Animal Physiology
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Lecture - 33
Amyotrophic Lateral Sclerosis Disease

Welcome back to the lecture series in Animal Physiology. We are into week 7 and today we are starting the lecture 3. So, in the first two lectures if you recollect we started with Alzheimer's disease, then we talked about Parkinson's.

In both the cases though the effects are different: in one case you use your own identity, which is a case of Alzheimer's where most of the neuron in the hippocampus and the surrounding cortical region dies out for an absolute unknown reason and it is being postulated and kind of. One of the accepted paradigms are that the trafficking along the axon is being compromised, because the proteins which are laid across the axon to carry the neurotransmitter cargo and other cargos kind of that lead pattern of proteins is distorted. And just like there are break points on the road traffic gets stopped, exactly in the same way the molecular trafficking is compromised and eventually the axon starts to die out and that leads to the Alzheimer's.

Pretty much in the same line in the neurons of substantia nigra, which is involved in locomotion and coordination of movements the dopaminergic neuron loses or dies out for again an unknown reason and their synapse on the lower motor neuron which are sitting in the ventral horn of the spinal cord do not receive the necessary signals

Thus, discontinuing the circuit; if you remember in the last class I mentioned the circuit kind of gets discontinued, because from the message goes from the ascending or the dorsal pathway or the sensory pathway to all the way to motor cortex in substantia nigra and the message gets processed and from there the process message is sent to the lower spinal cord or lower motor neuron in the spinal cord and from there by series of computation the message is being relayed to their specific organ. Now, the problem comes when that motor neuron which is sitting in the ventral horn do not receive the necessary signal from substantia nigra and I talked you about L Dopa therapy.

So today, now we have dealt with two different case studies which involved a brain neurons. Today we will talk about a very similar fate which happens in the ventral horn of the spinal cord, the motor neurons which are sitting in the ventral horn. And the progression of death or the story line of death is very similar as the Alzheimer's and Parkinson. Absolutely for an unknown reason bearing aside couple of cases of mutation in some of the SOD genes; SOD stands for Super Oxide Dismutase it is one of the antioxidant enzymes. Like just for your knowledge say there are three antioxidant enzymes in our body: glutathione peroxidase GPx x, in short they call it catalase which involves in quenching the peroxides. And the third one is super oxide dismutase which get rid of the super oxide radicals.

So, essentially these three enzymes hold the fort in our body to counter the problem we face because of living in an oxygenated environment. Because, while living in an oxygenated environment it leads to generation of series of free radicals for oxide radical super oxide radical bunch of them.

In the case of SOD there is a mutant of SOD which accounts for death of small population of motor neuron or there are patients who suffer from death of motor neuron because of a mutation in the SOD-G. Bearing aside that there is a huge number for whom why the death occurs in these motor neuron is not clear.

So, today our aim will be to explore that particular aspect which otherwise commonly known as ALS- Amyotrophic Lateral Sclerosis, which is caused due to the death of the lower motor neuron which are present on the ventral horn.

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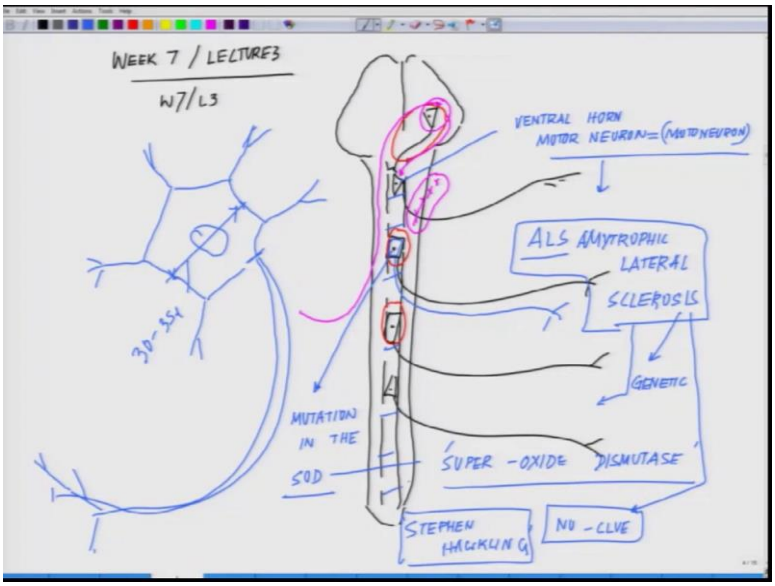

So, let us start this chapter we are on week 7 lecture 3: W 7 L 3.

Now, let us again redraw the brain and spinal cord connectivity. Here is our spinal cord, talked about the brain, and here we have the ventral horn, the dotted line showing the ventral horn motor neuron. So, most of the motor neuron are sitting here in laminar structure I have already explained that to you, in previous classes. And this motor neuron gets input from the higher motor neurons like this.

So, we have already talked about the problem happening in these ones. Now I will talk about the problem happening in these ones. So, in this situation the circuit is like this, signal going by the ascending pathway, reaching the motor cortex, getting processed, the process in information comes back, but from here it fails to transmit the message.

So, if you compare it with Parkinson where the central processor or the brain feel to convey the message, here the spinal cord motor neuron or the one which are called ventral horn motor neuron, and sometime you will see this spelling written in American literature as motor neuron also, so both are same; do not get confused. So, ventral horn motor neuron exactly had the same fate as we have seen further hippocampal neuron. They started to die out, and these are the biggest neuron in our body and these are the oldest of all neurons which are formed.

So, in the mothers wound these are the neurons which are the first one to form, and they are really big. They have a fairly good cell body which is around 30 to 35 micron and they have a process which is fairly long because think of it like from the spinal cord all the way to the hand their process goes along. So, you see they are significantly longer, their process is significantly longer.

So, in ALS or amyotrophic lateral sclerosis: trophic lateral sclerosis. A disease which has affected several people across the world and only one sub fragment of it is known which is those who are having a mutation in the SOD- Super Oxide Dismutase. So, the SOD mutant is only a count for probably 1 or 2 percent of ALS patients. So, there is one aspect which is genetic.

But there is another aspect which we have no clue why these neurons die. Stephen Hawking, one famous name who suffers from ALS and interestingly the motor neurons which are sitting at different level of ventral horn, they have a different time or different level of sensitivity to get effected by the disease. What does that mean is? Say for example, some of these neurons, some of these ventral horn neurons are much more prone because of ALS, where some of them do not get that badly affected. So, apparently if you think of it in a way.

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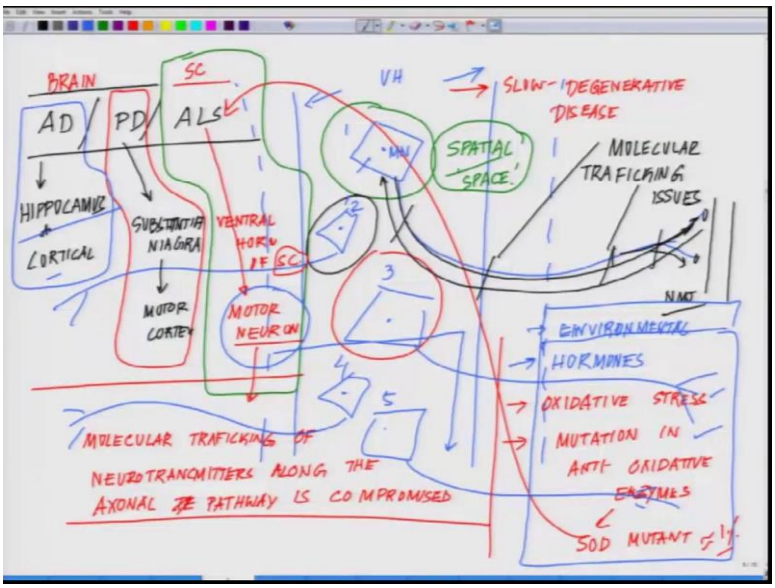

Apparently, along the ventral horn if I in this kind of enlarging the ventral horn view and where these huge motor neurons are sitting they are pulling out just let me mark it for your convenience this is your ventral horn and these are your motor neurons.

So, different population of motor neurons which are sitting here and conveying the information to different parts of the body they have different, like how to put it, like see for example I number them 1 2 different families. So, may be one family say 3, maybe more susceptible as compared to the 1 or may be this one may not get easily effected

So, most of this patient if you look at them you will see that they can move there, like this part, this muscle which is blinking your eye rashes. That is not effected, they can really you know their muscles of the eyes which are controlled by the motor neuron do not get easily effected by ALS. Contrite with some of the other ones which involved in the movement they are much more easily affected. So, it is absolutely not clear why all of a sudden at a certain point of life some population of neuron goes for or decides or meets in the fate of dyeing out we really have no clue.

The symptom what has been observed is again the same. If you really highlight this part or this part or this part you will see there are molecular trafficking issues. So, apparently the neurotransmitters which are to be transmitted at the axonal site or at the junction or at neuromuscular junction (Refer Time: 14:56) we will come to this neuromuscular junctions in subsequent section.

So, these neurotransmitter transmissions which or neurotransmitter transport transmission is wrong word here, neurotransmitter transport which is happening along the axon which I have mentioned in the previous class is kind of getting compromised. So essentially it boils down, there are certain thematic which is emerging over a period of time is that these cells if I have to kind of draw a correlation between AD- Alzheimer's disease, PD- Parkinson disease, ALS.

So, the first difference is if I look at it AD effecting hippocampal neuron and cortical neurons, hippocampus and cortical. PD on the country effects substantia nigra or motor cortex and these two are essentially in the brain, whereas this one is sitting at spinal cord the ALS and here you are affecting the motor neuron of; so this is affecting the ventral horn of spinal cord ventral horn of spinal cord SC stands for spinal cord specially affecting the motor neurons.

All three has this one common feature where molecular trafficking of neurotransmitters along the axonal pathway is compromised and it is not clear, so there are several factors which are associated with, there are school of thoughts which believed these are oxidative stress related, there evidences of mutation in anti oxidative enzymes. At least one classic example is SOD mutant involved in ALS, but that is only account for approximately 1 percent of the cases what we know off.

But apart from it and there is one more aspect, it is a slow degenerative disease and this will happen very fast, it is slowly kind of progresses and apart from it they have a spatial feature to it, they do not spread all over, there is spatiality involved. It means they have certain space preference. So, spay less pattern you see only in the motor neuron of the ventral horn. It does not affect the dopaminergic neuron. Country in the PD Parkinson's disease effects substantia nigra motor neuron: and whereas AD Alzheimer's disease effect only hippocampal mostly and part of the cortical system.

So, you see that there is an emerging pattern which is coming through though the disease progression is fairly the same but, their location is specific and within location two among the motor neurons if I have to put it their preference for certain category of motor neuron if you remember when I told you- that they have a preference for some like certain category of motor neuron this is they have a preference for one category over the others. So, disease progression is kind of different for even for that same kind of tissue.

So, essentially it is not really clear that how these things; there are theories all over if you see through the research articles, there are tons of research article which have been documented in this field. But, as of now for Parkinson disease of course we have L Dopa therapy with partly or in a small way help the patients. For ALS we hardly have any therapy, for AD we have a long way to go.

So, as of now and there is another theory. So, I talked about the oxidative stress certain probably, the mutation in anti oxidative enzyme. Some talks it about hormones which may have involved in it, but to save it absolute confidence and of course some blame it on environmental toxins or whatever. But to tell with absolute certainty at this point is a far crime.

So, with this aspect of comparing these three different kind of degenerative disorders which are happening in the spinal cord substantia nigra of the brain of the motor cortex, hippocampal region of the core processing unit of the brain.

I will conclude this part. And in the next class what we will do, we will talk about the spinal cord injuries which is another form of problem which happens because of the injury which happens on the motor neuron which are sitting in the ventral horn. So, please read through these things and kind of formulate your understanding.

Thanks for patient listening.