Animal Physiology
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Lecture - 32
Parkinson's Disease

Welcome back to lecture series on Animal Physiology. So, we are into week 7th the first lecture this week we have started with Alzheimer's. So, today we will talk about another aspect. So, we have devoute a time on memory and learning, and epilepsy and Alzheimer's.

Today we will talk about movement related disorders. So, on one hand in Alzheimer's disease you lose your own self or you forget who you are. There is another disorder exactly of similar kind in terms of molecular or cellular pathology. That is called Parkinson's disease

Parkinson's disease is a disorder where a certain population of the neurons, a certain part of the brain which controls your movement started to starts to die off. We do not know why, exactly that is why the similarity between this disease and Alzheimer's lies why all of a sudden at that specific or a particular part or the loci of the brain certain neurons started to die off we do not know, but it does happen.

Now, once they start to die off these neurons at that particular location has the projection in the spinal cord which governs your movement. So, that leads to the; because since those neurons which are sitting in the spinal cord do not get the signal coordination that leads to a movement disorder. Or you really cannot you know control the movement of your hands or legs or in the series of issues.

So, let us try to see how really the circuit works and where that drawback is.

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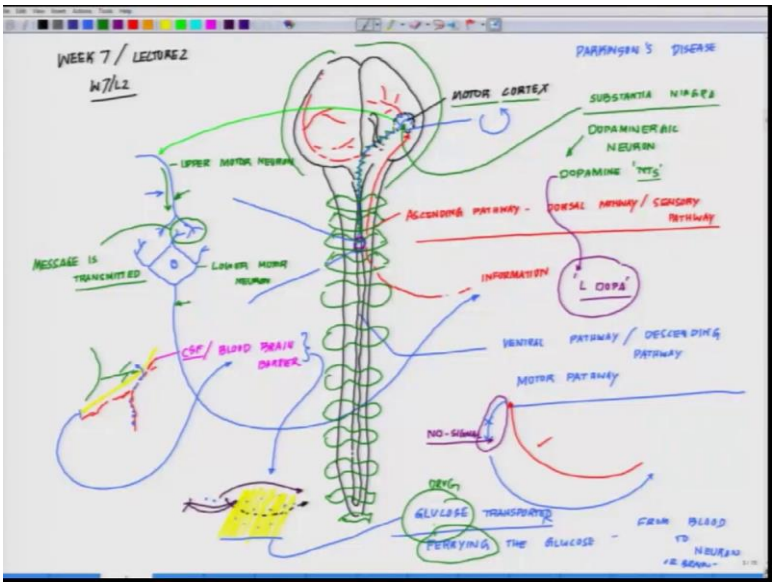

If you remember when you talk about ventral and dorsal pathway; so this is your brain and this is the spinal cord, this is out here is the ventral horn like here. And there is a spot, so this is of course we have talked about the hippocampal regions. And you have say motor cortex somewhere here; motor cortex. So, just before I forget this is behind to week 7 lecture 2: W 7 L 2.

So, here is the motor cortex. So, the way your movement thing occurs is this. So, there is information, some kind of information which goes. Say for example, you have to pick up a glass or something, the information travels all the way to the motor cortex like this. So, this is the info and along the ascending pathway which is also called dorsal pathway, the information the electrical and pulse goes to the motor cortex. At the motor cortex there are certain in their processing of that information takes place, specific zone in this case when you talk about Parkinson's disorder, Parkinson disease. At this point there are certain degrees of processing which takes place. And from here there are certain neuron which has projections like this on the ventral horn. So for example: on the ventral horn neuron there are projections like this.

Now at the ventral horn neuron let me blue up the ventral horn now. So, here is that process of the neuron which is coming, this is what you meant by projections. At that spot there is a bigger motor neuron which is sitting, which will take the info back for your action right. And this is that projection which is coming from here.

So, this neuron which is bringing the information from the motor cortex to the motor neuron which is sitting out in the ventral horn which is your; this is ascending pathway or the dorsal horn, and this is the central A is your ventral pathway or descending pathway. Why you call it descending? Because it is coming down from the brain, descending pathway or you can call it also motor pathway. And by the same token they are all same and by the same token you can call the dorsal pathway as sensory pathway.

So, now as the information is coming down out here, at this location there is a synaptic contact where the signal which has been coming from the motor cortex all the way to the ventral horn out here the message is passed, message is transmitted.

Now, suppose from the motor cortex no message arises here. So, automatically this motor neuron which is sitting at the ventral horn will not be able to execute anything. Now, such thing could only happen when the motor neuron from, so these both are motor neuron one motor neuron projection comes from the motor cortex to the ventral horn. So, there are names. So, the motor neuron which is coming from the motor cortex is called hyper motor neuron and the second one is called the lower motor neuron or somatic motor neuron because it is in contact with the specific cell type or whatever where it has to executes its action.

So, the only situation where the upper motor neuron feels to deliver message to the motor neuron could be either or somewhere other they become silent. Or this neuron which is coming as a projection started to degenerate. So, there is no signal which is happening from here, such situation arises in the case of Parkinson where these upper motor neurons which are located in this location which is called substantia nigra started to die off and exactly the same way as we have reserved in the case of Alzheimer's these neurons started to regenerate.

Once they degenerate and these neurons are Dopaminergic neuron, when we talk about Dopaminergic means these neuron secrete dopamine as a neurotransmitter. I am just putting NT S.

So, this Dopaminergic neuron at the substantia nigra started to die off, and they did not signal the lower motor neuron. So, the circuit which was essentially something like this we know the way up its perfectly fine, but now from here signal no more signal arrives this part of the circuit is all, but if you do not receive a signal out here there is no signal;

that means, there is a issue. And that is precisely what happens in the case of Parkinson disease there is something called L Dopa Therapy for which Nobel Prize which is gone, I will leave it up to you to see that what it is.

L dopa is a analog of dopamine which is being implanted slowly releasing which kind of feed bees, neurons some where other you have to really have a slow releasing stuff which is there. You can read through it, I will leave it up to your wisdom to read through this L Dopa therapy and you will you will like it. There are some very interesting aspects about the L Dopa therapy.

What is important is in both the cases whether it is Alzheimer's whether this is Parkinson, the progress of the disease is same. If you remember what I was drawing in the last class; so this is the pyramidal hippocampal neuron.

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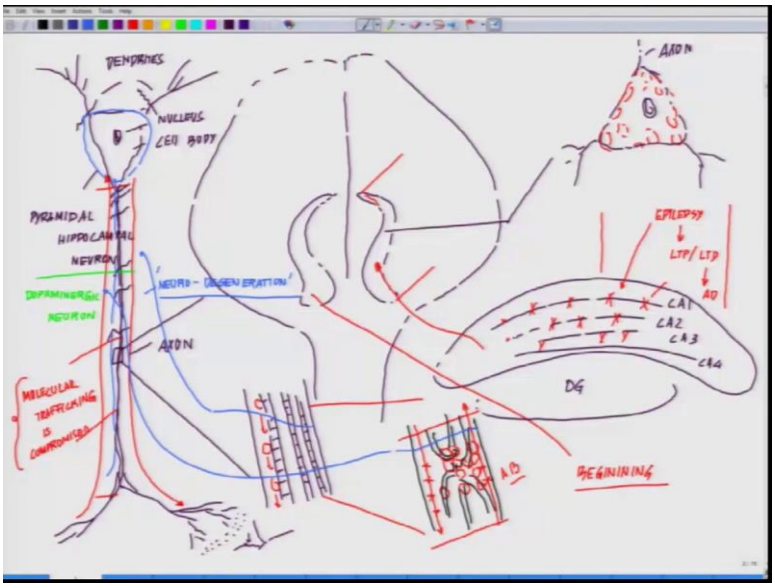

Now if you replace this pyramidal hippocampal neuron with a dopaminergic neuron just you change the name, and of course definitely that will lead to the change in the shape it will it is not as pyramidal as this one. But, if you look at what is happening at this zone and this zone for both of them it is a similar train.

So, apparently there is same type of neuro-degeneration and this neuro-degeneration is very unpredictable and why it happens at a particular age, and what is the geneses is it genetics or is it physiology or is it both or is it environment we really do not know.

Exactly we are on the same page as Alzheimer's about how this degeneration gets initiated and leads to a compromised living compromising the quality of life forever. If you think over it that unless we have a way to repair; so you have injuries in your hands legs wherever you have a (Refer Time: 14:47) kind of get around it. But in these situations you hardly can do anything, you are fairly helpless.

So, for Alzheimer's we really do not have anything. In the case of Parkinson at least we have some degree of recovery, I will not say recovery some degree of restoration of function in the form of L Dopa therapy; that is all we have. So, these are conditions or these are situations which happens in the brain where you have very limited access in terms of the drug entry or in terms of course surgery is a big challenge, or even in terms of regenerative medicine where you think of even in planting stem cells.

Why the access is tough? First of all is because of the blood brain barrier. If you look at the structure it is always surrounded by another lining. And these vessels are never in direct contact with the neurons, there is always a layer. So, it is something like if you have the neurons out here if this is the neuronal terminal, so there will be always a kind of a very thin film which I am showing in yellow, which will the fill cavity what we call as CSF or cerebrospinal fluid, which is covering the blood brain barrier.

The blood vessels will be all travelling like this, but they will never be indirect contact. So, now you realize that for a drug to jump; suppose you introduce a drug these blue dots are the drugs and for a drug to jump to this side it has to cross through the blood brain barrier. And blood brain barrier is not so easy to cross unless you have specific boats, molecular boats or the cargo boats which can carry this small drug molecule in a boat like this or ferry this molecule in a boat to the side where the neuron is present. So, it has to cross to this channel out here. Unless it cross through this channel it will not be able to interact with the neurons on the other side.

So, the biggest challenge of any kind of neuro-degenerative problems or any removing a or brain tumor or any kind of problem in the brain is how you easily you can do the surgery. The answer is very challenging, because this whole thing is enclosed in a strong structure which is your skull. And this whole spinal cord is once we will come we will talk about the spinal cord injure in the very next section you will realize the challenge.

So, there are these columns through which this whole thing passes. And these are bony columns; it is not easy access for these kind of surgeries to be conducted easily.

In terms of the drug therapy the problem is the same, because this drug molecule has to diffuse into through this space and in this space, the blood brain barrier fluid unless otherwise you have a carrier molecule: say for example, brain uses glucose as its major source of energy. Now, there are glucose transporters which are sitting out here where this glucose transporter molecules. These glucose transporters help in transporters help in ferrying the glucose from blood to neuron or to brain.

So, if you replace glucose by say drug molecule here- higher drug molecule, now unless there is a ferry for the drug molecule to reach to the other side that will remain stuck on this side. So, even if you take a drug there is no way, there is no guarantee that that drug is going to reach to your brain or in the specific part of the brain.

Your other option is that you inject something through this skull at that specific spot. By drilling through the skull which is not so easy, and then to the very moment you do some anything of that sort it means you are now exposing your brain to something which you do not wanted to do so easily unless otherwise. Or you surgically cut open the skull access the brain, and that is what they do most of the time in the case of brain tumor, where the glial cells kind of you know out numbers at a specific spot and those glial growths has to be removed.

So, in summary accessing brain is a very very challenging task. And understanding the uncertainty of this disease to approach is another very challenging scenario. So, with these two cases where ones individuality is being compromised in the form of Alzheimer, in the other case Parkinson where your movement is being compromised; I will close it on this lecture.

So, in the next lecture we will pretty much take over from here, if the damage happens in the lower motor neuron which will bring us to the situation of two more diseases: one is spinal cord injury and the relevant disease what could happen, and the second one is a amyotrophic lateral sclerosis lateral sclerosis followed by we will talk about multiple sclerosis which is a problem of the glial cell. And in that process we will talk about myelination and myelination related disorders.

Thanks for your patient listening.