A Guided Revision

Physiology of the Autonomic Nervous System

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Ph.D, MBBS

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DISCLAIMER

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I would like to extend my deepest gratitude to my family for their unconditional love and unwavering support throughout the years. Your encouragement has been the cornerstone of my journey.

I am also immensely grateful to all my teachers and friends, whose inspiration and assistance have been invaluable. Thank you for being part of my journey and helping me grow along the way.

BIOGRAPHY

Dr. Aszrin earned her medical degree (MBBS) from the University of Adelaide, Australia, in 1999. Following her graduation, she began her medical career with the Malaysia Ministry of Health in 2000. In 2006, she joined the Faculty of Medicine at the International Islamic University Malaysia (IIUM). Dr. Aszrin was awarded a doctorate in Physiology in 2010 and has since been actively involved in teaching medical physiology to both undergraduate and postgraduate students.

PREFACE

As a medical graduate, the author recognizes the challenges students face in reviewing complex topics efficiently. This book is designed as a revision tool that provides concise yet comprehensive coverage of essential information. All content has been carefully checked and reviewed to ensure accuracy at the time of publication. However, as medicine is an ever-evolving field, the knowledge presented may expand or change over time. Therefore, readers are encouraged to verify any information they find in this book with other sources, especially if discrepancies arise.

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Learning Objectives

1. To describe the characteristic function and organization of the sympathetic and parasympathetic nervous systems.

2. To describe the autonomic neurotransmitters and receptors, and their deactivation mechanisms.

5. To apply the basic knowledge and explain autonomic dysfunctions and the action of autonomic drugs.

3. To describe the autonomic responses of the effector organ.

4. To discuss the exceptions to the general rule of autonomic responses.

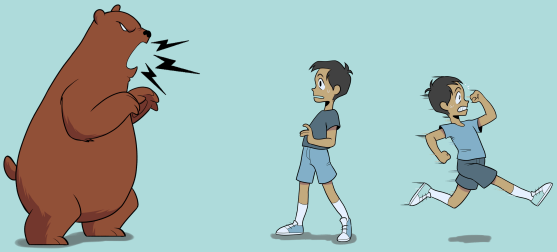
01

General

Functions & Organization of Autonomic Nervous System

The Function of Autonomic Nervous System

Innervates & maintains a stable & optimal internal environment of body viscera, secretory glands & smooth muscles.



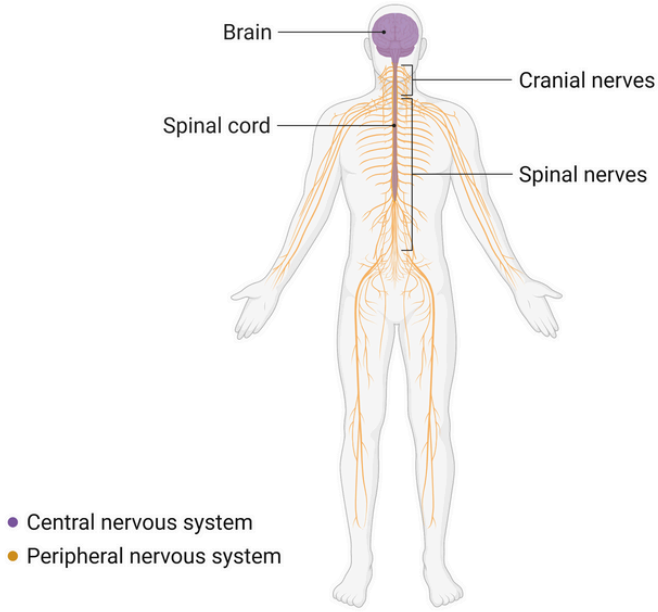
SYMPATHETIC NERVOUS SYSTEM

It is associated with preparing the body to fight against or flee away from threat. (Fight or flight)

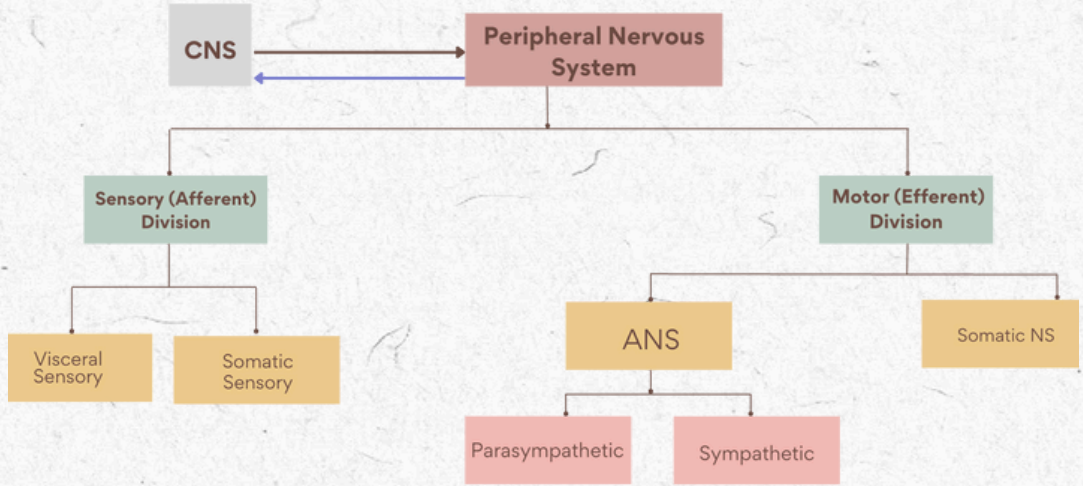
PARASYMPATHETIC NERVOUS SYSTEM

It dominates in queit, relaxed situations. (Rest and Digestion)

The Major Components of the Nervous System



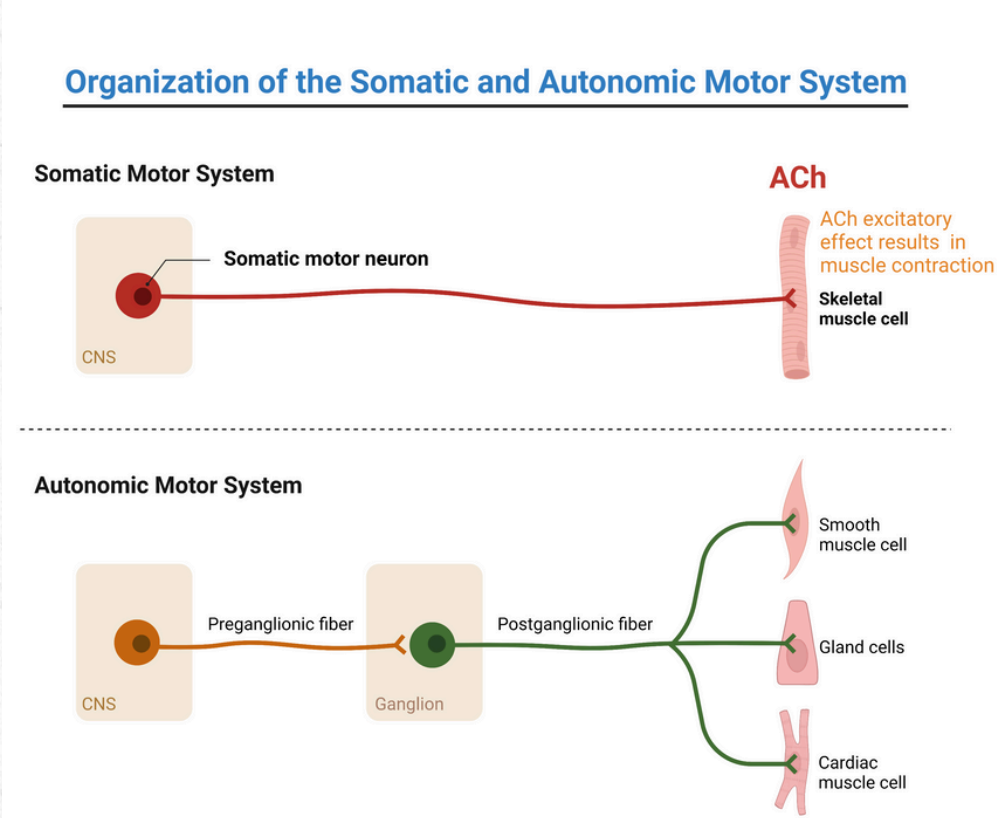
Divisions of the Nervous System



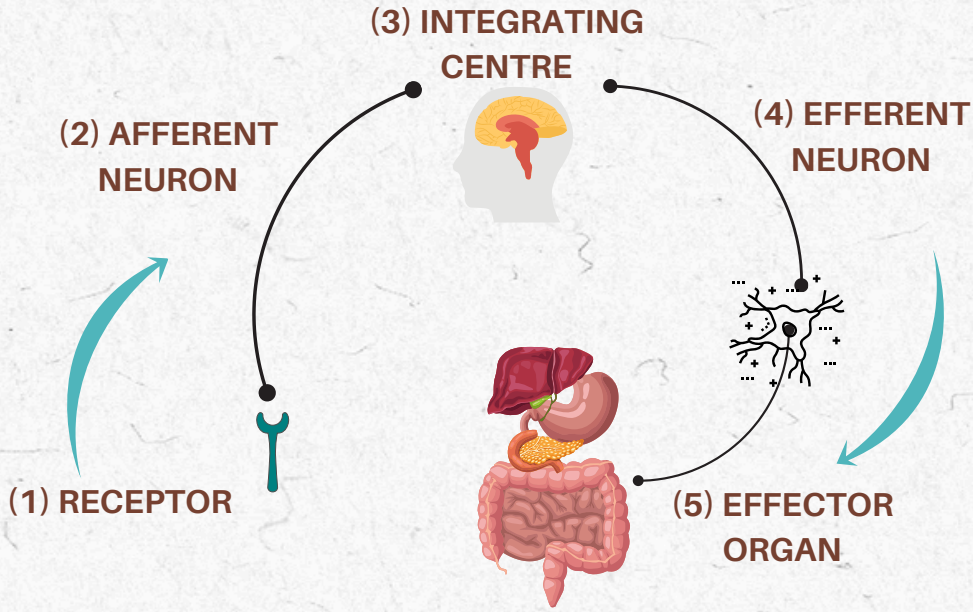
Divisions of the Nervous System

FUNCTIONAL DIVISIONS

VOLUNTARY vs **INVOLUNTARY**



ANS Organization : Components of the Autonomic Pathway

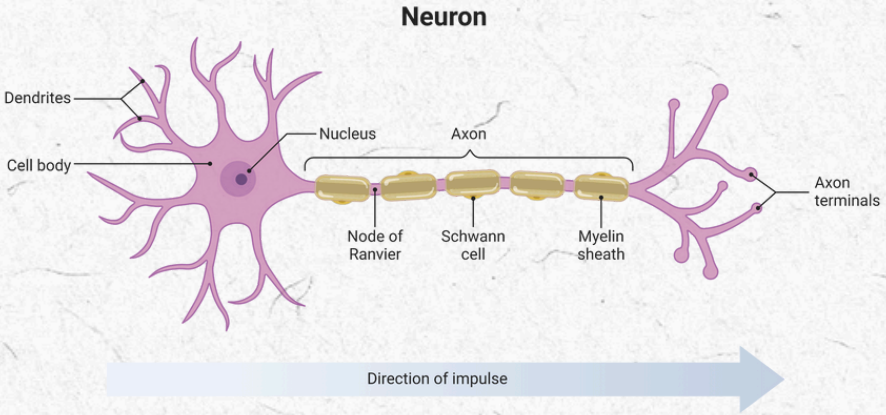


- To achieve its function, the ANS is organized on the basis of the **reflex arc 5 components**.

* [Reflex arc: The pathway by which a reflex occurs in an involuntary stereotyped response to a stimulus]

ANS Organization: EFFERENT Neuron

- Cell body of the FIRST NEURON is located in the CNS (forming the integrating centre).
- FIRST NEURON axon (preganglionic neuron) synapses with the cell body of the SECOND NEURON (within a ganglion).
- SECOND NEURON is also called the postganglionic neuron.
- Postganglionic neuron terminals synapses with the effector organ.

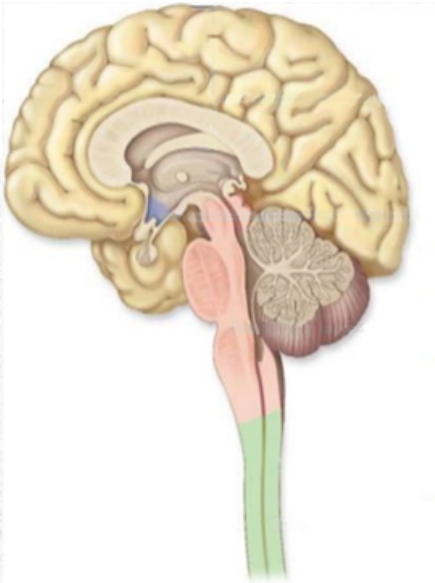


* [Ganglion: A cluster of neuronal cell bodies outside the CNS].

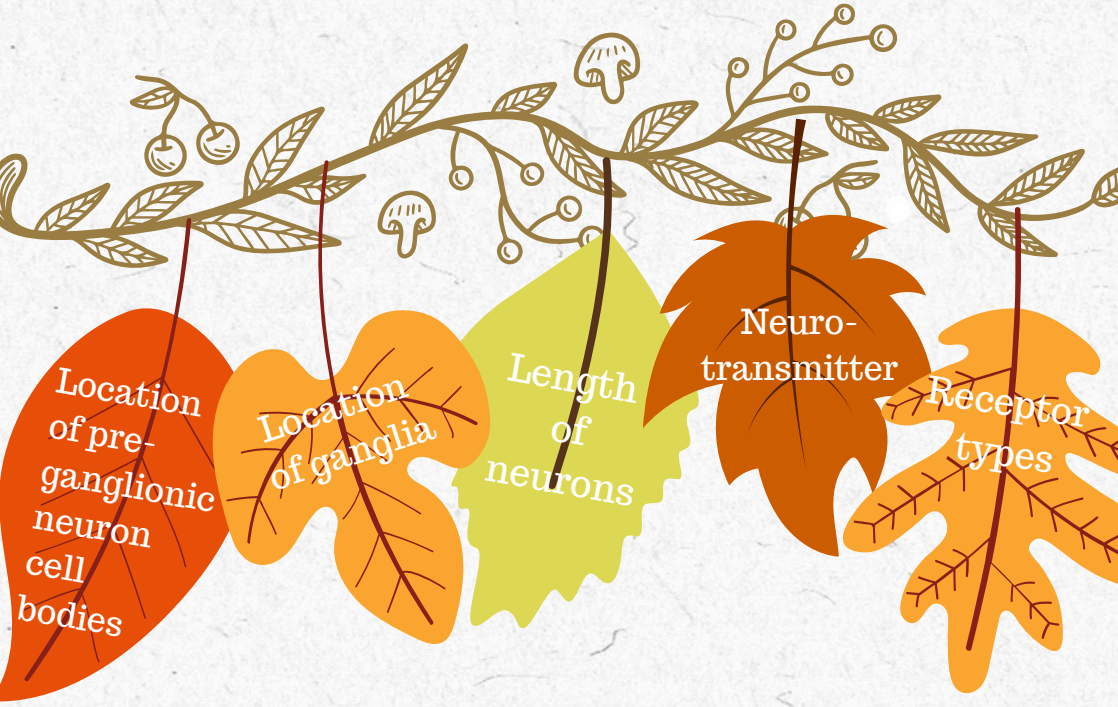
ANS Organization: Integrating Centres

A group of neuron cell bodies
at various levels in the CNS that control the ANS

Hypothalamus	Limbic system	Cerebral cortex	Brain stem	Spinal Cord
• **main integration centre** for autonomic functions. • receives autonomic regulatory input from the limbic system to do so.	provides subconscious input from the cerebral cortex to the hypothalamus.	provides subconscious cerebral input.	the medulla - **major control centre** for the ANS.	coordinate **quick responses** to external stimuli that is **only** managed by the spinal cord.



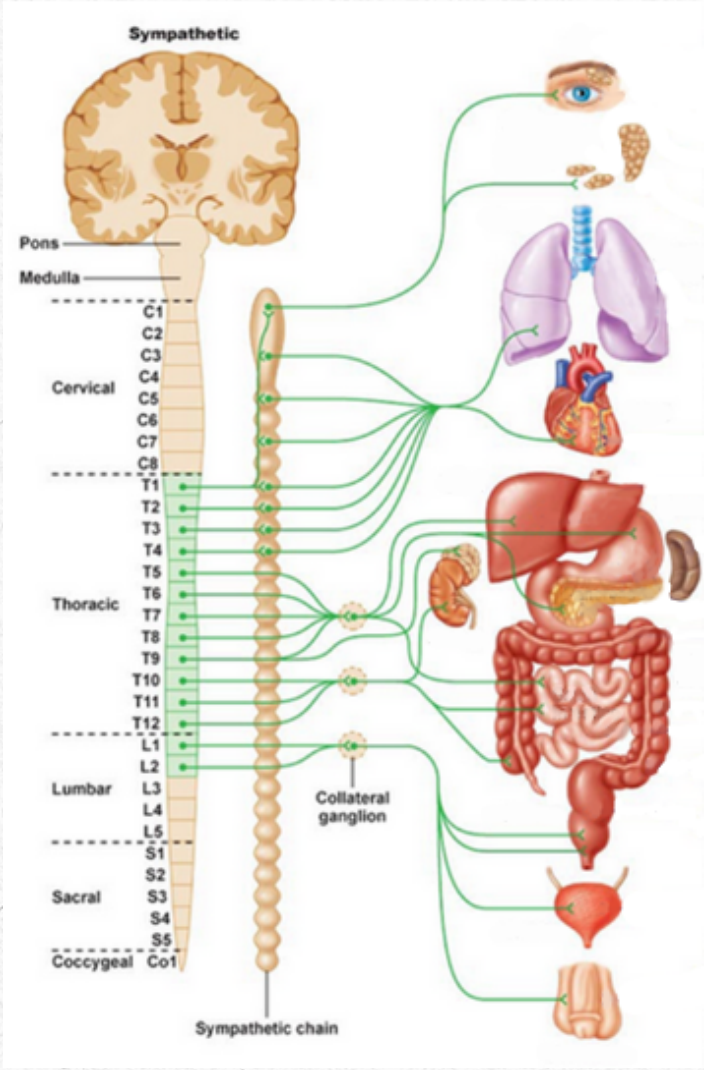
ANS Organization: Structural Characteristics



Structural Characteristics: Sympathetic NS

Location of preganglionic neuron cell bodies:

Lie within lateral horns of T1-L2 segments of the spinal cord

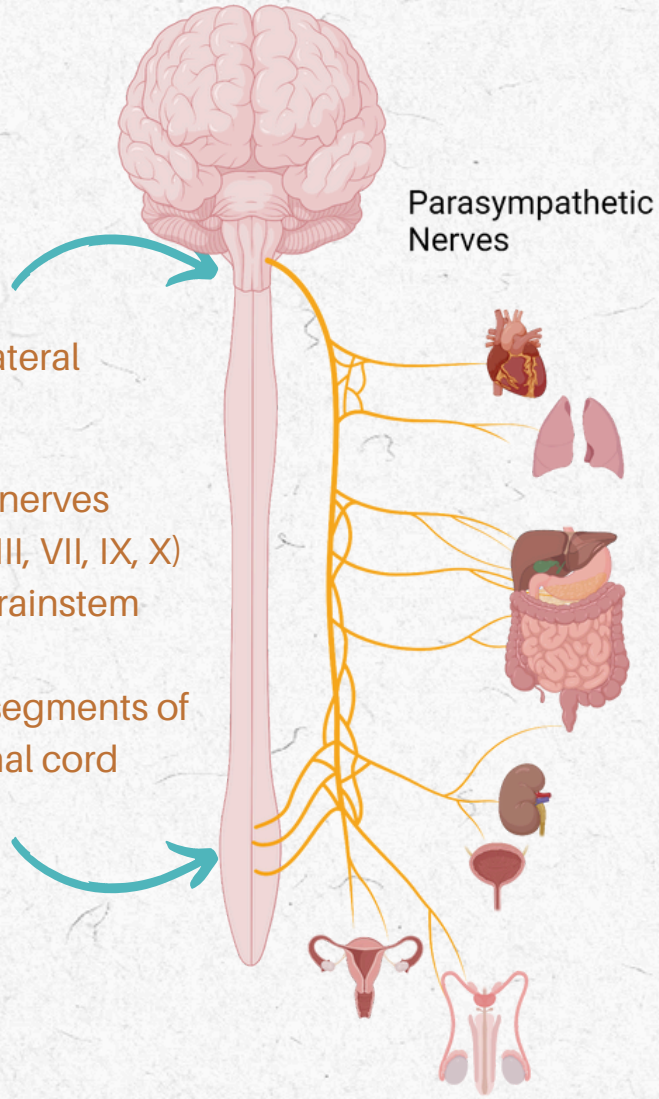


Structural Characteristics: Parasympathetic NS

Location of preganglionic neuron cell bodies

Lie within lateral horns of :

- Cranial nerves nuclei (III, VII, IX, X) in the brainstem
- S2-S4 segments of the spinal cord



Structural Characteristics:

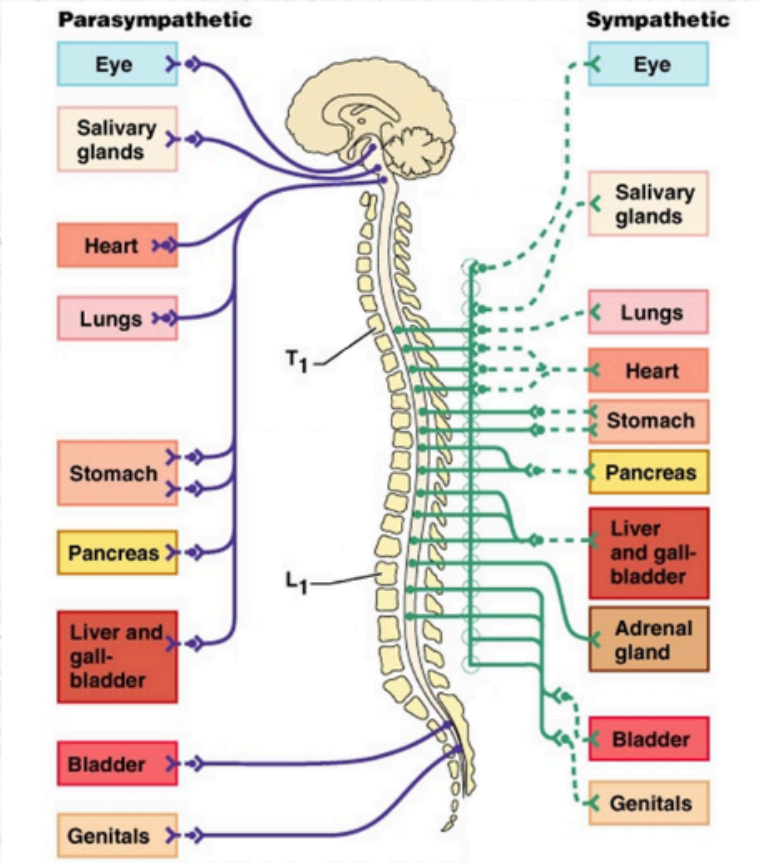
Location of ganglia

Parasympathetic NS

- Near the effector organs. Examples: Ciliary ganglia - Eye, Myenteric plexus - GIT

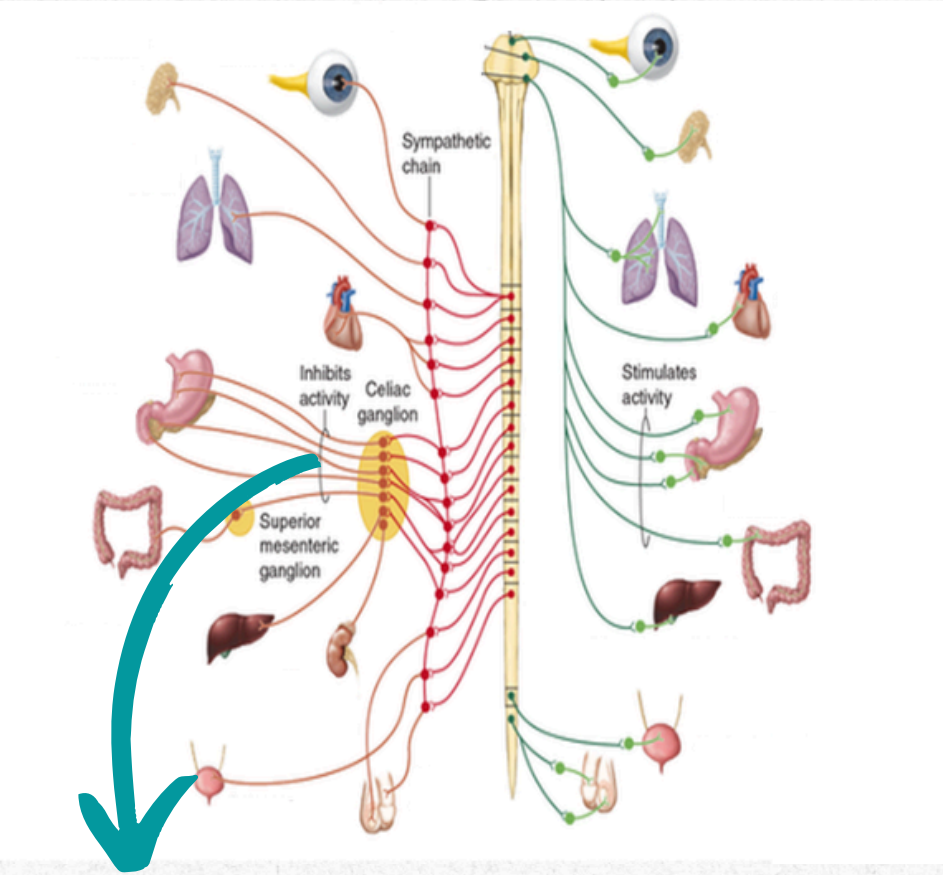
Sympathetic NS

- Lie on either side of the vertebral column.
- Away from the effector organ.



Structural Characteristics: Sympathetic NS

Length of neuron



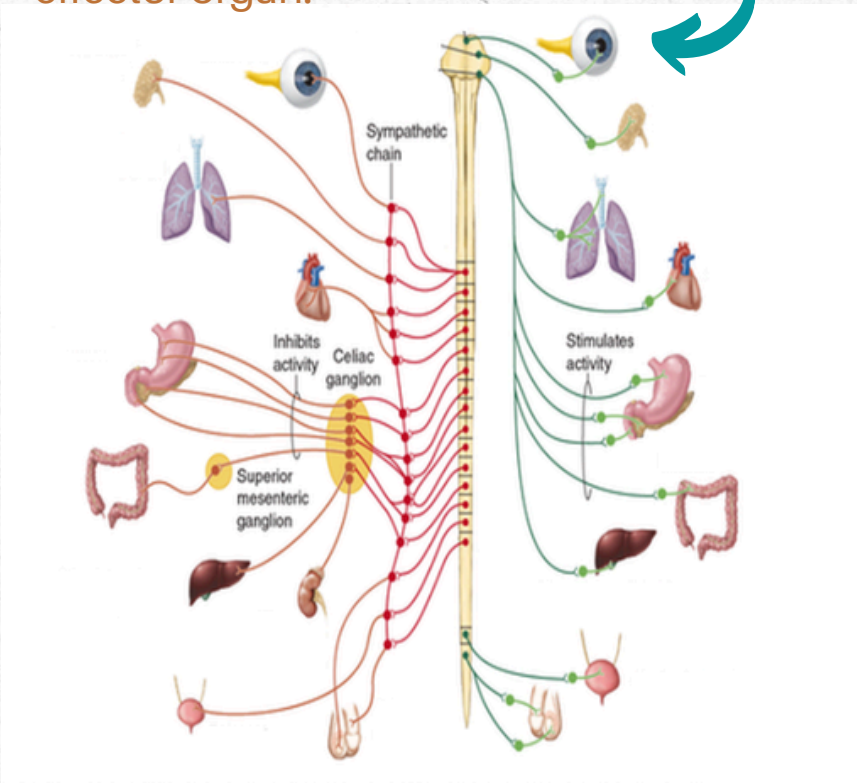
- Long **post**ganglionic neurons (relatively shorter preganglionic)
- **Pre**ganglionic neuron axon synapses with **MANY** **post**ganglionic neuron of more than 1 effector organ .

Structural Characteristics: Parasympathetic NS

Length of neuron

- Short **post**ganglionic neurons (long preganglionic)

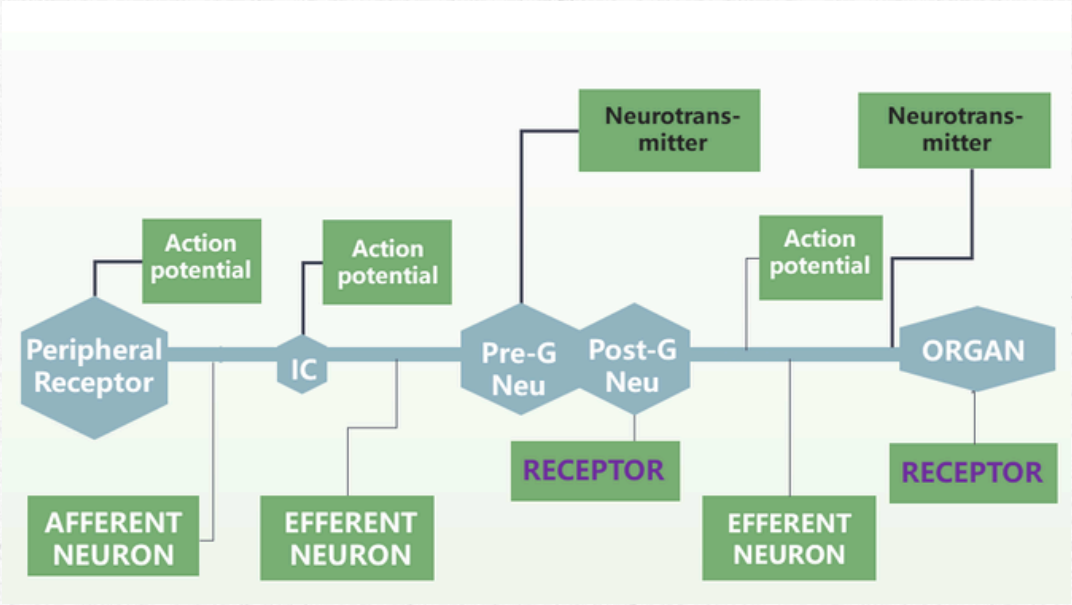
- **Pre**ganglionic neuron axon synapses with postganglionic neuron of a **SINGLE** effector organ.

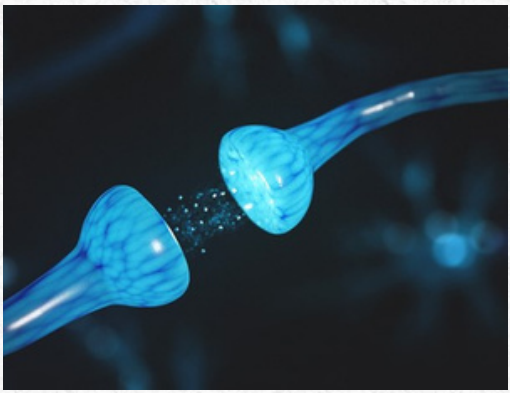


02

Autonomic Neurotransmitters & Receptors

Communication between Components of Autonomic Pathway





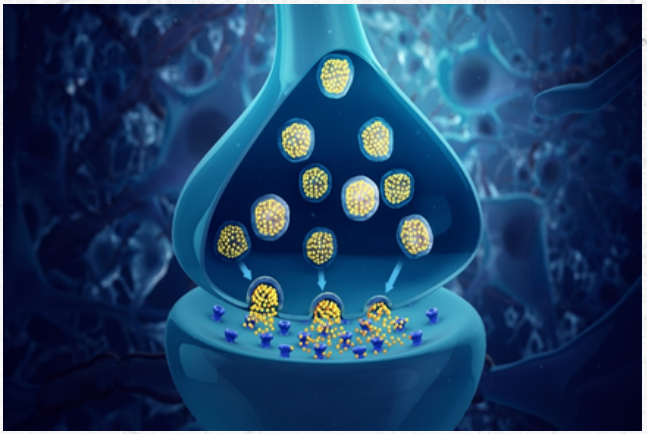
Structural Characteristics: Principal neurotransmitter

Sympathetic NS

- Noradrenaline (NA)
- Adrenaline

Parasympathetic NS

- Acetylcholine (ACh)



Structural Characteristics: Parasympathetic Pathway Receptors

ACh acts on 2 types of receptors that are located postsynaptically

Nicotinic receptor

on the parasympathetic ganglia/ the cell body of the **postganglionic neuron**.

Muscarinic receptor

on the **effector organ** cell membranes.

Structural Characteristics: Sympathetic Pathway Neurotransmitter

PREGANGLIONIC NEURON

- Preganglionic neuron terminals of the SNS release **ACh**.
- It synapses with the cell body of the **postganglionic neuron** of the SNS.

POSTGANGLIONIC NEURON

- Postganglionic neuron terminals of the SNS releases **NA.**
- It synapses with the **effector organ**.

Structural Characteristics: Sympathetic Pathway Receptors

The receptors are located postsynaptically on

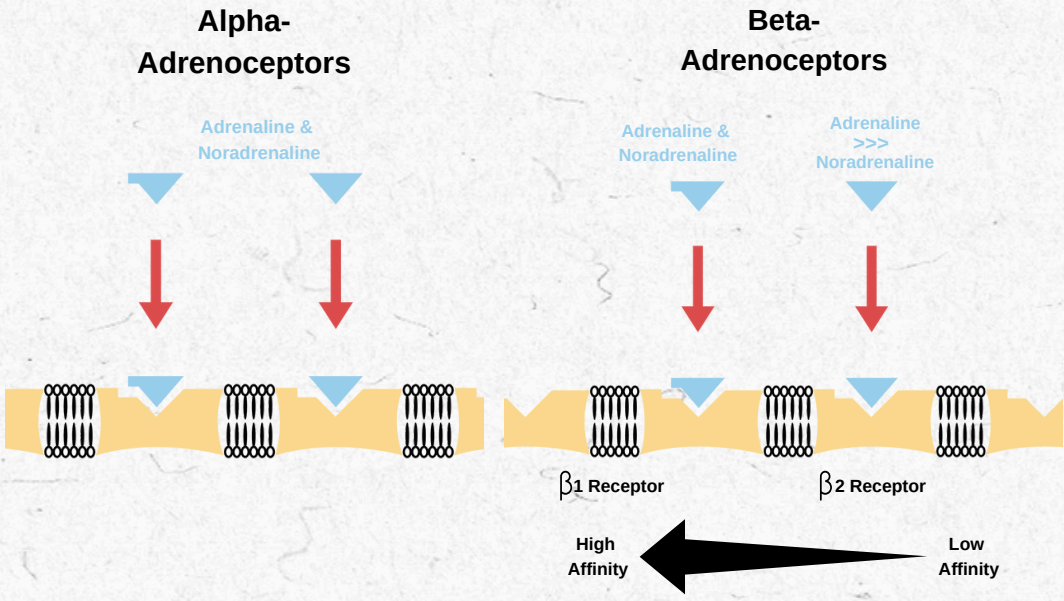
Nicotinic receptor

the sympathetic ganglia/ the cell body of the **postganglionic neuron**.

Adrenoreceptor

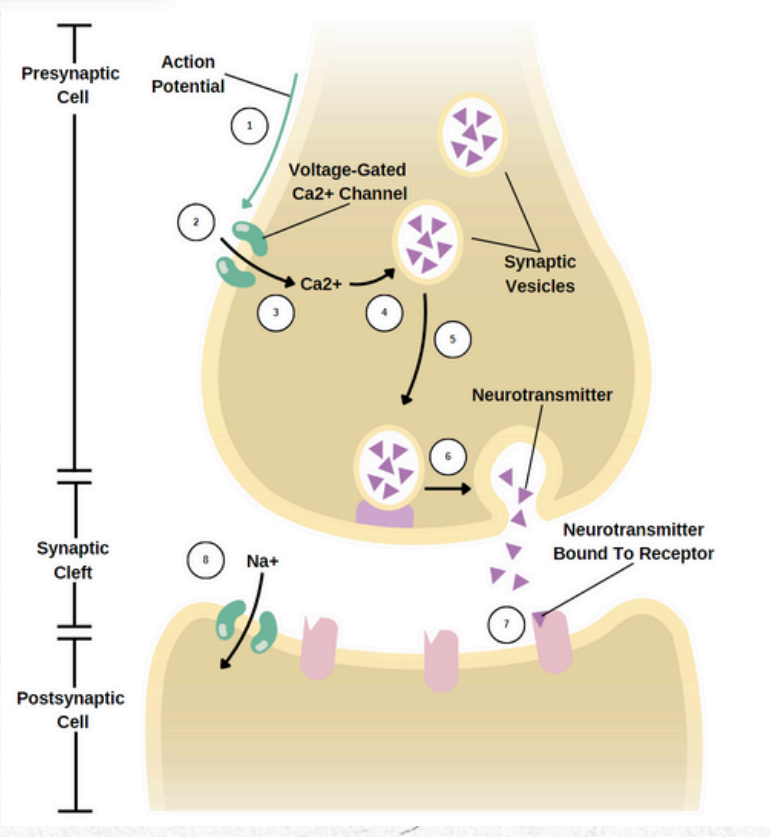
the **effector organ** cell membranes.

Receptors on Effector Organs: Postganglionic sympathetic neuron terminals



- **Alpha**-Adrenoceptors are responsive to both Adrenaline & Noradrenaline, but more responsive to noradrenaline than to adrenaline.
- At low concentration of adrenaline, the effects of **β2- Adrenoceptors** are dominant.
- At high concentrations of adrenaline, the effects of **Alpha-Adrenoceptors** become more pronounced.

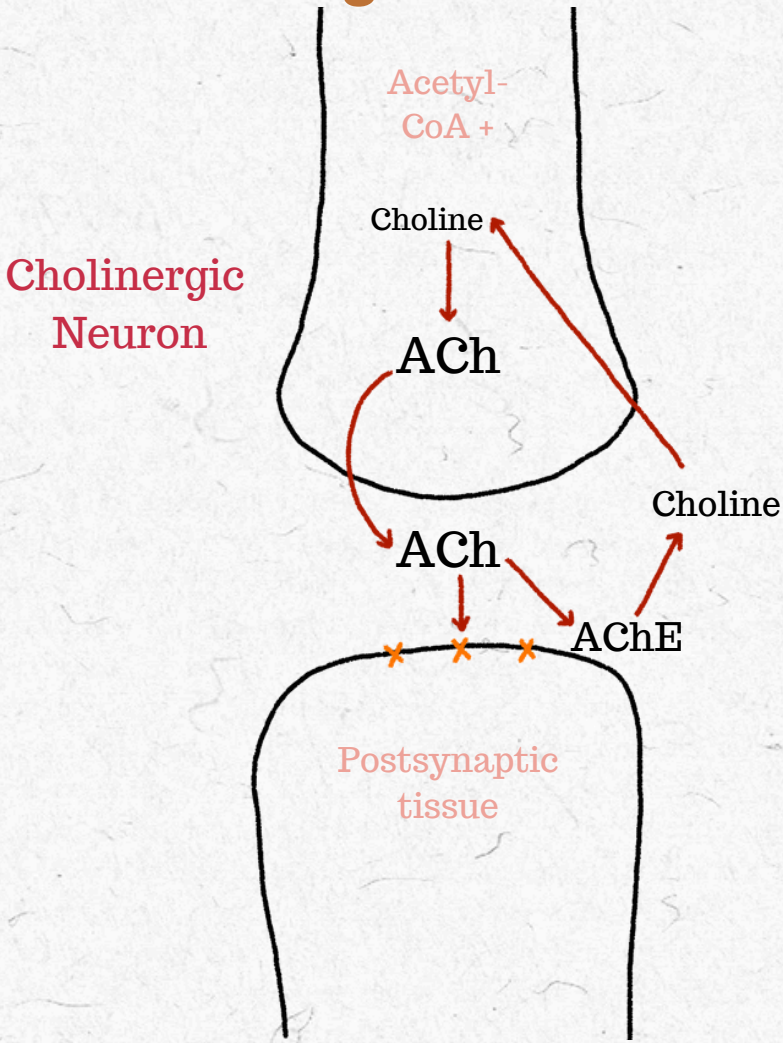
Neurotransmitters Synthesis: Parasympathetic NS



Acetylcholine:

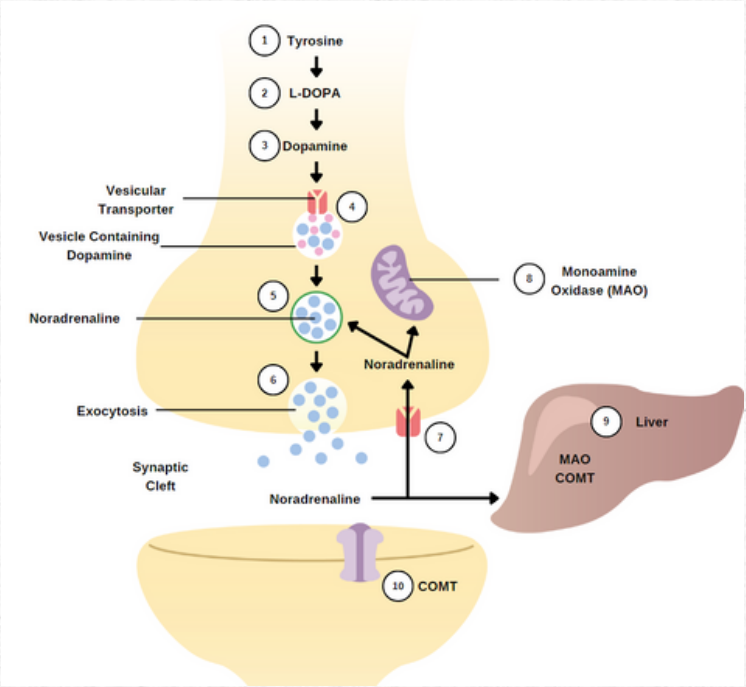
- Synthesized & stored in vesicles in the neuron terminal portion.
- Released when an action potential is conducted through the neuron.

Deactivation of Acetylcholine at cholinergic nerve endings



Deactivation mechanisms are very fast by **acetylcholinesterase (AChE)**

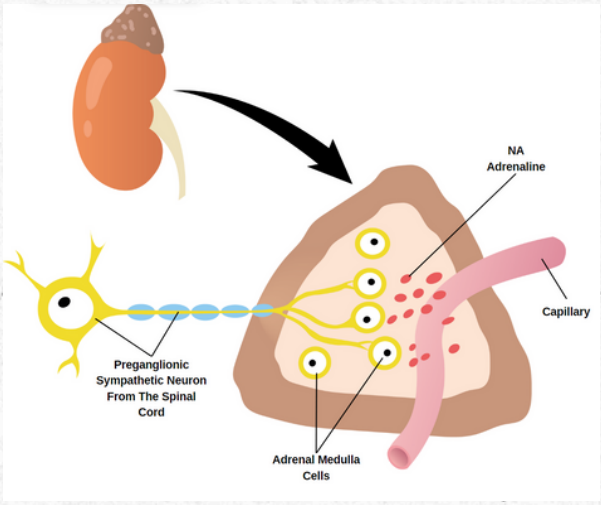
Neurotransmitters Synthesis: Sympathetic NS



Noradrenaline (NA) is synthesized at:

- nerve endings
- adrenal medulla.

Adrenaline is **NOT** synthesized at nerve endings.



Neurotransmitters Synthesis: Sympathetic NS

Phenylethanolamine N-methyl transferase (PNMT)
is required to covert

PNMT is present in:

- adrenal gland medullary cells
- postganglionic neuron terminals of Sympathetic NS
- some neurons in CNS

Deactivation of Noradrenaline at sympathetic nerve endings

Deactivation mechanism is very slow.

1

Broken down by enzyme

Monoamine oxidase (MAO)

2

Remaining neurotransmitter is broken down by enzyme

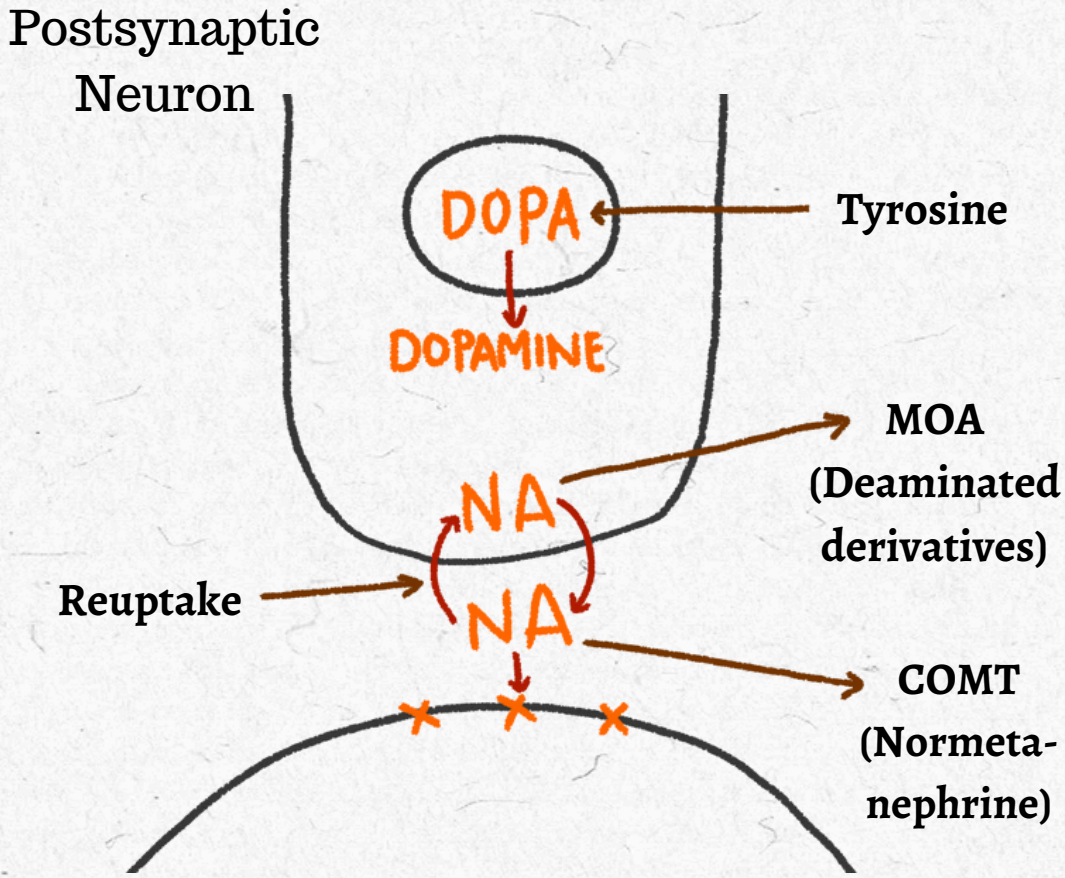
Catechol-O-methyl transferase (COMT)

3

NA Reuptake by the synaptic knobs at postganglionic terminals

which also leads to a prolonged sympathetic effect.

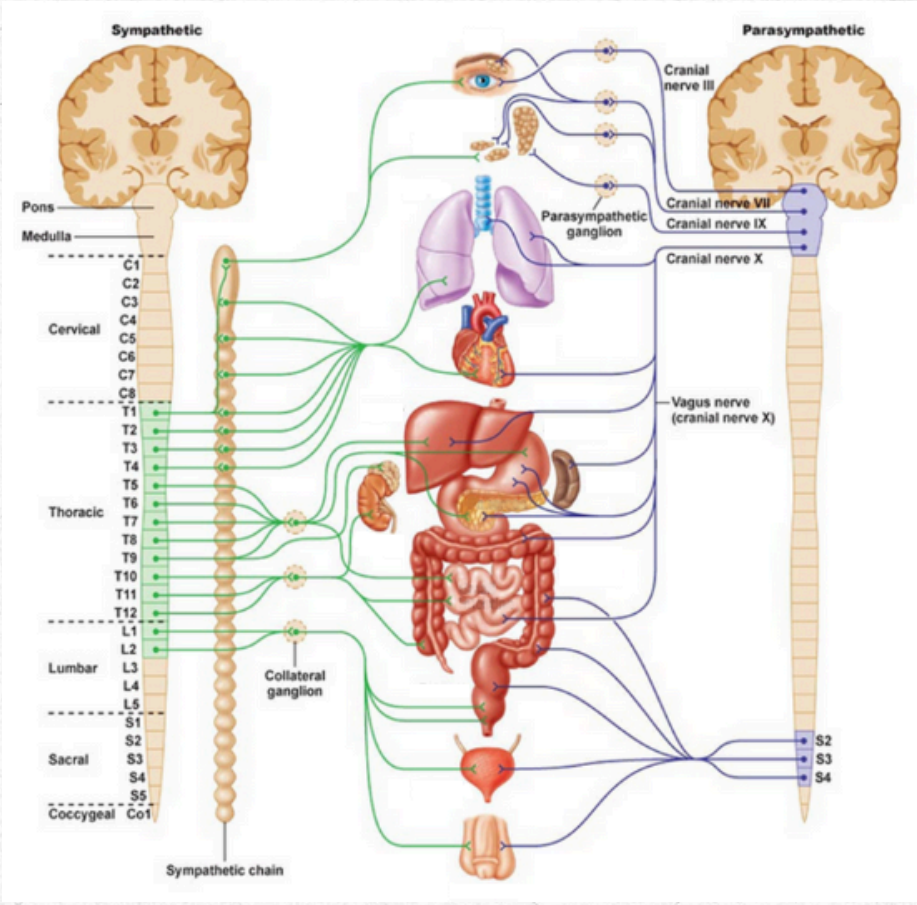
Deactivation of Noradrenaline at sympathetic nerve endings



03

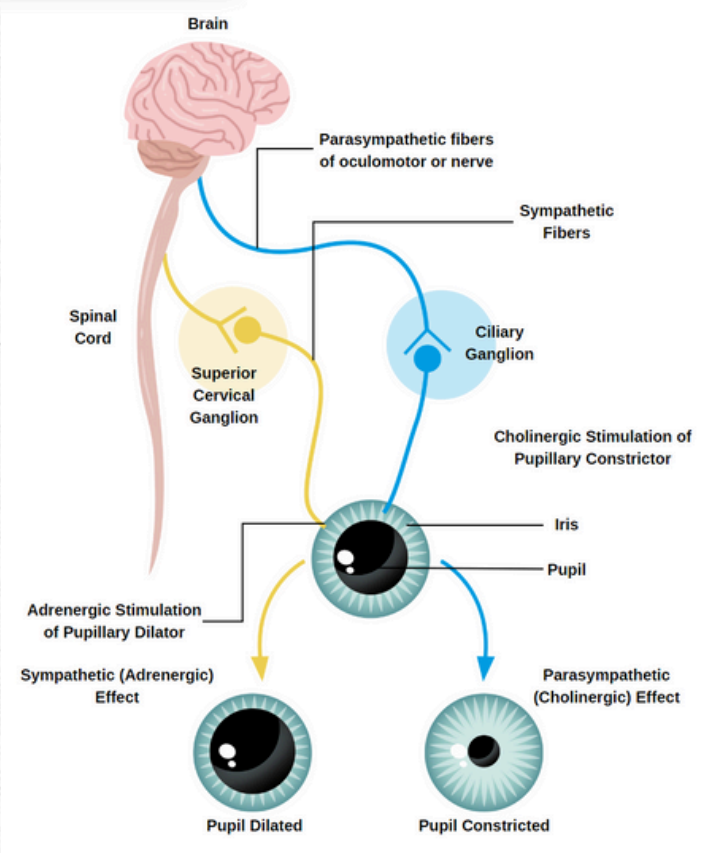
Effector Organs Responses

ANS Organization: Effector Organs Responses



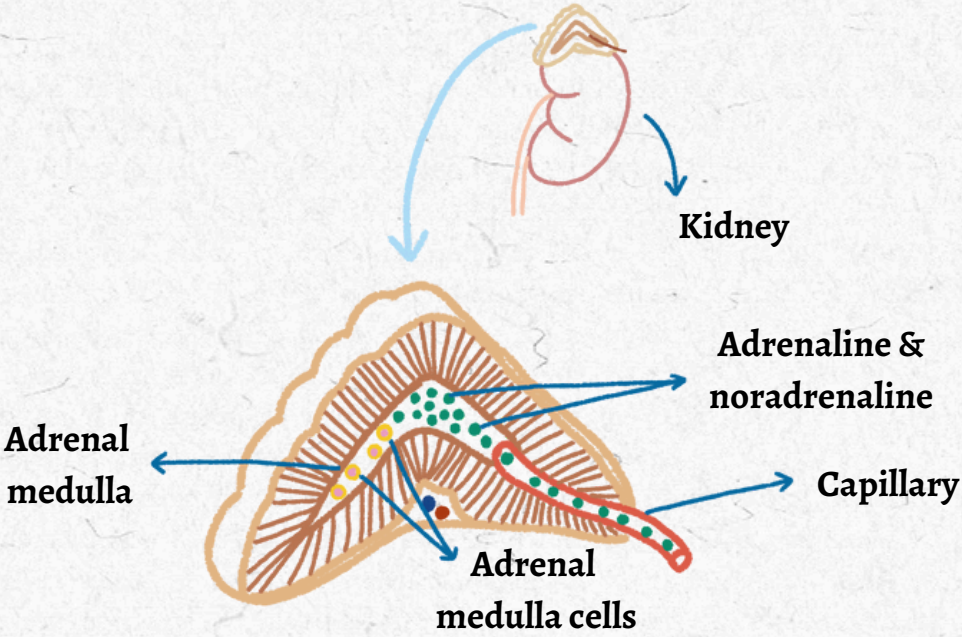
- Most organs have dual nerve innervations (sympathetic & parasympathetic nerves).
- Sympathetic nervous system innervations are widespread .

ANS Organization: Effector Organs Responses



- Generally sympathetic & parasympathetic nervous systems exert opposing (antagonistic) effects on the effector organs, allowing precise control over the organs.

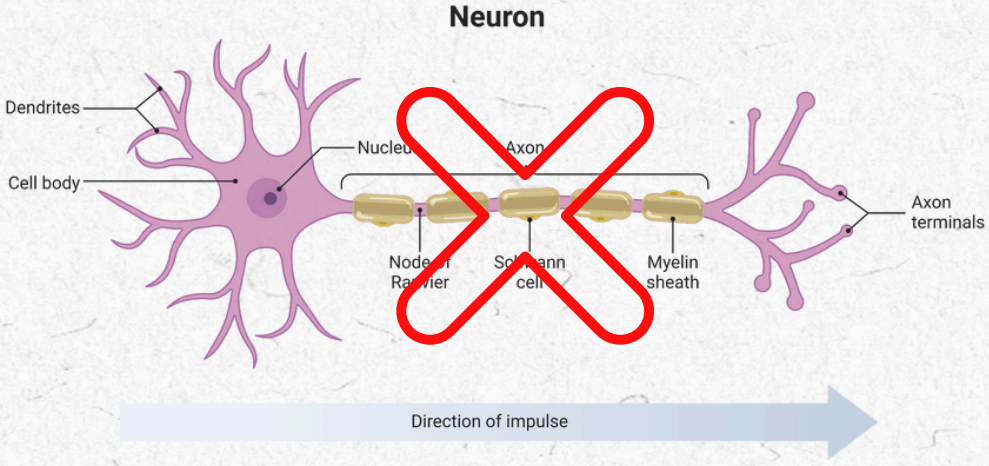
ANS Organization:
Effector Organs Responses
The Sympathoadrenal Axis



- The adrenal medulla is a part of the Sympathoadrenal Axis.

- It releases the hormones catecholamines (**adrenaline** (80%), **NA** & **dopamine**) into the circulation to a distant organ. This prolong sympathetic effect.

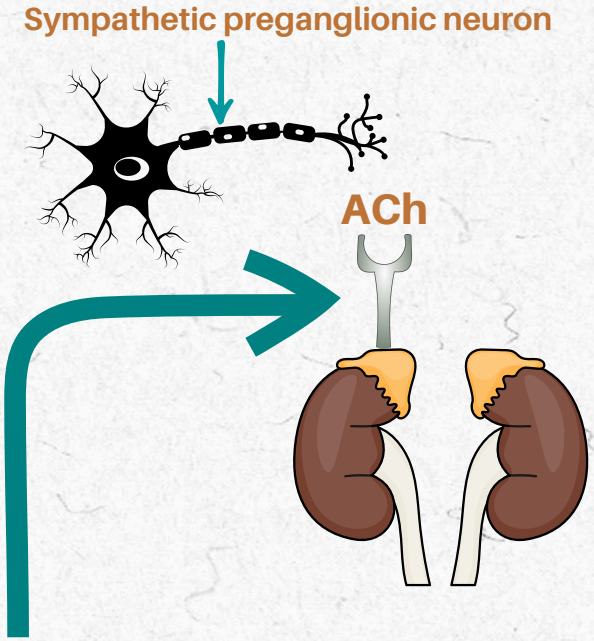
ANS Organization:
Effector Organs Responses
The Sympathoadrenal Axis



- The adrenal medulla is a modified sympathetic ganglion.
  - [Postganglionic neuron cells without axons].

- Upon stimulation by the sympathetic preganglionic neuron, adrenal medulla effect is exerted through the release of **ACh**.

ANS Organization:
Effector Organs Responses
The Sympathoadrenal Axis



The receptors on the
adrenal medulla chromaffin cells is :

Nicotinic Receptors

[Eventhough it is a gland (an effector organ)]

Effector Organs Responses

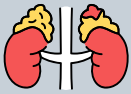
Effector Organ	Response to Sympathetic Activation (Adrenergic Receptor)	Response to Parasympathetic Activation (Muscarinic Receptor)
Eyes	Pupil dilation (α1)	Pupil constriction Lacrimal gland secretion
Arterioles	• Vasoconstriction (α1) – e.g. in splanchnic vessels, skin • Vasodilation (β2) – e.g. in skeletal muscles, coronary art.	--
Systemic veins	• Venoconstriction (α1) • Venodilation (α2/β2)	--
Heart • Pacemaker cells: • Atria, Ventricles:	• ↑ Heart rate (β1) • ↑ Cardiac contractility (β1,β2)	• ↓ Heart rate • ↓ Cardiac contractility
Lungs • Bronchial smooth muscle : • Bronchial glands:	• (sparse sympathetic innervation) • Bronchodilation (β2)	• Bronchoconstriction • ↑ secretion
Intestinal • Sphincters: • Wall smooth muscle : • Secretions:	• Contraction (α1) • ↓ motility (β2,α1 ,α2) • --	• Relaxation • ↑ motility • Stimulation

Effector Organ	Response to Sympathetic Activation (Adrenergic Receptor)	Response to Parasympathetic Activation (Muscarinic Receptor)
Bladder • Sphincters: • Wall:	• Contraction (α1) • Relaxation (β2)	• Relaxation • Contraction
Gallbladder	Relaxation (β2)	Contraction
Kidney	Renin secretion (β1)	--
Male genitalia	Ejaculation (α1)	Erection
Uterus	• Pregnant: Contraction (α1) • Pregnant & Non-Pregnant: Relaxation(β2)	--
Metabolic stimulation: • **Liver** • **Adipose tissue**	• Gluconeogenesis & glycogenolysis (α1, β2) • Lipolysis (β3)	--
Salivary, Submandibular & Parotid glands	Thick viscous secretion (α1)	Watery secretion
Skin	• Piloerector muscle Contraction (α1) • Sweat glands secretion - *sympathetic cholinergic neurone* - (Muscarinic)	--
Lacrimal glands	--	Secretion

04

Exceptions to the General Rule of ANS

Most organs have dual nerve innervation, EXCEPT the following effector organs, which receive receives SYMPATHETIC effect only:

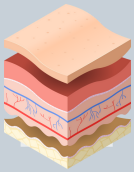


Adrenal medulla

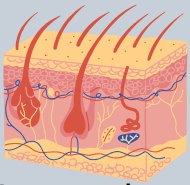
Blood vessels (except in penis/ clitoris)

Liver, Adipose tissue Kidney, Uterus

Piloerector muscles of hair follicles



Skin



Sweat glands

Most organs are dually innervated, & the nerve fibres activities in these effector organs are typically antagonistic,

EXCEPT:

Salivary glands

- The sympathetic & parasympathetic nerve activities are not antagonistic.
- Both nerve fibers stimulate salivary secretion.
- However, the saliva produced has different volume & composition
  - depending on which autonomic branch is dominant.

Viscous saliva (Sympathetic)
vs.
Watery saliva (Paraympathetic)

Postganglionic sympathetic neuron terminals at effector organs typically release noradrenaline, which acts on α1, β1, or β2 adrenoceptors,

EXCEPT:

sweat glands & piloerector muscles

They are innervated by sympathetic nerve fibers.
BUT,
the sympathetic postganglionic fibers secrete ACh instead of noradrenaline, which acts on muscarinic receptors at the effector organs.

Sympathetic adrenoreceptors activation generally has "stimulatory" effects that prepare the body for a fight-or-flight response.

Heart: β1

- positive chronotropic
- positive inotropic effects

Arterioles: α1

- vasoconstriction [Leading to ↑ BP]

Sympathetic adrenoreceptors activation generally has "stimulatory" effects that prepare the body for a fight-or-flight response

EXCEPT

β2- Adrenergic receptors activation often results in vasodilation and relaxation, rather than stimulation. This occurs through the relaxation of arteriolar smooth muscles, notably in specific areas such as:

- coronary circulation.
- skeletal muscle circulation
- lungs (bronchial cells)

NOTE:
THE NEURONS THAT ARE referred to as CHOLINERGIC

All preganglionic neurons.

Parasympathetic postganglionic neurons.

Sympathetic neuron which innervates adrenal medulla.

Sympathetic postganglionic neuron which innervates sweat glands piloerector muscles.

05

Clinical Relevance:

Autonomic Dysfunctions & Pharmacological Terms

AUTONOMIC DYSFUNCTIONS

SYMPATHETIC VS. PARA-SYMPATHETIC

SYMPATHETIC OVERACTIVITY:

- **Hypertension**
- **Excessive sweating (hyperhidrosis)**
- **Vasospasm (Raynaud's phenomenon)**

PARASYMPATHETIC OVERACTIVITY:

- **Gastric hyperacidity**
- **Irritable bowel syndrome**

OTHER AUTONOMIC DYSFUNCTIONS

Horner's syndrome

- A sympathetic disruption in the cervical sympathetic pathway from the hypothalamus to the eye.

Neurogenic syncope

- Neurocardiogenic syncope (or vasovagal syncope) is the commonest type of reflex syncope.
- There is an abnormal autonomic response, causing vasodilation and increased vagal tone.

Orthostatic hypotension

- An efferent sympathetic vasomotor fibers disruption.
- It causes a prolong drop in blood pressure after postural change (from lying down to standing).

Neurogenic erectile dysfunction

- It is caused by a deficit in nerve signaling to the penis corpora cavernosa.

AUTONOMIC PHARMACOLOGY

Sympathetic NS	Parasympathetic NS
Drugs that **mimic** noradrenaline: • adrenergic / • adrenergic agonist/ • sympathomimetic	Drugs that **mimic** acetylcholine: • cholinergic/ • muscarinic agonists
Drugs that **block** noradrenaline • anti-adrenergic/ • adrenergic antagonist/ • sympatholytic	Drugs that **block** acetylcholine • anti-cholinergic • muscarinic antagonist • parasympatholytic

AUTONOMIC PHARMACOLOGY: EXAMPLESOF DRUGS

ADRENERGICS

Agonists:

- Norepinephrine (α1)
  Phenylephrine (α1)
- Clonidine (α2)
- Norepinephrine (β1)
- Isoproterenol (β1)
- Epinephrine (β2)
- Isoproterenol (β2)
- Albuterol (β2)

Antagonists:

- Phenoxybenzamine (α1)
- Yohimbine (α2)
- Propranolol (β1)
- Metoprolol (β1)
- Propranolol (β2)
- Butoxamine (β2)

CHOLINERGICS

Nicotinic Agonist:

- ACh Nicotine
  Carbachol

Nicotinic Antagonist:

- Curare

Muscarinic Agonist:

- ACh Muscarine
  Carbachol

Muscarinic Antagonist:

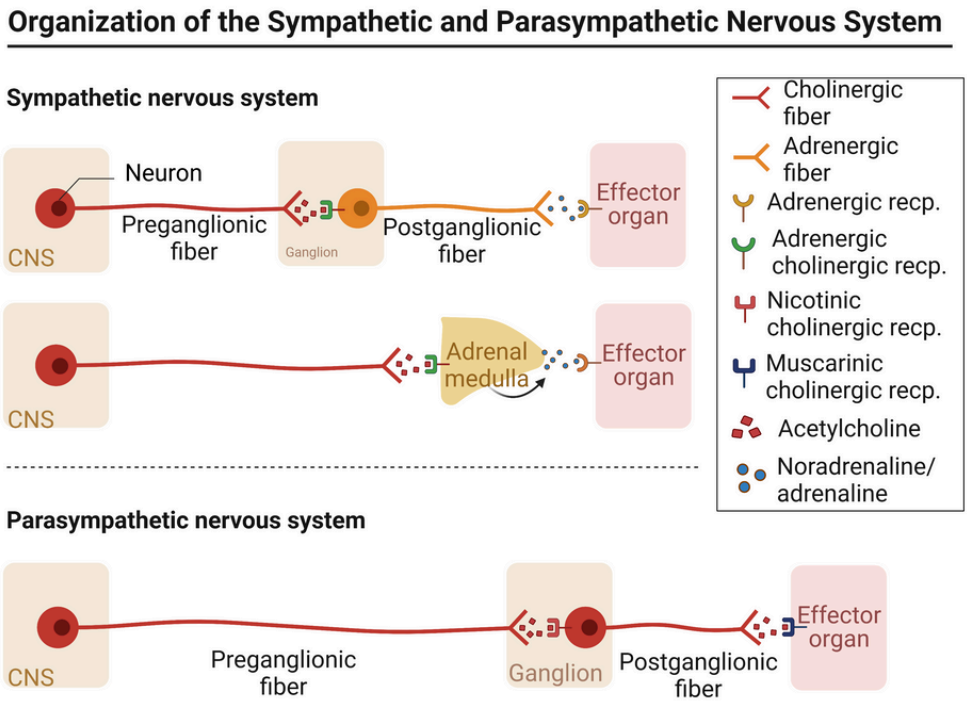
- Atropine

Summary

ANS Organization: Structural Characteristics

Characterized by:	Sympathetic NS	Parasympathetic NS
Location of preganglionic neuron cell bodies	• T1-L2 segments (within lateral horns of spinal cord)	• S2-S4 segments • Cranial nerves nuclei III, VII, IX, X (brainstem)
Location of ganglia from the effector organ	• Away	• Near
Postganglionic neurons • **Length** • **(Pre-G neu) Synapse**	• Long • Preganglionic neu. axon synapses with MANY postganglionic neu. of more than 1 effector organ	• Short • Preganglionic neu. synapses with postganglionic neu. of a SINGLE effector organ.
Principal neurotransmitters (at postganglionic neuron terminals)	• Noradrenaline • Adrenaline	• Acetylcholine
Effector organ receptors	• α-adrenoreceptor • β-adrenoreceptor	• Muscarinic receptor
Effects & Function	• Fight-or-flight	• Rest & digest

ANS Organization: Neurotransmitter, Receptor & Effector Organs



REFERENCES

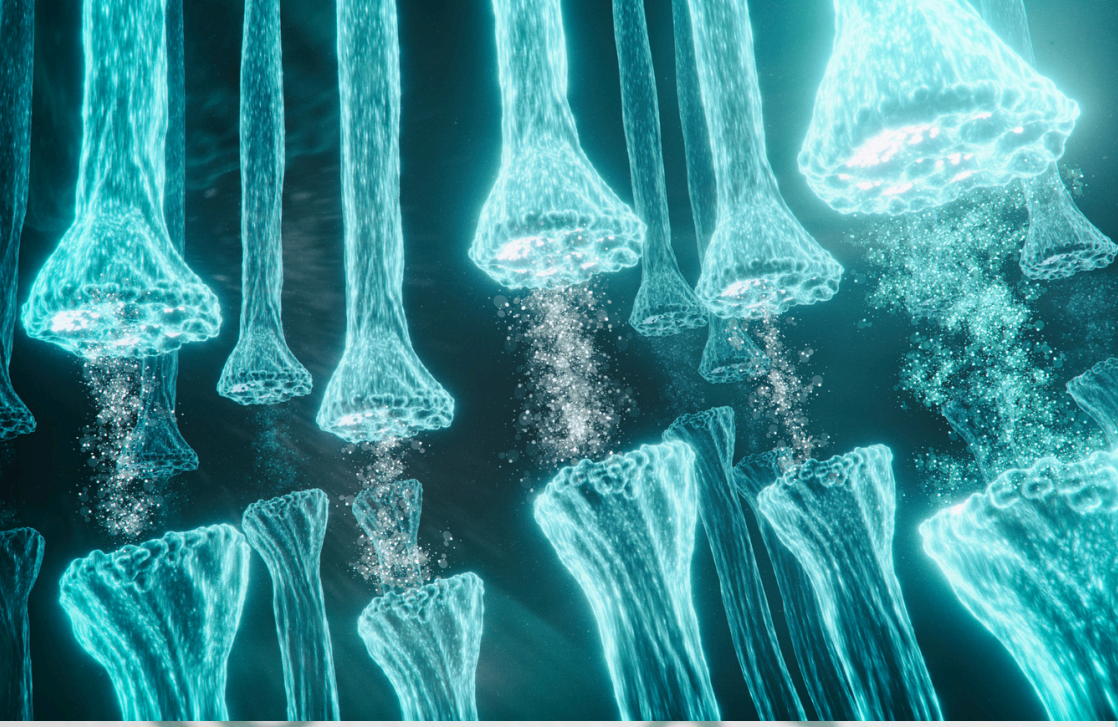
Barrett, K. E. & Ganong, W. F. (2016). Ganong's review of medical physiology (25th ed.). Mac Graw Hill.

Costanzo, L. S. (2021). *Costanzo Physiology*. Elsevier Health Sciences

Hall. J.E & Guyton A.C (2016). Guyton and Hall textbook of medical physiology (13th ed.). Elsevier.

Sherwood, L. (2016). Human physiology: From cells to systems (9th ed.). Cengage Learning.

The contents are based on the author's experience in teaching physiology and reliable sources for the relevant topics.



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