Cognition and its Computation
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Lecture - 41
Learning in Biological Neural Networks

Welcome. So, you have been learning about learning and memory in the recent in the last lectures. And, you have gone over theories of learning theories of memory and the disorders of learning and memory and so, in this weeks lectures you will learn more about how learning occurs in actual biological networks in; that means, in the brain. And, it is not necessary I mean we will discuss examples even from the vertebrate system in even from the in vertibate system like the aplasia and of course, rodents and primates, non-human primates.

And of course, humans you have we have very little understanding from the single neuron level as to how learning occurs. However, it is easily extendable from the primate and non-human primate and the rodent cases, even the nature and properties of the neurons that both share and even in vivo even x vivo experiments that show similar properties across different species, even humans and non-human primates and rodents.

So, as you have seen before that learning or as you have been told before that learning is based on plasticity, synaptic plasticity to be more specific. And, we have discussed how this kind of synaptic plasticity manifests itself in the single neuron level. And, how the input activity of synapse at synapses that is the if we go back to our canonical structure of the pre synaptic neuron and postsynaptic neuron.

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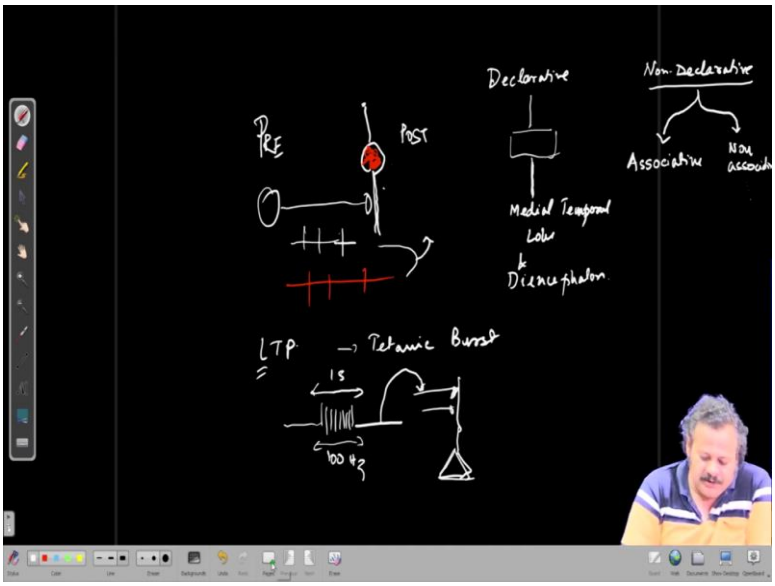

Pre synaptic neuron and postsynaptic neuron whose, the synapse is made on a dendrite of the postsynaptic neuron and this is the output of the postsynaptic neuron. So, we know how the activity or action potentials in the pre synaptic neuron and how the activity simultaneous activity in the postsynaptic neuron. If we mark it with red, at the same time the relation between these two determine how this synapse changes over time based on the rules of plasticity, that we have learnt about it.

It can depend on the type of synapse of course, as we have mentioned. So, this kind of learning is or this kind of synaptic changes is happening at the network level as a whole when an organism or an animal learns to perform a task. And in fact, as you have learnt in the previous weeks that memory and learning are inherently tied together. In the sense, that with memory only we learn something and then we recall it from memory to actually act based on the learning.

So, we cannot really tease them apart so easily. So, in these discussions, we will be talking about either or kind of scenarios where we will be talking of learning or memory depending on the kind of structure we are talking about. So, it really depends on which structure is involved in that particular process, that determines the particulars of learning and memory that is involved in that process ok.

So, if we think of memory, there is two kinds basically declarative and the non-declarative. So, declarative memory is as you have known is basically about facts and

points to remember directly which have particular form that is they can be declared. And, this kind of memory is associated or is based on learning at the medial temporal lobe and diencephalon.

And, non-declarative memory can be of many different kinds of which the broad two categorizations are associative and non-associative. And, these involve variety of structures in the cortex, in the cerebellum and in the periphery, the ones that are involved with reflex pathways in the non-associative memory. They are involved they involve much more peripheral systems.

And, associative memory again depending on which structure is involved and what kind of paradigm is used in learning or the kind of learning that is associated or rather kind of learning it is based on, the structure can be very different. And so, it is mainly corticalum and some sub cortical elements are of course, involved as we have seen in reward pathways and so on.

So, in general the declarative memory part is thought to be controlled or rather based on the titanic burst kind of stimulus. So, as you have learnt it is mainly based on LTP: Long Term Potentiation based on titanic burst, where if we remind ourselves it is basically if we have a strong stimulation in the pre synaptic side at about100 hertz for 1 second for a period of 1 second, that is if we have synapses here and this is the postsynaptic neuron, the this is the dendrite.

And, we are providing a stimulation onto one of these afferents or axons projecting on to the stimulus. Then, this synapse strengthens in a form that the EPSP produced by this synapse is much stronger after the titanic burst and it lasts for a very long time. And, it is in fact, the long term potentiation or long term memory.

This kind of potentiation inherently is associated with in with an association which we will discuss more in the non-declarative memory and associated learning which is that without this kind of titanic burst stimulation, we wouldnot get this kind of learning, this kind of long term potentiation.

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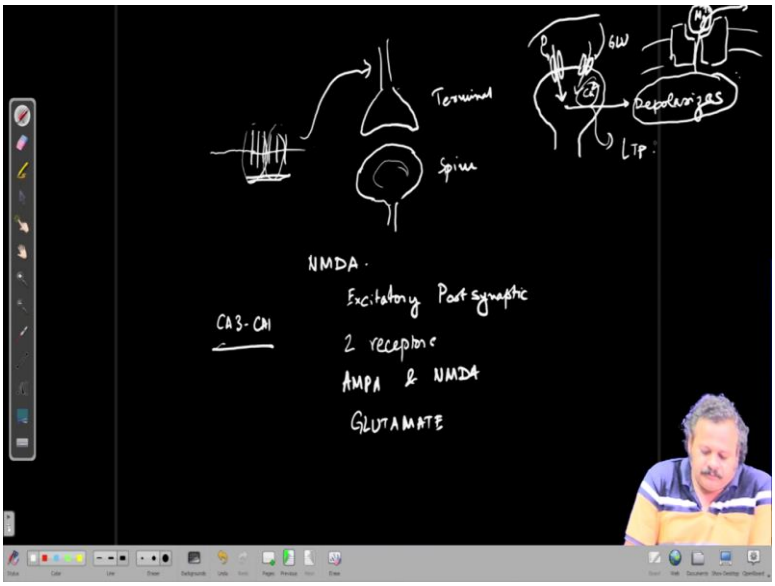

And, that is because what is understood is that with this titanic burst stimulation, if you recollect so, this is the synaptic terminal. And, here we have the dendritic spine on the postsynaptic neurons dendrite, it is the spine and terminal. So, this high level of stimulation applied pre-synaptically for a brief period of time, what this does is actually causes a depolarization in the postsynaptic spine initially.

And, that depolarization then as you may recollect actually opens up the N methyl D aspartateion channels, that are involved in the long term potentiation process. So, the way it happens is so, this is in the CA3 CA1 synapse, the one that is involved that is in the hippocampus, the kind of synapses in the hippocampus. The CA 3 and CA 1 are types of neurons in the hippocampus, that you have learnt in hippocampal structure.

And, it is the it is synapses in here that are involved in the declarative memory part and learning of such things. And, the experiments in this case show that if we stimulate on the input spines on the inputs to the spines of the CA 1 neurons, these spines are form the excitatory postsynaptic parts postsynaptic part. And, there are two kinds of receptors that are involved that is AMPA and NMDA and the glutamate is the pre synaptic neurotransmitter.

So, if we look at this pine like so, there are AMPA receptors. So, glutamate is released that goes and binds to the AMPA receptors and allows cations to go in. So, this flow

depolarizes the post synapticside. And, there are NMDA receptors here which are also activated by glutamate, then require glutamate to bind in order to activate them.

But, they have their structure is somewhat like this, where there is a room for a magnesium ion Mg 2 plus to be present and block the pore of the NMDA receptor. And, because of this positive ion, when only when this depolarization happens in the postsynaptic side, this magnesium gets knocked out and that allows with the binding of glutamate, that allows calcium to come in.

So, inherently there is this association that is forming that initially the depolarization is finally, causing the calcium to come in. Without that initial depolarization, the calcium flow wouldnot happen and this calcium is responsible for the long term potentiation as we have learnt before. So, primarily this kind of mechanism in the hippocampal circuits are involved in the declarative memory associated learning.

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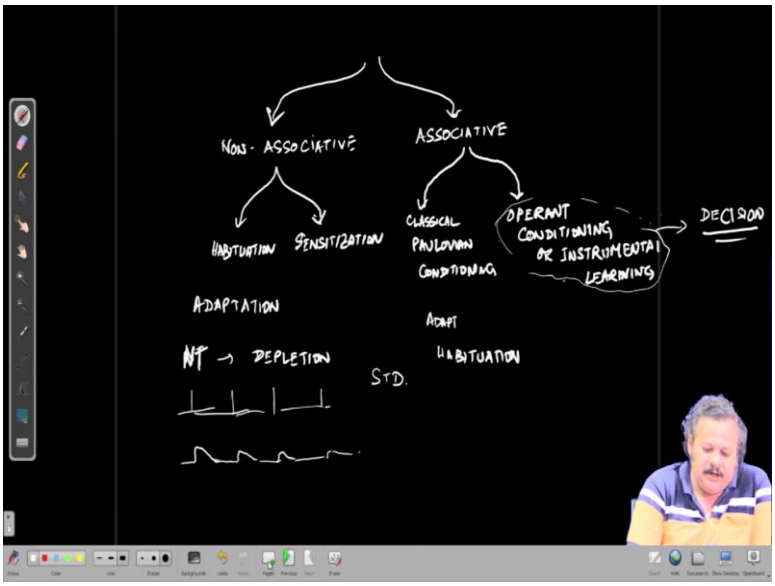

Now, if we go to the non-declarative memory associated learning; so, we will talk about the two kinds of learning here. One is non-associative and the other is associative. In the non-associative cases, there are primarily two kinds of learning and that is habituation and second is sensitization. And, in associative learning there again are primarily two kinds.

Of course, there are many variants that are studied in the literature, but broadly there are two kinds. The one is the classical Pavlovian conditioning and the other is the operant conditioning or instrumental learning.

We will see that it is this operant conditioning or instrumental learning plays a big role later on when we discuss about decision making. It is the choice of action that is involved in operant conditioning that actually leads to decision making. So, that will be taken up later on. And so, if we think about habituation, it is more like an adaptation phenomena. It can happen at multiple levels, that is at the level of the whole organism or a whole human or even at the level of a single synapse or a network of neurons.

Like we have talked about the neurotransmitter, for the neurotransmitter case in the single neuron level; the neurotransmitter depletion with repeated activity essentially leads to adaptation or habituation. That is if we, if you remember in terms of short term depression, if we keep on repeating a stimulation at a synapse, the synapse synaptic output on the postsynaptic site, gradually keeps on decreasing, leading to no final response in the postsynaptic site.

So, a similar thing is our situation when we adapt to loud sounds, initially when a loud sound comes on; we are astonished or rather we are startled. And, as the loud sound keeps on repeating, gradually we get habituated. And, this habituation leads us to accommodate our environment in order to accommodate in the environment where there are stimuli that initially produce an effect.

But, we soon find that they are inconsequential in terms of our goal directed actions or goal directed behavior that we are constantly performing in our real life. And so, we phase them out and in fact, attention can play a big role in this habituation. In fact, we initially as you may remember from the framework work of attention, the saliency filters in the bottom up side of attention, the saliency filters pull out these kind of stimuli into our working memory initially.

And, we initially provide a behavioral response also like a startle response or in case of the loud sound. And, but eventually it it phases out from our attention in the sense that it goes out of our working memory. And so, we adapt to it and that is the basis of habituation, adaptation or habituation ok. So, this is a form of non-associative memory, in the sense that there is only one stimulus or only one element in the environment to

which we about which we are learning or about which we are reacting in a particular way in a learned way.

I mean in the sense that we are no more interested in that kind of sound or in that kind of stimulus.So, that is why it is non-associative, that is there is no other stimulus or no other outcome associated with it. On the other hand, associative memory we will see that there are there would be two kinds of elements involved in the learning.

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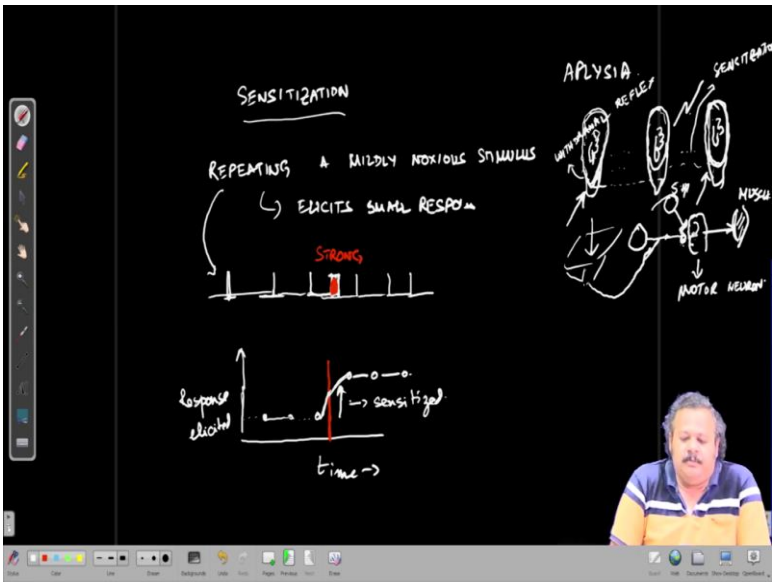

So, going on with the non-associative part of learning, the other important phenomena is sensitization. This is a particular kind of learning which is seen in invertebrates and vertebrates and rodents and even humans. In the sense that, if we have a mildly noxious stimuli stimulus presented to us, we react to it by avoiding it um. I mean not vehemently in that sense that not so strongly, that is the the response that noxious stimulus elicits is a mild, because it is a mild noxious stimulus.

But, if we keep on repeating a mildly noxious stimulus, it elicits a small response every time until maybe we habituated. But so, if let us say this tick is this repeating noxious stimulus, that is occurring once every few minutes and then in there a very strongly noxious stimulus is embedded. So, this is a strong negative stimulus and then our original mildly noxious stimulus continues. Then, what is observed is if we have some measure of the response to the noxious stimulus and this is time, this is response elicited.

Some quantification of the response in the sense of how much we pull back or something like that. Then, for each of the stimuli, we have a response each of the mildly noxious stimulus, we have some response. And, what happens is if we have the noxious stimulus, the strongly noxious stimulus in between; then there is a jump in the strength of the response to the mildly noxious stimulus.

So, in other words this jump is being caused, that is we are sensitized to the environment. Initially, what is thought to be at play here behind this kind of learning is that with the mildly noxious stimulus, we are ok or the organism is ok initially. But, if all of a sudden that strong noxious stimulus comes, it is almost like the organism believes or seems to understand that it is a avery aversive environment in general.

And so, its responses to such stimuli has to be even more and that is what happens during this sensitization. And, the this phenomena was first studied in the Aplysia and a lot about a learning is based on this model organism Aplysia, because it has a very simple nervous system. And, many initial ideas at the molecular level for learning came from this system and led to lot of understanding about the mechanisms of learning underlying in the synaptic level and the molecular level.

So, the experiment that was done is actually in the Aplysia, it has a long it has a tail side and it has a gill region in the middle with a spout. And so, if we produce if we provide a mechanical small stimulus to it what happens is the the Aplysia pulls back its tail like so and the gills. So, this is like a withdrawal reflex. So, now if along with this stimulus going on for some time, if all of a sudden the same animal or the Aplysia is gills and then a spout is given a strong electrical shock.

It retracts its tail very strongly and much more compared to there is the retraction here, in the case of the mechanical push or pinch. And so, also the gills are withdrawn internally to a great degree. And, beyond that again when the mechanical stimulus is applied, now it elicits a much stronger response or stronger withdrawal like close to what it was observed during the electrical stimulation. So, this sensitization (Refer Time: 26:25); this sensitization occurs through strengthening of synapses.

So, actually what happens is that; so, this is the skin surface let us say and there are receptors, that are encoding this mechanical touch on there. And, this is going as input to a sensory neuron that projects onto a motor neurons, motor neuron that is driving a

muscle that is controlling the pull and push of this gill and the tail. This is the muscle that is doing that.

So, this is the motor neuron. Now, there is an extra element which is a serotonergic serotonergic neuron, that is modulating this synapse. During this sensitization what happens is that this serotonergic neuron comes into play and it enhances the postsynaptic response through the inflow of calcium in the postsynaptic site. And, that produces more receptors on the postsynaptic site leading to a much stronger response when the same stimulus is coming in.

So, this extra noxious stimuli is activating another pathway where this phi HT or serotonergic neuron is activated which is the neuro modulatory system; I mean system of neurotransmitter that is involved in modulating other synapses. So, that causes the strengthening of this synapse which leads to a stronger response. Again, just like what was happening when the actual response, when the actual electrical stimulation took place. So, with that single short sort of learning in this case this sensitization is happening by strengthening this sensory to motor synapse.

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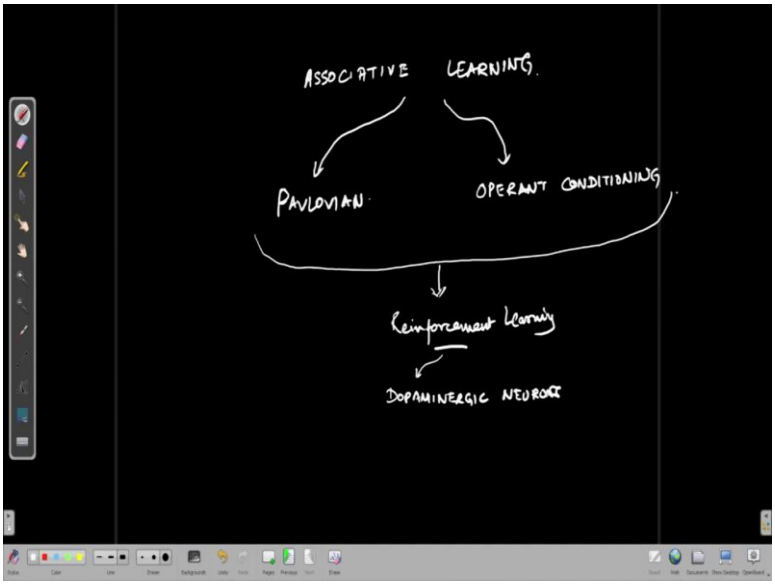

So, beyond this we now have the following to discuss, that is in terms of associative learning and as we said this has the classical or Pavlovian and the operant condition. What we will see in the next lecture is both of this can be cast into a form of reinforcement learning.

And, this kind of reinforcement learning involves different neurotransmitter systems, but primarily we will keep our discussion to the dopaminergic neurons, that are as we have known involved in the reward pathway. So, with this we end our lecture, initial lecture on the learning and the second lecture on learning and further examples will be taken up in the following lecture.

Thank you.