Human Physiology
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Lecture – 15
Rhythmicity of heart beat-Part 2

Let us go back and I will ask you one question of what we have done already. Remember when we talked about the innervation of the skeletal muscle, the neuron is located somewhere in the central nervous system, it gives rise to a motor fibre, that motor fibre terminates on the skeletal muscle and releases what neurotransmitter? Acetylcholine. Very good. It will act on what kind of receptor? Ligand. The second answer was little muted. It was nicotinic acetylcholine.

What was it? Acetylcholine nicotinic type. Then another statement that I want to make is if you remember our yesterday's class where we talked about the autonomic supply or the sympathetic or the parasympathetic supply in which the peculiarity was, there were two neurons in the series. How many neurons in the series? Two neurons. Two neurons in the series.

All the first neurons, I will make another general statement, all the first neurons whether it is sympathetic or parasympathetic are cholinergic. Are again what? Cholinergic. Cholinergic and like the earlier system they are also acting on the second neuron via the nicotinic acetylcholine receptor. What did I say? So, first neuron, first neuron, first of all in sympathetic and parasympathetic we all agree that there are two neurons in series. No doubt there, there is no dispute there.

The first neuron, I am making a statement now. What is it? The first neuron is what? Is what? Cholinergic. What is it? Cholinergic. Cholinergic. What is it? Cholinergic.

It is talking to the second neuron and that second neuron and that second neuron is having what kind of receptors? acetylcholine. acetylcholine. It has to have acetylcholine receptors again of nicotinic type. Again at what type? Nicotinic. Nicotinic type.

So, far the story is very simple. Now I am talking about the gross ganglion receptor of the parasympathetic nervous. So, let us go to yesterday's image. I am not going to draw the image, but the fiber starts somewhere in the middle of long hair tie travels over the vagus. It goes as far as the heart, it is cholinergic, cholinergic, cholinergic.

It goes, it talks to the second neuron, the second neuron is very close to the heart. It talks

to the second neuron via the nicotinic acetylcholine receptor, no doubt so far. The second neuron goes and talks to the heart muscle, particularly what muscle? Particularly talks to the cells of the SA node and the V node, talks to those and that receptor is now different kind. It is not nicotinic, not nicotinic, not nicotinic. It is another type which is called as muscarinic.

What do you call it as? Muscarinic. Now here is a very interesting point. I mean, I will take you back to about 1930 or 32 when they knew that, well, acetylcholine is there, it acts on the receptor, it is there. It acts on the receptor on the skeletal muscle, yes, on the receptors in the heart, yes, on the receptor, everywhere it acts. But then the beauty was or the differences were when you take a particular drug which acts on the same receptor, but the same drug does not act on all the receptors.

What do I mean by that? What do I mean by that? I will go to the preganglionic fiber. Preganglionic fiber acts on the ganglion, nicotinic type. Means what? Nicotin can combine with the, why am I calling that particular receptor of acetylcholine as nicotinic type? Because the molecule nicotin which I get from tobacco can act with that receptor, therefore it is nicotinic type. Then what am I? I am making another statement. The receptor on the heart which again this is acetylcholine, on that receptor nicotin does not act.

It does not act. Then what is, then how do I know? I classify it because it combines with another molecule and that molecule I get from a particular mushroom and I call that molecule as muscarine. What do you call it as? Muscarine. So, please remember this is my classification of the different types of acetylcholine is not possible if I do not resort to pharmacology. You get me? See, we do not have nicotin, we do not have muscarine, we do not have them.

But we have the different receptors and I am in a position to differentiate them because they interact with different molecules taken from nature. I get nicotin from nature, I get muscarine from nature. When I administer them into the right, I find that some acetylcholine it binds to nicotin binds to some acetylcholine receptors nicotinic. Muscarine binds to another muscarinic. Now, having done that classification then I want to know more about each of the type of the receptors.

So, I use all the modern techniques and I want to find out what the proteins are and what are their structures and I find that the nicotinic type of receptors essentially belong to this type of chemistry which means there are 5 subunits. What am I talking about? Nicotinic type. What am I talking about? So, it is on the skeletal muscle. Hello? Skeletal muscle. It is on the plasma membrane of the cell membrane, listen to this, cell membrane of the

ganglionic neuron which is receiving the preganglionic fibre.

Is it Greek and Latin? Am I making sense? Again, again parasympathetic nervous system, first neuron located in the middle of longata yesterday. What was the name of the nucleus? Let us see. Let us test your memory.

Dorcell. Dorcell. Wagle. Wagle.

Motor. Motor. Nucleus. Very good, very good. Every word has a meaning? Dorcell, dorsal, wagle, it gives us to wagle. And it is giving rise to preganglionic fibres or postganglionic fibres, please? Preganglionic. Preganglionic.

What is it? Preganglionic. Is it cholinergic or what? Cholinergic. It is going to talk on the second neuron now. The second neuron on the plasma membrane will have what kind of receptor? Nicotinic. Nicotinic.

What is it? Nicotinic. Nicotinic. Now, I am talking about the second neuron. The second neuron is going to talk to what? Heart. Heart.

Going to talk to what? Heart. Where is the receptor located? On the heart. Now, what kind of receptor? Muscarinic. Muscarinic. So, the information is taken in the nature information taken by acetylcholine, acetylcholine, but acetylcholine, nicotinic, acetylcholine, muscarinic. And now I am going to isolate those proteins which are of the nicotinic type and I find that the structure is consisting of what? How many, can you actually count how many subunits or proteins subunits are there? Five.

Five. Five, always five. Always what? Five. And what is the, and whenever acetylcholine combines with it what do they do? These five proteins they open and then they let, they allow the ions to pass through. Therefore, I can also cause call the channels as ionotropic. What did I say? Ionotropic. Everybody, what is it? Ionotropic.

Ionotropic. Why ionotropic? Because it directly allows the ions to pass through ionotropic. So, I will say that whenever this receptor combines with its ligand, in this particular case ligand can be a natural acetylcholine or it can be taken from outside which is nicotine and it can respond and it may respond by opening the channel it will allow the ions to pass through and therefore, I will call it as ionotropic. Done, concept clear? Great. Now, when I go to the muscarinic type of receptor I find that its structure is totally different, but we are aware of that kind of molecule. What are those kinds of molecule I want you to identify? They are 7 transmembrane proteins.

Hello, G protein coupled. Hello. And they will take the signal inside, they will take the signal inside to the from outside to the inside. So, outside the molecule has to combine. In nature that molecule is again acetylcholine. But it is combining with that kind of protein. Acetylcholine you can see there is acid is combining that kind of protein and it will undergo configurational change.

When it undergoes the configurational change it will act with a G protein which may be inhibitory type or excitatory type I will not talk about it here and then it will take a signal it will take a signal down into the cell and that signal may have different paths different paths either it may open a channel it may not open a channel it may just act on a sarcoplasmic reticulum release it can there are different pathways. But since they are all metabolic, I will call that type of receptor as metapotropic. So, I will make a general statement that whereas, the nicotinic type of receptor in acetylcholine is ionotropic. The muscarinic type of receptor which is a receptor of acetylcholine is of what type? Metapotropic.

Metapotropic say that again. Metapotropic. Metapotropic good good good good. So, I give here the structure of nicotin the acetylcholine and the muscarine just for your general information. So, you can read about the muscarinic type of receptor. What happens when the muscarinic type of receptor? So, here is a you have done an interesting experiment.

You are working on a rat you have opened a rat you are placed an electrode or you just look at the heart and find out how many times the heart is beating. Good good ok. It is a rat it is beating 250 times no problem ok. Then you take a pair of electrodes you dissect out its vagus whose vagus that rats vagus you place your electrode on the vagus and give a small current shock give a small shock are you with me. So, what you are doing you are electrically exciting the vagus nerve ok.

Along it lot of fibres are excited we do not worry about them, but I keep on looking at the heart and I find that the heart beat which was about 250 beats per minute has come down to 200, it has gone down come down to 150 ok. So, what is my what is my conclusion that there is some information that is going from the heart I have made a mistake that is going from the medulla elongata over the vagus to the heart ok. And when the muscarinic fibres in the muscarinic receptors in the heart are excited heart slows down in bits. How does it happen that explanation is here it is again the same muscarinic type of receptor you can see the plasma membrane and you can see the acylcholine molecule combining there. What is this acylcholine molecule coming from? It is coming from the post ganglionic fibre.

Hello vagus pre ganglionic. Post ganglionic acylcholine talks to the muscarinic receptor the metabotropic you can see the 7 times the membrane is going the protein is going up and down and when it does it gives a signal to the G protein which is inhibitory type there are there are one or more steps then it finally talks to a channel. It is talking to the channel what is this channel it is the potassium ion channel. It opens the potassium ion channel when it opens the potassium ions go out when they go out the outside becomes more positive when it goes more positive it means now the membrane is hyperpolarized whenever a membrane is hyperpolarized it is inhibited. Now these two words we will never forget hyperpolarized membrane is inhibited what did I say? Hyperpolarized. Hyperpolarized so this plasma membrane plasma membrane inside is 0 take any membrane inside is 0 so outside is 70 outside is how much? 70 may be nerve muscle whatever outside is how much? 70 or if I make a if I turn it other round outside is 0 outside is 0 the inside will be how much? Minus 70.

Minus 70 inside is how much? Minus 70. Minus 70 if minus 70 becomes minus 80 it is hyperpolarized what is it? Remember this it is what? Hyperpolarized. Hyperpolarized means it is inhibited it is now difficult to stimulate the cell but from 70 if I go to 60 and 50 it is depolarized now it is easy for me to stimulate the cell side the cell. So do not mess up with these terms. Now we are suppose we are still looking at the same rat and we are looking at the beats you know there are two traces there one is a continuous one is a dotted the continuous one is the normal one that is a control you have not excited the vagus nerve and then now you excite it and what difference do you find that in the time period in which you had the three peaks how many dotted peaks are you having? 2. 2 which means what? The frequency of beats has gone down are you with me? I cannot ask a very simple question instead of instead of putting my electrode on the vagus and electrically stimulate stimulate it is it a good idea for me to take a pipette in the pipette take very dilute solution of Acetylcholine and directly do it on the heart what will happen? What will happen? Be bold.

Be bold you are you are permitted to make mistakes but most logical answer Acetylcholine will combine with muscarinic receptor and then you will have the sequence of events and then the heart will go down. So actually whether you are giving Acetylcholine from outside or whether you are electrically stimulating the vagus you are ultimately resulting doing what? You are releasing Acetylcholine on the plasma membrane of the cardiac cell and then this sequence of events which we have seen in the previous slide and the heart will slow down are you okay so far? Okay now change of gears I am going to take you to some other aspect of the heart very interesting very interesting okay now let us go to the moment when the when the heart is not excited okay what is happened what is the position of the SA node not excited not excited SA node not excited just catch on to that moment not excited okay now excited okay excited

means what suddenly there is reversal of polarity on the plasma membrane similar rest of the heart is still it is it is still not excited will go very slow although although the whole thing happens within 0.345 seconds okay will go very slow and the little later then the action potential has spread from the SA node over the internodal pathway to the AV node okay you have gone that far okay or maybe you have crossed through the bundle of his okay so this part of the system or this part of the heart has undergone reversal of polarity means what outside has become 0 outside of the plasma membrane was 0 now it has become plus 20 hello are you with me but the rest of the heart rest of the heart is still polarized so now you can I want you to look at this image and try to make sense of it this is this is after 0.1 second after the SA node has excited and you can see the negativity gone as far as as far as the partition it has gone you can see the partition the right and left ventricle you can see that there is negative but the rest of is still positive as a result of some positivity there some negativity there there will be flow of current are you with me there will be what there will be a flow of current within the heart okay now now I can directly put the electrode on the heart and get that try to find out how much that current is I can do that but for that I will have to put an electrode all the way through your through your skin into your heart that's not a good idea so what they do what they do now I'm going to talk about very very simple and very useful pathologic tool which you call as what ECG electrocardiogram what did I say say that again electrocardiogram okay in which what you really do is you place your electrode on your chest and out of that current generated whatever little comes out are you with me little comes out you see because it has to pass through a lot of other body parts whatever little comes out you pick it up and then try to plot it and try to make sense of it okay that plot we will call as ECG but this explains to you why in every cycle a current is generated and you can pick up the current by you can see the patient here you can see the different electrodes the information from the electrodes is being taken to that oscilloscope which we call as cardioscope and then you are seeing it and you find a very interesting pattern there is a pattern okay and that pattern in standard language which has evolved in the language of cardiologists by the cardiologist we have certain waves what do this wave represent they represent electrical current where are you picking it from from the periphery why is it very good because you are not you know there's nothing invasive okay you you can just I can I make a lot of interpretation of your working of your heart without actually going to the heart the little current that I can pick up from the skin I can plot it up and take a look at it and then try to find out whether your heart is okay or not okay and then I get certain curves and now what I'm going to do another two minutes is try to try to understand what those curves really are and how do the cardiologists interpret to them the first there is a tiny peak there tiny curve there which the cardiologist will call as the P wave what do you call it as P wave what do you call it as P wave okay and on the on the x axis you can see the time duration taken by the P wave are you there with me okay and on the on the y axis you can see the voltage being generated every time the card goes through the

circle goes through the cycle after that then there is a little dip after Q after P can you see it flattens and then little dip and then it shoots up and then again comes down this is called as QRS complex it is taken together what do you call it as this is a terminology which doctors use I am only I am simply trying to convey to you they have they have they describe the P wave then they describe the QRS complex and after that again there is an interval there is an interval there is an interval and then there is what wave is there T wave P wave QRS complex and T wave are you with me and in a in a person who is having 72 beats per minute how much time it will take has been shown on the so if you have if you can just count the number of hours there is R you can you see Q at that R the highest peak point of the QRS complex so I if I plot this over a minute okay and if I if I can get pulse rate of 75 I will actually get 72 hours over a period of minute are you with me this is 72 hours it is very simple it is 72 hours okay all right now please remember this and I will take you to another image in which we have better interpretation of the different timing the what is the P interval what is the what is the P what is the PQ interval here what is the QRS interval ST interval and author tells us that heart rate the the the QT interval is dependent is heart rate dependent means if the heart rate if the heart rate is more than the interval will be will be less okay now now this is very interesting just focus on this I am sure you can make out look at the image and try to draw your own conclusions we can see the heart you can see the heart okay then in the first image you can see the the area that is near the AV node and we are catching the moment when the AV node had just fired and the colored part there has depolarized are you okay and now if you go on the on the lower traces there there we are trying to draw the relevant ECG so when this part of the SA node is excited and the current is spreading in the then you get this little rise in the P wave secondly when it spreads on the so what is the difference between the first diagram of the heart and second diagram of heart in the second diagram of heart the the wave of depolarization has spread over both the oracles simple both the oracles it is spread over both the oracles when it has spread now now it has spread over both the oracles at that moment if I look at the trace what do I find P wave what do I find P wave what do I find so P wave is essentially because the two oracles are depolarizing what is it are you getting the language what does P wave represent that really then as the as the action potential spreads over the bundle of phase and then it spreads over the the Purkinje fibers and it goes as far as the tip but it has not passed over the entire ventricles then it goes as far as the as to the from P it has gone to Q and then when the entire ventricles are depolarized you get what complex your is complex are you with me and then a little later a little later when the vent when both the ventricles see they have depolarized they have depolarized after a little while they will repolarize when they repolarize you get the T wave you get what you get T wave I will I will explain this in the let us take a look at so what have we learnt in last five minutes what have we learnt we have learnt a correlation between the cardiac cycle in which the oracles depolarize the ventricles depolarize a little later and the ventricles repolarize and

how this can translate into the ECG trace you can simply get by placing electrodes on the chest and getting the readings are you with me so far now you can ask a very simple question what about the auricular repolarization why do not I see it we do not see it we do not see it because we do not see it it is there but we do not see it because it is completely dominated by the depolarization of the ventricles it is the QRS complex is so strong that is it is somewhere in the QRS complex and we cannot delineate it. Now what is the most important use of ECG one of the very important uses is that if there is any cardiac arrhythmia the rate at which the SA node should keep on firing on its own if there is any problem or anywhere or there are the interval between the two firings is not good enough or instead of you see heart can go wrong in many ways if the instead of SA node the AV node starts firing at higher sequence so all kinds of different arrhythmias can happen and those arrhythmias can be detected with the help of ECG.

So what am I trying to tell you the great importance of ECG as a simple non-invasive tool to find out whether your heart is doing okay or not so you can please read about the different okay just a few examples you know if the yeah yes see the thing is we are not placing the electrode directly on the heart so actually it is not a 100% representation of the cycle through which the heart is going it is means you see the current is the current is going from many places and then it is coming filtered through a system and this is how it is represented so it is it is not just it is it is it is not just just the just the repolarization that is that is influencing many things are there okay and all this is the this is an output of all things put together okay but broadly it is report not we it is not possible for us to go into every for doing that you will have to place the electrode on the heart and then and then you will get the positive whatever in positive negative for that again you go to a cell and then you place an electrode there you will get a very clear correlation between the two if the heart starts beating very fast now I'm introducing I will introduce you to a few terms it's called as tachycardia what do you call it as tachycardia so if the the one at the top is a normal normal trace the below that one is you can see the the r-picks are are coming at higher frequency the top one is the normal this one is the tachycardia okay the lower than that is called as bradycardia means what the heart is the heart is slowed down okay and really interesting is on the right one okay the SA node SA node fires fires fires fails to fire what did I say there's a problem in the heart fails to fire and then therefore so so SA node SA should have fired fired their SA block what is author what is Gaitan trying to tell us there SA SA for some reason SA just didn't just didn't fire okay it doesn't mean it may fire the next time the next time it has not come on completely bad okay okay so so SA SA block is there okay so these are the these are just a few examples in which you can and there are many many examples in which you can okay I am in a rush so I want to okay okay okay we are done with the heart heart per se okay we will move on. you