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

Lecture - 12

Hello welcome back to the lecture series in the NPTEL on animal physiology. We are in section 5 with the nervous system. One thing I forgot to tell you people that there are almost 8 to 10 lectures, dedicated for the nervous system, because of the white control mechanism it executes. As of now we are done with two lectures, where we have talked about the different kinds of neurons, the classifications of the neurons and how the neurons transmit electrical signals in the forms of action potentials, and all or none in the form of action potentials.

Apart from it, in the second class we moved on to glial cells; the supporting cells or the second type of cells of the nervous systems. We talked about the complete classification of the glial cells and what are their individual functions. We talked about the myelination and few other details, about the electrical activity comparison of glial cells and then neuronal cells. Today, what we do is that we will talk about little bit about neurotransmitters. I have just introduced the neurotransmitters. Today, I will talk about the classification of neurotransmitter, structure at the neuromuscular junction nerve muscle because, I talked to you, that there could be connection between neurons to neurons, to transmit signals. There could be a information, to be a processed when neuron sends a signal to a muscle, and accordingly the muscle to which is or to move.

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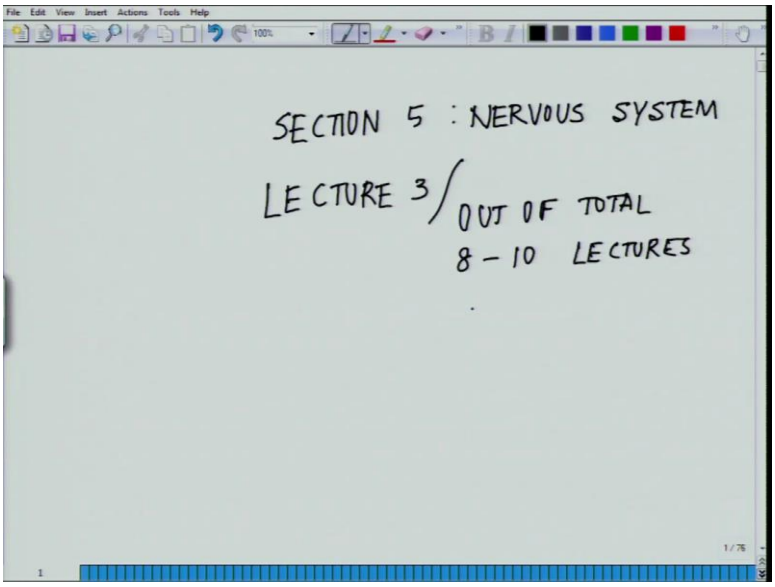

We will talk about some of these small circuits today. From there we will move on. So, let us start the class. We are into the section 5. This is the third lecture out of the 8 to 10 lecture, which are dedicated to this section.

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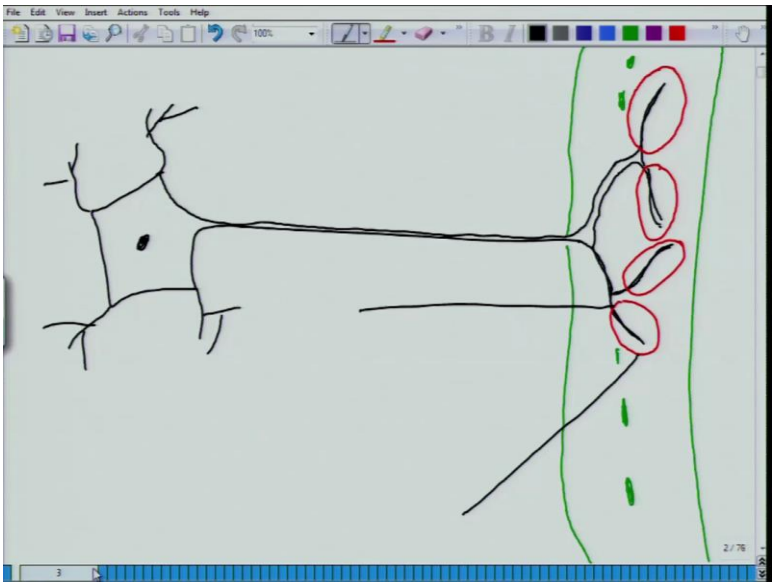

The first thing I will do is, we talked about this synapse in the last class. I will again revisit the synapse. I told you that possibilities are there, that neuron may form synapse on other neurons, or it may form on muscles. Historically speaking, the first of the

synapse, which were discovered and people understood the most, were between the nerve and the muscle, which were the neuromuscular junction.

We will take that example. I am putting the muscles in green, for example, this is the muscle and probably, in the next class what I will do, we will talk more about the muscle structure and everything, that will help you to understand some of the features out here. This green color is the muscle, and these are the nucleus of the muscle, and this is the connection where, let me highlight the connection in red. These are the zones synapses are formed; electrical connectivity has formed. Now, if I blow up this picture, it would be something like this.

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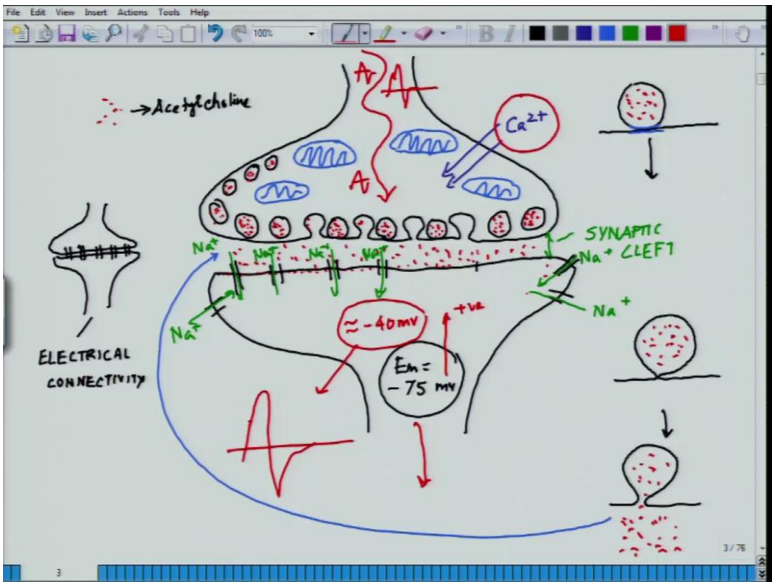

Let us move on to the next page. Let me blow up this picture. It would be something like this. I will talk about this; what are these invagination and everything. Imagine the other side. In this case it is muscle. If it is a neuron, that will look something like this; another membrane out here. It could ne neuronal membrane; here, I am drawing neuronal membrane. It could be a muscle membrane, if I discontinue. What exactly is happening? I have already shown you, that electrical impulse reaches all the way to the end. Then, what happens is the most important part. Few specific terminologies, this gap is called synaptic left. This is the small gap between one neuron and another neuron, or between one neuron and their target tissue, which may be muscle or something else.

I expect you guys to go through the notes, and just check, what is the nanometer difference between the two? It is a very small gap and this is one exercise, I wish you guys carry out. In this zone, where there axon is making synapses, there are lot of mitochondria. These are the mitochondria. Mitochondrias are power generators or energy generators of the cell. There are enormous amount of mitochondria out here. What the electrical signal does, when the electrical signals reaches here, say for example, I told you there are several kind of neurotransmitters, and one of the very widely read neurotransmitter is called acetyl choline. Soon after this, we will come to the classification of the neurotransmitter. But, before I go to the classification, just assume that this is the neurotransmitter; one of them is acetyl choline.

That will help me to explain, how the synapses really function. Once the electrical signals reaches out here, the next thing what happen is, electrical signal leads to entry of calcium ions from outside. In this zone, what you will see, you will see a lot of vesicles like this. These vesicles are filled with, likewise, these vesicles are all filled with neurotransmitters; this red are the neurotransmitter molecules in this. These, the close one are the vesicles. So, ignore the one, I have just drawn, likely in advance. I will come to that. Look at this synaptic left. There are two options. The electrical signal may jump to the next one through gap junction; we have talked about that in the electrical synapse, but in this case, that is not happening. In this case there is a physical gap.

You have to realize, this is the basic difference between an electrical connectivity and a synaptic connectivity. There is a physical gap in the range of nanometers. Whereas, in the case of electrical synapse, if I have to draw it, just side by side, it will look something like this. This is the upper one and this is the lower one, the one which is receiving. There are physical tubes in between them, likewise. This is what is in an electrical connectivity, in the form of gap junctions, whereas in the case of synaptic left, there is a gap. Now, the red color, what I showed you, the electrical signal is reaching.

As the electrical signal reaches at the terminal, there is an entry of calcium ions. These calcium ion leads to couple of events, which takes place here. These vesicles, they are bound to this membrane. If you look at these vesicles, they are bound and now, you recollect back. You remember, in the beginning of the transport phenomena and membrane physiology, I taught you people about exocytoses and indocytoses. I told you one of these processes helps you to throw away something outside the cell; throw away.

What happens? This membrane, this vesicle, which is form of a small membrane, this vesicle binds to the master membrane, which is this, filled with neurotransmitter, and imagine the membrane, underneath where it is binding. It is binding to this membrane like this.

Next thing, what happens? These two membrane merges, which two membrane merges? Like, this part of the membrane and this part of the membrane; they merges and what happens eventually, is something like this. While they are merging, they are almost there. Next thing, what you see is that, mind it, is all filled with neurotransmitters. Then, this opens out on the outer side, like this. This happens in pico or a fem to seconds range. These neurotransmitters are given out into that cleft. This the next step, what happens now, if you follow, this is what is happening out here. Now, stage two; this particular cleft, soon is filled with all neurotransmitters. These neurotransmitters, once they are into the cleft and in this case, we are assuming all this red to be acetyl choline.

Once these neurotransmitters are in the cleft, they bind to the target membrane; it could be a muscle; it could be another neuron or whatsoever. Once these start binding along this, you see all of them, like, on top of these red lines or all over this surface. As soon as they bind, they open up a series of cation channels. In terms of, from outside to inside, if something has to move, this leads to the opening of the cat ion channels. This promotes the entry of sodium inside the cell Na plus, Na plus, Na plus, from all over the place, and mind it, this is happening in a fem to or a pico second time interval. This is very fast. So, these neurotransmitters bind.

If you have a confusion out here, that I have drawn these on the surface; these are on the surface, mind it, these are not inside the cell; inside, there are (( )) cell. They are all on the surface. If you a confusion, you can rub this off so that, you should not have any confusion out here, that these, just for your better understanding, I will redraw this. So, they bind to the surface of the membrane and opens up the cat ion channels, and all these cat ion channels lead to the entry of sodium. As the sodium enter, mind it, this cell is sitting at say, minus 75 mili volt negative, with respect to Em, the membrane potential minus 75 milli volt; minus 75 with respect to the outside.

As soon as there is the entry of these sodium ions, from minus 75 it starts to shoot towards the positive direction. As soon as it reaches something around minus 40 milli

volt, it shoots up an action potential. Now, from one action potential, which was generated out here, this action potential is transmitted through second neuron and the second neuron again carries the same process, and wherever it diverges and whatever it does. Still, the story is not complete because, what is happening to these red molecules which are bound out there? Because, if they are bound, the next series of signals, which is going to come; what will happen to that? Because, those neurotransmitters, which will be ejected out from the center neuron, will not find a place to bind to the one, where the message has to be sent.

Just for the technical terms, the one which is sending the signal is called pre synaptic, and the one which is receiving the signal is called the post synaptic. In the case of neuromuscular junction, muscle surface or the muscle membrane is called the post synaptic membrane, and this whole phenomena is called synaptic event. This is, you can say this, one of the central theme or the central procedure. Because, the way I am drawing it, is very simple. But think of it, when this was discovered, this was something, one of the most path breaking discoveries, of discovering synapse in the biological system.

For last 70 years, people are rigorously researching up on these structural details of this and the features and everything, using electron microscopy, patch climb physiology, intracellular electrode, extracellular electrode and a whole series of bioelectrical techniques, are being employed to understand field effect transistors and likewise. What will happen to these neurotransmitters, which are present here? These neurotransmitters have to be removed immediately; otherwise, the next signal would not be able to do. These are, again, I am repeatedly trying to tell you, that these all happen in a pico second or fem to second level domain.

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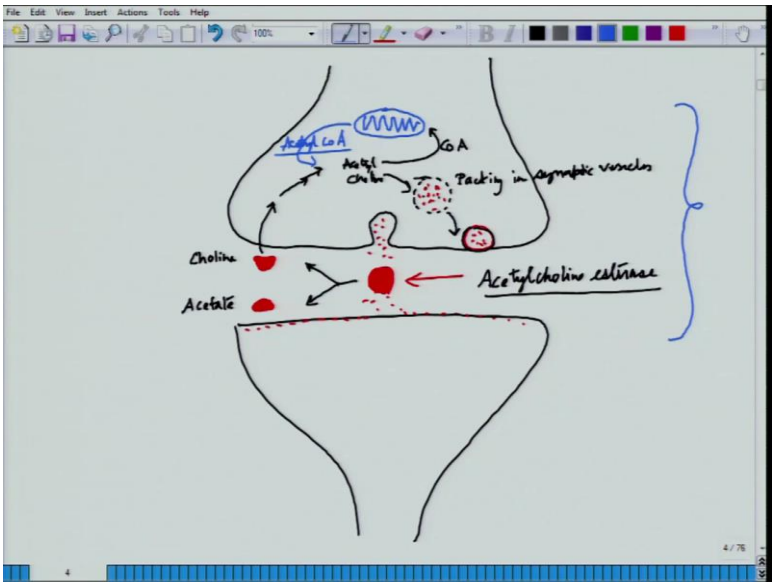

So, what will happen is that, now, let us do a little bit of small chemistry out here. What is happening here? Let us make this diagram little bit simple, so that we can appreciate what is happening out here. This makes synaptic cleft slightly bigger because, I have to put some of these features out there. Now imagine, this vesicle has given the acetyl choline out here, simplest to it, only one vesicle buying to it. What will happen to this acetyl choline is, here you have the, just take up a bigger molecule, imagine. This is an acetyl choline molecule; a single molecule. I am just blowing it up now. What will happen? There is an enzyme present in the synaptic cleft, and that enzyme is called acetyl choline esterase. This enzyme immediately come and what it does is, it splits this molecule into two parts; one side is called acetate; the other is called choline. Here is your acetate part, which gets metabolized and the other one is called choline.

This choline is immediately taken back by the cell. It goes back inside the cell. Now, you see exocytose, while acetyl choline is being given out by the pre synaptic membrane, into the synaptic cleft. Now, you see another molecule, a part of that molecule is taken back by the cell, inside the pre synaptic membrane. So, that is how the choline gets back inside the cell. Once the choline gets back inside the cell, what would happen, simultaneously, I told you that there are lot of mitochondrias out here, which are the energy rich or the energy producing machinery. What it does? This gives out an acetyl moiety here; acetyl COA; acetyl coenzyme A. So, acetyl coenzyme A, with the choline moiety coming from this side, is forming acetyl choline.

The COA goes back to the mitochondria. This acetyl choline now, is packed. This is a very complex process, where it is packed; packaging of acetyl choline into synaptic vesicles and then, this stuff comes here. Now, it is filled with, sorry, acetyl choline and it comes here and it bounds again, likewise, and then again, it is being sent out. This whole complex event has to take place, in order to ensure, and this is all happening at a very narrow time window. This is like, think of it, neuron in the central nervous system is synapsed by; a single neuron is synapsed by 10000 other neurons. In other words, there are very minimum, if assumed that one neuron form one synapse with another neuron, at least 10000.

But actually, one neuron forms multiple synapse on another neuron. So, think of the complexity of information transfer; single neuron receiving inputs from 10000 other sources at one point of time. I mean this is something, which is unfathomable. This unfathomably complex and one of the phenomenal network, where you have 1000s and 1000s of such neurons, in the nervous system and they are continuously, based on your experience, the information are getting stored in this form of electro chemical mode.

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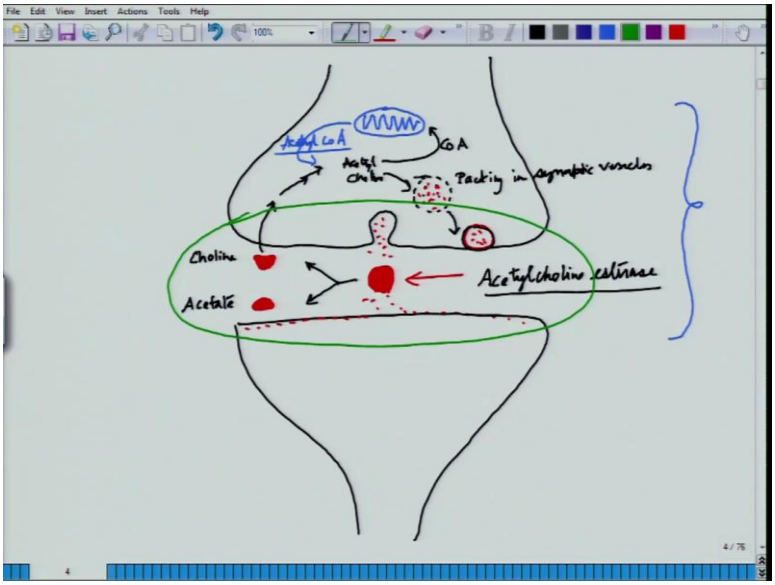

It is believed that all your memories, all your information are stored in this wonderful zone; synapse. This is a region where it is, just like something, similar to that you can think of is, membrane of CD; or surface of CD or a membrane of older days audio tapes, where the scratches taking place, where the sound waves are getting stored, something of

that kind. But, how this structure persists? How our information are being stored in the system? We will come to this section, with memory and everything, while we will be talking about learning and memory. At this point, what is most important for you people is to understand this. This is the central; very core to nervous system.

I mean, there is enough detail I can go into it, but at this point, what I expect you people to understand the very basic fundamental synapse, which are present. From here, we will talk about, before I move up on to classification of the neuron transmitter, we have talked about acetyl choline. So, we will talk about this information processing part with slightly more details.

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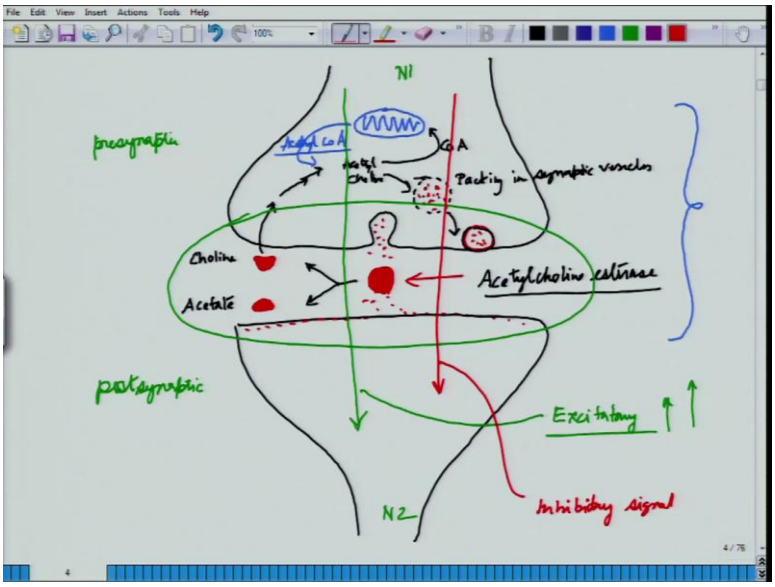

Think of it, there are multiple options. Once again, let me go back to the slide to tell you. The information from, if this is the pre synaptic membrane, and this is the post synaptic membrane. There are multiple options here. In terms of information processing, one option is this, that this one this cendence, is N1, I call this and I call this N2. N1 send an excitatory signal. If N1 sends N2, an excitatory signal, the signal is getting transmitted. But, think of it, if N1 from here send an inhibitory signal, in other words, what is an inhibitory signal? Say for example, N1 leads to the secretion of a neurotransmitter, which upon binding, to a post synaptic membrane, leads to the opening of chloride ions or chloride channels. So, what will happen? Before this, I told you cat ions are moving. So, sodium are moving from outside because outside the cell, sodium is higher; inside the

cell sodium is lower. By the diffusion gradient, sodium gushes inside the cell. Think of the reverse situation. Think of the another situation, say for example, instead of acetyl choline there is another neurotransmitter, which upon binding, say XYZ neurotransmitter, upon binding to the post synaptic membrane, leads to the opening of the ports, which allow the entry of chloride ions inside the cell. If the chloride ion enters inside the post synaptic cells or N2, what will happen?

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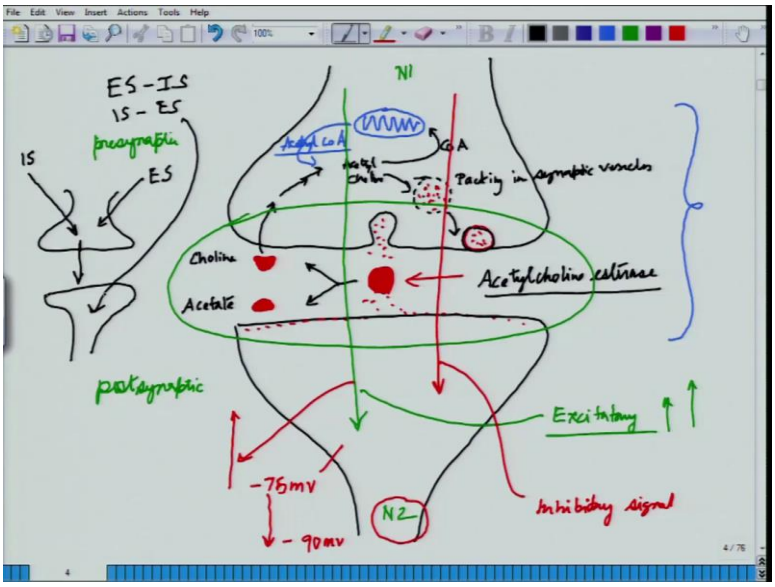

Say for example, this cell is sitting at minus 75 milli volt. So, from -75, instead of going up, which was happening in the case of excitatory, this will go down to -90 milli volt. So, the signal which is coming from N1 to N2, will stop there for some XYZ reason, or part of the signal will remain; part of the signal get stopped; or maybe, at same point of time to increase your complexity of thought. This may receive an inhibitory signal and an excitatory signal. Based on that, it does a computation and it decides what to transfer. What will happen is this, the excitatory signal minus inhibitory signal, or inhibitory signal minus the excitatory signal will decide, how much signal will be transmitted to the next neuron.

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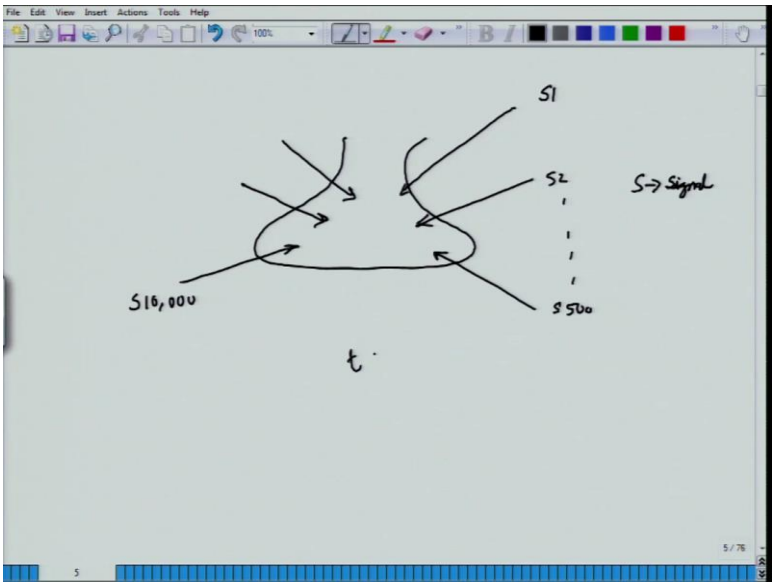

Think of it. Now, just to help you to think more complex, imagine here, is one neuron sitting and this is receiving at one point of time, say for example, S1, S2, S500; I am not adding those, and I have to say, S10000, and S stands for signal. At one point of time, at time T, this cell is receiving 10000 inputs. 10000 inputs could be excitatory; could be inhibitory; could be silent; or could be anything or everything, which we do not know.

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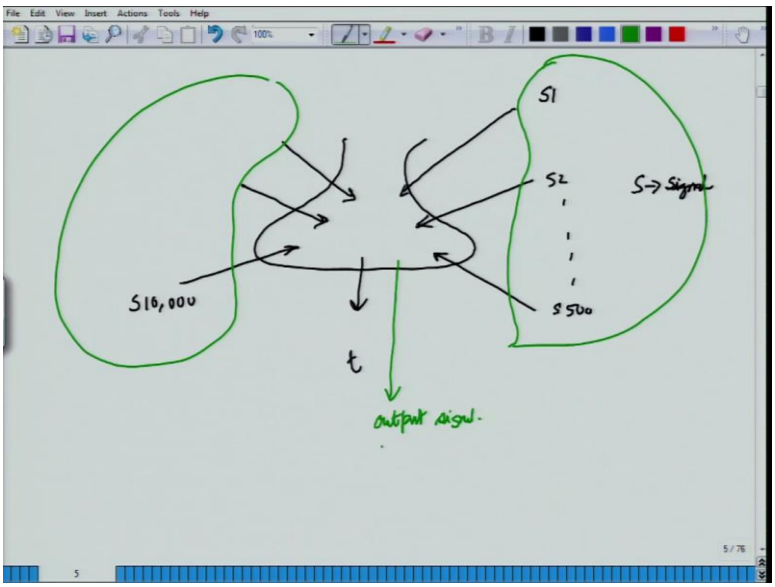

Based on that, in a fraction of a movement, this cell makes a complete algebraic addition of these signals, and that is we call as neuronal computation. It does all this computation

with all this, all this, and all this different signal and decides a lump of signals, what has to be transmitted. The output signal is decided out here. This output signal decides wherever it sends it; sends it to the muscles; sends it wherever XYZ target organ, decides what to do. It is that level of complexity, we are dealing with. The best computer in the world, the best super computer whatsoever you call that, can never ever match this complexity, because of another important thing. If a computer has to do this much calculation, the amount of heat it is going to generate will be enormous. But, when the brain does this computation, it does not generate heat. It functions in a totally different way. So, in other words, you can call those were from electrical or have some bend.

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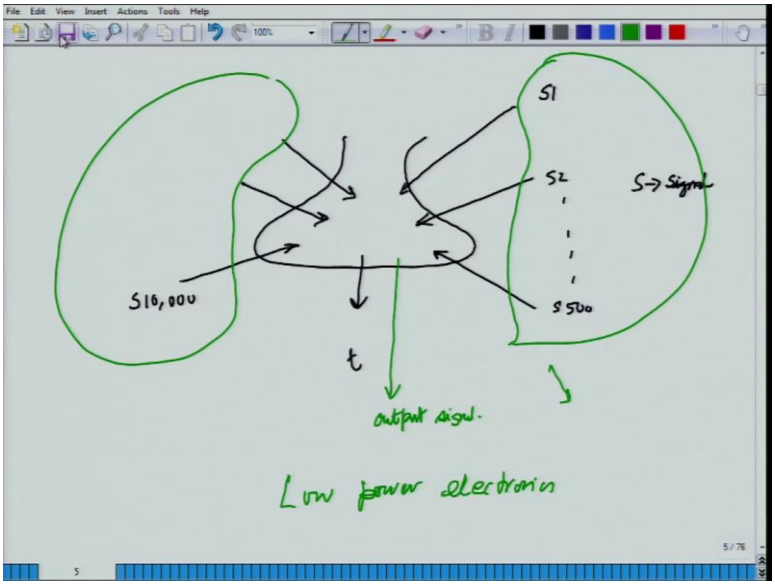

This is the classic situation of low power electronics. Everything happens at a very low power. This is very important to you people to appreciate. This excitatory, the numbers of currencies are very few. This is one way to you to look at it. While I was introducing you there is excitatory and inhibitory neurotransmitter, think of it. That is another way of classification, which adds up to the complexity of this whole procedure, that whether it is inhibitory or whether it is excitatory. What kind of neurotransmitter? That is why, we have to come to the classification of neurotransmitter. Next, I told you a delta time t.

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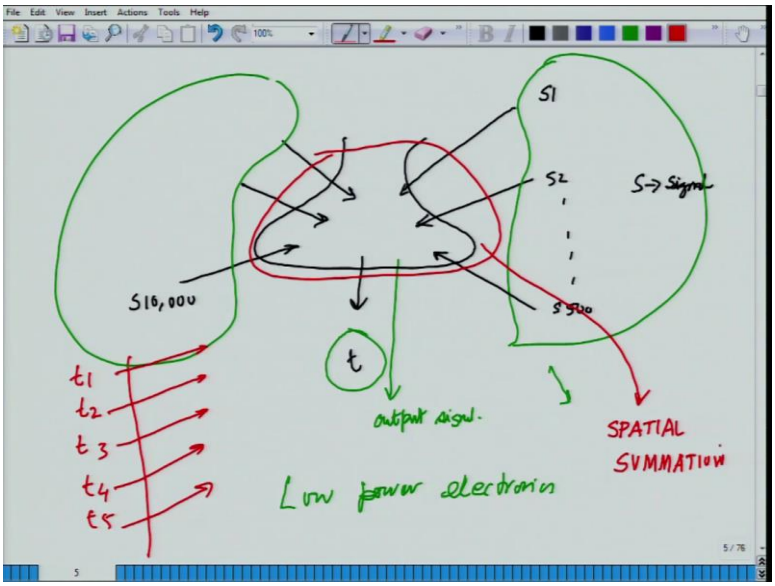

All these things are happening, but think of a situation, where, say for example, I have the time t1 second, t2 second, t3 second, t4 second, t5 second or even less than a second or fem to second or pico second, the signals are coming to this; to this target. There will a different kind of addition that is called, if this one is in the same space; in the same location there, all coming at the same time, mind it, all the signals at say, now, all the signals are coming, likewise. That is on the spot, and that is called spatial summation. Summation is only a function of space; spatial summation. Whereas, think of another situation, where signals are coming like this, over a period of time. It means, my ah is the signal; ah, ah, ah, likewise, tak, tak, tak, tak, tak, these are the signal. So, they are coming over a period of time. So, those kinds of signals, what happens? Say for example, think of this situation.

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All the signals are coming at the same time on a target. This leads to a spatial summation. Now, think of it, here is the base t. So, x axis is the time. Here is the time seconds; signals are coming like this; different amplitude, different magnitude, different time window. So, those, your y axis is the signal; amplitude of a signal. So, if this is the spatial summation, this one is called temporal summation. This is even much more complex.

So, ten thousand inputs over a period of some fem to second or pico second or nanosecond is coming think of it. So, this is the level of complexity a nervous system hardwires it a very very complex and very very interesting system that is why has a call it that our next code. So, we know in biology there is something called as genetic code where we know how the genes demonstrate a function or a protein or a our phenotype now the next code which will the next frontier one of the very profound frontier that would be the neural code what we meant by neural code of this is something very important for you people to appreciate before we go in depth with the nervous system.

So, say for example, someone must have thought you some must have told you that this is a cell phone this is the cell phone who thought you this a cell phone you saw this and you figure out if you see another cell phone ohh this is a cell phone I know this this is a cell phone fine whenever we tell this is a cell phone. Now let us take another example this is say for example, a notebook we call this is a notebook. So, somebody must have

taught you, that this is a notebook. What I meant by that or say for example, I say this looks like a pen or say for example, I have a mic here. So, by looking at it, I can say there is a mic. This is very important. I never call this cell phone as computer or as calculator. I never call this notebook as something, say, stool or something. I never say this. Why I do not say this? This is very important part.

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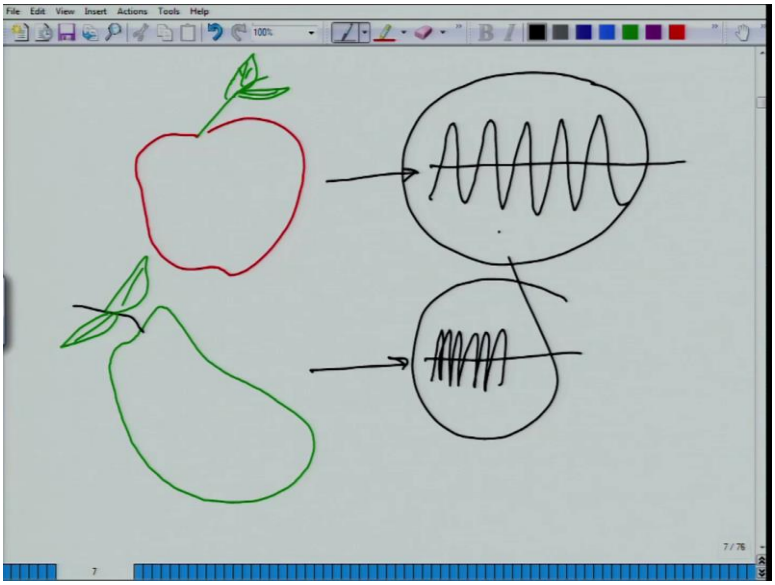

In my system, whenever you look at, say for example, I have an apple out here, something like this. While we were small kids, someone has taught us, that this is an apple. If this is an apple, then it has a neural code. It has a neural signal which is stored in your system as an apple, whereas, if you see, say for example, mango. So, this is kind of, people are eating lot of mangoes today. So, somebody must have taught us, that this is a mango, and it has different kind of signal. Same way, everything what we see has a correlated neuronal code.

That code teaches us, that this is a mango, this is an apple, this is a cell phone, this is a book, this individual is your mother, this individual is your father, this individual is your sister, this individual is your friend, this individual is you wife. They are information stored in your system.

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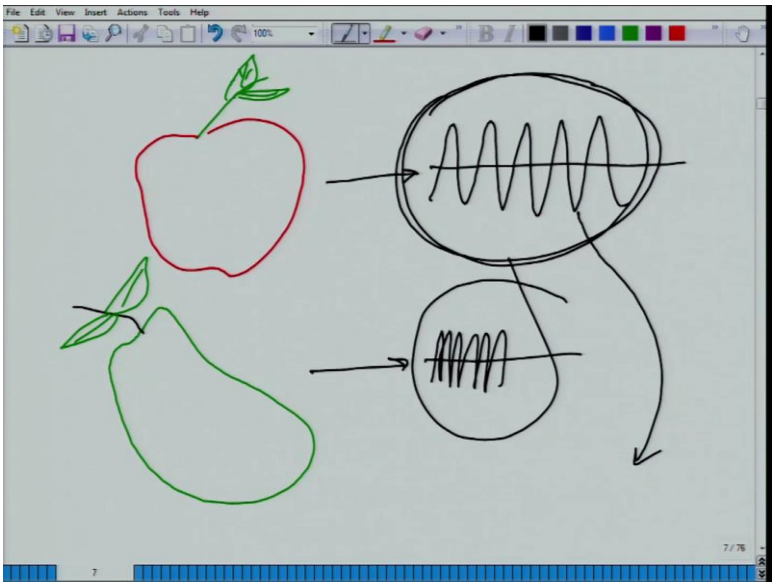

If some way or the other, I know that this signal is the signal for apple. Now, say for example, somebody does not have an eye, who is blind. If I could feed into that individual's brain, that this is the signal of an apple, the person, technically, should be able to visualize that. In other words, could we see a song, you understand what I meant.

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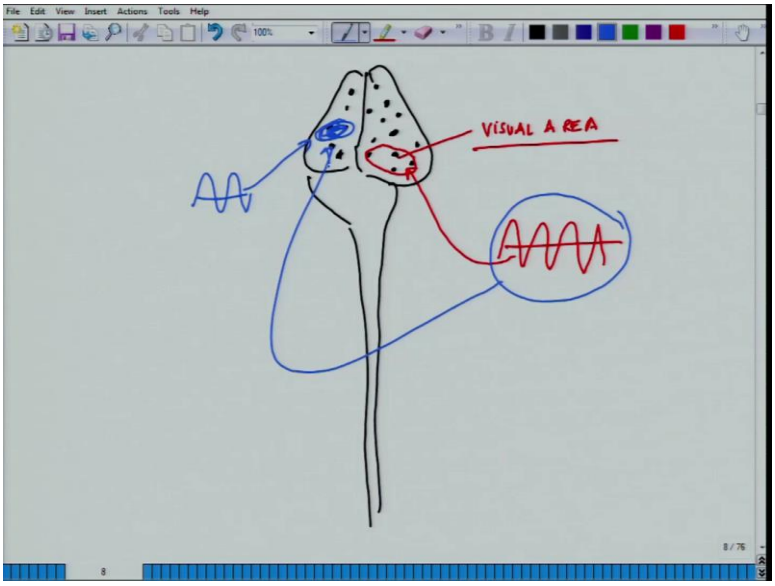

That means like this. If this is your brain and it has different areas which is storing different kinds of information. There are visual areas, there are olfactory areas, which you can smell. There are hearing areas, where you hear, where the sound information is

being coded. So, these are the different areas of the brain. Let us take the example of this. Say for example, this is, I call this as the visual area. In terms of the visual area, I told you, there are signals, which say that this is an apple. This signal is for an apple. Now, imagine if this is a sound area, where sounds are decoded. After all, end of the day, that is nothing, but an electrical signal which is reaching out here. Now, if I feed this signal, the signal of an apple to the sound area, what will happen? A very fundamental question.

If I feed this signal of an apple, that electrical signal to the sound area, could we hear an apple? I may sound very bizzard; I may sound very, like, am I a mad to tell, could I hear an apple. But, think of it. That is what exactly prompts you guys to think, that could I hear an apple; could I see the sound. Because, in the visual area, I am feeling a sound signal. Something, which is sound; could I see the sound. Because, as of now, you are hearing me; you cannot see the waves. Could you see the sound? Could I hear the apple? These fall under one of the most beautiful and challenging area of nervous system called neuronal codes.

What are those codes, which ensure that we identify our parents; we identify the roads through which we are travelling? Because, errors in those leads to dreaded disease like Alzheimer; some of the disease like Parkinson, and we will come to those. What is dementia and all other aspects. So, this is called neural code. Coming back, there are a couple of more things, we talked about spatial summation, and we talked about temporal summation.

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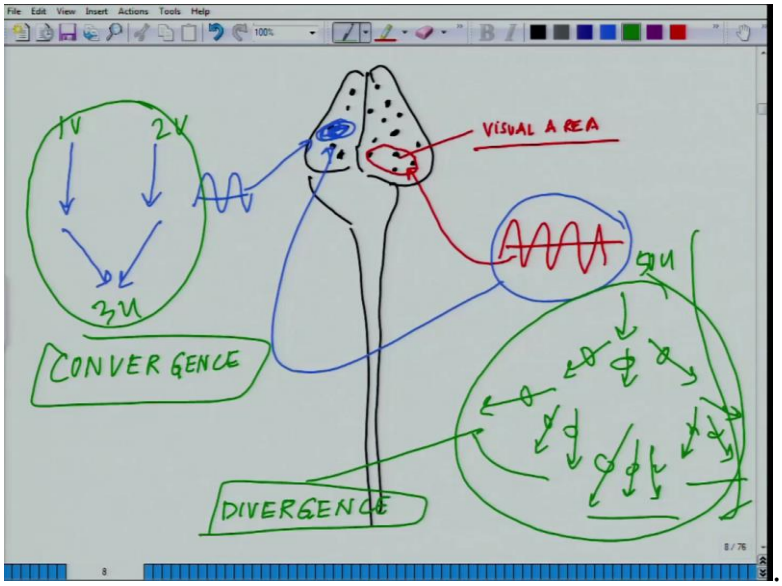

Now, we will talk about another set of summation; say for example, information are coming. These are neurons; they may converge at a point or what may happen is, a signal coming and it is getting split up into, likewise. These are called divergent circuits that you see here. The signals are getting diverged; one signal or it could be a convergent circuit out here.

This is convergence and this is called divergence. So, this is another mode by which signals are getting computed. Say for example, 1 unit signal comes from here; 2 unit comes from here; they may add up to 3 unit, or there may be inhibition or whatsoever. Say for example, 50 unit comes from here, and it is getting divided equally, unequally at these different nodes, then it may again divided equally, unequally, likewise. That is how the signal is getting diverged into different networks. This is how it happens because, think of it, whenever you remember something, you do not remember with one feature; you have multiple feature, say for example, you see a building.

Suppose, you have come to this building previously. How you remember the building? How you remember is, that building is somewhere in this location. Then, you remember who you met in that building. Then you remember what the color of that building was. Then, you may remember, how the building smelling was. Think of it. Smell; olfaction, color; a visual , whom you met; is emotional. So, all these different things gives you a complete picture of that building. In other words, all the information you are gathering at

one point, are being discritised into different component; a visual component; a olfactory component; a sound component; a consciousness component; and the emotional component.

Then, when you recall all of them as one unit or part of it; some of them missing; some of them you may have forgotten; or something. What is forgetfulness and why we forget? How we acquire information is the most, if I have to say, what are the challenging problems of this century; what are those kinds of million dollar problems? Memory; what is memory, what is learning? We will come in depth into this memory and learning.

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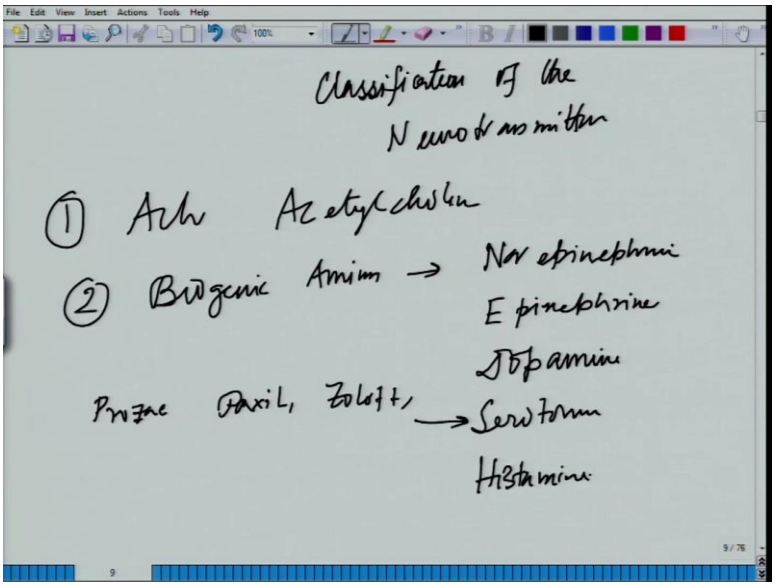

For now, just as I told you, that we will talk about the classification of the neurotransmitter. Let us come to the classification of the neurotransmitter, and then, we will again come back to this debate. Neurotransmitters are wide range of chemicals. It may sound bit of a drab, to go through this classification, but it is really essential. The first one, which we have already dealt is acetyl choline. Second one bigger group is called bwgenic amines. Under this, you have nor epinephrine, epinephrine, then you have doamine, then you have serotonine. While talking about serotonin, those of you who take anti depressant or something like, prozac zoloft paxil, they are nothing, but all serotonin. Paxil zoloft Prozac; it is a bias product. Then, you have histamine in that.

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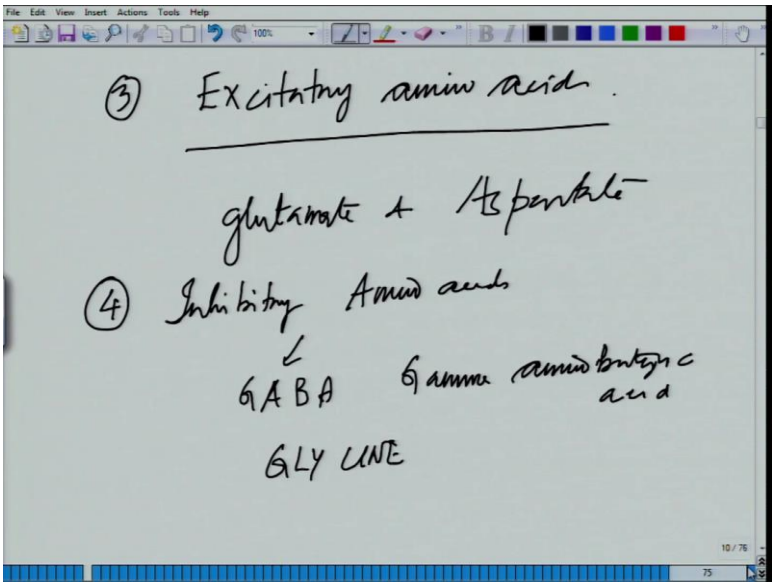

Then, coming to the third one, is the excitatory amino acids. Excitatory amino acids includes glutamate and aspartate. I kindly want you people to go through the structures, just for the curiosity sake. Then, you have inhibitory amino acids, which are opening up the chloride channels. Inhibitory amino acids which includes gaba, gama; full form is amino butyric acid, glycine.

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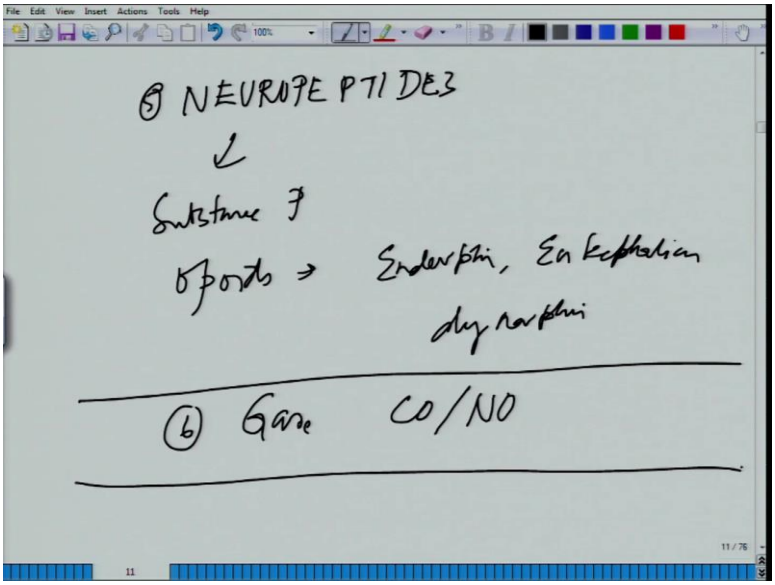

It is the fifth class, which belong to neuropeptides. This is one of the very emerging classes of it. Substance p and opoids, endorphins, enkephalins and dynorphins. Then, you

have some specific gases; one of them already won a noble prize; carbon monoxide nitric oxide, because these gases do not need any kind of getting. They could really go through the membrane as we already disused this.

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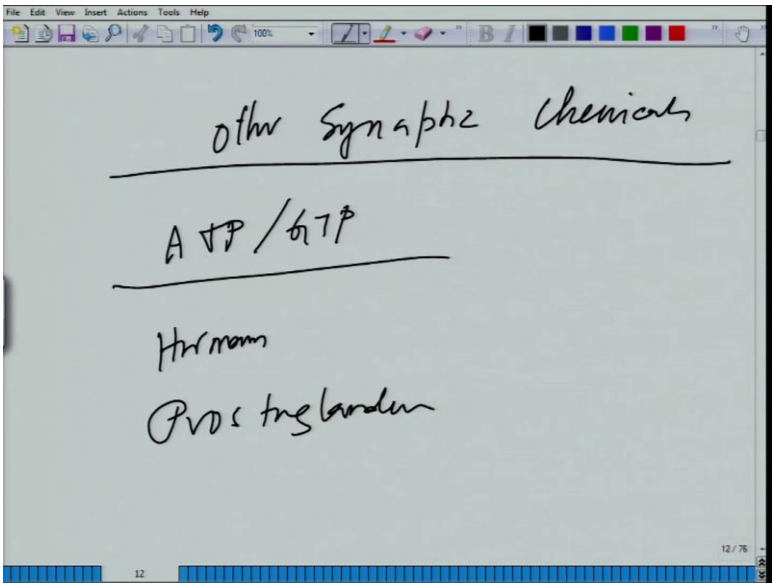

And other synaptic chemicals like, ATP, GTP, hormones; we will come to this and something, like this prostaglandins, for example. These are the broad classification of the neurotransmitters. After giving you this broad classification of neurotransmitters, and as you mentioning about that prozac paxil, and all these kinds of drugs, which are. In other words, what does this mean?

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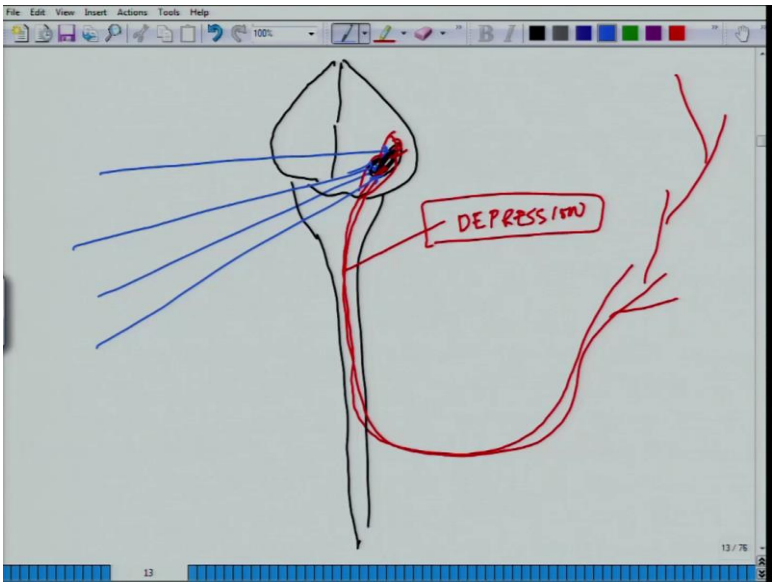

Say for example, if I have some way to define, let us think of it. This is the brain and this is the spinal cord, likewise. Now, if some way or the other, say for example, this is some kind of a circuit which is governing our multiple processes coming through and like, and there are lot of network. Imagine this is the circuit, which I have put in red, is dictating this person, is getting more activated. Whenever, this circuit is getting more activated, this person goes for depression. In other words, some way or the other, if I could modulate this circuit with some XYZ component, whenever we talk about depression or high or anything; what does that essentially means is this.

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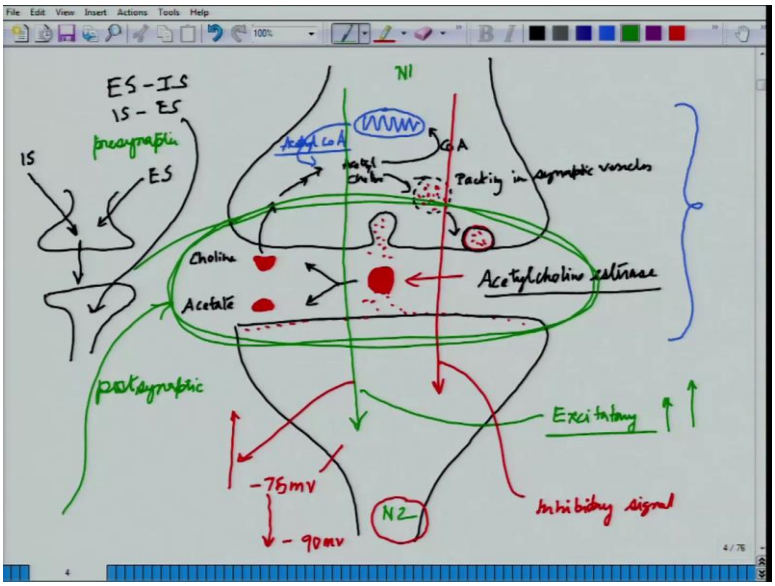

In a very simple term, in a very most fundamental term, if I had to tell you, your depression, your happiness, your everything lies in this zone. This is where all these behavioral trades of individuals are being regulated. If you could modulate this, you can modulate several things, but to modulate this is a very challenging task. At your synapses lies that in that particular, coming back, where I was trying to draw the circuit.

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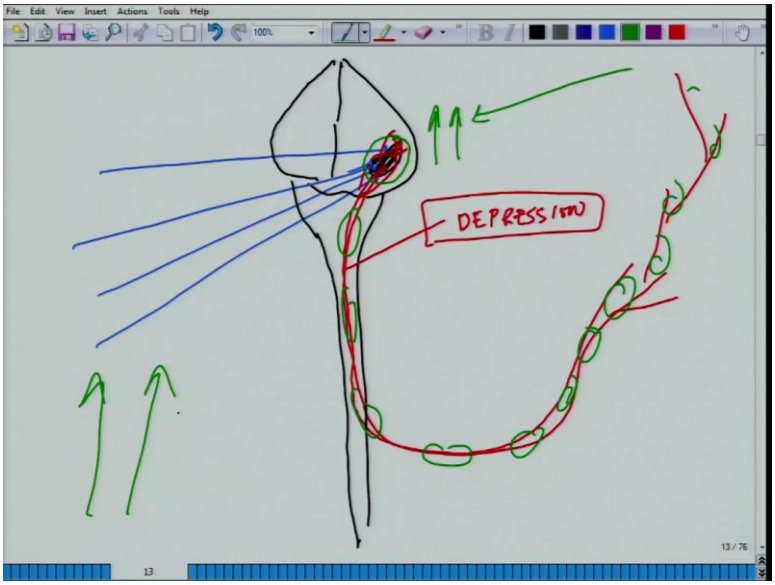

All the synapses which are involved all this pathway, ensuring that this person goes in some form of a depression on something. This kind of circuits leads to; you are continually fed with some specific kind of neurotransmitters here. Now, your option is that, either you may oppose those neurotransmitters by XYZ chemicals, or if the case is reverse, that there is a lack of those neurotransmitters, that is why, this person is suffering from XYZ kind of disease. Then, you enhance the amount of those neurotransmitters, and we will to this, in terms of eldopa and the Parkinson and everything.

This is the overall understanding what I expect from this class for you people to understand. End of the day, it is the brain which dictate several things; all our behavioral traits; all our patterns; all our behavior; how we react to situation; These are all governed by the brain and it is governed through the most simple, yet, most complex structure called as synapse, and the network of synapses. By this time, I believe, you people must be trying to appreciate that. If at one point of time or over a period of time, there are

10,000 inputs coming to an individual neuron, and there are 1000s and 1000s and 1000s of such neurons.

What a complex super computer are we talking about? Not even a computer; this is above that. This is one of the bionic computation machines, which helps us to be what we are. It is that complex and that serious. So, with this I will close on this class. We will come to the next class where, we will be talking about the neuromuscular junction, in depth, about how the electrical signal is being translated into a mechanical signal. Before we start that, what we will do; we will talk about the structure of the muscles. Then, in the next class, we will talk about three circuits. We will talk about reflex circuit and what is reflex circuit. We will talk about the neuromuscular junction, and we will talk about how the electrical energy is translated into mechanical energy.

Thank you guys for your attention.