move on to electroencephalogram – EEG, for monitoring brain activity, stands for electroencephalogram. Now what essentially happens, so for example, what you do is that you put place different electrodes like this on the head. These are just surface electrodes and what you are essentially measuring here, you are measuring, these are the electrodes, which are placed, you are measuring the field potential. So, at one point, there are thousand thousands of neurons and the summation of the electrical activity that is what we are measuring, it is a very gross measurement, one you cannot figure out what is exactly happening at individuals cellular level or at individual synapse. What you are essentially getting is a pool of synapse arising from thousands of neurons at one point. The total summation of that and how that influences, how that could tell you or how you could picture this treat of the brain based on those waves all over the brain.

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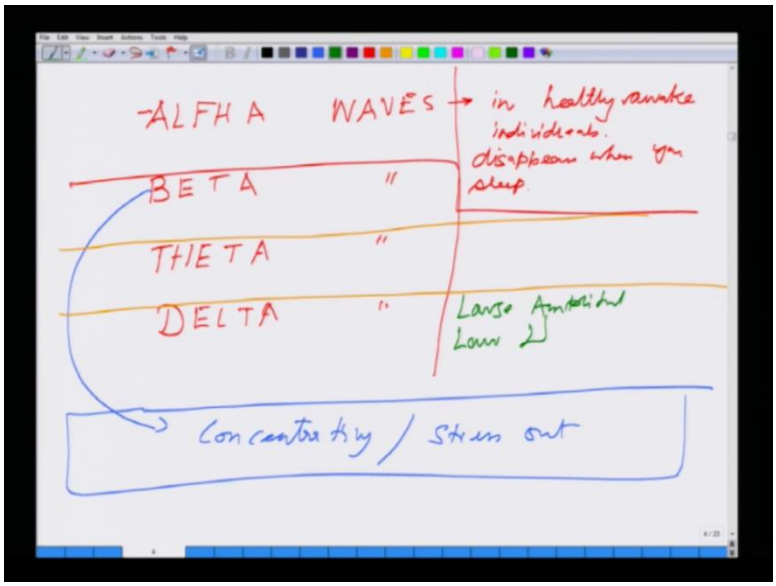

What are the different waves, which are involved in the brain. You have alpha waves, you have beta waves, I will come to the details of all these. Alpha waves, you have beta waves, you have theta waves then you have delta waves. What these are? So if you look at alpha waves, alpha waves occur in the brain of a healthy awake individual. Whereas, very interesting these alpha waves disappears with when you are sleeping. So, let me just and it disappears when you sleep; whereas, the beta waves are typical individuals who are either concentrating on task or they are in a stress situation. So, just I will use another color.

So, your say for example, you are concentrating or stressed out, you see the beta waves. Then you have the theta waves. The theta waves may appear transiently during sleep in normal adult but are often observed in children and intensely frustrated individuals. This is a very interesting kind of a situation. Mostly it is seen in children or when a person is very very frustrated, you see the theta waves. Whereas, you have delta waves these delta waves are very large amplitude low frequency waves, and there are normally seen during deep sleep of an individual's of all ages.

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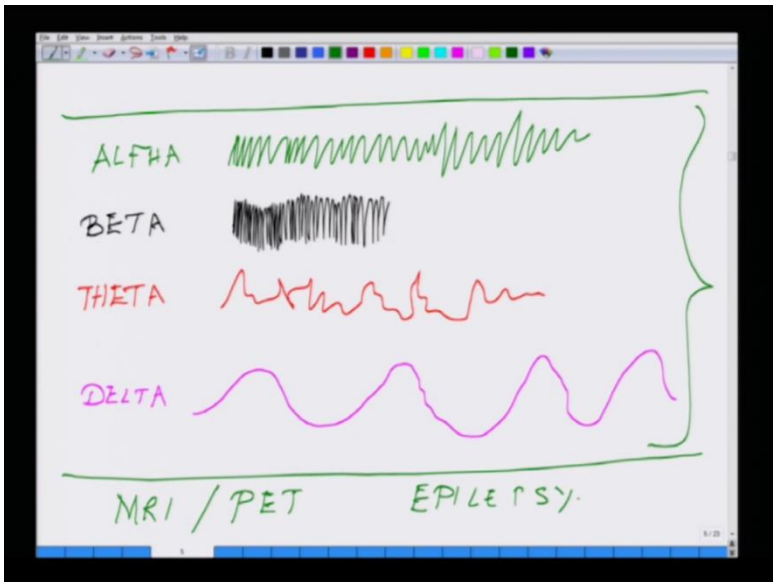

So, if you realize these are the ones, which are something like if I had to just draw a comparative picture of the different waves. So, there will be something like alpha will be when a person is awake you know this is what you see as an alpha. What is the beta is even much more like, this is the intense situation, when you are concentrating or you are very very stressed out or something. This is the kind of beta waves which are coming. Then you have the theta waves, which is person is frustrated or you see in the children likewise and then you have the delta waves which are much more. So, these are the delta, these are theta, this is beta and this is alpha. So, these are the four different wave patterns which are being seen in the brain. So, these are the different four patterns which ensures what state the brain is and however is kind of you know altering depending on the state of the individual.

So, based on this several physiological tests are being done is the nature of this person, how intense this person is and the doctors make whole lot of observations on these kind of individuals at which wave are prevalent on which individual. They also highlight a lot of physiological disorders, say for example, in the case of epilepsy, you see a huge change in all these things. In the case of epilepsy, where there is a basically a seizure is taking place, you see there is a absolute asynchronous behavior among all these different waves. And this is something which those who are expert in reading these waves can figure out that this person suffers is has the tendency to suffer from epilepsy or the wave

pattern completely changes is over a period at that particular point of seizure. Just before that started kind of you know it is balancing.

So, we started with in the class about when I talked to you about that will be talking about how to measure electrical signal at the single cell level. We talked about how we studied the different kind of channels, then we talked about how we could pattern the neurons on top of microelectrode arrays, how we could use sharp electrodes to make the measurements. Here we are talking about electroencephalogram, which is on a live animal, you are making this field potential recordings. So, all these different kind of recordings had their advantages and disadvantages. When you do a field potential kind of measurements like alpha, beta, theta, delta waves, you get the gross picture of the brain how it is functioning; and without any technique, it is fairly straightforward.

Of course, these techniques of the waves are being being further assisted by the MRI and the positron emission tomography, and magnetic resonance in the gene; these two other techniques very profoundly powerful technique helps in really picturing the brain what essentially happening inside the brain at a specific point of time. But they would not tell you anything at what is happening at the cellular level. Whereas, if you come down at the cellular level, you can understand the phenomenon at a single cell level or maybe a group of cell, but you have no idea about how the population is behaving at that point of time.

Then you can further go down, you can make circuits of one neuron, two neuron, four neurons, six neurons likewise and you can understand the small network behavior. But what is the take home message of this whole process is, this whole process are slowly diverging or disclosing the secret stories of our own self. Why we are like this, why are behavior is like this, why certain people have sleep related disorders, why certain people have hallucinations, why certain people cannot concentrate at certain things whereas others can concentrate, why certain people gets stressed out on the other end, why certain people does not get stressed out. There are series of such things, which are highlighted by these different techniques, which eventually leads us to understand our final frontier - the brain.

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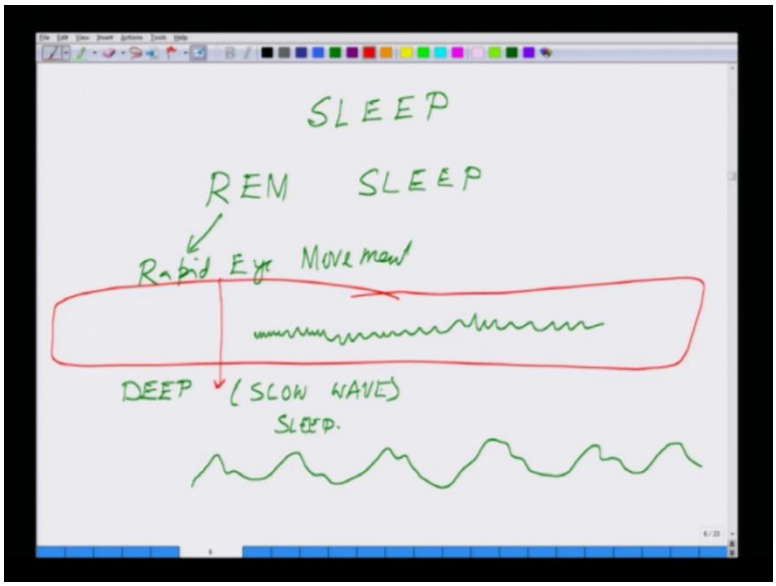

Now I will give you a very brief very very brief outline about some of the sleep rhythms what is there and move on from there. So, see this is a very very interesting phenomenon and sleep related disorders. So,in the deep sleep basically, so there are different kinds of there is something called a rem sleep; and rem sleep, because this is called rapid eye moment sleep, this is where you see all your dreams. And this rapid eye moment it is something like this then you go to the deep or slow wave sleep, and that this slow wave sleep is the time when the waves are much more, so whatsoever dreams you see you see pretty much out here and this is all electroencephalogram recordings.

And essentially you will observe that deep basically as you are kind of initial phase of the sleep which is basically the rem sleep and then there is a transition phase between the rem and the deep sleep. So, from the rem to the deep, there is a small transition phase and then you realize that most of the deep sleep in an average individual takes place between 10 am to that midnight period. It is very interesting this is where maximum deep or slow waves functions and after that again the rapid eye moment and likewise and so on and so forth.

So, one of challenges what we are going to face is we will be needing more and more tools which could couple with the existing tools of MRI, pet, electroencephalogram, in order to understand or get a much more holistic picture of the brain, what exactly is happening. And the more and more research is going on in field of imaging especially

the brain imaging to understand some of this very deep rooted phenomenon of consciousness, learning, memory, sleep, dream and the relevant disorders. As we will be moving through, we will be talking about the man machine interface on this one more part we will be dealing with there we will see how we really could you know how sedation and how could we control the brain activity. Of course, not in the human level, but at least definitely at the levels of the monkeys, I will be giving you certain handout and discussing that with you. Now, I will just take a small ditto with this background, I will close in here with this part of the sleep and I will come back to one of the part that we talked about about the spinal cord.

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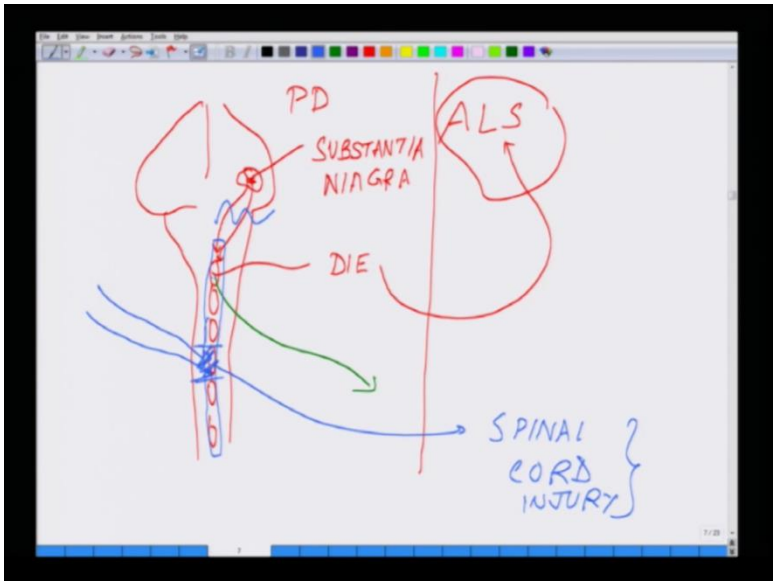

So, yesterday I talked about alzhiemers, I talked about parkinson disease, but what I have not talked about is the amyotrophic lateral scleroses - ALS. In the case of ALS, what happens is that. So, I told in the case of PDor the parkinson disease say it is substantia niagra within the brain which is kind of getting affected. So, there is region called substantia niagra. So, these neurons fail to send electrical stimulus. Whereas in the case of ALS what happens, so these neurons sends the message to the lower motor neurons which are sitting in the ventral horns. These motor neurons when they start to die that neuro degenerative disorder is called amyotrophic lateral sclerosis. So, essentially your substantia niagara is all fine.

So, the electrical stimulus is coming from here, but from here, what it is suppose to relieve the electrical information's to the target tissue is not taking place. So, this is the situation in amyotrophic later sclerosis. And further there are situations when because of accidents or because of certain some kind of mess up, basically these neurons started to die or dies out, certain part of the circuit you know kind of get damaged, which is essentially spinal cord injury. This is which mostly happens during you know automobile accident or some other very hasty situation.

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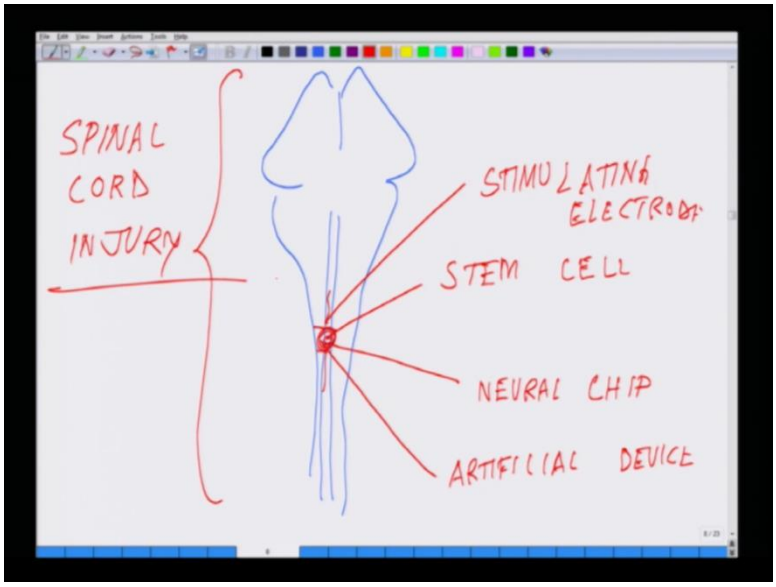

So, in the case of spinal cord injury, there are several routes; and in one of the possibilities of future will be somewhere or rather, if you could regenerate those neurons which are kind of damaged at a specific part. You implant the stem cells and they somehow rather get incorporated or you can put a neural chip out here something like, which will take care of it or you could have an artificial device which will rebuild the connectivity between. So, it almost like a fuse. A fuse goes off, then this connectivity has to be reestablished or you follow a stem cell therapy or somewhere rather you do a put some stimulating electrodes, which will help to regain or maintain some of the activities. So, there are several techniques at the level of neuro prosthesis. So, this is all regarding spinal cord injury situation. So, there are several techniques by which people are trying to counter the spinal cord injury patients.

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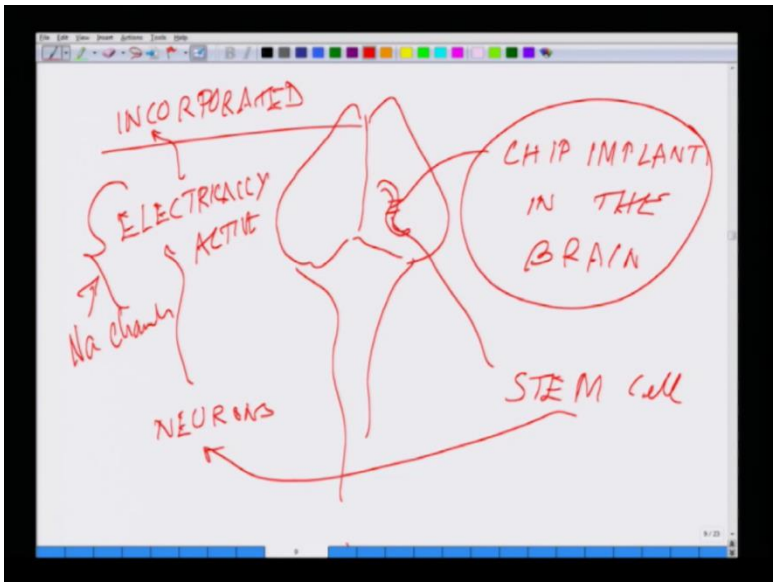

Similarly, on the same line, if I go back to the brain say for example, what will happen if part of the brain dies out something like this. Say for example, out here, people who are trying to know implant chips on the brain attempts are going on that if you could implant a chip on the brain at the place where the damage has taken place. Of course, the other therapy will be a incorporate stem cells out there and those stem cells become electrically active. First of all, they become neurons and those neurons become electrically active. So, it means, whenever we talk about electrically active that means, essentially they should be able to generate their sodium channels, and then they get incorporated in the circuit. But we do not know really, if these such cells get incorporated into the circuit, how the connectivity will be dictated what kind of connectivity they will establish with the rest of the circuit where the previous cell has died.

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So, just to visualize this situation it is something like this. Say for example, you are in a network like this. These are the individual neurons what I am drawing. So, for example, this neuron dies out, this one dies out, and say this one dies out and these. So, now, instead of them, here you are putting some new neurons which you are assuming they will be you know they will form neurons from stem cells, but will they form this same connectivity or not is a big question. So, these are the challenges of the future, will they become neuron, will they press all the necessary ion channels to become neuron, we really do not know at this stage. We are just speculating yes it may happen, it will be helpful, but we really do not know or could we put a what certain electronic device out there which will get incorporated and reestablish the connections, we really do not know.

These are some of the final frontier. So, a mankind this is kind of you know a dreaming, struggling and moving towards to understand who we are. So, at this stage, after covering through the central nervous system, peripheral nervous system briefly talking to you people over last two classes about the memory, learning, sleep very briefly about the sleep and giving you overall picture. I will close this part of the talk. In the next class, I will touch few smaller topics, which I missed out in the course, which will make much more sense at the cellular level especially in terms of the neuro transmitter excitatory inhibitory circuits, and that is where we will be closing down on the animal bioelectricity.

Thanks a lot.