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

Lecture – 63
Cerebellum Part -12

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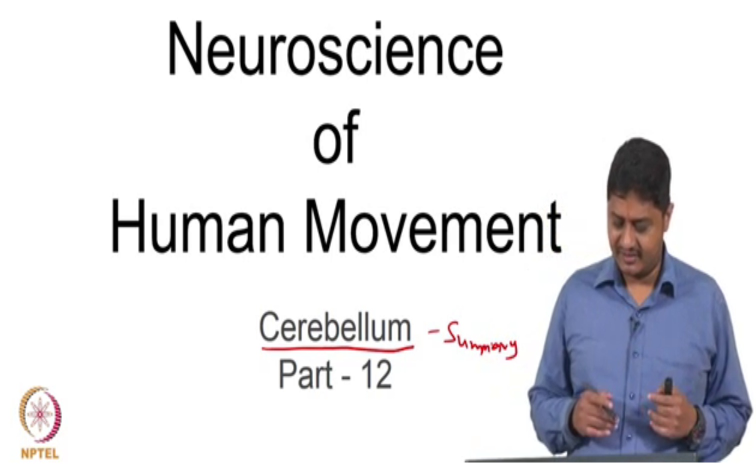

So, welcome to this class on a Neuroscience of Human Movement. In today's class, we will be discussing cerebellum. And it will be a summary of the discussion, the previous discussion. So, for the past 11 videos we have been discussing, cerebellum its anatomy, its functions, pathways and what could happen in case of lesions etcetera. In this class, we will summarize, so some details may be missing, please do check back the original video to understand the details. Here, the idea is to provide just relatively brief summary of the topics.

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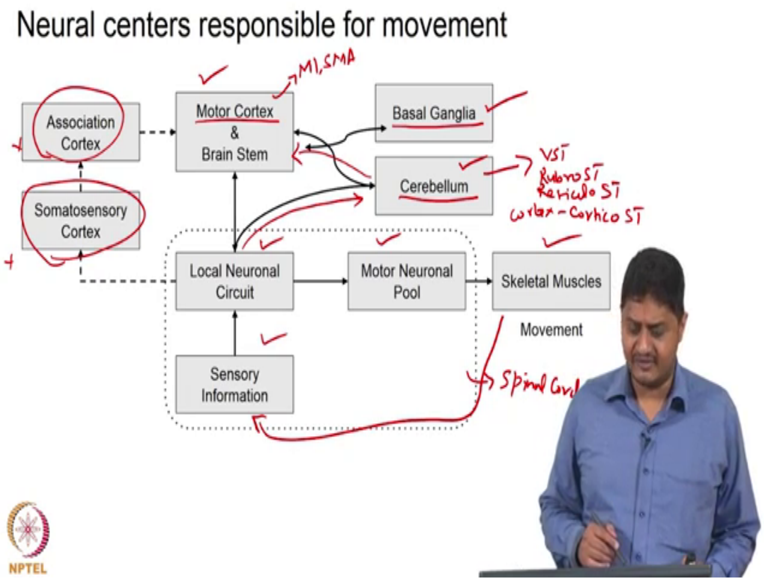

So, let us remind ourselves of the situation with movement system or the neural control of movement. The system that is responsible for neural control of movement. We said that movements are generated through skeletal muscles. And skeletal muscles are controlled by alpha motor neuronal pool in the spinal cord, so that is the spinal cord; the dotted box is a spinal cord. And these alphabet a neuronal pool or control by local neuronal circuits, there is sensory information that also comes from the muscle for example and from other sources of course.

And we have discussed the skeletal muscle physiology of that and how movements are generated, how muscles are responsible for movement generation, we have discussed the connectivity within the spinal cord excitation and inhibition within the spinal cord, how alpha motor neuron circuiting excited, how they may be inherited, how sensory information crosses alphabet and neurons to fire or get inhabited as the case may be.

And we have discussed how these spinal motor neuron circuitry, and its function is controlled to a large extend by the motor neurons or the motor areas of the cortex; this is a primary motor cortex or simply M 1, or supplementary motor area. And then other motor areas we have discussed the other areas, which is the pre supplementary motor area. And the dossal pre motor area, ventral pre motor area, pre dossal pre motor area, etcetera; we have discussed all this cased in the previous classes.

And we have discussed so far, in the last 11 lectures we have discussed, the role of cerebellum in modulating movement importantly, please note that the cerebellum receives input from the spinal cord that is one way arrow. And it communicates not directly with the spinal cord, but rather with the motor cortex and the brain stem. So, it does not directly mod, directly control movements whereas, it modulates movements or it regulates movements.

So, in other words, it does not communicate with the spinal cord. The cerebellum has no direct projections to the spinal cord, although the cerebellum has projections through the vestibulo spinal tract; Rubro spinal tract, Reticulo spinal tract. And through the cortex, as in it projects to the ventro lateral thalamus; from the thalamus to the cortex and from cortex to through the cortico spinal tract right.

So, we will discuss these topics, we have discussed cerebellum. Somatosensory and the sensory areas we will not discuss as part of this course, we have we have mentioned this previously. So, the next topic of discussion will be basal ganglia. So, let us remind ourselves of what we learnt in the past 11 lectures.

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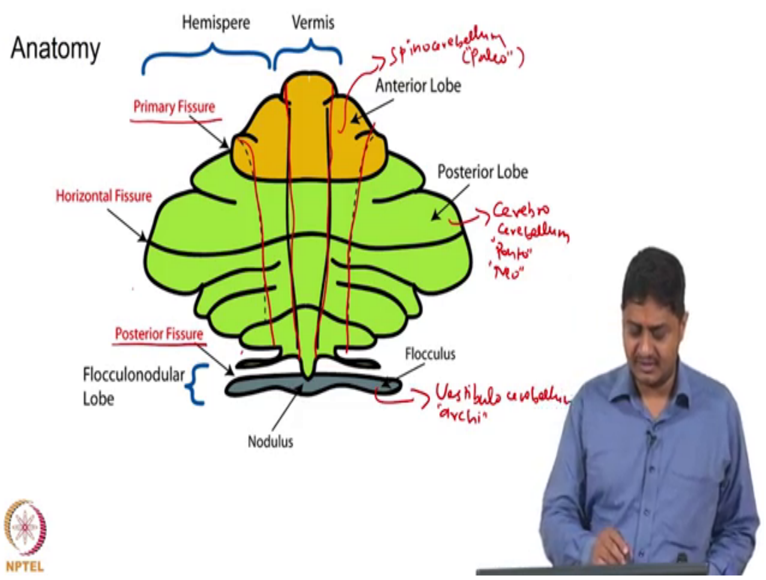

So, this is an picture that shows the anatomy of the cerebellum. There is the anterior lobe, and there is the posterior lobe, so that is the posterior lobe relatively big lobe is posterior lobe; these two are separated by the primary fissure. And there is a fissure that separates the posterior lobe from what is called as the flocculonodular lobe to remind ourselves, a the flocculonodular lobe is also called as the vestibulo cerebellum are the archicerebellum. This is the old cerebellum that is found even in fissures right.

So, evolutionarily this is the earliest precursor to the cerebellum. Further development lead to what is called as the spinocerebellum that is spinocerebellum is basically the vermis, and the intermediate zone are the paravermal area, this is called as the spinocerebellum; this is called as the vestibulo cerebellum.

Vestibulo cerebellum are the archi cerebellum, it is called as the spinocerebellum are the palio relatively old, but not too old palio cerebellum. The lateral areas are well developed in advance species in more developed species such as primates and humans that is called as the cerebro cerebellum, also called as ponto cerebellum, also called as the neo cerebellum it is a relatively new, so it is called as the neo cerebellum. Their functions are different the areas to which they project and different the inputs the areas from which they receive inputs are different.

So, we have discussed these cases separately in vestibulocerebellum for a couple of classes or maybe the spinocerebellum for 1 or 2 classes and the cerebro cerebellum for 1 or 2 classes. And the lesions that happened to these regions also cause characteristic differences. So, there will be a difference depending on the region of the lesion, the response of the system of the organism will be different etcetera, etcetera. So, the flocculonodular lobe what is not mentioned is the flocculonodular lobe is separated from the posterior lobe, through the posterior fissure and the anterior lobe and posterior lobe at the separated by the primary fissure.

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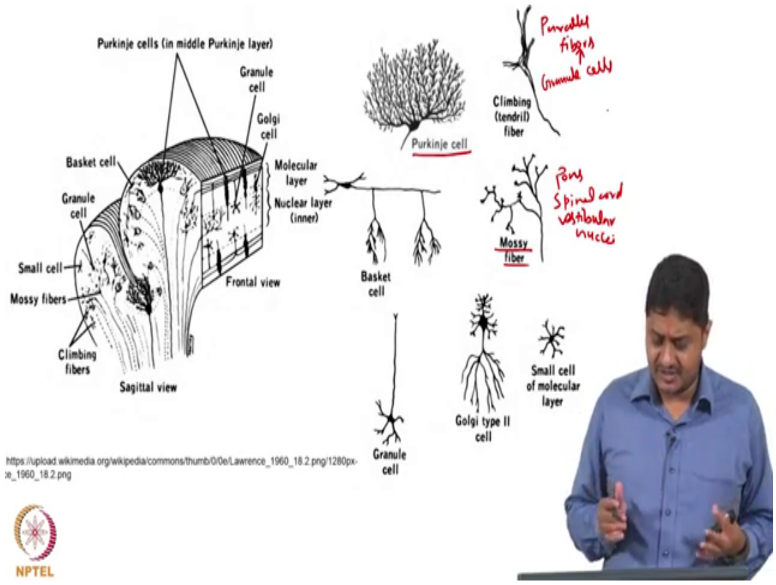

Now, also in the discussion of the micro circuitry we said that there are this climbing fibers that originate in the inferior olive. So, there are two major sources of inputs; one is the climbing fiber, exclusively originating from the inferior olive if fiber originates from the inferior olive, and projects to the cerebellum it is called as a climbing fiber. There is a reason why this is called as a climbing fiber, because this claims through the tree like structure of the purkinje cell, and makes multiple synopsis with its dendrites.

And all the other inputs that originate from all other sources, such as pons what is the source of information to the pons; pons receives input from the cortex and then projects, so pons acts as the relay center by receiving input from the cortex and then projecting to the cerebellum. And these inputs are coming through, what are called as mossy fibers and spinal cord, vestibular nuclei. Any source that is not the inferior olive if it enters, if it gives an input to the cerebellum it is called as a that fiber is called as a mossy fiber ok.

The way these two systems work is fundamentally different. So, we will discuss that very briefly, we had a relatively long discussion of this topic in previous classes, so but I will try to remind you of this. It turns out that the purkinje cell is two-dimensional; so it is thick in one dimension and relatively thin in the other dimension right. So, in it in the dimension in which it is thin, it receives inputs from millions of parallel fibers. This has not been discussed previously in this class, as in this has not been discussed previously in today's class.

The mossy fibers make synopsis with water called as granule cells, the whose actions go on to become parallel fibers. So, granule cells so granule cells, receive input from mossy fibers and their actions go onto become parallel fibers. And each purkinje cell which is in inhibitory neuron, receives input from hundreds of thousands of parallel fibers right.

So, let us remember that there are about one hundred billion granule cells. So, there is a great divergence of information from the mossy fiber system, there is a smaller number of mossy fibers and so each mossy fiber makes a synopsis with thousands of granule cells whereas, each granule cell receives in information only from a few mossy fibers. Also note that the climbing fiber relationship with purkinje cells is also special, the climbing fibers each climbing fiber projects to about 1 to 10 purkinje cell, but a given purkinje cell this is input from 1 and only one climbing fiber.

The way these two function and the balance of excitation between these two systems, probably form crucial role in the function of the cerebellum as a whole.

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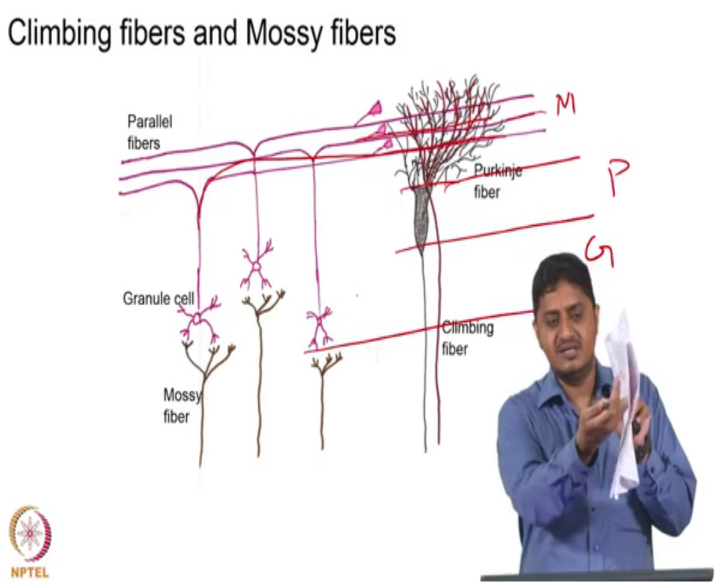

So, what you see here, once again let us remind ourselves how the situation the so the layer were the dendrites of the purkinje cell is located and other neurons and the actions of the parallel fibers located, this is called as the molecular layer. The layer where the purkinje cell bodies are located is called as a purkinje cell layer. And the layer where the granule cell bodies are located at just below the purkinje cell is called as a granule cell layer right. And so mossy fibers inner wet granule cells, and they go want to become parallel fibers and they inner wet the purkinje cell perpendicular to each other.

We showed this example of cables passing through sheets of paper, so the so the sheet of paper is th[ree] is two-dimensional and it is very it has area in this dimension, but in this dimension its relatively thin; and the parallel fibers go through this. So, this is the purkinje cell as in that is the purkinje cell, and the parallel fibers are perpendicular to the purkinje cell, this we discussed in the previous class. So, because of this reason the parallel fibers are able to inner wet a number of purkinje cells, and each purkinje cell receives input from a whole bunch of parallel fibres; hundreds of thousands of parallel fibers.

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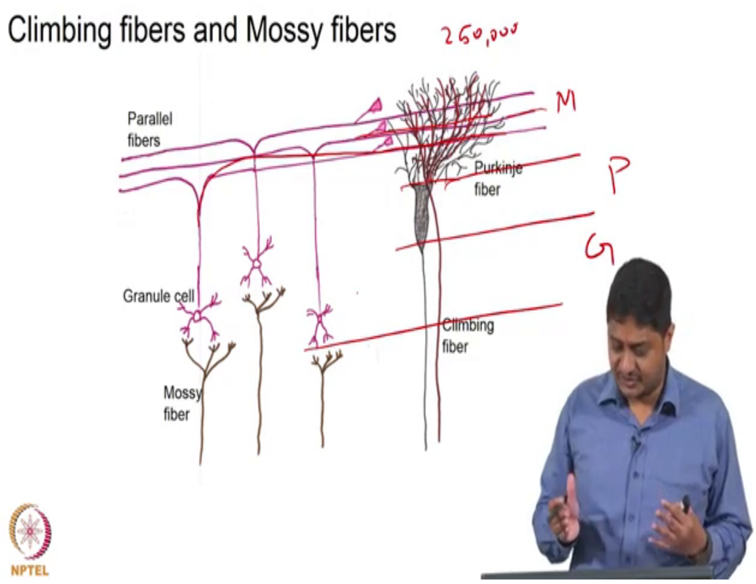

The number of dendrites in purkinje fibres can be as high as 250000 ok, relatively large numbers this ok. So, this important feature of the cerebellum or this micro circuitry of the cerebellum gets repeated multiple times thousands of times. So, this function of the cerebellum is probably predictable by function of this simple micro circuit.

So, if you if we are able to understand, how this micro circuit works to some extent at least to some extent, we should be in a position to understand how the cerebellum works The details of how exactly the cerebellum works, all its functions and its abilities continue to remain a mystery, but to some extent we are able to uncover that mystery by understanding of the neurophysiology of how this micro circuit works.

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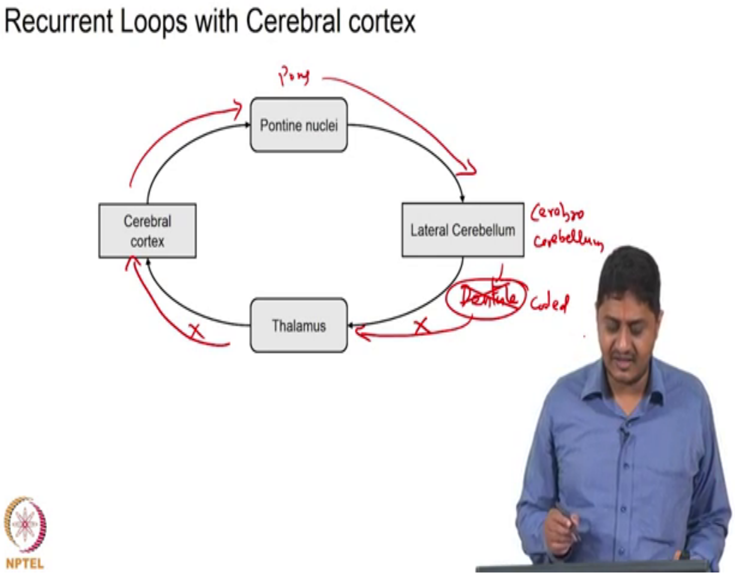

And we discussed the recurrent loops that the cerebellum has with cerebral cortex. So, cerebral cortex since neurons are sends information to the pons, and pons acts as the so that is pons or pontine nuclei. Pons acts as the relay center and it sends information to lateral cerebellum, lateral cerebellum means the cerebro cerebellum. And without the detail of how exactly this is happening, from the lateral cerebellum basically there is projection back to the dented nucleus, that is not discuss; so there is projection to the dentate nucleus which is one of the deep nuclei of the cerebellum.

So, there are four nuclei of the cerebellum; these are dentate nucleus, fastigial nucleus, globus and amboli from nuclei right. And the globus and amboli from together are called as the inter post nuclei sometimes right. So, the dentate nucleus projects to the thalamus, and from the thalamus the information goes back to the cerebral cortex. Most of the time this information goes back to the motor areas of the cerebral cortex, thus modulating the motor function right.

And let us remember that if the dented nucleus is cooled, cooled in activated or deactivated, then what happens is that information does not go from the cerebellum to the thalamus, and from the thalamus to the cerebral cortex; but this just not prevent movements from happening, but rather this delays the movement and reduces coordination. We saw this in one of the previous classes, where we showed that cooling of the dented nucleus produces symptoms typical of the cerebellar disorders right. So, there will be drummers, there is overshoot and undershoot, etcetera.

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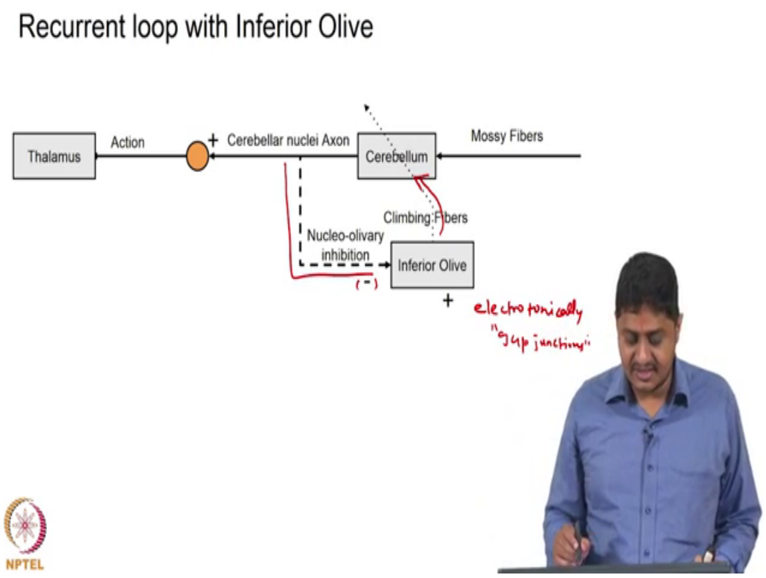

Also another recurring another recurrent loop is with the inferior olive. It turns out that the cerebellum receives input from the climbing fibers actually it is a very strong input, because the climbing fibers produce what is called as the complex spike, this is because of protracted or prolonged calcium conductance in the climbing fiber purkinje cell synapse right.

So, this causes this has a strong effect on the purkinje cell, and the purkinje cell inhibits the dip cerebral nuclei right. It turns out that what is also true is that the deep cerebellar nuclei can have inhibitory effect; actually there is an inhibitory sign that is there. So, I have an inhibitory effect on the inferior olive, a special feature of this inferior olive neurons is that these neurons or neurons within the inferior olive can communicate with each other electro tonically, through gap junctions.

So, very special feature not present in many other cases right. So, in a way the cerebellum controls its inputs to some extent, at least it regulates what sort of input it recession to what extent this inputs are influential to the cerebellum itself. So, cerebellum this is inputs, it also it also regulates its inputs or it regulates at least one of its strong inputs which is the climbing fiber through the inferior olive. So, this is the recurrent loop that the cerebellum has with the inferior olive. This is the previous case that we saw where the cerebellum having recurrent loop with the cerebral cortex.

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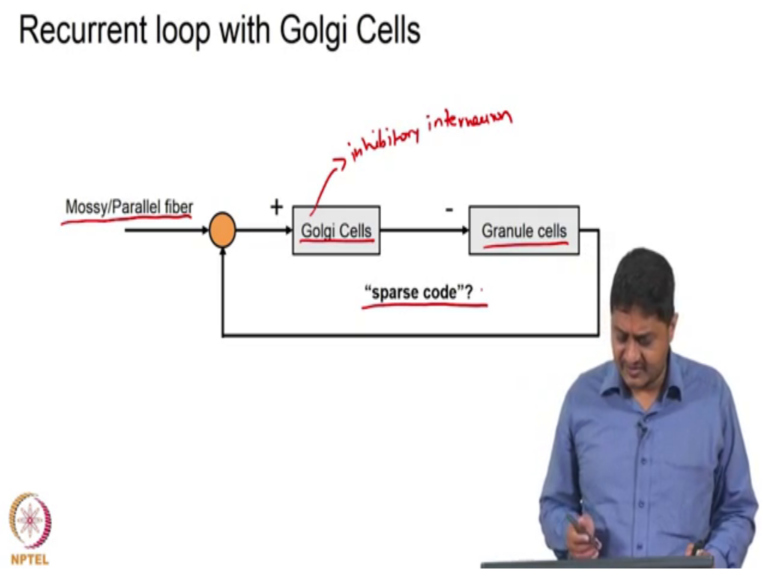

Another recurrent loop involves loops that exist within the cerebellum. In this case, it turns out that the mossy parallel fiber system excites and interneuron type of interneuron, inhibitory interneuron called as Golgi cells. These Golgi cells intern inhibit granule cells, actually it is the granular cell or the parallel fiber that excites the Golgi cells; they intern inhibit the granule cells.

Let us remember, let us remind ourselves this granule cells a very large in number, we have one hundred billion granule cells if all of this are active simultaneously it is not clear, what is the information that is being communicated. So, to ensure that we get the information that we want, while avoiding unwanted information or in other words noise.

It is important to keep a large number of this granule cells silent, in that sense Golgi cells it is believed or an interesting hypothesis is that the Golgi cells are keeping a large number of granules cells silent, so that whenever the granule cells are active the information that is communicated by them is, in some sense more informative or in some sense this is helping the cerebellum code information; in some form of sparse code.

What is what could technically be called in engineering parlance, as sparse code yes probably. This is an interesting hypothesis, this continues to be researched actively and the pathways within the vestibulocerebellum.

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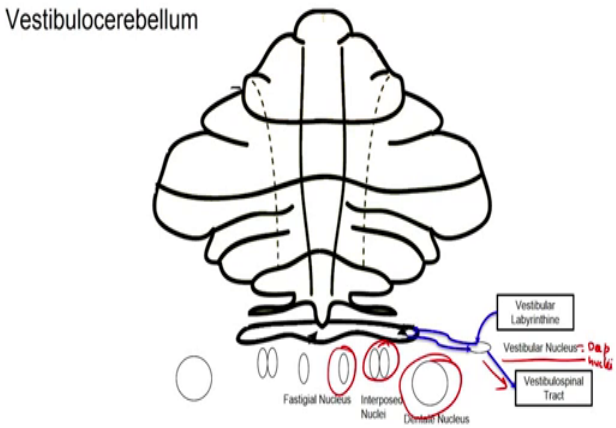

So, it turns out that the information from the vestibulo labyrinth was to the vestibulo nucleus and to the vestibulo cerebellum, which is the flocculonodular lobe here. And from there, it projects back to the vestibulo nuclei and from there to the vestibulospinal tract. And interesting point to note here is that information from here does not go to any of these, these are the deep cerebral nuclei; these are the major output structures of the cerebellum.

The vestibular nuclei are considered as both input also as the major output system. So, in some sense the vestibulo nucleus is comparable to the deep nuclei, in the sense that it is acting as an output nucleus of the cerebellum ok.

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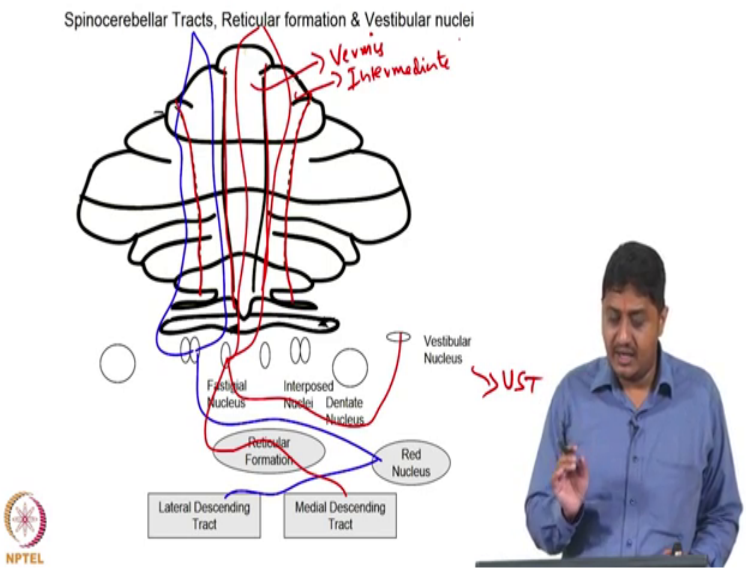

And within the spinocerebellar case there are few pathway. So, here you have the interposed nuclei, these are the interposed nuclei, we said this is the globose and emboliform are the interposed nuclei. So, information coming in from the vermal and the paravermal area, right. So, they project to the red nucleus and from the red nucleus to the lateral descending tract. Important to note here is that the cerebellum controls movements or controls parts of the body that are on the same side.

So, this may happen in multiple ways, this may happen in a way where the projection from the cerebellum is to the same side of the body, it is not going to be direct; the indirect projection is go going to be on the same side of the body or it is possible that there can be two crossovers like it happens in this case ok. So, it is crucial to note whether there are two crossovers or not, but regardless of whether there are two crossovers or whether there is no crossover is important to realize that cerebellum controls body parts that are on the same side or ipsilaterally, whereas cerebral cortex, whereas the motor cortex, controls parts of the body that are on the opposite side or the contralateral side.

So, within the vermal area for example, there is projection to the fastigial nucleus and from the fastigial nucleus to the vestibular nuclei, through the reticular formation and from the reticular formation through the medial descending tract also called as the reticulospinal tract, this is called all the red nucleus pathways also called as the rubrospinal tract. And from the vestibular nucleus, there is output that is called as the vestibulospinal tract.

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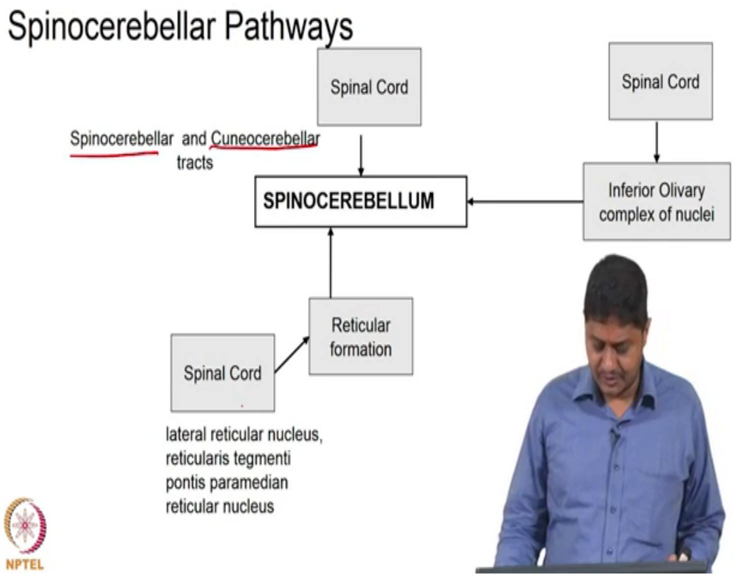

There are multiple inputs that the spinocerebellum receives, what is the spinocerebellum; spinocerebellum is this intermediate zone, this is the vermis that is vermis and this is the paravermal area are the intermediate zone right. The most medial and the neighboring areas are called as the spinocerebellum is it not. It receives inputs from multiple sources, but all of them are coming from the spinal cord mainly. So, what are the pathways, these are called as the spinocerebellar and the cuneocerebellar pathways.

And spinal cord projects to the reticular formation and multiple nuclei within the reticular formation such as the lateral reticular nucleus, such as a reticularis tegmenti and pointis paramedian reticular nucleus. For example, from there is projection to the spinocerebellum so that is one, there is more actually.

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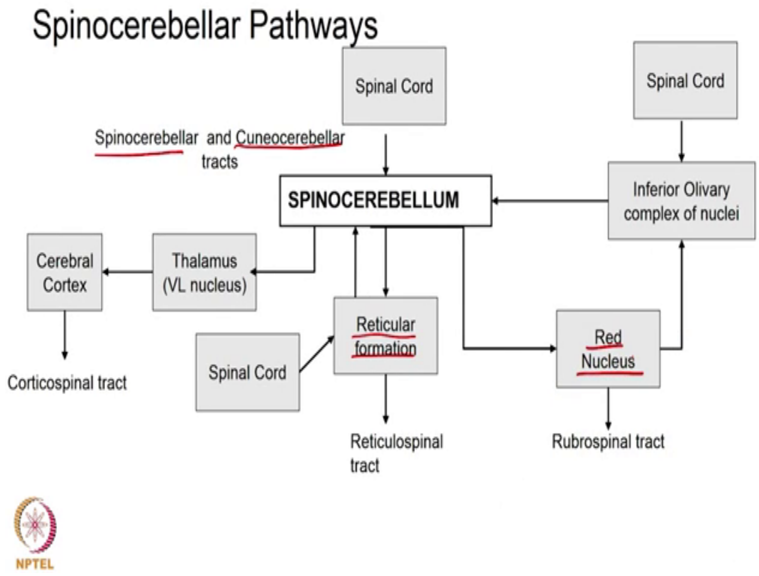

And the spinocerebellum projects back to the reticular formation, and the reticular formation controls the spinal cord via the reticulospinal tract. And spino cerebellum also projects to the red nucleus, and through to the rubrospinal tract controls the spinal cord. So, note here from the spinocerebellum there is in direct connection, this is not there. There is an direct projection to the spinal cord, but rather it is only through reticular formation and red nucleus in the case of spinocerebellum. In the case of cerebrocerebellum it is going to be though thalamus and cortex, that is in the next few slides.

So, there are multiple cases. So, for example, so there is it also projects in some cases to the ventrolateral thalamus and cerebral cortex through the corticospinal tract. So, information is coming in from multiple sources, from spinocerebellar, cuneocerebellar tract from the reticular formation and it is projection the outputs are projected to reticular formation, red nucleus and to thalamus cortex and the outputs are finally implemented, the final execution is performed through reticulospinal tract, rubrospinal tract, corticospinal tract, etcetera.

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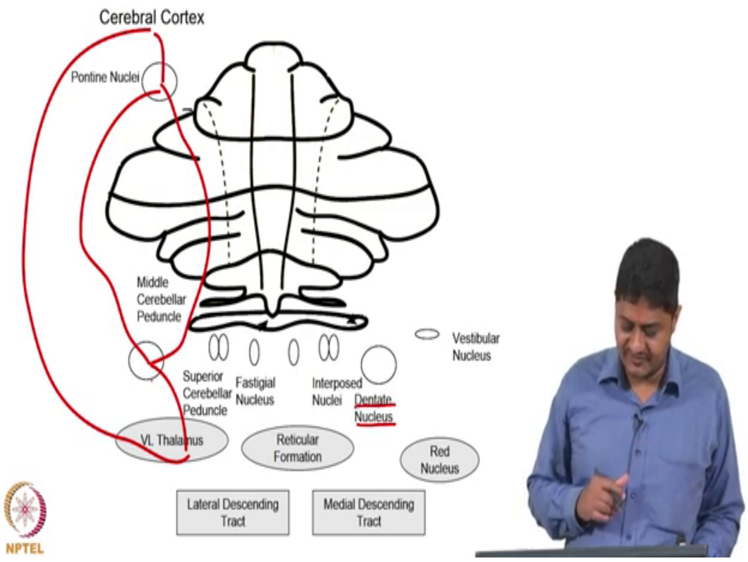

And for the cerebrocerbellum case, information comes in from the cerebral cortex to pons, and from pons to through the lateral areas are this is the cerebro cerebellum through the lateral hemispheres, and projects to the dented nucleus that is the big nucleus right. Through the dented nucleus, this is relatively well developed in advance species such as humans, right.

And this is mainly through the middle cerebral peduncle. So, middle cerebral peduncle is exclusively dedicated for communication with the cortex right, and from there to the ventro lateral thalamus through the superiors peduncle, and from the ventro lateral thalamus back to the cerebral cortex; this is the recurrent loop that we saw in one of the previous slides right.

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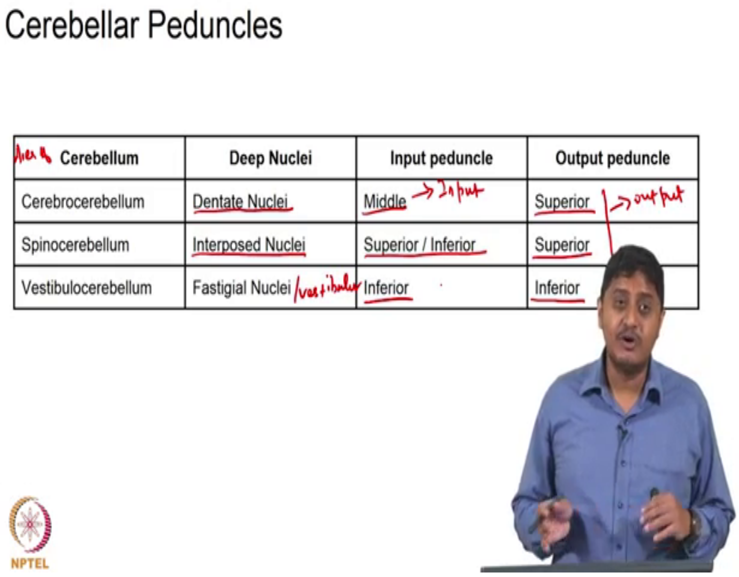

So, very brief overview of the cerebellar peduncles here. So, parts of this is the sub part of the cerebellum or area of the cerebellum. If it is a cerebrocerebellum, it receives input from the cerebral cortex via the pons, and it outputs through the dented nucleolus; and the input peduncle is mainly middle peduncle, and the output peduncles is mainly superior peduncle. If it is the spinocerebellum, it receives input from the spinal cord from multiple sources through the cuneocerbellar tract, through the spinocerebellar tract.

Actually there are two divisions of that the dorsal spinocerebellar tract, the ventral spinocerebellar tract, etcetera and the cuneocerebellar tract. And the deep nuclei involved or usually the interposed nuclei. The input peduncle is are not just one, in this case it may be either superior or inferior, the output peduncle is mainly the superior peduncle.

And if it is a vestibulocerebellum, then it receives input mainly from the vestibulo nucleus, and the deep nuclei involved are fastigial nuclei sometimes it is the vestibular nuclei. And the input peduncle is mainly inferior, the output peduncle is also inferior right. So, one could see that in this case in by looking at the peduncles, you could say that the middle peduncle is mainly an input peduncle; the superior peduncle is mainly an output peduncle mostly. The inferior peduncle is a relatively complicated structure, it is a it is a smallest, but its relatively complicated there has both input and output projections.

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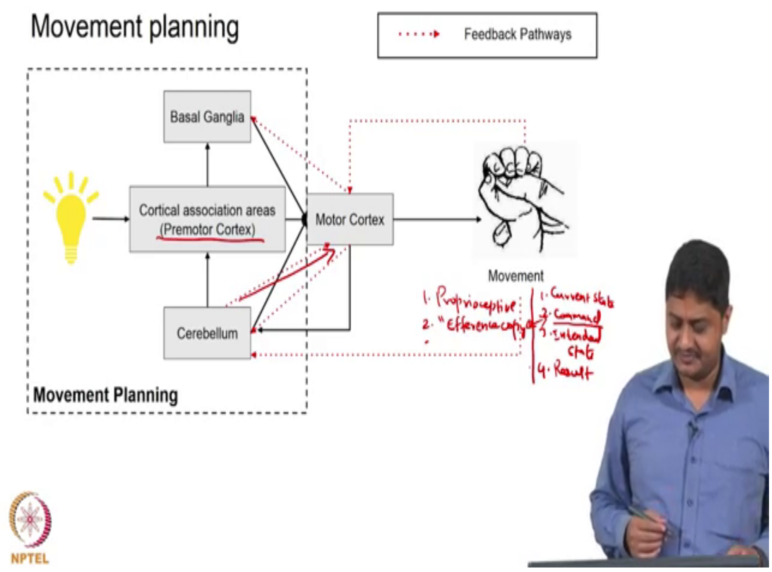

And we discuss the case of the role of cerebellum in planning and a regulation of movements. So, feedback about movements arrive at the cerebellum through multiple sources, it also goes to other sources such as motor cortex; for example, the movement is being made, motor cortex receives input the or feedback via the association cortices that is shown here, that is shown here. And cerebellum receives information about the plant movement, how does this received information via the dorsal and the ventral spinocerebellar tract; what it receive what is the kind of information that it receives, proprioceptive information and what is called as efference copy, so cerebellum knows the current state.

Cerebellum knows what is an what is the state that is going to happen, what is the current command, and it knows the results; so, it knows the current state, it knows the command, it knows the intended state, it knows the result of the command. How does it know the result of the command, the result of the command is known by proprioceptive information, I have given this command I want to make that movement, but an whether or not I have made that movement can be understood by comparing the intended state and the result. If these two are the same, then there is no need to make any correction; if these two are not the same that is a movement error that must be corrected.

So, there are multiple sources of information, how does the cerebellum know the intended state that is coming from other sources from motor areas of the cortex and brain stem that project to the cerebellum, this is what the intended state is how does it know the command that is the efference copy, command is the efference copy. How does it know the current shape, once again through the proprioceptive information. So, multiple sources of information are integrated in the cerebellum, and it functions mainly as a error correcting engine right.

So, and it does not perform this error correction directly, it always projects to the cortex via the thalamus or to brain stem via the other sources such as red nucleus reticular formation right. It projects to other motor areas, and these motor areas project to the spinal cord via the vestibulo spinal tract or rubrospinal tract, retriculo spinal tract or corticospinal tract. So, in other words cerebellum gets this information on multiple factors and helps to regulate or modulate movements.

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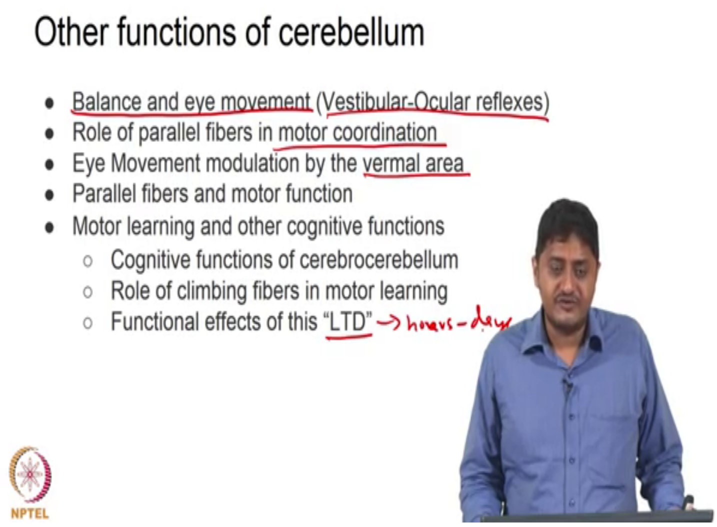

So, it is also believed that there are other functions of the cerebellum such as cognitive functions, but before that there are function such as balance and eye movement, such as vestibular-ocular reflex we discuss this case, in one of the previous classes. And it is believed that parallel fibers perform a crucial role in motor coordination, parallel fibers project perpendicularly to the purkinje cells, because they innervate purkinje cells at multiple levels. It is possible that the these purkinje cells, which project to the deep nuclei in a somato topic manner, so that means if different purkinje cells are activated, that means that there could be multi muscle coordination or multi effecter coordination; in other words motor coordination.

And modulation of eye moments by area in the medial cerebellar cortex, so the vermal area and the other contributions of parallel fibers in motor function and then most importantly motor learning. What we said about motor learning was that the climbing fiber acts as a teaching or instructing signal by simultaneously activating the error causing by simultaneous activation of the purkinje cell along with an error.

So, whenever an error is happening, a set of parallel fibers have fired right or firing at that time. At around the same time, if the climbing fiber is also firing this causes what is called as a long term depression in the purkinje cell, parallel fiber synapse. So, in other words, it is telling the purkinje cell or it is informing, it is communicating to this purkinje cell that these parallel fibers are causing errors, repeated effects or repeated repetitive actions of this.

For example, multiple times and the same thing happens as in the same error is happening, this climbing fiber is again informing causes this long term depression to become are the to for the climbing fiber to continuously activate the purkinje cell that way it is reducing the possibility that these parallel fibers are going to be responded to in future. So, that way there is an error correction that happens in relatively long term, this could last two hours, two days ok.

So, with this we come to the end of this class, thank you very much for your attention; and we will continue our discussion on basal ganglia in future classes, so.

Thank you very much.