Neuroscience of Human Movement
Department of Higher Education Ministry of Human Resource Development
Indian Institute of Technology, Madras

Lecture – 25
Excitation and Inhibition within Spinal cord Part – 1

Hello all, so welcome to this class on Excitation and Inhibition within Spinal cord. So, this is part 1 of I suppose many parts.

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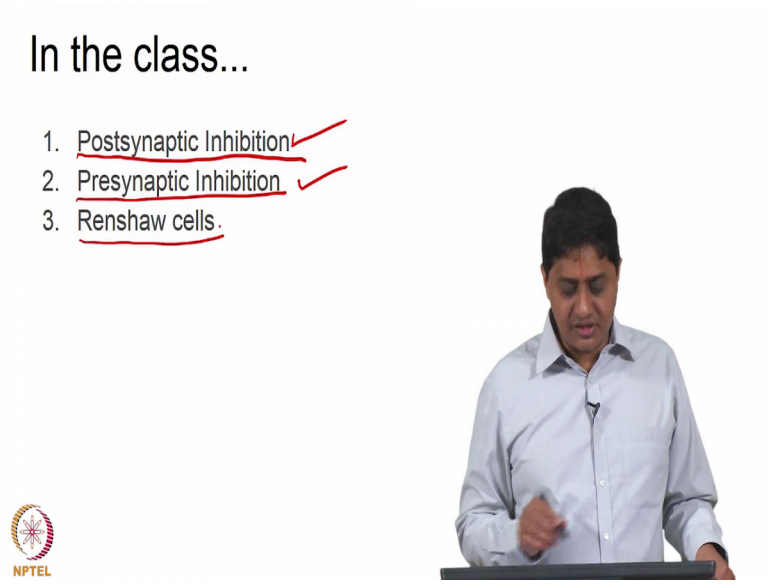

In this class we will be talking about inhibition, specifically what is generally called as postsynaptic inhibition or so when I mention just inhibition we are referring by default to this Postsynaptic Inhibition. What does this involve? This involves a chemicals neurotransmitters that function as a inhibitory neurotransmitters or perform inhibition on the postsynaptic.

So, in general when we say inhibition we are referring to postsynaptic inhibition. Or then a special case of inhibition that could be cause due to excitation how can this happen, we will see how this can happen in today's class, in this class. And then one example of an inhibitory interneuron performing a critical function this example of a Renshaw cell more details on this cell and it is function in future classes.

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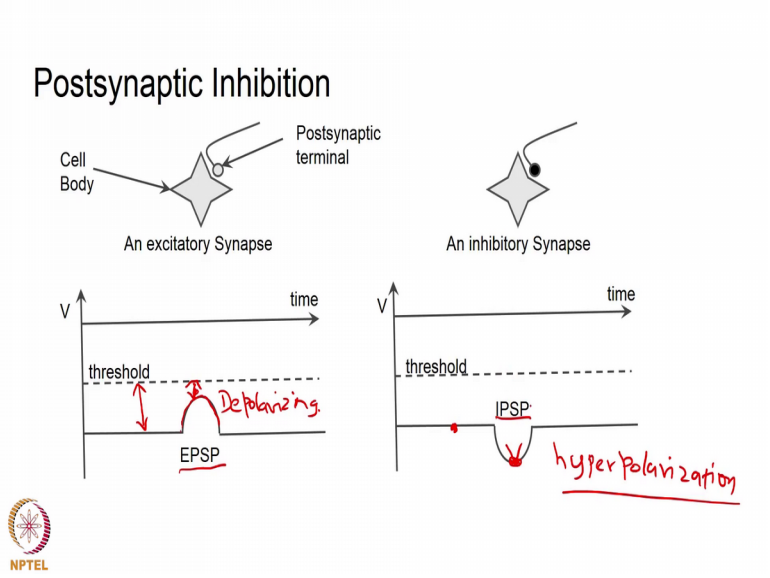

So, in general we have seen that an excitatory Synapsis one that causes an excitatory postsynaptic potential or and EPSP. What does this involve? Sometime above we have seen for example, the case of neuromuscular junction. So, whenever acetylcholine is released into the synaptic cleft, the nicotine cholinergic receptors or the ligand gated ion channels, sense the presence of a acetylcholine and open and allow a lot of sodium to enter inside the muscle cell causing; an action potential in the muscle cell and then contraction of the muscle excitation contraction coupling etcetera is it not.

So, this postsynaptic potential if it takes the cell to closer to it is threshold right, this potential when it takes the cell closer to the threshold. So, here is the earlier the difference between the threshold and the membrane potential was so much. Now because of this the amplitude of the difference between the membrane potential and a threshold is reduced are and the probability that this membrane, this part of the cell or this membrane is going to be taken to threshold. And an action potential caused in this part of the membrane is increased when an excitation happens this is called as an excitatory postsynaptic potential.

We have seen how this could be achieved right, we will review that in the next slide. So, by the way let us let us remember that this is called as depolarizing the membrane, is it not? How is this caused? By a inward current. So, by the influx of sodium we decided to call the currents across membrane, as an inward current and outward current in our

earliest classes in the first few classes we said what is an inward current and what is an outward current. Inward current is this current that involves an influx of a cations into the cell or an out flux of anions from the cell, this is called as inward current.

If the opposite happens right or if cations leave the cell, when would this happen for example, even potassium leaks from the cell potassium channel opens and a lot of potassium leaves from the cell. Or when chloride enters the cell when either of these 2 happens and anion enters the cell or a cation leaves the cell. So, an outward current is happened so this causes a hyper polarization, is it not; this is called as an hyper polarization. This reduces the probability at this point the probability that this cell is going to be taken to threshold and action potential happening in this part of the membrane is relatively reduced when compared with say for example, that part is it not?

Here is a resting membrane potential this resting membrane potential is taken to a value below the regular resting membrane potential reducing the probability or increasing the difference between the threshold and the membrane potential. This potential is called as Inhibitory Postsynaptic potential or IPSP. This synapsis that cause an IPSP or a hyper polarization are called as inhibitory synapsis. So, synapsis that cause a depolarization or postsynaptic cell neuron or excitable cell, any excitable cell goes to threshold and produces an action potential are called as a excitatory synapsis. And those synapsis that reduce the probability are called as a inhibitory synapsis.

And this inhibition can be caused due to chemicals or can be due to other mechanisms ok. So, in this case we have seen an earlier case where acetylcholine acts as the excitatory neurotransmitter opening a sodium channels on the postsynaptic membrane and sodium serves as the carrier for as the as the mediator for inward current increasing the chance that it is going to go to threshold. In the inhibitory case there may be similar neurotransmitters that cause the IPSP in the postsynaptic cell ok.

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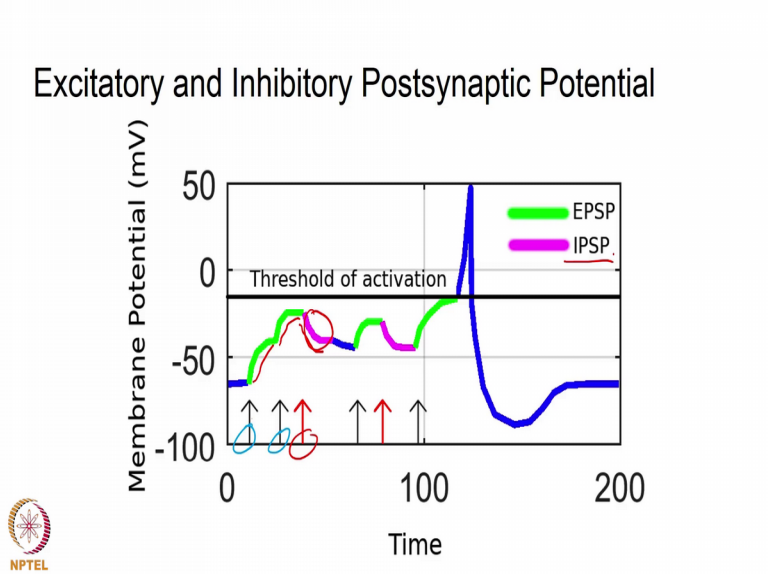

Let us see other reasons how this can this can happen; we saw in previous classes just remind ourselves. I can have several stimulations several EPSPs one after the other that some to reach a threshold. If these are arriving from the same spot, but are following one after the other temporally there is a temporal summation. Or these could arrive at the same time from multiple dendrites, from multiple spaces, from multiple points in space. Then the summation happens spatially we call this as spatial summation in previous classes, is it not?

Note here the stimulation positive stimulation or excitatory stimulation is shown in black like here. And the inhibitory stimulation are shown in red like here. So, every time an excitatory stimulation happens there is a depolarization, taking the membrane closer to threshold, but then whenever an inhibitory stimulation happens or an or an inhibition happens; it is broad farther away there is a hyper polarization. So, this phase that is shown in a rose or pink is an IPSP inhibitory postsynaptic potential. Reducing the probability that the membrane is going to be taken to threshold and an action potential is going to be caused in the in this part of the membrane.

Let us say something when and we said several of the postsynaptic EPSP several EPSPs could combine together a in time to cause an action potential or in space to cause an action potential. Or several IPSPs could combine together in time and space to prevent the happening of an action potential ok. So, there could be spatial and temporal

summation, and that is applicable for both EPSPs and IPSPs equally. So, how does this part function, how does this the inhibitory postsynaptic potential functions, how does inhibition itself functions.

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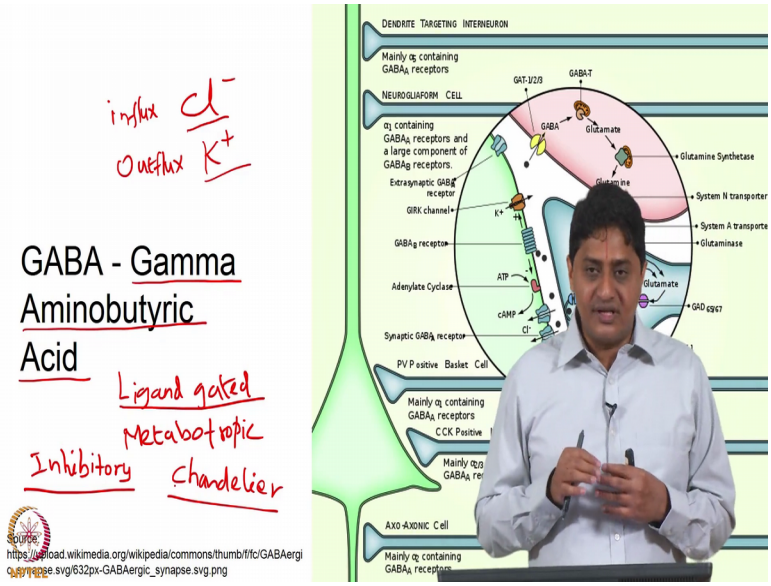

Once one simple example is the case of GABA, which is a neurotransmitter or an inhibitory neurotransmitter. This is Gamma Aminobutyric acid, so we discussed several cases of several types of a neurotransmitters. We said the amino acids, we said neuropeptides right. We gave a several examples of each. So, here is a Gamma Aminobutyric acid that is that is usually, in the usual case an inhibitory neurotransmitter how does it function. We will only discuss an important function here.

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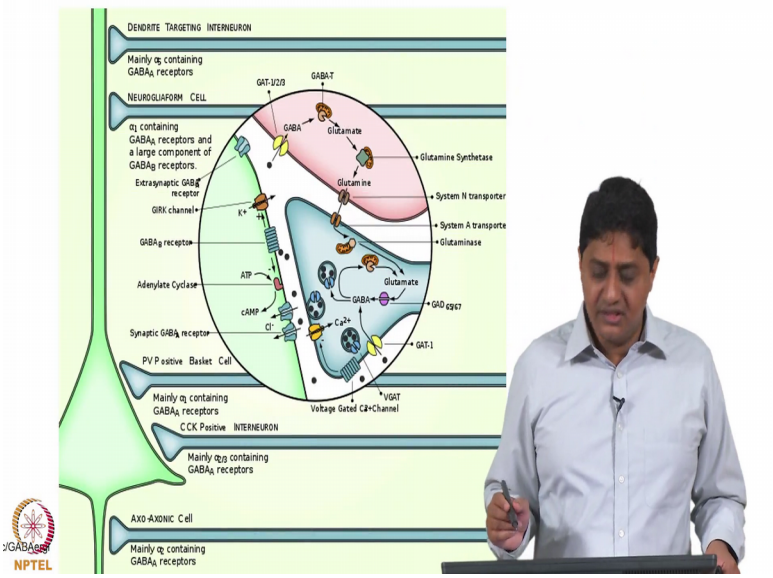

You see a picture that is depicting the lifecycle of GABA, which we are not going to discuss. We will only discuss what it does because in previous classes we have seen the lifecycle of a acetylcholine.

Here we will only discuss function of a GABA alone. What this does is when GABA sensitive receptors sense the presence of a GABA; so how is GABA itself released the usual mechanism. So, whenever an action potential arrives neurotransmitters are packed, neurotransmitter in this case is GABA. GABA is packed into vesicles the usual method GABA is packed into vesicles an action potential arrives in the presynaptic neuron. And it activates a calcium as usual this presence of calcium is detected by the membrane proteins and the neurotransmitter is released.

However, this neurotransmitter is inhibitor in nature previously, we talked about acetylcholine when acetylcholine goes and binds to the nicotine cholinergic receptors or the ligand gated channels the it causes an influx of sodium. Here we have a chemical which when binds to the receptors. It causes an influx of chloride or depending on specific cases it could cause an out flux of potassium, both have if you analyze both have similar functions, is it not? And influx of chloride into the postsynaptic cell brings the cell to makes the cell go more negative or this is an outward current, is it not?

So, it reduces the probability that this membrane is going to be taken to a threshold and an action potential caused in the postsynaptic cell same with the out flux of potassium.

So, there is not going to be sodium that is involved in this case, but rather whenever these channels are activated; potassium either leaves the cell or chloride enters the cell, thus reducing the probability that this cell is going to go to action potential or reach threshold and produce an action potential. In the brief time that is concerned by the way this changes is a function of time after sometime, there could be an excitatory neurotransmitter the receptors for which may will also be present on the cell membrane will be detected and will produce, but that in the future. At the particular point in time under discussion this could cause an outward current.

Thus reducing the probability that this is going to happen. And how is this receptor functioning, earlier we said nicotine cholinergic receptors in the case of a acetylcholine. Here there are 2 methods one is the ligand gated GABA channel, ligand gated channel. Similar to the nicotine cholinergic receptor, which is a also ligand gated channel. The other one involves the metabotropic receptors are involve, what are called as mediators. Those that involve G protein, the details I am skipping for brevity.

And the sufficient if you know that there is not just a simple method by which this function, there are at least a 2 mechanisms by which GABA could function the receptors are of at least 2 types. Those that involve mediator such as a G protein and those that involve a ligand gated ion channels, that and note that this ligand gated ion channel is not a sodium channel, but rather can be one of these, 2 can be either chloride channel that opens inside or can be a potassium channel that opens on the outside.

Thus reducing the chance that this cell is going to go to the threshold and note in many of this cases in almost all of these cases the this neurotransmitter GABA is inhibitory. Most of this cases, so when I say most whenever I say most; that means, that there are cases where this is not inhibitory. For example, in many insects GABA functions has both excitatory inhibitor, how is this possible? Also in mammals for example, there are specific cells this cells are called as I think chandelier cells. Check the spelling specific cells in which these this chemicals serves as an excitatory neurotransmitter.

So, a particular chemical can function either as an excitatory neurotransmitter or as an inhibitory neurotransmitter, how is this possible? By the way acetylcholine is in general an excitatory neurotransmitter, but there are cases in which it can also cause inhibition. There are examples of that we will see that in future classes while we are discussing the

specifics, how is this possible. Because the channels that are sensitive to the presence of this chemicals say for example GABA. If there is a channel that is sensitive to the presence of a GABA, which opens whenever GABA is there, but allows sodium inside let us take such a hypothetical case.

If there is a channel which opens and allows sodium to go inside it is going to cause an excitation. So, it is not just dependent so the synapsis and their function is not just dependent on the chemical alone, it is also dependent on the particular receptor on the particular channel that we are talking about. In many cases or in most cases GABA channels are those that produce an outward flux or those that cause an inhibition in most cases.

So, in general GABA is a inhibitory neurotransmitter, and in general acetylcholine is an excitatory neurotransmitter because it involves the opening of sodium channels inside the cell so bring in sodium inside the cell. So, in general this is true, but not in every specific case in biology exception is the rule. So, for every rule that we speak about there are exceptions. So, we will in so whenever I say you know this is a this is a GABA ergic neuron. So, this is going to cause an inhibition that is true in most cases.

So, by default whenever I am saying this is a GABA ergic neuron you should immediately put an negative sign next to it. You should immediately say that that is an inhibitory neurotransmitter, that is true by default. In specific cases where this function varies, if and when we discuss that specific cases I will tell you that you know there is a there is here is a case where that does not happen, the opposite happens please note this exception. So, in most cases it is sufficient if you know that in most cases GABA is an inhibitory neurotransmitter, acetylcholine is an excitatory neurotransmitter, glutamate is an excitatory neurotransmitter and so on and so forth.

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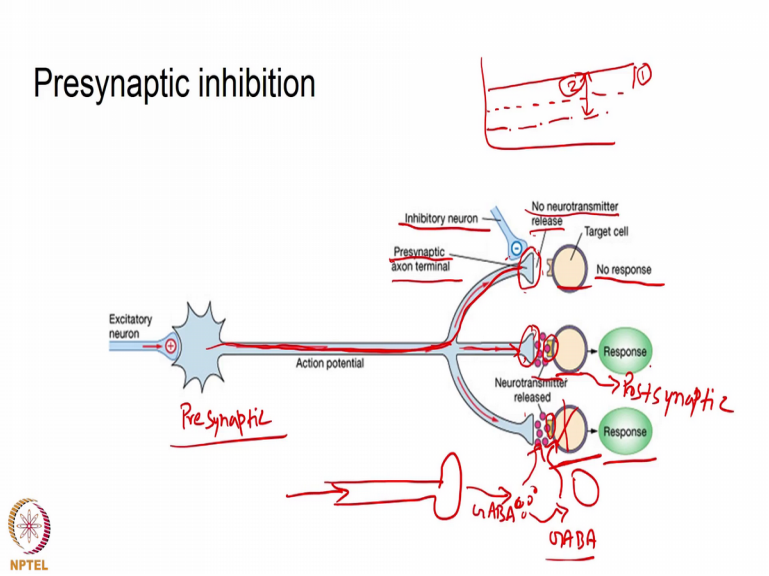

So, this is a case the so, what we have seen here is a case in which inhibition is caused due to postsynaptic mechanisms involving chemicals involving neurotransmitters. And then I said there is a case in which I could excite a neuron to cause inhibition in the postsynaptic neuron, how is this possible that is the question.

So, this mechanism is very special case for this to understand how this function, we need to know how the release of neurotransmitter itself functions. We said how neurotransmitter release is happening; that is due to the presence of calcium channels on the presynaptic cell. And which release calcium whenever an action potential whenever depolarization arrives as soon as depolarization arrives in the presynaptic terminal calcium is released. And this calcium is detected by the proteins and chemicals neurotransmitters are released from the vesicle into the synaptic cleft.

This is the mechanism that was discussed, but suppose for whatever reason I am keeping the membrane potential at a sufficiently high value. The arriving depolarization is not going to open many more calcium channels then are already open. So, in other words; suppose the membrane potential say was at that value. Earlier the resting membrane potential was at that value for example, and so suppose this is the membrane potential and I am reaching a new action potential brings the membrane close to that value right.

In this case the difference in the potential is smaller. The number of calcium channels that will open for this difference is smaller. Whereas, in this case the difference between

the potentiall, the membrane potential and the earlier resting membrane potential is larger. So, the number of calcium channels that will open will be larger. So, the amount of influx of calcium will be larger in this case, which I am going to call as case 2 and this I am going to call as case 1.

In case 1 the amount of a influx of calcium is going to be smaller and in case 2 the amount of a influx of calcium is going to be larger. And note depending on the difference in this difference in the amount of calcium that is detected. The number of the vesicles that are opened up or the amount of neurotransmitter that is released varies. So, in other words it is not dependent on the absolute value, but rather the difference in the amount of calcium that is detected. Since this difference is going to be a smaller in the first case the amount of neurotransmitter that is going to released is also going to be smaller.

So, if I can somehow maintain the membrane at a relatively high value of potential. Thus opening the calcium channels some of the calcium channels already, then the difference that is going to be detected is going to be a smaller affectively, preventing many or preventing a lot of neurotransmitter from getting released or much. Or no neurotransmitter can also it there may be a case when no neurotransmitter will be released because you are already at the maximum. So, that is a how is that achieved; by having an neuron that excites this part of the presynaptic terminal. And whenever that excitation is coming these calcium channels are going to open and sent in a lot of calcium.

But when a new excitation comes from the action potential of the same neuron cell body this is the presynaptic neuron, presynaptic neuron whose cell body is lying somewhere, but here is a different neuron that is activating this part right. When so when an action potential arrives it reaches this part or the synaptic end bulb right? Already this part is you know excited sufficiently that all the calcium channels are already open, there is not going to be any new calcium channel that is going to open due to the arrival of this action potential.

So, because of that no neurotransmitter will be released. Whereas, here is a case where there are no such excited state of this part of the synaptic end bulb. So, whenever an action potential arrives here, there is going to be more calcium channels that are getting opened, more vesicles that are going to open and a neurotransmitter is going to be

released into the cleft which is going to be detected by the postsynaptic cell. Here is the postsynaptic cell this is the postsynaptic cell or these are the postsynaptic cells that one, that one, and that one.

These 3 are the postsynaptic cells, when I am not activating this cell or when I am not activating this part of the cell. The action potential causes calcium channels to open and neurotransmitter to be released and detected by the presence of these receptors here and a response from this cell can be expected. So, this cell response why because there is no, in there is no excitation here that is causing an inhibition, but here there is an excitation that has taken the that has practically opened all the calcium channels everybody is already open new action potential arrives no more excitation.

New action potential arrives it is not like I can open any more calcium channels because they are all already opened. So, no difference in the amount of calcium is going to happen because of this reason. No new amount of neurotransmitter is going to be released. So, amount of neurotransmitter release is proportional to the difference in the amount of calcium that is present. Before the excitation arrives and a after the excitation arrives. So, depending on that if that difference is going to be small then no neurotransmitter or if that difference is 0 no neurotransmitter will be released.

So, this response or this target cell this postsynaptic cell will not respond at all so; that means, it is possible for me to selectively activate by the way; I can choose to not activate this. Suppose the this cell is present, but is not exciting this part, then what will happen? Then what will happen is that the what is happening here will happen. So, this part of the cell is not excited. So, all the calcium channels are closed before the action potential arrives then the action potential arrives, calcium channels are opening neurotransmitter is released.

So, I could selectively close a specific parts, a specific neurons using this presynaptic mechanism. So, here inhibition is happening due to this presynaptic mechanism or inhibition is happening due to an excitation. I can excite and ensure that there is an inhibition. So, it is a very special case of inhibition, which allows us by the way there are this could also have not is not what is not discussed is that; it could have another branch say, for example here that is going to release an inhibitory neurotransmitter like GABA that causes an inhibition this is postsynaptic inhibition.

This is a chemical that is you know inhibiting this cell or may be travels to these cells and inhibiting these cells that is possible. That is postsynaptic inhibition, this is presynaptic inhibition. So, there are there can be multiple cases of this or there maybe another neuron better still there may be a another neuron, that is an inhibitory neuron. For example, which through which whenever an action potential comes GABA is released ok.

So now GABA travels to these places and you know inhibits these neurons and there will be no response that is postsynaptic inhibition ok. So, fundamental difference presynaptic inhibition is caused due to excitation at the synaptic end bulb, ensuring that the calcium difference remains relatively small. And no neurotransmitter or very small amount of neurotransmitter is released causing an inhibition. Postsynaptic inhibition is that case in which a chemical, a neurotransmitter that is inhibitory in nature is released into the synaptic cleft preventing the possibility or the probability, excitable cell is going to go to threshold and produce an action potential ok.

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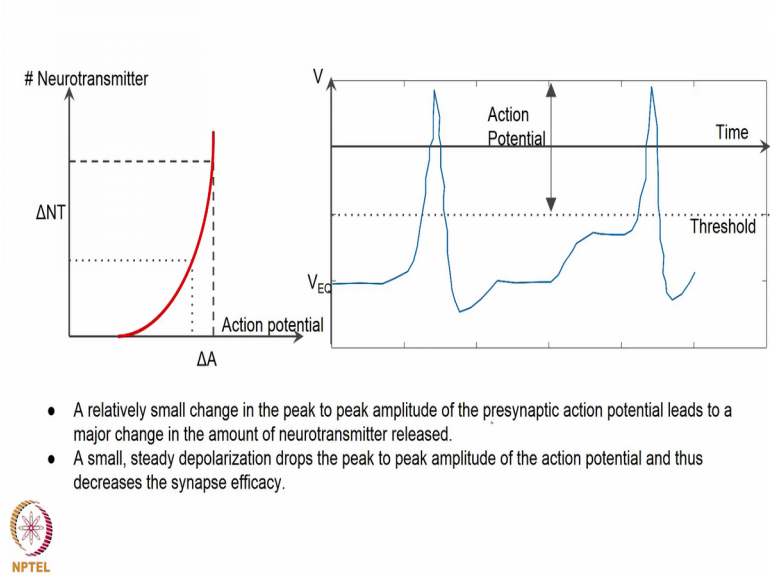

So, again, that the difference is discussed here. So, the difference in the amount of neurotransmitter that is released depends on the difference in the peak to peak amplitude that is what I was discussing. So, the peak to peak is the peak to peak amplitude of the presynaptic action potential is relatively small. Then the amount of calcium that is

released is also relatively small. So, this varies as function that is shown here for example, this is an example data.

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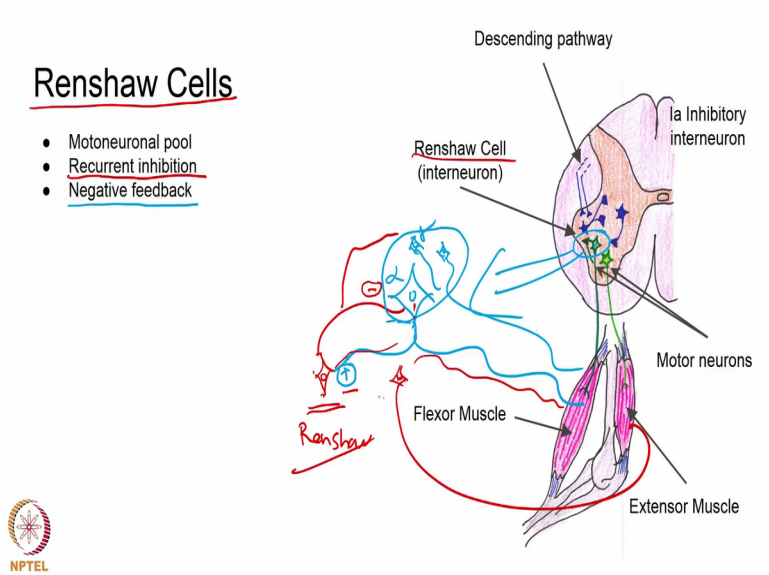

Here we discussed a particular case of an inhibitory interneuron within the spinal cord. So, these inhibitory interneurons are called as Renshaw cells, there are more inhibitory interneurons and other interneurons within the spinal cord not discussed in this class, but we will be discussed in future classes. But just wanted to touch upon one particular example, it is functions in reflexes it is functions in a other in other domains to be discussed in future, just briefly we will touch upon this function.

So, Renshaw cells are present in the motor neuronal pool where whereas, this is present to remind ourselves in the so how are these arriving to the to the muscles from the ventral roots is it not from the ventral root of the spinal cord so these are motor neurons. So, these whenever a motor neuron is a activated these Renshaw cell is a also activated. What this does is it activates the Renshaw cell that is shown as triangle here so that is that one.

So, this is activated along with the motor neuron, which is which I am going to circle with blue here for the sake of clarity. That is that one that is the motor neuron zoom this out for clarity. So, that is a motor neuron, that is going to take information to the and there are 2 of these. We will consider an alpha motor neuron for the case of, so a alpha motor neuron means that the one that is going to excite the extra visual fibers are the

force producing fibers, just going to contact the muscle this activates and the smaller neuron I am going to draw that in red which inhibits it is this is a plus and that is an. In other words, this motor neuron activates this interneuron which inhibits the motor neuron that activated it, what does this means?

So, whenever this motor neuron is activating the muscle; it activates an interneuron that inhibits the motor neuron that activated it, why would this happen? You cannot keep a increasing the excitation to the muscle forever you need to control that the, if the in excitational level to the muscle goes beyond a particular point it could cause physical damage. It could cause a it could have negative consequences which are undesirable.

So, you want to control the amount of excitation that is sent. So, as soon as a excitation is sent and inhibition is sent back to that motor neuronal. Actually what it does is more than this what is not shown more, more than this. So, this also branches out to other motor neurons. So, it actually causes an inhibition so that may be gamma that may be alpha and other motor neurons of distant, but agonistic muscles. So, it is going to cause an inhibition for the action not just for the cell.

So, if I am fluxing for example if I am performing fluxion, usually I give this example as if there are only 2 muscles that are involved, actually there are multiple muscles that are involved in this elbow fluxion function. There are 3 muscles that are involved Biceps, Brachii, Brachioradialis and Brachialis these are the 3 muscles that are involved. When I am fluxing the command for the fluxion is given by a motor neuron. And that information's received by the muscle, but simultaneously it also activates this inhibitory interneuron that is going to inhibit that motor neuronal pool. So, it is going to inhibit the whole pool or a large number of cells in this pool many of the cells in the pool are going to be inhibited by this guy.

This cell that produces an inhibition that causes an inhibition in the motor neuronal pool by the way whenever we say motor neuronal pool this could be any motor neuron. This could be alpha motor neuron of that muscle, gamma motor neuron of that muscle and alpha and gamma motor neurons of the other agonistic muscles. So, agonistic muscles are those that performs similar function. So, whenever Brachii Biceps is activated it could or this in inhibitory interneuron could inhibit the function of not just Biceps, but also Brachialism Brachioradialis.

So, it sense it inhibits a whole bunch of neurons motor neurons. So, in a way to perform the important function the critical function of negative feedbacks. So, I am interested in reducing or controlling the amount of excitation that is sent to the muscle. So, I am interested in placing a road block or interested this is like having a speed breaker or. So, in some sense I want to ensure that it does not increase to a level, where I cannot control this; this kind of inhibition. That is caused due to excitation, why by the way who is activating this to remind ourselves, who is activating this inhibitor interneuron; the same motor neuron it is this cell that is exciting is it not. So, the cell that is exciting it is getting inhibited by itself or in other words because this is called as a recurrent inhibition ok.

There may be cases where the in other interneurons maybe there. So, this kind of this interneuron that cases a inhibition of the same motor neuronal pool that activated it is called Renshaw cell, this interneuron is called as a Renshaw cell. Already written elsewhere also written here. There may be other interneurons not shown in this picture that will inhibit, the opposite muscle antagonistic muscle or that may excite the opposite muscle. When that happens; right that is different that is different will be discussed in future classes.

Here we are discussing one particular case we will just discuss the case of a one level of hierarchy in which, negative feedback is introduced. There are multiple levels of this negative feedback that comes into the picture. So, inhibition is present at a various levels this is a lowest level at which it is present there are other levels. So, we will discuss a each of those levels in future classes. So, to ensure why so much inhibition, why so much control, why so much control over how much excitation is going because it is necessary for us to perform functions, motor functions at that level maybe there is some demand; there is an necessity for us to perform motor functions at that level that requires control at multiple levels.

So, may be control or negative feedback at a multiple levels function functions to ensure that the excitation level does not go beyond a bounds, does not go beyond a limits causing physical damage. Note the muscles is made of you know materials that could undergo a physical damage or we want to at least minimize the amount of fatigue that is filled or at least, other such things other such considerations. So, which is why negative feedback is present that is enforced by this particular cell called Renshaw cell, its function is more functions or of this particular cell we will be discussed in future class or

way more, more complications are going to arrive as we continue the discussion in future classes ok.

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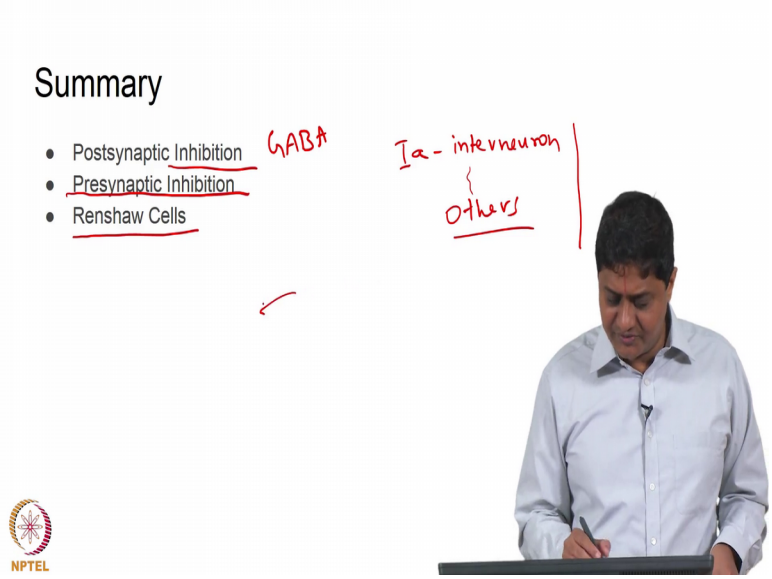

So, what we have seen is a particular case of inhibition that is caused due to chemicals such as GABA. That are mediated by the presence of postsynaptic ion channels, postsynaptic channels that open due to that are sensitive to the presence of these chemical that are called as postsynaptic inhibition. Or inhibition that is caused due to an excitation that is ensuring that the calcium channels are already open or the difference peak to peak difference remains sufficiently small that the amount of neurotransmitter release is sufficiently small, this is called as a presynaptic inhibition; that can be selectively opened and closed, selectively switched on and off. Presenting one more layer of control, one more method by which you could switch on and off specific synapsis.

And then one particular case of inhibitory interneurons called as a Renshaw cells that inhibit the motor neurons that activated it; are called as this is also called as recurrent inhibition. In future classes we will be seeing other cases that are called as a one a interneuron and the what it is function and other inhibitory interneurons to be discussed others, not the not giving the specifics. We will reserve those discussions for future classes and the various loops of excitation in inhibition which particular part of the spinal cord is responsible for what excitation and inhibition; we will discuss in future classes. So, I will stop here with this we come to the end of this class. Thank you very much.