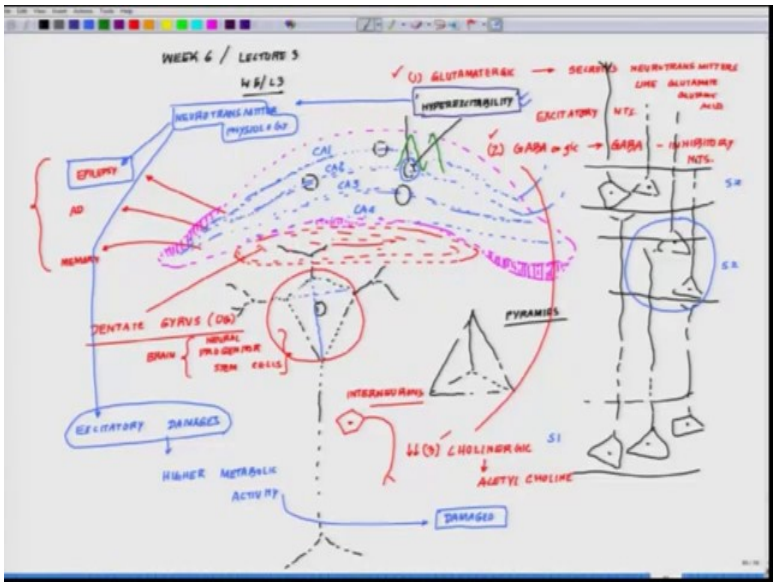
Animal Physiology
Prof. Mainak Das
Department of Biological Sciences & Bioengineering & Design Programme
Indian Institute of Technology, Kanpur

Lecture – 28
Epilepsy and Memory

Welcome back to the lecture series in Animal Physiology. So, we are into week sixth and we have finished two lectures and I have introduced into the anatomy of the brain specifically with anatomy of the hippocampal region which is where we will be concentrating for next two three classes where we will be talking about epilepsy Alzheimer's disease and memory.

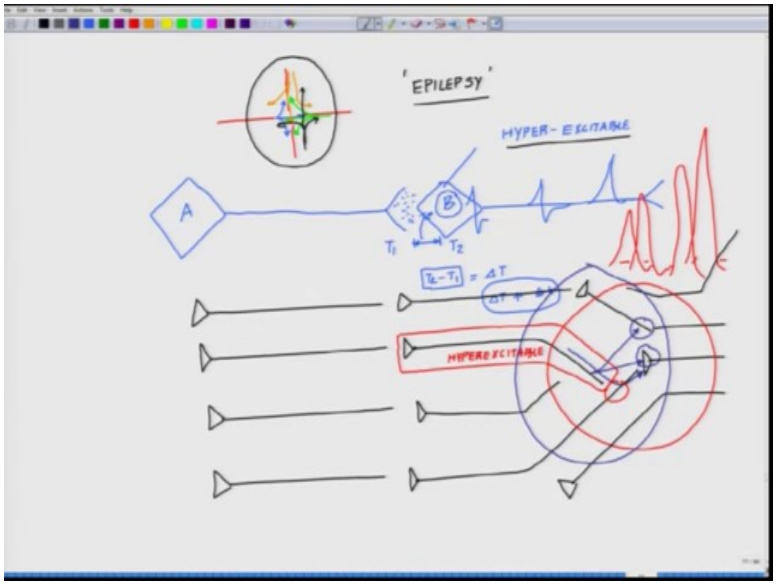
So, if you remember in the last class I told you that you know there are two major neurotransmitter which are secreted by the hippocampal neurons. The glutamatergic, the glutamate or the excited neurotransmitter, gabaergic - gaba which is an inhibitory neurotransmitter. And I told you there is a small population of cholinergic neurons which are present there, but which are more with controversies for a different reason, we will not get into that. There is a small population indeed as the emerging studies are indicating towards its. And from my own research account I can tell you which certainty that they are present there. So, now what happens in epilepsy in the circuit? So, I have we have briefly dealt about the circuit, try to you know how they are connected CA 1, CA 3 region.

(Refer Slide Time: 01:51)



So, during epilepsy, in this structure if you. So, let me just put it so this is week sixth and this is lecture three – W-6, L-3. So, what happens is that at certain small loci or locus where with I mean this is very difficult to pin point small locus there is an hyperexcitability and I have given you the examples in the first class, if you remember and this week's first class I told you, when we talked about the hyperexcitability just think of it what does it mean that means, due to hyperexcitability the neurons which are present there, they secrete neurotransmitters more than they are required right. If you remember?

(Refer Slide Time: 03:03)



So, if you just go back to the class where I was trying to show you this aspect something like this hyper-excitable and because of hyperexcitibility say for example, these are network now let us put neuron or shape into them and this is if how this is how the signal is rolling. Now, see for example, let us pick up one of them. Let us say this one this particular neuron which I am putting boxing up becomes hyper excitable. Now, the hyperexcitibility of this neuron, what it will do, it will kind of make this one hyper excitable if it has processes to this one, it will make it hyper excitable or process to this one it will make hyper excitable. So, if it is only supposed to send signal like this because of its hyper action it will send anomalous signals to these locations and if such sites are more so what will happen, there will be huge amount of anomalous signal which will be coming up which was not suppose do be there.

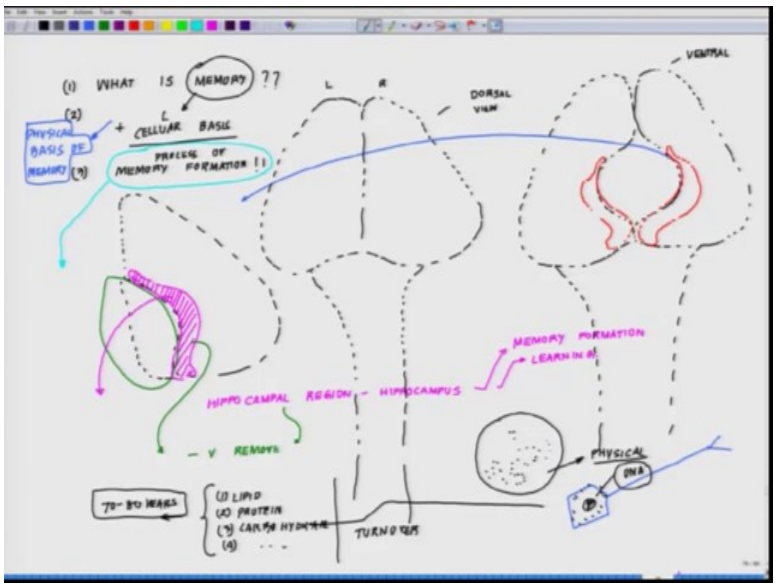
Now, one second coming back to the circuit one fine. So, these are those hyper excitable regions what we are talking about. These are different locations I mean you just have to break down the image according to the neuronal connectivity and everything. So, say for example, this is the region which becomes hyper excitable. So, such patients have in terms of the molecule one of the possibilities is that of the pathology is that they may have a defect in neurotransmitter release or neurotransmitter physiology. How that happens, why that happens is something which is a area of constant research, but it looks like some of the neurons possibly either genetically predisposed or there are certain modifications, which happens over period of time what makes them very hyper excitable but such patients suffers from what we know as epilepsy. So, this is where most of the epileptic bouts happen in this region. There are other places, but this is the major one. And this hyper excitability physiologically further lead to excitatory brain damage excitatory damages.

So, because in that location there are hyper excitable situation such hyper excitable situation leads to change the excitable properties of the neurons around it. And they at times because of higher metabolic activity are gets damaged. So, this is what happens in epilepsy. When this is going to happen cannot be protected, at certain specific time it happens it does not happen continuously, so that makes our hypothesis kind of wavy because you cannot even predict when this is going to happen. They are intensively thinking or some stress or something, we do not know we cannot tell anything with certainty. Some of the patients, do say they have feeling that they will get about like that,

but we really cannot say with certainty, but this is something what happens. And this is known to the clinicians or the neuron atomists, neurophysiologist, neurologist, neurosurgeons for a long period of time.

So, back in 1940s in Canada, there was one surgery which was done to a patient. The surgery was done because this patient was suffering from epileptic bouts frequent basis very frequent. So, he was a coal miner was suffering from epileptic bouts time and again, time and again, time and again. And every time he has to be admitted in the hospital for proper care and this was becoming a really a clinging issue for both the employers and for the patient. So, doctors were aware of the location within the brain where there is epileptic waves are getting generated. So, automatically if there is an hyper excitability, so the waves will be generated you know, they knew it is happening in the hippocampus. So, they did a simple surgery for that time, it was a simplest surgery they can think of.

(Refer Slide Time: 09:37)



So, they remove. So, this was anatomy anatomical aspects what I drew earlier in the earlier classes. So, they remove or the hippocampus and the results were stunning. This individual was suffering from epileptic bouts got rid of the epilepsy definitely. From the surgical perspective, it was a complete success. But then he never ever acquired any further memory that was the stunner. So, from that point till the last moment of his life or her life, this individual lift without acquiring any memory based on the memory is what he has earlier or whatever that was not something which was expected by the surgeons.

Sometime things happens, and you really do not protect, it just happen to happen that it was just like that so that one whatsoever protect exploration, medical twist, changed in the story of neuroscience forever. So, this is 1940s and 48 when this happen.

So, before that earlier to that we were never sure that where information are being stored, so some of the questions which completely were beyond our reach even to address were few questions the first one is what is memory? The question one it was beyond our anything you know approach this question. So, most of the research you might wonder what was happening is that mostly on behavior, the whole field was purely on psychological parameters which are very well established and thanks to all those psychologists who really established their feelings such a wonderful way that you know today they come so handy. So, now, we have travelled almost in a sixty, seventy years since that time.

Psychology and behavior, these are the only way you can approach the brain then there was nothing after that there is no cellular basis to understand anything. So, what is memory, this was one of the question which was not really there relevant to that was cellular basis of memory. If you do not know where memory is happening, you cannot even address that question. What is memory formation or the process of memory formation?

Well to answer or address, answer is a wrong word to address the first question, what I put there what is memory. Well, if I ask you what you understand by memory your immediate response will be we have memory cards, we have hard drives, we have computer memories, where basically on some platform or on a some surface or something there are some kind of inscription. Where the information are getting stored either in some kind of a bytes using you know 0, 1 or binary logics this is what mankind as whole best understanding on memory till this date.

So, there are 0 1 0 1 binary coding 0 0 1 1 0 0 0 1 likewise there are physical. So, if say for example, if there is a plate like this, on a plate like this, there are physical signature of any event which is put in some mechanical way into that zero one coding different ways and all and that is what we understand by memory. So, it means our understanding of memory is physical something which is physical. Now, the question arises in a biological system where is that physical parameter, what is that physical basis of memory, cellular

basis. So, let me add one more here, physical basis of memory. What is the physical basis right because whenever we talk about biology, we talk about there are proteins, there are DNA, there are carbohydrates, there are vitamins, there are minerals there is water and there are cells.

Now, when we talk about a physical basis like this if I draw this and if I say draw a neuron, and if I say a neuron store information my first question which will be coming is where is that physical aspect of it. Say for example, if there are some kind of a change happening something which will be stored, and if it has a change has to happen the change can only happen in either in a lipid which is forming the biolipid layer of the membrane or it can happen in a protein or it can happen to a carbohydrate. Or it could happen to a you know some other x, y, z or to even water right and not only that, whatever changes which are happening there that has to processed 70 to 80 years.

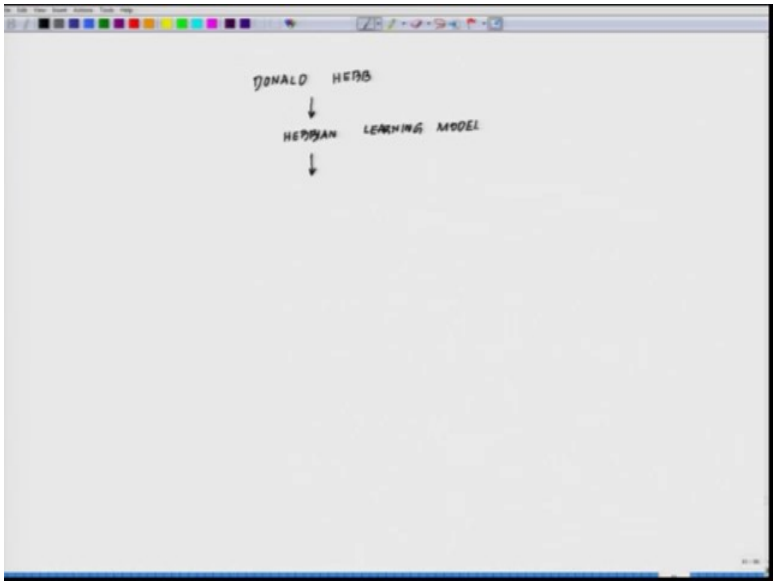
So, it means that molecule which see this change has to retain that change for next 70 to 80 years. Now, going by your cell biology logics and the word what we have used time and again in biology turnover of molecules. Turnover of molecules means you have a protein which is becomes older than it is replaced by the newer proteins; similarly you have carbohydrate molecule they replace similarly you have. The base molecule which are getting replaced I mean again and their dynamic structure, they are moving around slowly gradually within even in the membrane the lipid molecule shift their position lateral shape diffusion, flip flop and series of such things.

If you go through Albert's book a Cell Biology, you will see this and the question arises if there is a permanent change where the change is happening, what is that change. Or do you want to believe or do you want to except that every memory storage what is happening has something to do with the DNA which means there is a permanent change happening in the DNA that does happen though I am not ruling the doubt. But for everything that is something we do not know. As (Refer Time: 18:43) nobody knows, it is not that we do not know like you ask anybody, they can give you several mathematical zigmos and biological zigmos. But to tell with absolute clarity that yes this is the change, this is what is happening this is how it is happening and likewise and so and so forth, I guarantee you that no one can tell this with absolute certainty. Because we do not know we can only tell when we know do not know as of now we do not know.

Because of this one discovery that if you remove a part of the brain which is termed as hippocampus further memory formation does not occur opens up a pandora's box to approach memory from a different angle. So, it means the second question which is there. This question process of memory formation. So, now, we have some point in the brain to put our probe our electrode to figure out ok, now I have this point in the brain from where I can start the story. So, that is why I told you this particular accident or whatever you call that exploration opens up a whole new dimension about neuroscience. It took us the different to world altogether. And we are inducted to those people whatever they did to save that patient from epilepsy really gave mankind and access to understand how the memory formation has happening, we are not saying what is memory how possibly this is happening,but then having said this we have to go little bit backward to the psychologist what kind of theories they have proposed earlier to that.

So, I told you that is the field has been ruled by the physiologist, eminent psychologist, behaviorologist or ethologist for a long time before these kind of discoveries which allow this anatomists cell biologist really to understand or try to explore these events at the molecular level. Early to that it was all this treating brain as a block box I am doing some kind of a white noise analysis. So, what where the theories of learning and memory proposed by eminent psychologist earlier to that. The gentleman who proposed the very first learning model was Donald Hebb, I will put it here one second.

(Refer Slide Time: 22:06)



His name was Donald Hebb and what way commonly known as Hebbian learning model. So, what I will do in the next class is we will start exploring what was Hebbian learning model, and what were the subsequent studies which took place in the field of hippocampal neurotransmission which bring us at this point where we have a some fair degree of understanding how memory formation is occurring possibly in the brain.

So, thank you. So, in the next class, we will start with Hebb's proposition and the follow of experiments.