Sheet

Number
12

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Gentlemen, let's shock the world!

As we have discussed in the previous sheet regarding to the sympathetic and parasympathetic nervous system:

*The pre-ganglionic neuron refers to the first neuron even if there were no ganglia as in the exception of the sympathetic nervous system.

**In previous lecture, we were introduced to the types of tissues that are innervated by sympathetic division, and how do divergence and convergence result in diffusion of the stimulation, while No diffused effects will happen by parasympathetic stimulation (they are limited to organs only)

***Sympathetic stimulation will affect the heart by increasing the heart rate, called Tachycardia.

**And here we go:**

In this lecture we are going to focus on **the effects of the parasympathetic stimulation** & then on **the molecular basis of the physiological actions of the ANS**.

But first let’s see parasympathetic effect on the following:

A- Gastrointestinal system:

Now, regarding to the parasympathetic nervous system, we have previously discussed that it doesn’t have any direct influence over vessels, yet it Does have an indirect effect, and this is due to secretory cells which when stimulated by parasympathetic; releases vasodilators which in turn cause vasodilatation of vessels and thus affecting the gastrointestinal tract and results in what we can call **vasodilatation** which will increase the blood flow towards the gastrointestinal tract. However, you should know that the **main system** which is under the parasympathetic innervations: is the gastrointestinal system. So these are the effects of the parasympathetic over the gastrointestinal tract.

B- Glands:

Let’s take a closer look at glands, and specifically about the gastrointestinal glands: like salivary glands, pancreas as a gland, other secretory cells, or glands within the mucosal or within the walls of the gastrointestinal tract, all these glands and their activities are controlled by the parasympathetic **except sweat glands they are not under control by the parasympathetic**.

C- Heart muscle:

In addition, we have effects over the heart as we have talked previously, the sympathetic can increase **heart rate**, and can increase the **force of contraction**.
**However,** the parasympathetic can only decrease the heart rate and has no effect over the ventricular muscle (which controls the force of the contraction); to reduce its force of contraction, so without reducing the force of contraction, only the heart rate can be reduced by the parasympathetic stimulation.

So, what is the physiology behind decreasing and increasing the heart rate?

As we have taken in previous classes, heart muscle undergoes slow De-Polarization process, but what if this process was slower. Nevertheless it may get slower through the parasympathetic effect, which will result in longer time to reach the threshold, but on the other hand, the sympathetic nervous system is increasing the rate of depolarization thus the heart rate becomes faster, and this happens by changing the permeability of either sodium or potassium:

1- Increasing the permeability of Na will result in fast heart rate which is affected by the sympathetic nervous system.

2- Decreasing the permeability of Na, leakage for example, will result in a slow heart rate, which is affected by the parasympathetic nervous system.

D- Eye pupil:
   Either myosis (constriction) or mydriasis (dilation) could occur, but what determines either ways:

Myosis: when there is a high intensity of light directed towards the pupil, the pupil becomes constricted in order to reduce the amount of light that pass through the retina.

Mydriasis: when the eye is under little amount of light, the pupil gets dilated in process called mydriasis, which will allow more amount of light to enter the eye.

Such movements happen daily, especially when you try to read you have to change the convexity of your pupil according to the distance, to adapt your eyes to the required distance.

E- The urinary bladder:
   The voiding of the urinary bladder is under both the voluntary & involuntary control.
Part two:

The molecular basis of physiological actions of ANS:

Now we are going to understand deeply how does each system work?

First, in the picture below we can easily notice the similarities which are:

1- In both sympathetic and parasympathetic divisions, the preganglionic fibers release Acetylcholine as neurotransmitters.
2- The Acetylcholine is acting on receptors called **Nicotinic receptors**; to generate action potential at the second neuron by activation of sodium channels.
** Why are they called nicotinic receptors?
Simply because nicotine can bind to and activate that receptor not only acetylcholine.

And now the differences arise:

a- In sympathetic division, the second neuron releases norepinephrine as a neurotransmitter. Which indeed do need receptors which are called **adrenergic receptors**

Exception: Fibers of the sympathetic system which are innervating sweat glands, they are releasing acetylcholine, so they are sympathetic but acting like parasympathetic.

b- In parasympathetic division, the second neuron as well as the first neuron do release acetylcholine as a neurotransmitter. However, these neurotransmitters DO need receptors, which are called muscarinic receptors.

**But what is muscarin?**

**Well, muscarin is what we can easily find in toxic mushroom.**

*So, let’s assume this situation:*

What do you expect to find on someone who ate toxic mushroom?

**Answer:** all of the parasympathetic effects will start to happen; as muscarin bind to its receptors, the parasympathetic system will be stimulated and thus it will affect the gastrointestinal movement, hyper salivation, tearing, nasal discharge, and his pupil will be constricted.

And the patient will also have sweating; although sweating is considered to be under the control of the sympathetic nervous system, yet it’s receptors are affected by acetylcholine (remember the exception) so we can notice sweating
over that patient.

Actually, we have several types of muscarinic receptors:

**Muscarinic Receptors (M1-M5):**
These receptors are divided into either excitatory or inhibitory receptors:

M2&M4: are *inhibitory* receptors.  
M1, M3&M5: are *excitatory* receptors.

**Inhibitory:**
- **M2 in the heart:** G protein $\rightarrow$ K+ channel $\rightarrow$ slow the rate of depolarization.
- Other inhibitory receptors:
  - Gi $\rightarrow$ reducing the activity of adenyl cyclase $\rightarrow$ reduce cAMP

**Excitatory Receptors: (M1, M3, M5)**
Found on *smooth muscle and glands* are coupled  
Gq protein $\rightarrow$ phospholipase C.

This enzyme increases production of inositol-1,4,5-trisphosphate (IP3), which will result in releasing calcium ions and thus having contracted muscles.  
** So we either have inhibition or excitation depending on the type of receptors we are having.

Let’s review what might happen to our patient after eating toxified mushroom:

*Stimulation of secretory activity:* salivation, tearing, sweating, nasal and bronchial secretion.
- *Increase gastrointestinal tract motility* $\rightarrow$ vomiting and diarrhea.
- *Contraction of urinary bladder* $\rightarrow$ urination.
- *Slowing of the heart* $\rightarrow$ Bradycardia
We can’t only stop these symptoms but also we can reverse these effects, simply by blocking those muscarinic receptors using **Atropine**.

**Blocking of Muscarinic Receptors by ATROPIN:**

Inhibition of glandular secretions: dry mouth, dry eyes, and dry nasal passages.
- Tachycardia. (Increase heart rate).
- Loss of pupillary light reflex.
- Loss of ability to focus the lens for near vision.

**Receptors and Signal transduction mechanisms:**

**Adrenergic receptors:** *these receptors respond to both epinephrine and norepinephrine.*

**Alpha receptors:** *divide into alpha1 & alpha2 receptors.*

**Alpha1:**

Which are surrounding the vessels and arterioles, and when stimulated it will result in constriction of the vessels through the usual mechanism:

Excitatory: PLC → IP3

**Alpha2:**

Located at the neuron terminals, and it has **inhibitory effect**, which will result in reducing the norepinephrine and thus having inhibitory effect.

**Alpha 2 Heteroreceptors:**

Are found over neurons that are not releasing norepinephrine, and also have an inhibitory effect.

Question:

If someone is playing football and then he was injured, does he feel pain at that time?

Answer:
No; because most of the axons that are transmitting pain sensation are releasing epinephrine, reducing transmission of pain during activity, and after relaxation, pain starts to be transmitted gradually.

**Beta receptors:**

- **Beta 1 ($\beta_1$) receptors:** found on heart

- **Beta 2 ($\beta_2$) receptors:** found on tracheal and bronchial smooth muscle, in the gastrointestinal tract, and on smooth muscles of blood vessels supplying skeletal muscles

  \[ \text{Gs} \rightarrow \text{Adenylyl cyclase} \rightarrow \text{increase cAMP} \]

**Patient with asthma suffers from constriction in his bronchioles, but what if he had a heart problem what would you give him?**

First of all, a patient with asthma needs epinephrine which binds to beta 2 receptors and results in bronchodilation.

Also, an asthmatic patient with tachycardia (increased heart rate). You can’t give him beta blockers (general beta blocker for all beta receptors) because that will result in lowering the heart rate but on the other side will cause bronchoconstriction. What to do?? **We give him a beta “1” blocker which will lower the heart rate without affecting bronchioles.**

Note: - the asthmatic patient must be given epinephrine to dilate the bronchioles; you have to be careful as they might have tachycardia. The epinephrine will result in even higher heart rate; because epinephrine will activate all beta and alpha receptors which include beta 1, so you have to be careful and watch his heart rate so it doesn’t reach dangerous levels.