Pharmacology

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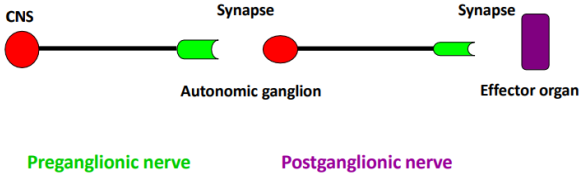
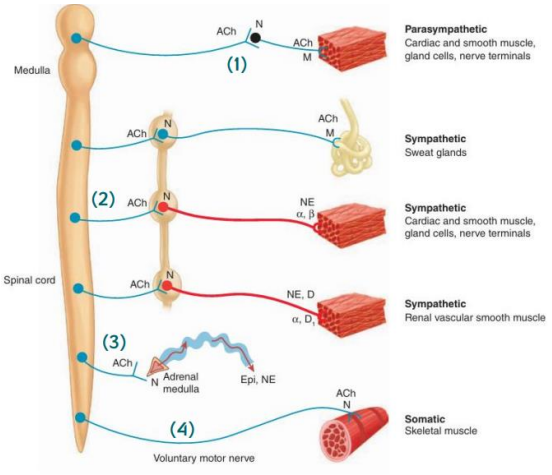
Autonomic Pharmacology

- The autonomic nervous system activities are NOT under direct conscious control (*Involuntary*)
- It is concerned with *visceral functions* such as cardiac output, blood flow and digestion
- It consists of 2 major divisions:
  - **Sympathetic** (***thoracolumbar***)
  - **Parasympathetic** (***craniosacral***)
- Both divisions originate in ***nuclei*** within the central nervous system, giving rise to *preganglionic efferent* fibers that exit from brain stem or spinal cord and terminate in autonomic ganglia



- From the autonomic ***ganglia***, *postganglionic* fibers run to the tissues involved
- Parasympathetic System
  - The preganglionic neuron releases acetylcholine (ACh) at nicotinic (N) receptors in the ganglion
  - The postganglionic neuron releases ACh at muscarinic (M) receptors to target cardiac and smooth muscle, gland cells, and nerve terminals



- Sympathetic System
  - Preganglionic releases ACh at N receptors in ganglia
  - Postganglionic neurons release:
    1. **Norepinephrine (NE)** at alpha (α) and beta (β) receptors to affect cardiac and smooth muscle, gland cells, and nerve terminals
    2. ACh at M receptors for sweat glands
    3. **Norepinephrine and dopamine** (D) at α and dopamine (D1) receptors for ***renal vascular*** smooth muscle
  - **Adrenal Medulla** functions as a modified sympathetic ganglion that releases epinephrine (Epi) much more than norepinephrine (NE) directly into the **bloodstream**
- Somatic Motor System consists of a single motor neuron release ACh at N receptors to activate skeletal muscle under voluntary control
- Neurons of the ANS release neurotransmitters into the synapse, which carry information to/or activate the next cells, which can be:
  - Co-transmitters which are chemicals released by most ANS fibers
  - Acetylcholine and the nerves that release it are called **cholinergic**, which include:
    - ✓ All autonomic ***preganglionic*** fibers
    - ✓ ***Most parasympathetic*** postganglionic fibers
    - ✓ Few sympathetic postganglionic fibers (***sweat gland***)

- Norepinephrine (noradrenaline) and the nerves that release it are called **adrenergic**, which includes:
  - ***Most sympathetic*** postganglionic fibers
  - Some sympathetic postganglionic fiber release ***dopamine***
  - Adrenal medulla releases epinephrine and norepinephrine

Adrenergic fibers releases norepinephrine more than epinephrine

- Neurotransmitters have many features that represent potential targets for pharmaceutical agents
  - **Synthesis** of neurotransmitters occurs in the neuron
    - Choline acetyltransferase (ChAT) synthesizes Ach from choline and acetyl CoA in the neuron
    - Choline is uptaken into the neuron by cotransport with Na^+ via choline transporter (ChT)
  - NTs are **stored** in the synaptic vesicles in the presynaptic terminals
    - Ach is loaded into the vesicle by vesicle associated transporter (VAT) which is an exchanger (counter transporter) with proton
    - Vesicles Co-store neurotransmitters with ***ATP*** and ***peptides***
  - NTs are **released** by *calcium-mediated exocytosis*
    - When the action potential reaches the axon terminals, calcium channels open which ***triggers the fusion*** between the vesicle membrane with the presynaptic membrane
    - All the contents inside the vesicle are released (ATP, peptides, NTs)
  - NTs diffuse through synaptic cleft then act on post-synaptic **receptor** proteins to produce a response
  - After producing the needed effect, NT activity is **terminated**
    - Acetylcholinesterase (AchE) ***breaks*** Ach down into choline and acetate which are reabsorbed into the presynaptic neuron by ChT to be recycled
    - ***Negative feedback:*** **auto**-receptors on the presynaptic terminals cause reduction in NT release

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