Animal Physiology
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Lecture - 14

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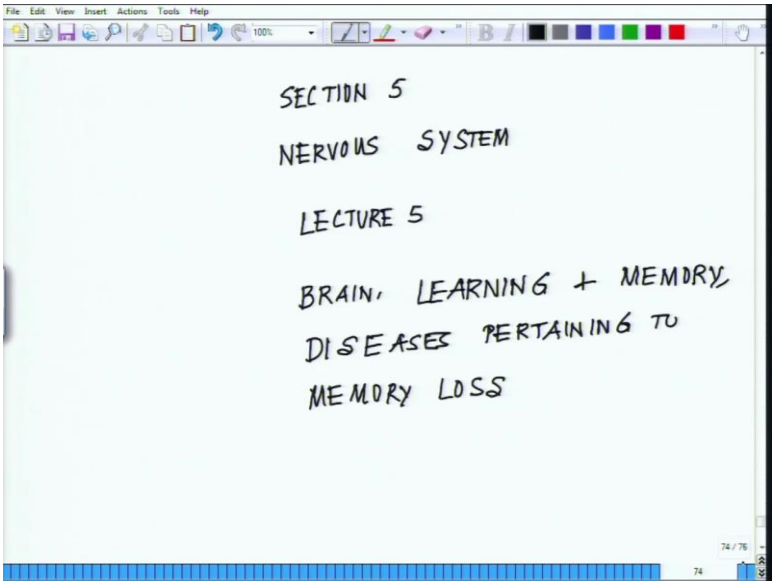

Welcome back to the lecture series on animal physiology. So, we are in section five and in nervous system and today we are on the section 5 lecture 5. So, basically there are almost 8 to 10 allotted lectures for this section. So, we are on the fifth lecture. So, today we will be studying about the brain, the key central processing unit of our body in terms of cognition thinking process learning and memory. We will talk about some of the models of memory and the diseases pertaining to that particular memory deficit or dementia or any other form of information storage loss. To start of with, just look at the geometry of the brain. So, that will help you to kind of understand. So, we are ((Refer Time: 01:17)) section five which I have already mentioned.

So, will be talking about the Brain, Learning and Memory and we talking about diseases pertaining to a to memory loss. So, before we start, let me tell you some stories which may help you. So, back in nineteen forty eight sometimes in forties or forty exactly I do not recollect the year, there was individual who was getting frequent bout of Epilepsy. Now, those of you who do not know about Epilepsy. Epilepsy is a disorder when a all of a sudden the brain becomes hyper active. It is said that one of the theories says that there is a uncontrolled secretion or release of excitatory neuro transmitters like glutamate it

may be a resultant of glutamate excess secretion or glutamate toxicity or something like that. So, all of a sudden brain become completely hyper active and the person looses complete control on its peripheral system and most of the time a Epilepsy patient pretty much falls down and after sometime, he or she regains conscious and then they are fine, but, the problem is that you really cannot predict when they will be getting that kind of a violent bouts of Epilepsy.

So, here was a patient or an individual say x or y what is ever. So, this individual was a mine worker he was working mines in Canada. So, he was getting this frequent bouts of Epilepsy and every time he had to he had to be admitted to the hospital and you know doctor used to do give a medication and this is forty's and fifty's much even before I think the DNA also was not discovered by the time. So, this fairly early. So, eventually there was one surgery which was performed on him by some of the neuro surgeons. What they did is that, they specifically removed a part of the brain which was supposed to be the origin of this a hyper activity. So, brain has and will come to that. Before that I will tell you the stories and I will come back to this. Next what happened is that of course, this person did not suffer from epileptic bouts since then but he never learnt anything from that day, he could not never remember anything what he learnt from that day on he could only live on the information which he gathered in the past.

So, this was the first I can call it an accidental discovery or you can call it a just a freaking chance that because of one surgery or surgical removal of a specific part of the brain. Human being came to know as a raise we came to know for the first time that this particular part is involved in some form of information acquiring. It something like, if I had to give a computer analogy the something like a Random Access Memory you need to have a RAM in your computer. So, in that you can you know. So, higher the RAM the more are the ability to download information's and all the other things. So, it is almost like a RAM and that sets the tone for a series of experiments in nineteen forties we are into twenty thirteen. It is since then it is almost 70 years, 43 years there are series of experiment across the world. A good number of scientists who are involved in understanding what is learning, what is memory. And in that process several new information have come to known to mankind and in this section and the subsequent section of these lectures will be discussing about some of these discoveries which took place.

So, having said this what I will do, first of all I will go to the structure of the brain and I will try to show you that part of the brain which was actually removed in that patient. So, that way you will have a visualization of that area, so going back to the slides.

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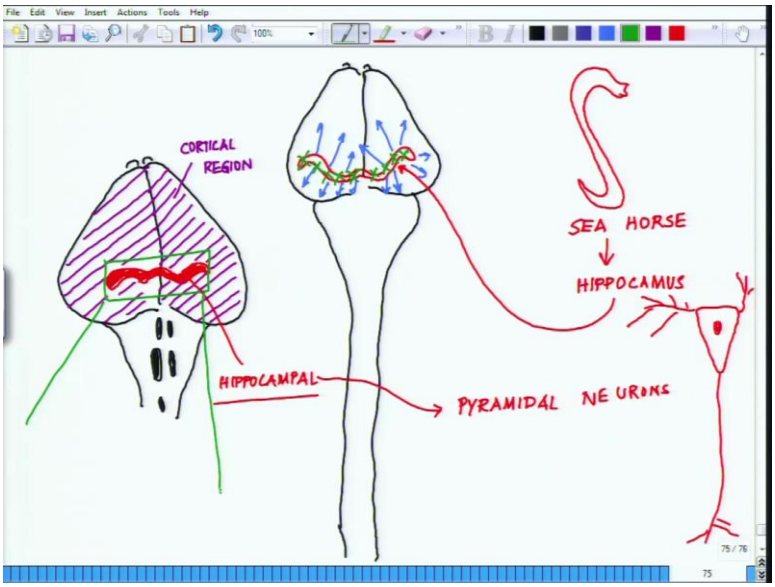

So, if I draw the brain like this. So, this is from the top you are seeing the individual. So, for example, you are lying down and. So, this is the brain stem and this is the spinal cord coming I am not doing completely because I will be dealing with there is small bouts here fine. So, the region which was removed in this patient, I am highlighting that region was an organ like this a billowed. This structure and this structure is termed as if you look at this structure shape of this structure if I had to put it like this it is almost like this, which for the Greeks, this is the Greeks used to call this kind of structure this kind of animals sea horse and in Greek sea horse the word in Greek is hippocampus. So, this region of the brain based on this got the name called hippocamus.

So, in that particular patient this was the part, where there as uncontrolled electrical activity all of a sudden without any time without any prediction or anything. So, what the doctors did is they removed this part they got rid of the surgically remove this part and next what they found this person never gathered any kind of the information. Now talking about the other parts of the brains if this is the hippocampal region, and then let me redraw another picture, which will kind of help you people to appreciate. These are the left lobe and the right lobe and here you have the hippocampal formation likewise the

rest of the region, which is called the cortical regions. And within the cortical regions there are several areas the language area which is called brokas area, varnicase area. You have visual cortex, you have areas which are involved in hearing .You have areas, which are involved in motor control and especially most of the motor control are in the brain stem regions out somewhere here there are nuclei.

So, here the nucleus does not mean the nucleus of a cell it is the aggregation of a neurons at a specific point which are controlling.So, there are areas which are controlling nuero-respiration. There are areas which are controlling other motor activities. Then, there are areas which are controlling your appetite and there areas which are not well defined have some role to play with different kind of pain circuits.

So, just by removing this small area of the brain with respect to this is a smaller area this patient this individual loses any information gathering here. So, this is your cortical region cortical region and this is the hippocampal region. The neurons which form a hippocampal region are called pyramidal neuron pyramidal neurons. So, why it is called pyramidal neurons because these neurons if you see the structure of these neurons they look like pyramids like this the cell bodies are like this and these are the axonal processes and these are their dendritic tree here is the nag here is the nucleus of the cell. So, and apart from it. So, if I kind of you know magnify this image how this looks like in a cross sectional view of this. So, let us move on to the next page to tell you the cross sectional view.

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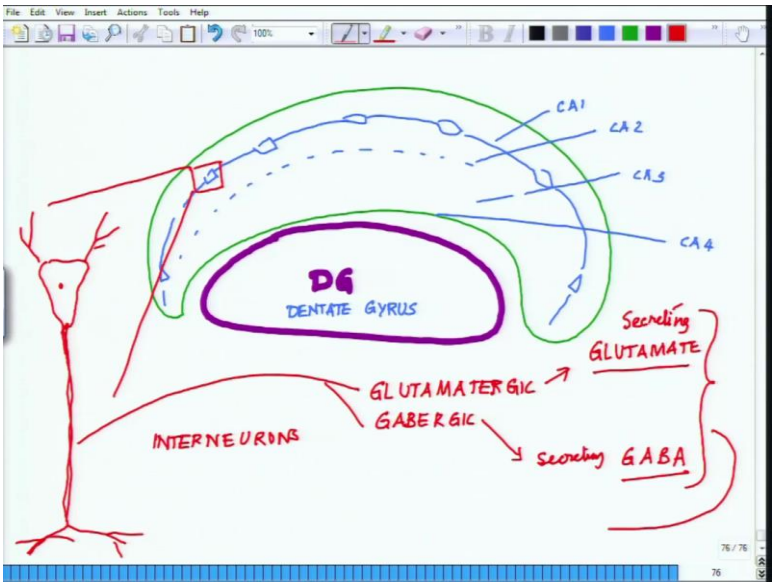

So, the cross sectional view of this structure is almost like this. So, what will you see is there are kind of circuits all over the place likewise there are specific regions and there are and these regions are consist of several circuits and these regions have different names and I will come to the namings CA1 region. Then you have similar regions, which are called CA2 regions, CA3 regions, CA4 regions and underneath this, is a area called many books you will see it is written as DG. DG stands for dentate gurus. So, this is the cycle architecture of the hippocampal neuron which are mostly consist of...

So, if I have to kind of you know blow up on this these mostly they are consist of those pyramidal shape neurons like this with the dendritic processes and likewise ok. So, these are the and apart from it there are series of inter neurons if you remember inter neurons we talked about the inter neurons in this spinal cord circuits. They are a series of inter neurons and most of these neurons are neppercampial region are either glutamatergic and I will tell you what does that mean Glutamatergic or Gabergic. So, this means if they are Glutamatergic or Gabergic. Glutamate means. So, if you remember the classification neuro transmitters. So, most of these neurons secrets and excitatory neuro transmitter called Glutamate, secreting Glutamate and Gabergic means the secreting Gaba, Amina Beta acetic acid as neuro transmitter. So, based on the neuro transmitters these are been classified. Apart from these so another thing remember one more thing while study about the brain none of these regions are kind of isolated they are not isolated regions.

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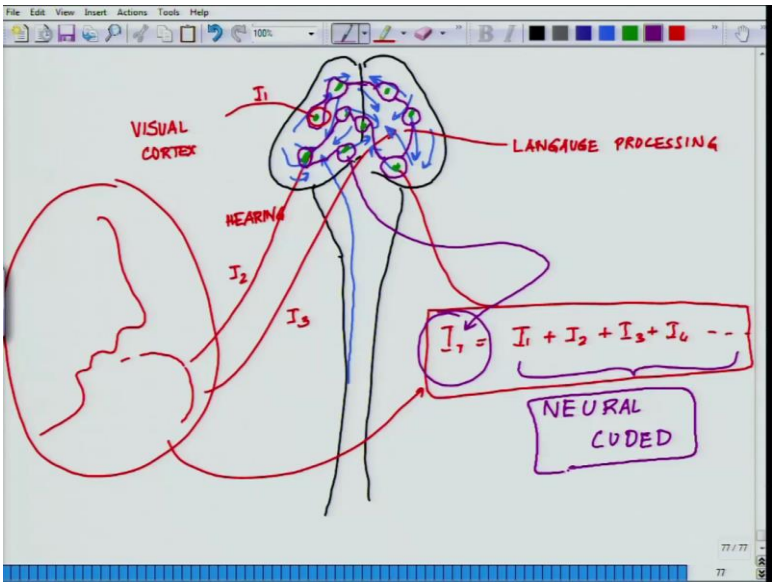

So, in other words say, for example again let me redraw the brain if and this is how the brains look like and this is the brain stem. So, and from these spinal cord you are getting all the signals, which are coming. All the motor neurons which sorry sensory neurons which are bringing the signals and then they are all interconnected with multiple kind of connections likewise. Somewhere there converging they are all interconnected with neurons and they are a circuit. Its imagine you open a radio or you open a computer or you open a super computer circuit or you open or you see a I c chip hundred and micro hundred very high end microscope it is a huge circuits and these circuits. We call them as neuronal path ways and these path ways are kind of you know linked up with one and other.

In other word, if you remember in the last class I was telling you something and whenever we see an individual say for example, I have to remember something there are several ways by which I can remember an individual. Say for example, today you are seeing me I am putting on a particular color of the shirt, have a shaved, my facial expression, my voice. I mean look at it already a sound modality, my voice, shirt color, face, visual cues, color codes, visual cues, color codes to individual section. Voice is another section apart from it some other aspect of it. So, a piece of information is being stored. If say for example, if somebody has to store in his or her memory the face of an individual or about to know like you know to remember individual there are several ways we remember. So, say for example, now let me give you a practical situation. So,

say for example, you see this individual and you have to remember this individual. So, part will be say for example, you have the visual cortex which is ensuring the visual cues about this individual, visual cortex if this person is speaking something. So, that will be stored in some region called you know hearing or hearing region ok. Then you have something called a language processing area where language. What I am speaking you are processing it language processing. So, in other word what is happening us individual whom you are seeing as a whole? All the information's for example, if this is the set of information, two this is information three.

So, all the information about an individual if that I called as I t the total information is divided into I 1 plus I 2 plus I 3 plus I 4 likewise. And these pieces of information's are stored at different parts of the brain all over the brain they are stored now what happens is this. So, say for example, if I call show them as the memory traces about this individual these are the different memory traces for x y z whom you want to recollect. So, now, if I have to recollect this individual as a whole what I have to do is, either I have to gather all this points and gathering all this point means, I have to get this piece of information, this piece of information I am drawing this piece of information, this piece of information about this individual. This piece of information, this piece of information, this piece of information, this piece of information and this whole piece of information then eventually should be able to recollect this individual.

And this only happens, when they are all connected with each other. So, when you started you know you remember like we also remember he had a very husky voice or we remember his or her eyes were like this or on that day, he or she was putting on the or specific kind of cloth or specific color. These are those bits and pieces of information's and this is what I was trying to tell you. This falls under the final frontier of human existence .understanding the neural code in this circuit in this huge circuit these falls under their neural coding. How we are been coded. How all these information's are been coded. Neural coding or neuraly coded. So, we are all neuraly coded. So, coming back where I took the D Tour. So, talking about the hippocampus. So, I started this with the hippocampus well talking about this circuit.

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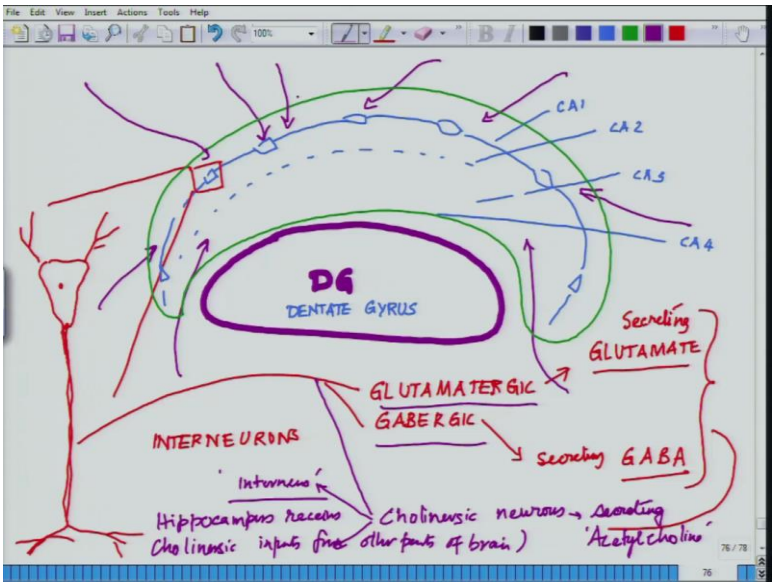

So, this circuit what you see out here is getting inputs from other areas, several other areas it is getting input likewise and some, of the inputs which are coming in the form of Cholinergic neurons. Cholinergic neurons are the once. So, I talked about the Glutametargic neurons which are secreting Glutamate. I talked about the Gabergic neurons which are secreting Gaba. Yet there are series of Cholinergic neurons, it has been proved that hippocampus has some of the inter neurons which has the ability to secret Acetyl cholines. So, Cholinergic are the once which secreting Acetyl choline .

So, this Cholinergic neurons either they may be the inter neurons or, this is the debatable topic that whether there are Cholinergic neurons as it is other than inter neurons in the hippocampus or not, but it has been documented in the literature that hippocampus indeed have some Cholinergic neurons where the beginning of its development, but then that dumble goes down, but apart from it gets cholinergic inputs from other parts of the brain. So, in other words to put it. So, let me put it. So, hippocampus or receives Cholinergic inputs from other parts of brain. So, the cholinergic inputs what you see. So, the hippocampus receives cholinergic neurons. So, what I wanted to tell you highlight.

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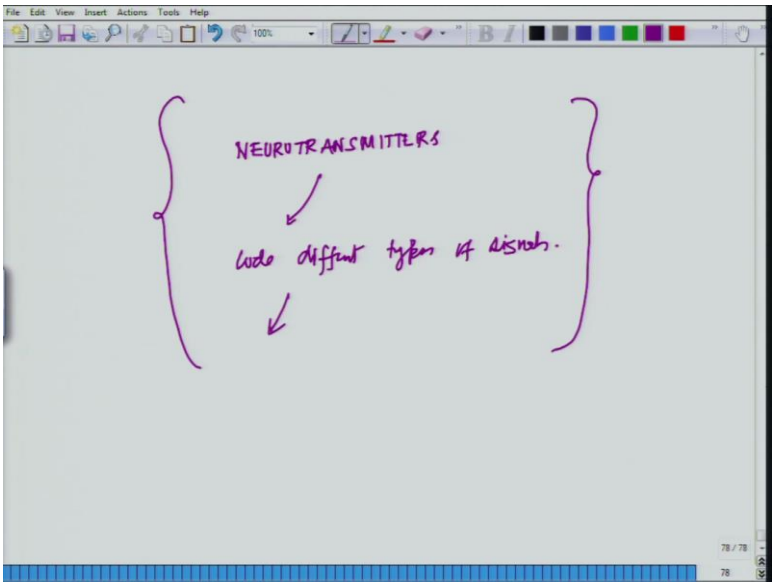

Here something very important that each one of these Neurotransmitters decides. So, apart from that time and space we talked about. So, the Neurotransmitters have the ability to code different type of signals. So, depending on what kind of Neurotransmitters are functioning at specific regions of the brain our coding pattern kind of changes.

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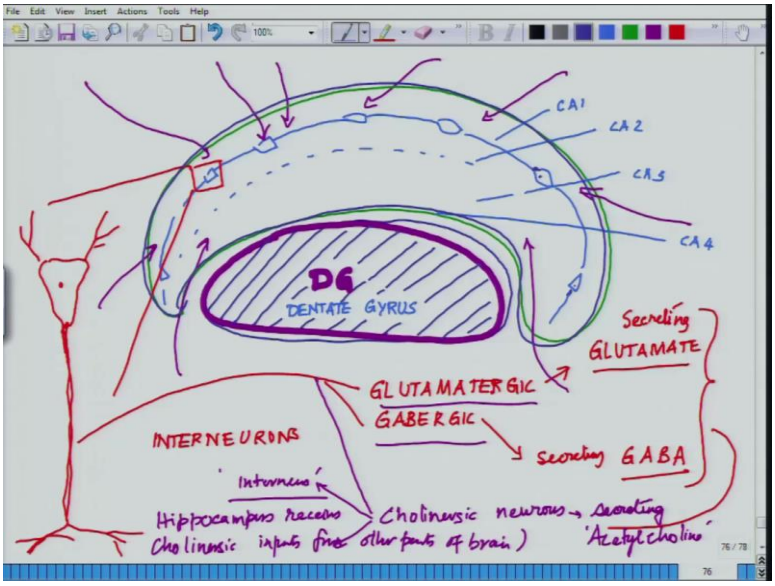

So, this is very important for people to understand. So, coming back to the hippocampal part. So, this was the region which was removed from this particular patient. So, where it all started a structure of the hippocampus and it is having the pyramidal shape neurons

and CA1, CA2, CA3, CA4 and the dentate Gyrus region of the brain. So, since we are talking about this thing, let me and highlight another part of the aspect of the brain which is very contraventional. Come to this in depth in the subsequent lecture this is the part. So, if you people remember in the beginning I told you that the real cells are dividing cells and the neurons are non-dividing cells, but it I told you that there are certain regions of the brain where indeed the neurons do divide and dentate Gyrus is one such hot spot where the neurons are dividing. And will come to the whole controversy across the world among the scientist that do they really divide and they do the form functional neurons or not. This is something, which is under intense investigation from different groups across the world. Really what is happening are they dividing are they becoming neurons or not and all that processes ok. Now coming back to the circuit what we are talking about. So, next thing was that. So, now, we have since we have talked about the geometry of the or the morphology or the structure of the hippocampus hippocampal region of the brain now will talk about some of the why this region is. So, very important.

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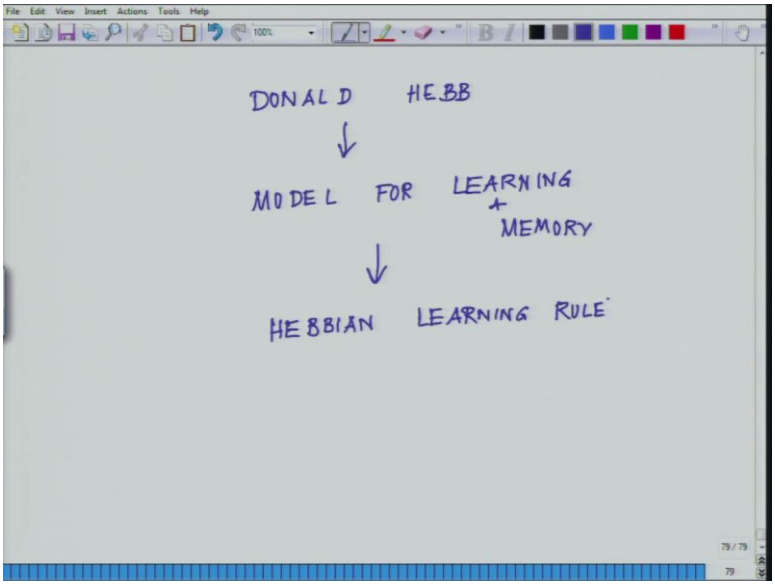

So, of course, we saw from the patient, but by the same during the same time during there was an psychologist who proposed a model of learning and memory his name was Donald Hebb you people can check it out from the web. If you do. Donald Hebb was a psychologist and he proposed a model for learning and memory. So, what and that was eventually called as learning and memory which was eventually called Hebbian Learning rule. So, what exactly is hebbian learning rule. So, hebbian learning rule states that. So,

first of all I have to make you understand this then I will kind of schematically draw it at one point of time. There is say for example, this hand this is sending some signal and this one is receiving some signal and both of them are equally excited this is sending a huge train of signals and this one is receiving. Now one hand is sending signal the other one just imagine this is one object and this is another object. One is sending signal other is receiving and a very high train of signals after some point even after and both of them are very active if the sender this one is the sender and this one is the receiver, this one which I am moving now is the receiver. If sender stops sending signal to the receiver yet receiver still keeps on receiving signal this may sound bit bazzare.

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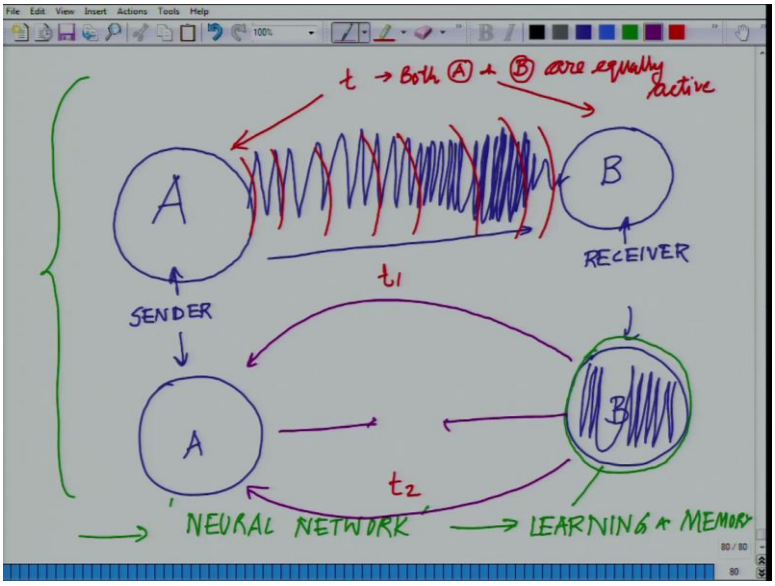

So, think of this situation what is happening. So, now, let me put it in terms of schematically. if this one is A and this one is B . So, A is the sender and B is the receiver. So, A is a training sending a train of signal like this to B very strong train of a very high frequency signal which are reaching to A like this and A and B are both active at some point. So, the pre condition is that at one point of time at t point of time both A and B are equally active. So, at t 1 we made this recording. That this one is sending signal and which one which was being received by B. After some point of time say t 2 point of time here is B and here is A. A is no more sending any signal yet B is perceiving that it is getting signals like this in other words say for example, I teach you something very intensely and you are listening to it very intensely I stop teaching, I finish my class, but still your brain is processing that information continuously you remembering the you

know somewhere or the something is getting changed in your circuits it is slightly bit abstract for nineteen forties when this whole theory was proposed, but that was the first learning model that is how we learn we reargue it.

We see, you know in our childhood our parents, teachers us you know learn something by heart like you know learn by heart. You know second two oneza two, two twoza four, two threeza six, two fourza eight likewise. You know, you remember it or there is some poem you continuously listen to it and you remember it. This something like that and this was and that is been said at that time that this is how the information. So, what happens essentially what Hebb says it is that in that process there are permanent changes which I am showing in green happens on the receiver side. And this is a form of learning which was proposed by learning and memory, which was proposed by Donald D Hebb this was the first model, it was just a model and the whole feel of neuron network and all these things all those who are from that field knows that these were some of the initial models which are been thought, but then does this model well this is a mathematical model out there thus this model has physiological significance that was the question.

So, now, going back what all we have talked about because I will come to this. That is why I am giving some discrete pieces of information. So, we talked about this structure and we talked about the patient where this structure was removed and this person could never gather any further information could never remember anything. So, this was proved by the time nineteen forties and fifties that hippocampal region is involved in learning and memory a first set of learning. Second thing was which was known at that time. So, there was existing learning model by Donald Hebb and the learning model looks like this. When A is intense sending an intense signal with very high frequency and B is receiving and both A and B are active at that point of time after some point of time in spite of the fact whether a is sending any signal or not B is receiving certain signals.

So, in other word there are two possibilities. One possibility which comes suppose that B request A to send more information that is more of an inter active. So, this loop becomes much often a inter active loop. Now could this be proved in biological system that was a challenge the story from here shifted from nineteen forties and fifties to late nineteen sixties or somewhere in nineteen sixties. There was one study, which was done by three individual Bliss, Lomu and Collingridge.

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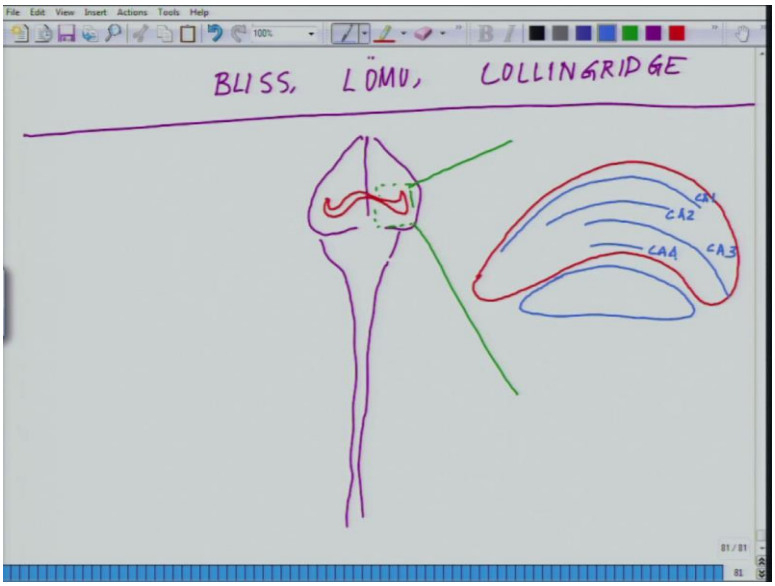

This was one of the very seminal paper Bliss, Lomu and Collingridge believe the spelling may have some mistake, but kindly correct it. So, what they did is that they took out hippocampal region from the brain of I think ginny pig or something like that. So here is they dissect out an animal basically, they sacrifice the animal because you know taking of the brain or sacrificing the animal. So, from here we are trying to do they removed the hippocampal region. So, this part was removed likewise. So, already I have told you that there are specific circuits on this part CA1 region, CA2 region, CA3 region CA4 region and you have this dentate Gyrus sitting underneath it. So, here you have the CA1, CA2. CA3 circuit, CA4 circuits and they are all interconnected in a complex manner.

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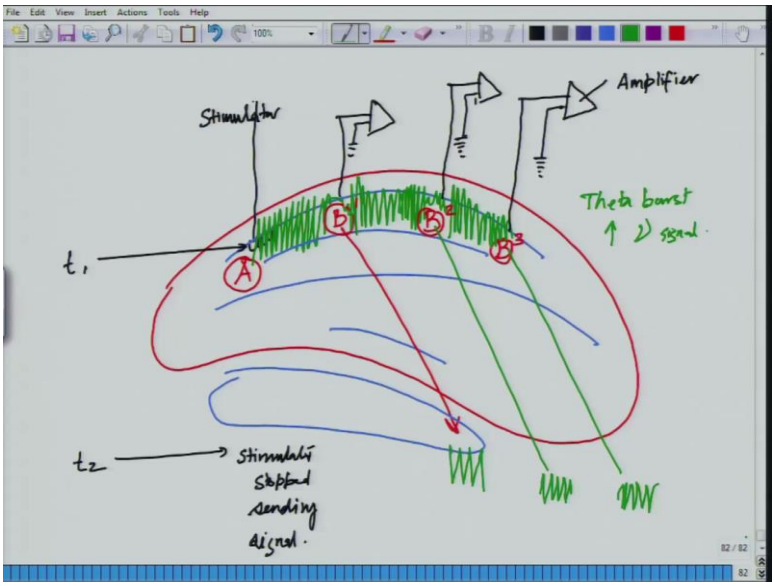

So, what they did is they placed it in a bath likewise take the next slide and redraw the whole thing that will help you to understand. CA1, CA2, CA3, CA4 dentate Gyrus. So, they placed it in a bath where this tissue can live for at least few hours and then they did, by that time there was lot of good development in electro physiology. So, they placed multiple electrodes like this. These are the electrodes placed and they were making recording. So, this is the amplifier out here very high end amplifier though at that point also the amplifiers were just kind of in the developing phase because this was the time just after the discovery of the transistors in nineteen fifties and this was the stimulator. So, imagine this part to be your A region in the previous diagram if you go back to the previous diagram when I am showing you A and B and imagine this to be the part B and they are connected like a circuit.

Say for example, this is I put multiple B1, B2, B3 fine. Now A is sending a train of signals from here to B of course, not only to B, this will continue all the way to through this circuit to B2 and this will continue of course, to B3 fine. So, these are the train of signal at time t1, time t2 this continues say for few minutes or few seconds, a very very strong train of signal is to call that as Theta Burst. It is a very high frequency signal. Then at time t2 the stimulator stopped sending signal. Yet it was observed that B2 is getting some signals. So, do at B3 is getting some. So, B1, B2 and B 3 all are getting signals why is it so. Now, if you go back I was talking about Hebbian learning model this

was the study we change the way we think it is these are some of the seminal discoveries which helped us to appreciate.

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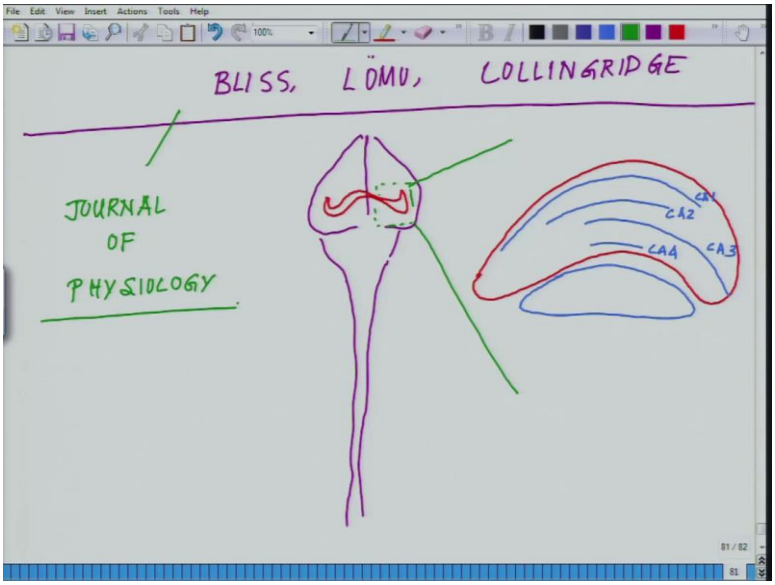

So, this was this seminal paper which was published in journal of physiology that point of time was the first documentation of the Hebbian learning model or memory.

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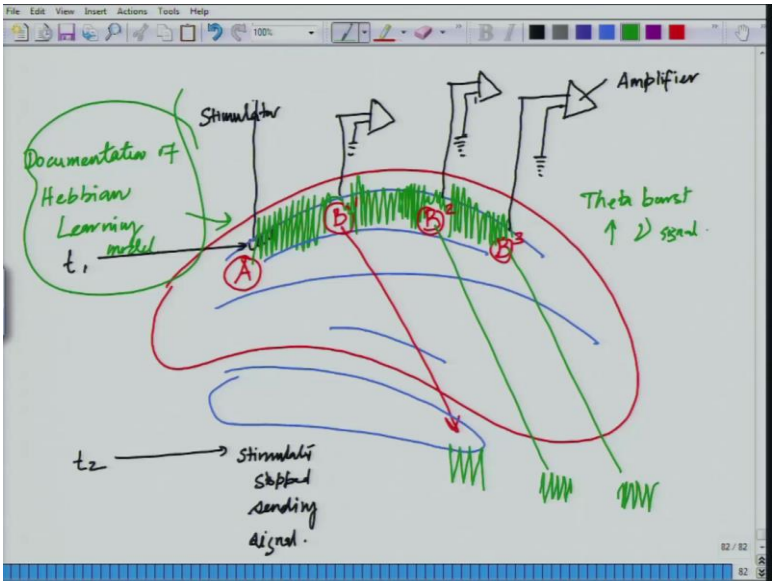

So, first documentation of Hebbian learning model it was this experiment which helped us to develop the whole field into another level and they term this process.

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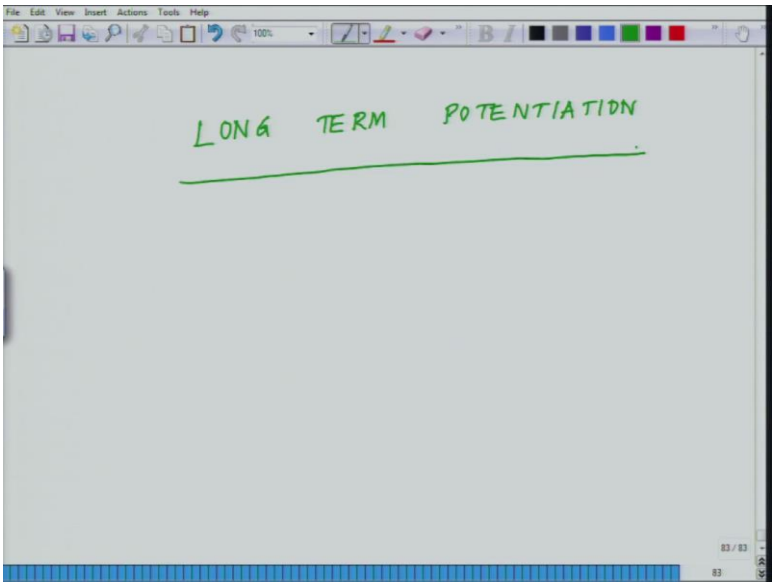

As first memory model biological system was termed as Long Term Potentiation. What exactly is does that mean and what exactly happens here. So, coming back to again I will refer back to the Hebbian learning model because that is the starting of this whole journey.

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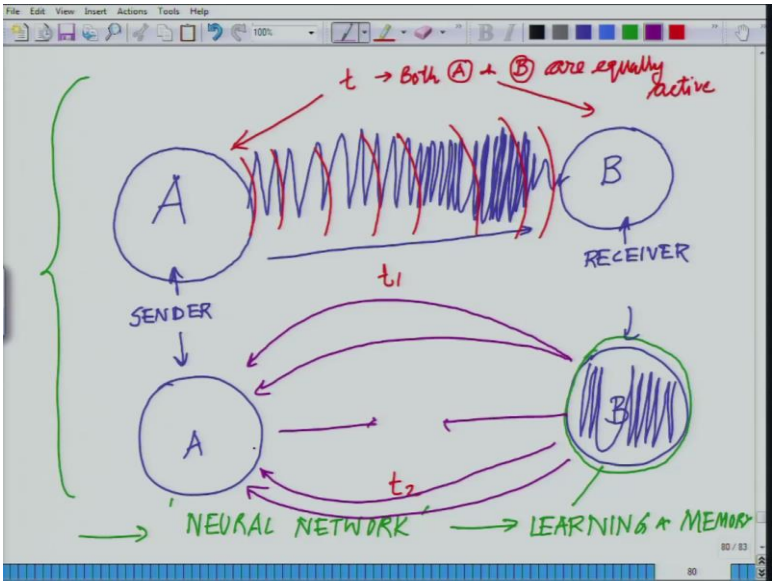

So, if you remember well I was explaining that I told you there are certain signal which is which was believed that B is sending to A that when A is no more sending signal asking A to send more signal.

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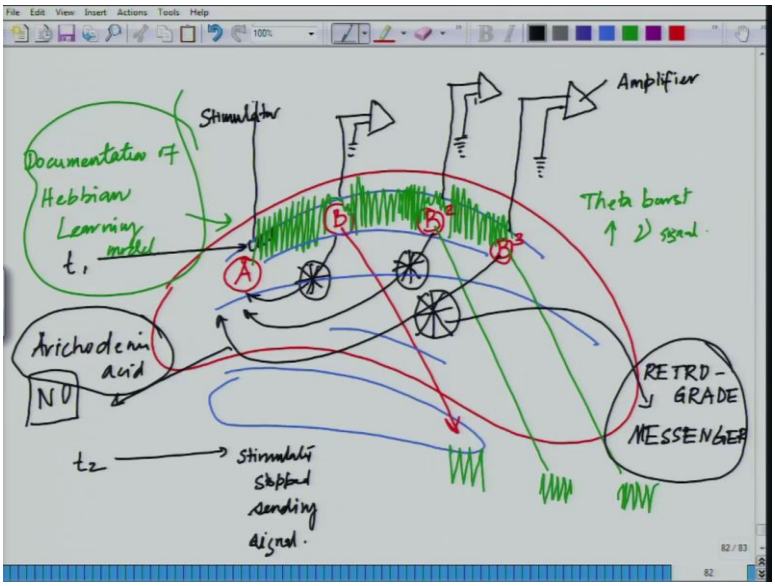

So, the next idea was in this model in nineteen seventies when during sixties and seventies when this was discovered it was thought that, there may be some signals, which are sent out by B to A telling A that you send more signals. In other word those signals which are been send from B to A out here what you see which I am putting in black and like I am putting a astric mark on those these were termed as retro-grade messenger retro grade messenger. Now, what are those retro-grade messengers? Till date this is nineteen seventies and forty three years have gone since then we are in twenty thirteen we are not really sure what the retro-grade messengers are.

They are potential molecules which have been implicated in that one of them is the nitric oxide. If you remember I was telling you about this molecule in the classification of neurotransmitters then one of the fatty acid Arichodenic acid which is involved in it possibly. And few other molecules, but nobody with certainty can tell which are the retro-grade messenger till date and there is intense investigation on the way that what are those retro-grade messengers. Are they, are at all and if they are. who are they in how they are communicating from B till A or from the receiver to the sender that you react accordingly. Now what really, is long term potentiation now that is what I was where I stopped? So, at what does that mean?

So, at this stage what I will do I will stop with this lecture and in the next lecture will talk about what are what are long term potentiation and the other model what is long term depression and will come to the diseases what will be dealing with thanks a lot .