Autonomic Nervous System

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Peripheral Nervous System

A. Sensory – Somatic Nervous System

B. Autonomic Nervous System
   1. Sympathetic Nervous System
   2. Parasympathetic Nervous System
   3. Enteric Nervous System
I. Peripheral Nervous System
A. Sensory – Somatic N.S.
   1. sensory (afferent) and motor (efferent)
   2. nerve fibers project to SKELETAL MUSCLE
   3. VOLUNTARY FUNCTIONS
B. Autonomic Nervous System

1. sensory (afferent) and motor (efferent)
2. Nerve fibers project to smooth muscle, cardiac muscle, and endocrine glands
3. INVOLUNTARY FUNCTIONS
Autonomic Nervous System

• Involuntary system
• Concerned with visceral functions
• Target is body’s smooth muscle, glands, cardiac muscle
• Cell bodies lie in ganglia outside the CNS
• Efferent Motor Output
• All preganglionic neurons utilize acetylcholine as a neurotransmitter; postganglionic neurons vary.
Autonomic Nervous System

- ANS can be divided based on anatomic and functional grounds into two portions:
  1. Parasympathetic (craniosacral)-ganglia are found near target organs
     Neurotransmitter: acetylcholine
  2. Sympathetic (thoracolumbar)-cell bodies lie in chains of ganglia on either side of spinal cord
     Neurotransmitter: norepinephrine
Parasympathetic System

• Preganglionic fibers originate from the brainstem and sacral region of the spinal cord.

• Travel outward in the cranial or sacral nerves to ganglia located near or within various viscera.

• Short postganglionic fibers continue from the ganglia to specific muscles or glands within the viscera.

• Pre- and postganglionic fibers utilize acetylcholine as their neurotransmitter.
Cranial Parasympathetics:

- Preganglionic fibers originate in brainstem and travel with one of four cranial nerves (III; VII; IX; X)

- Preganglionic fibers terminate on postganglionic cell bodies in ganglia close to target tissue: ciliary, pterygopalatine, otic, submandibular.
Structures innervated by cranial parasympathetics include:

- Head: ciliary body, sphincter, lacrimal glands, salivary glands, nasal & palatine glands

- All viscera in the thorax

- Viscera of abdominal cavity except the terminal one-third of large intestine
Sacral Parasympathetics

- Preganglionic fibers originate from neurons in lateral gray horn of sacral spinal cord.
- Preganglionic fibers exit spinal cord via ventral roots of spinal nerves to form pelvic splanchnic nerves.
- Structures innervated:
  - Terminal one-third of large intestine
  - Urinary bladder
  - Genitalia
Sympathetic System

• Preganglionic fibers originate from neurons in the gray matter of the spinal cord.
• Second order neurons leave the cord through the ventral roots of spinal nerves from T1 to L2 and enter one of the paravertebral ganglia.
• After synapsing with second order neurons, postganglionic fibers leave the ganglia to travel to the visceral effector.
• Postganglionic fibers primarily utilize norepinephrine as their neurotransmitter.
In the sympathetic chain, preganglionic fibers may:

- Synapse with postganglionic fibers at the level of entry
- Ascend or descend in the chain to synapse with neurons in ganglia at the cervical or sacral level
- Pass through the sympathetic chain without synapsing (splanchnic nerves)
- Go directly to the adrenal gland without synapsing in a ganglion
In The EYE
Sympathetic and/or parasympathetic systems innervate:

- Intrinsic muscles of the eye (ciliary muscle, dilator, and sphincter pupillae)
- Vascular smooth muscle
- Some smooth muscles of eyelid (tarsal muscles)
- Glands (lacrimal gland)
Oculosympathetic Innervation

- Dilator muscle of the iris
- Choroidal arterioles (smooth muscle)
- Tarsal muscles (Müller)
- Sweat glands
Parasympathetic Innervation to the Eye

- Sphincter Pupillae
- Ciliary muscles (involved in accommodation)
- Lacrimal gland
- Tarsal muscle (sympathetic portion)
- Choroidal vasculature
- Ophthalmic artery and branches
Direct and Consensual Light Reflex

- **Afferent Signal**
  - Retinal Ganglion Cells
  - Optic Nerve
  - Optic Chiasm
  - Optic Tract
  - Synapse in Pretectal Nucleus
  - Project to both sides of Edinger-Westphal Nucleus

- **Efferent Signal**
  - Preganglionic fibers synapse in ciliary ganglion
  - Postganglionic fibers travel in short ciliary nerves to sphincter pupillae
Neurotransmitter Chemistry

Cholinergic Transmission:

• Neurons that utilize acetylcholine are said to be cholinergic

• Remember, all preganglionic ANS neurons use acetylcholine as the neurotransmitter (parasymp. and symp.)

• Postganglionic parasympathetic neurons use acetylcholine
Synthesis of Acetylcholine

- Acetylcholine (Ach) is synthesized in the cytoplasm from acetyl CoA and choline in a reaction catalyzed by choline acetyltransferase (ChAT).
- Acetyl CoA is synthesized in mitochondria.
- Choline is transported across the cell membrane by a sodium dependent membrane carrier.
Storage of Acetylcholine

- Once synthesized, ACh is transported from the cytoplasm into vesicles by an antiporter embedded in the vesicle membrane.
- ATP and peptides are also stored in vesicles.
Release of Acetylcholine

- AP reaches the terminal activating a voltage sensitive Ca\(^{2+}\) channel triggering an influx of extracellular Ca\(^{2+}\).
- The resulting increase in intracellular Ca\(^{2+}\) causes fusion of the vesicles with the surface membrane.
- Once vesicles fuse, there is an exocytotic expulsion of ACh and cotransmitters into junctional cleft.
Action of Acetylcholine

• After release from presynaptic terminal, ACh binds to and activates ACh receptors on the postsynaptic membrane (cholinoreceptors).

• ACh must then be cleared from the synaptic cleft to allow another round of synaptic transmission.
Termination of Acetylcholine

- Catabolism: Released ACh is degraded by acetylcholinesterase (AChE), a degradative enzyme secreted in the cleft.
- AChE hydrolyzes ACh into choline and acetic acid thus terminating the action.
- Choline is taken back up into the presynaptic axon to be reused for ACh synthesis.
Adrenergic Transmission

Tyrosine—amino acid precursor to three different amine neurotransmitters with a catechol structure:

1. Dopamine
2. Norepinephrine
3. Epinephrine

- Neurons that use any of these neurotransmitters are called adrenergic.
• Tyrosine is converted to Dopa by tyrosine hydroxylase
  - Rate limiting step

• Dopa is converted to dopamine by dopa decarboxylase

• Dopamine is converted to norepinephrine by dopamine $\beta$-hydroxylase

• Norepinephrine is converted to epinephrine by phentolamine N-methyltransferase (PNMT)
• Tyrosine is transported into the nerve by a sodium-dependent carrier.
• Tyrosine is converted to dopa
• Dopa is converted to dopamine
• Dopamine is converted to norepinephrine
• AP opens voltage sensitive Ca^{2+} channels, causing fusion of vesicles to membrane and release of NE, cotransmitters and dopamine β-hydroxylase
• NE activates receptors on postsynaptic neurons
• Reuptake or Uptake 1: NT is taken up into nerve terminal and stored in vesicles for reuse
• Catabolism by MAO
• Diffusion
• Uptake 2: transport to postjunctional cell where it is metabolized by COMT
Neurotransmitter Receptors

• NT released into synaptic cleft bind to specific receptors on postsynaptic membrane
• Binding is like inserting key into lock causing conformational change in protein
• Two general categories:
  1. Ligand-Gated Ion Channels
  2. G-Coupled Receptors
Ligand-Gated Ion Channels

- Ex. Nicotinic ACh receptor in skeletal muscle
- Membrane spanning proteins embedded in plasma membrane
- Five subunits form a pore
- Four different polypeptides make up subunits: $\alpha$, $\beta$, $\gamma$, $\delta$
- Complete channel made up of 2 $\alpha$ units and one each of $\beta$, $\gamma$, and $\delta$
• One binding site on each a subunit and ACh must bind simultaneously to each site for channel to open.

• When no NT is present, pore remains closed and impermeable to ions.

• When NT is present and binds, induces conformational change in the receptor causing pore to open and allow flow of ions.

• Lesser degree of ion specificity than voltage-gated channels.
• Influx of Na\(^+\) causes postsynaptic neuron to depolarize from the resting potential toward the threshold for generating an AP.

• If ligand-gated channel is permeable to Cl\(^-\), then net effect will be to hyperpolarize the postsynaptic cell from the resting potential
G-Protein Coupled Receptors

- Guanosine triphosphate (GTP) binding proteins

- Provide slower, longer lasting, and more diverse postsynaptic reaction
• Activation of G-Protein Coupled Receptors involve three steps:

1. NT molecules bind to cell surface receptors.

2. Receptor proteins activate G-proteins located on the cytoplasmic face of postsynaptic membrane.

3. G-proteins then change the activities of an effector element, usually an enzyme or ion channel.
• Many types of G-proteins:
  Ex. $G_s$: stimulates adenylyl cyclase which in turn converts ATP to cAMP
  $G_i$: inhibits adenylyl cyclase to decrease $[\text{cAMP}]_i$

• Can initiate extensive metabolic effects: referred to as metabotropic receptors.
Cholinergic Receptors

- One NT may bind to several types of receptors referred to as receptor subtypes:
  - Ex: ACh binds to receptors in heart to slow heart rate and in skeletal muscle to cause muscle contraction. Because ACh binds to these receptors, they are called cholinergic receptors.
Other drugs may bind to cholinergic receptors but may have different effects on the heart and skeletal muscle.

Ex: Nicotine is a receptor agonist in skeletal muscle but has no effect in the heart.

Muscarine has no effect on skeletal muscle but is a cholinergic agonist in the heart.

Thus, ACh receptor subtypes can be distinguished by different drug actions.
• These agonists gave the subtypes their names: Nicotinic and Muscarinic Receptors

• To date, five distinct muscarinic G-protein coupled receptors have been pharmacologically identified (M1-M5).
Adrenergic Receptors

- Determination of adrenergic receptor subtypes occurred when it was revealed that epinephrine was more effective than norepinephrine for stimulation of smooth muscle in the vasculature, uterus, and dilator pupillae.

- Proposed that two types existed: $\alpha$ and $\beta$
  - $\alpha$: now $\alpha_1$ and $\alpha_2$
  - $\beta$: now $\beta_1$ and $\beta_2$
Why Do We Need to Know about the Autonomic Nervous System?

- Horner’s Syndrome:
  - Sympathetic Lesion—may lie in (1) CNS, (2) preganglionic or (3) postganglionic
  - Signs: Ptosis, miosis, anhydrosis
  - Causes:
    - Lesions in brain stem or spinal cord
      - Due to Multiple Sclerosis or Vertebral Artery Dissection
    - 2nd Order Neuron
      - Tumors of lung or breast
      - Trauma (including surgery)
      - Epidural anesthetic
    - Postganglionic neuron—
      - Carotid Artery Dissection
      - Tumors and inflammation of the neck
      - Neck Trauma