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

Lecture - 76
Basal Ganglia – Various Disorders

Welcome to this class on Neuroscience of Human Movement. In this class we will discuss other disorders of Basal Ganglia; that means, disorders other than Parkinson's disease.

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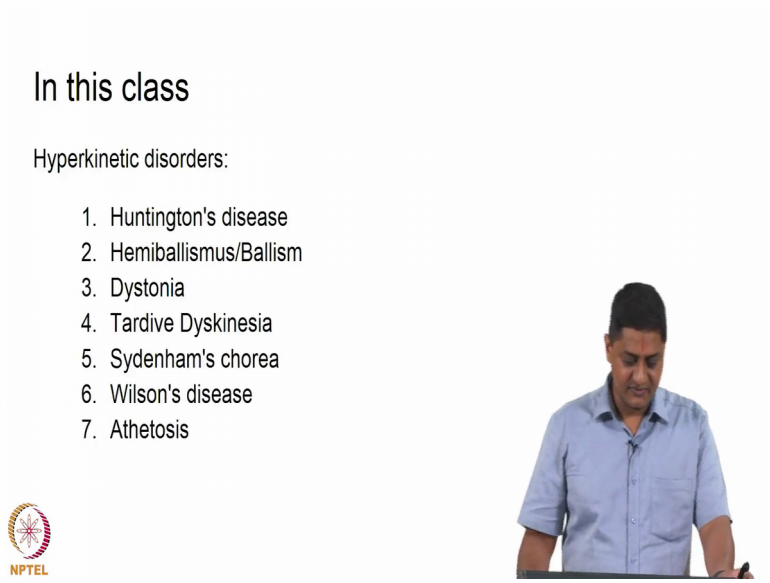

So, in this class we will discuss specifically hyperkinetic disorders in particular huntington's disease and ballism and other disorders such as dystonia, tardive dyskinesia, sydenham's chorea, Wilson's disease and athetosis.

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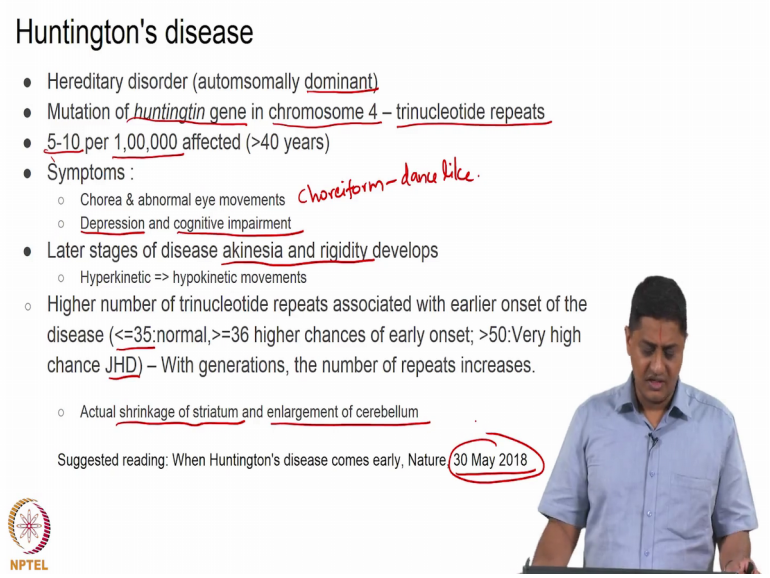

Huntington's disease right is a genetic disorder, it is a hereditary disorder and is autosomally dominant; that means, what if one of the parents has the disease the child has a 50 percent chance of getting this disease right. The fortunately the gene responsible for causing this disease has been identified. This is the mutation of the huntingtin gene in chromosome 4 that causes higher number of trinucleotide repeats right. The occurrence is about 5 to 10 per 100000 so, 5 to 10 100000 years right. Symptoms are chorieform movements dance like movements chorieform or dance like.

So, this of course, shares the route with what is called as choreography right. So, like you see in movies choreography means what dance related to dance right. So, chorieform dance like movements so, these individuals when they make movements it looks as if they are dancing right and eye movements are abnormal.

And, usually this also is accompanied by other non-motor symptoms such as depression and impairment of cognitive function. Although, the exact details of the non-motor functions or dysfunctions have not been understood, the motor form has been documented relatively well right and it turns out that in later stages of the disease hypokinetic form right.

And, akinesia rigidity form a phenotype involving rigidity and akinesia is developed and that leads ultimately to death; usually death happens after about 15 to 20 years after onset right. And, it turns out that the number of this trinucleotide repeat determines when the

person is going to get the disease right. If this number is below 35, this is a relatively normal and if it is greater than or equal to 36, there is a higher chance of early onset. Above 50 well this is just a ballpark number, above 50 repeats of this trinucleotide repeat usually signals that the person will develop what is called as Juvenile Huntington's Disease that is what I have called us JHD; Juvenile Huntington's Disease.

So, in some cases these children develop diseases at round the age of 1213. So, very early onset this is very different from the original discussion. This is very different from the original description made by Huntington in his paper right. And, it turns out that with the generations as a generation's progress the onset happens earlier. So, if in one generation the onset happens at 40 years then in the next generation it turns out that the number of trinucleotide repeats increases.

So, if the father gets the disease at around 40 years, the child has a chance of getting the diseases at around 35 say for example, of 38 depending on the number of trinucleotide repeats. And, in children with JHD it turns out that there is an actual shrinkage of striatum and then enlargement of cerebellum. This is a mall adaptation, this is an adaptation due to pathology. This leads to a situation where the person does not this child does not go through the chorieform stage and directly reaches rigidity.

So, in other words people in whom the disease sets in at an early age right, like in the case of Juvenile Huntington's disease it turns out that these people have a higher chance of directly going to the rigidity form without going through the chorieform right. Without going through the dance like symptom of typical of this disease although, the specific gene and the chromosome on the particular molecular details have been identified still a lot of research is needed to further understand this.

Let us remember that in comparison with Parkinson's disease, Huntington's disease and it is pathophysiology are relatively poorly understood right. Please do read the most recent article on this topic in nature when Huntington's disease comes early, 30th May which is just a few days ago right where the details of disease discussion, there are few other accompanying articles that I suggest you read alright.

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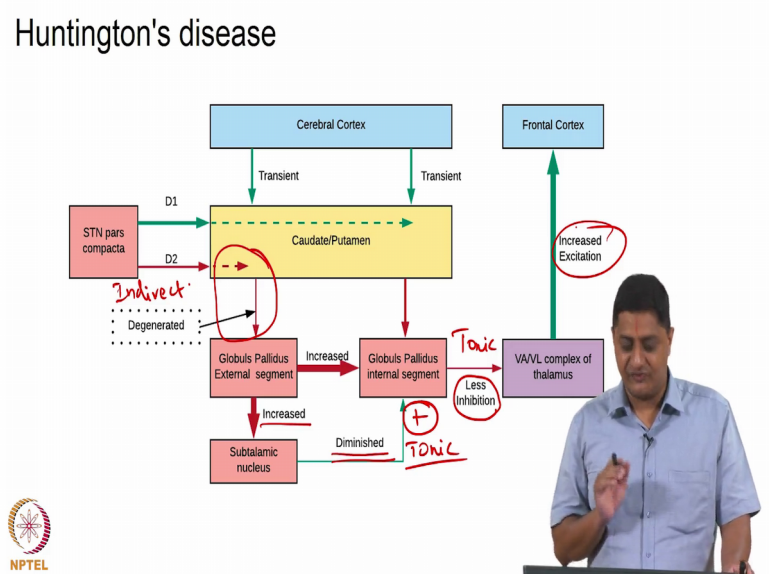

So, what exactly is happening in this is what pathway is affected, it turns out that Huntington's disease involves selective degeneration of the indirect pathway. So that means, what the neurons from the striatum to the GPE right are affected, this leads to a situation where the subtalamic nucleus is inhibited to a greater extent. Thus, diminishing the subtalamic nucleus input to GPI right.

Let us remember that the subtalamic nucleus actually is exciting the globus pallidus internal segment; that means, in the absence of the subtalamic nucleus excitation the amount of inhibition. Let us remember this is tonic and this is also tonic right. So, this means a situation is developed in which the amount of inhibition that is received by the thalamocortical neurons is reduced.

Because, of this reason what happens is that there is an increased excitation at the cortex level right leading to unwanted movements being performed, unwanted dance like chorieform movements being performed right. However, this model is too simplistic there are a specific cases when this model cannot explain the actual details right. So, let us remember that this model can only do so much justice a lot more research is required for an actual deeper understanding of the pathophysiology of this disease.

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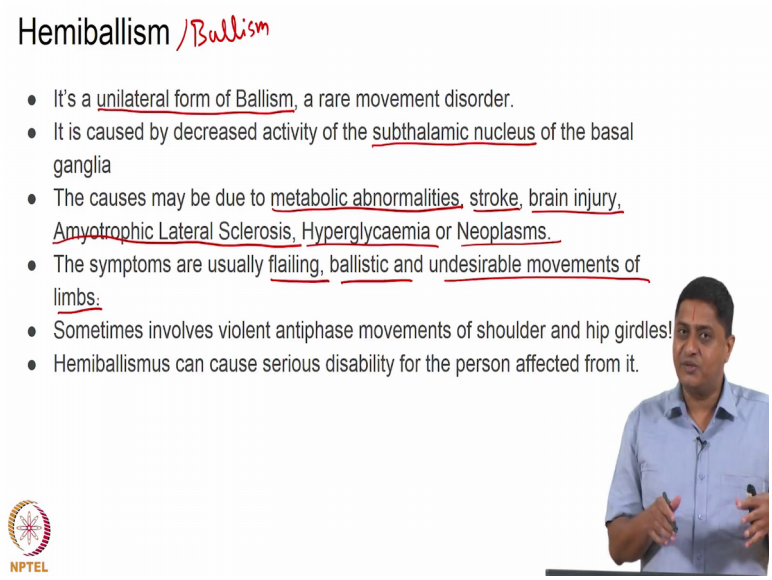

Then the case of hemiballism or ballism, if ballism happens in one side of the body that is called as hemiballism. So, a unilateral form of ballism is called as a hemiballism; this is happening usually due to dysfunction of subthalamic nucleus of the basal ganglia. So, this means if for whatever reason the subthalamic nucleus is not toned, then what happens is unwanted movements are produced why? Because, of subthalmic nucleus is tonically exciting the GPI right in this picture so, this is happening. So, this is a so, if the subtalamic nucleus is not toned; that means, what that means, the tonic excitation this is by GPI which is tonically inhibiting the thalamocortical neurones is reduced; that means, that the output of GPI is reduced.

But, the output of GPI is inhibitory in nature or ballism or hemiballism leads to a situation where there is going to be unwanted movements. So, the exact reasons why the subthalamic nucleus neurons are not toned maybe due to multiple reasons metabolic abnormalities, stroke, whatever brain injury, the ALS several causes, hyperglycaemia, neoplasms several could lead it to selective degeneration or selective death of neurons in the subthalamic nucleus right. What are the symptoms? The symptoms are flailing ballistic and undesirable movements of the limbs; usually what happens is that ballism even hemiballism involve violent out of phase movements between the shoulder girdle and the hip girdle, like you would see in Bollywood dance right.

When you watch Bollywood song what you see is that there is violent; that means, very fast out of face movements of the shoulder girdle and the hip girdle right. This leads to a very violent and unwanted and very difficult disability for patients. Of course, in the movie this is fun to watch, but in the lives of people this is really horrible because, all the time they will have to be going through right. This causes serious disability for the person who is affected by this particular disease right. Why is this happening once again, due to death of neurones in the subthalamic nucleus?

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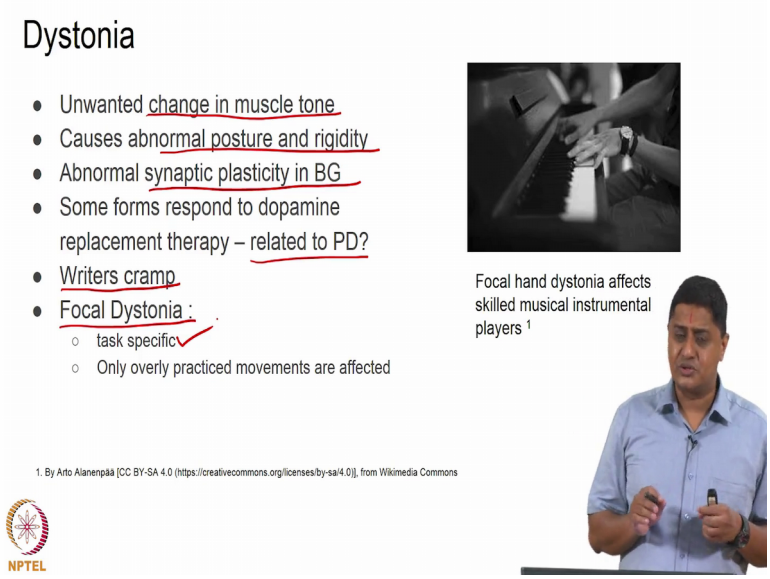

Then dystonia, this is an undesirable amount of muscle tone than required right. So, this leads to a situation of abnormal posture and many times rigidity right. So, why it is called the hypothesis is that this is caused due to abnormal synaptic plasticity in the basal ganglia. In the then the question is how exactly is basal ganglia even implicated in this disease. Actually, some forms of dystonia respond to dopamine replacement therapy then the question is it somehow related to Parkinson's disease. In fact, the truth is that the exact link of how basal ganglia is linked to dystonia remains a mystery.

We actually do not understand the pathophysiology or the connection between basal ganglia and dystonia. One particular form of dystonia is of course, writer's cramp or focal dystonia for example, in musician related dystonia. This person can do practically everything using the same effector, but the moment he is going to perform a well practiced task right, it is a task specific thing overly practiced task then that movement is

affected this is called as musicians dystonia right. Relatively rare such condition, but a debilitating condition of this very poor understanding of why this happens, what are the details, how to treat this, what are the so, and the exact relationship to basal ganglia is also relatively poorly understood.

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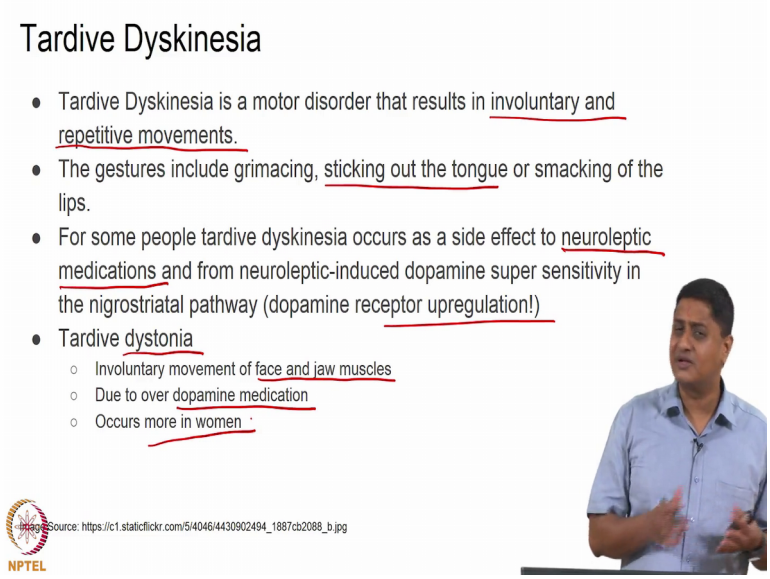

Another, disease is tardive dyskinesia right, in this case what happens is there are involuntary and repetitive movements that are caused usually as a side effect of neuroleptic medications right and dopamine super sensitivity. So, in other words that is upregulation of dopamine receptors right. This leads to situation where the person is frequently performing that kind of movements, grimacing you know like that, like sticking out the tongue or you know smacking of the lips or various other unwanted and socially awkward movements right.

And, one particular form of tardive dyskinesia is tardive dystonia right. So, this is related to tardive dyskinesia and also related to dystonia right. Again in this case there are involuntary movement of face and jaw muscles again due to dopamine medication. Again it occurs more in women when compared with man and it occurs more in older people when compared with younger people. In some cases it also happens as a result of other medication side effects right so, this is tardive dyskinesia.

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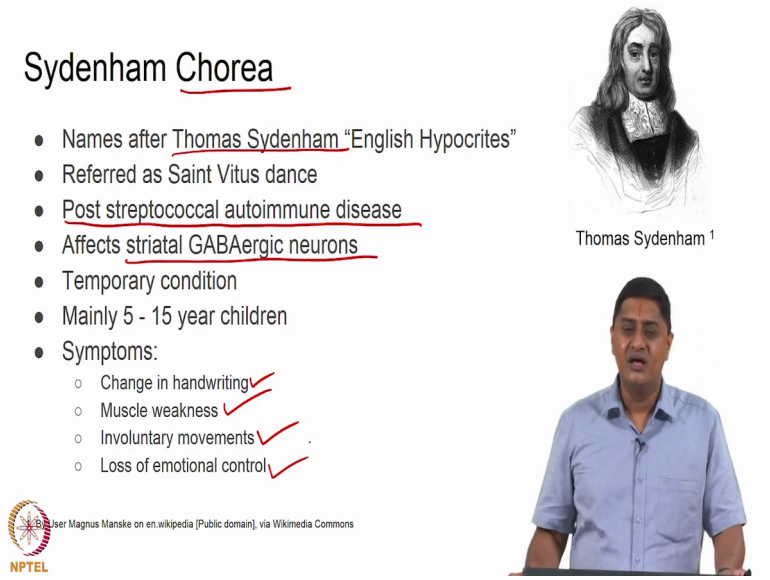

Then another disease is chorea, that are dance form movements dance like movements related as after effect of romatic fever or post streptococcal autoimmune disease right. So, this is named after Thomas Sydenham right, it is a relatively temporary conditions such fortunately it is a temporary condition it affects striatal GABAergic neurons, it happens between the age of 5 and 15 years right.

What happens what are the symptoms? Changes in handwriting, muscle weakness and unwanted or involuntary movements, unfortunately this is also accompanies by frequent loss of emotional control right as after effect. So, after the person survives the streptococcal disease then the person gets this disease.

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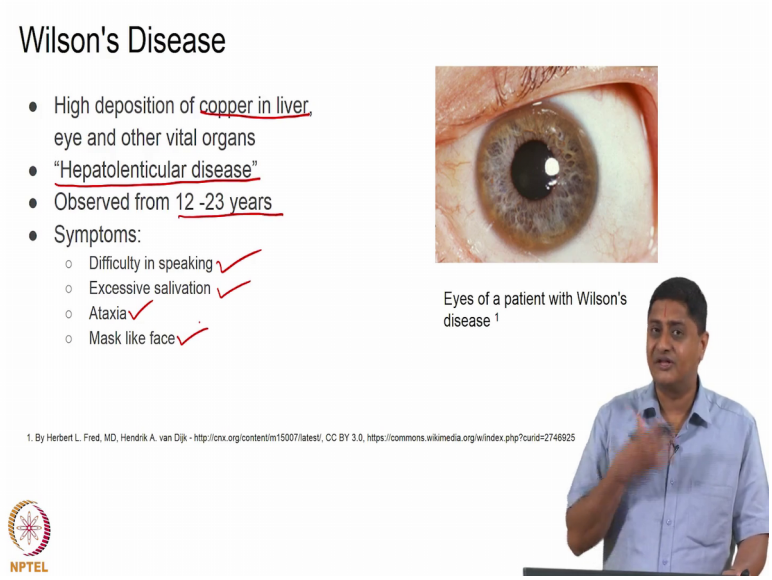

Then the so, called the hepatolenticular disease or Wilson's disease. This happens due to high deposition of copper in liver; hepato means liver related, lenticular means basal ganglia related right. So, this unwanted high deposition of copper in liver actually leads to a situation, when the lentiform nucleus other lenticular nucleus is and its performance is affected. Usually, the age of occurrence is between 12 and 23 years. What happens, what are the symptoms?

Difficulty in speaking, excessive salivation unable to control salivation, ataxia and unfortunately accompanied by mask like face in other words unable to express an emotion through facial features right. So, facial features and expression of emotion through the face is associated with movements of relatively small muscles as I mentioned in a previous class. So, this disease leads to a situation when the people are not able to move those muscles, when the person is showing a face that resembles a mask showing no emotion.