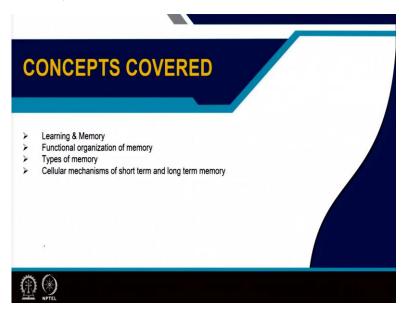
Basics of Mental Health & Clinical Psychiatry Doctor Arijita Banerjee Doctor B. C. Roy Multispecialty Medical Research Centre Indian Institute of Technology, Kharagpur Lecture 22 Learning & Memory - 1

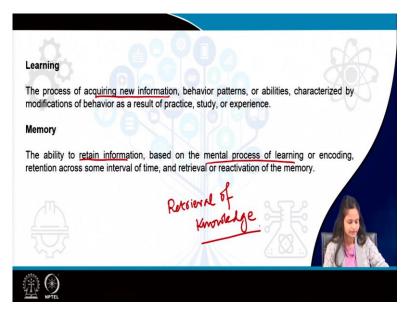
Hello everyone, our next topic is Learning and Memory.

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So, in the first part of learning and memory will cover what is learning, what is memory, what are the functional organization of memory, what are the types of memory and what is the cellular basis of cellular mechanisms of short term and long term memory.

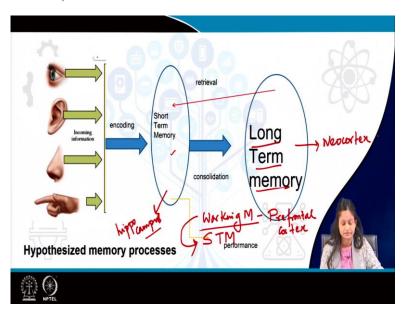
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Now, by definition what does learning means learning is the process of acquiring new information, behavior patterns or abilities characterized by modifications of behavior as a result of practice study or experience. So, learning means you are acquiring knowledge in whatever way you acquire knowledge, whether you study practice experience, the new knowledge the new information is acquired, that is your learning, whenever you use that new information or whenever you retry that new information or storage or whenever you try to retry the stored information that is memory.

So, the memory is ability to retain information based on the mental process of learning or encoding, retention across some interval of time, retrieval or reactivation of memory. So, mainly memory means, the retrieval of knowledge. So, whatever knowledge you have gained whenever you are driving it and using it, that is memory and learning is acquiring of new information.

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Now, hypothesized memory processes will see, now, we get various sensory cues or sensory heads from the surroundings. For example, we see there are visual stimuli, there are auditory stimuli, we hear many things, then we get sensory stimulation from the nodes like the smell many things, then we touch many things.

So, in this way, there are various receptors, tactile receptors, visual receptors, auditory receptors, olfactory receptors, through which there are informations which we receive, whatever information which we are receiving our body is transforming those information into sensory signals. So, this transformation of this information new information into sensory

signals is known as encoding. And this encoding is further done in the form of short term memory.

Now, whenever we are transforming the new information in terms whether it is auditory information, visual information, tactile informations into the sensory signals, that we are creating short term memory, now, short term memory has got various parts for example, there is working memory which is a form of short term memory and then you have the short term memory that is STM.

Now, what do you mean by working memory? Working memory means, suppose, if I asked you to remember my recollect my phone number 860-763-3688. So, at once you may not be able to recollect, would you be able to recollect? No. After two or three times either I will repeat the phone numbers or you will repeat on yourself by yourself and then you will be able to recollect. So, what you were doing that is your working memory, you could be able to recollect for a short span of time for a very brief span of time, a few chunks of ward or number that is working memory.

Now, this center of this working memory is prefrontal cortex. The prefrontal cortex is already very important a seat for planning or initiation of any goal. So, prefrontal cortex is a site of working memory. Now, if this working memory, if I asked you to recollect my phone number after 5 minutes, then you will not be able to recollect because you have not revised that enough to convert it into short term memory. So, after repeated exposure to the stimuli after repeated if you had repeatedly revised it, you would have converted this working memory into short term memory, the short term memory usually lasts for few hours or few days.

And this is not only with the few chunks of what you could remember quite a number of things with short term memory. So, the short term memory the sight of the short term memory is hippocampus. This has already been discussed in the limbic cortex mainly the CA one region of the hippocampus.

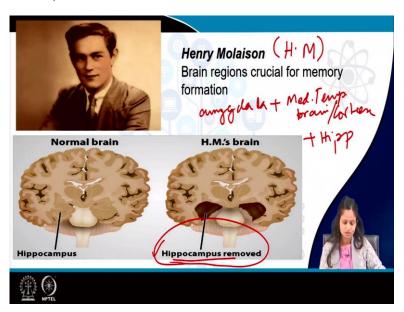
Now, this short term memory further on repeated revisions, they get consolidated or consolidation. So, this consolidation occur and gets converted into long term memory, this long term memory is seen in the neocortex, I mean the seat of long term memory is neocortex. So, encoding is occurring, it is converted the information is converted into signals. And we could just remember for a short span of time that is short term memory that is mainly occurring at the region of hippocampus very short term memories working memory that is the

level of prefrontal cortex, further on consolidation or repeated revision, the short term memory gets converted into long term memory. This occurs at the level of neocortex.

Now, from long term memory, what do we do? We did try the information suppose, if I asked you a question, you try to remember what you had learned? So, this is known as retrieval, when you try to recollect your information from long term memory and after recollection, what you will do? You will perform the activity that is performance, either you will write the exam or either you will talk or either you will try to recognize what has happened. So, this is known as performance. You are retrieving something from very old memories or long term memory and you are performing the act.

Now, at any point of this, whether during the encoding or during the consolidation or during the retrieval or during the performance, anything gets hampered that results in dementia that is seen in neurodegenerative disease, dementia does not mean only the consolidation only short term memory is not getting converted into long term memory. Other processor also there, it is getting converted but I am not able to retrieve it, or I am able to retrieve it but I am not able to perform it. So, at any of the state if any of the states gets affected that results in your dementia seen in various neurodegenerative diseases.

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So, we will come to this handsome guy known as Henry Mollison and he is very the scientists name him very specifically as H. M. Now, what his childhood though it was not that handsome because of the age of nine, he suffered a road traffic accident. Now, after the accident, what happened he started developing seizures, which later on initially the partial

seizures and in later on, it got converted into intractable epilepsy, he used to get intractable epileptic fits.

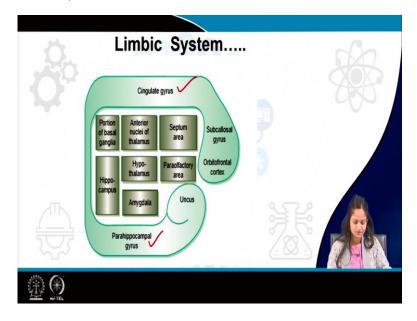
Now, at that time doctors what they did, they tried to remove certain portions of his brain to help him get rid of this seizures. Now, the doctors removed hippocampus, along with that they removed amygdala and medial temporal portion of the brain that is a medial temporal lobe of the cortex I mean the cortex, medial temporal cortex and the amygdala and hippocampus. So, these three structures were removed.

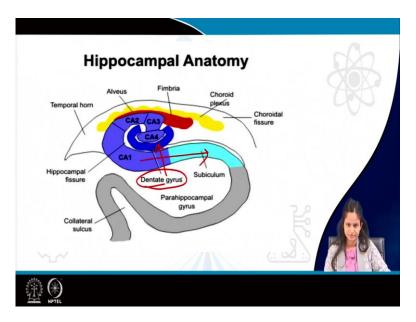
Now, what is the role of medial temporal lobe and amygdala, I had already discussed in the limbic system. After this what happened when the doctors after performing the surgery when the doctors asked him about the condition, what was seen that this person was able to remember everything before the surgery, but this person is not able to form new memories.

So, the new memories he was not able to form used to every time forget the new memories after the surgery, but everything every memory before the surgery was intact, which means the his retro (())(9:49) memories were there preserved, but he was suffering from anterograde amnesia.

Anterograde memory amnesia means after the surgery, he was not able to form new memories. So, with this person with the help of this person fortunately or unfortunately the scientist came to the conclusion that hippocampus plays a very important role in conversion of the memories from short term to long term. So, that is the role of Henry Mollison.

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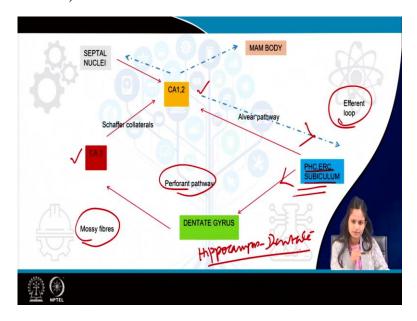




Now, limbic system I had already discussed that these are the structures of limbic system because limbic system I will go a bit in brief because it is plays a very important role in memory, the cingulate gyrus and the parahippocampal gyrus, they form the limbic cortex with the help of cingulate gyrus and parahippocampal gyrus, the entorhinal cortex receives the information as well as the output, I mean, it is also from the entorhinal cortex.

So, mainly the input to the hippocampal anatomy, if I see is to the dentate gyrus, this has already been told the dentate gyrus receives the information from entorhinal cortex and the output is mainly from the CA 1 region of the hippocampus.

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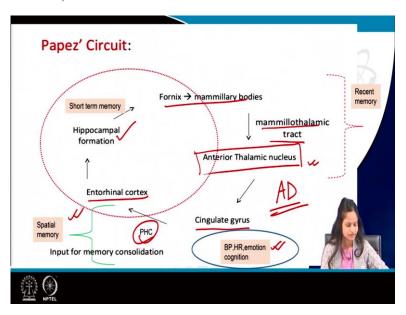


So, this is the circuit which is very important that is a hippocampus dentate circuit, where the entorhinal cortex is receiving every information and sending two pathways to the CA 1

region and the dentate gyrus. And this pathway as I already been discussed, that is very important to the dentate gyrus, dentate gyrus sending further information to the CA 3 regions of the hippocampus with the help of mossy fibers, and CA 3 further sense the informations with the help of scrapper collaterals, that is the exons of the CA 3 to the CA 1 region and CA 1 region also receives information from the septal nuclei, another gray matter of hippocampus.

And finally, the efferent pathways is back to the septal nuclei and the mammillary body and entorhinal cortex which completes this loop efferent loop so, you can see entorhinal cortex is giving out like input to the hippocampus to the dentate gyrus and entorhinal cortex is receiving information from the CA 1 region of the hippocampus. So, this is very important this is the hippocampus dentate pathway, it forms a very important role in the short term memory formations because in this loop, the processing of memory occurs.

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Now the Papez' circuit is very important it was discovered after James Papez'. Now this portions I had already discussed when the entorhinal cortex is receiving the information from other cortex and giving the information to the hippocampal formation. Hippocampal formations giving the informations or out to the Fornix and mammillary body.

From the mammillary body via mammillothalamic tract, it is going to the anterior nucleus of the thalamus. From the anterior nucleus of thalamus it is giving output to the cingulate cortex of the cingulate gyrus, again, which is completing the loop with the help of parahippocampal cortex to the entorhinal cortex.

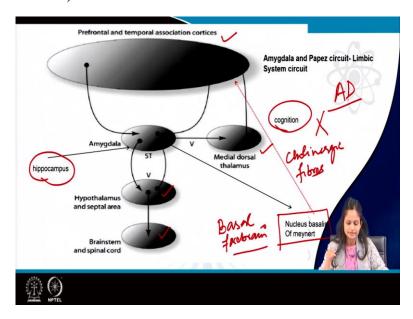
Now we will see what are the memories relevant to this Papez' circuit? This hippocampal formation has already told you it is important for the short term memory. Short term memory I told you working memory is there and after that, the short term memory is there working memory is mainly important for very small span of time.

Now, this recent memory is mainly played by mammillary body mammillothalamic tract and anterior nucleus of thalamus. Recent memory means when you ask a person suppose what you had in your dinner? So, in my dinner, what if you asked me what I had in my dinner, I should be able to recollect and say okay, roti, dal, chapatti like this things.

So, if the person is not able to answer that questions, that means there is some problem with the recent memory that is the recent memory. Now, the cingulate gyrus is mainly important for BP, heartrate, regulation, emotion and cognition. This is the main role formed by the cingulate gyrus and entorhinal cortex and parahippocampal gyrus that is mainly responsible for the three dimensional memory that is spatial memory.

All these four types of memory gets disrupted in a very important neurodegenerative disease known as Alzheimer's disease. The patients of Alzheimer's they are not able to recollect recent memory. The remote memory is intact I mean old memories will be intact. But the recent memory, the short term memory, the cognitive function, the spatial memory, if you leave the person in a road, the person will forget the berries his house, they will not be able to know, they will not be able to perceive the 3D dimension of the road, where to go right or left or straight. So, all these things, all these types of memory gets disrupted in Alzheimer's disease of neurodegenerative conditions.

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Now, how these are linked? These are linked mainly by the amygdala purpose circuit of the limbic system. Hippocampus is giving the output to amygdala from the CA 1 region mainly to the basal lateral nucleus of amygdala. And there is also an into, like, association cortices, prefrontal, temporal various cortical areas, information is coming to the amygdala.

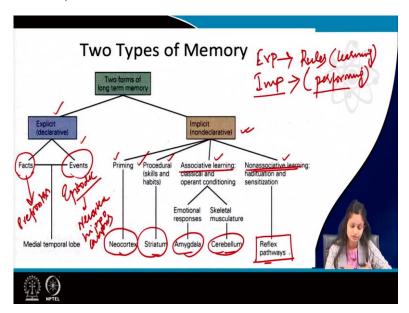
Amygdala is giving again information to the dorsomedial nucleus of thalamus which is again giving information to the cortex. Amygdala is giving information to the hypothalamus, where the information is further relate to the brainstem and spinal cord, as well as amygdala gives information to another structure known as nucleus basalis of meynert.

These I had also told you while describing the cholinergic pathway of brain, nucleus basalis of meynert or known as basal forebrain. Nucleus basalis of meynert is the cholinergic nucleus present in the brain, the most important cholinergic or the main site of the cholinergic neuron, which is present in the brain.

And this nucleus basalis of meynert give further projections to the various areas of the cortices. So, this is mainly responsible for the cognition, this because these projections are from cholinergic fibers, these are cholinergic pathways. So, this cholinergic fibres project from the nucleus basalis of meynert or basal forebrain to various areas of the cortex.

Again, if this function or if this pathway gets destroyed in case of Alzheimer's disease, typically it is seen in the Alzheimer's patients the cholinergic pathways get destroyed.

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So, in this way, we can see the circuit which are important for the memory formations in case of limbic system, associating limbic system hippocampus and the cortical areas. Now, two types of memory we will mainly discuss. The two types of memory is long term memory of course, explicit memory and implicit memory. Explicit memory is declarative memory and implicit memory is non declarative memory.

Now, what do you mean by explicit memory and what do you mean by implicit memory? At explicit memory or declarative memory in short, I will tell you, when you try to learn new facts, you take the help of your cortex as well as your hippocampus because new learning is going on that is explicit memory or declarative memory usually abide by various rules and regulation.

Implicit memory when you have already learned the you have learned the fact learned any problem or anything, learned the activity and now you have to perform. So, explicit memory is mainly learning and implicit memory is mainly performing. A very common example if I give you suppose when you try to learn driving a new car, you are trying to learn driving as a new comer.

So, what you will do it is a very important task very dangerous task when you do not know driving and you are trying to drive a car. So, you will try to learn, this is accelerated, this is brake, this is clutch, in this way you will learn so, this will take the help of and your brain will always be alert.

So, this was this will take the help of hippocampus. So, this is known as explicit learning you are learning. Now suppose you have already learned driving and now you are driving along the road, what will happen even if you listen to music or even if the persons are talking behind you or even you are talking with anybody, you know when to put the clutch, when to put the gear because you have learned that behavior now you do not require that consciousness or awareness.

So, now you just have to perform. So, that is known as implicit behavior or implicit learning that means, explicit learning is declarative learning when you have rules and regulations for learning and when you take help of your brain that is hippocampus. Implicit learning is when you perform a learned act, you do not take help of your hippocampus. So, that is implicit learning. Now, this two types of learning is further divided into various types of learning.

Now for example, explicit learning is two types. One is facts and one is events. Now, if it is based on facts that is known as semantic or factual learning, for example, if I try to facts means you are remembering fact, if I asked you what is the capital of India? So, you will tell Delhi is the capital of India so, you are remembering facts, so, that is known as explicit factual or semantic memory, the main role the main prefrontal cortex the main site is prefrontal cortex and temporal cortex.

Then, episodic learning that is events when you try to recollect any event any past event, suppose if I asked you what happened in your first day of your college, or how was the first day of your college, you are trying to remember an event, so or episode that is known as episodic memory. And again episodic memory is neocortex, the seat neocortex and hippocampus. So, these are the types of explicit or declarative memory.

Now coming to the implicit or non-declarative memory, what are the types of non-declarative or implicit memory. Here you will not see any hippocampus over here because we do not need hippocampus because it is already a learned behavior you have just to perform. So, there is a priming there is a procedural memory, there is associative learning and there is no associative learning. So, what do you mean by priming? The seat of priming is neocortex.

Priming means before any action or before you are asking someone to perform any action you are if you just give a clue, or if you just give a hint or if you just prime the person's brain, then that will help in their memory. For example, if I give a hint, suppose the electrical

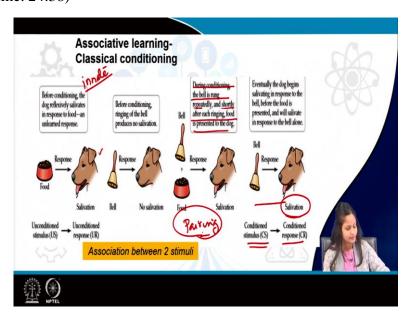
activity of brain the encephalograph, the electro-electroencephalograph EEG the discoverer of this EEG is Hans Berger.

Now, if I ask a student, can you tell me who has discovered EEG? Then if the student is not able to recollect by chance, and say the name, I will give him a head immediately that it is somewhat related to a eatable which is mainly found in McDonalds. So, he will remember I am trying to give him a hint of burger. So, the person will immediately tell that okay, it has been discovered by Hans Berger. So, priming means you are exposing the brain to a previous stimuli with the help of hence before actually performing the task. So, this is priming.

Then the procedural learning, which takes the help of stratum and cerebellum, you have learned that thing and now you are using the skills, you are using your hands for writing, remembering and then writing that is the procedural memory. Then associative learning, associative learning is again divided into classical and operant conditioning. So, I will tell that later.

Associative learning associates two stimuli or one stimuli and behavior, the person or animal, they try to associate two stimuli the relationship between two stimuli or a relationship between a stimulus and a behavior and they learn based on that mainly, amygdala and cerebellum plays a role. Non-associative learning is based on the strength of the stimulus, the person will learn its behavior. So, that is mainly by the reflex pathways.

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Now, based on this overall description of the types of memory, we will move on to the associative learning that is classical conditioning. This has been a very important and

classical example done by Pavlov that is Pavlov's experiment of classical conditioning. Now, what is been done over here? A dog is given, presented with the food before conditioning I have not conditioned the dog is given food. So, obviously the dog will start salivating food is in front of the dog. The dog is very much hungry. So, that there will be salivation.

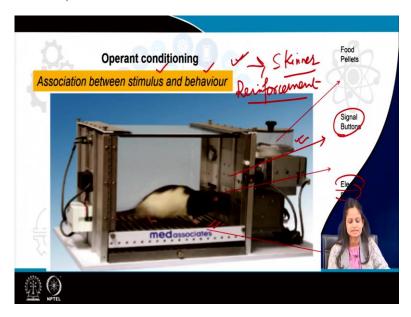
So, this salivation is innate response of the dog it is because the dog has not learned that food is there. So, I have to saliva it, it is an innate response which is already present since birth that food is there and the dog will saliva it. Now, second thing after this the dog is presented with not food, but a bell. So, here also no conditioning has been done, the bell is rung and it is seen whether dog salives it or not obviously, the dog will not salive it, because only bell is ringing.

The next step, the first bell is rung and then it is followed by food. So, during this conditioning the bell is rung repeatedly and shortly after each ringing the food is present to the dog. Now, the dog will see first time, second time, third time and then it will try to pair this two stimuli that okay whenever there is a ringing of the bell, soon after that it is followed by food. So, at that time what will happen after some time even on ringing the bell, there will be salivation even if I do not present the food, but still the bell is rung there will be salivation So, this is the conditioned stimulus which is giving the conditioned response.

So, what is happening? There is an association between the two stimuli, the dog could associate that two stimuli one the neutral stimuli and the other one is the conditioned stimuli, the neutral stimuli is the food, the condition stimuli is the bell. So, this is causing the dog to pair and learn, when these two stimuli are given together, so, I should like there will be salivation of the dog.

Now, the very important thing is to remember if you first present food to the dog, and after that, you ring the bell, then that is not conditioned reflex, the dog will simply bark at you because you are disturbing his food. So, the bell should be rung first and then that is followed by the conditioned stimulus, that is followed by the neutral stimulus that is the food. So, the bell is given first and then there will be the food given so, that in that way pairing is done. This is the classical conditioning.

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Next is the operant conditioning. The operant conditioning is the association between stimulus and behavior, how it is done, it is typically done in with the help of rat. This is the Skinner's experiment, because it has been discovered by Skinner, famous scientist and this box is known as Skinner's box. So, what will happen? There are food pellets and one pot and this rat is kept inside this box. There are electric panels. And there are electric panels, panels there are various signals buttons are there.

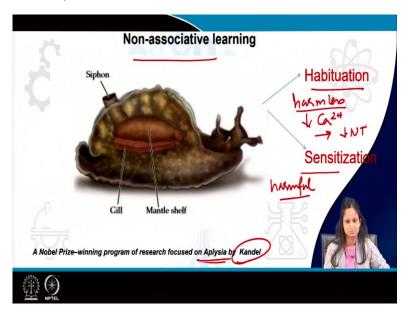
Now, when this rat will try to press a button what will happen after pressing the button this is these are the electric panels and there are certain buttons now whenever there will be signal buttons which is present say suppose here, when this rat will press the right button for the food pellets, the foot pellets will come to rat and rat will be happy that this is a reward for me. I have got food. But by chance if the rat presses the wrong button.

So, what that time will happen this electric panel will get activated and the rat will get electric shock. Now, that is a punishment for the rat, the rat is getting reward in terms of food whenever he is pressing the right button. Now the rat will learn that on pressing the wrong button, I am getting electric shock.

So, rat will try to associate the stimulus and the behavior whether it is reward or whether it is punishment. If the behavior is rewarding, it will continue with that button that will give him further rewards. So, that we will call that is known as reinforcement. And if the rat is getting punished, so rat will try to avoid that behavior and this is a normal phenomenon which is which happens in human also. If you encourage someone, if you give rewards to someone

due to for some act, the person will try to do that act more but (()) (30:00) punish that person obviously the person would avoid that act. So, that is the operant conditioning that person or the year the rat is trying to learn by associating the stimulus and the behavior.

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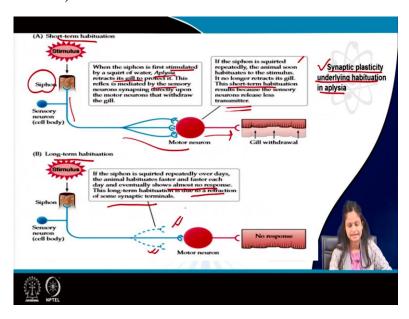


Now, the non-associative learning. The non-associative learning has already been discovered by a Nobel Prize winner candle in a sea snail the that as a scientific name is Aplysia. Now, in a sea snail what it has shown, there are two types of behavior which is seen in non-associative, habituation and sensitization. So, what has happening in habituation? In habituation what happens, you have to remember the stimulus which we give should be harmful. So, what happens in habituation?

If you constantly give a person harmless stimuli, at first the person will try to see okay, this is this thing, then after some time the person will ignore it, because it is not causing any exaggerated reaction or it is a harmless stimuli. So, that is habituation. Sensitization means, if you are giving certain stimulus to a person, which will cause harmful effect, so, basically that person or animal will try to give an exaggerated response. So, that is known as sensitization.

Now, habituation occurs because of decrease in the calcium levels in the signups. So, decrease in the calcium level in the presynaptic terminals will result in decrease in the neurotransmitter and so, there will be habituation there will be less generational impulse.

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And we will see how this habituation and sensitization takes place. Now, this is short term habituation, this is long term habituation. This is the siphon of that Aplysia sea snail. This is a sensory neuron cell body which is giving motor neurons to the you can see the motor neurons and this is motor neurons is supplying inhibiting the gill.

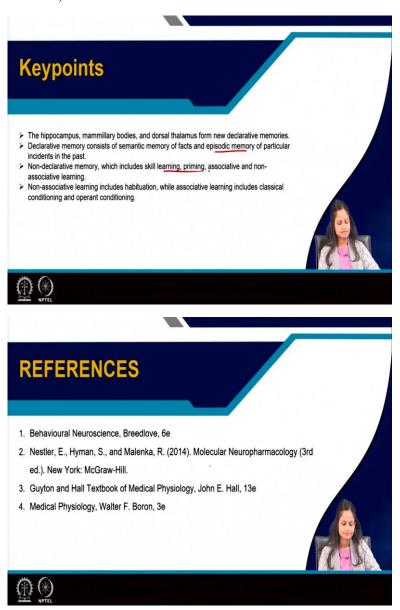
So, whenever I touch the siphon, what will happen there will be gill withdrawal, but after some time what is seen, even if repeated touching the siphon the Aplysia is not reacting there will not be any gill withdrawal, no real response because this sea snail has learned that with repeated touch, there is no nothing harm which is done. So, I need not to response, I need not to respond or I need not to withdraw my gill.

So, when the siphon is first stimulated, Aplysia retracts its Gill to protect it. The reflex is mediated by the sensory neurons that withdraw and finally the motor neurons that withdraw the gill. If this is done repeatedly, what will happen? That will habituate the animal and this short term habituation results in decrease of less neurotransmitter because of less calcium in the presynaptic terminal.

Now long term habituation, if this is done repeatedly over a number of days, number of weeks, the animal will develop this habituation faster, how, because it will show no response that will usually happen because of the retraction of some synaptic terminals. Later on what will happen this motor neurons will have less synaptic terminals. Now this change in the synaptic terminal behavior, because of this environmental stimulus is known as synaptic plasticity, because of the strength of the stimulus, now, had the stimulus been harmful, there

would have been more synaptic terminals to protect, but since the stimulus is less harmful or it is harmless, so there is habituation which is developing by synaptic plasticity, which is causing retraction of the synaptic terminals. So, hence this is causing no response.

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So, here we have to remember that hippocampus mammillary body and dorsal thalamus forms the new declarative memories. Declarative memory consists of the semantic memory of facts and episodic memory. And non-declarative memory includes skill learning, priming associated and non-associative learning, and which also includes habituation while associative learning includes classical conditioning and operant conditioning. Thank you.