Basics of Mental Health and Clinical Psychiatry
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Lecture 03
Basal Ganglia

Hello everyone. So today we will go to our third topic that is basal ganglia.

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Now, basal ganglia as I told you in my previous lecture, that whenever there is an initiation of an idea and execution of that plan, of that voluntary activity, always the cerebral cortex consults its

2 fellows one is cerebellum, the other one is basal ganglia. Now, how it consults with cerebellum that I had already discussed in the previous lecture. Today we will discuss how basal ganglia helps cortex to execute the functions. So, the concepts we will cover is components of basal ganglia, nuclei of basal ganglia, connections of basal ganglia, functions of basal ganglia and applied aspects.

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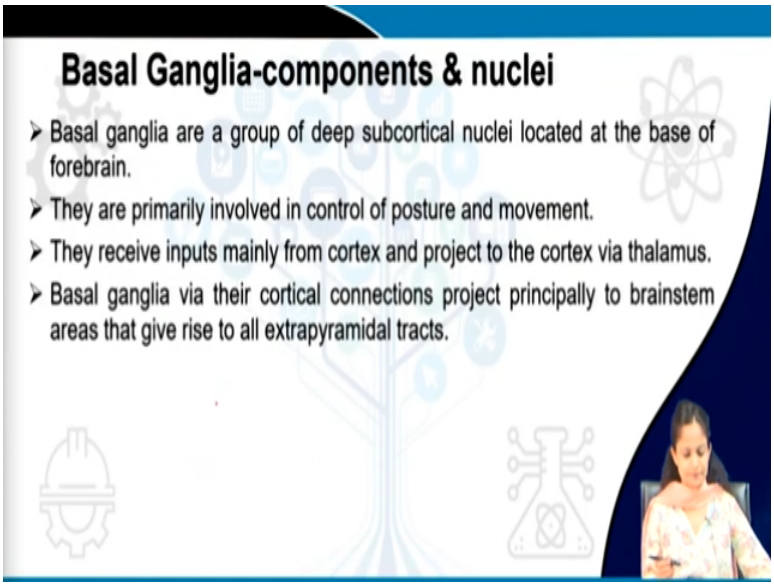

Now, what are the components and nuclei of basal ganglia? So, before coming to this main topic, I should say this ganglia is actually a misnomer, because ganglia is a collection of cell bodies outside the central nervous system, but this basal ganglia is present inside the central nervous system. So, it would be better if we call it as basal nuclei actually.

So, these are the gray matter masses, which are a group of deep cortical nuclei located at the base of the forebrain and they are mainly important for the control of posture and movement, as I told you they receive inputs from the cortex and they gave their feedback back to the cortex via thalamus. So, they are mainly concerned with the extra pyramidal activities that is outside of the cortical tracks corticospinal tracts the pyramidal tracks.

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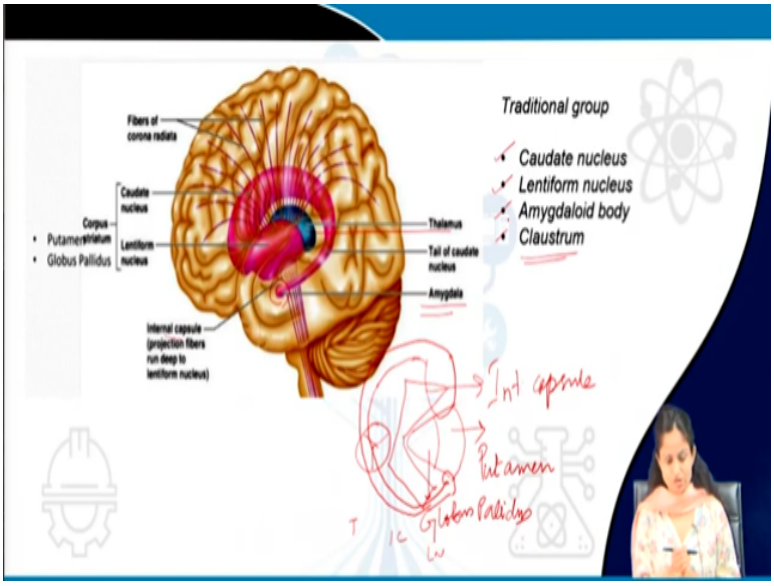

Now, coming to the structure of this basal ganglia. So, what basal ganglia is composed of? Now, this is thalamus, as you can see, lateral to the thalamus we have this lentiform nucleus. So if I draw it over here, suppose this is a thalamus we have 2 thalamus. So, this is thalamus and lateral to the thalami we have the lentiform nucleus. Now, this lentiform nucleus consists of 2 parts the lateral part is the putamen and the medial part is the globus pallidus.

So, this lentiform nucleus lies lateral to the thalamus in between thalamus and lentiform nuclei we have a collection of white band that is white matter this is known as internal capsule. As you can see, this is the internal capsule this is the projection fibers which are running deep to the lentiform nucleus. So, thalamus laterally internal capsule, then laterally we have lentiform nucleus then this lentiform nucleus is also related to another nucleus that is caudate nucleus, what happens? This caudate nucleus the head of the caudate nucleus, suppose this is the head of the caudate nucleus, it sits over the putamen of this lentiform nuclei.

So this caudate nucleus, as you can see this is the caudate nucleus, it tries to sit over the lentiform nuclei. Now caudate nucleus has got a head and a tail, the tail portion bears a small body known as amygdala.

And so, again if you just revise it thalamus we have then we have internal capsule, then we have this lentiform nucleus along with the caudate nucleus, lentiform nucleus along with the caudate

lobe head and the tail and then laterally we have another gray matter that is known as claustrum. So with the structures these are the traditional group of structures, which we see in the basal ganglia that is caudate nucleus, lentiform nucleus, amygdaloid body and claustrum.

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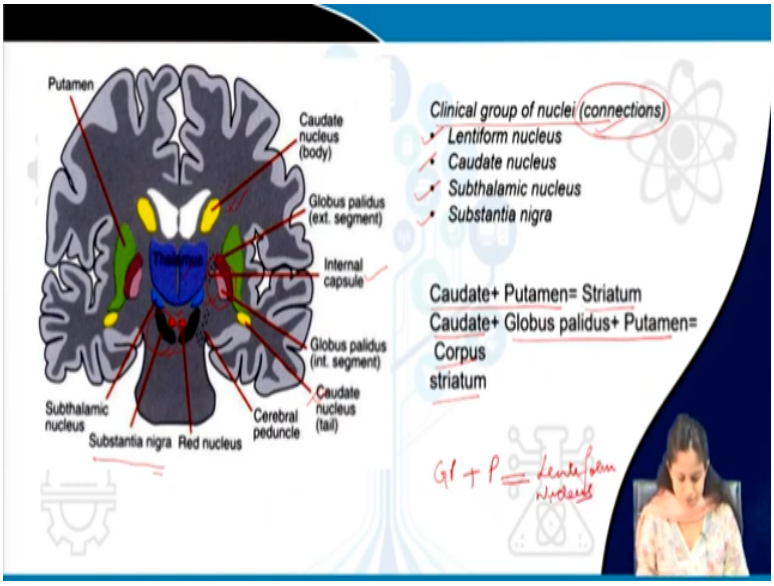

Now we will go to the functional classification or the clinical classification of the basal ganglia nuclei. Now, this structure is actually what I drawn, this is the thalamus. Laterally you can see this portion is the lentiform nuclei which consists of globus pallidus both internus and externa and the putamen then in between the thalamus and the lentiform nuclei we have internal capsule.

Then you have the caudate nucleus body and the caudate nucleus tail and then laterally we will have the another gray matter that is claustrum, below this thalamus another body is there that is subthalamic nucleus anything which is below thalamus is sub thalamus. So we have subthalamic nuclei.

Now coming to the midbrain region, this is the red nucleus. We are more concerned with this portion that is substantia nigra. The posterior part of the substantia nigra is very dense, it consists of dense neurons so they are known as substantia nigra pars compacta and the interior region is less than so they are known as substantia nigra pars reticularis. So for the time being, you will remember it as substantia nigra. So, why am I telling the structures? Because these structures are different from that of the anatomical classification we have already discussed.

The clinical group of nuclei and connections is lentiform nucleus, caudate nucleus, subthalamic nucleus which is lying below the thalamus and substantia nigra which is actually a part of midbrain, this is mainly because of the connections, we have classified it clinically and we have not taken into account the amygdaloid body because amygdala you will read or it is of more important in the limbic system which is associated with memory.

So emotional memory, so here we talk about 2 terms that is new striatum or striatum and corpus striatum, striatum whenever I will be talking about striatum it means I am considering caudate and putamen. Now, why this has been put together? Because of their similar neurotransmitter similar connections and when I whenever I will talk about corpus striatum that means I will put the caudate nucleus and the lentiform nucleus that is globus pallidus and putamen because as I told you globus pallidus and putamen this forms the lentiform nucleus.

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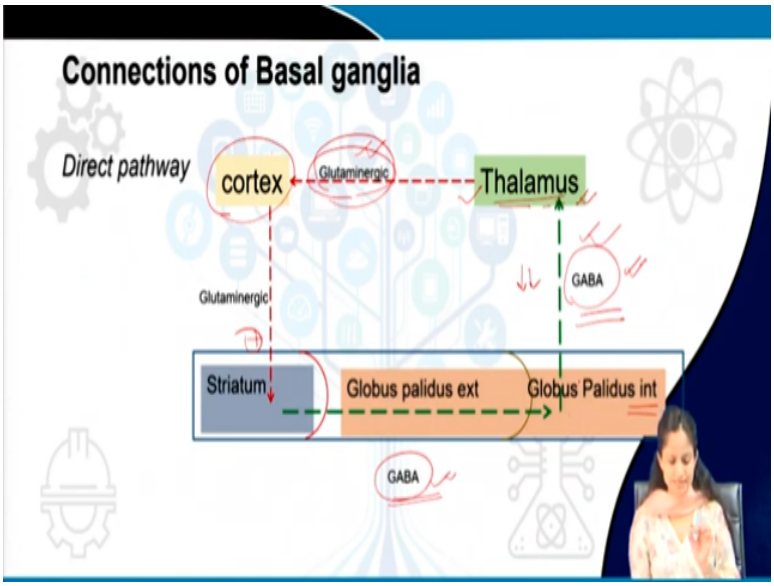

Now having understood this classifications we will move on to the connections of basal ganglia. As I told you that basal ganglia also consults with the cerebral cortex before execution of the final plan. So what connections are what intimations it gives we will see? Now there are mainly 2 connections one is via direct pathway and one is via indirect pathway. So obviously the connections will be from cortex, the input should be from cortex, the output we should also be towards the cortex.

So, the first input the cortex is given to the striatum, striatum means as I already told you about the previous I am talking about the new striatum. So, cortex is giving input to the glutaminergic with the help of glutaminergic fiber striatum, glutamatergic fibers means this fibers are excitatories.

Now after striatum this is in connection with the globus pallidus and globus pallidus internus. The next connection it will give from striatum to the pallidus. Now this striatopallido fibers, these are gabaminergic or inhibitory in nature, from the striatum the fibers will move to the globus pallidus internus mind it is internus not externus. So, this internus fibers will be gabergic. Now, after this internus again the fibers will move to the thalamus, this fibers are pallidothalamic fibers which are again gabaminergic that means inhibitory nature.

Then from the thalamus the fibers will move to the cortex again there will be fiber that is thalamocortical fibers which are again glutaminergic. So, basically what we are saying the main input from the cortex to the striatum and the output towards the thalamus to cortex I mean what is coming out of the cortex and what is going into the cortex both are glutaminergic that is excitatory neurotransmitter.

But what is happening inside the basal ganglia they are mainly having inhibitory neurotransmitter, so we will see exactly what happens during rest that means whenever we are not doing any motion, so whenever we are not doing any motion, whenever we are not acting anything. Suppose I am sitting so obviously I will not be doing any movement.

So, cortex is not firing anything, there is no impulses being fired from the cortex, when we are at rest when cortex is not firing anything at that time this pallidothalamic fibers which are gabaminergic these are very active, these are constantly firing inhibitory neurotransmitter on the thalamus, because of this the thalamus keeps the cortex under excitatory conditions, I mean it is not over excitatory it is under excitatory, it inhibits the cortex.

So, what will happen? Whenever that is why whenever we are rest, we are not doing any movements, but suppose this pathway gets destroyed what will happen even in the rest also I will do some kind of movements, I will keep my hands rolling I will keep chewing like this. So, this is when the pathway gets destroyed. So, under rest what is happening? This cortex is kept

inhibited with the help of thalamus with the help of this fibers this is mainly gabaminergic fibers that is pallidothalamic fibers.

Now what will happen we will see if we are doing any motion suppose I want to execute any activity this cortex will fire I want to speak or I want to take the glass of water then cortex building there, the person needs to take the glass of water the person needs to raise the hand so cortex will fire, when the cortex will fire to the striatum, this is glutaminergic that is excitatory input is there, this will cause this fibers that is tritopallidal fibers which are gabaminergic to secrete gaba. So now remember this gaba is getting secreted over globus pallidus internus, now this gaba is a inhibitory neurotransmitter.

Now this inhibitory neurotransmitter something which is inhibitory neurotransmitter obviously will inhibit the next pathway. So, this transmitter will inhibit this pathway. So, this pathway will get inhibited that means this pallidothalamic fibers which were keeping a check on cortex when you are at rest, this will get inhibit, it will stop firing.

So, when it will stop firing this thalamus will escape this fibers and it will start firing glutaminergic fibers and it will start acting via glutaminergic fibers, these fibers will fire and the cortex will act accordingly, that means the cortex will execute the function there will be hand movements there will be raising of the hand the motor function will get executed. So while the very important thing to remember is when at rest, this gabaminergic fibers are very active which is from pallidothalamas. These are pallidothalamic fibers which are gabaminergic, which are very active during rest. So this keeps on the check on the cortex.

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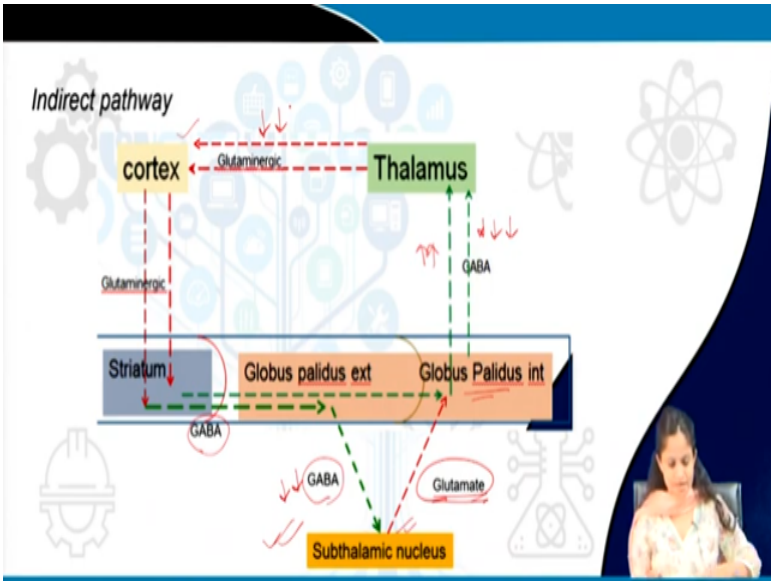

Now we will see the indirect pathway. This is the same diagram which I told you in the previous slide. Now if you asked me when there is already a direct pathway, why we need an indirect pathway it is more complicated? Now we need indirect pathway because suppose when my hand I am flexing, whenever doing any actions I am flexing my arm so the flexor muscles are acting, at the same time the extensor muscles are also relaxing.

So, the agonist muscle and the antagonist muscles are acting in opposite way. So, to carry out the motion in a forward direction we have to relax or inhibit some other pathway also. So that is why there is this indirect pathway. So we will see what is happening in this indirect pathway. This is the direct pathway.

Now, coming to the indirect pathway, again there is a motion so cortex is giving signal to the striatum the motion has started. So, cortex is sending glutaminergic fibers to the striatum, the striatum instead of now this pathway is different instead of sending signal to the pallidus internus which we seen earlier, it will send signal to the pallidus externus, now since it is an indirect pathway that means some extra loop has to be there so this striatum is sending again negative that is gabaminergic pathway or fibers to pallidus externus.

Now from pallidus externus this fibers will come to the subthalamic nucleus which is present beneath the thalamus this is also gabaminergic, from subthalamic nucleus glutaminergic fibers

will move to the globus pallidus internus and from globus pallidus internus this already we know the gabaminergic fibers moved to the thalamus and from thalamus the thalamocortical fibers moved to the cortex.

So, you can say this extra loop is done by this subthalamic nucleus. Now, whenever there is a motion, suppose, with the help of direct pathway what is happening this direct pathway is causing facilitation of the activity, my hand is raised up for the activity, now as my hand is raised up the other muscles in the hand should relax. So, what will happen? The cortex is sending glutaminergic fibers to the striatum, from the striatum the negative fibers GABA they are inhibiting the fibers pallido subthalamic fibers.

Now, again inhibiting pallido subthalamic fibers means these fibers are inhibited, the potential is inhibited. So, this glutaminergic fibers that means they are firing more, these are excitatory now, I mean there is no inhibition of this gabaminergic fibers.

So, when this glutaminergic fibers are excitatory they will cause globus pallidus internus to release more GABA, when more GABA will be released that means inhibitory neurotransmitter is getting released. So, the other pathway or the indirect pathway will cause decrease in the action potential or impulse conduction. Finally, this will inhibit the thalamus to act on the cortex or inhibit the firing of the thalamus, the thalamocortical fibers.

So on one hand, when there is flexion of the muscles which is happening because of the excitatory pathway, because of the direct pathway on the other hand my extensor muscles are getting relaxed because of the indirect pathway inhibitory action. So, this is the indirect pathway.

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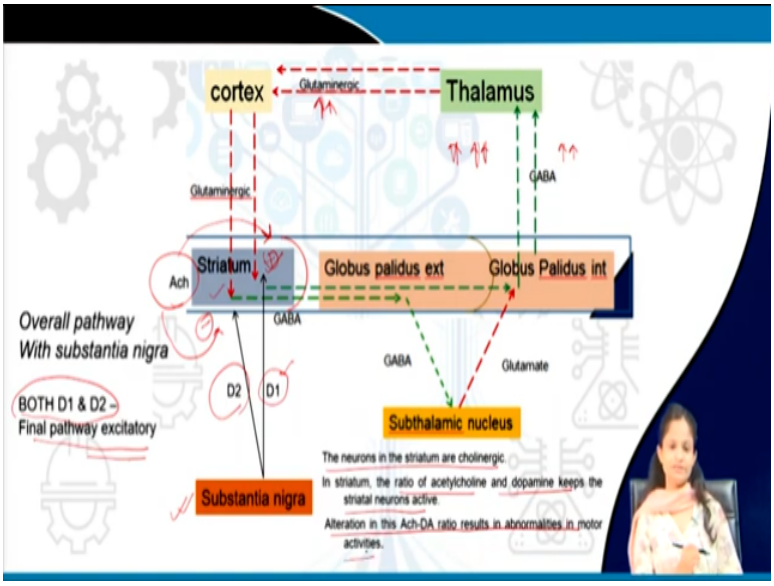

Now, again also there is a manipulation which is done by a third body, which is this third body? This is substantial nigra which is present in the midbrain, the substantia nigra secretes dopaminergic fibers or dopaminergic neurons, there are mainly 2 dopaminergic pathway, this dopaminergic neurons act on the striatum, it acts on the direct pathway, it acts on the indirect pathway with the help of 2 different receptors and this receptors are antagonistic to each other. For example, through D1 receptors the dopamine this is the nigrostriatal pathway, this is nigra and this is striata so nigrostriatal pathway.

So, this nigrostriatal fibers or dopaminergic fibers with the help of D1 receptors will stimulate the direct pathway and with the help of D2 receptors it will inhibit the indirect pathway. So, D1 receptor is stimulating the direct pathway, D2 receptor is inhibiting the indirect pathway. Now, if you see this pathway, when D1 receptor are getting stimulated this direct pathway is getting facilitated more. And when this D2 receptors are inhibiting this indirect pathway with the help of this extra loop, again this pallidothalmic fibers will also get facilitated that means the indirect pathway will also get facilitated.

So, finally the output with the help of substantia nigra or D1 D2 receptors that is that will be finally excitatory, so, the motor activity which we want to do that is actually facilitated by this dopaminergic neurons that is nigrostriatal pathway whether they act on D1 receptors or D2 receptors, they are acting antagonistically because the loop is different, one is direct loop one is

indirect loop, through whichever loop they act the action the output is always excitatory or facilitatory.

Now, there is another role of a neurotransmitter that is acetylcholine over here, what you have to remember is the action of acetylcholine is exactly the opposite of the dopamine that means if D1 receptors are facilitatory the acetylcholine will inhibit the D1 receptors. And if D2 receptors are inhibitory then acetylcholine will facilitate the D2 receptors.

Now, why there is opposite reactions? Because these reactions are keeping a check on the basal ganglia so that there is no error occur there occurs no error in the movement, once the movement starts for normal person there should not be any error. So, always there is a check or there is an eye which is on the basal ganglia through different connections and through different neurotransmitters.

So, even if you do not remember what is action of acetylcholine, you have to remember the most important action of dopamine that is D1 receptors facilitates the direct pathway D2 receptors inhibits the indirect pathway, but the common pathway is always excitatory and acetylcholine are present in that striatum always for any action, the ratio of acetylcholine and dopamine should be in balance, our system in our body this 2 neurotransmitters should be kept in balance for the functions to get executed. Whenever there will be imbalance we will get disorder. So the ratio of acetylcholine and dopamine keeps the striatal neurons active. Alteration in this ratio results in abnormalities of different motor activities.

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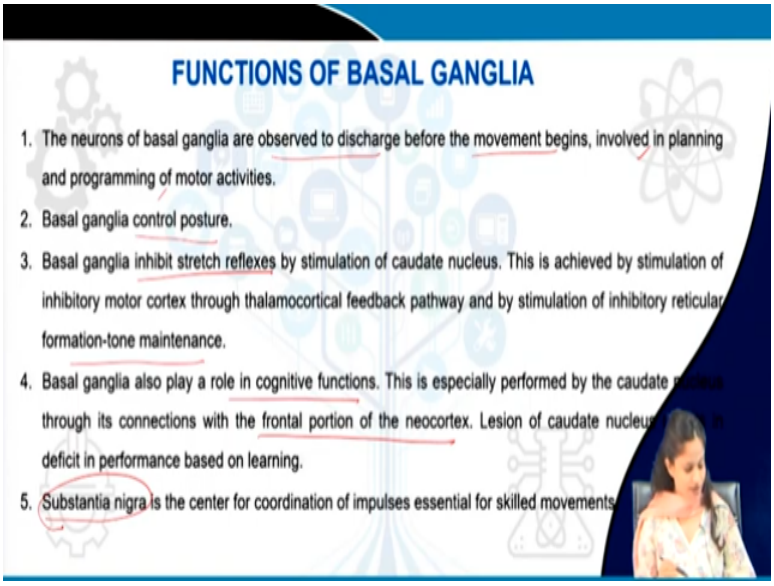

So we will see, after this connections we will come across the functions of basal ganglia. So the neurons of basal ganglia are observed to discharge before the movement begins, even the movement begins before it starts beginning, I told you that basal ganglia and cerebellum discusses with the cerebral cortex what you intended to do that is already been checked by the basal ganglia and cerebellum. So the planning and programming is done by the basal ganglia.

Basal Ganglia controls the posture by keeping a check on the reflexes because of the inhibitory responses or the inhibitory feedback on the thalamus, it inhibit the stretch reflexes and hence maintains the tone of the muscle. They also play a very important role in cognitive functions because it is linked to the neocortex with the frontal connection of the neocortex, that is why whenever there is lesions in the caudate nucleus, what will happen? There will be difficulty in learning, impaired learning, so, the coordination is very important with the help of substantia nigra, how this gets affected I will show you.

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Now, lesions of basal ganglia can be 2. The first one is hypokinesia when there is reduced movement, the other one is hyperkinesia when there is excitatory or exaggerated movement. So, hypokinesia occurs when the direct pathway gets affected, when there is dishamper or when there is hampering of the direct pathway that time hypokinesia occurs. The others disorders which is due to the hyperkinetic movements or exaggerated movements that occurs when there is an imbalance or dysfunction of the indirect pathway that means when it involves the subthalamic nucleus, the other loop.

Now, when it involves the direct pathway, a very common disease, we see that is Parkinsonism. What happens in Parkinsonism? It is mainly due to the degeneration of the nigrostriatal pathway. Now, if you just remember the slides which I had shown, the nigrostriatal pathway are the dopaminergic neurons, this dopaminergic neurons whether it acts on the D1 receptor or the D2 receptors excitatory or inhibitory, the final pathway is always excitatory.

Now, if this nigrostriatal pathway is destroyed or if I cut to this nigrostriatal pathway due to any reason, so, the excitatory output will be decreased, that means our cortex will be functioning less, that our cortex will be not functioning or under functioning. So that what happens in Parkinsonism, if you see a Parkinsonism patient, the Parkinsonism patient walks very slowly, they do not know when to react, they have very mask-like faces, the eyelids you know the movement of the eyes gets decreased, blinking of the eyes get decreased.

If you ask them to start any activity, they will they will not be able to start or initiate that activity, why? Because the cortex is under functioning because of the destruction of this nigrostriatal dopaminergic neurons, this can also happen because of any drugs, like in case of psychotic patients, we give dopamine receptor blockers we give various drugs so because of that as a side effect also we can get hypokinesia.

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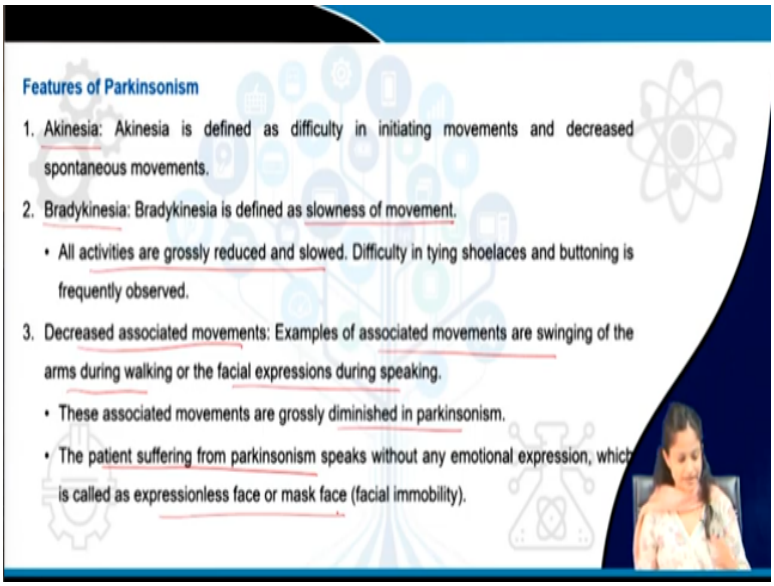

Now before going to the indirect pathway disorders a few I should like to tell about the Parkinsonism. Parkinsonism is mainly featured by akinesia or bradykinesia because of the slowness of the movements, the movements become slow, all the activities are reduced and slow, there is difficulty in tying the shoelace, buttoning the shirts, there will be decreased associated movements and during walking what happens, when you walk what happens your arms are when I am walking my arms are also you know moving, but there will not be any coordination when this person will be walking because obviously the coordination is lost the basal ganglia the nigrostriatal pathway are destroyed.

So associated movements like swinging of the arms during walking or when I am speaking I am giving some facial expressions, I know when to smile, when to cry of I know when I am going to get upset, so, there are some facial expressions, this facial expressions also get less or decreased to variable extent in case of Parkinsonism patients because the Parkinsonism patients will not be knowing when to smile, because that basal ganglia nigrostriatal pathway keeps the cortex under

functioning because of this under functioning of this cortex, there the planning the programming of all the movements get hampered.

Now, this movements are all decreased in Parkinsonism we clearly say there is a mask-like faces in Parkinsonism, that is the expression less face when whenever you will wear a mask the faces expression less. So, the patients suffering from Parkinsonism they usually have the facial immobility so there is a mask-like face or expressionless face.

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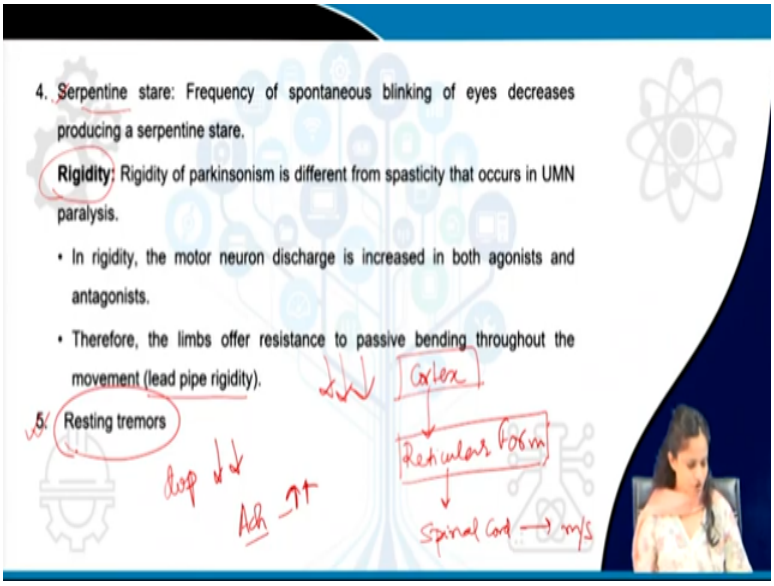

And a serpentine look serpentine look means what my eyes are not blinking for number of frequently I am not blinking my eyes frequently, I am staring staring staring so that is because of the difficulty in blinking of the eyes. So, this occurs in case of Parkinsonism patients. Now, the Parkinsonism patients gives a very important attribute that is rigidity. Rigidity means when the muscle tone I told you the muscle tone is also maintained by basal ganglia the muscle tone of our body is usually maintained by the reticular fibers.

So reticular fibers which are coming to the spinal tract, I will show you this is cortex, cortex gives input to the reticular formation and from reticular formation the input I mean the output comes to spinal cord and then to the muscles. So, whenever cortex get gives information to the reticular formation actually this information is what it is, it keeps inhibition inhibitory input that

means cortex when my cortex is normal, it tries to keep a check on the reticular formation, it should not overact, it should not fire as whenever it wants, it should not fire rigorously.

So, cortex keeps an eye on the reticular formation and hence the reticular spinal fibers, these are inhibited. So, our tone is maintained, but what will happen in Parkinsonism patients the nigrostriatal pathway are destroyed. So, because of nigrostriatal pathway destractions, this cortex is kept inhibited, that is under activity of the cortex. Now, my cortex does not know when to act, my cortex is not keeping any check on the reticular formation.

Now, what will happen if my cortex if the main center is not keeping check on the reticular formation? The reticular formation will over fire, will constantly fire. Now, when it will constantly fire, the tone of my muscles will get increased both agonist as well as antagonist both flexor as well as extensor compartment.

So, when you will try to flex the arm of this person that is Parkinsonism patient, you will feel very hard or very difficult to flex and very difficult to extend this type of rigidity is known as lead pipe rigidity. You know if you try to bend a lead pipe, it is very hard to bend or flex so this type of rigidity is known as lead pipe rigidity.

Then you get resting tremors, this resting tremors as I told you because of the disbalance of the acetylcholine and the dopamine whenever there is a destruction of this nigrostriatal pathway, the acetylcholine whenever this there is a decrease in the dopamine the acetylcholine what will happen? It will increase in concentration because it keeps a balance, acetylcholine and dopamine should be in balance.

So, whenever dopamine decreases acetylcholine should raise, now this compensatory mechanism which is happening our bodies actually harmful. So whenever acetylcholine it is harmful in the vice versa also if dopamine gets rest acetylcholine decreases. So actually both should be in balance. So, when dopamine decreases because of the destruction of the nigrostriatal pathway in Parkinsonism patients, the acetylcholine increases and this cholinergic neurons are the result for resting tremors.

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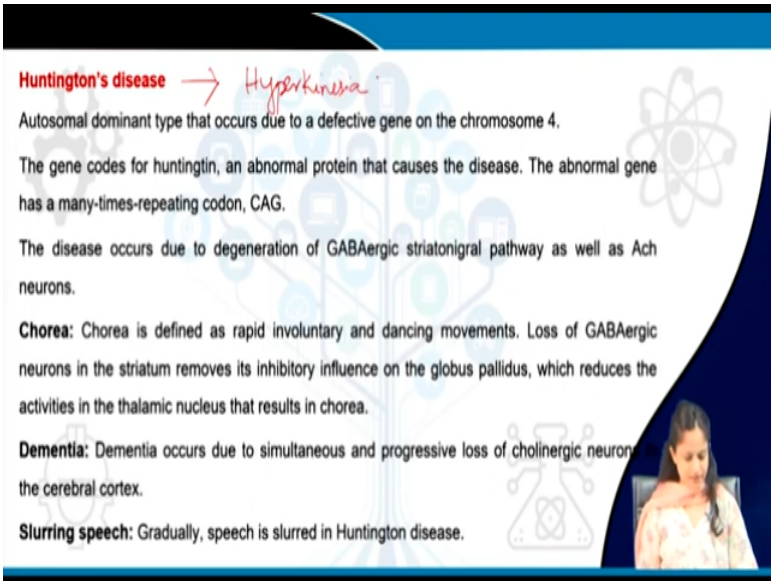

So, this is another disease known as Huntington's disease. Now, Huntington's disease is actually a disease which occurs because of hyperkinesha.

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Before that, I would like to go to the some of my previous slides. I told you hypokinesia occurs because of the involvement of the indirect pathway, indirect pathway means the gabaminergic pathway, which are inhibitory neurotransmitters, inhibitory pathway that will get affected, if that gets affected obviously there is no inhibition on the of basal ganglia on the cortex or the thalamus

so my cortex will always be over functioning or over excitatory whenever there is loss of inhibition, so, what will happen which will result in Chorea.

Chorea is purposeless jerky, involuntary movements; these movements are not to be done purposefully. I am not doing involuntary movements so I am at rest, but still my hands are moving here and there so this is Chorea.

Then there is athetosis, this is also involuntary movements which are a bit slow and occurs at the level of hands and the wrist fingers. Then again, this jerky movements if it occurs in the hip or the truncal region that is ballism, and tardive dyskinesia is also hyperkinetic movements which are mainly seen in oro facial regions, this is mainly because of the side effect of antipsychotic drugs. Many antipsychotic drugs we give, because of the side effect of antipsychotic drugs we see tardive dyskinesia, we see many of the patients like chewing or movement of the, you know, mouth, so, constant movement of the involuntary movement of the mouth that is tardive dyskinesia.

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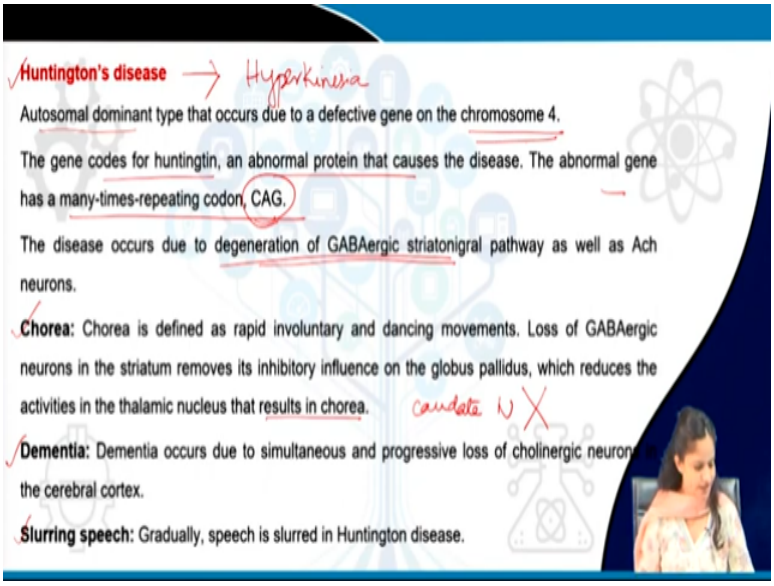

Now, a classical example of Chorea is seen in Huntington's disease. Huntington's disease is an autosomal dominant disease. It usually results because of the defective gene that has Huntington's gene on chromosome number 4. Now, what happens in this disease? There is degeneration of this gabaminergics tritonigral pathway that is indirect pathway. So there will be

Chorea that is rapid involuntary dancing movements that results in Chorea. Whenever the caudate nucleus gets affected, this occurs mainly because of the caudate nucleus destruction.

And it also results in dementia, loss of memory and slurring of the speech. So, and the patients are also seen to have depression. So, these are the features of Huntington's disease, this usually results because of the gene, which codes for Huntington, they that gene has got many repeated trinucleotide repeats that is CAG repeats, this trinucleotide repeats are amplified generation to generation.

That means, if I am having Huntington's disease, my son will have severe form of Huntington's disease, my grandson will have more severe form of Huntington's disease because this trinucleotide sequence gets amplified with generation. So this is an autosomal dominant disease, which has Chorea, dementia and depression.

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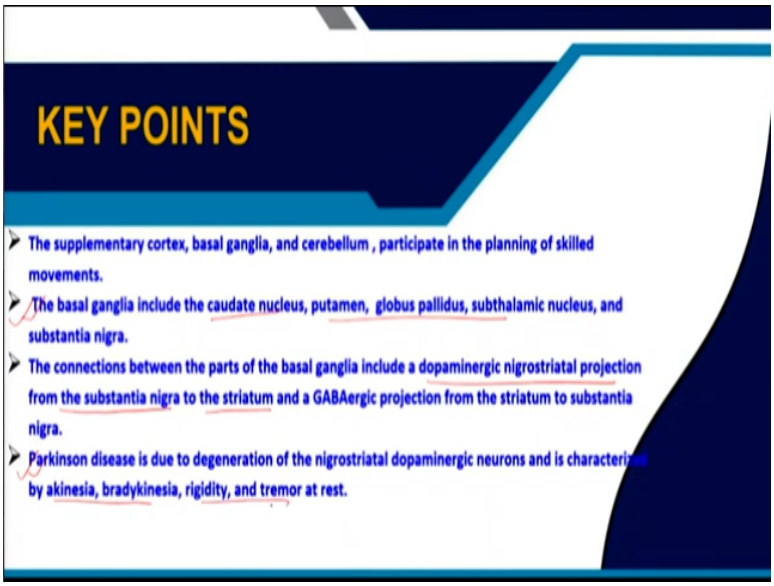

So the key points you have to remember is the basal nuclei. The basal ganglia consists of caudate nucleus, lentiform nuclei, subthalamic nuclei and substantia nigra that is a functional classification of nuclei you have to remember. The connections mainly the dopaminergic nigrostriatal projections from the substantia nigra to the striatum is very important because destruction of this pathway leads to Parkinsonism which results in the akinesia or bradykinesia, rigidity and resting tremors.

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So with this, I would like to conclude my lecture.

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Thank you.