(SECOND)

#9

Introduction to ANS

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**Introduction to Autonomic nervous system (ANS):**

Nervous system divided into: CNS & PNS

CNS>>>brain & spinal cord

PNS>>>efferent division & afferent division

PNS>>>"neurons located outside the brain and spinal cord"

- afferent division: sensory input from the viscera
- efferent division: reflex response>>ANS & somatic nerves

Somatic nerves: voluntary

ANS: involuntary>>1) sympathetic ("fight or flight")

2) Parasympathetic ("rest and digest")

3) Enteric ("GIT")
ANS:

* Autonomous mean Not under conscious control >> involuntary >> done without will or conscious control

There is some information from the text book:

Afferent >> bring information from PNS to CNS
Efferent >> carry signals from CNS to PNS
Somatic >> EX: contraction of the skeletal muscles
ANS >> visceral, vegetative, involuntary nervous system
ANS >> controlling, digestion, cardiac output
Enteric "brain of the gut" >> gut, pancreas, gallbladder

*FUNCTIONS OF ANS:

- Regulates involuntary visceral functions:
  Heart (cardiac output), SM, digestion, exocrine glands, Bladder and bowel action
  - Necessary to maintain life

* ANS Consists of:

Sympathetic system (Thoraco-lumbar) >> according to their origin (from T1 to L3)
Parasympathetic system (Cranio-sacral)
Enteric nervous system >> special to GI regulation

* Anatomy of ANS

ANS consists of:
Medullary centers (brain stem or spinal cord) → Preganglionic fiber → Ganglia → Postganglionic fibers → effector organ

*In sympathetic the nerves origin from the thoracic and lumber region (the origin connected with each other’s)
*In parasympathetic the nerves origin from the cranial and the sacrum (the origins far away from each other’s).

*origin of nerve > preganglionic>ganglia>postganglionic>>site of action (organ).

Preganglionic>>>before ganglia
postganglionic>>>after ganglia

*as we see the #preganglionic fibers in sympathetic are shorter than those in parasympathetic

As well as the #postganglionic fibers in sympathetic are longer than those in parasympathetic.

*the neurotransmitters: Chemical substance released from nerve ending, carries impulses across synapses >>Combines and stimulates receptors

*Main neurotransmitters in ANS are:
*Acetylcholine: on cholinergic receptors

*Noradrenaline (norepinephrine): on adrenergic receptors

*adrenaline (epinephrine)

*dopamine: on dopaminergic receptors

*Other neurotransmitters: Nonadrenergic Noncholinergic (NANC) as:

Neuropeptides, Substance P, VIP (vasoactive intestinal polypeptide)

Autonomic drugs:
Autonomic drugs: mimic or block actions of neurotransmitters

Modify functions of the ANS by stimulation or blockade

Have useful effects

In preganglionic the neurotransmitter is Ach in both sympathetic & parasympathetic

In postganglionic the neurotransmitter in parasympathetic is Ach whereas in sympathetic the neurotransmitters are epinephrine (adrenaline), norepinephrine (noradrenaline).

*the receptors that bind Ach are called #cholinergic receptors (divided into muscarinic & nicotinic)

*The receptors that bind adrenaline or noradrenaline are called #adrenergic receptors (divided into alpha (1&2), beta (1&2)).

*Locations of ganglia in sympathetic are close to spinal cord but in parasympathetic Locations of ganglia are in wall of end organs

Parasympathetic system (rest and digest):

Preganglionic fibers leave with cranial nerves (3rd oculomotor, 7th facial, 10th vagus nerves) & 3rd – 4th sacral spinal nerves

Ganglia in wall of end organs
From ganglia postganglionic fibers run to innervated tissues

Parasympathetic output discrete (individually separate and distinct) because postganglionic neurons aren't branched, but are directed to a specific organ

SO In parasympathetic there is no branching in the postganglionic fiber, that mean one nerve will go to certain organ and cause certain activity

The parasympathetic is dominant in rest and no risk >> that mean in normal cases the dominant is parasympathetic but in stress states the dominant is sympathetic

**Sympathetic system** *(fight or flight)* :

Preganglionic fibers leave CNS through thoracic and lumbar spinal nerves

Ganglia in the paravertebral chains

From ganglia, post-ganglionic fibers run to innervated tissues

Sympathetic outputs are diffuse because postganglionic neurons may innervate more than one organs

Because of branching of sympathetic post ganglia, the distribution is wide

SO in sympathetic is branches that mean certain nerve will affect many organs and will causes many affects

#you should see pictures in **slides 17** and you should know that:

*most of organs have both sympathetic and parasympathetic actions which are often oppose each other, or balance their actions.

**BUT** some organs have **only sympathetic** actions like:

Blood vessels, Adrenal medulla, kidney and genetelia in **female**

WHEREAS lacremlal glands only have parasympathetic action

**Enteric Nervous System (ENS):**

Collections of neurons in wall of the GIT

3rd division of the ANS

Includes:
Myenteric Auerbach plexus

Submucosal Meissner plexus

Regulates motor & secretory functions of GIT

**ENS contains:**

1) Cholinergic fibers

2) Adrenergic fibers

3) Nonadrenergic noncholinergic (NANC) neurons

NOW we will see every one of these types:

**NANC neurons** (nonadrenergic noncholinergic)  
(slide 21, minute 25)

they Motor & sensory neurons in autonomic target organs (gut, bronchi & bladder)

**Neurotransmitters:**

1) Neuropeptides  
2) Substance P  
3) VIP (vasoactive intestinal Peptide)

*Capsaicin (of chilli peppers) releases neurotransmitters from these neurons>>so it is agonist to these receptors (NANC) to facilitate the movement of the GIT.

**Cholinergic Transmission:**  
cholinergic = bind Ach

Acetylcholine is the neurotransmitter

Acts on cholinoreceptors present in:

- Autonomic ganglia (sympathetic & parasympathetic)>> all receptors in ganglia are cholinergic

- Postsynaptic fibers of **#parasympathetic** system

- Adrenal medulla

- NMJ endplates (neuromuscular junction)

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**Pathway of Acetylcholine**
SYNTHESIS:

\[ \text{Acetyl-co A} + \text{choline} \xrightarrow{(\text{CAT})} \text{Ach} \]

CAT: choline acetyltransferase

*Choline* is transported actively from cytoplasm into cholinergic nerve terminals

*Choline acetyltransferase* catalyzes the synthesis of Ach from Acetyl-coA + choline by ester bond between them

STORAGE:

After synthesis, Ach is protected from degradation by uptake it into storage vesicles

RELEASE:

*if there is an Action potential >> that mean there is a depolarization of nerve terminal so calcium will enter to the nerve terminals >> Increase intra-neuronal calcium causing Fusion of storage vesicles with membrane>> Expulsion & release of Ach into synaptic cleft (by exocytosis)

NOTE:

**release is blocked by botulinum toxins.**

**spider venom causes release of Ach.**

BINDING:

Ach binds to & activates cholinceptors On post-synaptic & pre-synaptic membrane Leading to various actions according to the organ

DEGRADATION:
*Ach* will rapidly (Very rapid) hydrolyzed by **Acetylcholinesterase** in the synaptic cleft into: acetate + choline.

*acetate* will be removed outside of the body by the urine whereas **choline** will be recycled (taken by neuron by cell barriers and spores).

**Cholinesterase**: in cholinergic synapses & RBC:

Specific for Ach (that mean it will affect only Ach because they recognize the ester bond between acetate &choline.)

**Pseudocholinesterase**: in plasma & liver:

Not specific for Ach (can bind other substances other than Ach)

**#RECYCLING:**

Recycling of choline back into neurons occurs to synthesis new Ach

**NOTE:**

****recycling inhibited by hemicholinium

**Inhibitors of Ach Pathway**

inhibit Of release:

Botulinum toxins: Botulism food poisoning ————— Respiratory paralysis

Some people use these toxins to eliminates wrinkles or paralyzes the facial muscles:
When a small amount of Botox is injected into a muscle, it blocks nerve signals that tell your muscles to contract. The effect is that it temporarily weakens or paralyzes the facial muscles and smooths or eliminates wrinkles in the skin for a few months.

**Inhibit Of binding of ACh**: Anti-cholinergic drugs

Now we will talk about Cholinoceptors in both their types Muscarinic and Nicotinic:

**Cholinoceptors**

Muscarinic receptors (bind muscarine)

Nicotinic receptors (*bind Nicotine*)
from the picture in slide 34 you should know that:

* muscarinic receptors have high affinity for muscarine and moderate affinity for Ach
* muscarinic receptors have low affinity for nicotine and will produce No effect.
* nicotinic receptors have high affinity for nicotine and moderate affinity for Ach
* nicotinic receptors have low affinity for muscarine and will produce No effect.

<table>
<thead>
<tr>
<th>Type</th>
<th>Location</th>
<th>action</th>
</tr>
</thead>
<tbody>
<tr>
<td>M₁</td>
<td>CNS</td>
<td>Excitatory</td>
</tr>
<tr>
<td>M₁</td>
<td>Parietal cells (in the wall of gastric or stomach)</td>
<td>Gastric secretion</td>
</tr>
<tr>
<td>M₂</td>
<td>Myocardium</td>
<td>reduce Rate, contractility, reduce CO(cadiac output) &gt; reduce the total blood volume that produced by contraction of the heart)</td>
</tr>
<tr>
<td>M₂</td>
<td>CNS</td>
<td>Inhibitory</td>
</tr>
<tr>
<td>M₃</td>
<td>Vascular SM(arteries &amp; veins)</td>
<td>Relaxation</td>
</tr>
<tr>
<td>M₃</td>
<td>Endothelium</td>
<td>Nitric oxide (EDRF)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>* Endothelium-derived relaxing factor (EDRF) is produced and released by the endothelium to promote smooth muscle relaxation</td>
</tr>
<tr>
<td>M₃</td>
<td>Circular M of iris</td>
<td>Miosis</td>
</tr>
<tr>
<td>M₃</td>
<td>Exocrine &amp; GIT</td>
<td>Increase secretions</td>
</tr>
<tr>
<td>M₃</td>
<td>GIT &amp; Bladder wall</td>
<td>contraction</td>
</tr>
<tr>
<td>M₃</td>
<td>GIT, Bladder sphincters</td>
<td>Relaxation</td>
</tr>
<tr>
<td>M₃</td>
<td>Bronchi</td>
<td>Bronchoconstriction(decrease the air of breathing)</td>
</tr>
<tr>
<td>M₄ &amp; M₅</td>
<td>CNS</td>
<td>Not well defined</td>
</tr>
<tr>
<td>Other muscarinic receptors</td>
<td>In corpora cavernosa of penis</td>
<td>Leading to erection through: Release of nitric oxide causing vasodilatation</td>
</tr>
</tbody>
</table>

|nicotonic receptors|
Adrenergic Drugs:

Neurotransmitters in adrenergic neurons are:

NA & dopamine

Sympathomimetics: >> sympatho=sympathetic.......mimetic=look like (substances produce the same activity of the normal sympathetic system= the same activity of adrenaline&noradrenaline)

"Mimic actions of sympathetic system"

Derivatives of phenylethylamine (chemical structure of all neurotransmitters in sympathetic :noradrenaline ,adrenaline,dopamine,serotonin)>all called catecholamine because they cotain catechol group which is benzene ring with two hydroxyl groups in ortho(o) position)

"Chemical modification results in various agents"

from the picture in slide 40 you should know that:

in preganglionic neurons there is the ganglionic transmitter Ach in both sympathetic and parasympathetic SO the receptors are nicotinic receptors on ganglia and on adrenal medulla.

the sympathetic innervations of adrenal medulla don't have postganglionic neurons ,instead, the adrenaline and noradrenalin released direct into blood and then affect the effector organ by binding to ADRENERGIC receptors .....see the table
Pathway of catecholamines in the body Binding:

Released NA binds with adrenoceptors:

post-synaptically & pre-synaptic

Termination of actions of NA (noradrenalene):

1) Reuptake 1 into nerve terminals (Main)
2) Reuptake 2 into post-synaptic membrane
3) Diffusion of NA into circulation
4) Enzymatic transformation by:

Monoamine oxidase (MAO):

In **mitochondria** of nerve terminals, intestinal mucosa & liver

Catechol-O-methyl transferase (COMT):

In **cytoplasm** of liver, lung, brain

# from picture in **slide 43** we should know:

1) synthesis of neurotransmitter:

hydroxylation of tyrosine is the rate limiting step
tyrosine in presence of sodium will be converted to Dopa which will converted into dopamine.

MAO is monoaminoxydase it oxidize dopa and dopamine and convert them to inactive metabolites so easily eliminated by urine

we protect Dopamine from this enzyme (MAO) by uptake into storage vesicles

**NOTE**: transport into the vesicles is inhibited by *reserpine*.

Dopamine will be converted to norepinephrine in vesicles.

**2) Release of neurotransmitter:**

Influx of calcium causes fusion of the vesicles with the membrane in a process known as exocytosis

**NOTE**: release is blocked by *guanethidine*.

**3) Binding to receptor:**

Postsynaptic receptor is activated by the binding of neurotransmitter.

**4) Removal of neurotransmitter:**

Released norepinephrine is rapidly taken into the neuron.

**NOTE**: reuptake is inhibited by SNRIs, cocaine and imipramine

**5) metabolism:**

norepinephrine is methylated by COMT and oxidized by MAO.

Locations & Functions of adrenoceptors in the body:

**Alpha-adrenoceptors (α-Receptors):**

Two main subtypes:
**α₁:** post-synaptic

<table>
<thead>
<tr>
<th>Location</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular SM</td>
<td>Vasoconstriction</td>
</tr>
<tr>
<td>Radial M. of iris</td>
<td>Mydriasis</td>
</tr>
<tr>
<td>Bladder sphincter</td>
<td>Contraction</td>
</tr>
<tr>
<td>Intestine sphincter</td>
<td>Contraction</td>
</tr>
<tr>
<td>Male sex organs</td>
<td>Ejaculation</td>
</tr>
<tr>
<td>Inhibits K entry into cells</td>
<td>Hyperkalemia</td>
</tr>
</tbody>
</table>

**α₂:**

Pre-synaptic (Nerve ending)

Post-synaptic in certain sites in platelets.

<table>
<thead>
<tr>
<th>Location</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presynaptic</td>
<td>Control NA release</td>
</tr>
<tr>
<td>CNS</td>
<td>-ve feedback inhibition</td>
</tr>
<tr>
<td>Islet cells pancreas</td>
<td>Inhibit insulin secretion</td>
</tr>
</tbody>
</table>

**β-adrenoceptors**

3 subtypes of β-adrenoceptors:

β₁ Heart: Increase rate, contractility

Increase automaticity & conductivity

β₁ kidney: Increase renin.

β₃-adrenoceptors:

Lipolysis → Post-synaptic in lipocytes
### **β₂-adrenoceptors**

<table>
<thead>
<tr>
<th>Location</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchi</td>
<td>Bronchodilatation</td>
</tr>
<tr>
<td>Bladder wall</td>
<td>Relaxation(slow)</td>
</tr>
<tr>
<td>Intestine wall</td>
<td>Relaxation(slow)</td>
</tr>
<tr>
<td>Skeletal M. arterioles</td>
<td>◆ slow peristalsis</td>
</tr>
<tr>
<td></td>
<td>◆ Skeletal M. arterioles</td>
</tr>
<tr>
<td></td>
<td>Vasodilatation</td>
</tr>
<tr>
<td>Glycogenolysis (breakdown of glycogen)</td>
<td>Increase blood glucose</td>
</tr>
<tr>
<td>Gluconeogenesis (synthesis of glucose)</td>
<td>Increase blood glucose</td>
</tr>
<tr>
<td>Uterus</td>
<td>Relaxation</td>
</tr>
<tr>
<td>Skeletal muscles</td>
<td>Skeletal muscles</td>
</tr>
<tr>
<td>Mast cells</td>
<td>◆ Inhibits autacoid release</td>
</tr>
<tr>
<td></td>
<td>◆ increase K entry into cells</td>
</tr>
<tr>
<td></td>
<td>Hypokalemia</td>
</tr>
</tbody>
</table>

**_ascii_art**

فأُخبركم بأنه الطَّبَ داري ***وقلب الناس قد أضحى مكاني**

موقفين جميعاً بإذن الله الفتاح