

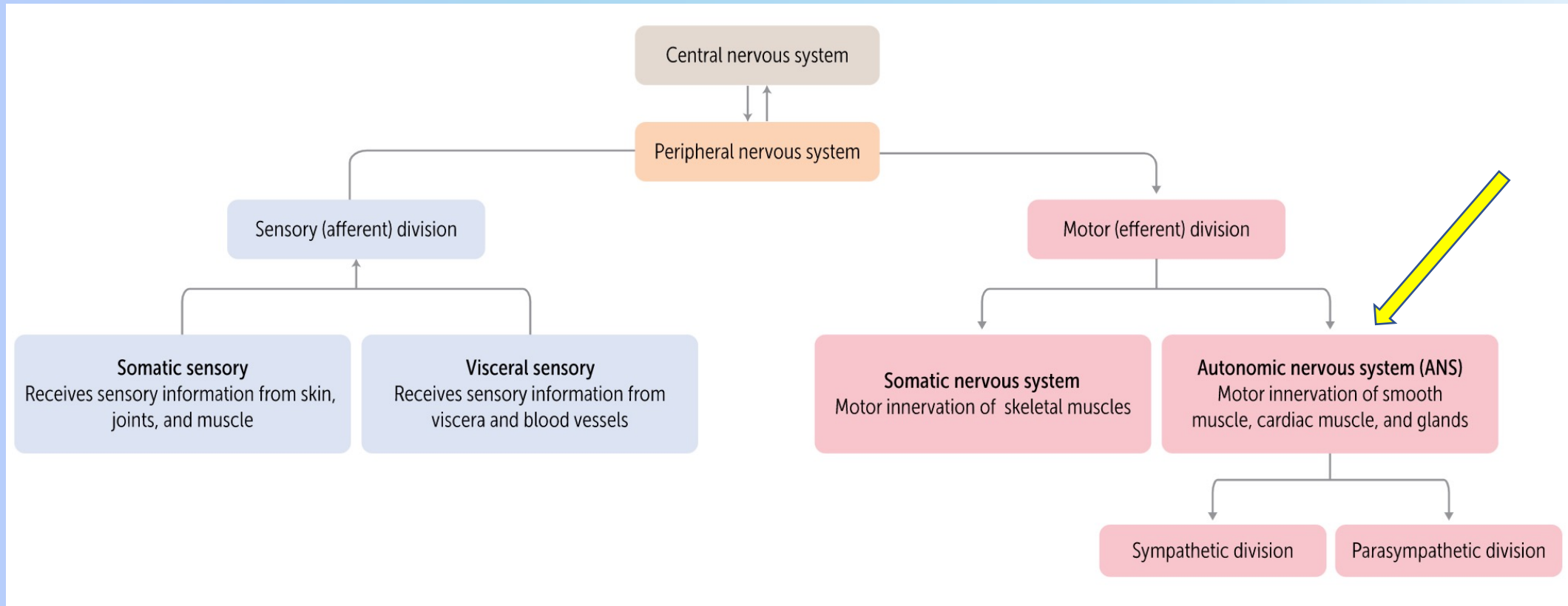
Autonomic Nervous System

L.D. Lord

Table of Contents

- Basic organization & functions
- ANS anatomy
- Neurotransmission
- Adrenergic receptors & autonomic effects in end-organs
- Basic ANS pharmacology
- Pupillary light reflex
- Wooclap!

Basic ANS organization & function (i)



Basic ANS organization & function (ii)

- **Sympathetic division** prepares the body for action
- **Parasympathetic division** supports rest, recovery, digestion (i.e. "maintenance functions")
- Sympathetic & parasympathetic divisions **oppose each other**

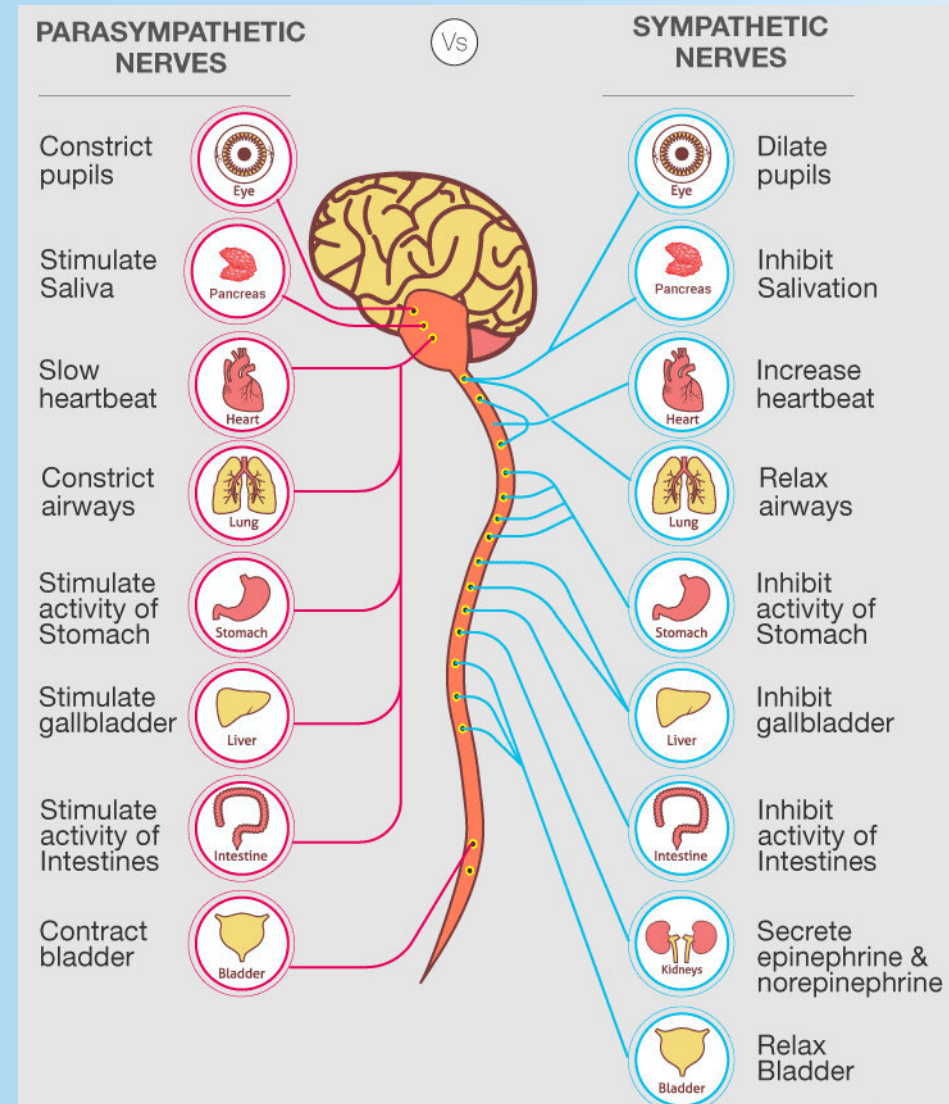
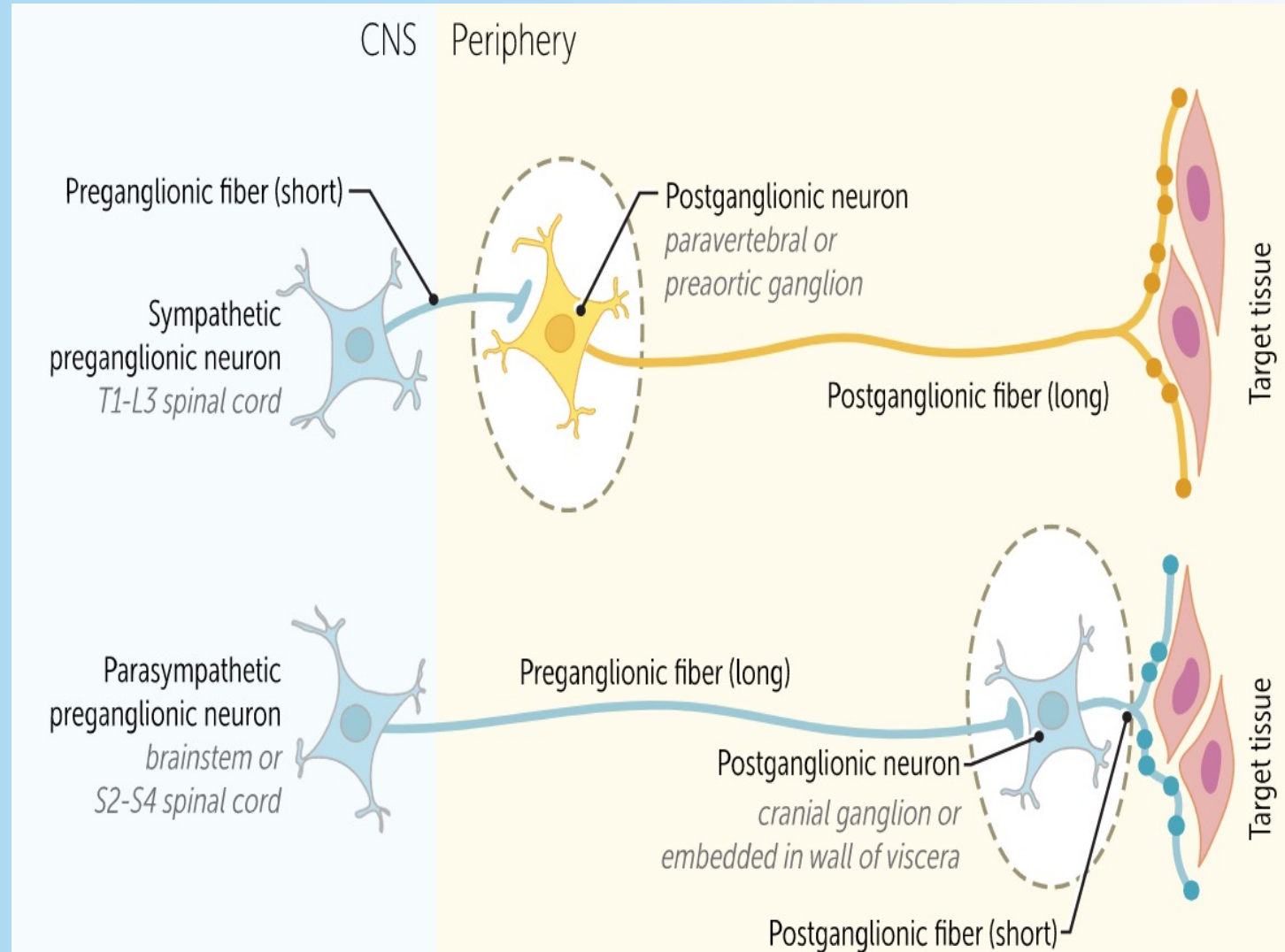


Table of Contents

- ~~Basic organization & functions~~
- ANS anatomy
- Neurotransmission
- Adrenergic receptors & autonomic effects in end-organs
- Basic ANS pharmacology
- Clinical correlations
- Wooclap!

General terminology

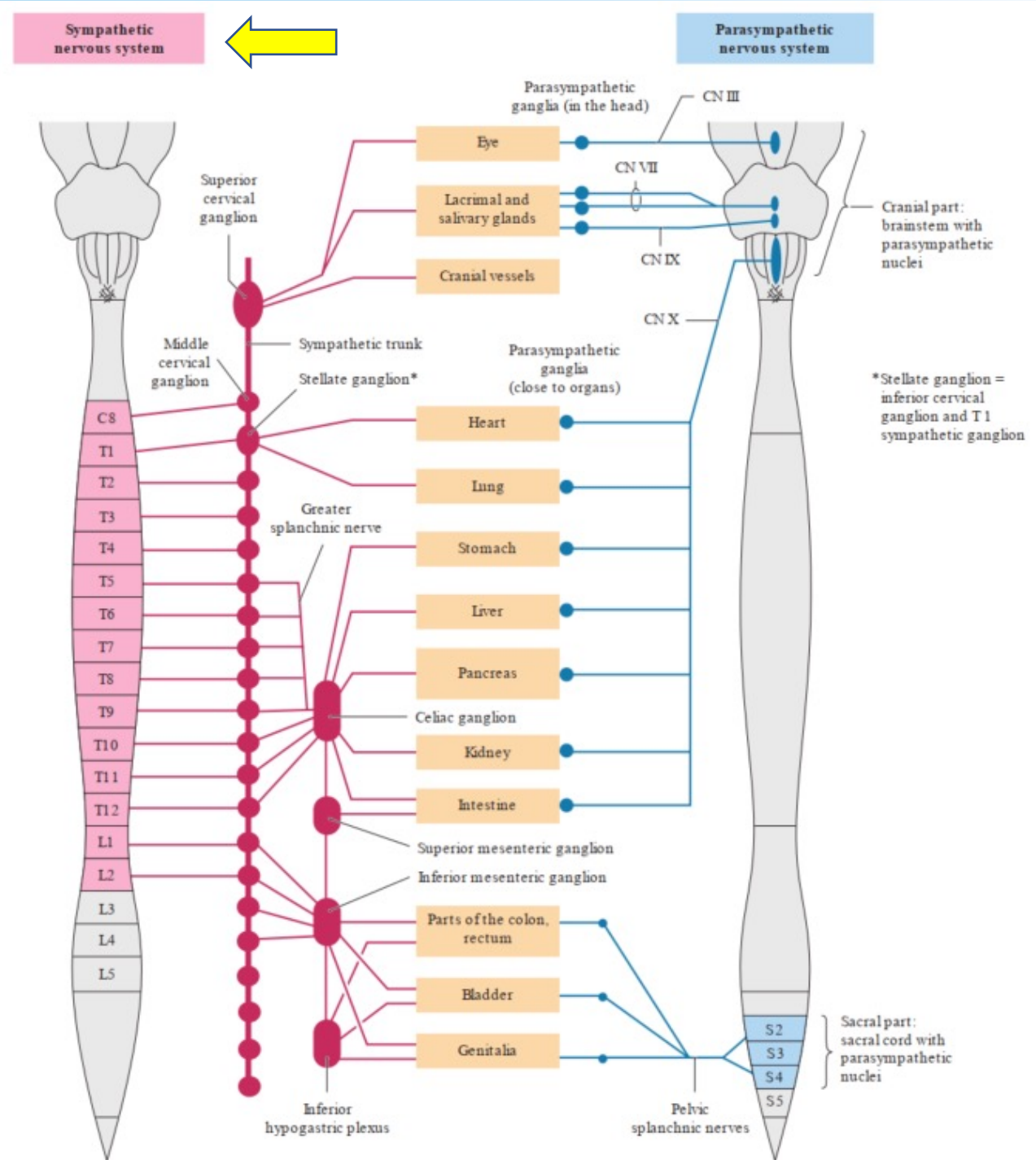
- Both branches of **ANS** use a **two-neuron connection** to transmit a signal from CNS to target organ!
- First neuron = “**pre-ganglionic neuron**” (found in CNS i.e. brain stem or spinal cord)
- Second neuron = “**post-ganglionic neuron**” (usually found in periphery) innervates the target organ



Note the relative axon lengths for sympathetic vs parasympathetic pre- and post-ganglionic neurons!

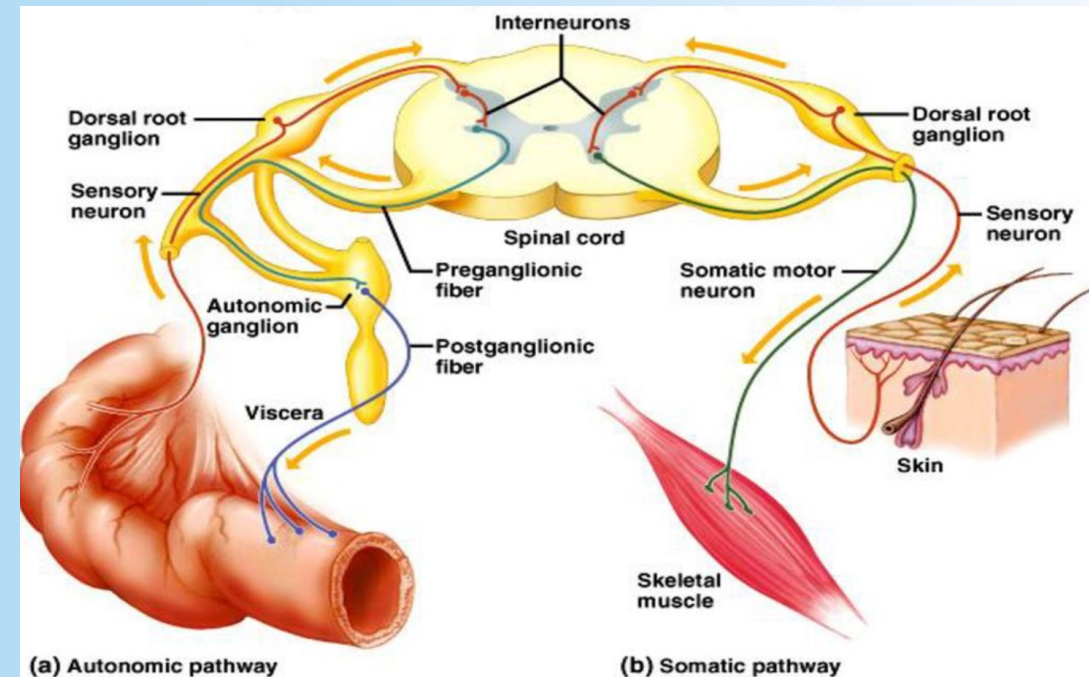
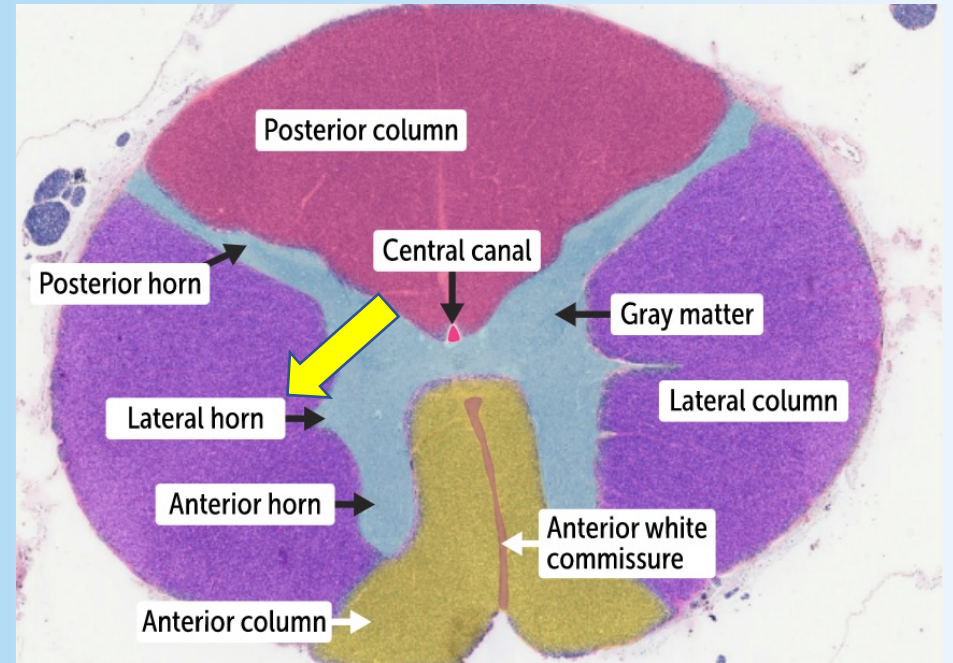
Sympathetic NS

- Cell bodies of pre-ganglionic neurons are found in **thoraco-lumbar spinal cord**
- Cell bodies of post-ganglionic neurons are found in the **sympathetic chain** (aka paravertebral chain) & **preaortic ganglia**
- Post-ganglionic neurons innervate **target tissues**



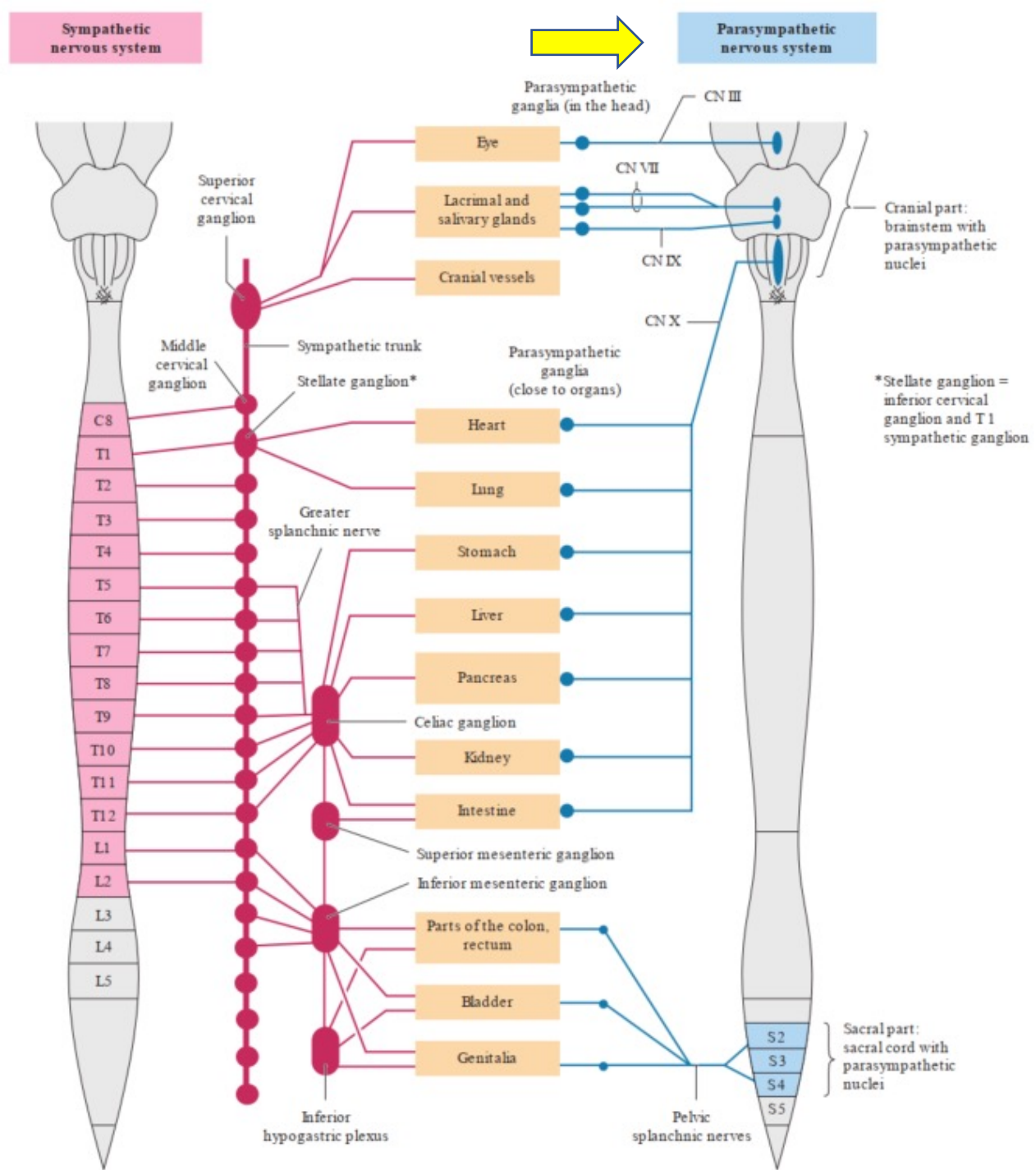
Sympathetic NS

- Cell bodies of **pre-ganglionic sympathetic neurons** are found in **lateral horn** of spinal cord
- Axons of **pre-ganglionic sympathetic neurons** exit the **ventral root** of spinal cord (alongside somatic motor fibers)
- reach the autonomic ganglia of **sympathetic chain** via the white ramus communicans
- the (long) **post-ganglionic neuron** innervates its target organ



Parasympathetic NS

- Cell bodies of pre-ganglionic neurons are in **parts of the brainstem** (i.e. CN III, VII, IX, X) & **sacral part of spinal cord**
- “Cranio-sacral” distribution
- Cell bodies of post-ganglionic neurons are in **cranial ganglia** & ganglia embedded in the **walls of target organs**



Parasympathetic NS

- **Cranial nerves with parasympathetic functions** innervate autonomic ganglia of the head (**CN's III, VII, IX**) or autonomic ganglia near their target organs (**CN X**)
- Post-ganglionic fibers then innervate their target organs

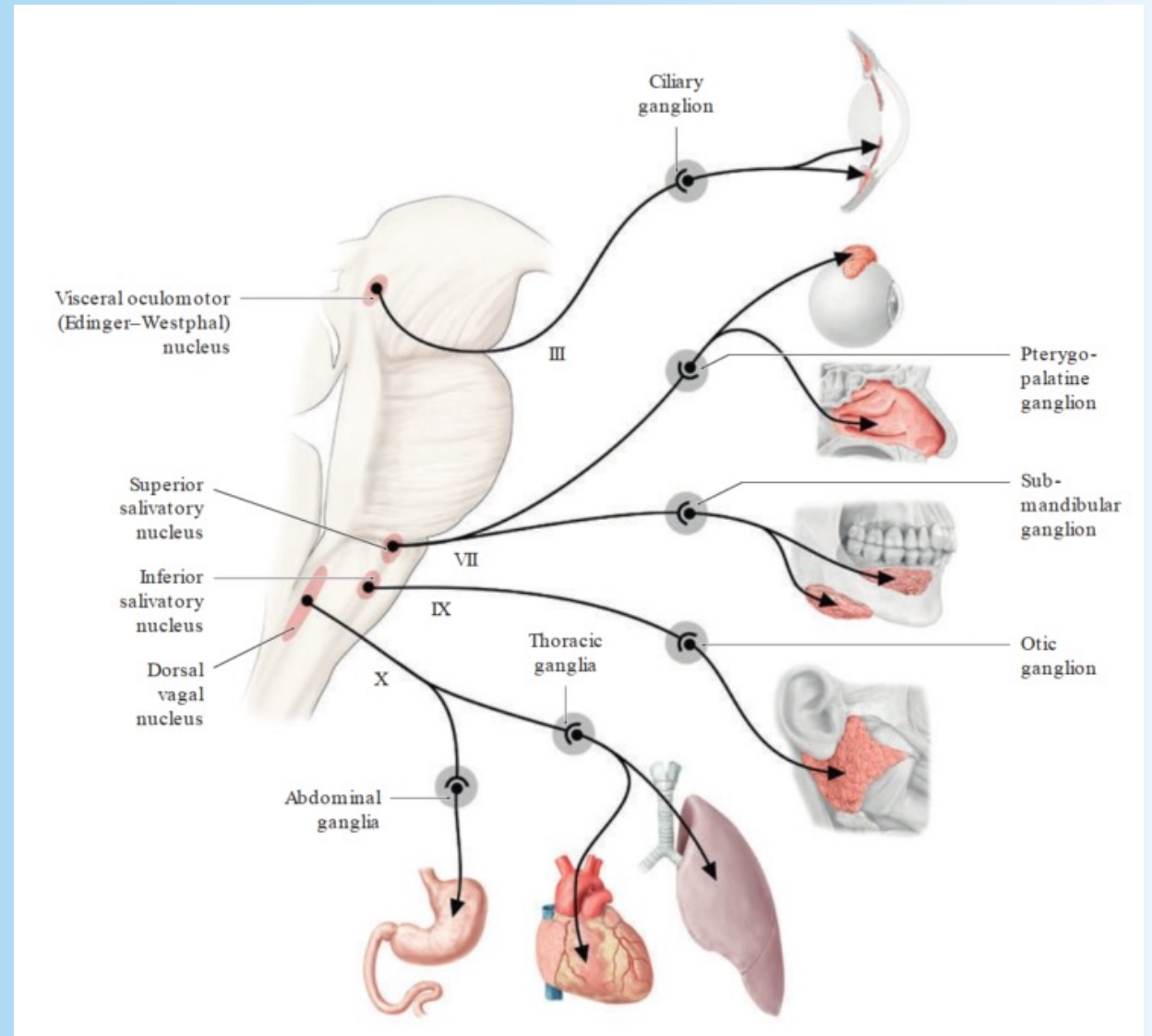
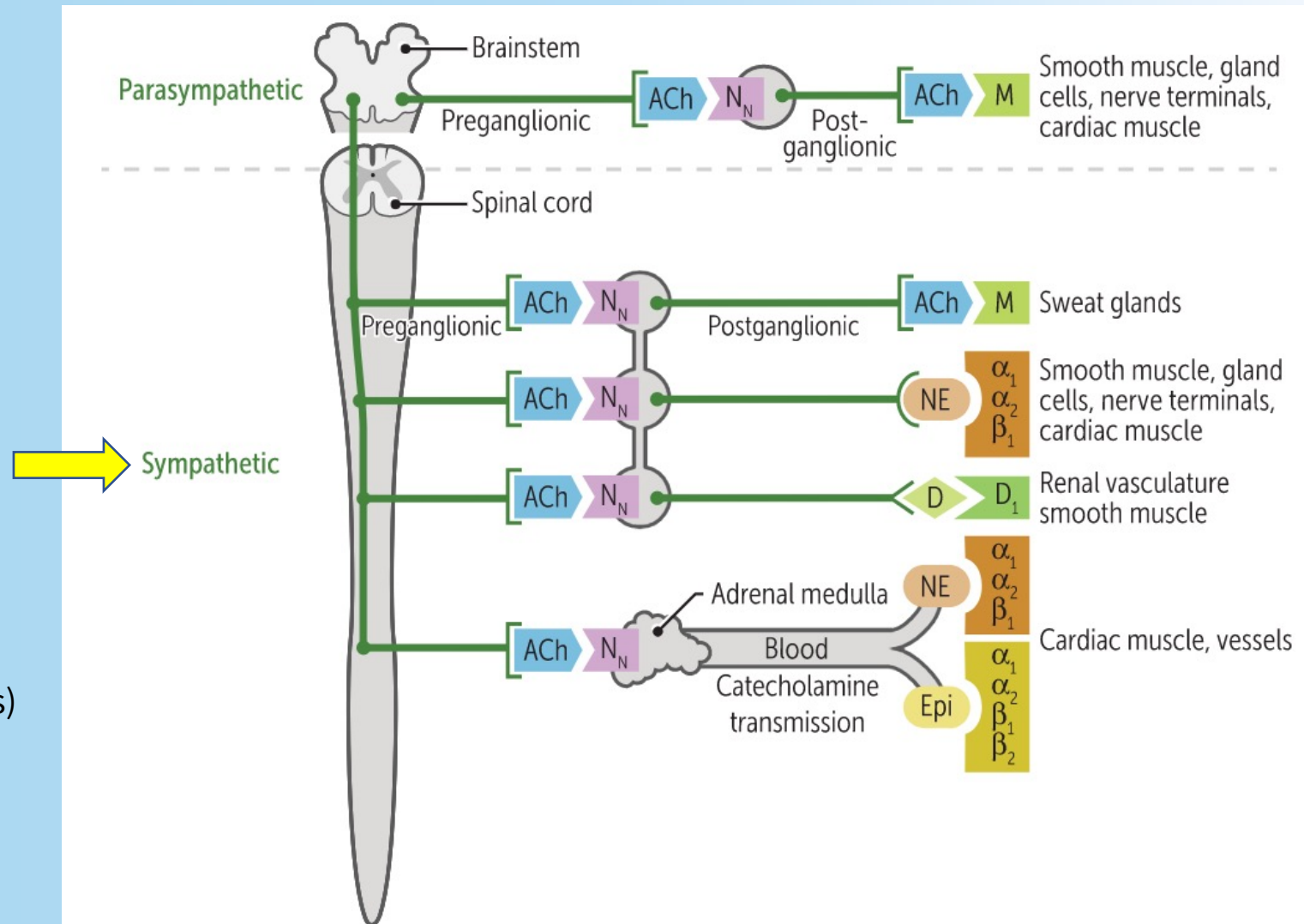


Table of Contents

- ~~Basic organization & functions~~
- ~~ANS anatomy~~
- Neurotransmission
- Adrenergic receptors & autonomic effects in end-organs
- Basic ANS pharmacology
- Pupillary light reflex
- Wooclap!

Neurotransmission: Sympathetic NS (i)

- First synapse:
 - **ACh** from pre-ganglionic neuron binds to **nicotinic receptor** on post-ganglionic neuron \rightarrow Na^+ influx
- Second synapse:
- **NE** from post-ganglionic neuron binds **adrenergic receptor*** in target organ
- * $\alpha_1, \alpha_2, \beta_1, \beta_2$ (G-protein coupled receptors)

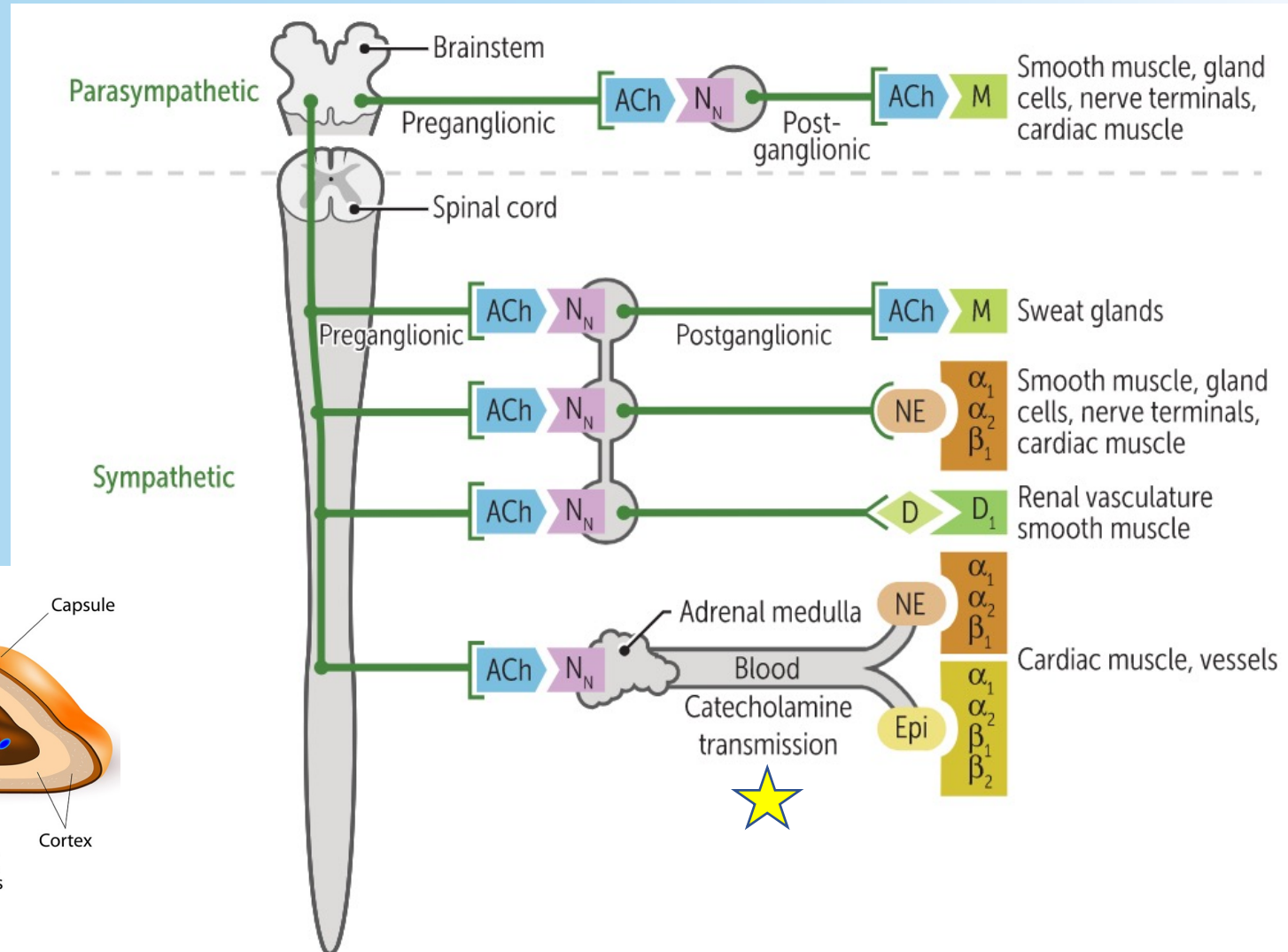
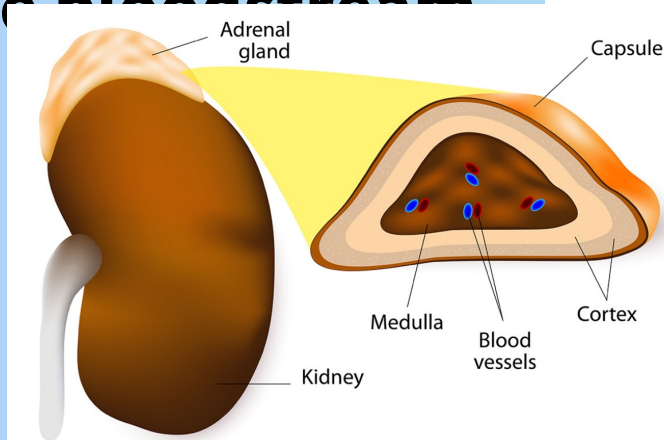


Neurotransmission: Sympathetic NS (ii)

- Adrenal medulla:

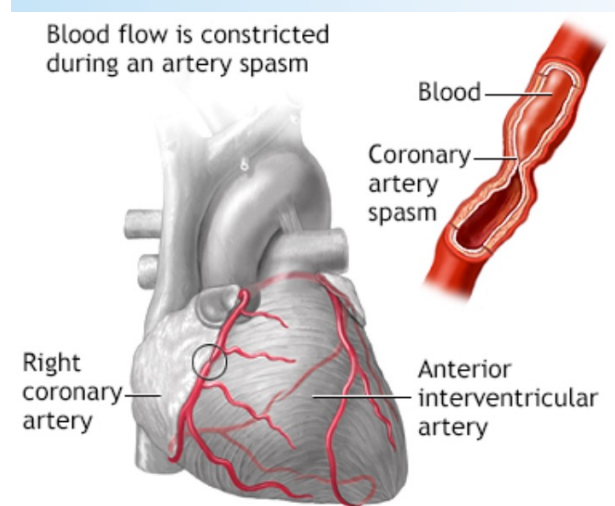
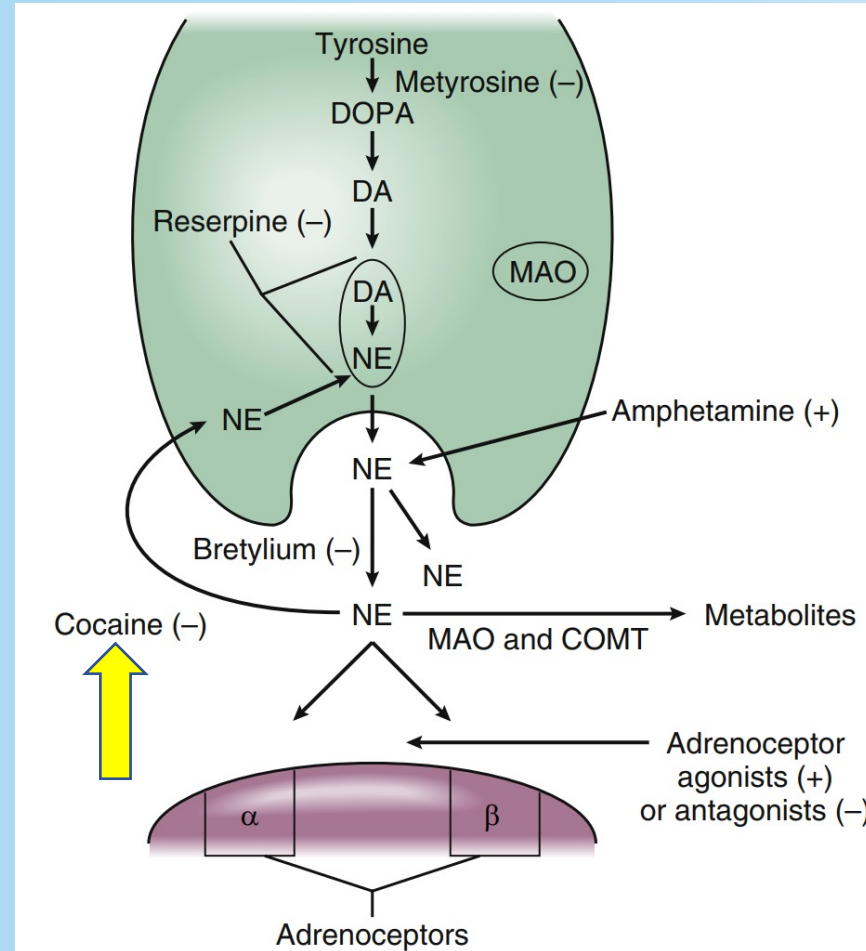
- **ACh** from pre-ganglionic neuron binds to **nicotinic receptor** in **adrenal medulla**

- Stimulates the **release of epinephrine & norepinephrine** from adrenal glands **into the bloodstream**



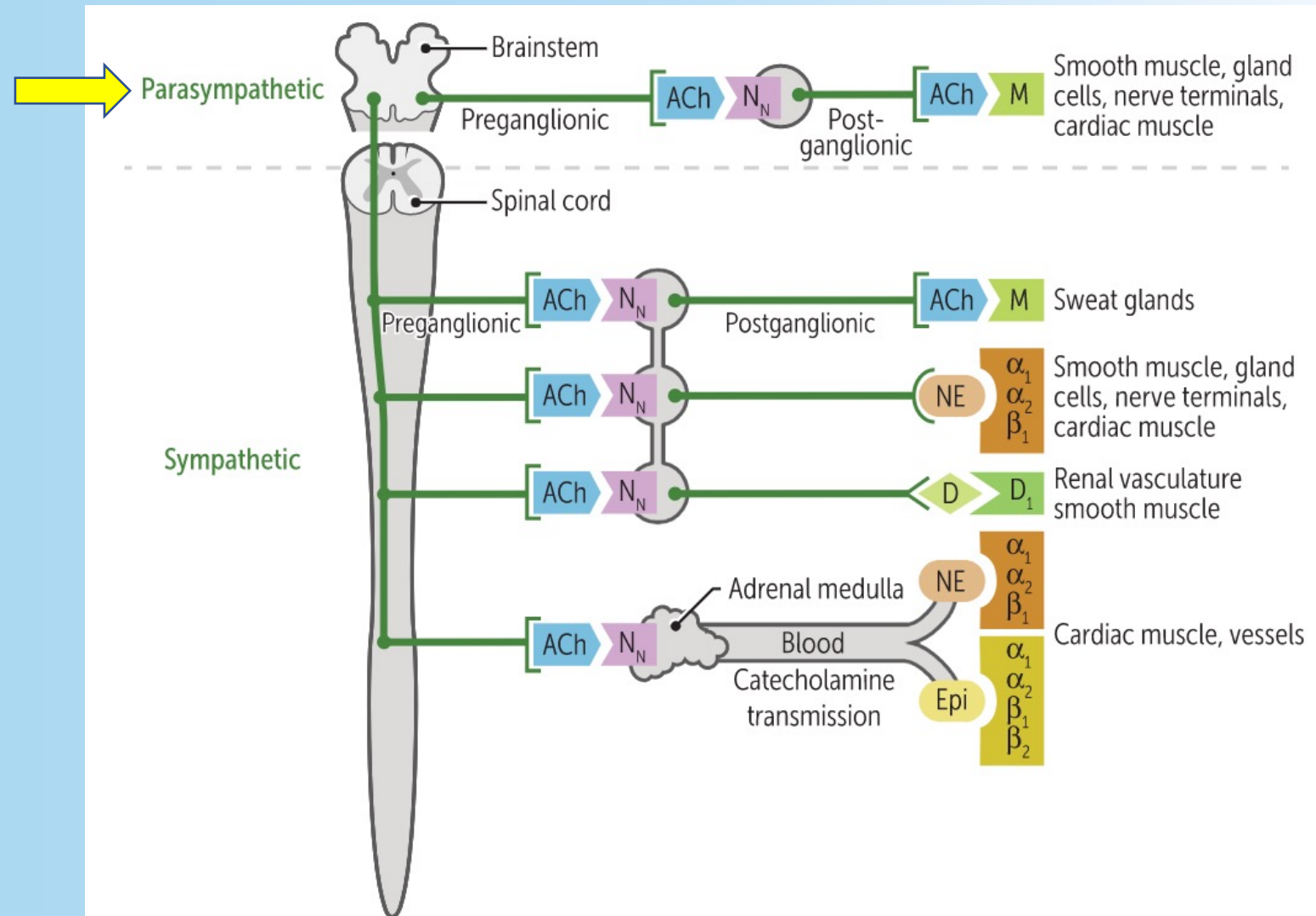
Sympathetic Neurotransmission: Cocaine

- **Blocks monoamine reuptake** by several membrane transporters (DAT, SERT, **NET**)
- NET blockade **increases NE levels** → overstimulation of adrenergic receptors (α_1 , α_2 , β_1 , β_2)
- Possible complication: **coronary vasospasm**



Neurotransmission: Parasympathetic NS

- First synapse:
 - **ACh** from pre-ganglionic neuron binds to **nicotinic receptor** on post-ganglionic neuron \rightarrow Na^+ influx
- Second synapse:
- **ACh** from post-ganglionic neuron binds to **muscarinic receptor*** in target organ
- * M_1, M_2, M_3 (G-protein coupled receptors)



Parasympathetic Neurotransmission: Atropine

- **Blocks muscarinic ACh receptors** (M_1 , M_2 , M_3), hence inhibiting parasympathetic effects at target organs
- Administered **before intubation to prevent vagal overstimulation**. Also helps reduce mucus secretions in airways.
- Administered before ophthalmology procedures to **induce mydriasis**

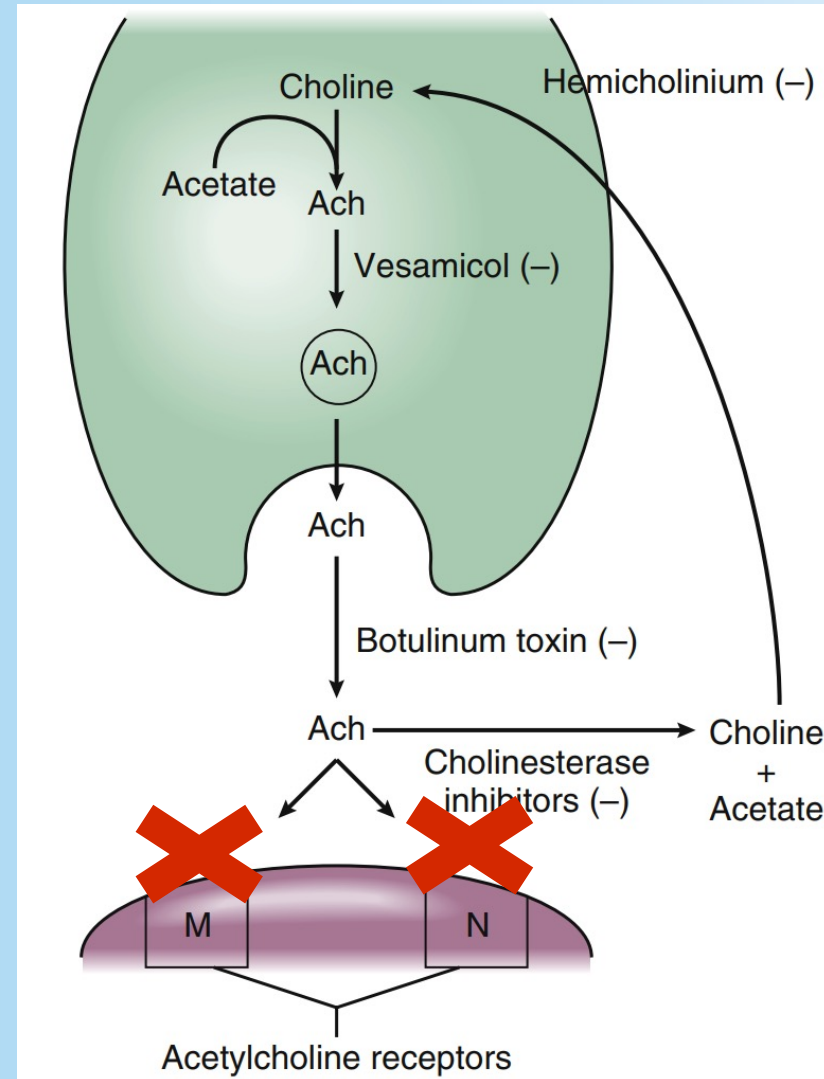


Table of Contents

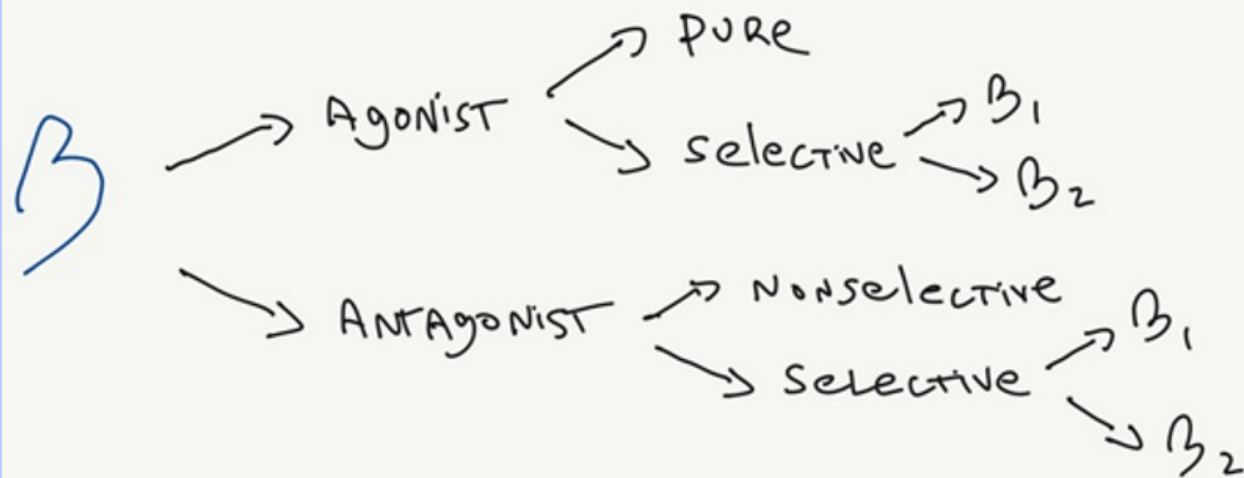
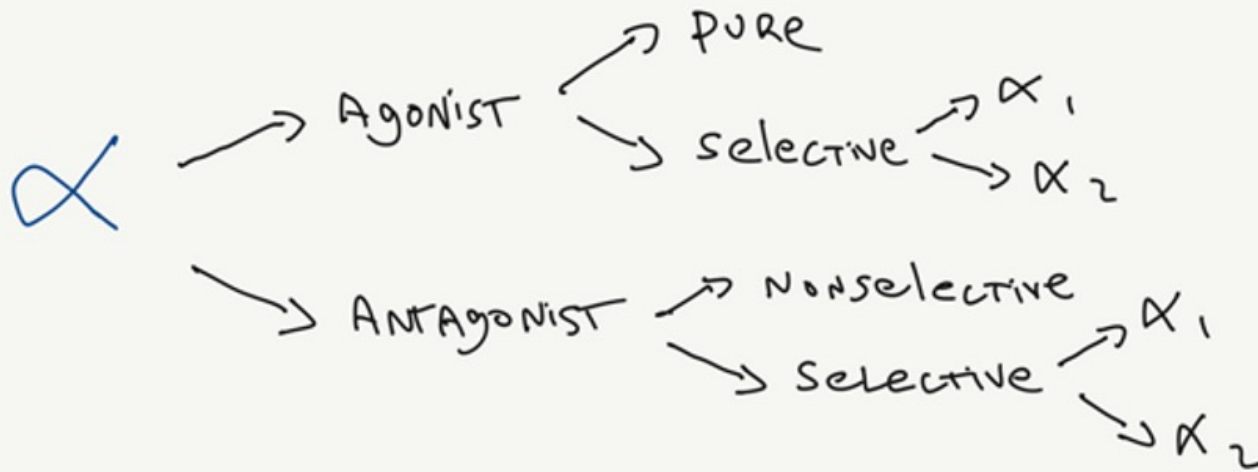
- ~~Basic organization & functions~~
- ~~ANS anatomy~~
- ~~Neurotransmission~~
- Adrenergic receptors & autonomic effects in end-organs
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ANS receptor effects at target organs

G-protein-linked second messengers

RECEPTOR	G-PROTEIN CLASS	MAJOR FUNCTIONS
Sympathetic		
α_1	q	↑ vascular smooth muscle contraction, ↑ pupillary dilator muscle contraction (mydriasis), ↑ intestinal and bladder sphincter muscle contraction
α_2	i	↓ sympathetic (adrenergic) outflow, ↓ insulin release, ↓ lipolysis, ↑ platelet aggregation, ↓ aqueous humor production
β_1	s	↑ heart rate, ↑ contractility (one heart), ↑ renin release, ↑ lipolysis
β_2	s	Vasodilation, bronchodilation (two lungs), ↑ lipolysis, ↑ insulin release, ↑ glycogenolysis, ↓ uterine tone (tocolysis), ↑ aqueous humor production, ↑ cellular K ⁺ uptake
	s	↑ lipolysis, ↑ thermogenesis in skeletal muscle, ↑ bladder relaxation
Parasympathetic		
M ₁	q	Mediates higher cognitive functions, stimulates enteric nervous system
M ₂	i	↓ heart rate and contractility of atria
M ₃	q	↑ exocrine gland secretions (eg, lacrimal, sweat, salivary, gastric acid), ↑ gut peristalsis, ↑ bladder contraction, bronchoconstriction, ↑ pupillary sphincter muscle contraction (miosis), ciliary muscle contraction (accommodation), ↑ insulin release, endothelium-mediated vasodilation

Basic Adrenergic pharmacology



Examples of agonists:

- **Epinephrine:** pure α agonist + pure β agonist
- **Clonidine:** selective α_2 agonist
- **Albuterol:** selective β_2 agonist

Examples of antagonists:

- **Prazosin:** selective α_1 antagonist
- **Propranolol:** non-selective β antagonist
- **Atenolol:** selective β_1 antagonist

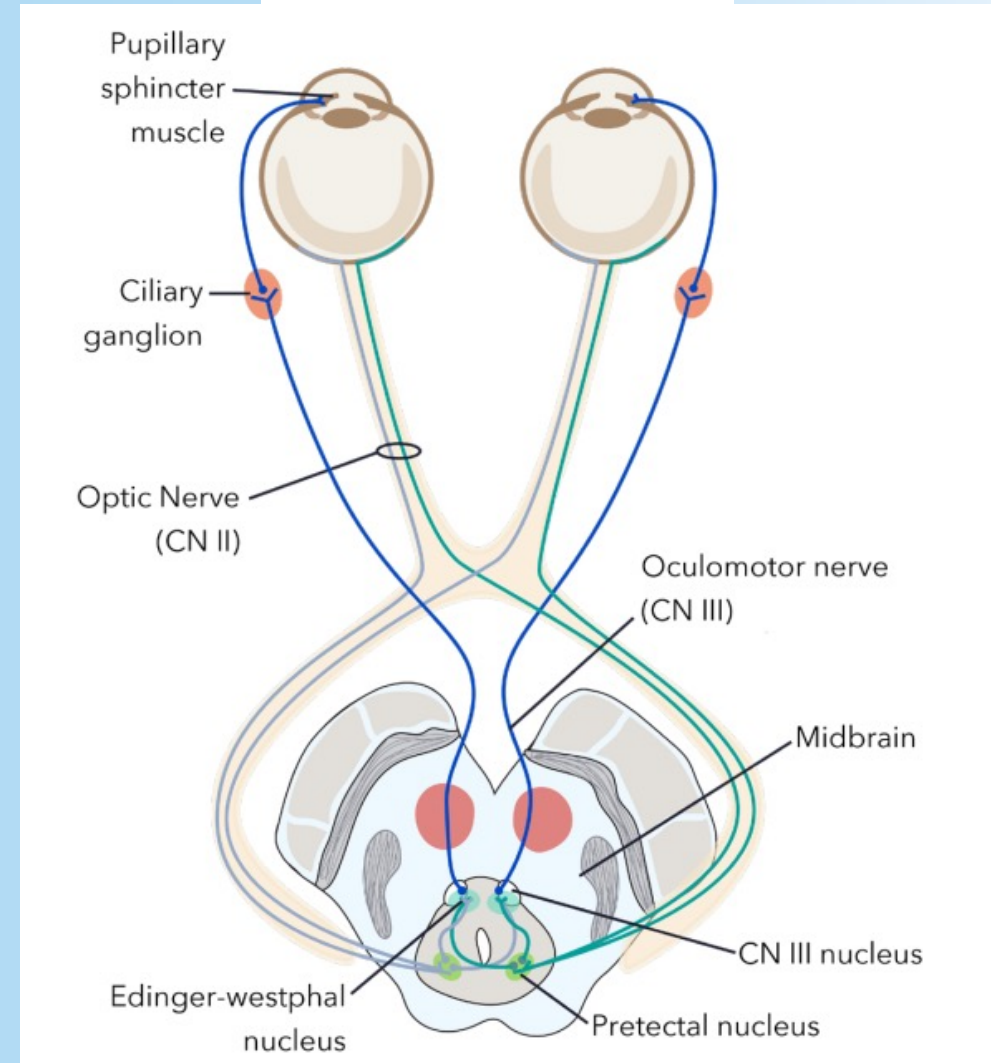
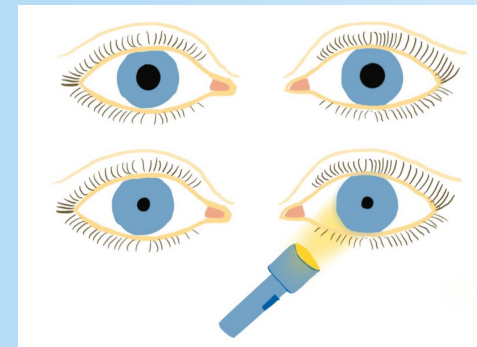
*"antagonist" aka "blockers"

Table of Contents

- ~~Basic organization & functions~~
- ~~ANS anatomy~~
- ~~Neurotransmission~~
- ~~Adrenergic receptors & autonomic effects in end-organs~~
- Pupillary light reflex
- Wooclap!

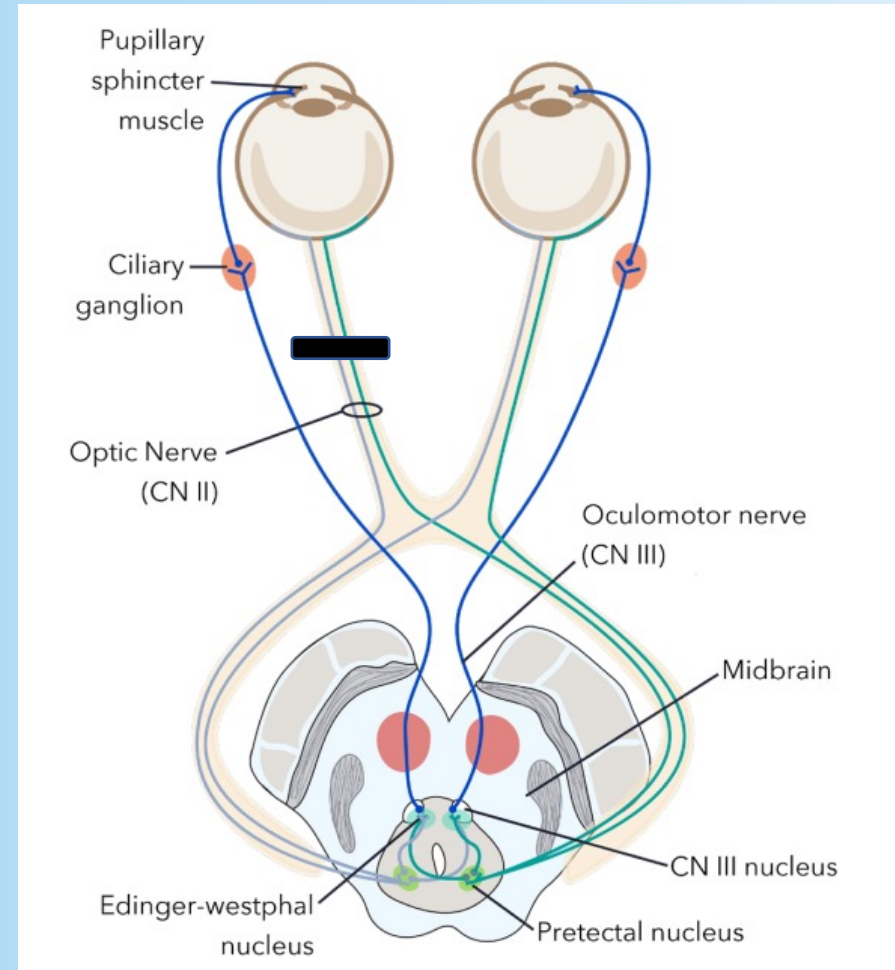
Pupillary light reflex (i)

- Clinically assess the **parasympathetic innervation** of pupillary sphincter muscle by **CN III & ciliary ganglion**
- Important to always check both the **direct** and **consensual responses to light (i.e. pupillary constriction)**
- Normal result: **positive direct & consensual responses** upon lighting each eye separately.
- Nb: nerve fibers from nasal hemiretina cross at the optic chiasm while fibers from the temporal retina remain ipsilateral!



Pupillary light reflex (ii)

- **Q:** Can pupillary constriction be elicited in the left eye if the left optic nerve (CN) is severed?
- **A:** Yes! A consensual response may be elicited by lighting the right eye.
- **Why?:** Nerve fibers from the **right nasal hemiretina** decussate at the optic chiasm, and reach the **left pretectal nucleus**.



Localized spinal cord trauma at the level of T5-T7 would be most likely to affect which of the following?

- a) Parasympathetic preganglionic fibers
- b) Parasympathetic postganglionic fibers
- c) Sympathetic preganglionic fibers
- d) Sympathetic postganglionic fibers

Which of the following is true regarding ANS synapses & neurotransmission?

- a) Sympathetic preganglionic are long
- b) Muscarinic receptors are stimulated by NE
- c) Parasympathetic postganglionic fibers are short
- d) Preganglionic sympathetic fibers release NE

What is the most likely side-effect of Phenoxybenzamine; a non-selective alpha-1 antagonist?

- a) Tachycardia
- b) Sweating
- c) Hypotension
- d) Heart failure

Find the correct statement:

- a) NE always causes smooth muscle contraction
- b) Cocaine stimulates release of NE
- c) NE release from postganglionic neuron is ACh-dependent
- d) Selective alpha-1 agonists are used to treat hypertension

Find the correct statement:

- a) Non-selective beta-blockers may increase heart rate
- b) Non-selective beta-blockers may be used to treat hypertension in asthmatic individuals
- c) Albuterol, a B2 antagonist, is a short-acting bronchoconstrictor
- d) Selective B1 blockers may be used to treat hypertension

Absent pupillary light reflex (both direct and consensual) upon lighting the right eye could indicate which of the following?

- A) Optic chiasm lesion
- B) Left CN III lesion
- C) Right prechiasmatic CN II lesion
- D) All correct

