Cognition and its Computation
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Lecture - 14
Synaptic Plasticity

Welcome. So, we have been discussing about neurotransmission and we introduced the concepts of synapse, the neurotransmitter, neurotransmitter receptors and how a synapse communicates with the how the pre synaptic side communicates with the postsynaptic side through the synapse and so, we introduced the term synaptic strength in the last lecture in the neurotransmission part.

So, let us look into that in a little more detail, where because as we said that the synaptic strength is what actually determines how much influence does the pre synaptic neuron have on the postsynaptic neuron.

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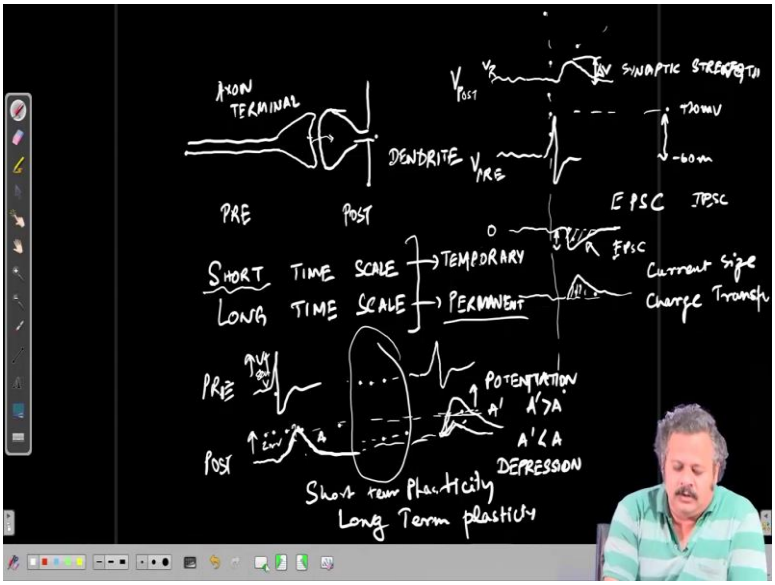

So, as if we remember the structure that, we have been using that there is a pre synaptic side with the axon terminal making a synapse on the dendritic spine on the postsynaptic side. So, this is the dendrite and this is the post side dendrite, there is the pre synaptic side and this is the axon terminal.

So, the neurotransmitter release finally causes a current flow in the postsynaptic neuron into the post synaptic neuron with positive ions going in or coming out or negative ions going in or coming out and depending on that, there is a change in the potential in the postsynaptic neuron that is if we are recording the voltage of the post synaptic neuron let us write it as V POST.

So, let us say it was at V rest initially and there is a spike in the pre synaptic side let us say V PRE looks like this and this voltage is about this is around minus 60 milli volts and this is around let us say plus 20 milli volts. If it is ionotropic neurotransmitter a release or ionotropic neurotransmission then there is an immediate change in voltage in the postsynaptic neuron with this height basically making the postsynaptic neuron change its voltage by that amount and that height is what we refer to as a measure of the strength of the synapse that is synaptic strength.

So, this height is usually in the order of few milli volts, but if we have a very strong synapse, it can be such that it causes the postsynaptic neuron to directly fire an action potential that is it crosses threshold with one input and such synapses are also there like in the brain stem in the auditory pathway which are known as like synapses that are called calyx of held that are very very strong and can basically every pre synaptic spike produces a postsynaptic spike.

Similarly, there are also synapses that are very small in the sense that the strength is very small physically also recently we have learnt that actually size correlates with the synaptic strength size of the synapse. And so, they are very small in strength and size and can be just half a milli volt or so, or even less and it requires many many inputs altogether to cause the postsynaptic neuron to fire an action potential.

So, there can be a wide variety of strengths and it is the modulation of this strength this delta V caused by the synapse caused by the pre synaptic terminal is what determines the strength of the synapse. There is another way we can measure it that is we can measure the actual current that goes into the synapse through the synapse into the post synaptic neuron.

So, instead of measuring voltage as we were doing if we could measure the current that flows due to the pre synaptic spike what we will get is the post synaptic current. It can be excitatory in nature or it can be inhibitory in nature that is IPSC or EPSC. So, what we

the convention is that for excitatory postsynaptic currents we draw it as an inward or a negative current and this is what is an EPSC.

So, initially the current is let us say 0 that the baseline there is no current flow at rest as we had a discussed earlier and so, this is an excitatory current or EPSC. So, this height is also a way to measure synaptic strength and particularly the area under this EPSC or area under an IPSC that is positive going current which is equivalent to the charge that is transferred into the postsynaptic side due to a spike in the pre synaptic neuron that also is a way to measure the synaptic strength.

So, either the current, size or the charge transfer which is the area under the EPSC or IPSC. This particular shaded regions in the EPSC profile or IPSC profile that also signifies the strength of the synapse. So, this synapse strength the change in it as you can imagine can occur in many ways and can take different amounts of time to occur though that is one side of it.

And the other thing is the change in the strength can be short lasting that is the synapse changes its strength is short lasting that is it changes the strength for a little while and then comes back to its original state or it can be long lasting that is the synapse changes its strength and remains like that for a long period of time hours minutes sometimes even years.

So, that brings us to the issue of the time scales of plasticity that is a short time scale or long time scale. Actually what we really mean is many different time scales of plasticity because either it is temporary for different varying periods of time, temporary or it is more permanent at least in the periods over which measurement is feasible. We cannot always may measure the strength of synapse in the brain for periods that are longer than hour or even sometimes half an hour to 45 minutes.

So, in that sense they are permanent, but we do have evidence to support the idea that these permanence is actually permanent which can last up to years; not direct measurements, but other indirect evidence. So, we so, basically what we mean by this plasticity is that ok, I had a pre synaptic spike I had a. So, this is pre, this is post. I had a change in the potential. So, this is the voltage this is also voltage, but at a much larger scale that is this is let us say 2 milli volts and this is around 80 milli volts this range.

I have this change let us say A milli volts and after a period of time due to some manipulation, I have the same input in the pre synaptic side that is a spike in the pre synaptic side that causes a very different output now and this is A prime let us say. So, this change that is beyond what might be expected from stochasticity or variability of responses. So, as we had introduced the term probability of ion channel being open or closed and similarly the synapses can have some unreliability.

So, what we are plotting here as EPSP of height A and A prime are actually average effects of many such of repeated input spikes or pre synaptic spikes and repeated measurements of postsynaptic potentials and that is the A that we are drawing here or representing here. So, after a period of time if this amplitude changes to A prime that is not statistically explainable from the variability in the measurements that is what is plasticity. It may increase or it may decrease.

So, increasing is potentiation and decrease. So, this was our height of A. The A prime may be greater than A that is potentiation and A prime being less than A is what we call depression. So, this potentiation and depression can be short lasting or temporary or long lasting or more permanent and so, this brings us to the two terms short term plasticity and long term plasticity.

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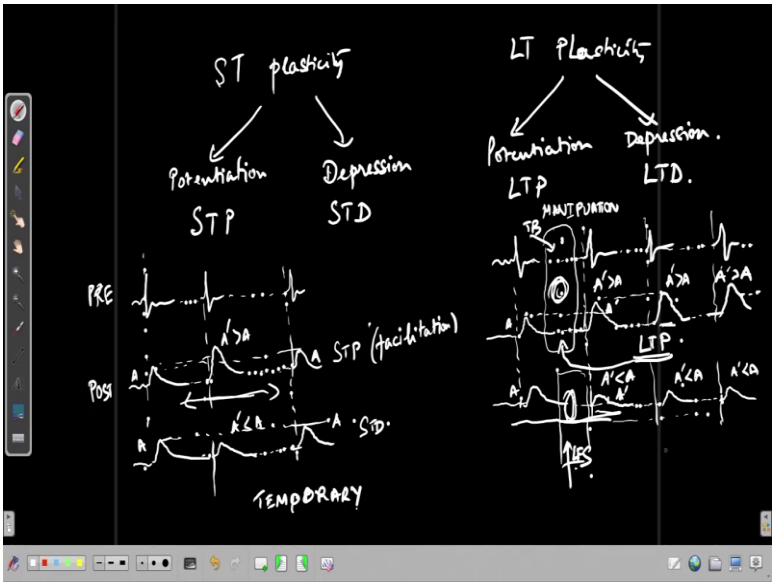

So, in this short term plasticity, short term plasticity it can be potentiation or depression that is strengthening of the synapse or weakening of the synapse that is depression.

Similarly, the long term plasticity can also be potentiation that is strengthening or depression or that is weakening. So, this is basically what we call short term potentiation, short term depression, long term potentiation and long term depression.

So, in short term potentiation and short term depression what we essentially mean is that let us say we have a pre synaptic spike and that produces this amplitude a of EPSP in the postsynaptic neuron with a short delay and after a while we do another spike and what we see that the strength of the synapse is increasing.

And that is short term potentiation because if we let the system be like this for a few seconds to minutes what will happen is that again if we have a pre synaptic spike the synapse goes backs to goes back to its original strength that is A. So, this A prime is greater than A for a short period of time in between and after that if we leave the system just like that at rest the system goes back to its original state that is the synaptic strength goes back to what it was originally that is A.

So, this temporary nature of change in synaptic strength is what we call short term plasticity. The corresponding thing for depression is that essentially this A prime will be less than A. So, let us for a sake of completeness let us draw it this is A and after that this A prime is less than A and if we leave it at rest for some time longer, it goes back to the original height A.

So, this is STP or also known as a facilitation; short term facilitation and this is short term depression. So, the temporary change is what we mean by short term temporary change. In the long term what we mean is that we have a pre synaptic spike there is a postsynaptic potential of height A then we do some sort of manipulation to the system. So, this is the key the for the long term changes.

We make a manipulation to the system some kind of activity post synaptic and pre synaptic activity we will go into the detail in a little bit. And what happens is let us say now we have a pre synaptic spike and the postsynaptic potential increases, let us say this is A prime and this A prime is greater than A.

Now, we let the system at rest for let us say few minutes. I again have a pre synaptic spike and I measure the postsynaptic potential it remains at A prime greater than A and I repeat that after many minutes and I get that same A prime greater than A. And this lasts

for half an hour to an hour and this is what we call long term potentiation and the key of this long term potent occurring is what manipulation we are doing in this period that induces the long term plasticity.

And equivalently we can think of long term depression as let us say the postsynaptic potential was A here at the first spike then again we have some kind of manipulation which will be different from what we saw what we did earlier. And now we have another pre synaptic spike and we see a smaller A prime and that is A prime is less than A and this lasts after many minutes we get the same A prime less than A again many minutes this for a pre synaptic spike we get an A prime.

That is less than A that same A prime actually that is it is this strength is lasting for scales of minutes to hours. So, all these are experimentally determined and so, there is a physical limitation to how long we can keep on doing these measurements for a particular pair of neurons connected via synapse.

So, the main difference is that in the short term and long term potentiation or depression is that there is involvement of protein synthesis or that causes the long term changes. The short term plasticity actually does not involve protein synthesis that is in the long term case actually there is there are more neurotransmitter receptors for example, that are generated because of expression of that particular protein and then it takes minutes I mean 20 to 30 minutes for this protein synthesis to occur.

And so, we having more receptors on the postsynaptic side actually causes the current to increase or let us say it reduces the number of postsynaptic receptors that can also cause change in the synaptic strength. So, let us go into some of the ways in which the long term potentiation and long term depression are induced. So, remember we had we said this manipulation here this manipulation or this manipulation.

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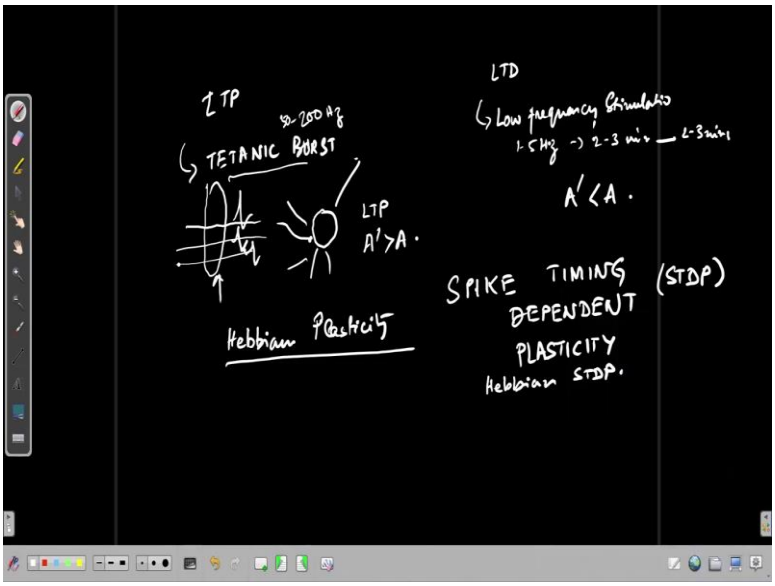

So, there ways in which this manipulation can be done and that is with what was originally shown is for LTP is tetanic burst of excitation; tetanic burst of excitation. So, this was shown in a particular system which has to do with the hippocampus. The particular region in the hippocampus CA1 and its input fibers that are thalamic that are the Schaffer collaterals.

And so, you if you is there is a tetanic burst of stimulation for let us say at 200 hertz for one second in the pre synaptic side that is let us say there are many fibers here and electrically we produce spikes on the pre synaptic side. These fibers are projecting onto a set of post synaptic neurons and let us say we are measuring from a postsynaptic neuron and many fibers might be projecting on to this same neurons dendrites ok.

And so, we are causing action potentials in these fibers that travel and cause the postsynaptic neuron to fire action potentials. And with this kind of a tetanic burst if we do the same measurements as we discussed in the earlier slide and the in this slide the measurements that we have shown here, so, that will show that there is LTP that is induced by this kind of stimulation. Similarly, the long term depression can be induced by low frequency stimulation low frequency stimulation.

Like, so, this is about 200 you know 50 to 200 hertz for a second to a few seconds. And here low frequency stimulation that is let us say 1 to 5 hertz for a few minutes 2 to 3 minutes and maybe with a gap and again for 2 to 3 minutes and this process shows as we

have discussed earlier this kind of behavior where this manipulation of low frequency stimulation is occurring here and this is the tetanic burst stimulation that is occurring here that induces long term plasticity where A prime is greater than A, low frequency stimulation induces depression that is A prime is less than A.

So, here this A prime is less than A if we do the same measurements and here A prime will be greater than A. So, these were how the synaptic plasticity was induced long term synaptic plasticity was induced and studied. There are many I mean lot of work that has been done beyond this that studies how this actually increases or decreases the actual synaptic strength. For the purposes of this course we will a not go into that detail, but we will remember it in this way.

That if we have pre synaptic activity followed by postsynaptic activity or pre synaptic activity that is causing postsynaptic activity in large amounts in a short period of time that will induce a long term change and this the opposite of that if we have very low frequency stimulation in the input and the post synaptic neuron is still firing action potentials then we get long term depression.

The overall implications of this process is that I mean when we get into the further details where we will try to understand different the different mechanisms behind let us say attention or some learning process these LTP and LTD is what we will keep on referring to as being involved in those processes.

And there is another particular way or more recently people have studied how this long term potentiation and long term depression can occur at synopsis or rather model at synopsis is based on spike timing dependent plasticity spike timing dependent plasticity. So, this is what is STDP.

So, so far whatever we have been talking about here is actually the classical Hebbian kind of plasticity. What this is refer I mean this is known as the Hebb's rule is that synapses or neurons that fire together wire together neurons that fire together wire together and this sort of scenario for tetanic burst causing LTP and low frequency stimulation causing LTD and Hebbian STDP which we will describe in the next lecture in more detail actually in detail.

These are all what are the synapses that follow Hebb's rule that is an input that causes an output that is this is firing the pre synaptic neuron is firing, the postsynaptic neuron is firing caused by this pre synaptic neurons firing this or within a very short window within a small window following the pre synaptic neurons spike or action potential. This kind of Hebbian plasticity is not necessarily true for all synapses.

So, it may be that some of the synapses are very different from this and so, we will refer to them in through the spike timing dependent plasticity rules. So, with these ideas of LTP, LTD and spike timing dependent plasticity, we will come to a close of these ideas of long term plasticity and in the next lecture we will discuss further on spike timing dependent plasticity and the mechanisms behind some of the short term phenomena that we have not talked about.

Thank you.