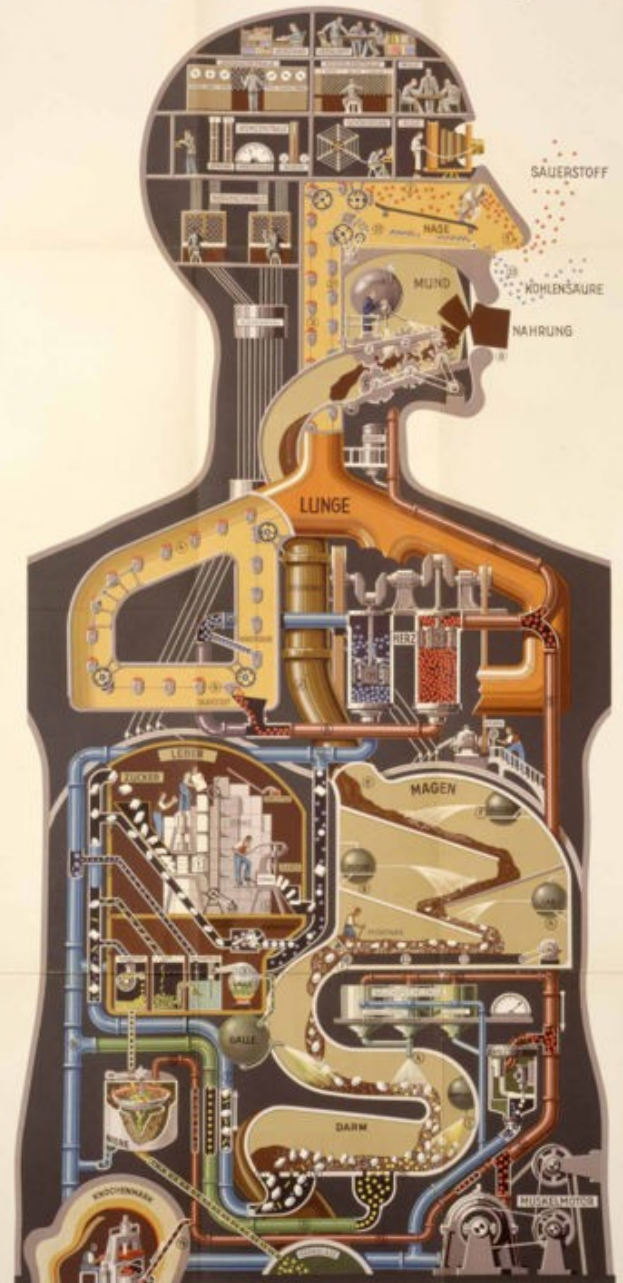


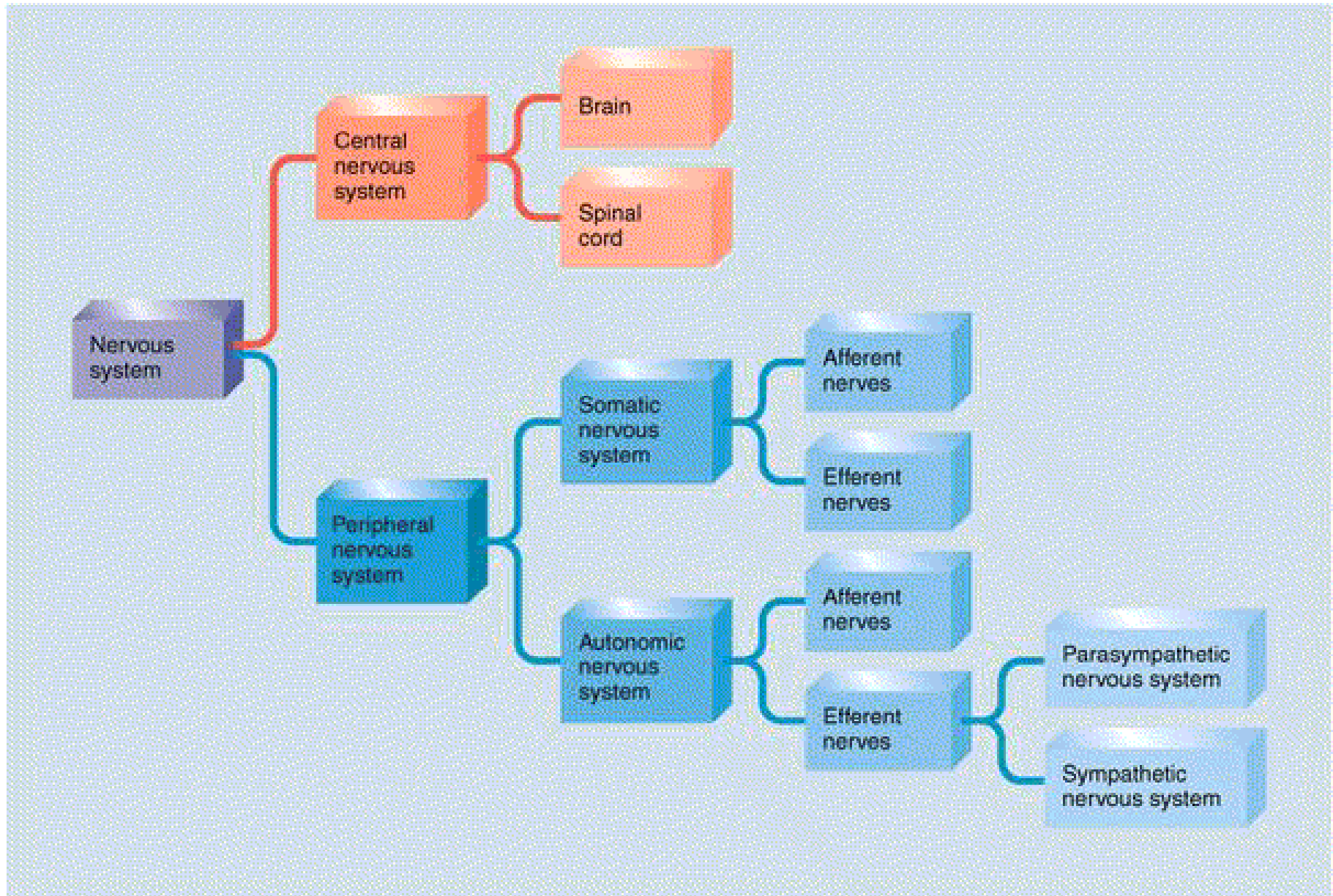
# PHYSIOLOGY OF AUTONOMIC NERVOUS SYSTEM

## Der Mensch als Industriepalast



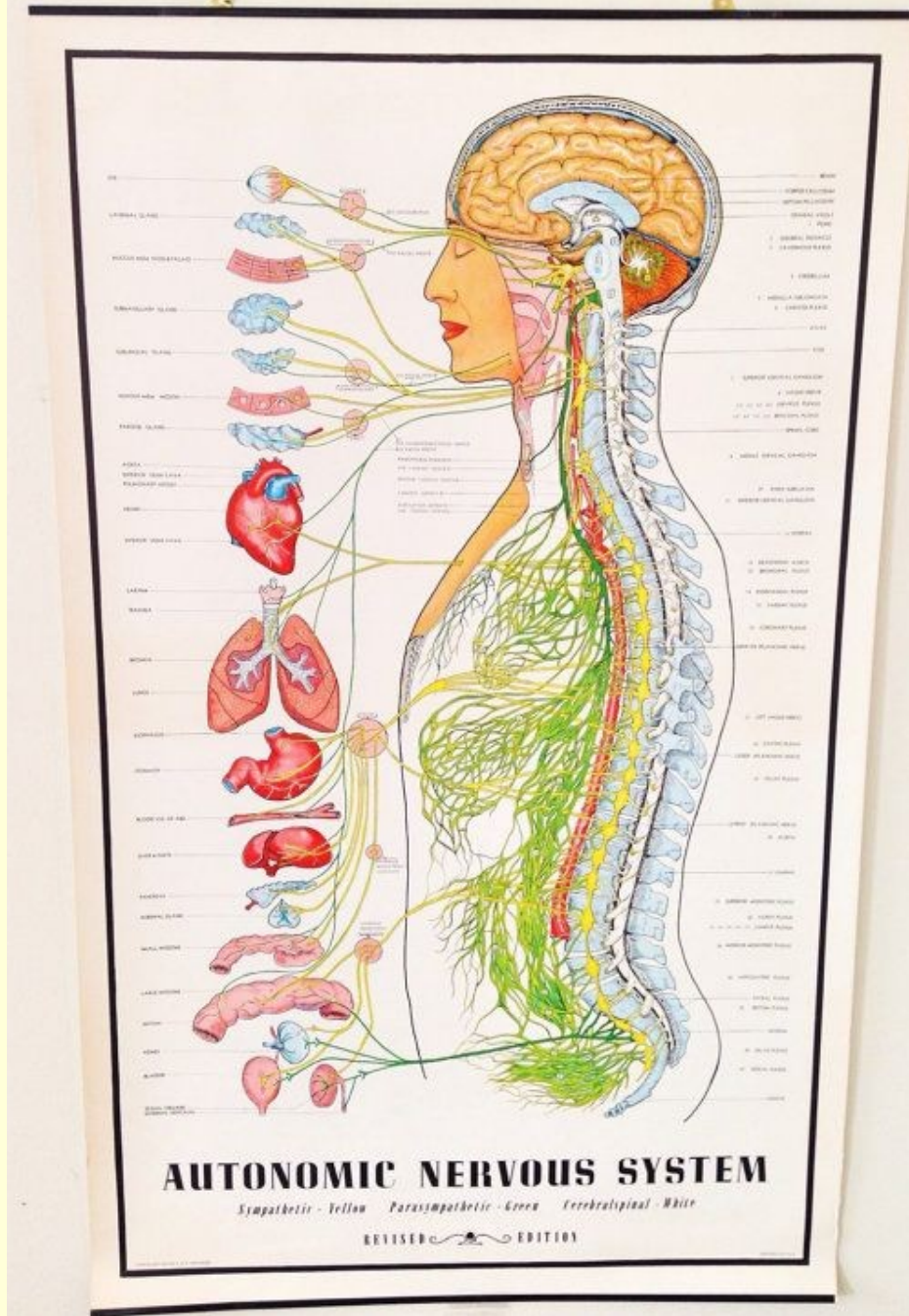
Aus Kahn, DAS LEBEN DES MENSCHEN / Franckh'sche Verlagsbuchhandlung, Stuttgart /

## ► Major Divisions of the Nervous System



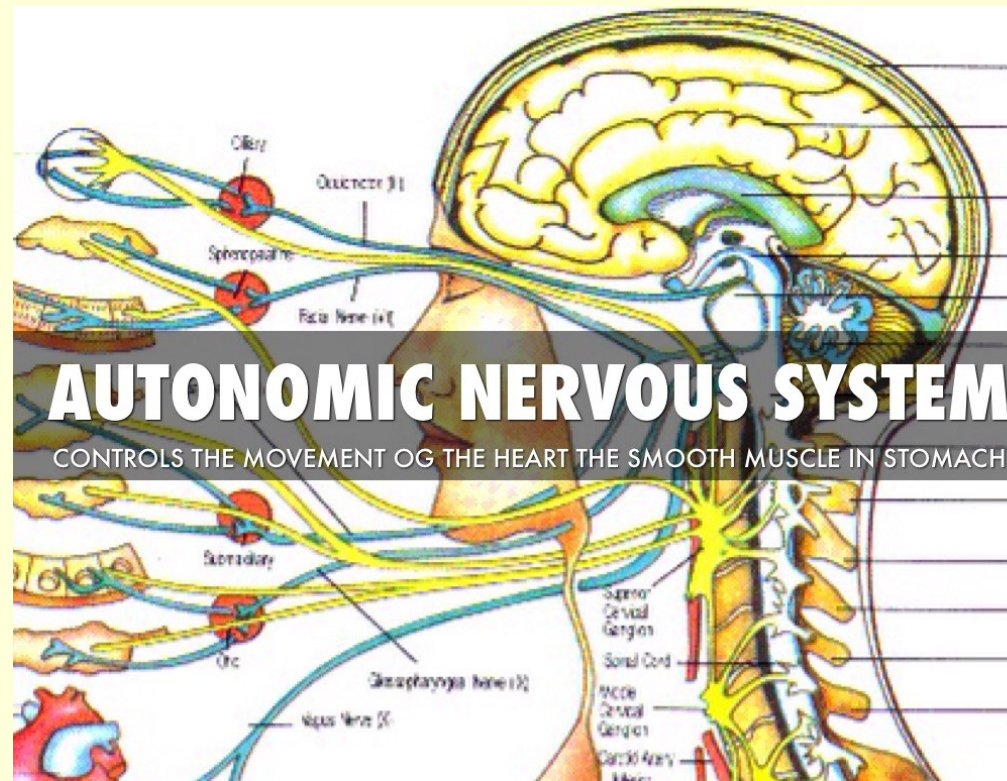
# ANS

- The autonomic nervous system consists of peripheral afferent and efferent neurons, and other neurons constituting a widespread CNS representation.



# ANS

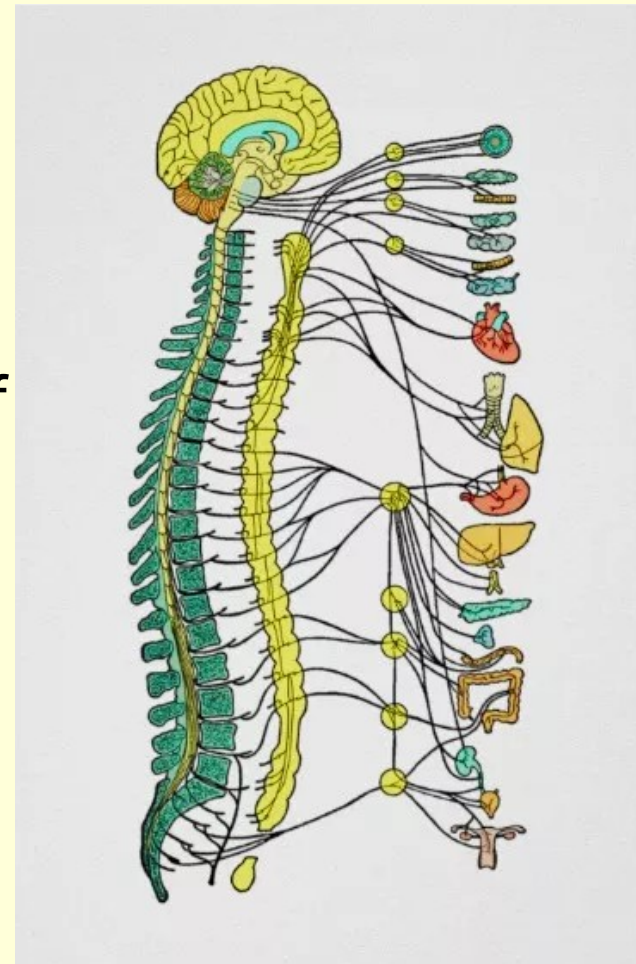
- ANS regulates the organism's internal environment and controls physical exchanges between the organism and the external environment.
- Together with the endocrine system, the ANS provides for homeostasis.



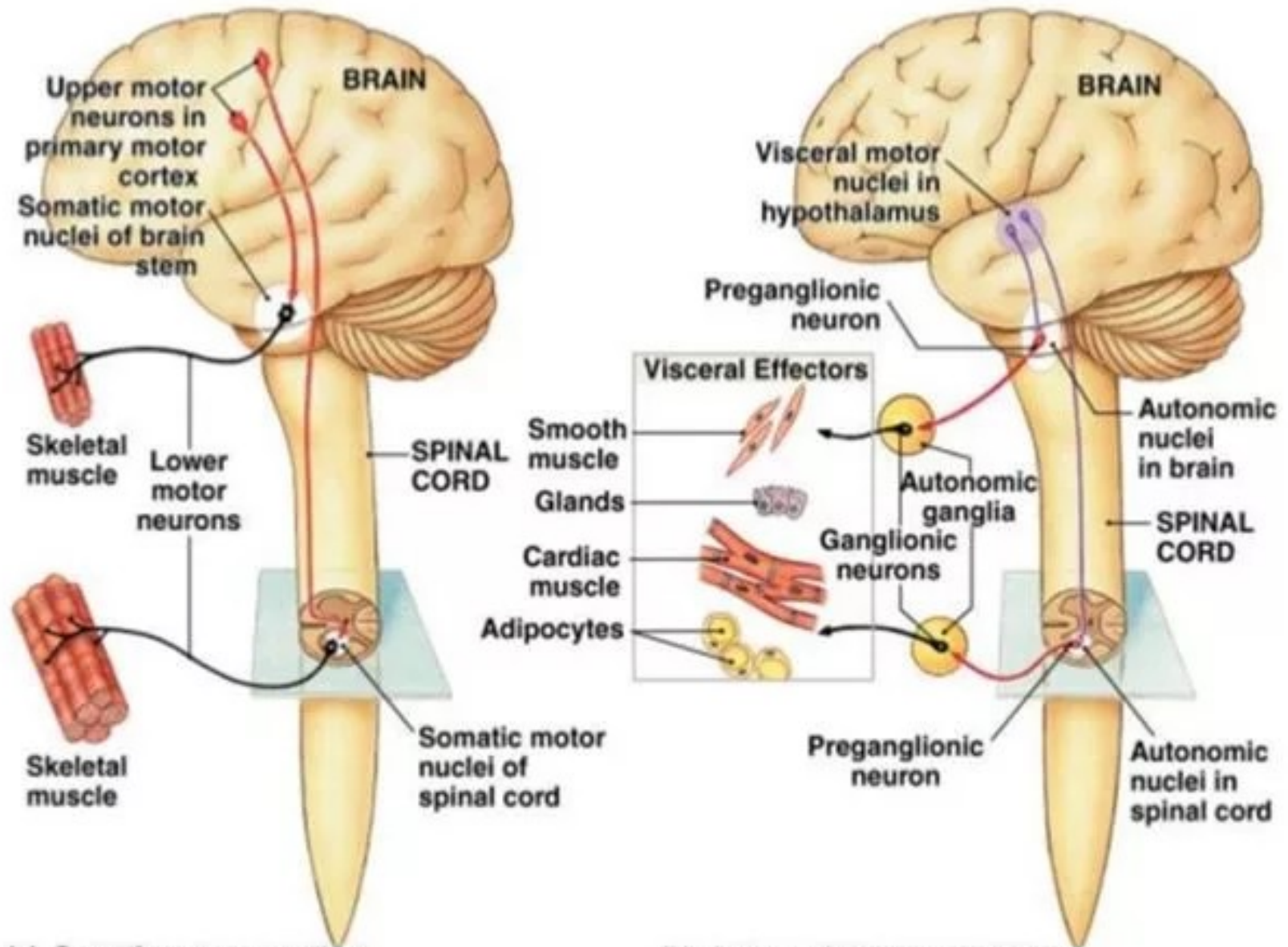
# HISTORY

The term “**autonomic nervous system**” being originally proposed by the Cambridge based Professor **James Langley**, is also called the “**vegetative nervous system**”, a term coined by **Reil** in 1807.

**Gaskell** (a London based Professor and the first editor of the Journal of Physiology) christened ANS as “**involuntary nervous system**” (involuntary, because, it is not under volition).



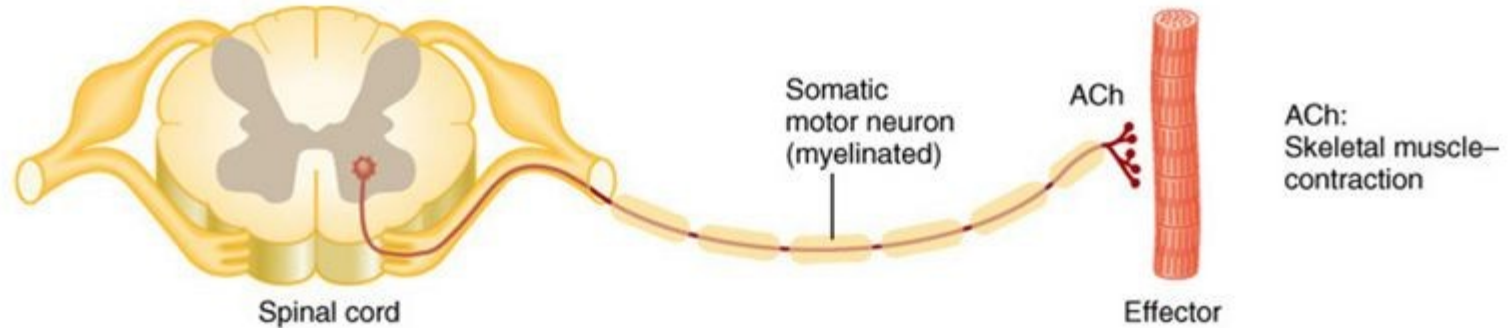
# Somatic vs. Autonomic



(a) Somatic nervous system

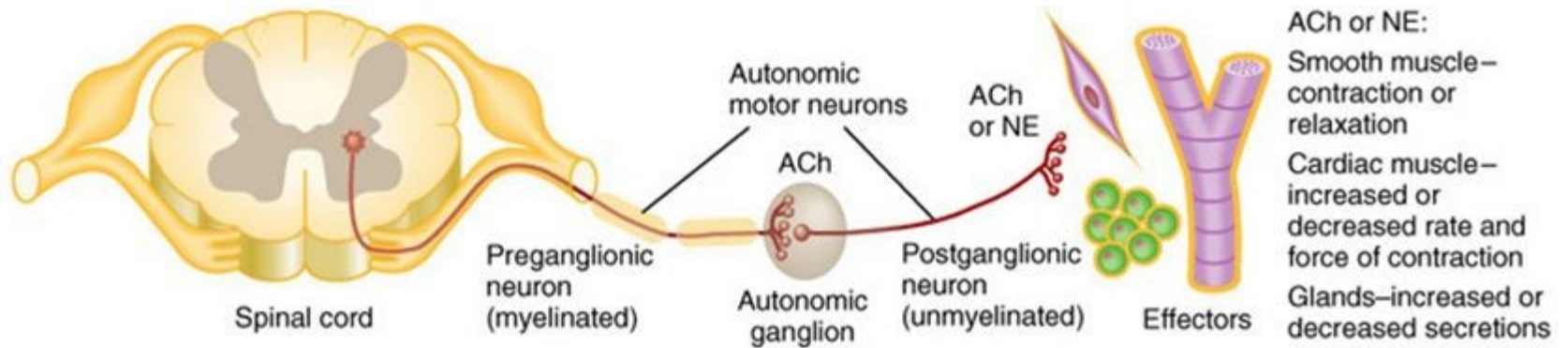
(b) Autonomic nervous system

# Comparison of Somatic and Autonomic Nervous Systems



(a) Somatic nervous system

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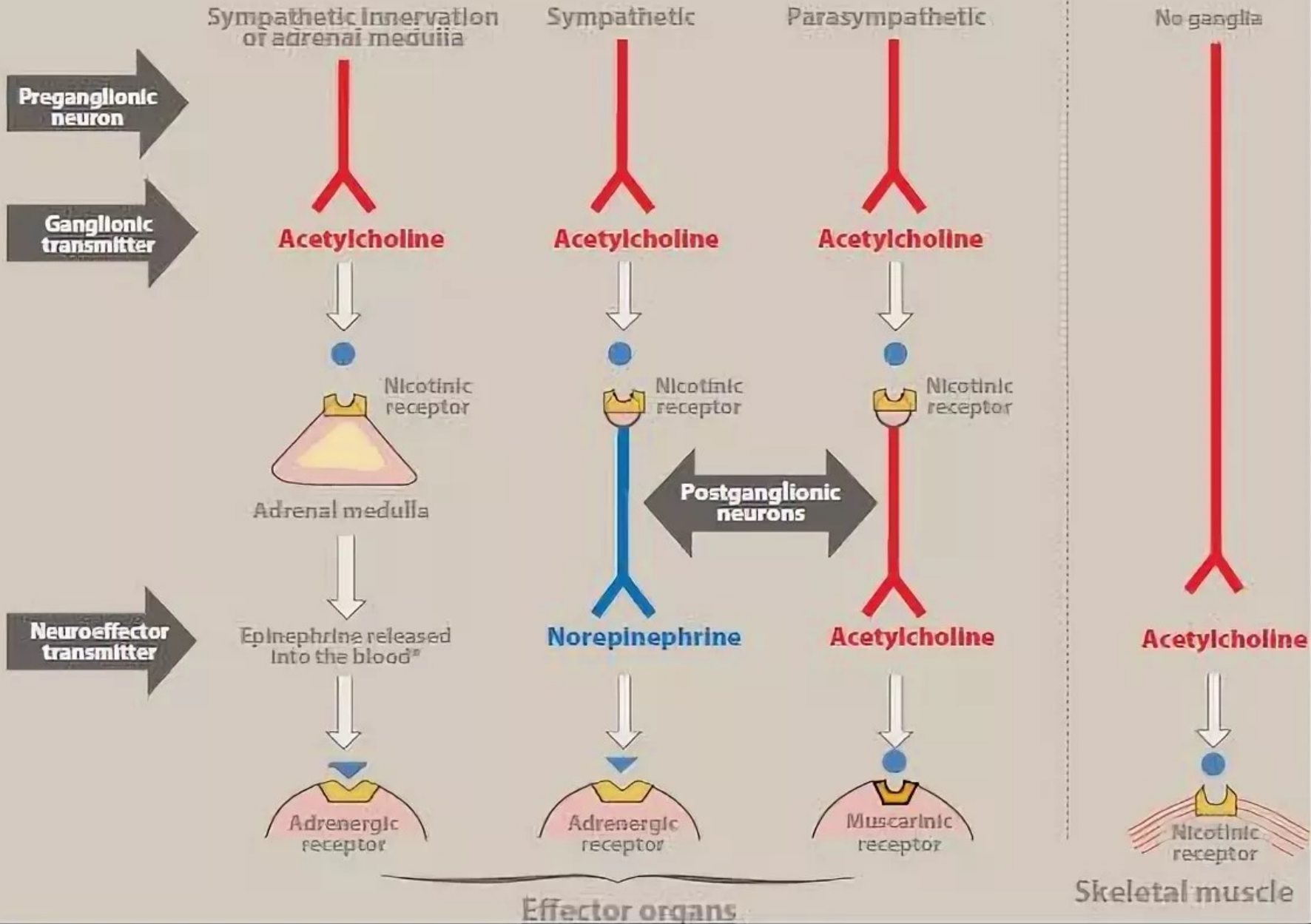


(b) Autonomic nervous system

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# AUTONOMIC

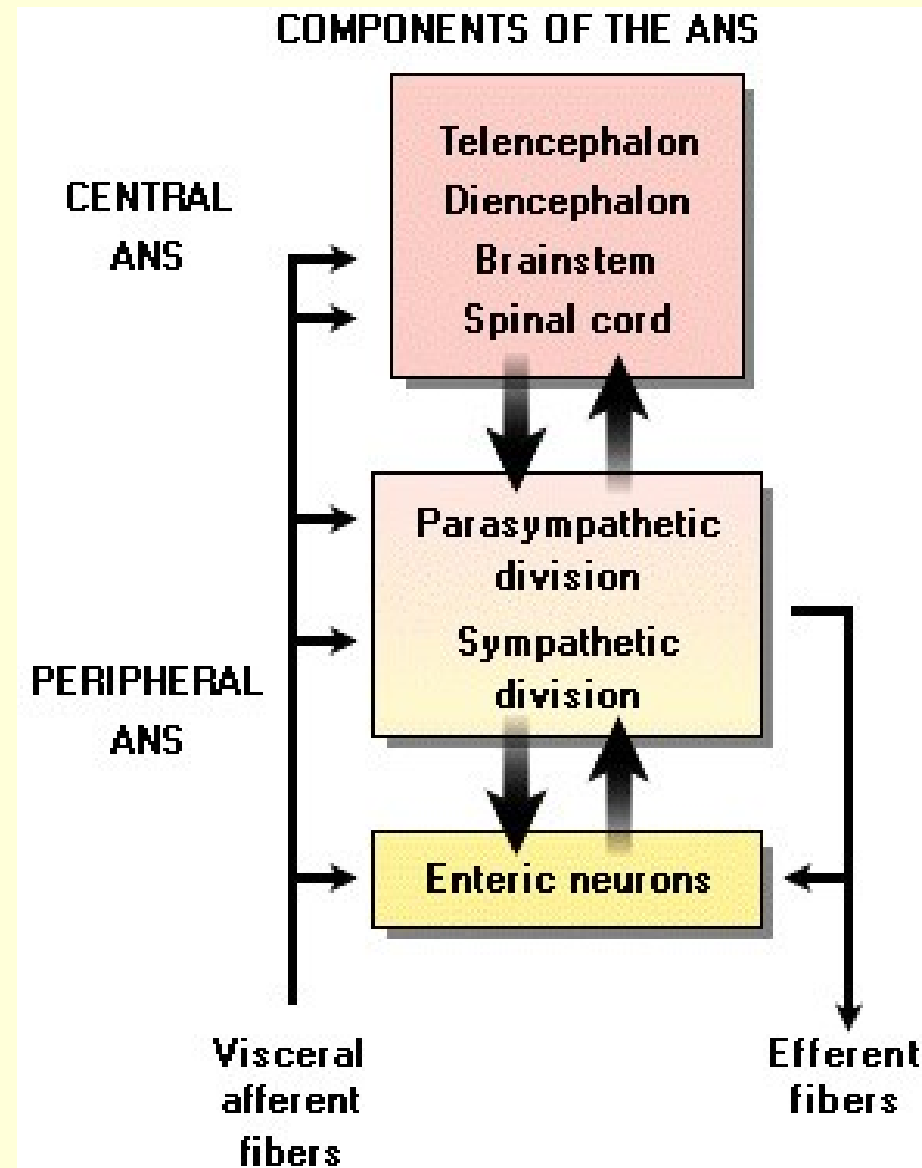
# SOMATIC





# Central & peripheral ANS

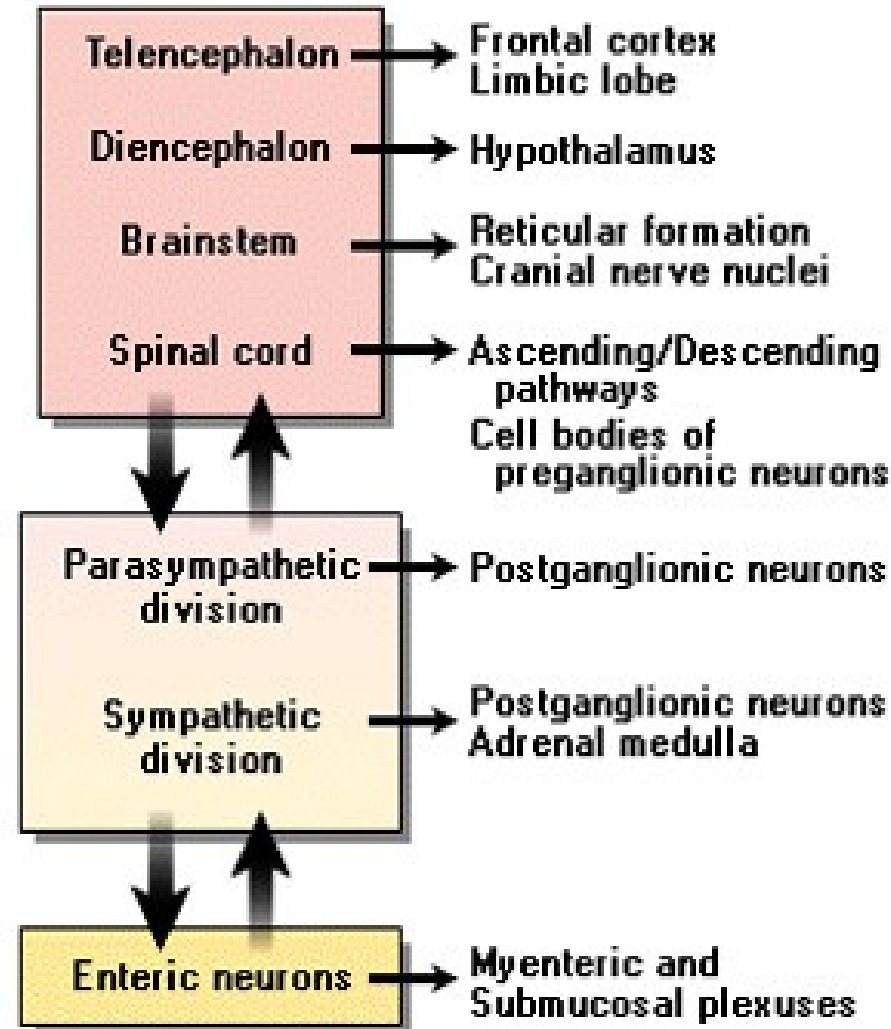
- *The central ANS* is quite diffuse, consisting of tracts and regions of gray matter in the spinal cord, brainstem, diencephalon, and telencephalon.
- *The peripheral ANS* includes the neurons of the parasympathetic and sympathetic divisions, the enteric neurons of the gut, and visceral afferent fibers.



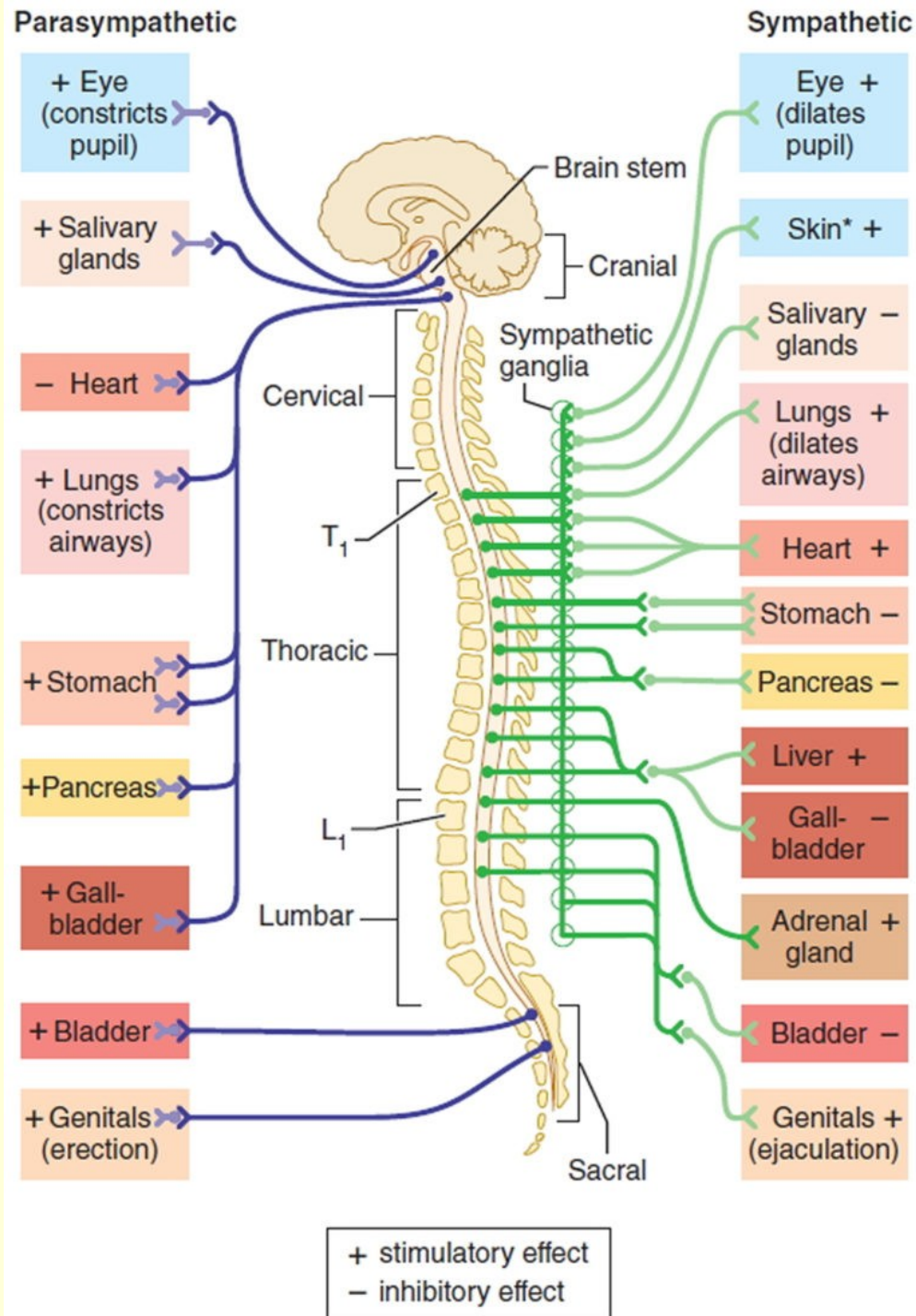
# Two divisions of ANS

- “Parasympathetic” nervous system – “craniosacral” (arises from the brain and sacral part of the spinal cord – L5-S5).
- “Sympathetic” nervous system – “thoracolumbar” (arises from the thoracic and upper lumbar segments of the cord – C8-L4).

## COMPONENTS OF THE ANS

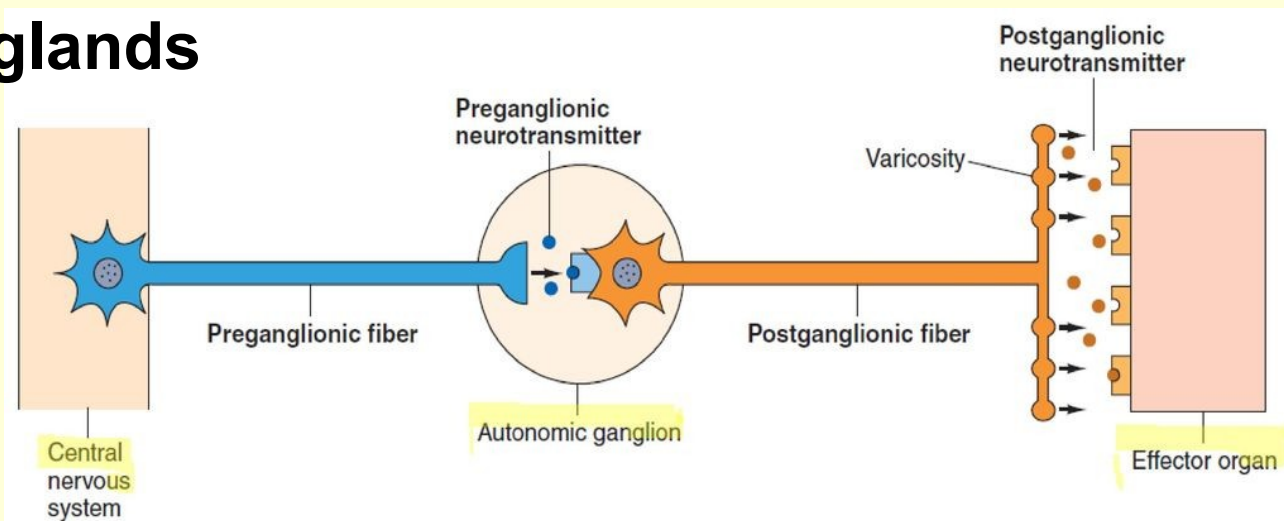


# Two divisions of ANS



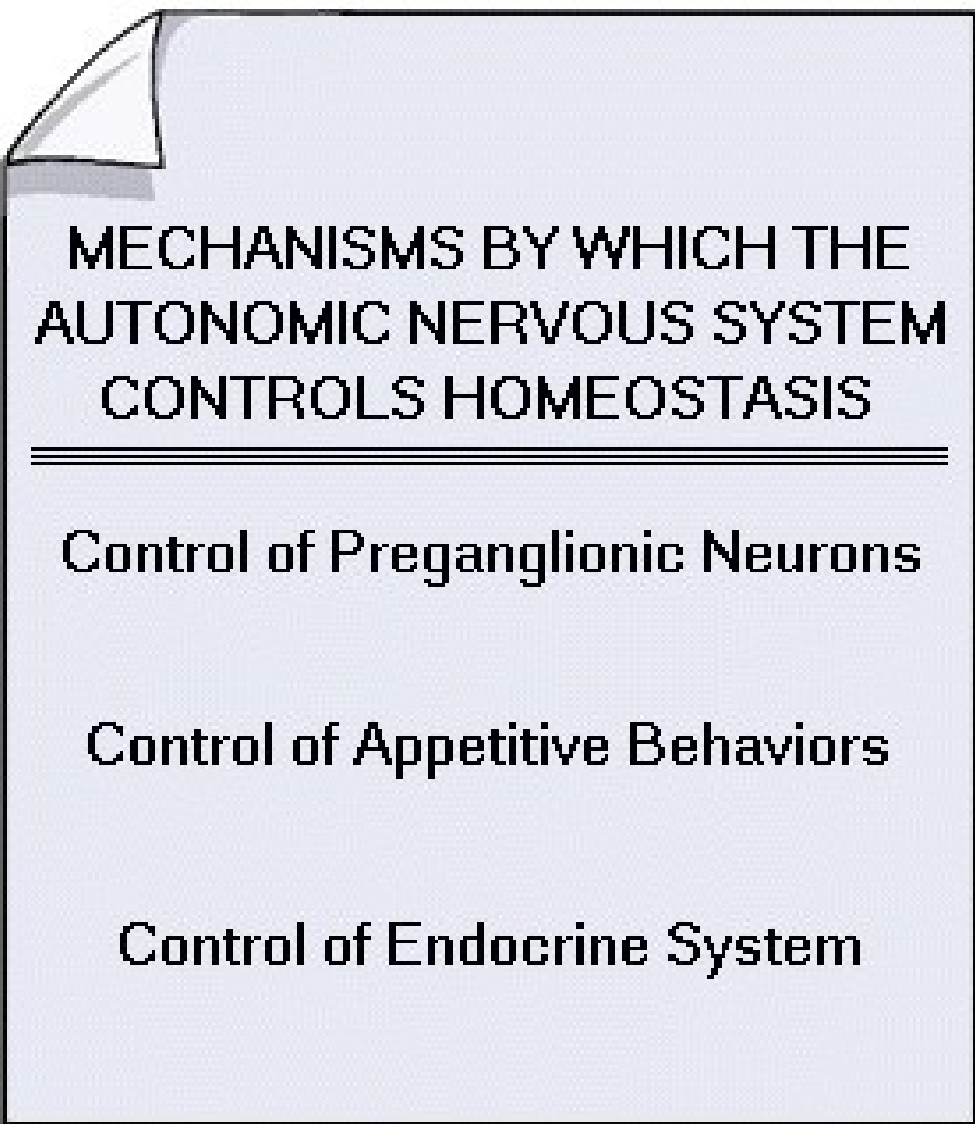
# Afferent & efferent ANS fibers

- The *afferent* of autonomic fibers bring information from the viscera (visceral pain sensation).
- The *efferent* (motor) fibers of autonomic system supply:
  - smooth muscles
  - cardiac muscles
  - exocrine glands



# The Central ANS (first)

The central ANS provides for homeostasis by three main routes. First, it controls the viscera via its connections to preganglionic neurons that control the heart, smooth muscle, and glands of the body through parasympathetic and sympathetic neurons.



## MECHANISMS BY WHICH THE AUTONOMIC NERVOUS SYSTEM CONTROLS HOMEOSTASIS

Control of Preganglionic Neurons

Control of Appetitive Behaviors

Control of Endocrine System

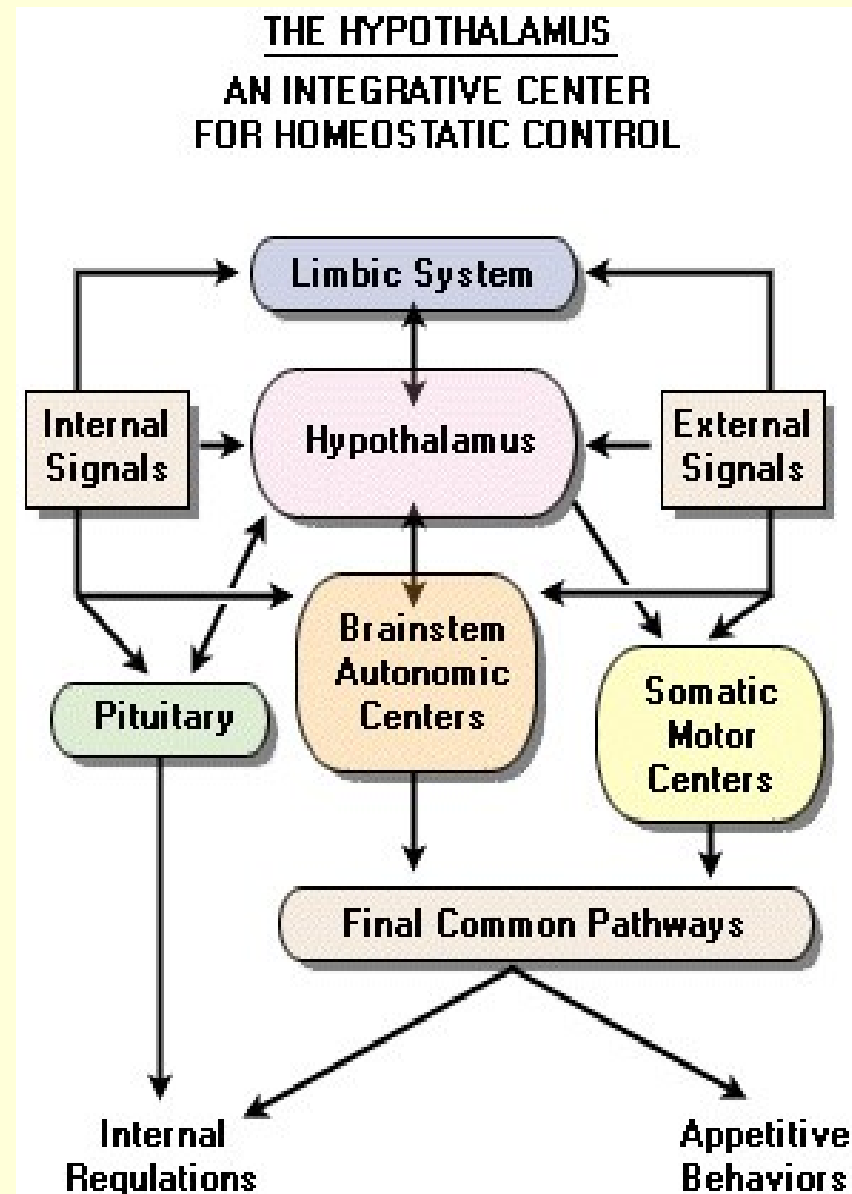
# The Central ANS (second)

- It controls behaviors responsible for physical exchanges between the organism and its environment via its connections to motivational and somatic motor pathways.
- Such behaviors are called "appetitive", meaning "appetite satisfying", and include ingestive (eating and drinking), excretory (micturition and defecation), and reproductive (mating and parturition) behaviors.
- Its control of the endocrine system contributes to both of the foregoing control mechanisms.

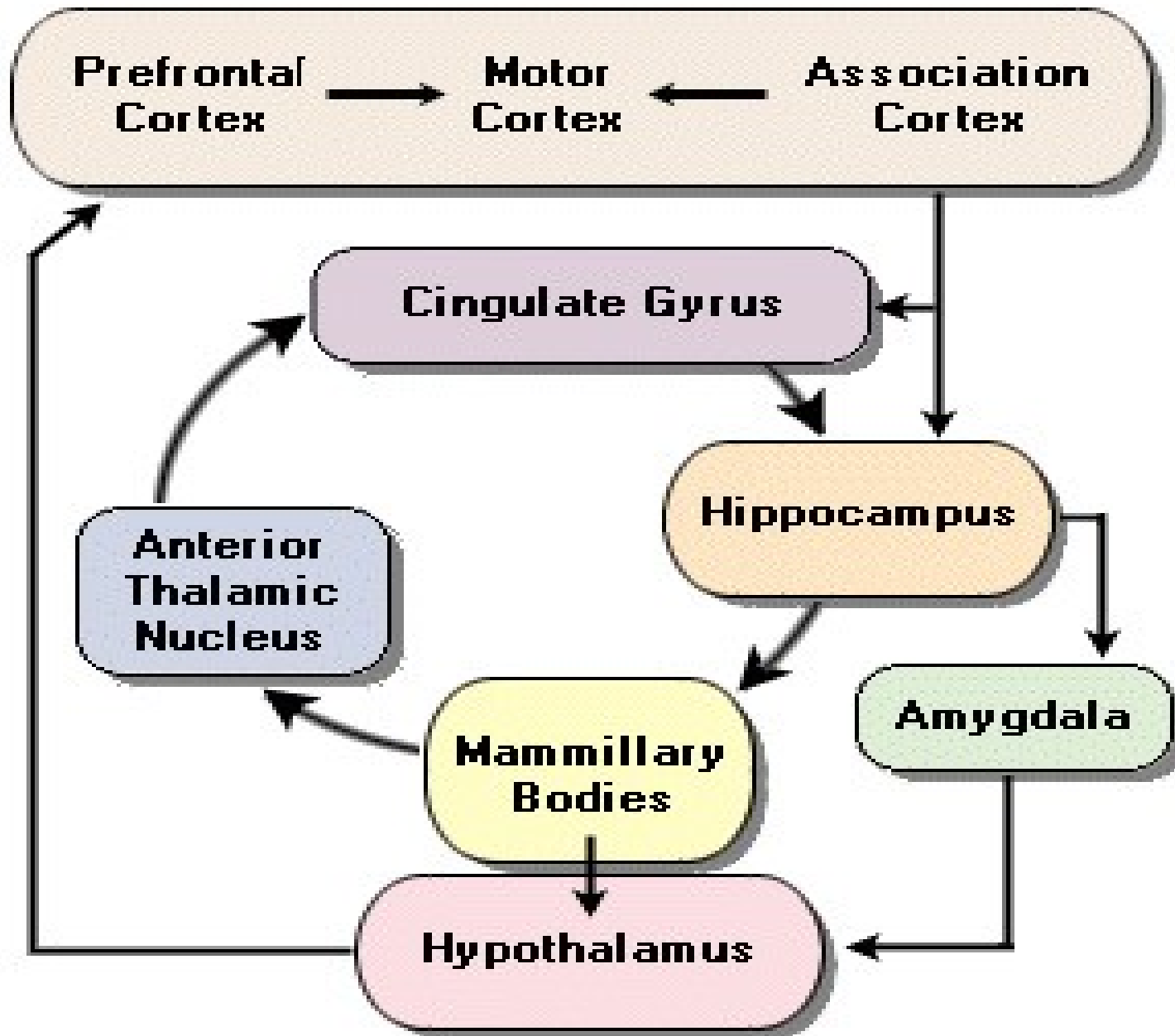


# The Central ANS (third)

- Within the central ANS, the hypothalamus is the major integrative center for homeostatic control.
- Technically, the hypothalamus is part of the limbic system, that provides for mood and affect, the appreciation of our emotional state.



# HYPOTHALAMIC CONNECTIONS WITH THE LIMBIC SYSTEM



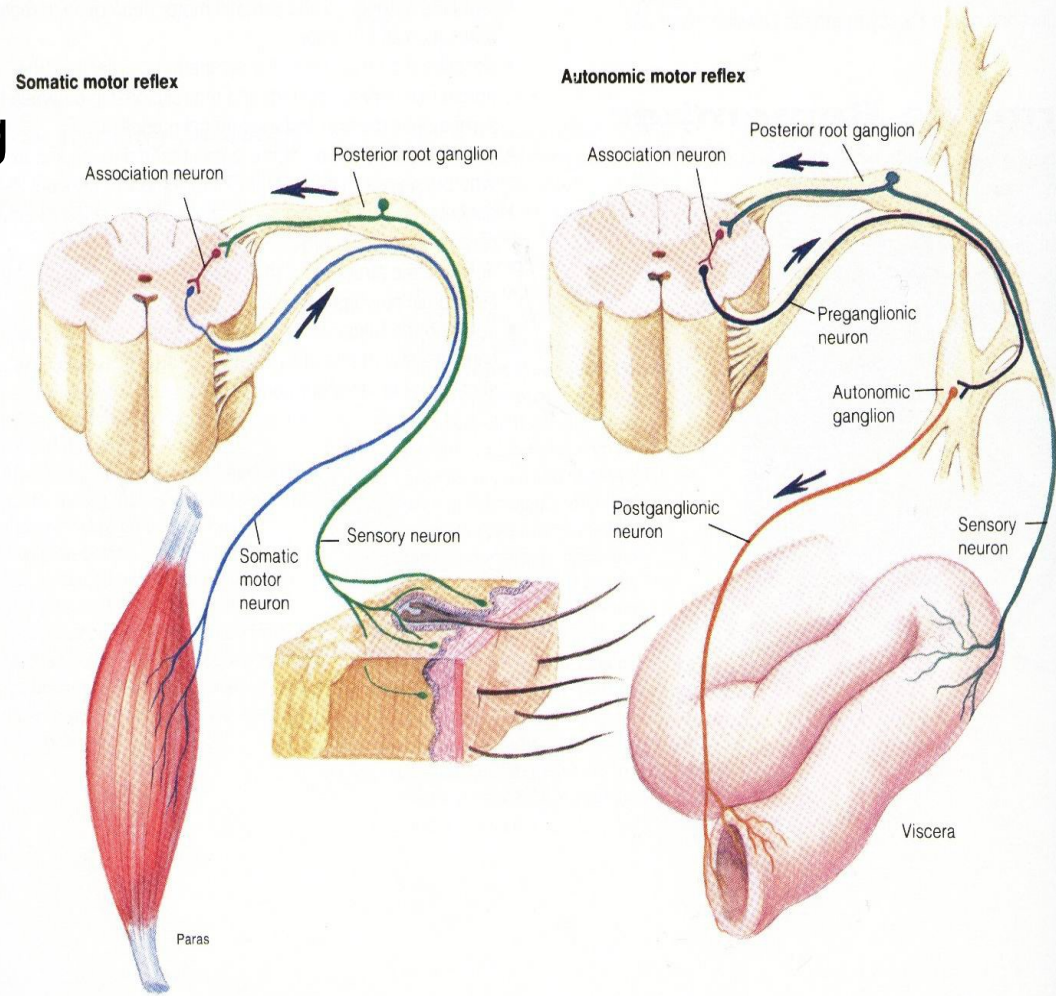


# The Peripheral ANS

The ANS is said to be responsible for preparing the body for the four F's:

- fighting
- fleeing
- feeding
- fooling around

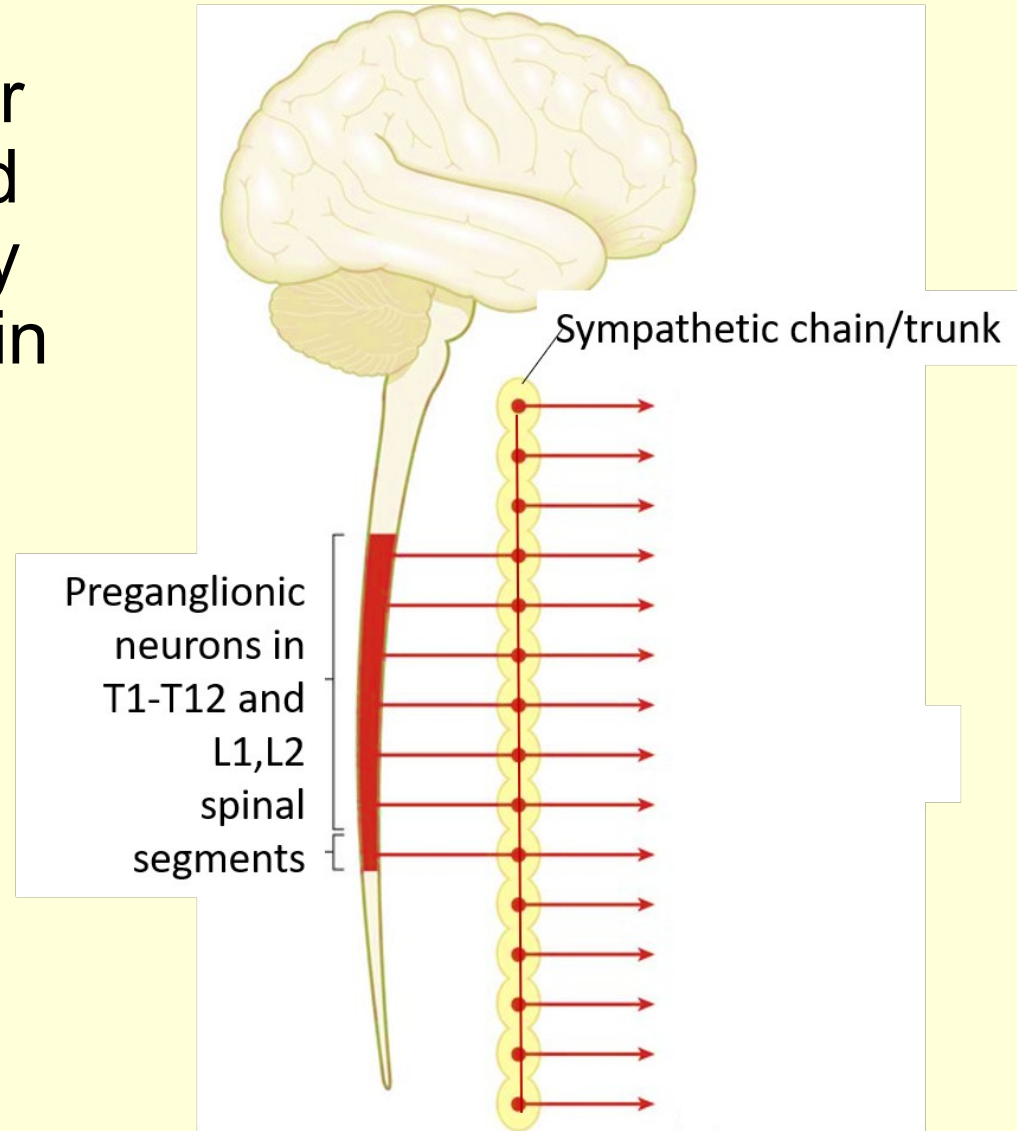
- The *sympathetic* division establishes conditions appropriate for *fight or flight*.
- The *parasympathetic* division for *feeding or fooling around*.



A comparison between a somatic motor reflex and an autonomic motor reflex.

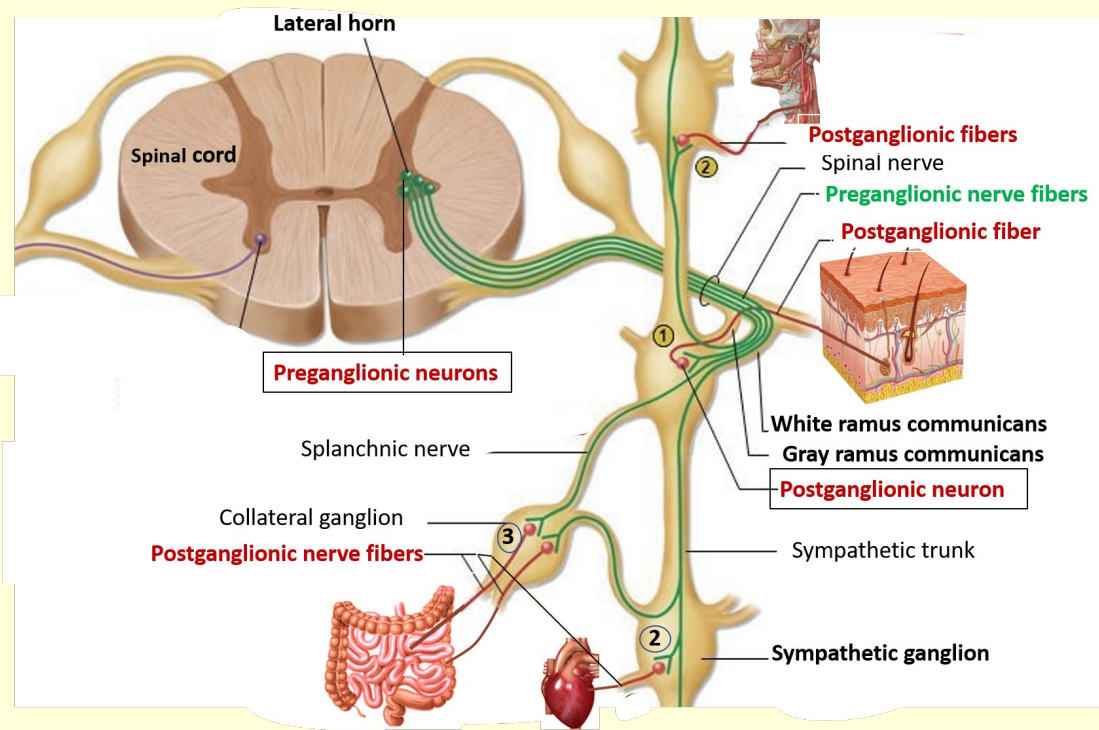
# THE SYMPATHETIC SYSTEM

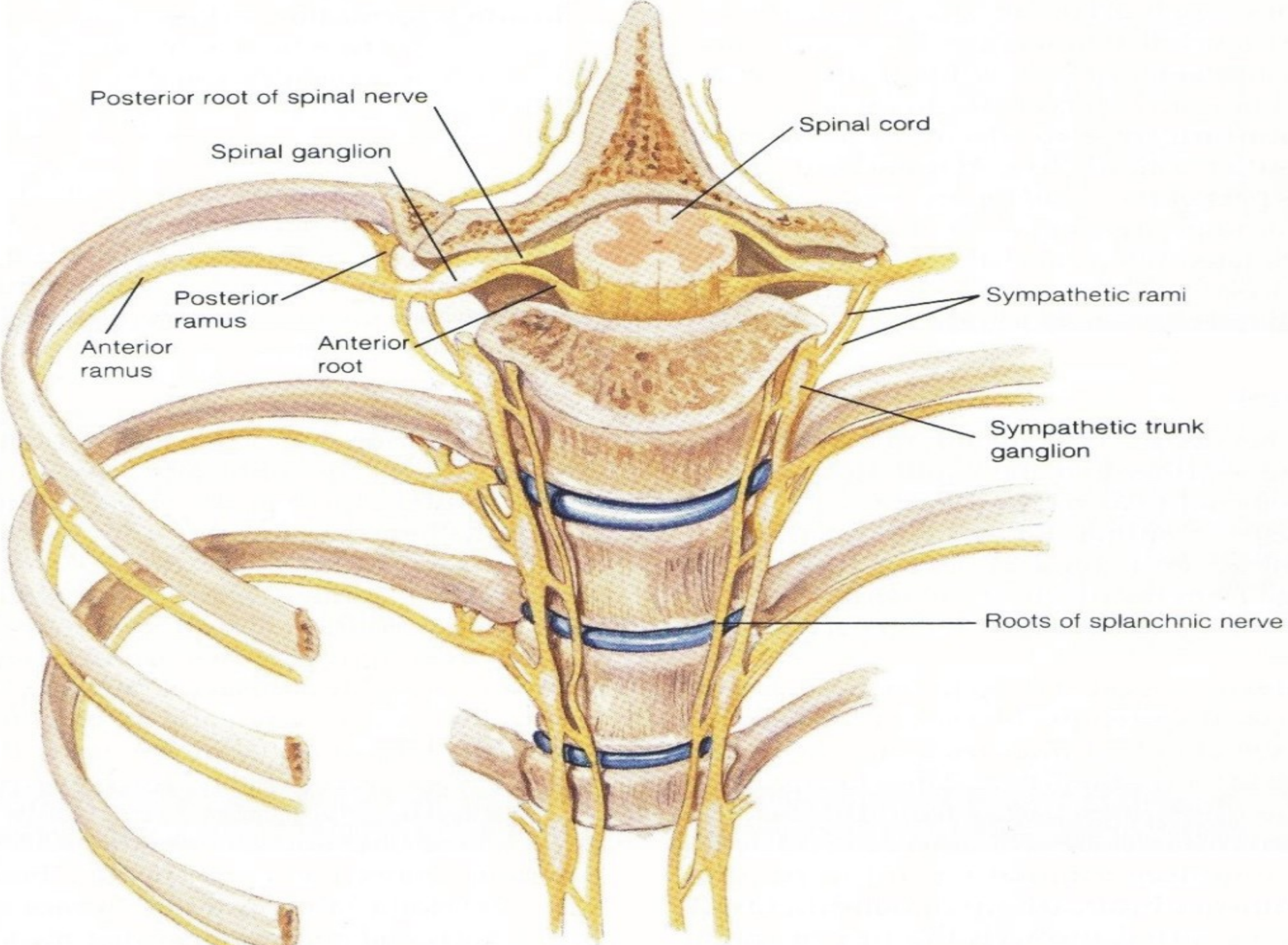
- The preganglionic fiber moves up or down and then synapses, usually with several neurons, in the trunk. From these synapses the postganglionic nerve fibers emerge and proceed to their destination.



# THE SYMPATHETIC SYSTEM

- Some preganglionic fibers leave the sympathetic trunk, still as preganglionic fibers, (i.e. without synapsing) and enter in another ganglion outside the sympathetic trunk (e.g. collateral ganglion) to synapse with the next order neuron (the postganglionic fiber).





Posterior root of spinal nerve

Spinal ganglion

Spinal cord

Anterior ramus

Posterior ramus

Anterior root

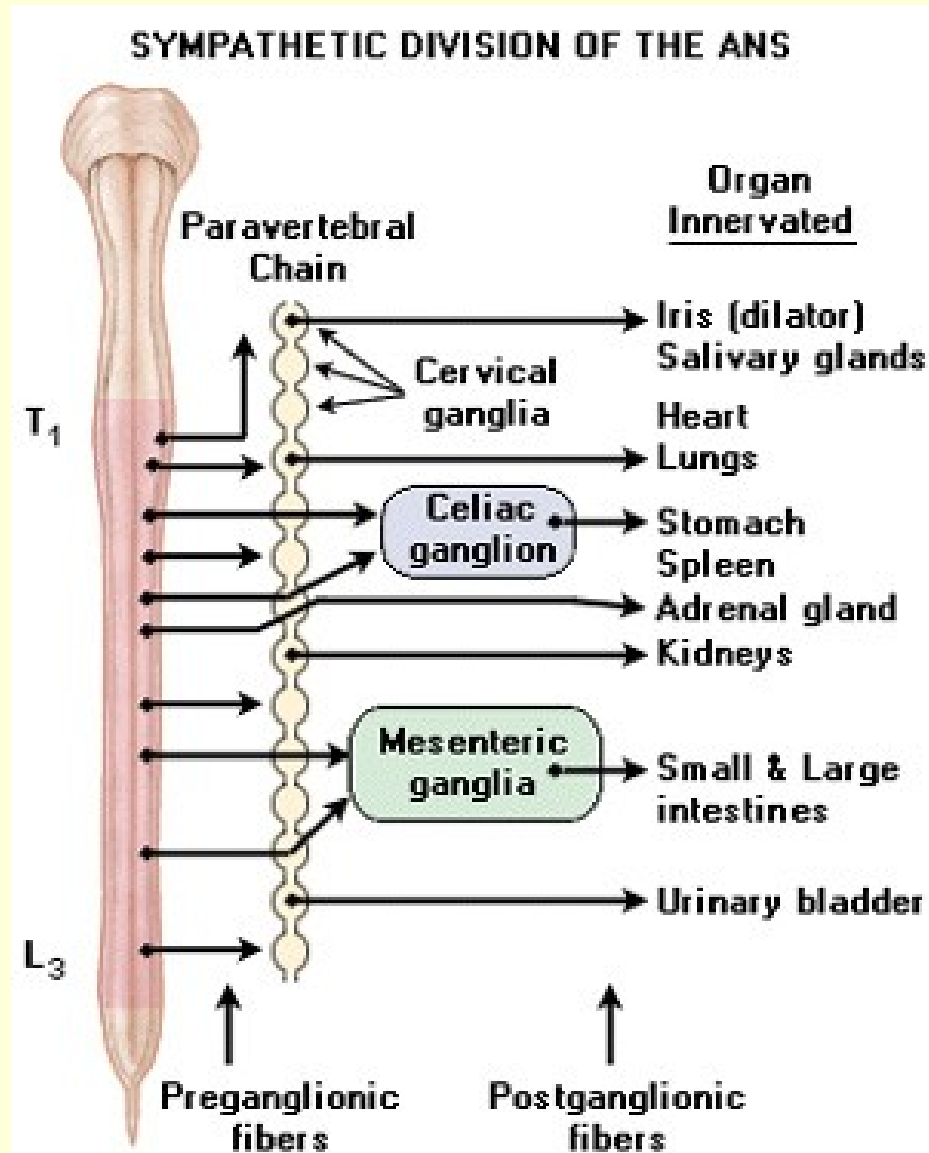
Sympathetic rami

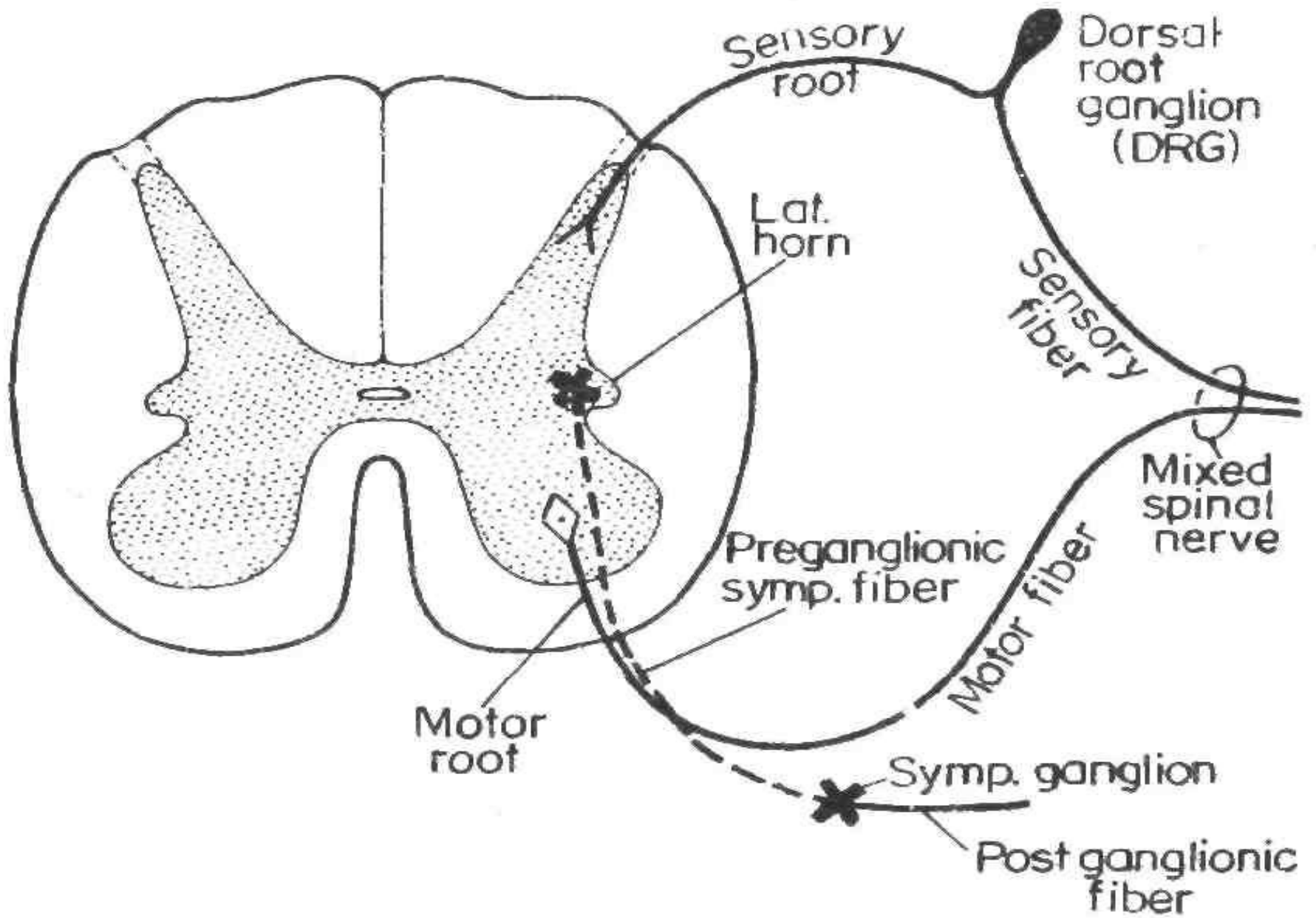
Sympathetic trunk ganglion

Roots of splanchnic nerve

# THE SYMPATHETIC SYSTEM

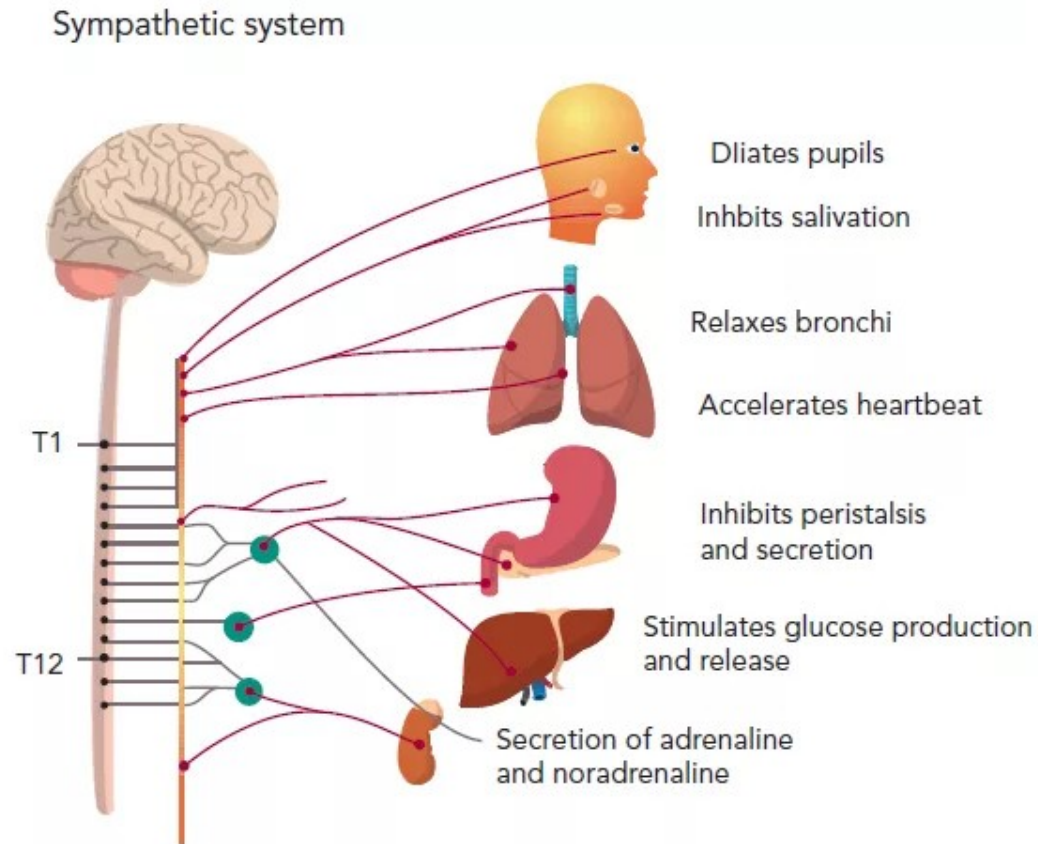
- The post ganglionic fibers, which emerge from the sympathetic trunk (chain) to join a spinal nerve, do so as gray rami communicantes (because these post ganglionic fibers are non medullated, they look grayish).

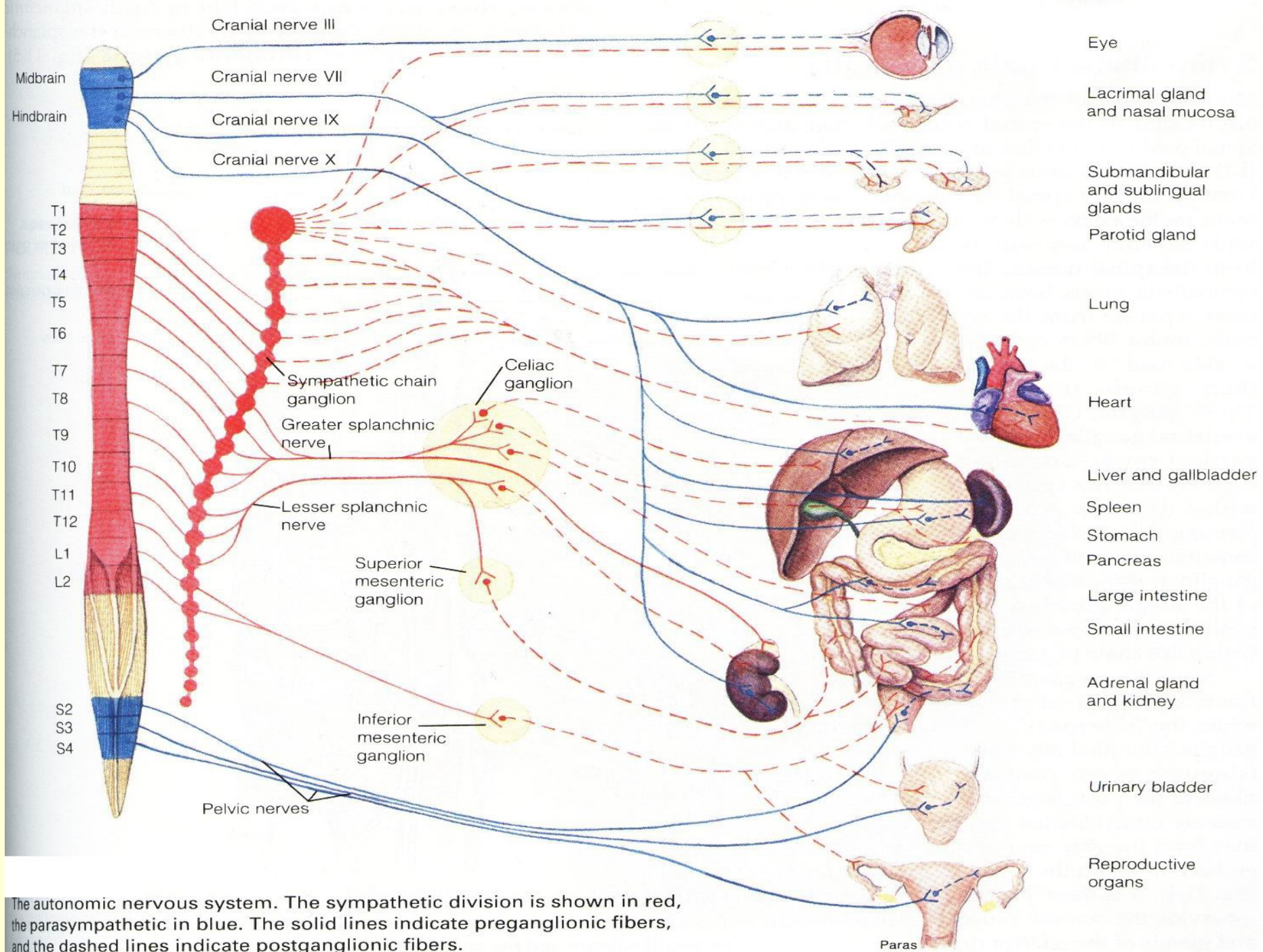




# The structures innervated by the postganglionic nerve fibers

- 1) the smooth muscles (respiratory tract, vascular tree, gastrointestinal tract);
- 2) the heart muscles;
- 3) the sweat glands;
- 4) the arrector pili muscles of the skin;
- 5) exocrine glands (salivary, pancreas, gastric glands).





The autonomic nervous system. The sympathetic division is shown in red, the parasympathetic in blue. The solid lines indicate preganglionic fibers, and the dashed lines indicate postganglionic fibers.

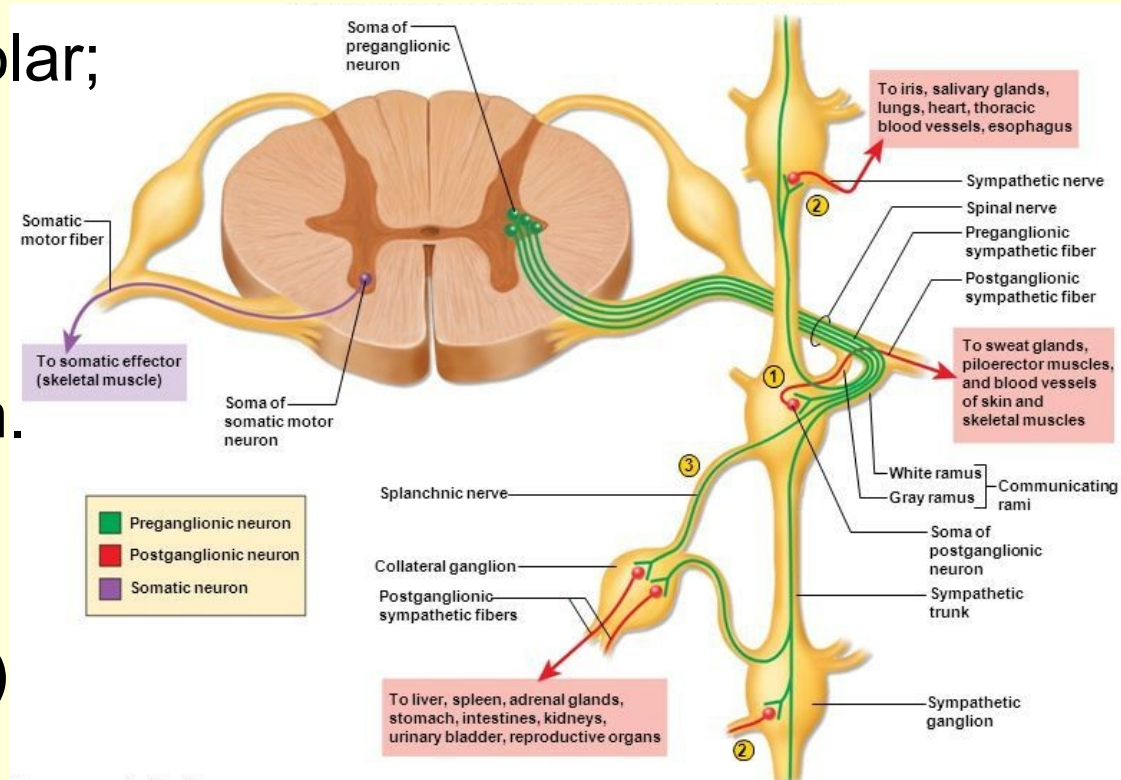
Paras

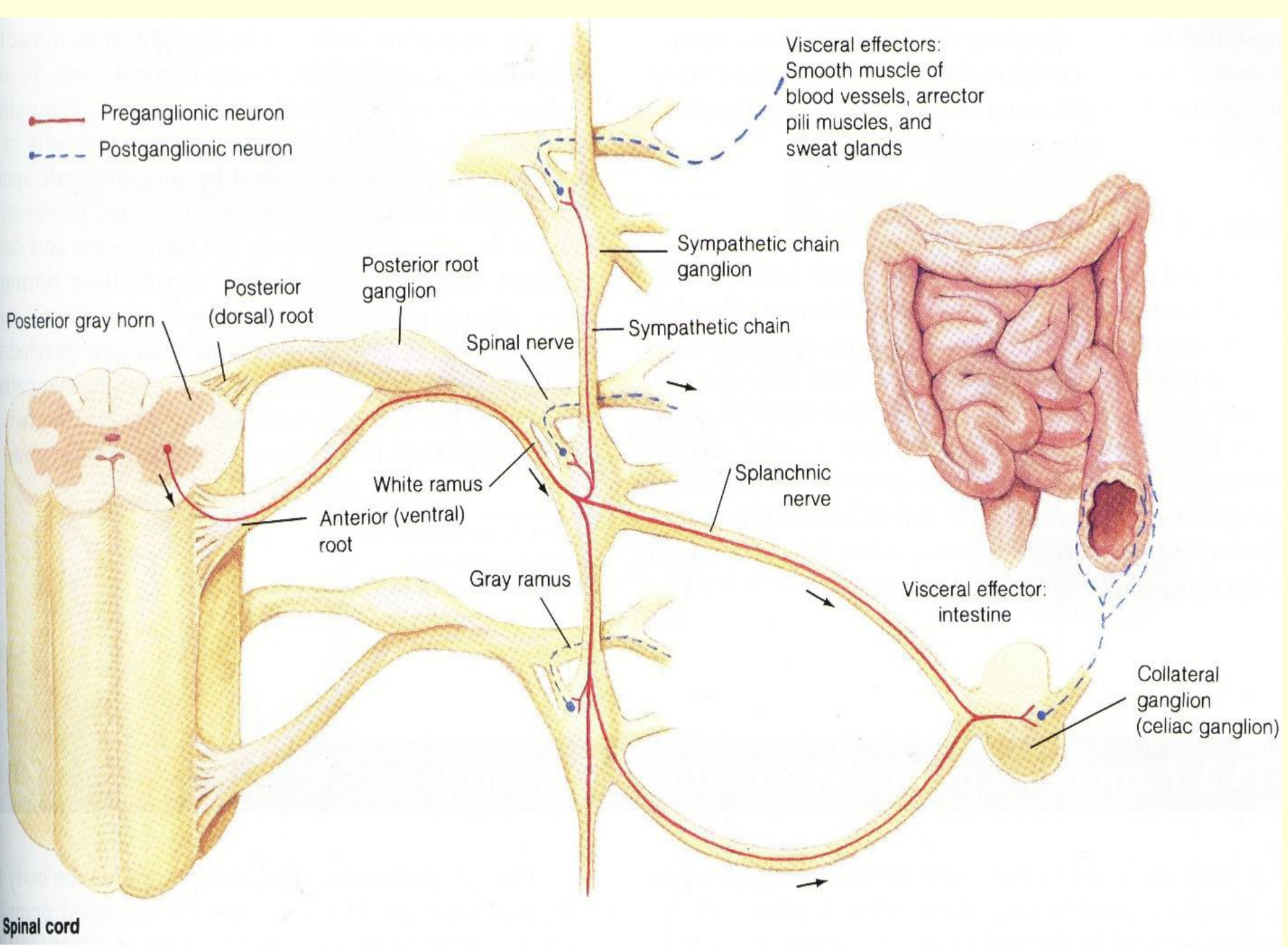


# THE SYMPATHETIC GANGLIA

(structures where synapsing between pre- and postganglionic fibers occurs)

1. The sympathetic trunk: two sympathetic trunks; each consisting of 22 paravertebral ganglia.
2. Prevertebral ganglia (“collateral ganglia”):
  - a) the celiac or solar;
  - b) superior mesenteric;
  - c) inferior mesenteric ganglion.
3. Terminal ganglia (situated near the bladder and rectum)

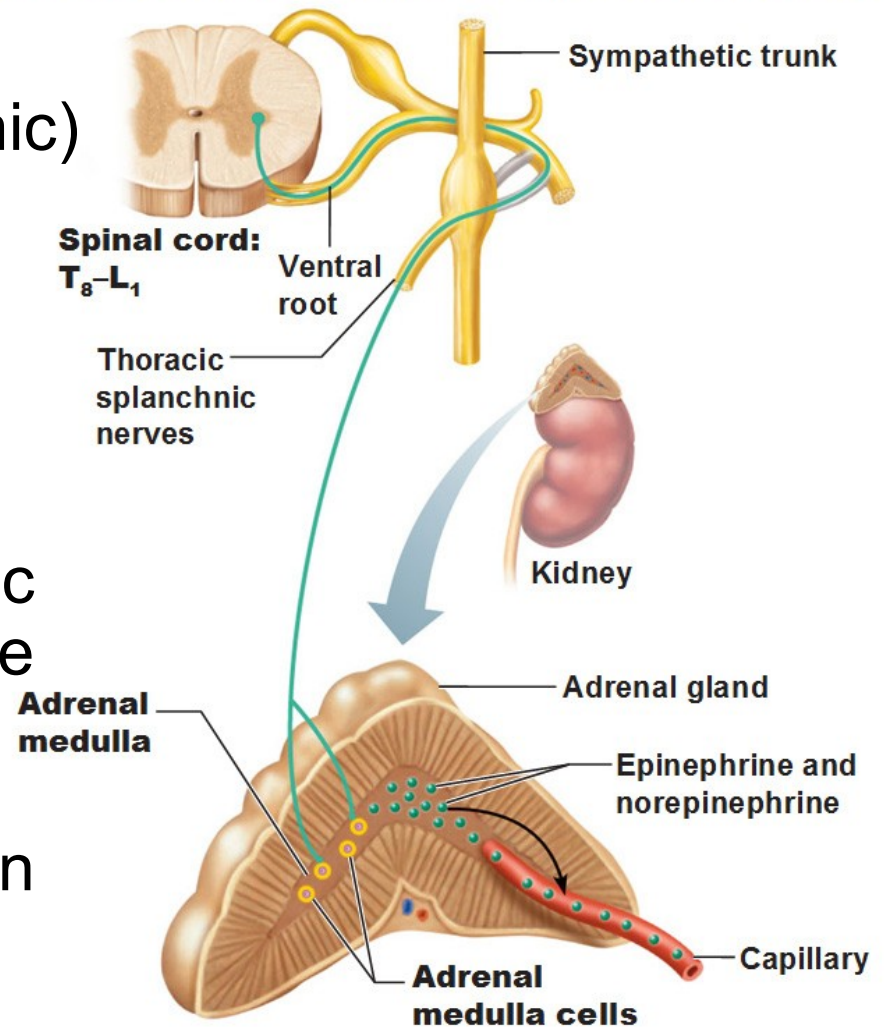




# “SYMPATHOADRENAL AXIS”

- Fibers of the greater splanchnic nerve (sympathetic, preganglionic) enter the suprarenal medulla and end in the chromaffin cells (secrete adrenalin as well as noradrenalin).
- Whenever the sympathetic system is stimulated, there is a concomitant stimulation of adrenalin and noradrenalin secretion from suprarenal medulla.

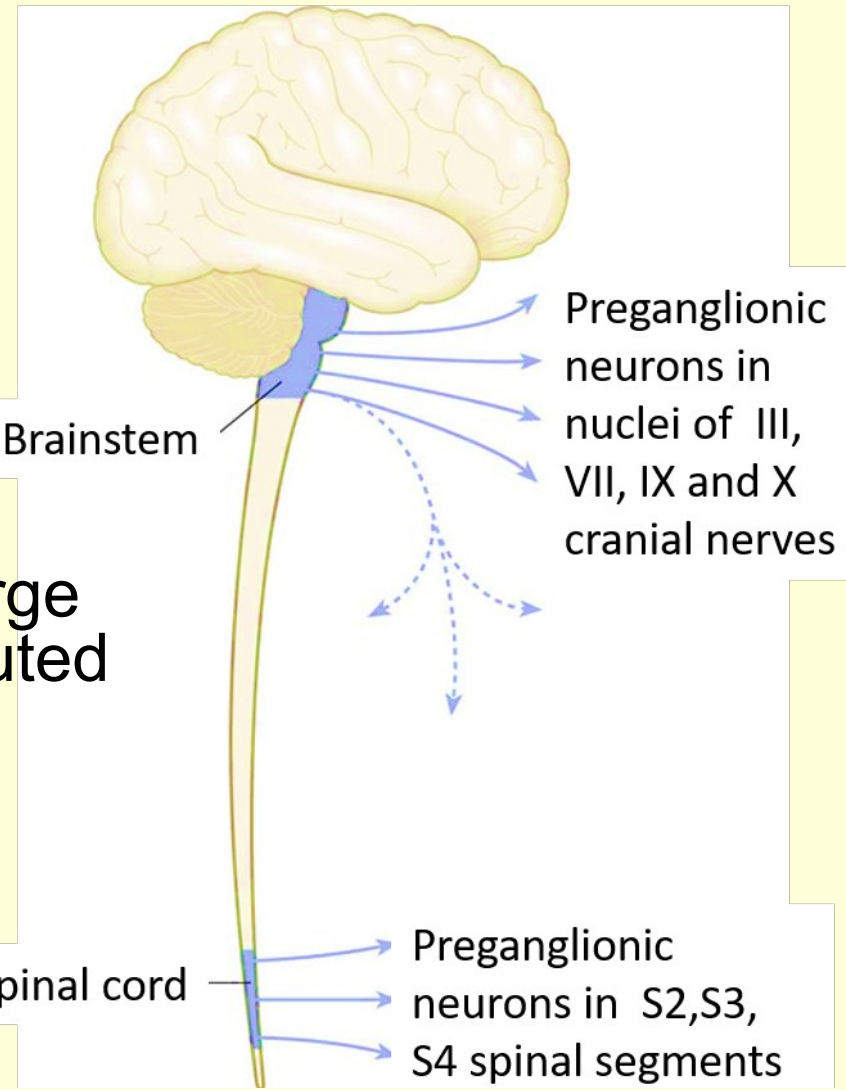
## The Adrenal Medulla of the Adrenal Gland



# PARASYMPATHETIC SYSTEM (craniosacral outflow)

## CRANIAL OUTFLOW (preganglionic)

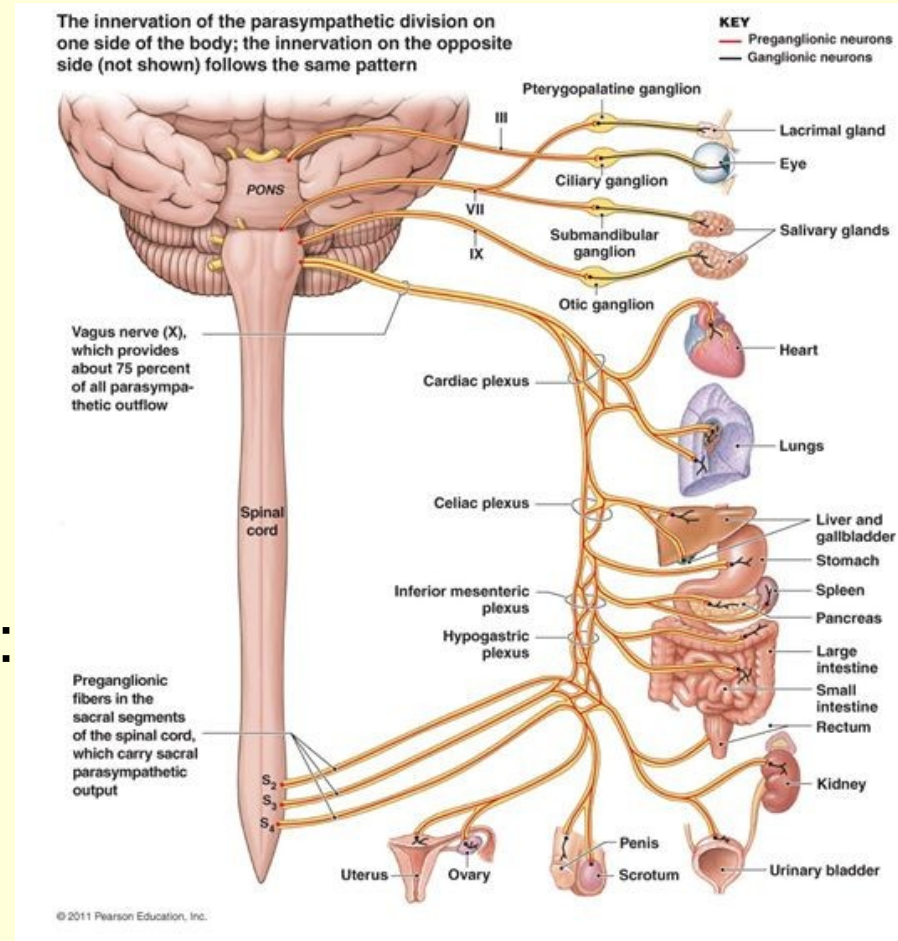
- The 3rd (oculomotor), 7th (facial), 9th (glossopharyngeal) and the 10th (vagus) cranial nerves are the nerves via which the cranial parasympathetic nerves emerge from the brain and are distributed to the peripheral structures. They relay in their ganglia: ciliary (3<sup>rd</sup>), submaxillary (7<sup>th</sup>), otic (9<sup>th</sup>). The ganglia for the vagal efferents are situated close to their target organs.



# PARASYMPATHETIC SYSTEM (craniosacral outflow)

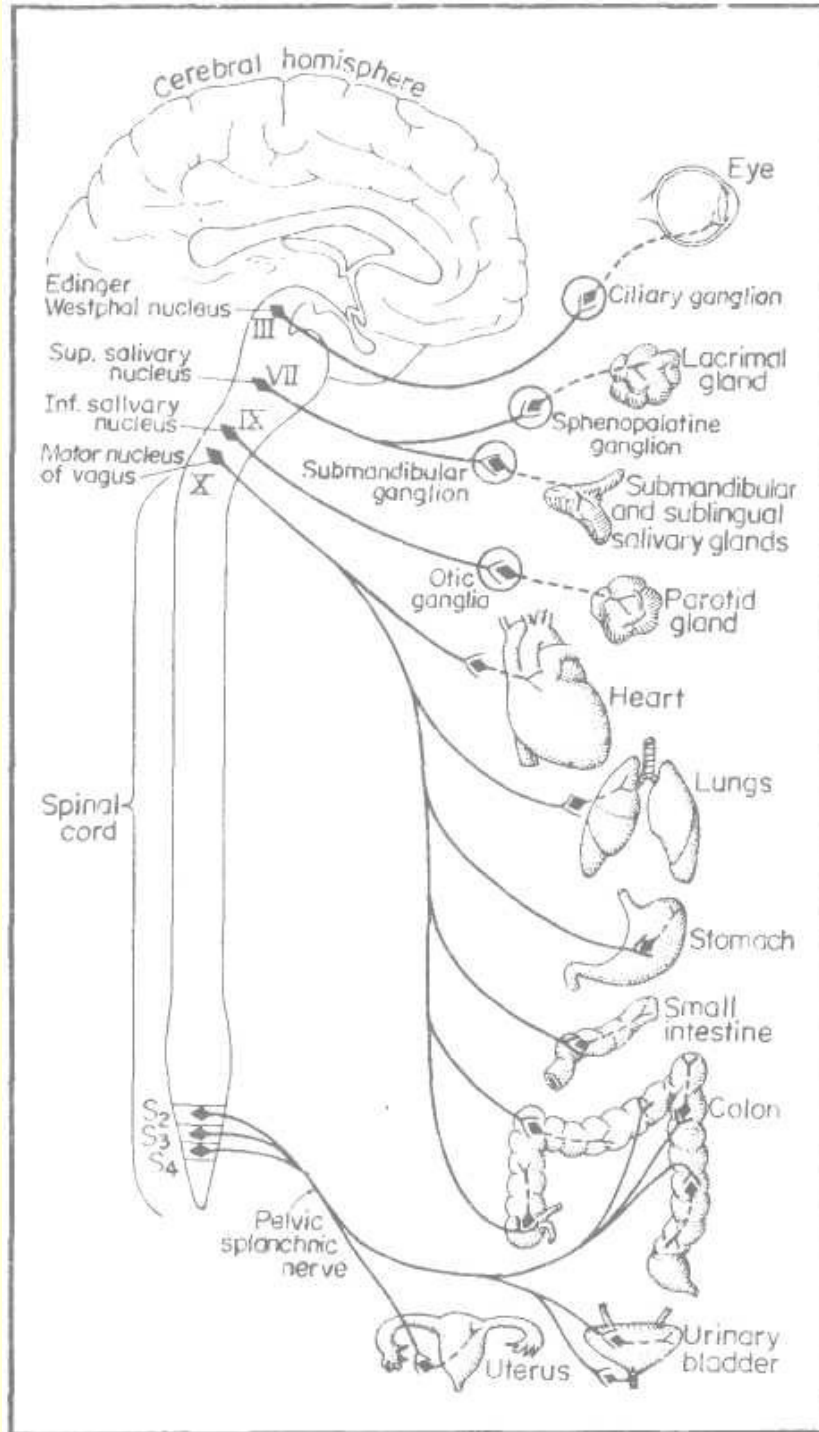
## SACRAL OUTFLOW (preganglionic)

- From the lateral horns of the 2nd, 3rd and 4th segments of the sacral regions, the parasympathetic fibers come out to form pelvic splanchnic nerves. The sacral autonomic supplies:
  - the last part of the colon and the rectum;
  - urinary bladder;
  - the uterus or the blood vessels of the penis.



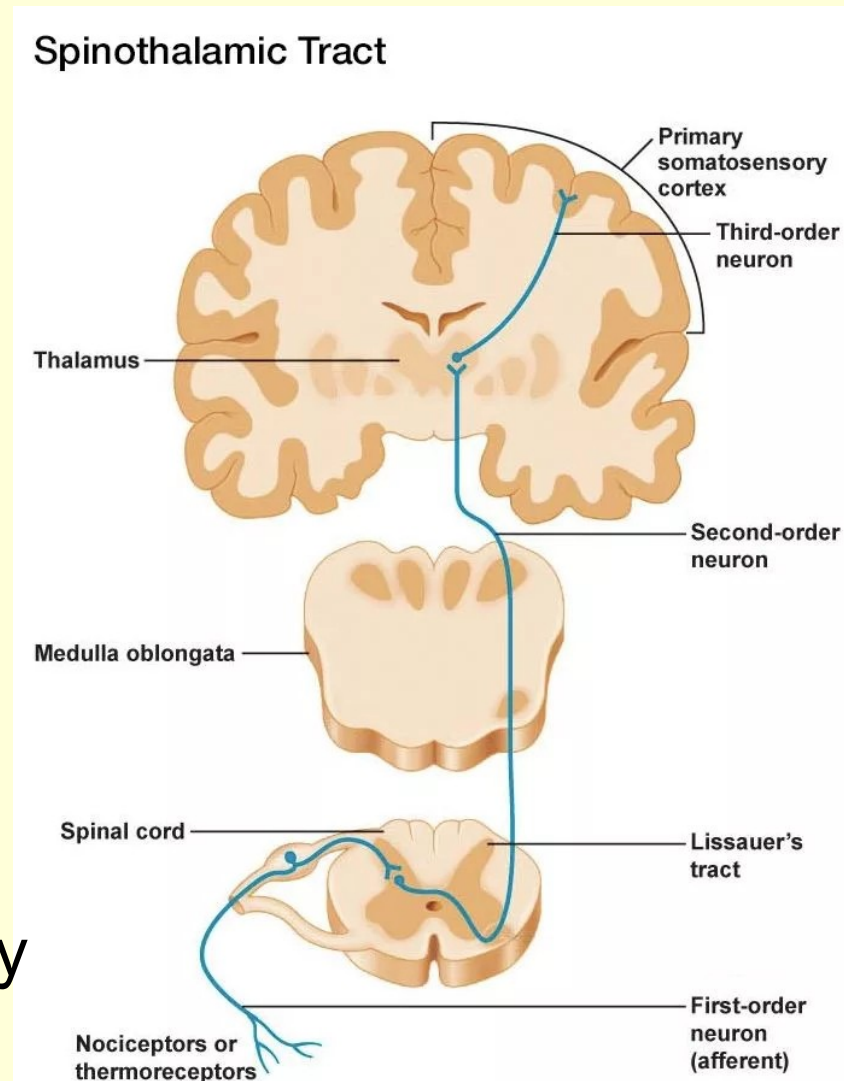
## PARASYMPATHETIC DIVISION OF THE ANS

Locus of cell body	Peripheral nerve	Ganglion	Organ Innervated
Edinger-Westphal nucleus	Oculomotor nerve (III)	Ciliary ganglion	Iris (sphincter) Ciliary muscle
Superior salivatory nucleus	Facial nerve (VII)	Pterygopalatine and Submandibular ganglia	Lacrimal, submandibular, and sublingual glands
Inferior salivatory nucleus	Glossopharyngeal nerve (IX)	Otic ganglion	Parotid glands
Dorsal vagal & Nucleus ambiguus	Vagus nerve	Various terminal ganglia	Bronchial tree Lungs Heart Liver, gall bladder, pancreas Kidneys Gut (esophagus to colon)
Sacral spinal cord	Splanchnic nerve	Pelvic plexus	Descending colon Rectum Bladder Genitalia



# SYMPATHETIC AFFERENTS

- Nerve cell soma of the **afferent fibers from viscera** are situated in the corresponding dorsal root ganglion. These fibers:
  - 1) may form afferent limb of an autonomic reflex arc;
  - 2) may be the first order neuron carrying visceral sensations (for pain sensation later order neuron travel up with the spinothalamic tract to end in the thalamus, and further relay occurs to the sensory cortex).





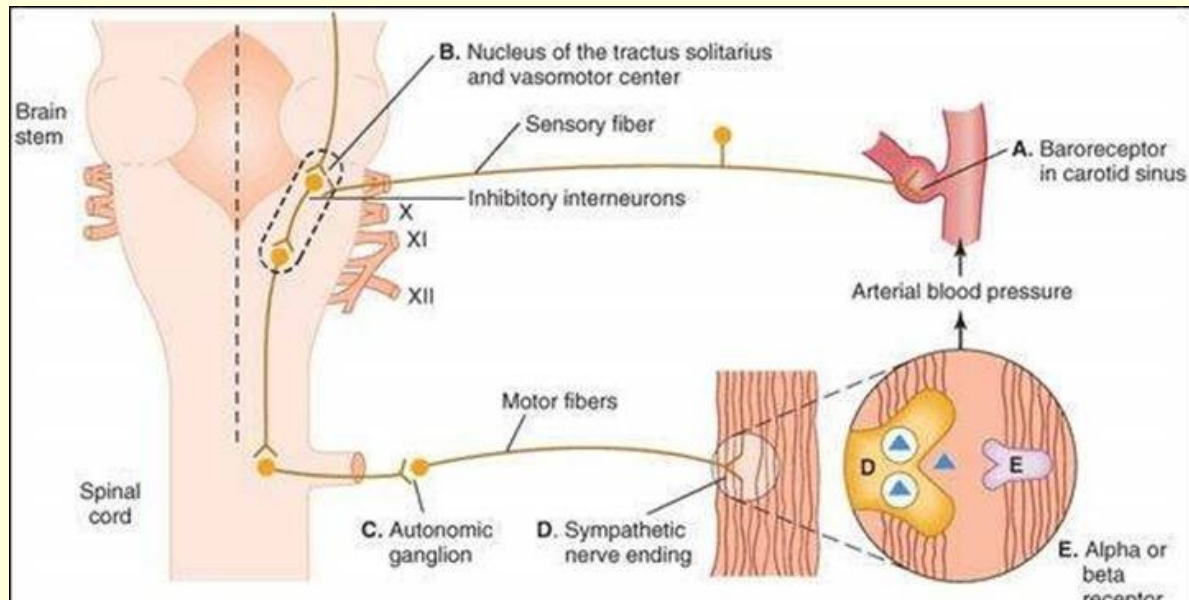
# PARASYMPATHETIC AFFERENTS

The central processes from the ganglia (afferents from the periphery are carried via the 7th, 9th and 10th cranial nerves) end in the nucleus of tractus solitarius (NTS).

The NTS is a center where ANS is integrated.

The NTS receives inputs from:

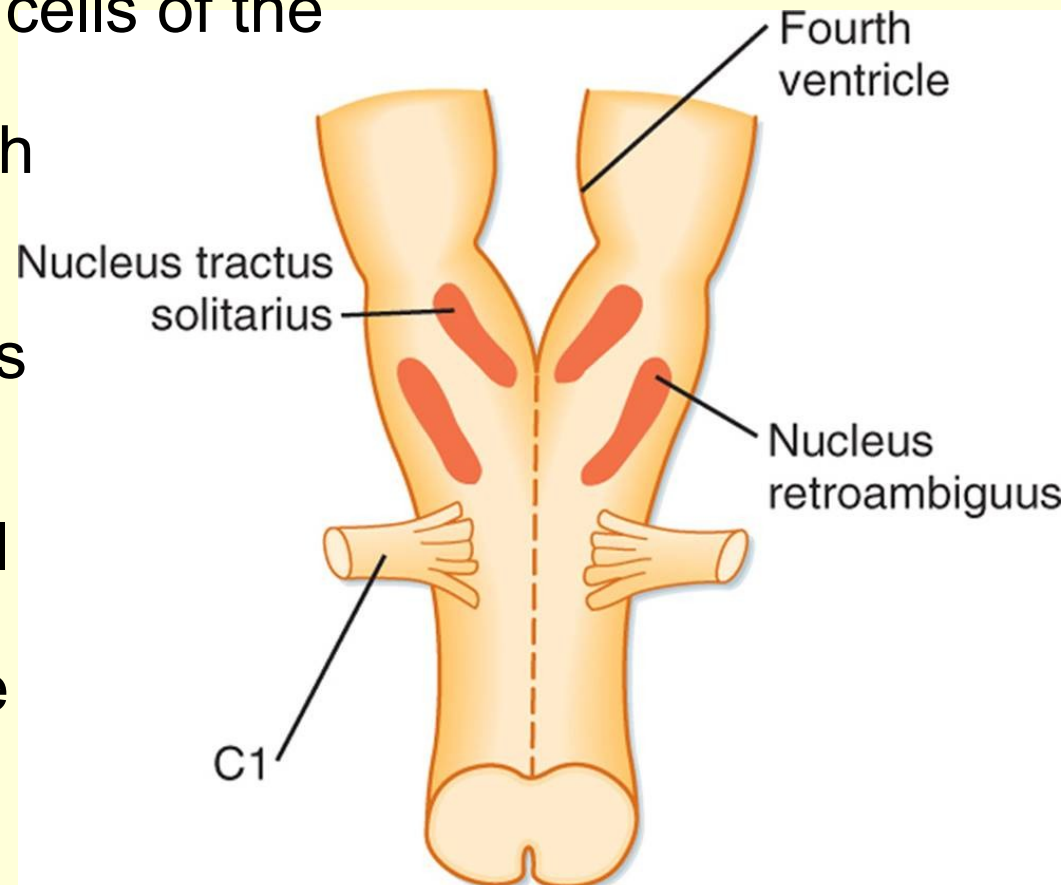
- 1) carotid sinus (baroreceptors) and carotid body (chemoreceptors);
- 2) baroreceptors from pulmonary circulation;
- 3) olfactory and taste sensations.



# PARASYMPATHETIC AFFERENTS

The NTS sends fibers to:

- 1) higher brain centers which, in turn control the lateral horn cells of the sympathetic system;
- 2) to hypothalamus (which can control the endocrines);
- 3) to dorsal motor nucleus of the vagus (which controls the heart/ bronchi/gastrointestinal tract);
- 4) to selected parts of the limbic system (which control the emotion).

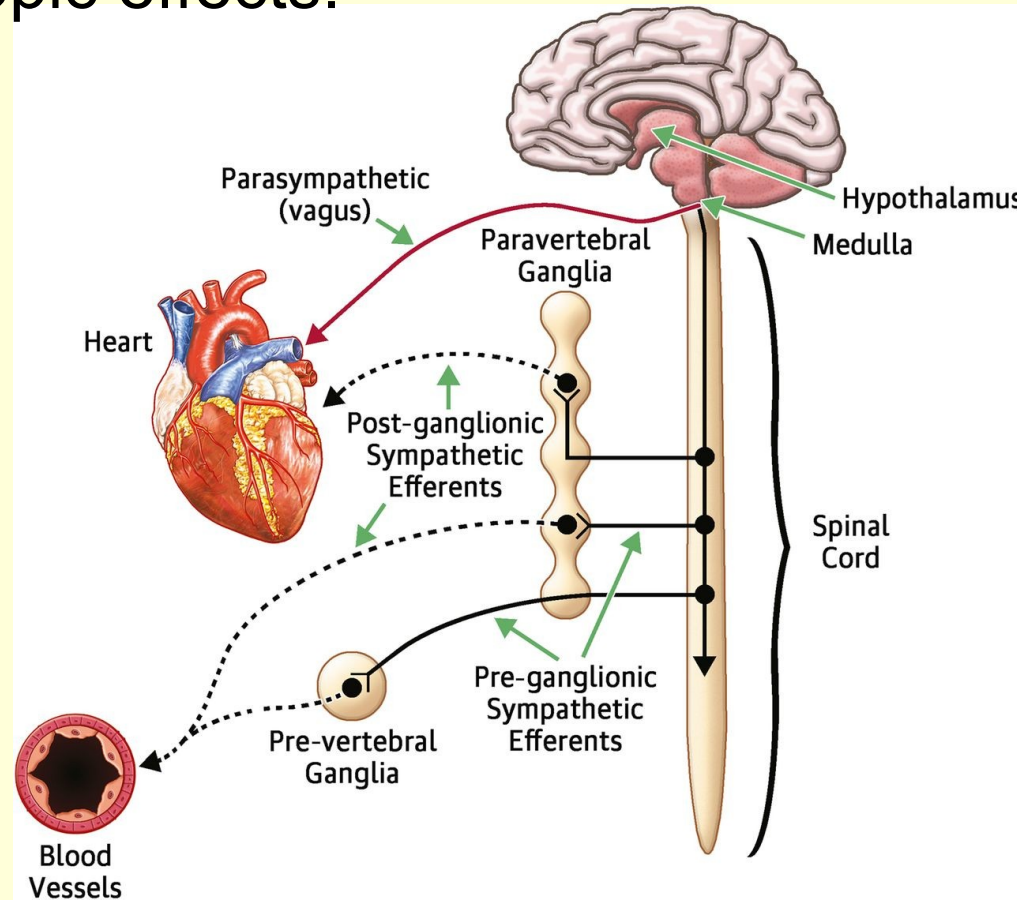


# EFFECTS OF SYMPATHETIC STIMULATION

## CARDIOVASCULAR SYSTEM

**Heart** (excitation) – positive chronotropic, dromotropic, inotropic and bathmotropic effects:

- a) rate of the heart increase;
- b) contractility of the heart increase (cardiac output rises);
- c) coronary flow increases.

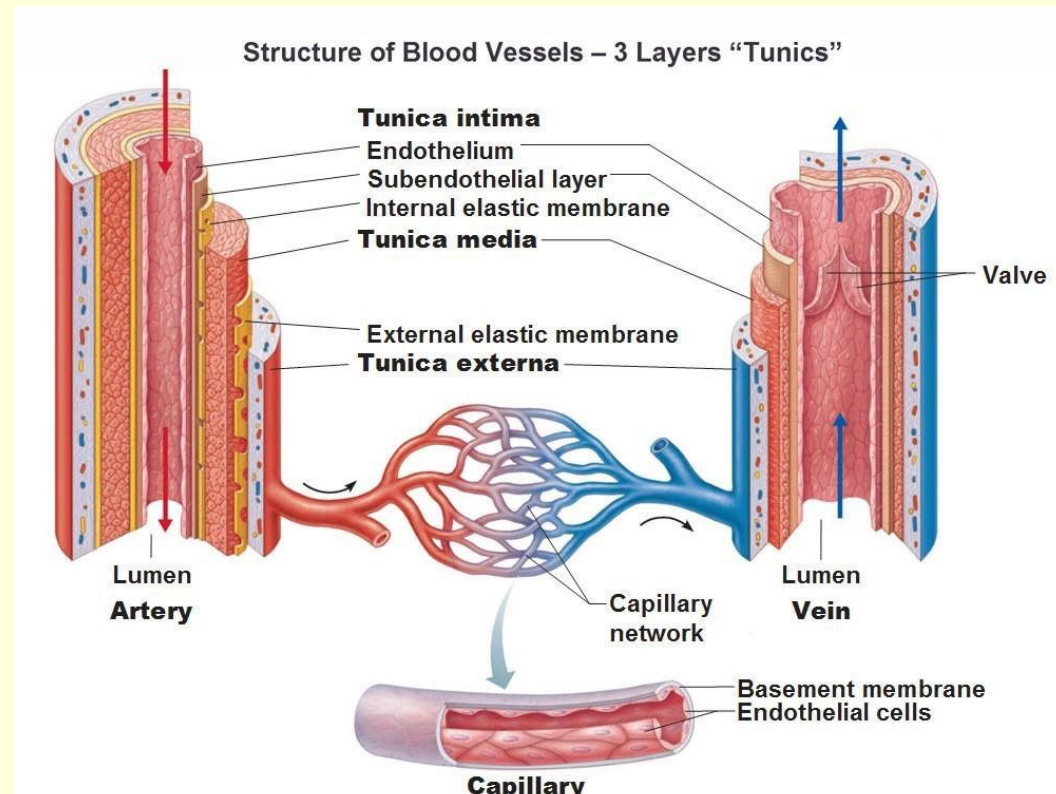


# EFFECTS OF SYMPATHETIC STIMULATION

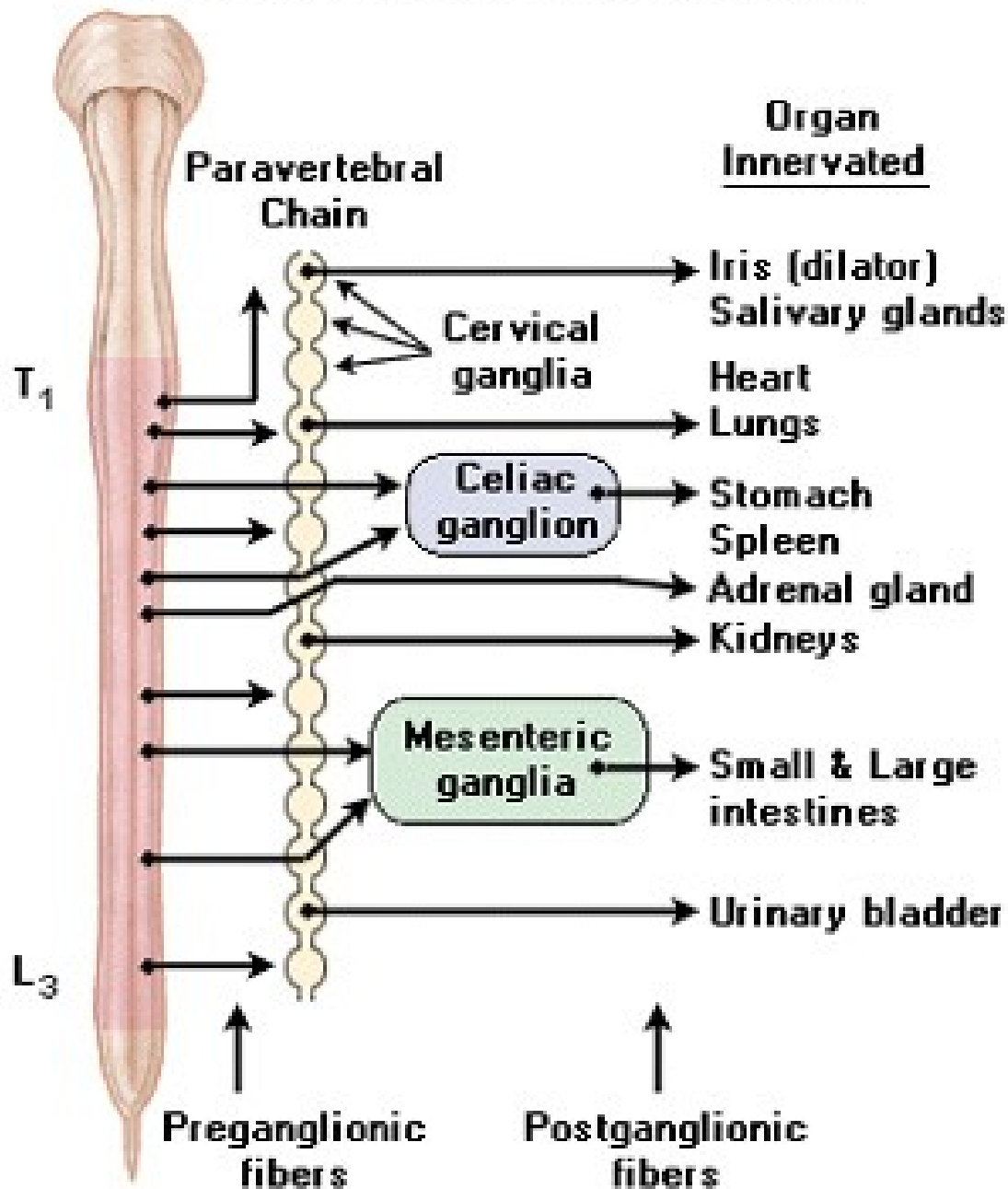
**Blood vessels** – target tissue is smooth muscles of the vessels.

- a) sharp vasoconstriction of cutaneous and splanchnic arterioles;
- b) vasodilatation of coronary and skeletal arterioles;
- c) venoconstriction.

**Blood pressure** rises – systolic, diastolic and the mean blood pressures.



# SYMPATHETIC DIVISION OF THE ANS

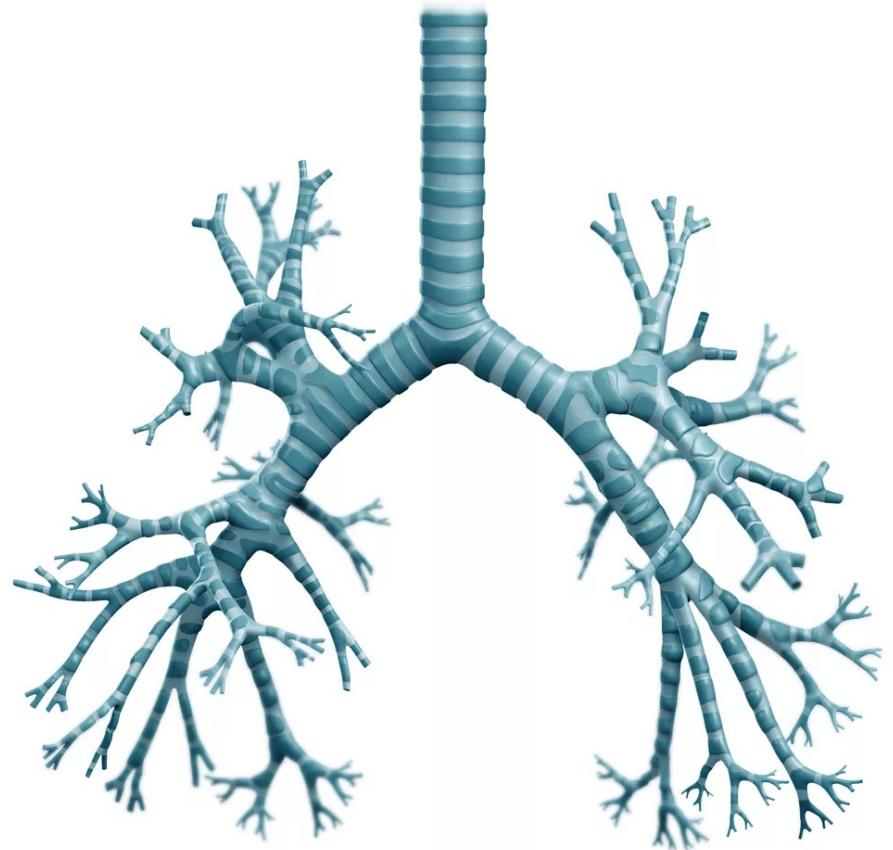


# EFFECTS OF SYMPATHETIC STIMULATION

## RESPIRATORY SYSTEM

Sympathetic stimulation leads to:

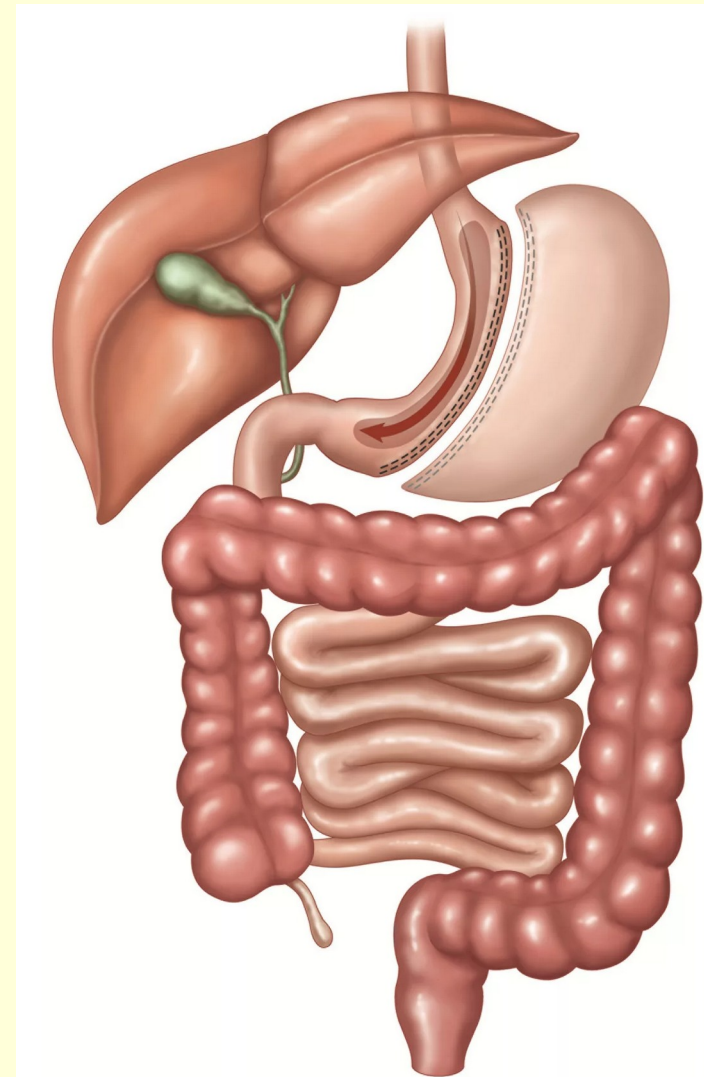
- a) bronchodilatation (due to relaxation of the bronchial muscles);
- b) tachypnea (rise in the rate of ventilation volume).



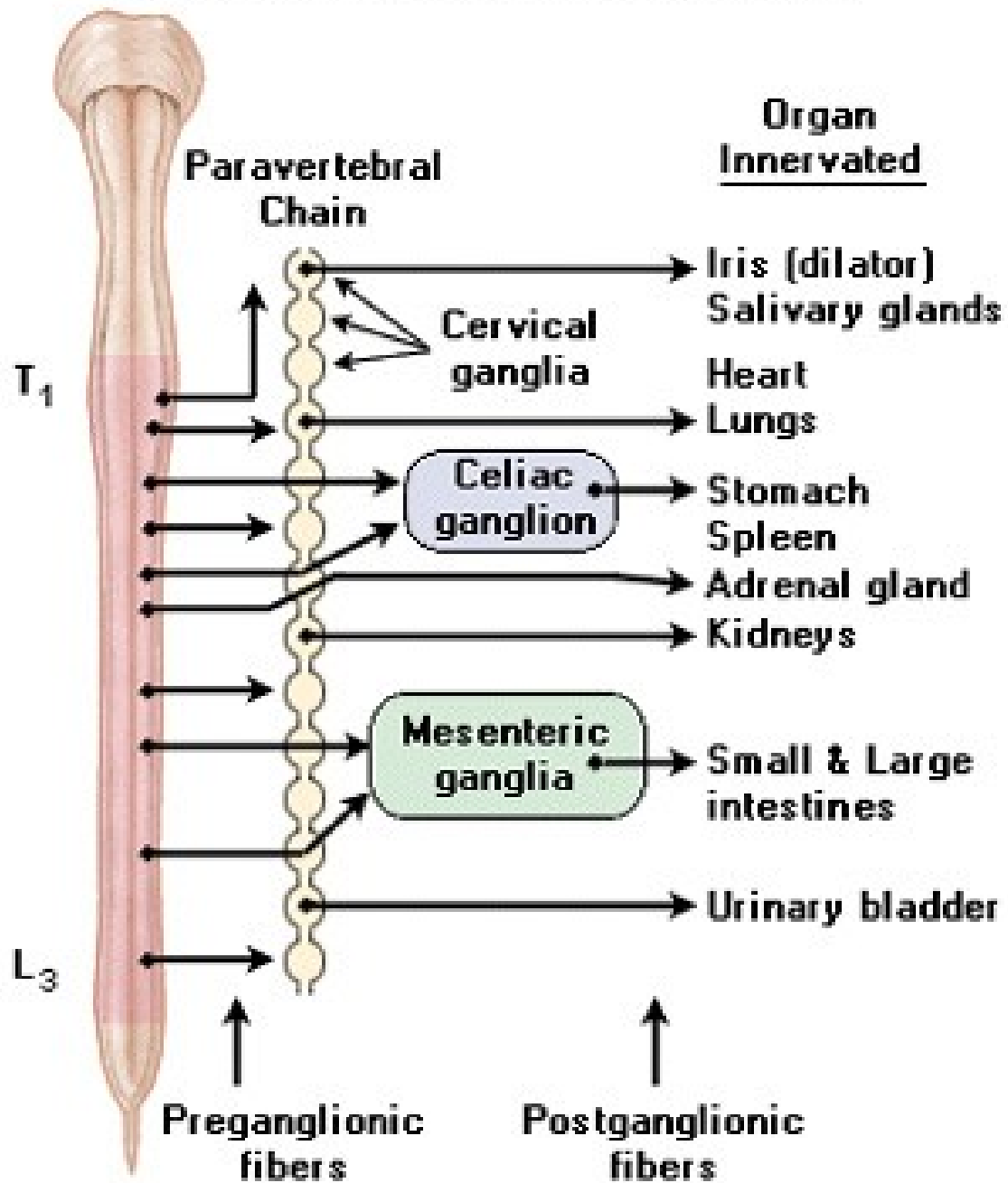
# EFFECTS OF SYMPATHETIC STIMULATION

## DIGESTIVE SYSTEM

- Stimulation of the sphincters (leading to their spasm) and relaxation of the general muscles of the gut (leading to inhibition of peristalsis) result.
- There is therefore, inhibition of peristalsis and holding up of the content of the gut.



# SYMPATHETIC DIVISION OF THE ANS

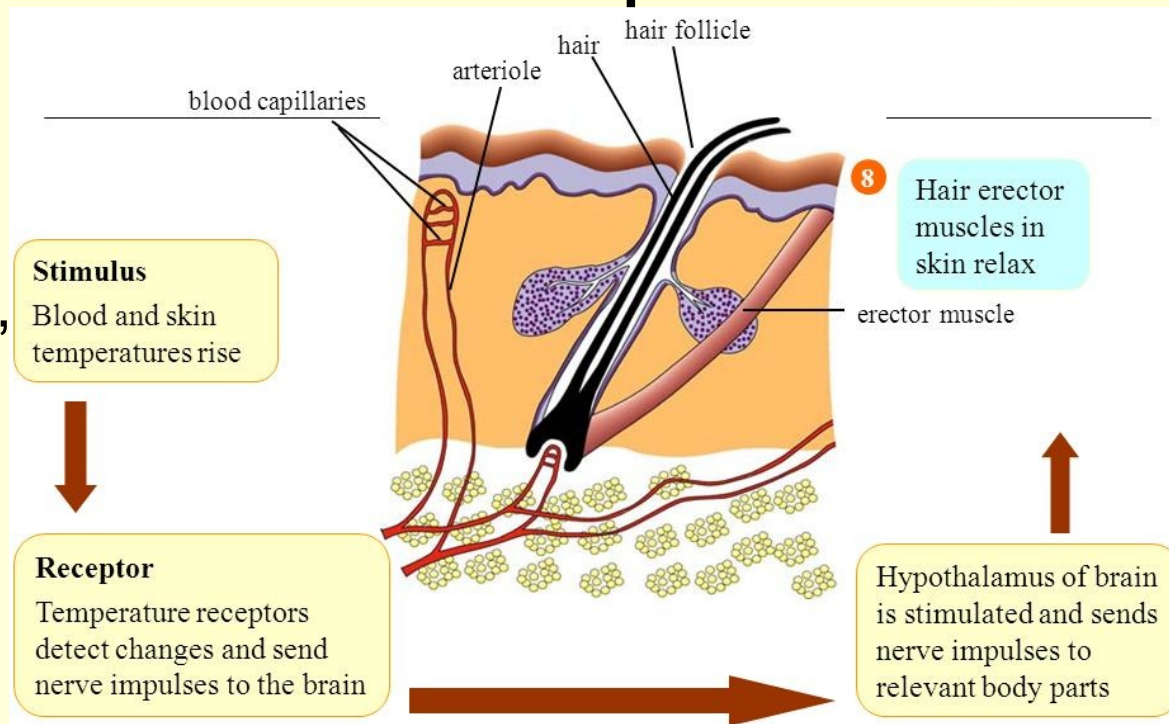




# EFFECTS OF SYMPATHETIC STIMULATION

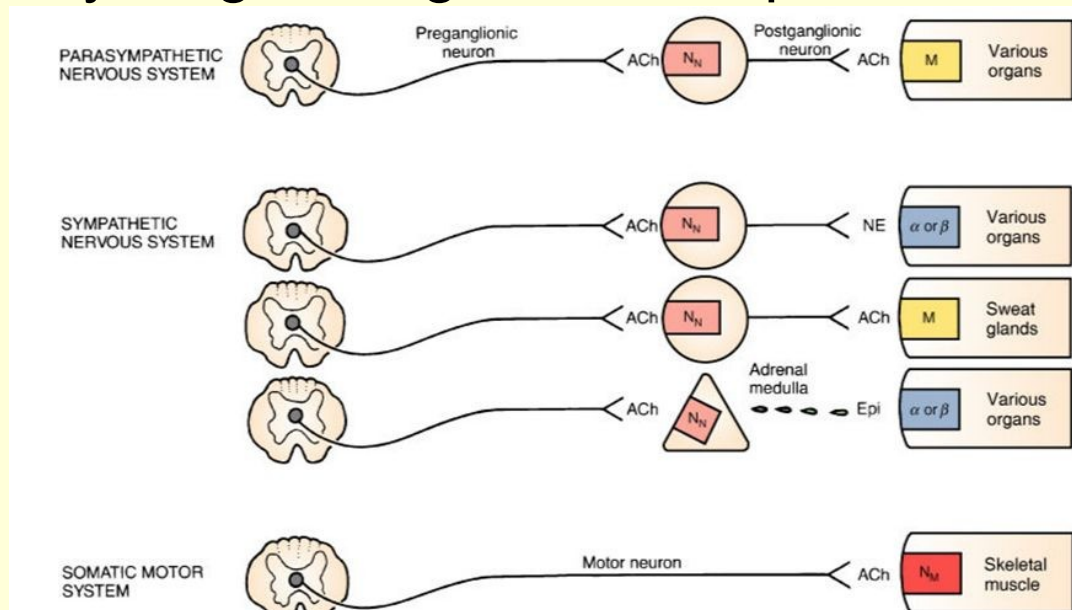
## SKIN, BODY TEMPERATURE

- Cutaneous **vasoconstriction** (leading to pallor), and **piloerection** result (due to the contraction of arrector pilorum muscles situated at the base of hair follicle).
- Together, cause **elevation of the core temperature of the body**, and thus is useful during exposure to cold. Sympathetic stimulation can, also, lead to sweating (sympathetic nerve endings of the sweat glands are **cholinergic**).



# ANS receptors – ANS neurotransmitters

- The ANS uses neurotransmitters and neuromodulators, as well as a hormone, that act at ionotropic and metabotropic receptors.
- The body needs to which the ANS must respond are relatively long-lasting, so the action of postganglionic neurons is mediated by long-lasting metabotropic mechanisms initiated by neurotransmitter binding to G protein-linked receptors.

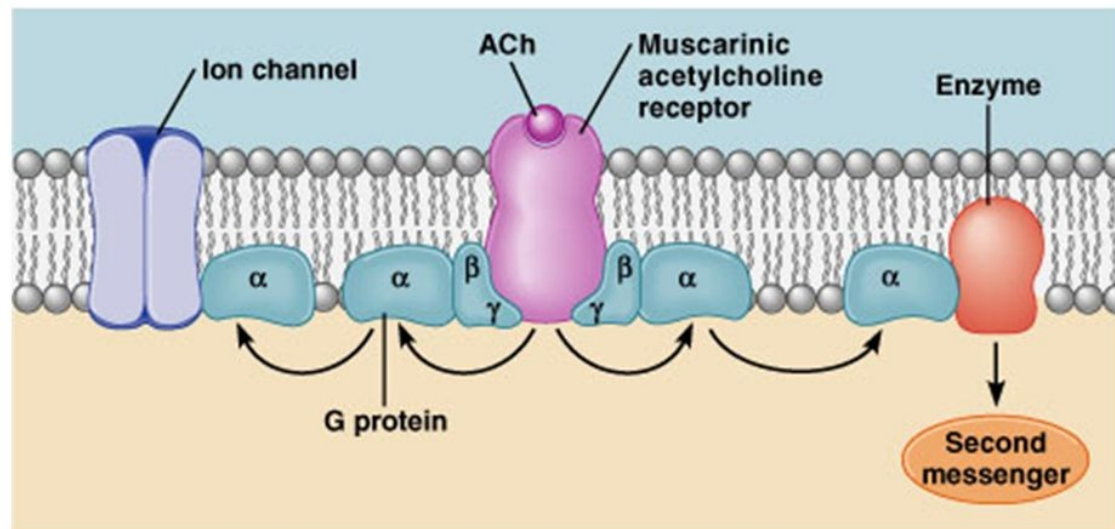


Cholinergic receptor subtypes: N<sub>N</sub> = nicotinic<sub>N</sub>, N<sub>M</sub> = nicotinic<sub>M</sub>, and M = muscarinic.  
Adrenergic receptor subtypes: α = alpha and β = beta.

# ANS receptors – ANS neurotransmitters

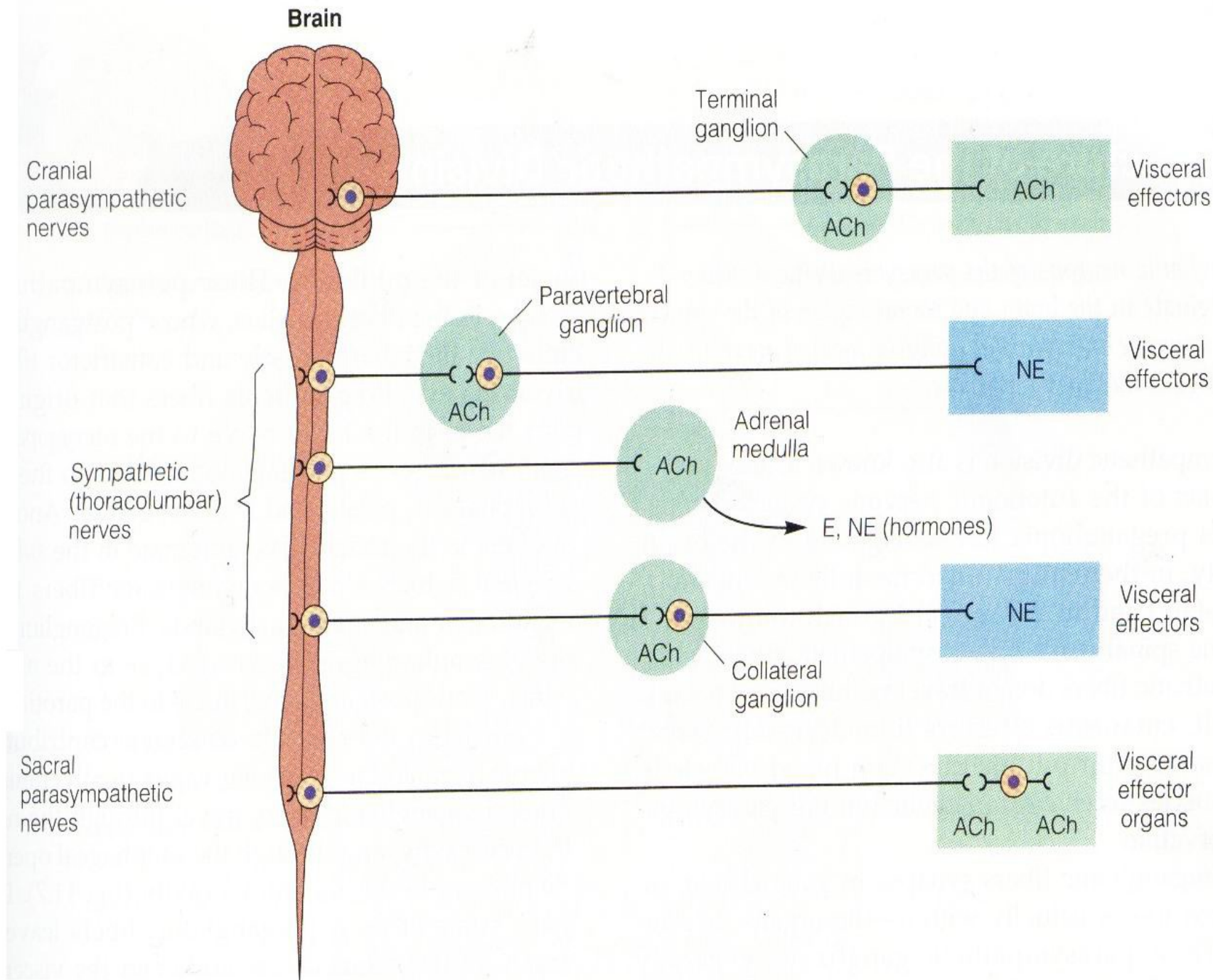
- Neuroactive peptides that act as neuromodulators are very common in the neurons of the ANS. Their long, slow synaptic actions are very important to the function of the ANS. Fast, ionotropic synaptic action is limited to cholinergic transmission between pre- and postganglionic neurons.

Actions at Muscarinic Cholinergic Receptors



## Receptors, Signaling Mechanisms, & Neurotransmitters Important For ANS Function

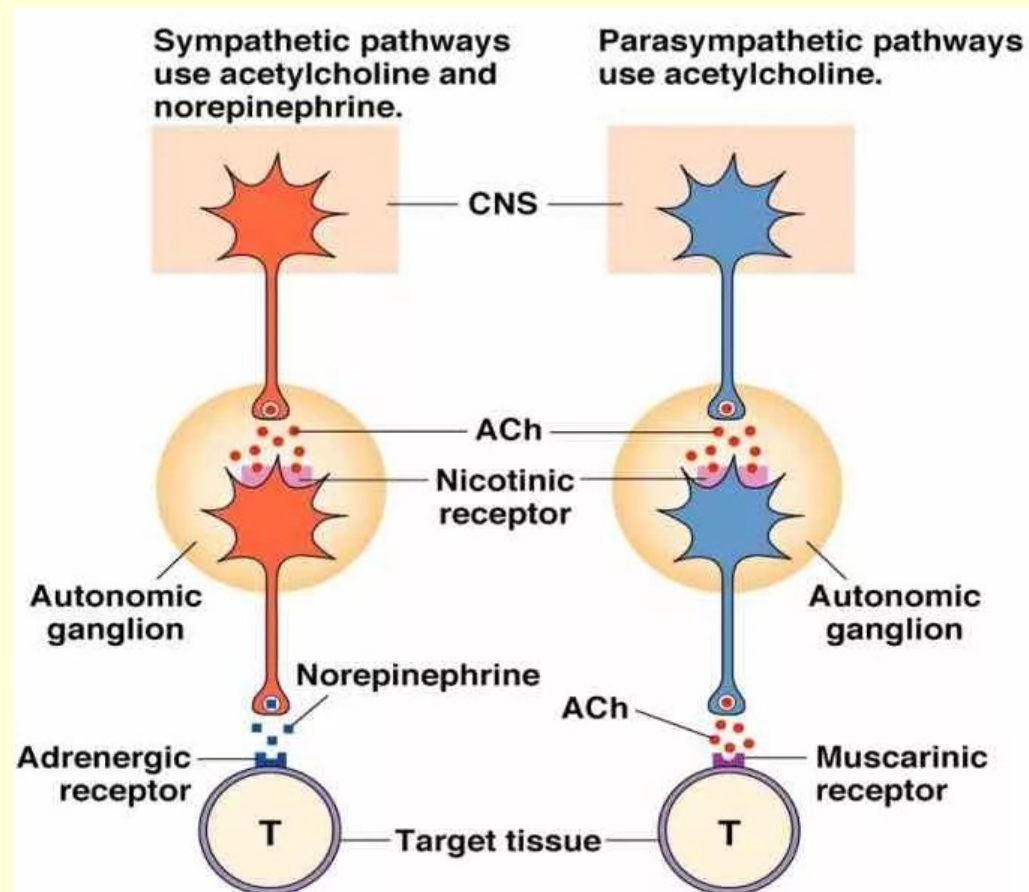
M <sub>1</sub>	Metabotropic	↑ IP <sub>3</sub> , DAG	Acetylcholine	
M <sub>2</sub>		↓ cAMP; ↑ g <sub>K</sub>		
M <sub>3</sub>		↑ IP <sub>3</sub> , DAG		
M <sub>4</sub>		↓ cAMP		
N <sub>N</sub> (Neural)	Ionotropic	↑ g <sub>Na,K</sub>		
α <sub>1</sub>	Metabotropic	↑ IP <sub>3</sub> , DAG	(E > NE)	Epinephrine (E) & Norepinephrine (NE)
α <sub>2</sub>		↓ cAMP; ↑ g <sub>K</sub> & ↓ g <sub>Ca</sub>	(E > NE)	
β <sub>1</sub>		↑ cAMP	(E = NE)	
β <sub>2</sub>		↑ cAMP	(E >> NE)	
D <sub>1</sub>	Metabotropic	↑ cAMP	Dopamine	
D <sub>2</sub>		↓ cAMP; ↑ g <sub>K</sub> & ↓ g <sub>Ca</sub>		



# CHEMICAL TRANSMISSION IN ANS

ACETYLCHOLINE is liberated at:

- 1) the postganglionic parasympathetic nerve endings;
- 2) the ANS ganglia (both sympathetic and parasympathetic);
- 3) the postganglionic sympathetic nerve endings supplying the sweat glands and some arterioles of skeletal muscles (cholinergic sympathetic nerves);
- 4) the preganglionic sympathetic nerves terminating on adrenal medullary cells.



## Parasympathetic Actions Mediated By Acetylcholine

Organ/Cells	Response	Organ/Cells	Response
<b>EYE</b>		<b>BLOOD VESSELS</b>	
Sphincter muscle, Iris	Contraction (Miosis)	Arteries	Dilation (by EDRF [NO])
Ciliary muscle	Contraction (Near Vision)	Veins	Dilation (by EDRF [NO])
<b>HEART</b>		<b>GASTROINTESTINAL TRACT</b>	
SA node	Decreased rate	Motility	Increase
AV node	Decreased conduction velocity	Sphincters	Relaxation
<b>LUNG</b>		Secretion	Stimulation
Bronchial muscle	Contraction	<b>GLANDS</b>	
Bronchial glands	Secretion	Sweat, salivary, lacrimal	Secretion
<b>URINARY BLADDER</b>		<b>REPRODUCTIVE SYSTEM</b>	
Detrusor	Contraction	Penus, clitoris	Erection
Trigone & sphincter	Relaxation		

### Sympathetic Actions Mediated by Adrenoceptors

Organ/Cells	Response	Organ/Cells	Response
<b>EYE</b>		<b>BLOOD VESSELS</b>	
Sphincter muscle, Iris	Dilation (Mydriasis)	Arterioles	Constriction, except coronary and skeletal muscle where dilation occurs
Ciliary muscle	Relaxation (Far Vision)	Veins	Constriction
<b>HEART</b>		<b>GASTROINTESTINAL TRACT</b>	
SA node	Increased rate	Motility	Decrease
AV node	Increased conduction	Sphincters	Contraction
Ventricles	Increased contractility	Secretion	Uncertain
<b>LUNG</b>		<b>SKIN</b>	
Bronchial muscle	Relaxation	Pilomotor muscles	Contraction
<b>URINARY BLADDER</b>		Sweat glands	Localized secretion
Trigone & sphincter	Contraction	<b>KIDNEY</b>	Renin secretion
<b>REPRODUCTION SYSTEM</b>			
Male sex organ	Ejaculation		



# CHEMICAL TRANSMISSION IN ANS

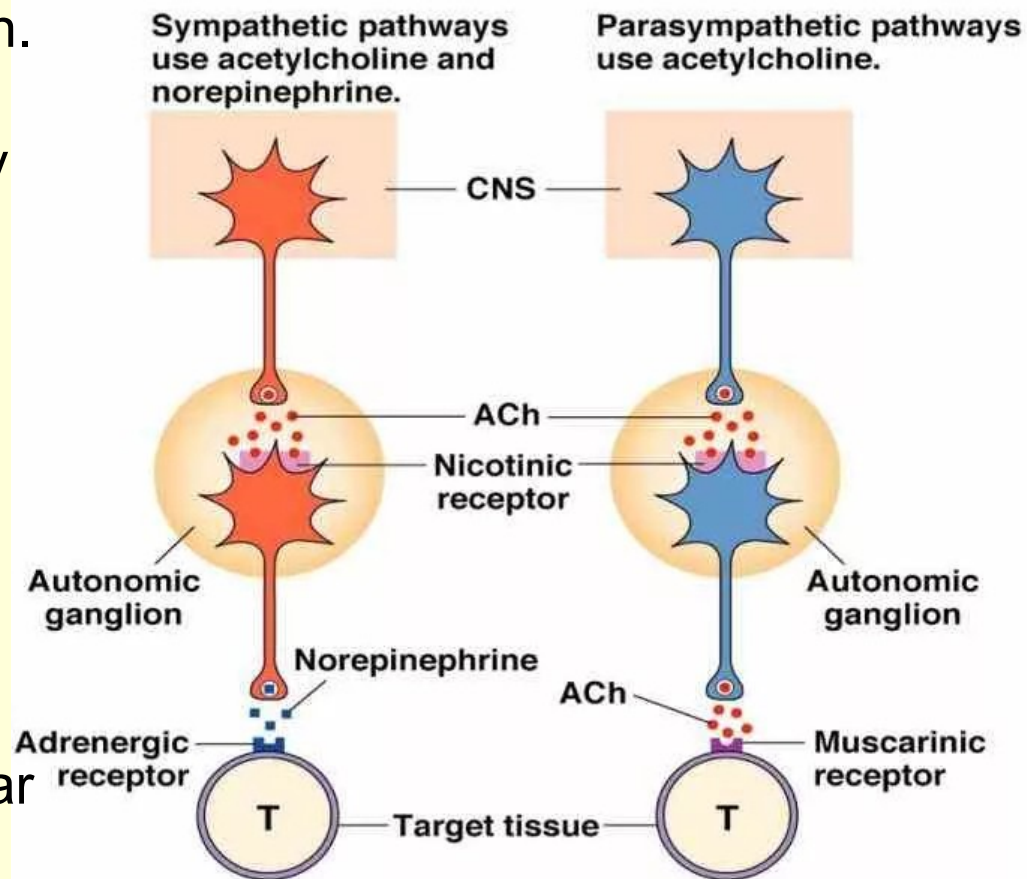
NORADRENALIN (NOREPINEPHRINE) – acts as a transmitter at:

- 1) postganglionic sympathetic nerve terminals;
- 2) some regions within the brain.

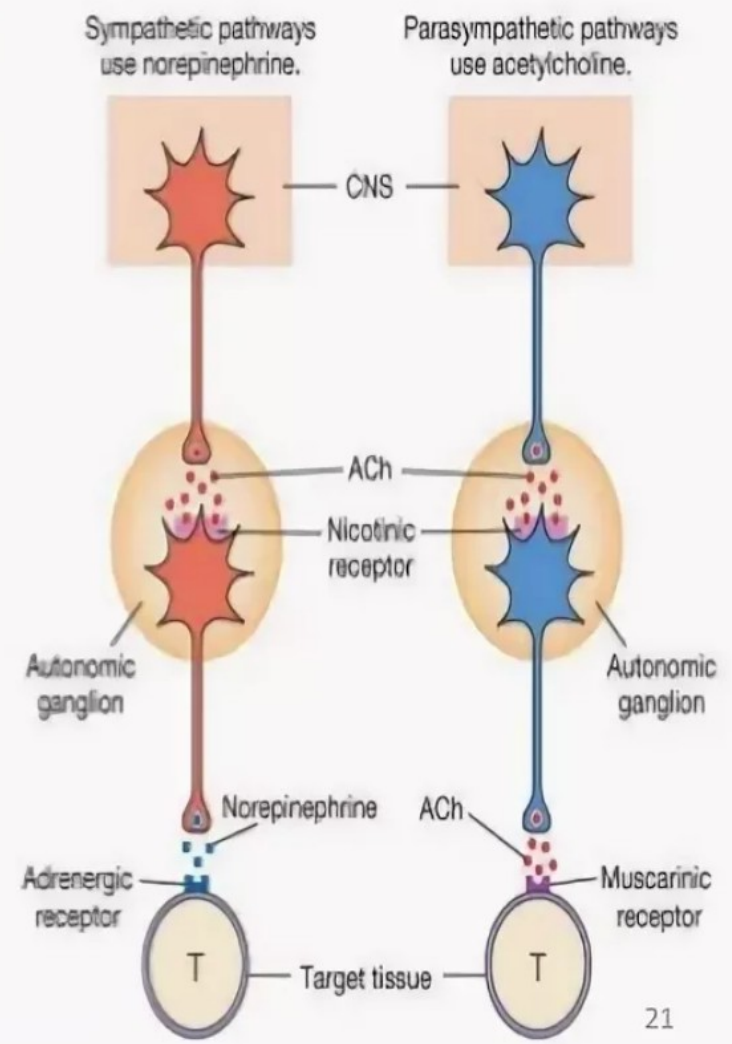
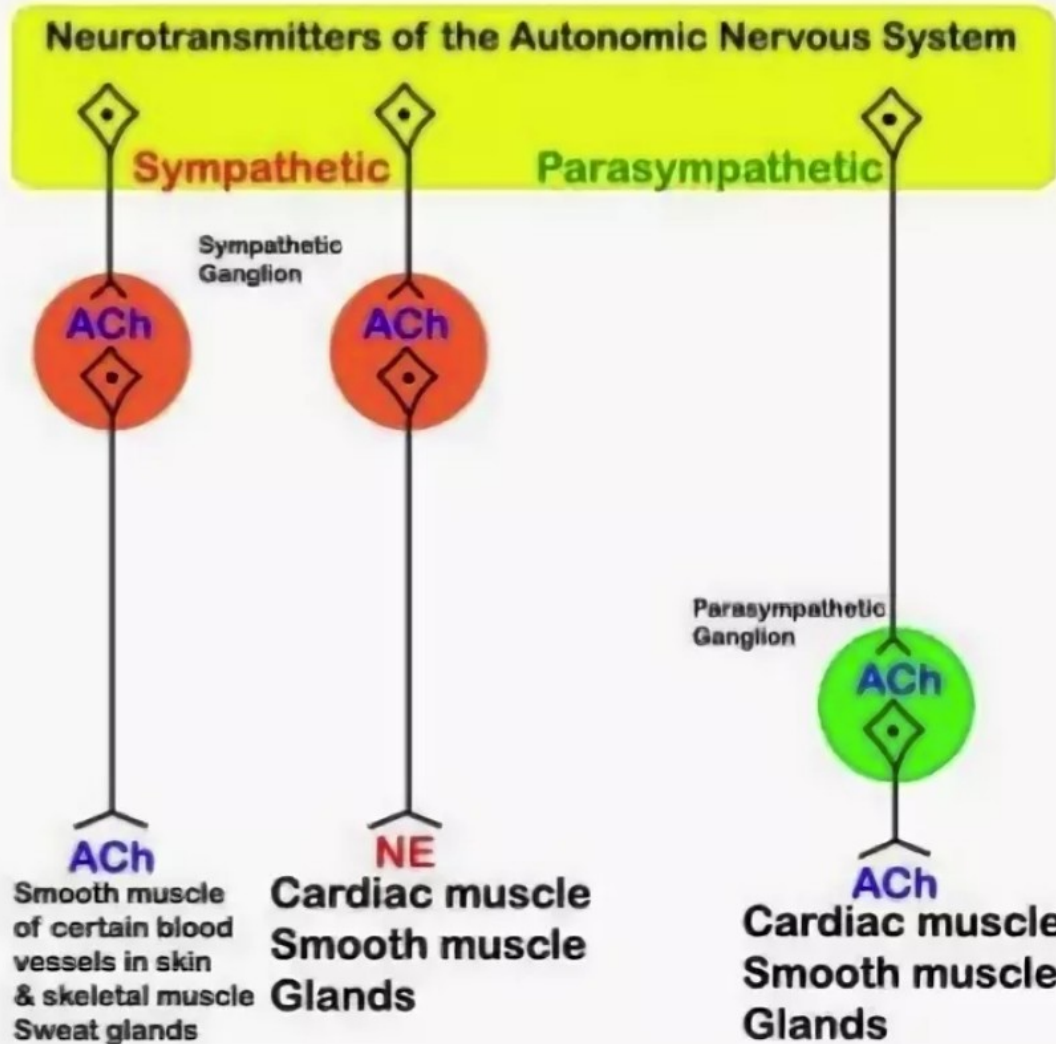
NORADRENALIN

RECEPTORS – are basically two types (in sympathetic system):

- 1) alfa-receptors occur both at the vascular smooth muscles in general and cardiac muscles as well as in some selective nerve terminals;
- 2) beta-receptors occur in the cell membrane of vascular smooth muscles (of skeletal muscles) and cardiac muscle.



# Neurotransmitter in sympathetic and parasympathetic nervous system



**Preganglionic Fibers**

**Postganglionic Neurons**

**Effector Cells**

Parasympathetic



Nicotinic ACh Receptors (Many)

Muscarinic ACh Receptors (Few)

Sympathetic



Adrenal Medulla

Sympathetic



Adrenergic Postganglionic Neuron

Sympathetic



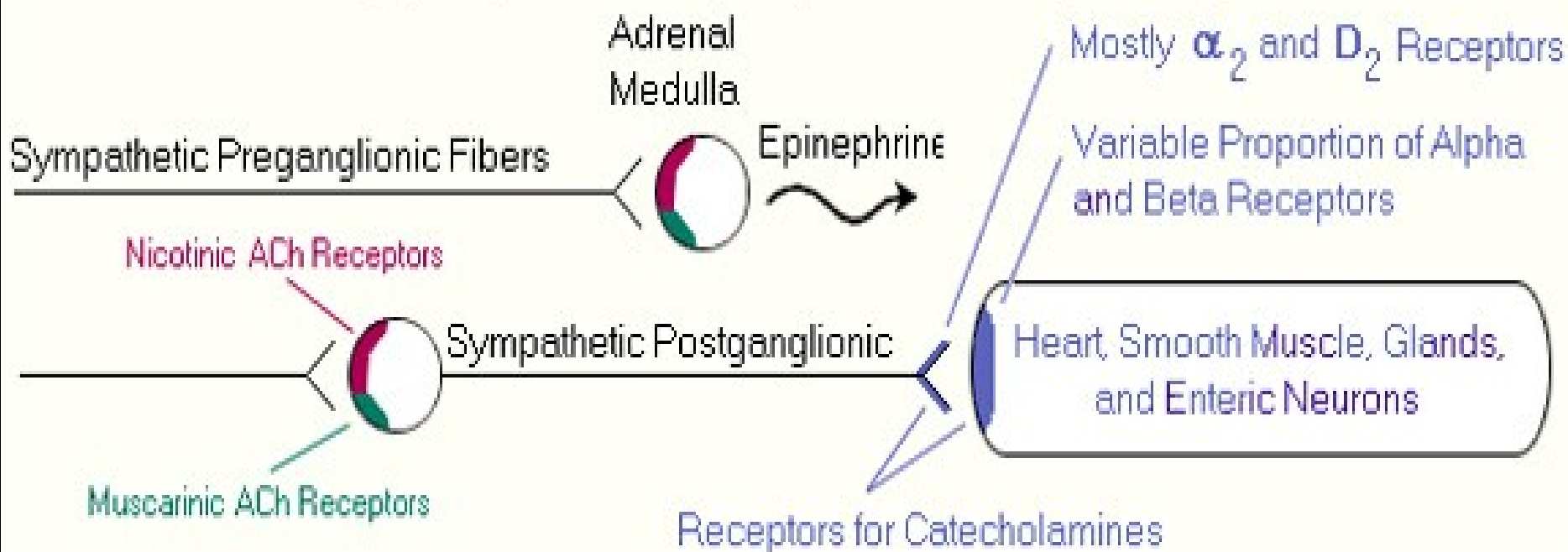
Cholinergic Postganglionic Neuron

Smooth Muscle, Glands, and Enteric Neurons

Muscarinic ACh Receptors

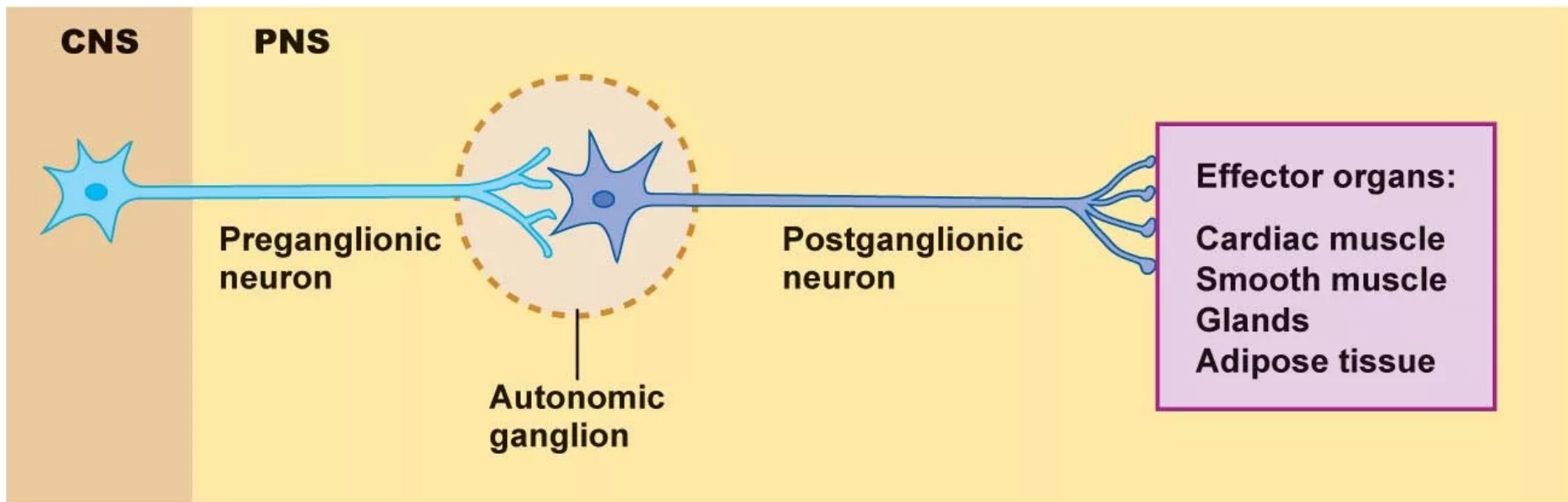
Sweat Glands

## LOCATION OF RECEPTORS FOR CATECHOLAMINES (Epinephrine, Norepinephrine, and Dopamine)



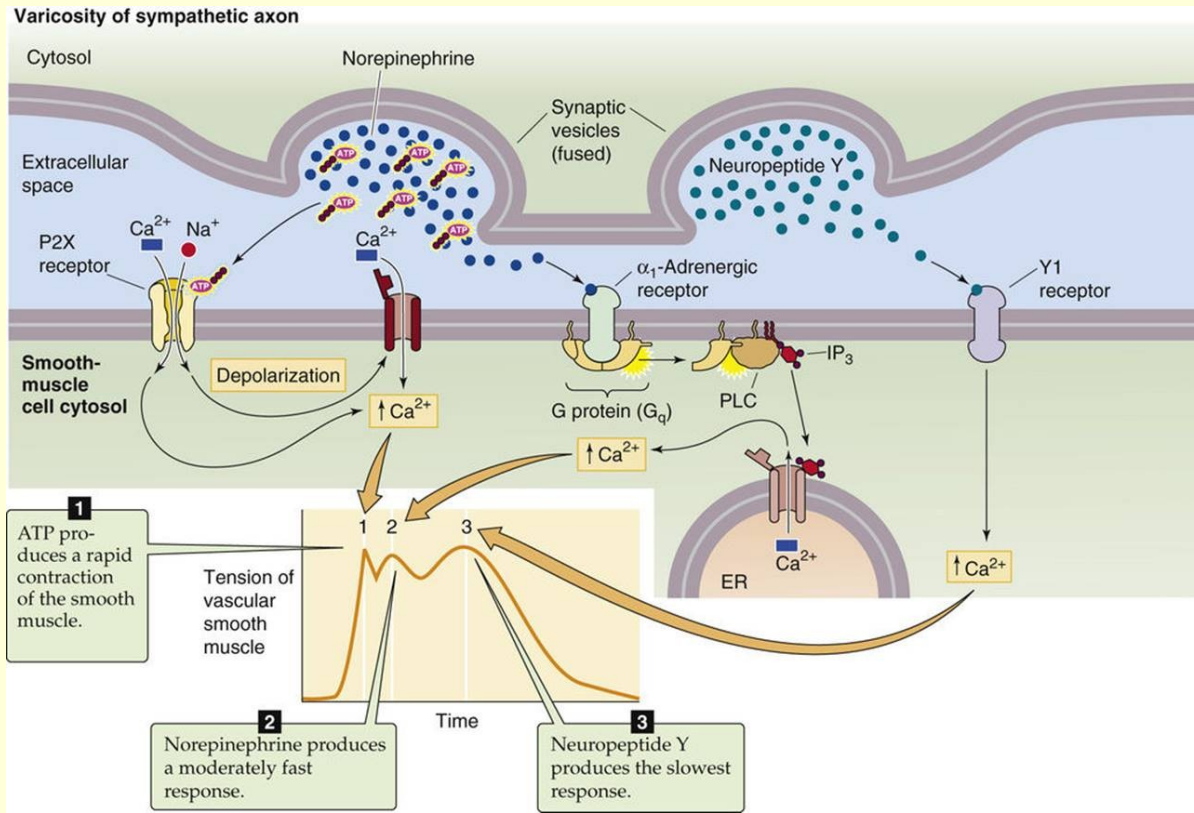
# Neuromodulators in the ANS

- Neuroactive peptides are found in preganglionic and postganglionic neurons of the ANS, including the chromaffin cells of the adrenal medulla, as well as in the enteric neurons of the gut.
- Receptors for neuropeptides are present on effector cells, neuronal cell bodies, dendrites, and presynaptic terminals.



# Neuromodulators in the ANS

- In many cases, neuropeptides act as neuromodulators, providing for, via G protein-mediated pathways, a long-lasting increase (or decrease) in the response of the cell to one or another of the primary neurotransmitters that act on it.



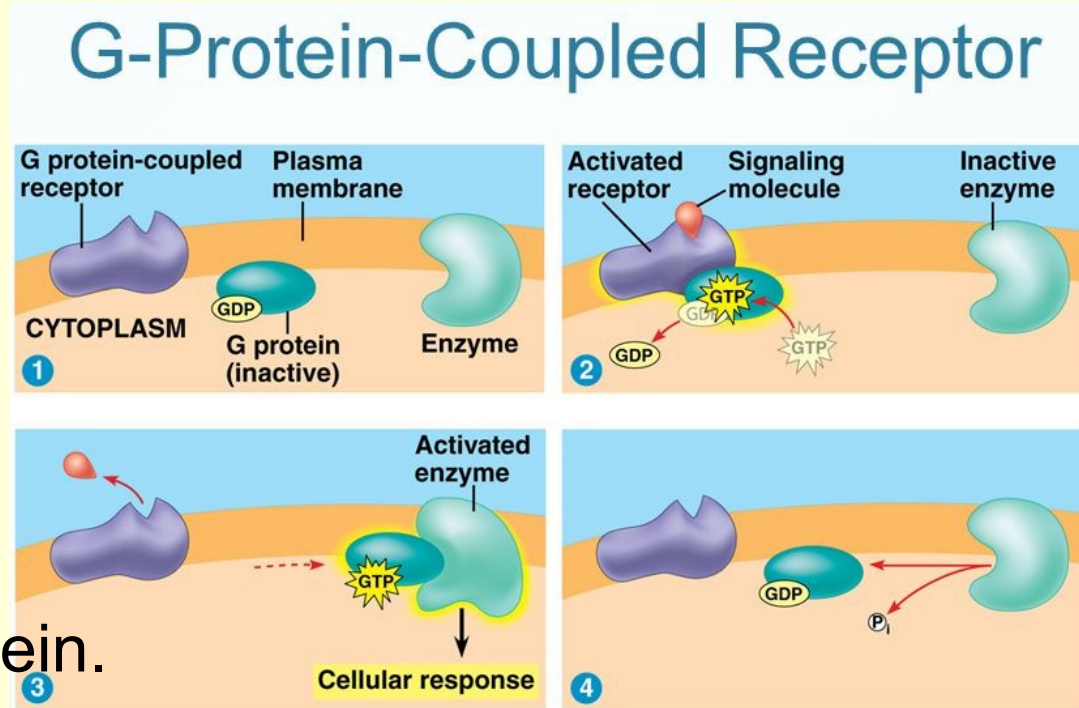
**Peptides in the ANS  
and Its Effector Tissues**

	<b>Location</b>
<b>Angiotensin II</b>	<b>D</b>
<b>Bombesin (Gastrin releasing peptide)</b>	<b>C D</b>
<b>Calcitonin gene-related peptide</b>	<b>B D</b>
<b>Cholecystokinin (CCK)</b>	<b>D</b>
<b>Dynorphin</b>	<b>C</b>
<b>Enkephalin</b>	<b>A D E</b>
<b>Galanin</b>	<b>D</b>
<b>Luteinizing hormone releasing hormone (LHRH)</b>	<b>A</b>
<b>Neuropeptide Y</b>	<b>B</b>
<b>Neurotensin</b>	<b>A</b>
<b>Oxytocin</b>	<b>D</b>
<b>Somatostatin</b>	<b>A D</b>
<b>Substance P</b>	<b>A B C</b>
<b>Vasoactive Intestinal Polypeptide (VIP)</b>	<b>B C D E</b>

**A = Preganglionic neurons    C = Enteric neurons**  
**B = Postganglionic neurons    D = Visceral afferent fibers**  
**E = Adrenal medulla**

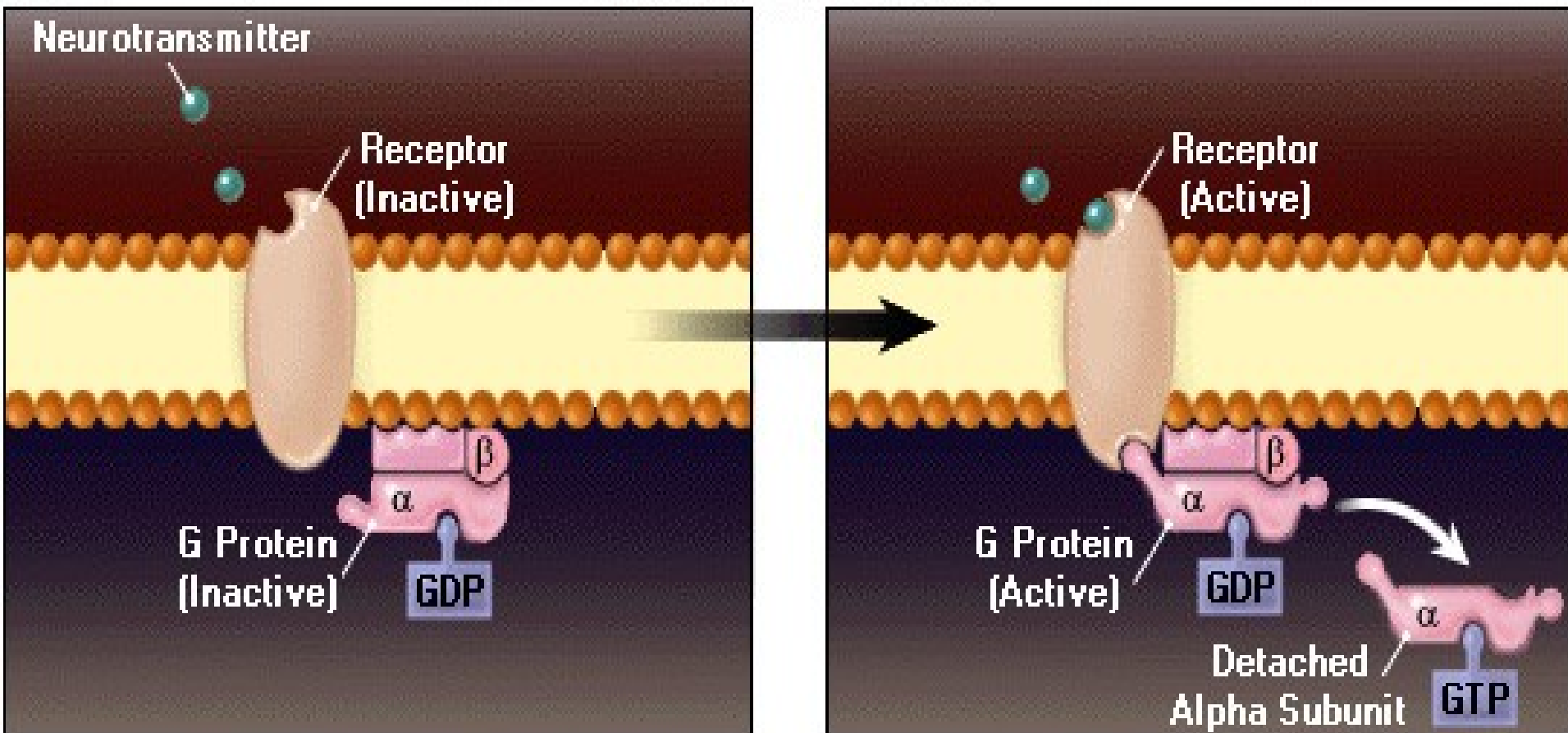
# Cell Signaling by G Protein Activation

- G proteins are a class of proteins that control the formation of intracellular second messengers by regulating the activity of enzymes in the plasma membrane.
- When the neurotransmitter (or hormone) binds to its G protein-linked receptor, a conformation change in the receptor protein activates the G protein.





## Activation of G Proteins



# Cell Signaling by G Protein Activation

This can produce several effects, including:

- increase or decrease in cyclic adenosine monophosphate (cAMP)
- increase in inositol trisphosphate (IP<sub>3</sub>) and diacylglycerol (DAG),
- direct effects on ion channels, and production of nitric oxide (NO).

## Intracellular Effector Mechanisms Regulated by G Protein Activation

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cAMP

IP<sub>3</sub> & DAG

NO

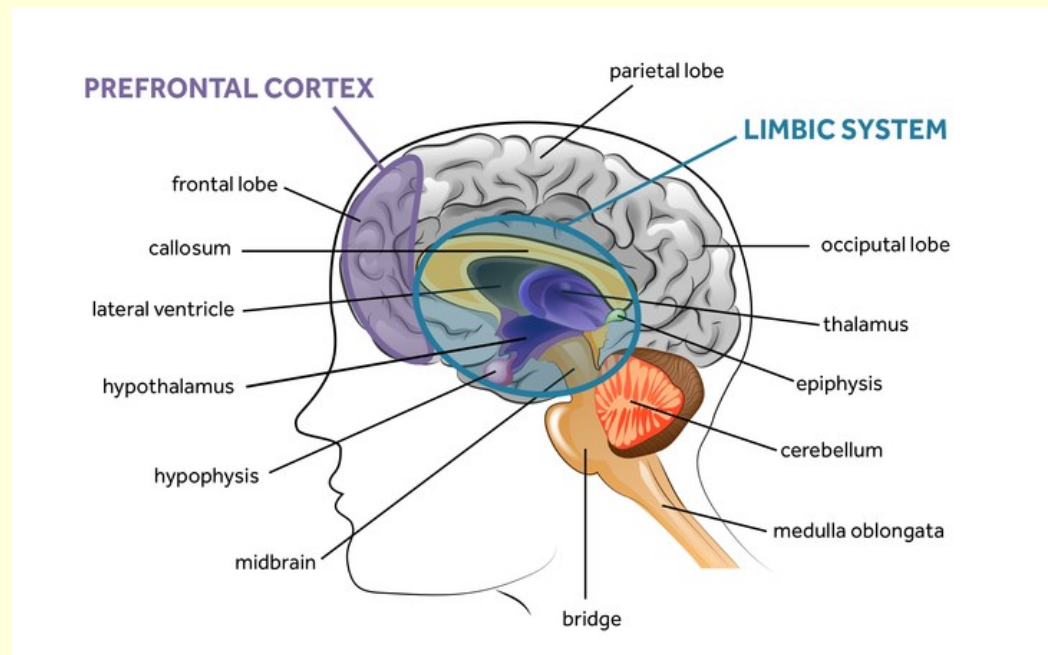
cGMP

## FACTORS REGULATING THE NUMBER OF RECEPTORS

FACTOR	TISSUE RESPONSE
Presence of agonist or endogenous ligand	↓ Receptors & sensitivity
Presence of antagonist	↑ Receptors & sensitivity
Denervation	↑ Receptors & sensitivity
Aging	↓ Receptors & sensitivity
Hormones	↑ or ↓ Receptors & sensitivity
Innervation (During development)	↑ Receptors & sensitivity

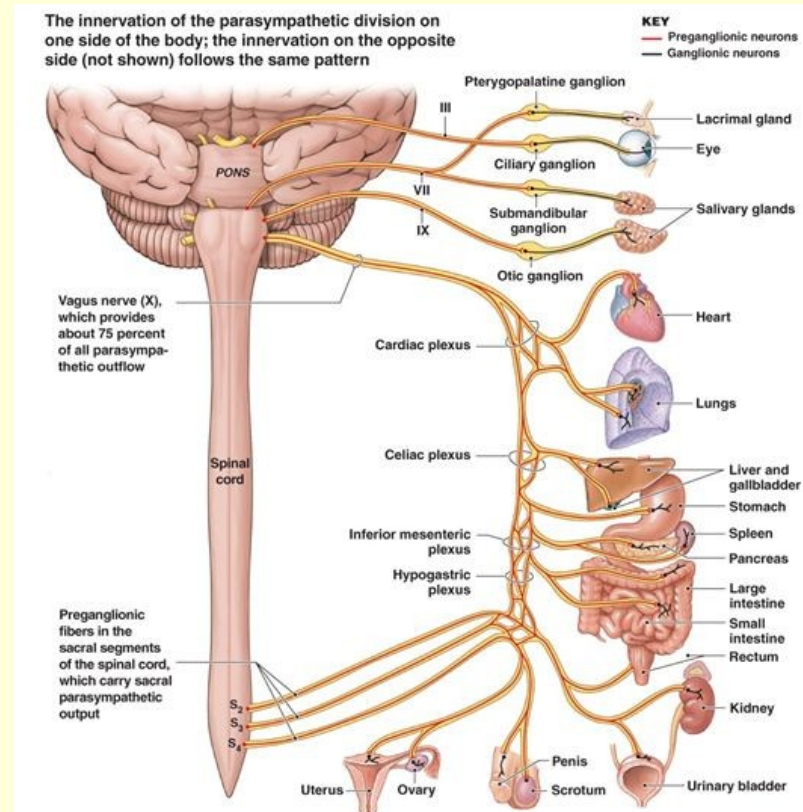
# HIGHER CONTROL OF SYMPATHETIC

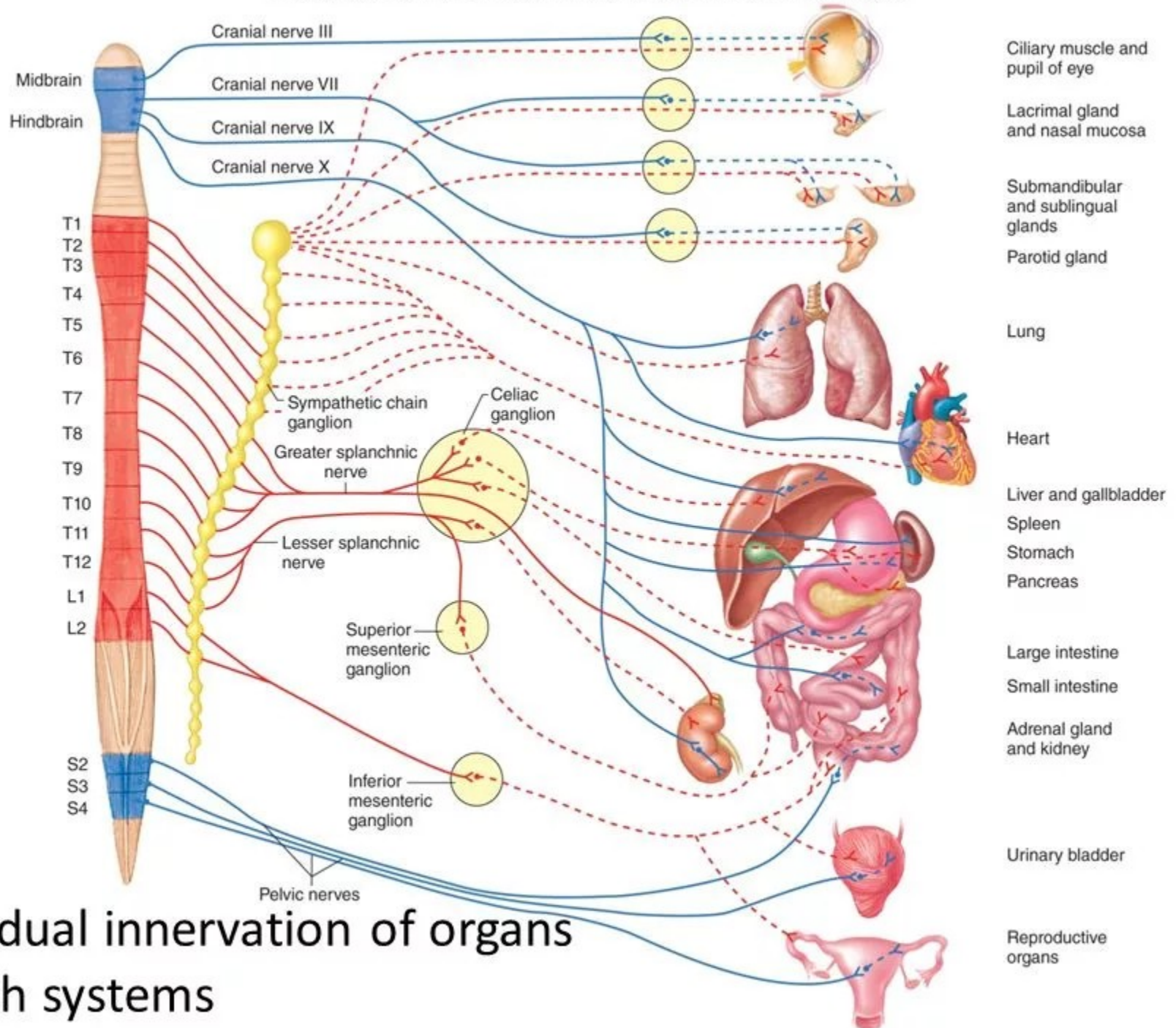
- The lateral horn cells of the spinal cord of the thoracolumbar regions are the “spinal centers” of sympathetic. These spinal centers are controlled by “higher centers”.
- An immediate higher center is “vasomotor center” at medulla. The “vasomotor center”, in turn is controlled and influenced by:
  - a) still higher centers like hypothalamus, limbic system, cerebral cortex (prefrontal lobe) and pontine nucleus;
  - b) reflexes like sinuaortic reflex;
  - c) blood oxygen tension and pH;
  - d) drugs.



# HIGHER CONTROL OF PARASYMPATHETIC

- Anterior region of hypothalamus is a higher center of parasympathetic activity.
- The dorsal nucleus of vagus is influenced by various reflexes like baroreceptor reflex.
- The superior (7<sup>th</sup>), inferior (9<sup>th</sup>) salivary nuclei and Edinger-Westphal nuclei (3<sup>rd</sup>) are influenced by various reflexes.





**Note: dual innervation of organs by both systems**

## **TYPICAL SIGNS OF ANS DYSFUNCTION**

**Postural (orthostatic) Hypotension**

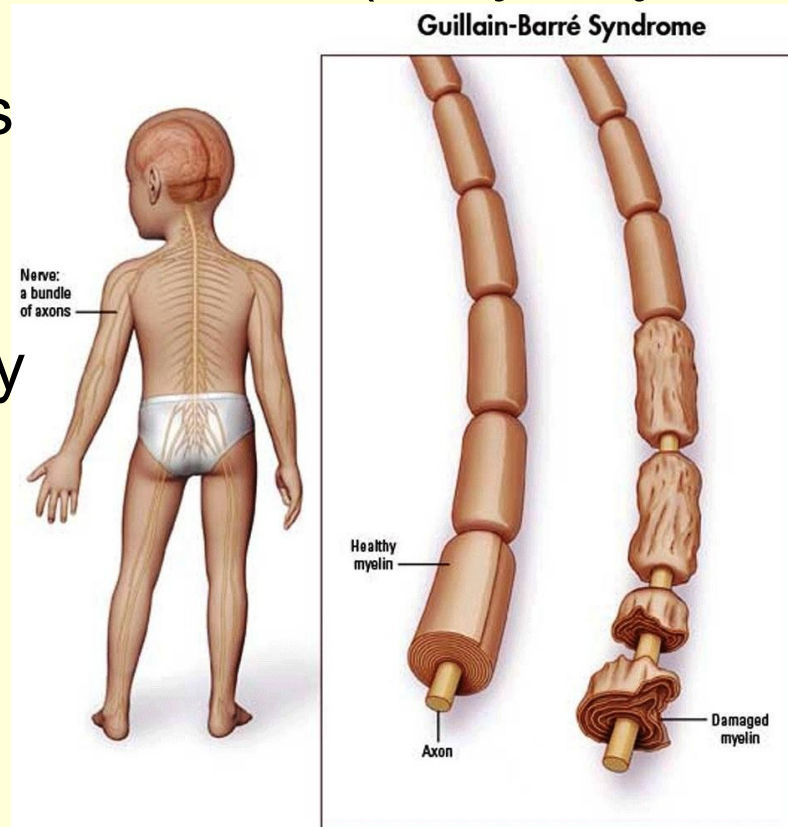
**Sexual Impotence**

**Disturbances of Micturition**

**Defective Sweating**

# Clinical Signs of ANS Dysfunction

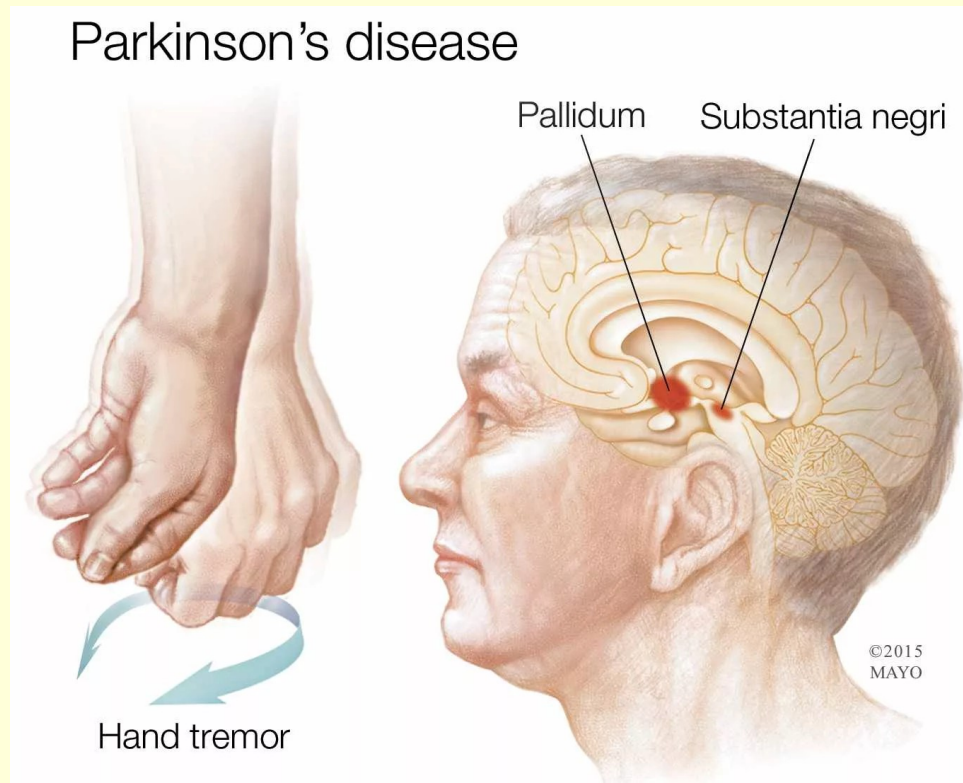
- Autonomic dysfunction may occur due to a disease process that is selective for the cells and fibers of the ANS. Examples are pure autonomic failure, multiple system atrophy, and familial dysautonomia (Riley-Day syndrome).
- In other cases, autonomic signs accompany other medical conditions. Examples are Parkinson's disease, diabetes, infectious peripheral neuropathy (Guillain-Barre syndrome), alcoholism, multiple sclerosis, and spinal cord damage.





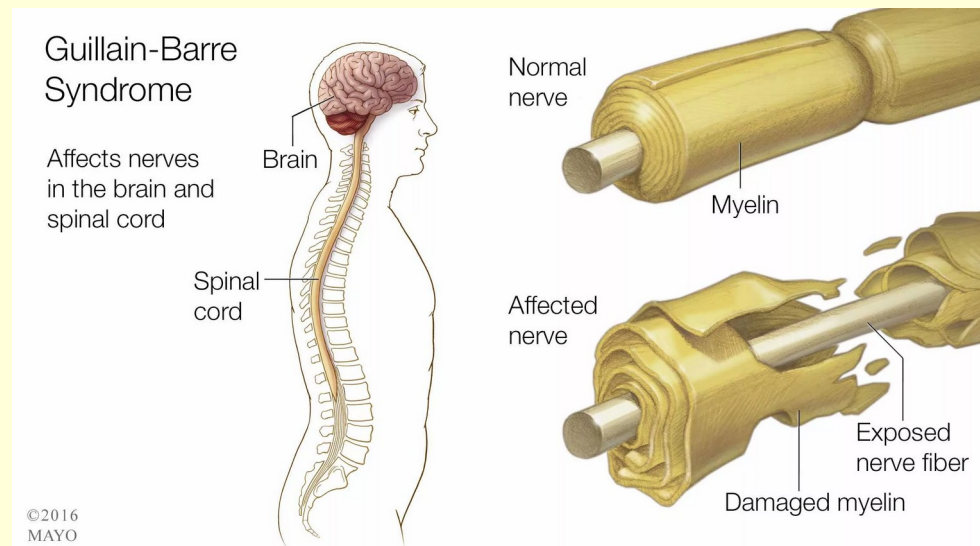
# Clinical Signs of ANS Dysfunction

- Some typical signs of ANS dysfunction, especially postural hypotension, impotence, and disturbance of micturition, may be the first signs of pure autonomic failure and multiple system atrophy.
- Degeneration of pre- and postganglionic autonomic neurons occurs in these diseases. This degeneration may progress and include lower motor neurons (multiple system atrophy) or cells in the substantia nigra (Parkinson's disease).



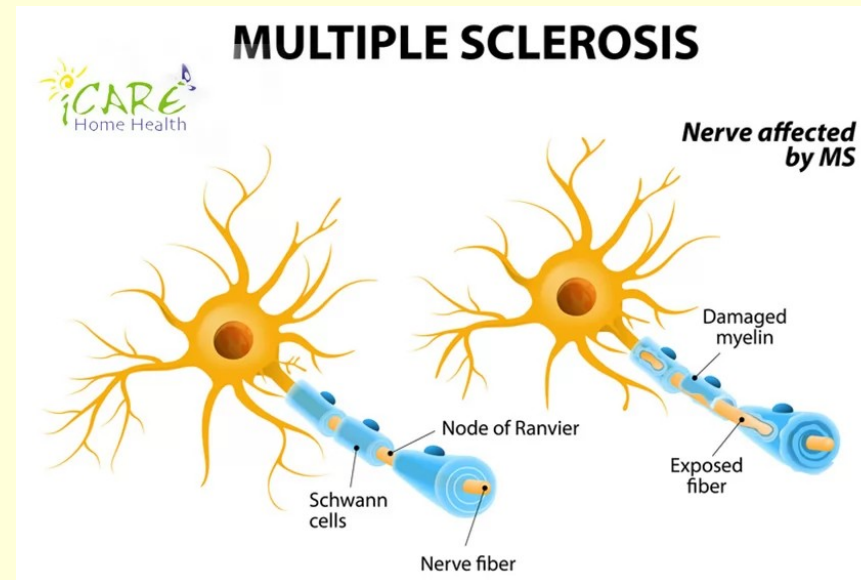
# Peripheral Neuropathies

- In peripheral neuropathies, similar signs may occur, but they are usually accompanied by the distinct signs of peripheral somatic sensory and somatic motor dysfunction that are hallmarks of damage to peripheral nerves.
- For example, in acute infectious peripheral neuropathy (Guillain-Barre syndrome), initial signs are distal paresthesias, numbness, and muscle weakness, the latter accompanied by muscle wasting and decreased stretch reflexes, but no fasciculations.

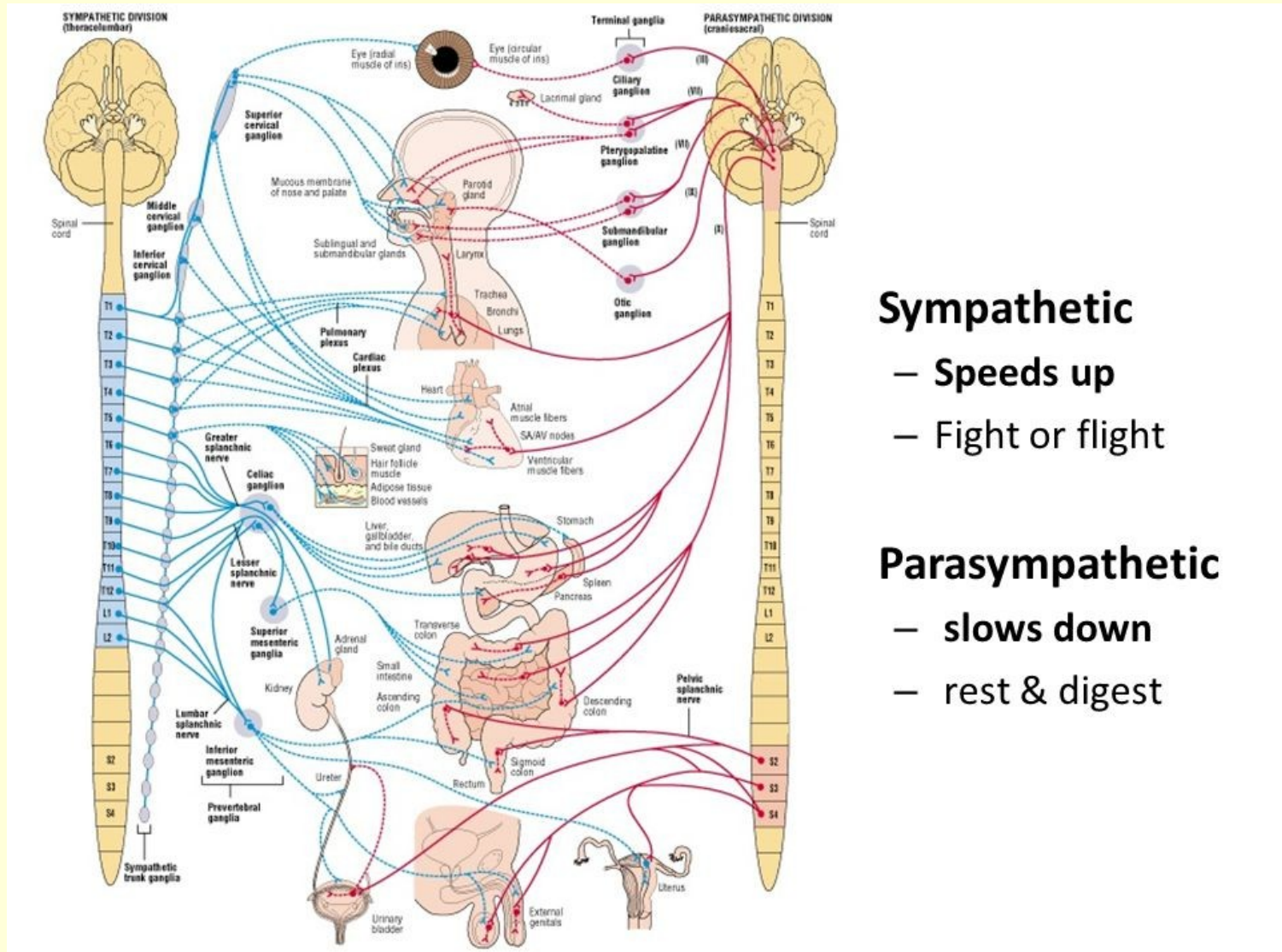


# Multiple Sclerosis and Spinal Cord Lesions

- These disorders mainly influence ANS function by disconnecting the preganglionic neurons of the spinal cord, the final common path for much of the ANS, from their supraspinal control.
- The effects depend on the level and severity of the lesion.
- Complete spinal cord transection is devastating to body temperature control, blood pressure regulation, and bowel, bladder, and sexual function.



# Thank You For Your Attention!



## Sympathetic

- Speeds up
- Fight or flight

## Parasympathetic

- slows down
- rest & digest