Neuroscience of Human Movement
Department of Multidisciplinary
Indian Institute of Technology, Madras

Lecture - 12
Neuromuscular Junction

So, welcome to this class on the Neuroscience of Human Movement. In today's class, we will be discussing about Neuromuscular Junction.

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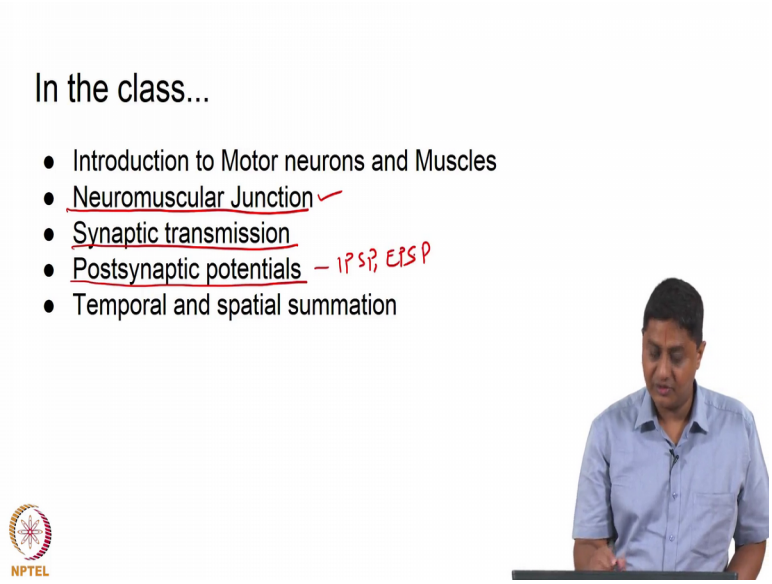

In this class, we will be introducing the notion of motor neurones and introducing muscles and muscle fibres. We will discuss the concept of neuromuscular junction in relatively good detail and we will discuss synaptic transmission, we will discuss postsynaptic potential and its types IPSP and EPSP and inhibitory postsynaptic potential and excitatory postsynaptic potential and temporal and spatial summation, right.

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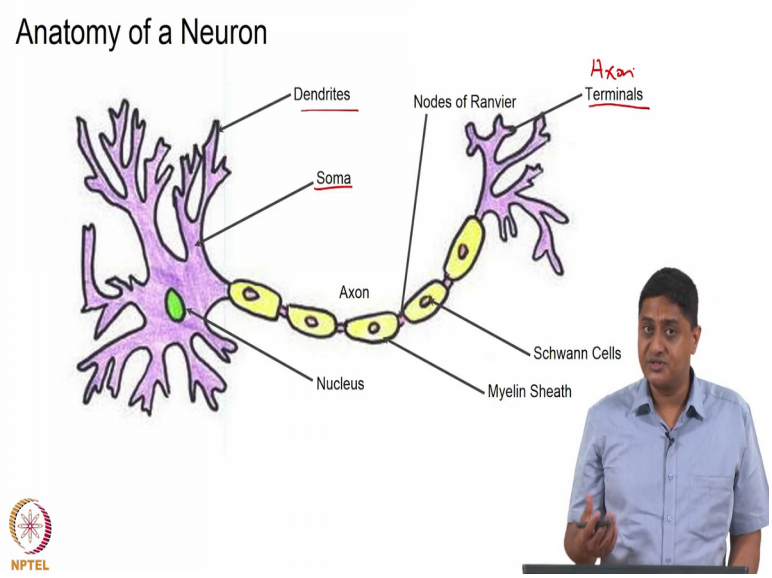

So, we are seeing earlier that a neuron has a cell body soma and several dendrites that are the input structures. And output structure is the axonal terminal; is it not; if this axonal terminal terminates at muscle or a muscle fibre, then it could cause depolarization after muscle fibre. Let us remember that both neurones and muscle fibres are excitatory cells, both of them can have action potentials in them because, they maintain a steady potential difference across their membrane. So, they both have the same characteristics or similar characteristics in terms of having sodium potassium pump having influx of sodium causing an action potential, etcetera, right.

So, if the neuron connects to a muscle fibre it not only causes an action potential in the muscle fibre, but it also causes the muscle fibre to contract or produce force. Now, in that respect the muscle fibre is different from a neuron and neuron can only produce and conduct action potentials whereas, a muscle fibre cannot only produce and conduct action potential, but also produce a force as to how the muscle producers a force we will discussing future classes, right.

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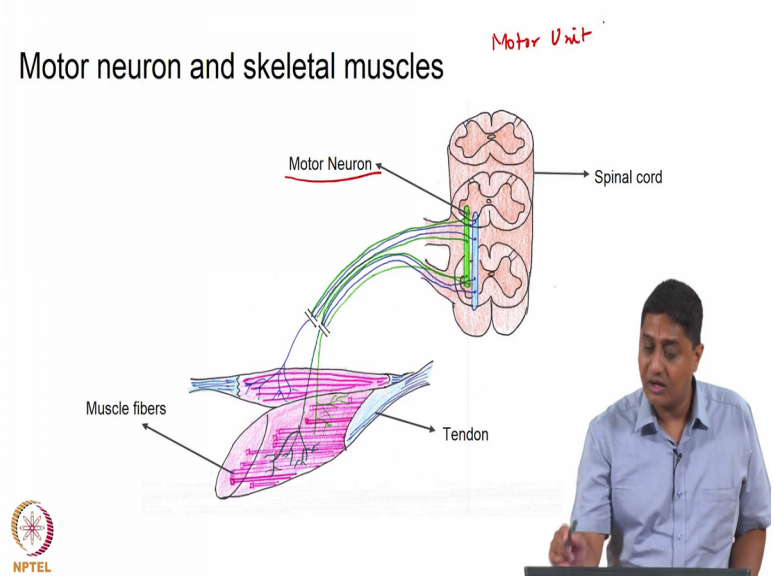

The neurons that synapse with that connect with muscle fibres are called as motor neurones, motor means movement and movement in the body is produced by contraction of muscles, right. So, neurons that cause muscle contraction are called as motor neurons. So, these motor neurons are located at the ventral side of the spinal cord. So, when an animal is on all force when an animal is on its four limbs, right. So, as in a quadruped as on its four limbs, the part of the body that faces the ground is called as the ventral side and the part of the body that faces the roof or the sky is called as the dorsal side ok.

So, the ventral side of the spinal cord houses ganglia or nuclei that contain a large number of motor neurons. These are the neurons that synapse with muscle fibres and cause the muscles to produce a force and there is also a relatively precise control of the force that is produced by the muscles. These neurons that synapse with or connect with muscle fibres are called as motor neurons and it turns out that one neuron can connect with a whole number of muscle fibres, one neurone and all the muscle fibres connected to it are called together as a motor unit. So, this is different from a motor neuron.

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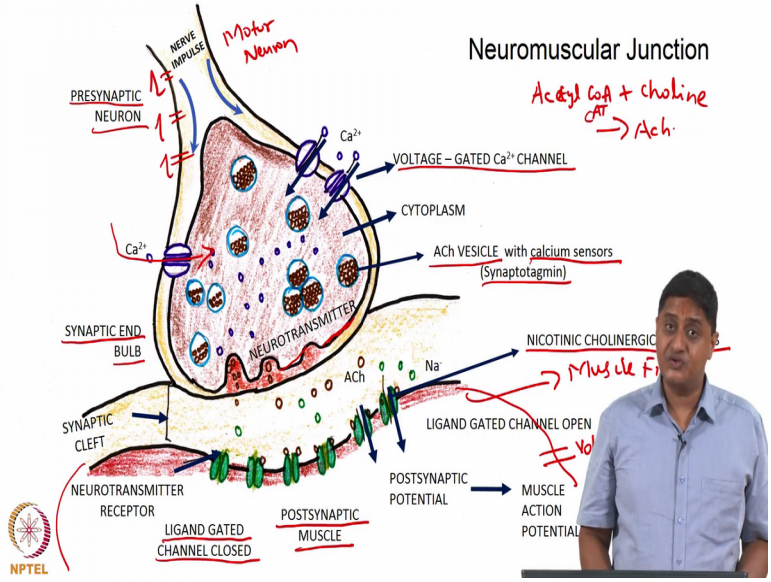

So, let us consider this part of the picture as the presynaptic neuron ok. So, this is the presynaptic neuron or the motor neuron and that side of the pictures shown here is the muscle fibre or the postsynaptic muscle fibre side ok. Now what happens, what causes an action potential in the muscle fibre. How is that conducted, that is of interest for us, what is the what are mechanisms that is of interest for us right. So, the nerve impulse or the action potential arrives from say the axon hillock towards the synoptic end bulb or the axonal terminal right. How does it arrive? The usual method of action potential propagation, basically one action potential causes the neighbouring areas.

So, when this action potential arrives say at that point ok, it is important to note that the synaptic end bulb or the axonal terminal of the motor neuron contains a relatively large number of these special channels, these channels are voltage gated calcium channels. Now, these channels are going to be opened whenever the potential is above a certain threshold.

So when action potential arise, when action potential arise to these points these voltage gated calcium channels open ok. So, this voltage gated calcium channels open and lot of calcium enters inside the cell. What does this do to the muscle or what does this do to the presynaptic neurone that is the question. So, it turns out we discuss in one of the previous classes that acetylcholine is synthesized by a protein choline acetyltransferase right choline acetyltransferase synthesis a acetylcholine from two components.

One is acetyl coenzyme A and choline both of these are combined together to produce acetylcholine. Who is producing this? The protein choline acetyltransferase. So, CAT is producing acetylcholine and it is packed into bags into relatively small bags called as vesicles ok. So, it is packed into acetylcholine vesicles and these acetylcholine vesicles have special calcium sensors called as synaptotagmin. So, this calcium sensors they detect the presence of calcium.

When the calcium level is higher what they do is they move the vesicle closer to the membrane right. They move the vesicle closer to the membrane and fuse with the membrane and then open on the outside, releasing the chemical acetylcholine on the outside through a process called exocytosis.

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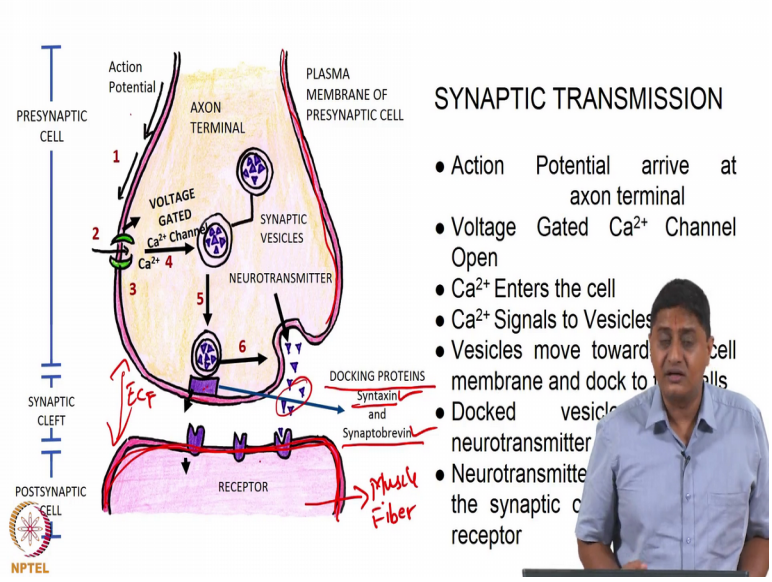

Let us go to a different picture and look at that situation. Whenever, action potential is caused in the presynaptic neuron and when it travels to the synaptic end bulb, these calcium channels are opened and the lot of calcium enters inside. And, these synoptic vesicles contain a calcium sensor which is the protein synaptotagmin and that synaptotagmin causes the or senses the process of calcium and begins a series of activities that lead to the fusing of the vesicle with the membrane.

This is mediated by docking proteins called syntaxin and synaptobrevin. So, by the action of syntaxin and synaptobrevin these vesicles fuse to the membrane and then open up on the outside. So, action potential arise and then that leads to opening of the calcium

channel and then as soon as the amount of calcium in the synoptic end bulb goes above a certain level that is detected by synaptotagmin. That causes moment of the vesicle towards the membrane and docking of the vesicle and docking of the vesicle with the membrane by the action of the docking protein syntaxin and synaptobrevin and then opening up of the vesicle on the outside.

Note once, the vesicles opens outside basically what is outside this; this is the extracellular fluid, is it not. This is the extracellular fluid, this is the gap between the muscle fibre, note this is the muscle fibre. This is the space between the muscle fibre and the neuron that is the extracellular fluid, right. So, how is this acetylcholine transported in the extracellular fluid, purely by diffusion. There is no control, there is no specific conditions that mediate that transport of acetylcholine from the presynaptic neurone to the postsynaptic muscles fibre, it happens only through diffusion. Of course, diffusion related last may come into the picture, but let us remember that this is a relatively small cap ok. So, acetylcholine moves from that side to this side. Now, what happens on the postsynaptic side that is the question.

What happens on the postsynaptic side? It turns out the postsynaptic side has receptors, these are like locks waiting to be opened ok. So, that is the ligand gated ion channel is called as a ligand gated ion channel or also called as a nicotinic cholinergic receptors. These are like locks whenever acetylcholine comes and attached to this lock so, acetylcholine is the key that is going to open this lock. So, whenever acetylcholine comes and attaches to the nicotinic cholinergic receptors, these receptors which are basically channels these channels open and let in sodium inside. So, basically these are slightly different from the regular stimulus driven sodium channels or voltage gated sodium channels.

These are ligand gated sodium channels which open only when that particular chemical, in this case acetylcholine attaches to them. When acetylcholine attached to this receptor the channel opens and lets in a lot of sodium. And, this influx of sodium could cause say for example, this is the muscle fibre and say here you have a voltage gated sodium channel say for example. Now, this influx of sodium could take this voltage gated sodium channel to threshold causing a greater influx of sodium and an action potential in the muscle fibre. How this muscle fibre produces force is a topic for future classes.

But for now, it is sufficient for us to know that when sodium enters inside via the ligand gated sodium channel or the nicotinic cholinergic receptors, it basically could and in many cases does cause the action potential in a muscle fibre.

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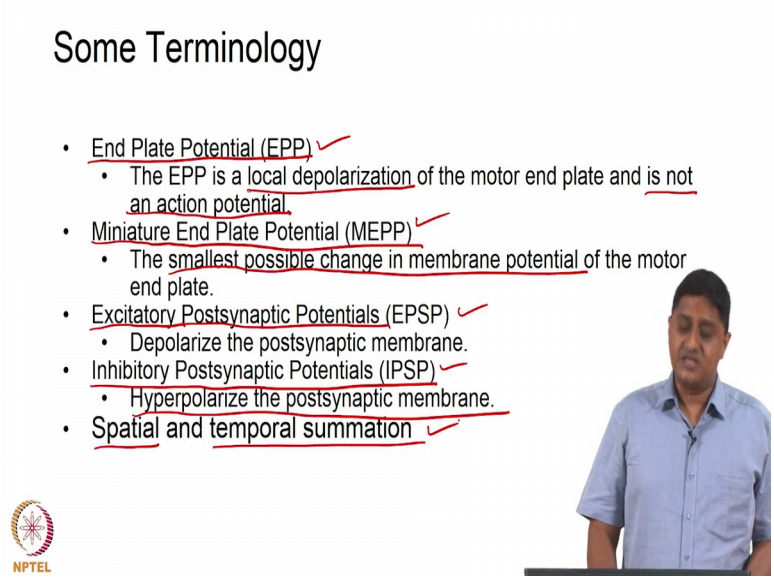

So, some terminology regarding the neuromuscular junction; end plate potential. So, spontaneously from the presynaptic terminal without the necessity for an action potential to arrive. Because, of this reason a small amount of acetylcholine reaches the postsynaptic terminal and causes relatively small amount of depolarization or a graded potential ok.

So, this graded potential or local depolarization is called as end plate potential ok. So, the end plate potential is a local depolarization or a graded potential of the motor end plate and this is not an action potential important. And, let us assume that only one acetylcholine molecule attaches to let us assume that only one acetylcholine molecular attaches to nicotinic cholinergic receptor, that causes entry of a small amount of sodium in the muscle fibre. That slightly causes depolarization, that causes slight depolarization of the muscle fibre.

This is the smallest possible change in the membrane potential of the motor end plate that is caused due to one acetylcholine molecule, that is called as the miniature end plate potential. So, the end plate potential is a local depolarization or a graded potential that is caused due to spontaneous release of acetylcholine from the presynaptic membrane, not

necessarily due to action potential. Whereas, miniature end plate potential is the smallest change in membrane potential of the muscle fibre that is caused due to one acetylcholine molecule.

Now, entry of acetylcholine and the influx of sodium causes an excitation in the muscle fibre right. This postsynaptic potential is excitatory and so, it is called as excitatory postsynaptic potential as we have seen in previous classes. This depolarizes the postsynaptic muscle fibre. It is also possible for postsynaptic potential to be inhibitory depending on the particular chemical, depending on whether that is acetylcholine or say GABA. There maybe either excitation or inhibition, also a depending on the particular receiver, depending on the particular receptor it is possible for a chemical to cause either an excitatory postsynaptic potential or an inhibitory postsynaptic potential. So, it is possible for a chemical for a neurotransmitter to cause inhibition in the postsynaptic side this is called as inhibitory postsynaptic potential.

This is usually caused for example, due to inhibitory neurotransmitters such as GABA, right. This hyperpolarizes the postsynaptic membrane, right and then we saw what are spatial and temporal summation. If at the same time several inputs arrive from multiple points in space it is called as a and that inform if at a point in time, if at a particular point in time multiple inputs arrive from several points in space and that information is summed or integrated to produce in action potential or cause some outcome that is called as spatial summation.

If at the same point in space multiple inputs arrive relatively close in time it is possible for the inputs to be summed one after the other, this is called as temporal summation as we have seen in previous classes. So, what we seen? We have seen end plate potential, we have seen miniature end plate potential, we have seen EPSP, IPSP and we have seen spatial and temporal summation.

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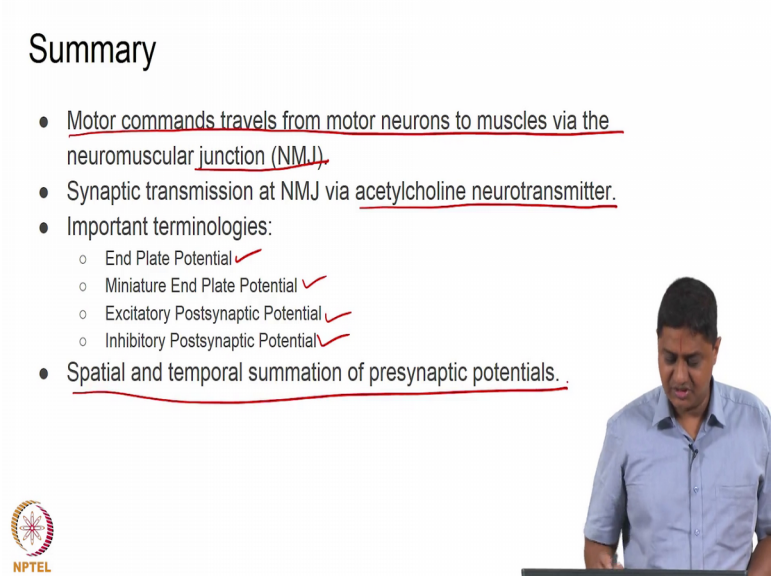

So, in summary we have seen that motor commands travel from motor neurons to muscles via the neuromuscular junction which is mediated by the neurotransmitter acetylcholine. The how acetylcholine causes this something that we have seen and synaptic transmission at neuromuscular junction via acetylcholine neurotransmitter, we have seen in relatively greater detail.

So, in summary what we have seen is motor commands reach the muscle via the NMJ or the neuromuscular junction and that is mediated by acetylcholine neurotransmitter right. Important terminologies we have seen end plate potential, we have seen miniature end plate potential, we have seen excitatory postsynaptic potential, we have seen inhibitory postsynaptic potential. And, we have seen spatial and temporal summation of postsynaptic presynaptic potentials.

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So far as contribution to our understanding of neurotransmission that happens, that the idea that neurotransmitters are packed in bags or in vesicles was first discovered by Sir Bernard Katz; for his contribution to this, he was awarded a Nobel Prize in Physiology or Medicine 1970. It is an inspiring story about him so, please to check Google for Bernard Katz and read his story. For science he had to practically run away from an antisymmetric Germany and took refuge in AV hills lab, where he lived practically until he could survive and what a fantastic career he has had.

So, it is an inspiring story please do read about it, I will stop here. So, with this we come to the end of this lecture, we will continue in future classes.

Thank you, very much for your attention.