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

Lecture - 67
Basal Ganglia – Outputs

Welcome to this class on Neuroscience of Human Movement. In today's class we will be discussing basal ganglia in particular the outputs of the Basal Ganglia.

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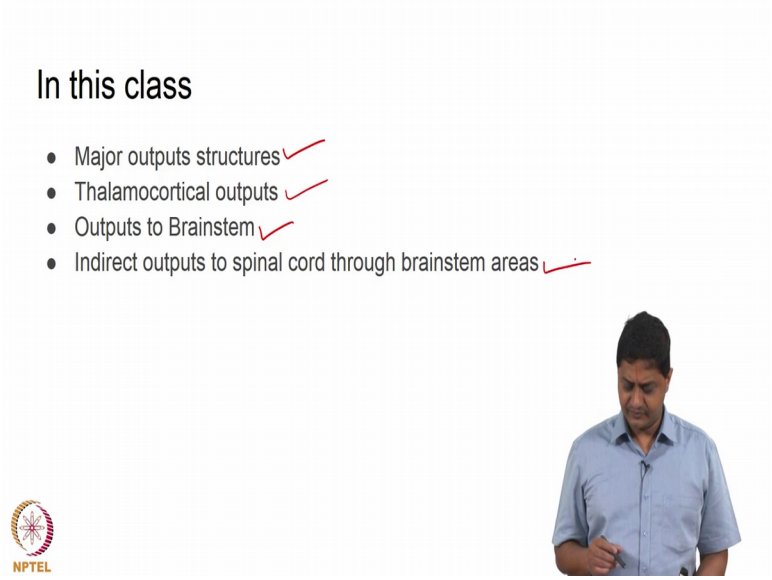

So, in this class we will discuss major output structures, they have already mentioned what this is this is globus pallidus internal segments and the substantial substantia nigra pars reticulate. And the outputs from the thalomatus to the cortex, which are basically the ones that are modulated by the basal ganglia output right. And outputs to the brainstem motor nuclii and indirect outputs to the spinal cord through brainstem areas in other words brainstem in this case acts as a upper motor neurons right motor areas in the brainstem act as the upper motor area for these cases.

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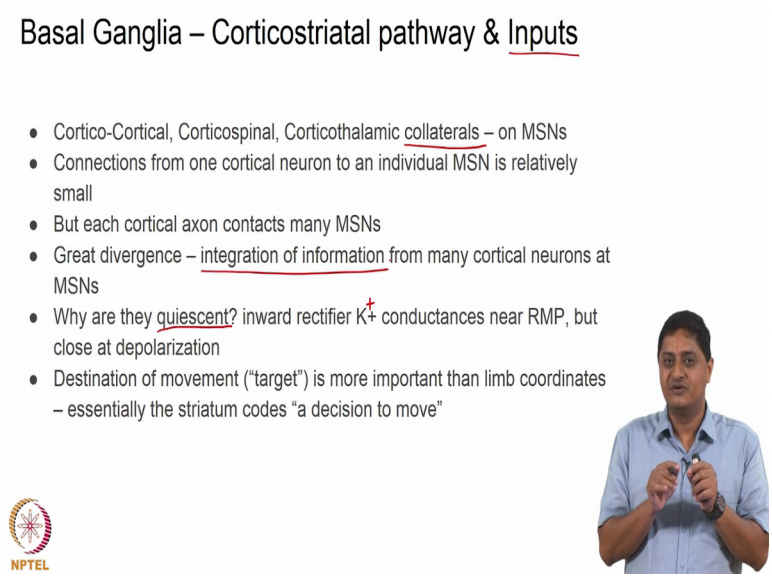

Something that we discussed yesterday, but we missed in yesterdays class are there is a Corticostriatal pathways in inputs importantly not only the corticostriatal pathway. So, there are exclusive projections from the cortex to the straitum right. Other than these cortico-cortical projections, corticospinal projections and carticothalamic projections are those that goes from one area of the cortex to the another area of the cortex or from the cortex to the spinal cord or from the cortex to the thalamus. These actions also send their branches are collaterals to medium spiny neurones. So, they terminate on medium spiny neurons thus exciting them.

Let us remember that medium spiny neurons are GABAergic and fundamentally inhibitory. If they are excited they are going to inhibit their target neurones, but they are usually quite, why are they usually quiet, why are they quiescent? Because of the inward rectifier potassium conductances that is potassium K plus inward rectifier potassium conductances that keep the membrane potential near resting membrane potential, but these conductances these rectifiers closed at depolarization. So, because of this unusual potassium conductance it turns out that the medium spiny neurons are usually quite.

And they need input from multiple cortical or nigral neurones to activate and we also saw what are the various kinds of input it receives that you know the inputs received from the cortical and the nigral neurones are actually at the distal end of the dendrites whereas, closer to the soma and cell body there are actually inputs coming from local

inter neurons and from thalamic neurons we are seen this. So, in that sense the local inter neurons modulate the output of the medium spiny neurons in a great way when compared with the cortical neurons.

So, multiple cortical neurons must send their input to the minimum spiny neurons for them to be excited spatial and temporal summation must happen, and then action potential will be generated in the medium spiny neuron. This is the case that we discussed yesterday. But regarding the cortical connections itself connections from one cortical neuron to an individual medium spiny neuron is relatively small. So, basically each cortical neurone sends one input to one medium spiny neuron or approximately that much, now too many connections to each medium spiny neuron.

However, each cortical acts on contacts many medium spiny neurons so, what happens is that one cortical neurones since multiple collaterals to multiple medium spiny neurons and one medium spiny neurons receives input from multiple cortical axons. So, what is there in this situation is a there is a great divergence; there is a great divergence of the cortical information on to many medium spiny neurons, and we saw yesterday that medium spiny neurons converge onto the pallidal neurons whereas, from the cortex there is in general a great divergence into the medium spiny neurons. This enables integration of information from multiple cortical neurones by the medium spiny neurons right.

And activity of the medium spiny neurons has been studied and people have asked the question what causes the medium spiny neurons to fire what activates them. In general it has been found that the destination of the movements, suppose I have this object I have to reach this object; where this object is determines which striatum neuron is going to be active not which limb is reaching or what movement is going to be done. So, this is to use a strong word this is encoded in the space of the target location not in the space of limb dynamics.

So; that means, essentially what the basal ganglia, what the striatum encodes is, a decision to move. The first whether or not to make a moment if the decision to make a moment is made, what movement must be made in other words to which target must be move a decision is what is being encoded by the striatum neurons. With this we finish the earlier discussion on inputs; now we will move on to the major output structures.

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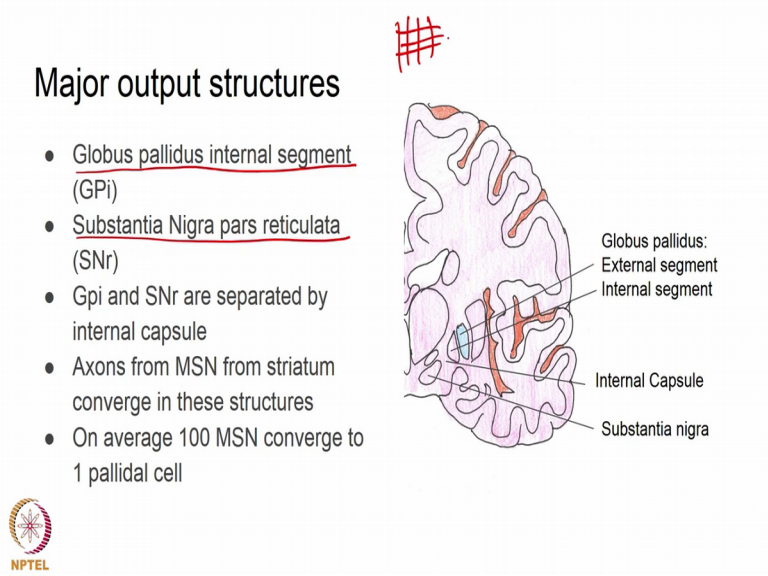

We have discussed this earlier; we said the major output structures of the basal ganglia or the globus pallidus internal segment and the substantia nigra pars reticulata.

Essentially the substantia nigra pars reticulata and globus pallidus internal are the same output structures separated by the internal capsule, note that the substantia nigra pars reticulata unlike the compacta the compacter contains compact packaging of cells which are composed of the many of these are dopaminergic. In the substantia nigra pars compacta, but in the reticulata the axons passing through the pars reticulata give the reticulata an appearance of net like that right. So, because of this reason this region is called as reticulata substantia nigra pars reticulate; both of these are the major output structures of the basal ganglia right.

And these are separated by the internal capsule in other words substantia nigra pars reticulata can be called as the downward displaced Gpi downward displaced globus pallidus internal right. And we already said that the axons from medium spiny neurons from the striatum converge onto the pallidal neurons right on an average 100 medium spiny neurones converge onto one pallidal cell what is also to be noted is that there is a broad spectrum of outputs to the pallidal neurons. So, what happens is that medium spiny neurons send outputs to multiple pallidal neurones right. So, they make synopsis with multiple pallidal neurons

But one pallidal neuron gets inputs from hundreds of medium spiny neurons. So, the situation is as follows the situation is that there is a broad inhibition that is provided by the striatum to the pallidal neurons; when the striatum itself is excited that excitation converts into a relatively sharp inhibition. So, there is in general a broad activation of the pallidal neurons are broad connections that are made by the spiny neurons on to the pallidal neurons, but some of these are sharp to.

In other words medium spiny neurons project to several neurones at the same time, but to some of the neurones they make very specific strong and sharp connections because of this reason when a particular medium spiny neuron is active a particular pallidal neuron is going to be inhibited from its activity. This is the way in which this functions somewhat similar are atleast comparable to our discussion in cerebellum about the purkinje cells right.

Something that we should remember that there is sharpening of focus in the purkinje cells by the parallel fibre inputs right something that we discuss some time ago in the previous classes. So, let us remember. So, there is divergence from the cortex into the striatum and then that is convergent from the striatum into the pallidal neurones and the pallidal neurones are the major output neurones right. So, they output to the thalamus or the substantia nigra pars reticulata outputs to the superior calculus right. The Gpi neurons output to the thalamus and they does inhibit the thalamo cortical neurones from being active something that we will discuss in future slides right.

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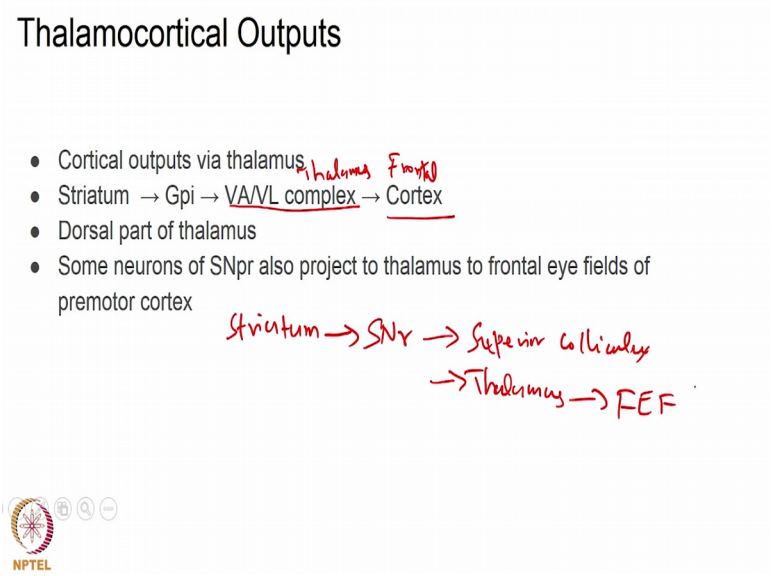

So, the thalamocortical outputs here thalamus are the neurons in the VA VL complex of the thalamus act as relay. They take the output of the Gpi, they take the output of the basal ganglia and inform the cortex of the basal ganglias modulation right. So, from the VA VL complex, from the ventral anterior and ventral lateral complex of the thalamus there are projections to the cortex. When you say cortex we will have to ask such which cortex this is right.

So, regardless of where the input is coming from to the basal ganglia. So, the basal ganglia may receive input from practically anywhere right in the cortex except the primary auditory and primary visual cortexes practically from everywhere else basal ganglia receiving input, but its outputs are always to the free central areas to the frontal cortices something to remember, either to the motor areas or to the executive and association areas of the frontal cortex of the pre frontal cortex.

This is where the basal ganglias output goes to, not to other areas in the cortex for example, not to the primary somatosensory cortex for example, right. So, what happens is from the striatum from the straitum, there are neurons that inhibit substantia nigra pars reticulata and they are directly project in one case to the superior colliculus. Some of these substantia nigra pars reticulata also projects to thalamus and from thalamus to the frontal eye fields once again the output is to the frontal area of the cortex FEF in the frontal cortex right something to remember.

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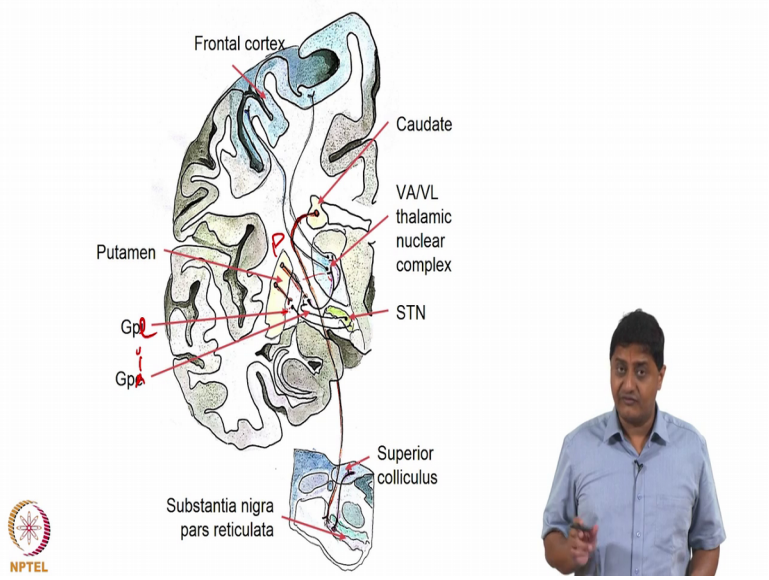

So, let us look at the situation one more time. So, basically there is output from the Gpi which is here. So, this is putamen sorry this is GPe and this is Gpi right.

From there the output goes to the VA VL neurons here and from the back to the cortex right. So, that is what happens and if it is from the substantia nigra pars reticulata the output goes to their superior colliculus right for controlling eye moments.

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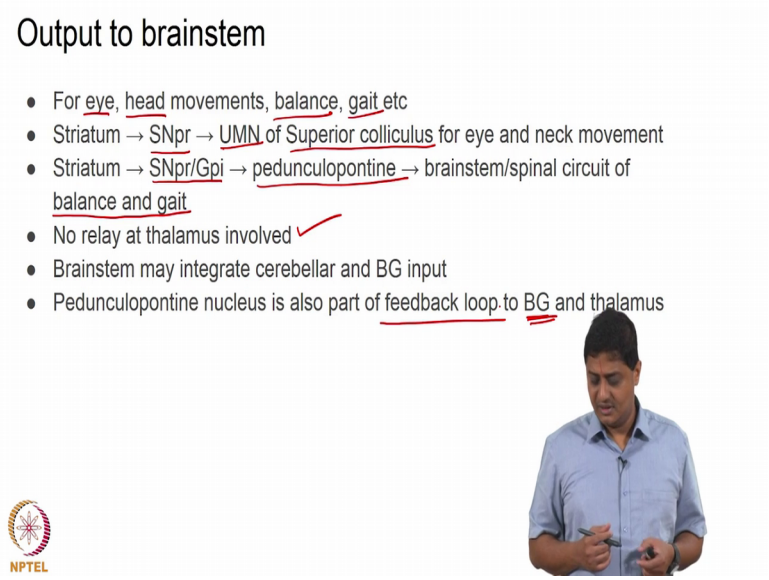

So, the output to the brainstem other than the cortical areas outputs, there are also output to the brainstem right. This is useful in the control of eye movements, head movements

balance and gait. So, from the striatum there is output to the substantia nigra pars reticulata which is the output structure, from there the output goes directly to the upper motor neurones of the superior colliculus without a relay in the thalamus right. In the case of substantia nigra pars reticulata there are many projections that go directly to the brainstem, directly to the superior colliculus without a relay in the thalamus.

Whereas if there is an output that is going to the frontal cortex from the substantia nigra pars reticulata for example, in the case of frontal eye fields, then what happens from substantia nigra pars reticulata there is an output that goes to the thalamus and through the thalamus relay it goes to the frontal eye field as we discussed. So, something to remember that if it is projecting to the brainstem there is no relay in the thalamus, if it is projecting to the cortex there is a relay in the thalamus right. So from the striatum substantia nigra pars reticulata or Gpi project to the pedunculopontine nucleus to basically control balance and gait.

In this case there is no relay in the thalamus that is involved crucial to note this point right. So, essentially brainstem may integrate outputs that come from the basal ganglia and also from the cerebellum, importantly Brainstem receive inputs from the cerebellum also. So, the control of balance and gait is managed not just by the cortex, by also these sub cortical structures basically cerebellum basically basal ganglia right. And also note pedunculopontine nucleus sends inputs to the basal ganglia via the thalamus something that is not generally mention pedunculo pontine nucleus is also part of a feedback loop that sends inputs to the basal ganglia via the thalamus right.

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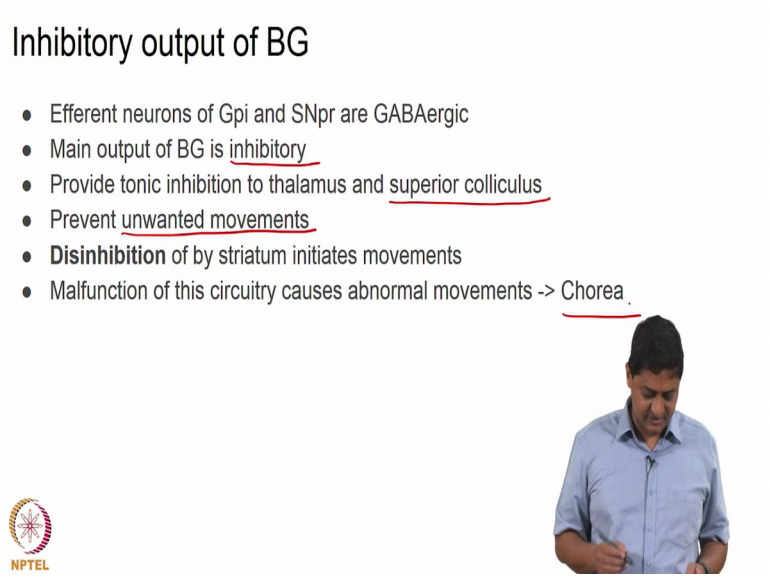

So, essentially the different neurones the output neurones of the globus pallidus internal and the substantia nigra pars reticulata are GABAergic and so; that means, there main output or the main output of basal ganglia is in general inhibitory. So, and this means that they provide tonic inhibition to the thalamus or the thalamocortical neurones and the superior colliculus. So, essentially what they are doing is, they are tonically inhibiting preventing unwanted moments and immediate hypothesis that we can make, you said if this function of the output neurons is somehow selectively compromise then what will happen.

They are tonically inhibiting preventing unwanted moments suppose this function is compromised then what will happen? Well immediately unwanted moments will start appearing right like in the case of chorea this is essentially what happens in huntingtons chorea something that we will discuss in future classes right.

So, selective degeneration of the indirect pathway leads to huntingtons chorea something that we will discuss. Essentially unwanted movements are prevented by this tonic inhibition and what ensure that the wanted moments are performed; the intentional moments are performed what ensure that? That is insured by transient selective disinhibition that comes from the striatum.

So, striatum essentially an inhibits for a brief period of time selectively some movements alone; now that opens the gate for that moment appear and the other moments are gated

this is this is the interesting and the dominant hypothesis in basal ganglia function right. By the way that also means that malfunction of this circuitry means chorea right something that we discussed.

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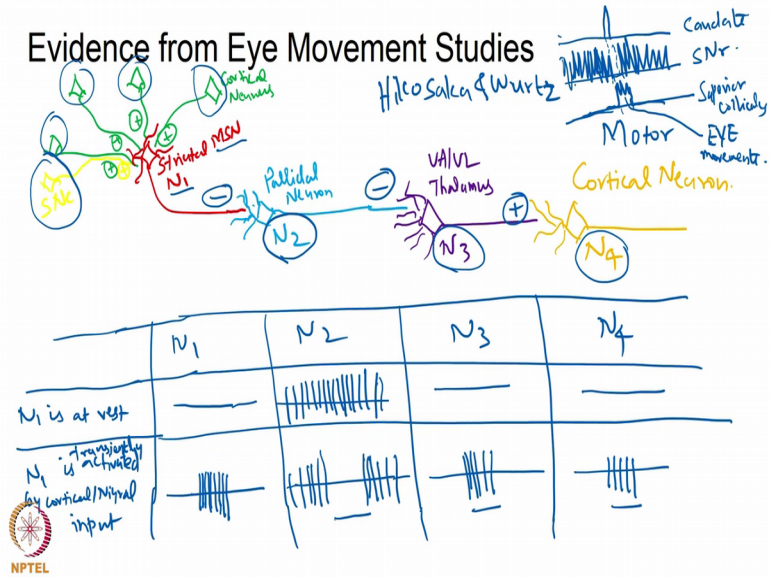

A lot of this evidence to support the presented ideas come from eye moment studies, I will draw the picture for this and we will discuss this in a minute. So, here I have drawn this situation a very simplified situation of what happens in the basal ganglia very cartoon type of diagram, done with my own hand, but it is going to explain the principle right. So, essentially what is happening is that the medium spiny neurons in the striatum which I am going to call us neurone 1 N 1 is receiving inputs from multiple cortical neurones which are shown in green here. The neurones in green are the cortical neurones and the neurone in yellow here is the substantia nigra pars compacta neuron or the dopaminergic neuron.

So, this medium spiny neuron is receiving input from several cortical neurons some nigral neurons. And this is making synopsis with palldal neurones neurones in the globus pallidus right which I am calling here as N 2; N 2 or the neuron 2 is the pallidal neuron which is inhibiting which is tonically inhibiting the neuron in the ventaro anterior or ventro lateral thalamus, and this neuron is called as a neuron 3 or N 3 and that is exciting the cortical neuron which I am calling as neuron N 4. Let us consider this is a neuron in

the motor cortex right N 4 is a neurone in the motor cortex for the purpose of this discussion, we will consider N 4 to be a neuron in the motor cortex right.

So, essentially suppose neuron 1 is at rest its activities like this right what will be the inhibition provided by neuron 1 to neuron 2? Nothing, because neuron one is quotient it is normally quotient let us remember that medium spiny neurons are normally quiet because of unusual potassium conductance is something that we saw right. N 1 is not inhibiting N 2 and because of this N 2 is tonically active and tonically inhibiting the thalamocortical neuron or the neuron in the thalamus right. So, essentially the activity of N 2 will be very high like this continuously it will be like this for that time period that is recorded this will be flat N 1 will be flat N 2 will be continuously active.

If N 2 is continuously inhibiting N 3 note the output of the pallidum is essentially inhibitory right it is continuously sending GABA to N 3 right because of that reason N 3 is not active N 3 is silent and because of that reason N 4 is also silent, why? That means, if the striatum neuron is quiet; that means that the motor cortical neuron is also quite preventing unwanted movements. Suppose I want to produce a movement, suppose I want to produce a movement what happens is it N 1 neurone becomes transiently active right. So, what happens is it this is flat for some time, but is active for a brief amount of time say that then what happens in the pallidal neuron here is what happens.

So, essentially for that time period alone there is silence in the pallidal neuron. So, during the time for which the striatal neuron is active the pallidal neuron is silent. When the pallidal neuron is silent what happens in the thalamus in the neuron in the relay at the thalamus usually it is silent during the time during which the palllidal neuron is silent that is excited. For that time alone it is excited and for that time alone the neuron 4 is excited thus, performing the intentional or movements that are needed I suppose to producing unwanted moments right. So, this is essentially what happens.

So, the caudate nucleus neurone is usually silent and when it is active for a brief amount of time it causes. So, this is caudate this is substantia nigra pars reticulata; substantia nigra pars reticulata neuron is continuously active and when the caudate nucleus neurone is active it is silent. When the caudate nucleus is active the substantia nigra pars reticulata silent and then it is active again is usually silent. During that time when the

substantia nigra pars reticulata neuron is silent the superior colliculus neutron is active and after other times it is silent.

This activity causes eye movements right essential this is how a specific eye movement is made right. However, note in this case that is no relay that is in the thalamus. So, this is simpler is an easier model to study, lot of data from animal morose especially monkeys have been performed by He de Hilco Saka and Robert woods Hilco Saka and woods this is data that I am trying to reproduce from the work of Hilco Saka and woods right. So, essentially this is what happens? Essentially the transient activation of the striatum neurons by the cortex transiently inhibits the pallidal neurones which are usually to tonically inhibiting the thalamus neurones, thus releasing the thalamus neurons from inhibition for a brief period of time or causing this inhibition.

So, basal ganglia or stratum is essentially disinhibiting the thalmo cortical neurones for transient brief amount of time, thus producing intentional or volitional movements.

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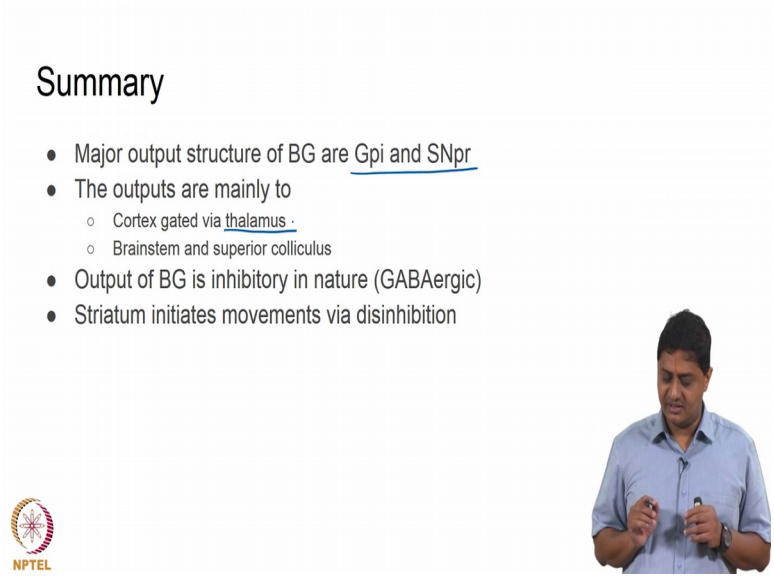

So, in summary what we have seen the basal ganglia's major output structures which are globus pallidus internal and the substantia nigra pars reticulata and the outputs to the cortex or gated by the thalamus are through release in the thalamus. And outputs to the brainstem and superior calculus are usually not get it and substantia nigra pars reticulata when it sends information to the frontal areas in the cortex, it sends it by other thalamus right. Output of basal ganglia is fundamentally in is output of the basal ganglia is

fundamentally inhibitory or GABAergic. And essentially whenever striatum initiates a activity it initiates movement by this inhibition with this we come to the end of this lecture.

Thank you very much for your attention.