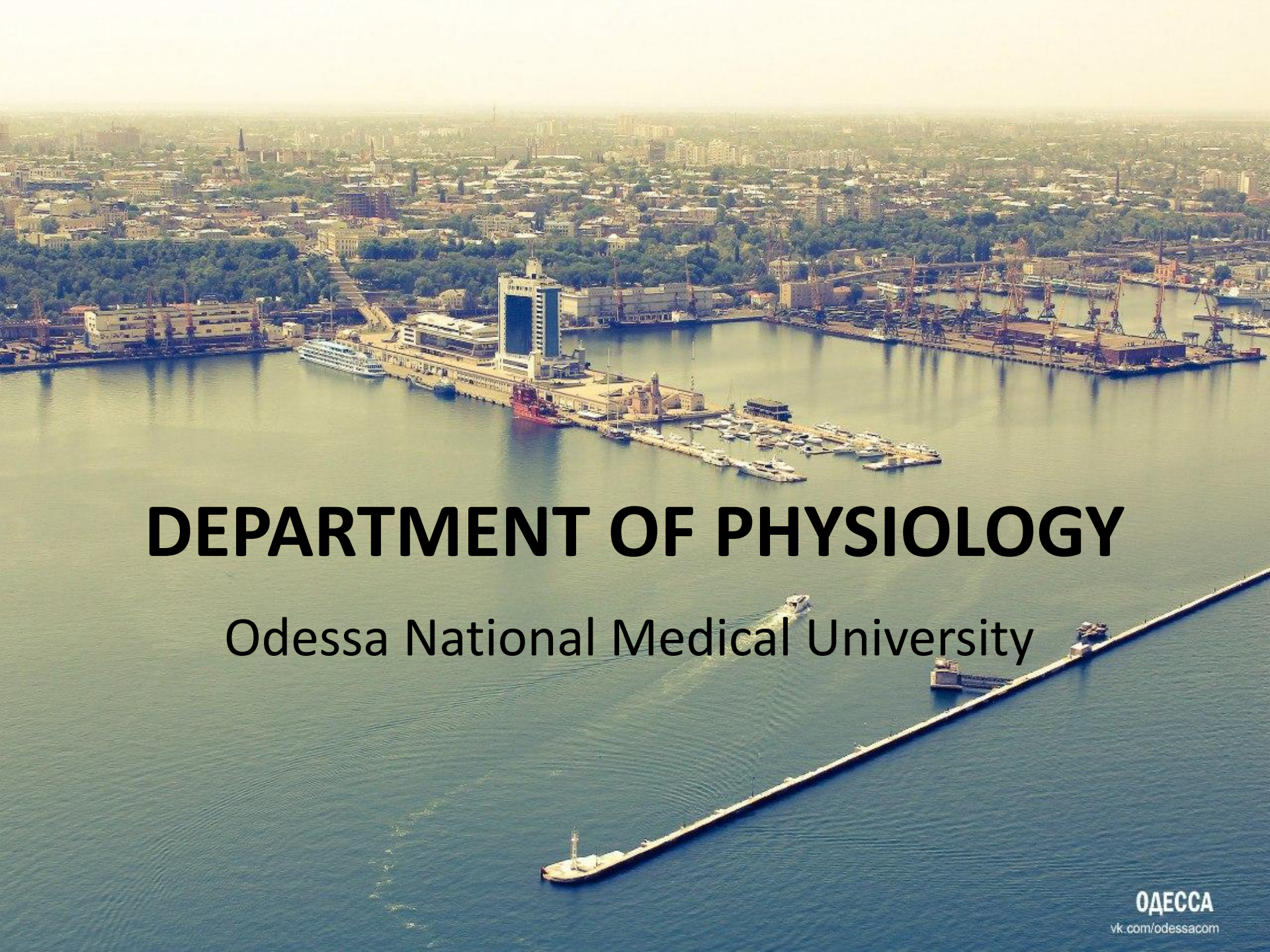


DEPARTMENT OF PHYSIOLOGY

Odessa National Medical University

Lecture № 5

STRUCTURAL AND FUNCTIONAL ORGANISATION OF THE AUTONOMIC NERVOUS SYSTEM AND ITS ROLE IN THE REGULATION OF VISCERAL FUNCTIONS.

As. DENYSENKO Oksana

Autonomic nervous system

ANS functions fall into three major categories:

- 1. Maintaining homeostatic conditions within the body;
- 2. Coordinating the body's responses to exercise and stress;
- 3. Assisting the endocrine system to regulate reproduction.

AUTONOMIC NERVOUS SYSTEM

- A part of the nervous system - complex of central and peripheral cellular structures - that regulates key involuntary functions of the body, including the activity of the heart muscle; the smooth muscles, including the muscles of the intestinal tract; and the glands.

CIASSIFICATION OF ANS

Vegetative,
autonomic,
visceral,
ganglionic,
involuntary

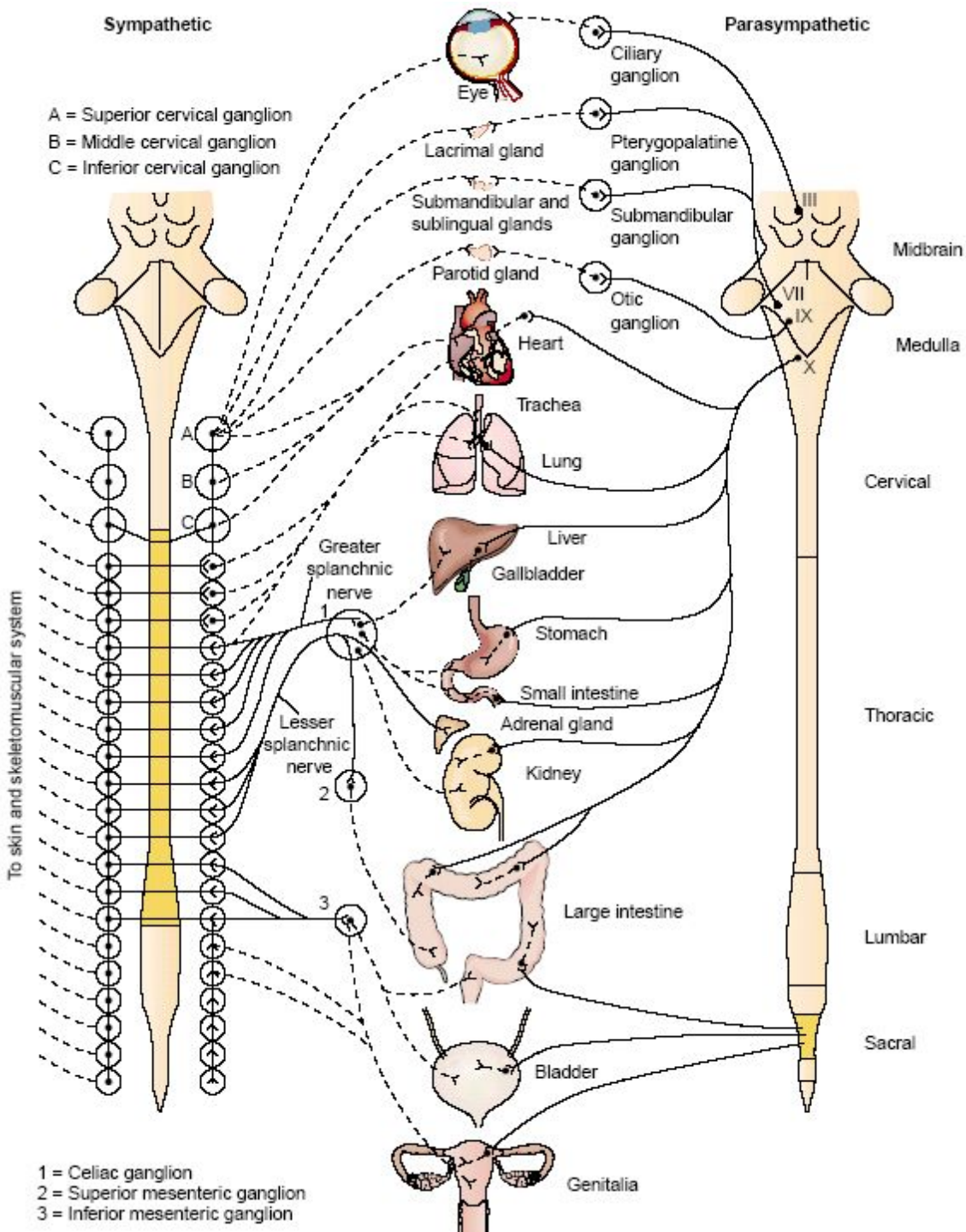
Sympathetic,
thoracolumbar,
adrenergic

Parasympathetic,
craniosacral,
cholinergic

Metasympathetic,
enteric,
intramural

General plan of ANS composition

- Central segmented neurons – preganglionic neurons, spinal cord, medulla oblongata, midbrain. Hypothalamus, RF, cerebellum, BG, cortex – supersegmentary centers
- Axons of segmented neurons – preganglionic fibers
- Vegetative ganglies – paravertebral and prevertebral - sympathetic, intramural – para- and metasympathetic
- Posganglionic fibers – go to organs


Sympathetic
Parasympathetic
A = Superior cervical ganglion
B = Middle cervical ganglion
C = Inferior cervical ganglion
Eye
Ciliary ganglion
Lacrimal gland
Pterygopalatine ganglion
Submandibular and sublingual glands
Submandibular ganglion
Parotid gland
Otic ganglion
III
VII
IX
X
Midbrain
Medulla
Heart
Trachea
Lung
Cervical
A
B
C
Liver
Gallbladder
Greater splanchnic nerve
1
Stomach
Small intestine
Adrenal gland
Lesser splanchnic nerve
2
Kidney
Thoracic
3
Large intestine
Lumbar
Sacral
Bladder
Genitalia
To skin and skeletomuscular system
1 = Celiac ganglion
2 = Superior mesenteric ganglion
3 = Inferior mesenteric ganglion

Main differences between somatic and autonomic nervous system

Indices	Somatic NS	ANS
Control	voluntary	involuntary
Action	Innervates skeletal muscles	Innervates internal organs
Main functions	Sensory, motor	Energy, nutrition
Spreading	strongly segments	All body
Fibers type	Mostly A	B, C

Main function of ANS

- Maintenance of homeostasis
- Mechanisms of adaptation
- Metabolism regulation
- Efferental innervation of all SMsc. of internal organs, vessels, sweat glands
- Trophic innervation of skeletal muscles (SNS), receptors and CNS

Autonomic pathway: Two Efferent Neurons in Series

Preganglionic neuron cell body in CNS

⇩

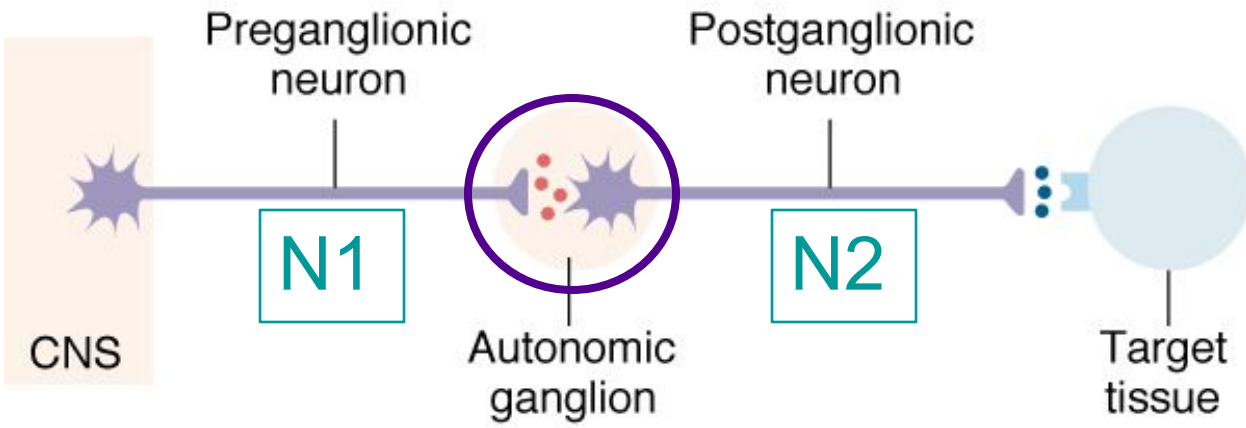
Synapse in autonomic ganglion outside CNS (often divergence!)

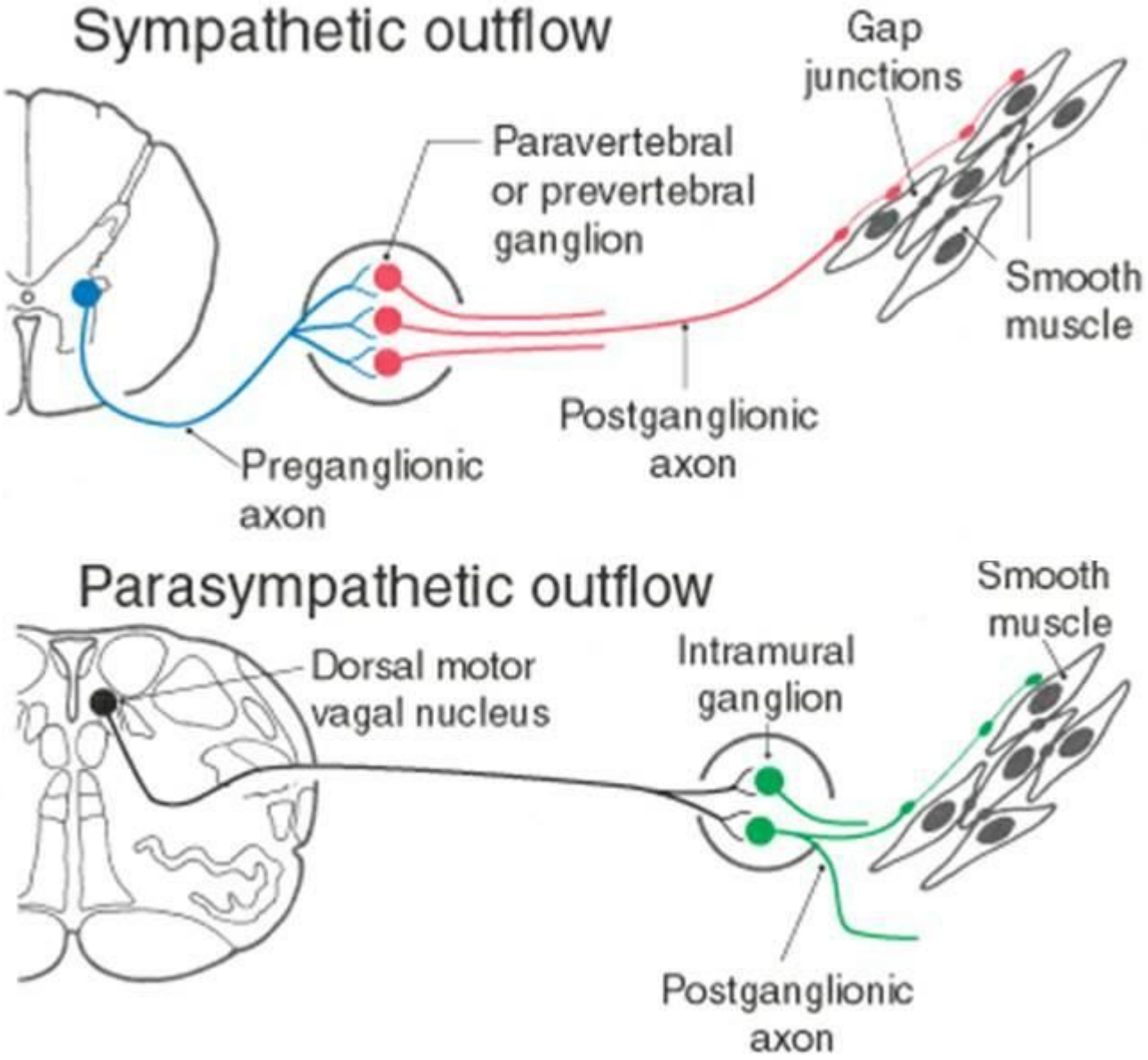
Postganglionic neurons

⇩

target cells

⇩

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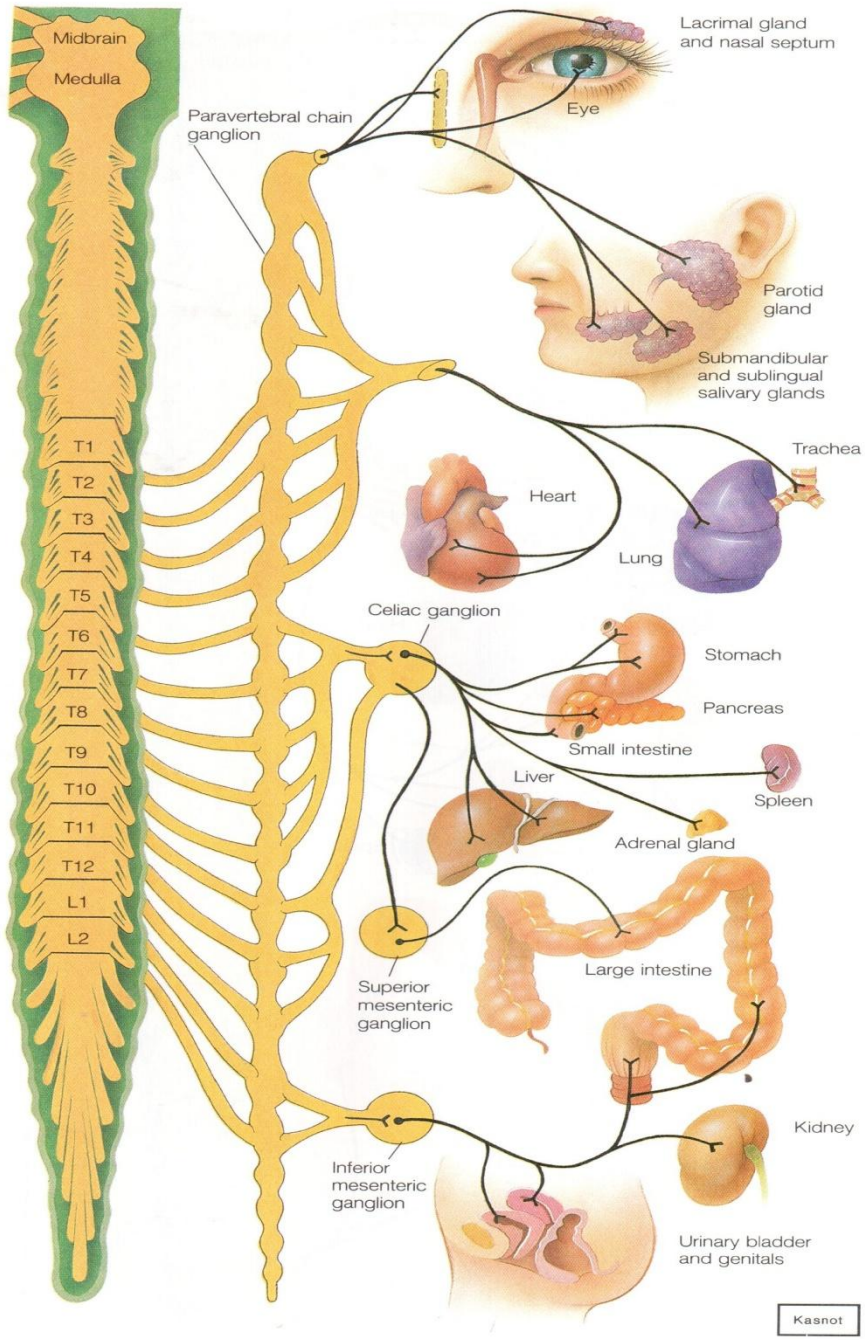
Smooth muscle
Postganglionic axon
Preganglionic axon
Parasympathetic outflow
Smooth muscle
Intramural ganglion
Dorsal motor vagal nucleus
Postganglionic axon

Sympathetic nervous system

innervates all organs and tissues



Sympathetic Nervous System
Figure 11.20

Sympathetic nervous system

- Preganglionic central (1-st) neurons – lateral horns of spinal cord C8-L2 :

- C8-Th2 – spinociliary centre – midriasis, exophthalmos

- T1-T5 – heart, lungs

- T1- L2 – vessels tonus, sweat glands

Sympathetic nervous system

- Main preganglionic fibers leave the spinal cord with the ventral roots of spinal nerves end in paravertebral ganglia (sympathetic trunk (vertebral chain)).

- Other part of these fibers – ends in prevertebral ganglia. These ganglia form different nervous plexus: celiac, superior mesenteric, inferior mesenteric, aorticorenal and renal.

- Neurotransmitter of preganglionic neuron – Ach.

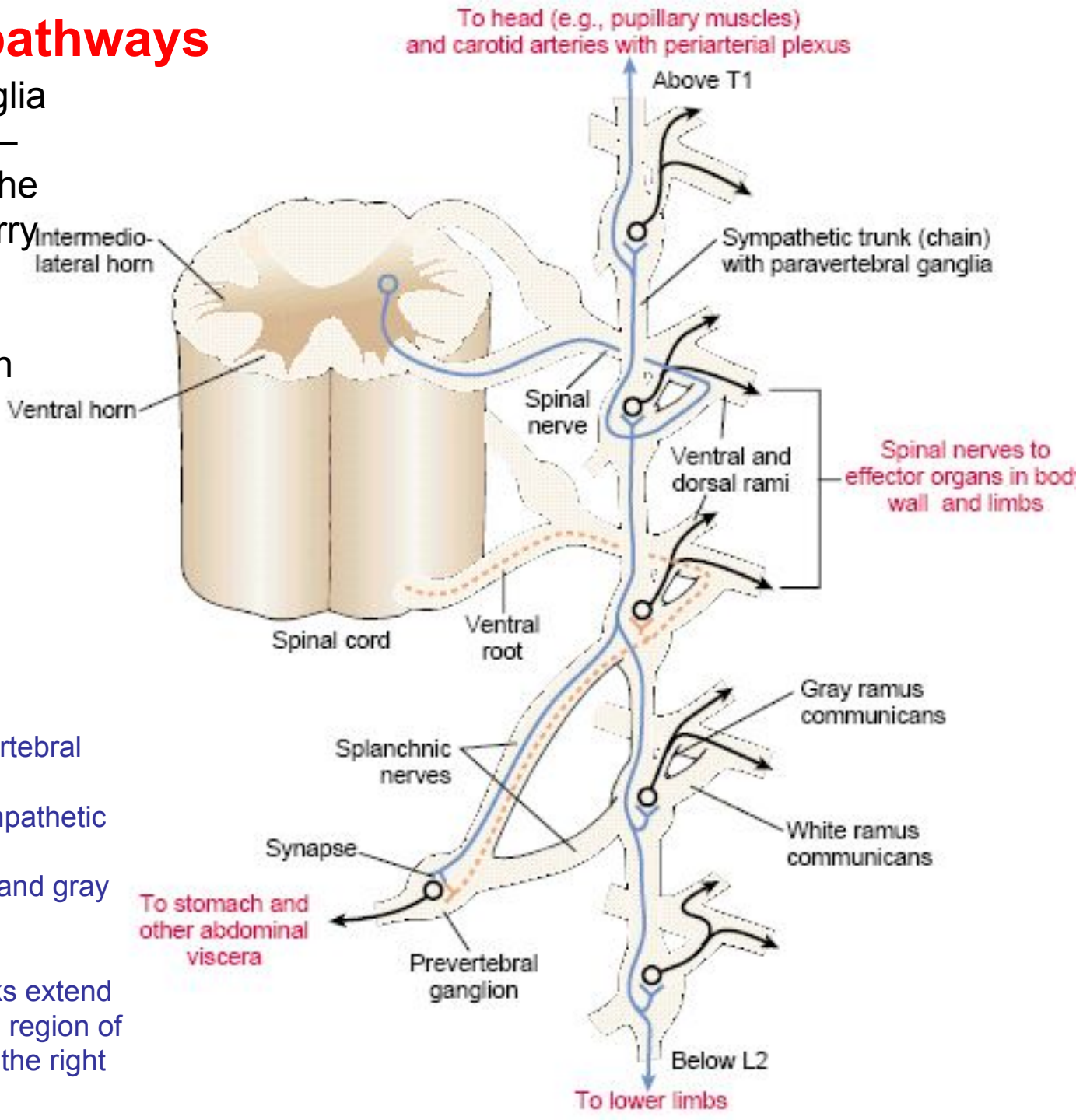
  It acts to N – cholinereceptors. These receptors are blocked by gangliablockers, but not curare like substances as in receptors of skeletal muscles

- postganglionics axons go as self-contained fibers or contained of somatic fibers (rami communicantes grisei)

Sympathetic pathways

Sympathetic chain ganglia (paravertebral ganglia) – preganglionic fibers of the sympathetic NS that carry motor impulses to the body wall or thoracic cavity synapses in chain ganglia

Collateral ganglia (prevertebral ganglia) – group of second order neurons that innervate organs in the abdominopelvic region



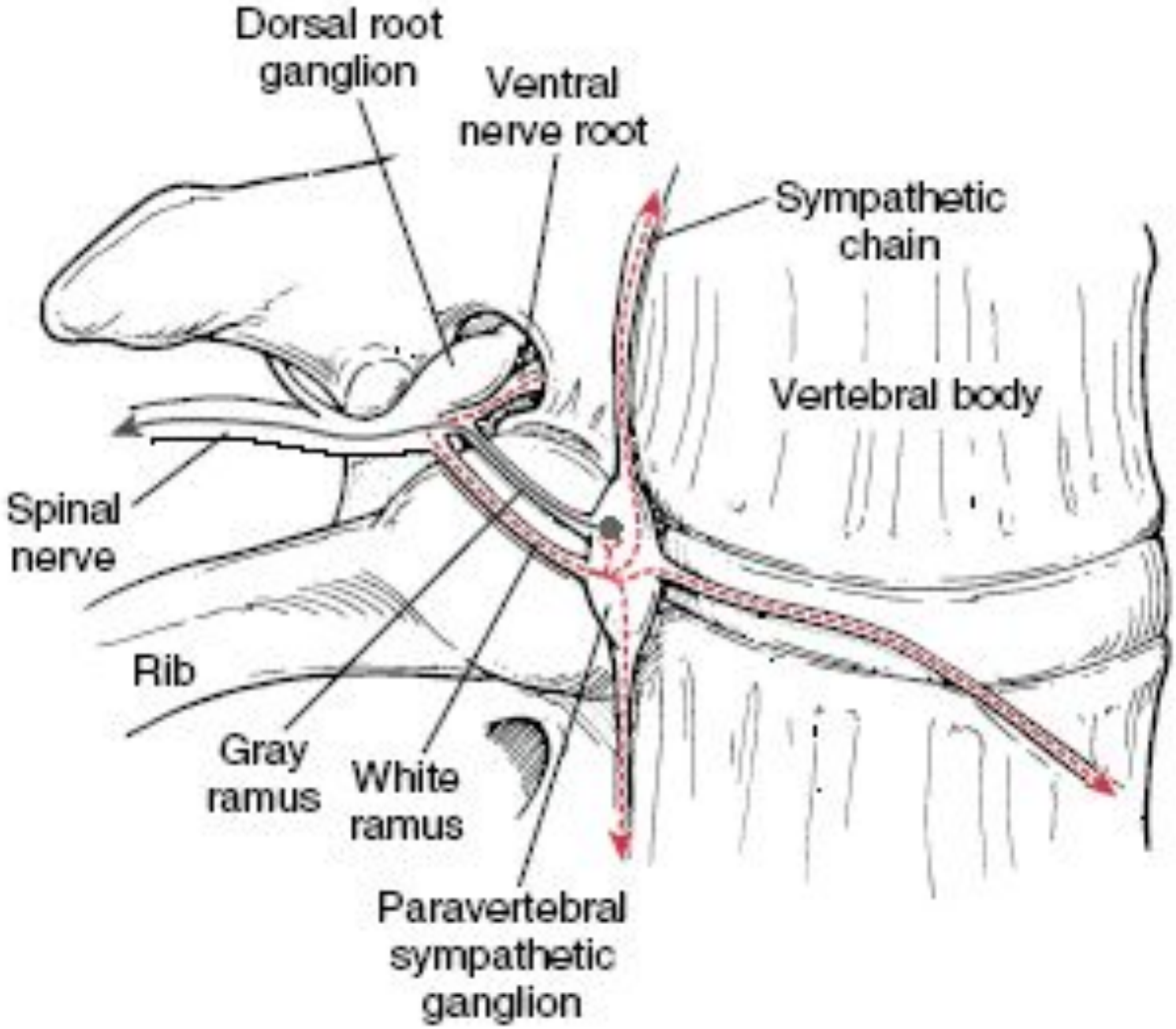
Located on both sides of the vertebral column

Linked by short nerves into sympathetic trunks

Joined to ventral rami by white and gray rami communicantes

Right and left sympathetic trunks extend from the base of the skull to the region of the coccyx; at their distal ends, the right and left trunks are fused.

Sympathetic pathways

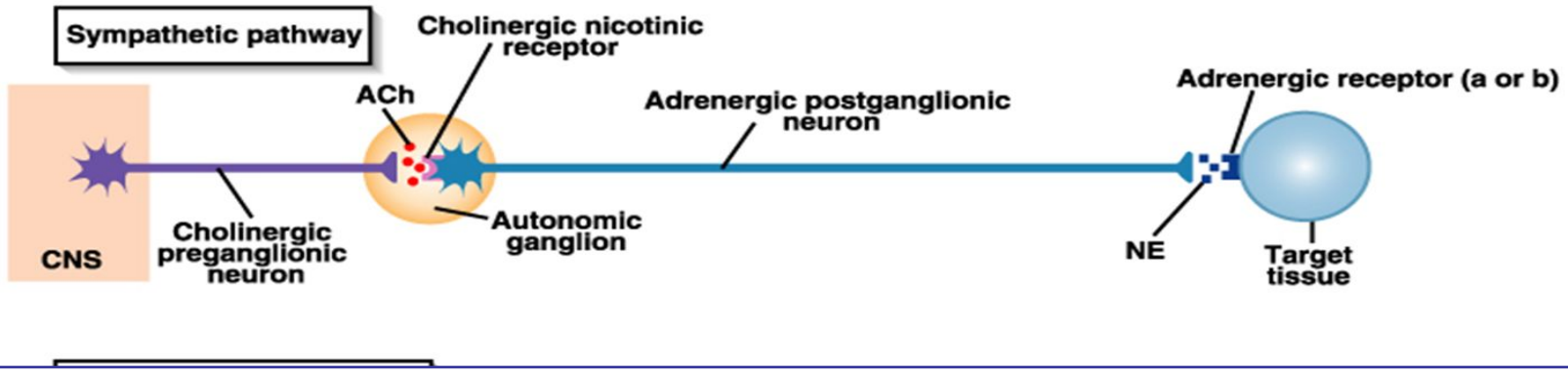


Abdominopelvic viscera

- Celiac ganglion
  - Innervates stomach, liver, gall bladder, pancreas, spleen
- Superior mesenteric ganglion
  - Innervates small intestine and initial portion of large intestine
- Inferior mesenteric ganglion
  - Innervates kidney, urinary bladder, sex organs, and final portion of large intestine

Other important considerations:

ganglion cells are usually located at some distance from the effectors. Accordingly, postganglionic sympathetic fibers are usually long fibers.



Acetylcholine (Ach) - pre-ganglionic ganglionic Neurotransmitter
Norepinephrine (NE) - post-ganglionic ganglionic Neurotransmitter

Sympathetic Division

- A single sympathetic preganglionic fiber has many axon collaterals and may synapse with 20 or more postganglionic neurons.

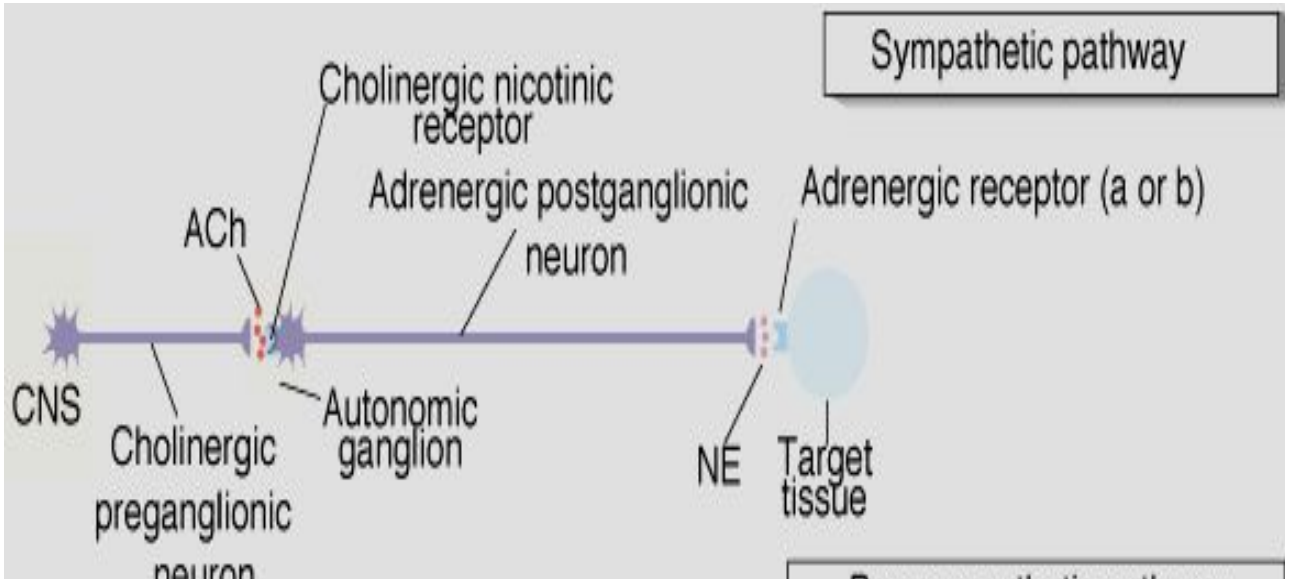
- The postganglionic axons typically terminate in several visceral effectors and therefore the effects of sympathetic stimulation are more widespread than the effects of parasympathetic stimulation.

Sympathetic nervous system

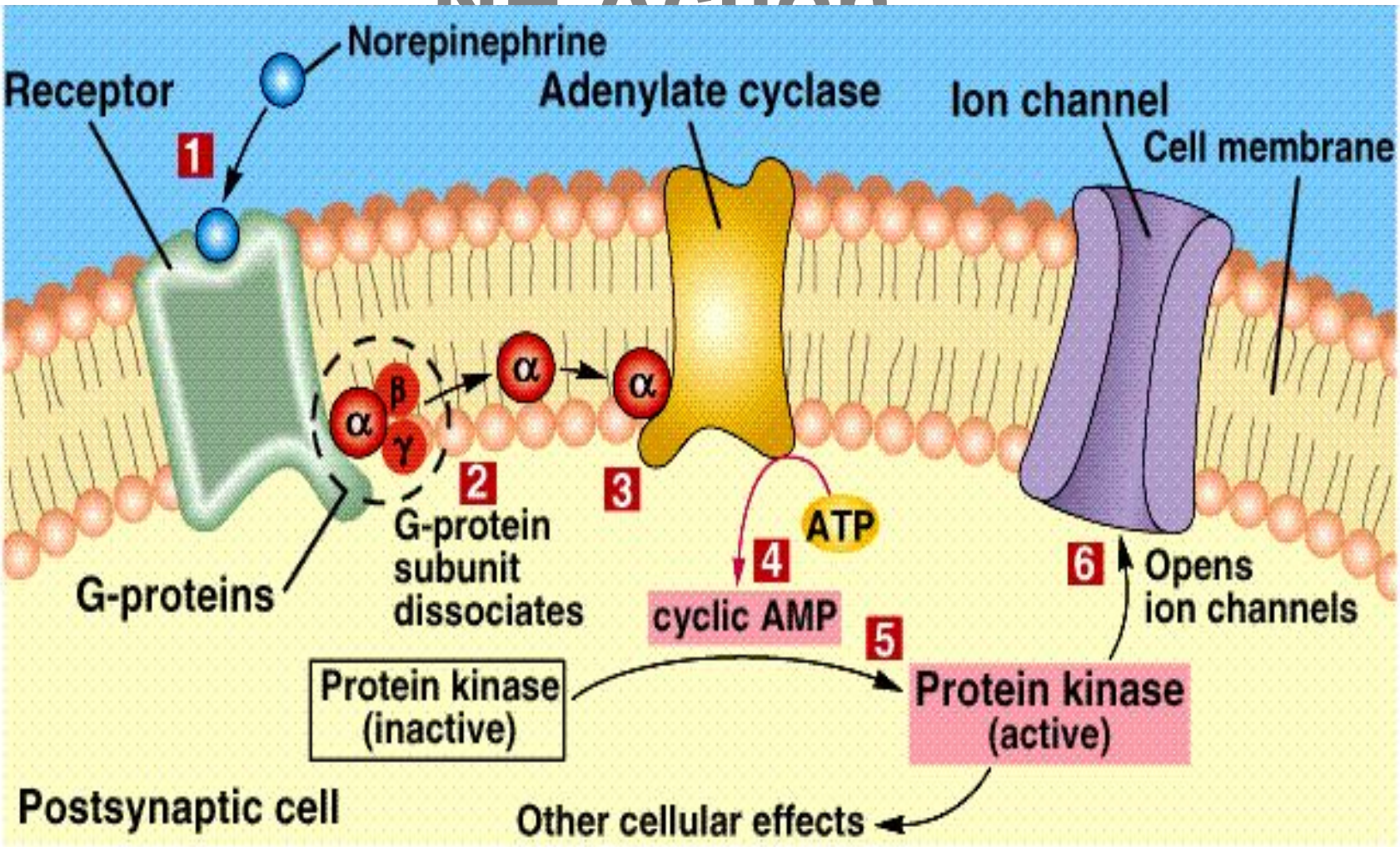
- Endings of postganglionic sympathetic fibers secrete NA.
- NA contacts to a1, a2 and ß1, ß2, ß3 AR. Kind of resulting potential depends on different amount of receptor on postsynaptic membrane.
- For example, if NA interacts to ß1-AR in myocardium, depolarization starts - > HR increases.
- if NA interacts to ß2-AR in uterus, hyperpolarization starts - > activity of uterus decreases.

Adrenergic Receptors

- **Found in neuroeffector junctions of sympathetic branch**
- **G protein linked, with various 2nd mess. Mech**
- **NT is NE**
- **α- and β- Receptors**



NE Action



The binding of norepinephrine to it's receptor (1) causes the dissociation of G-proteins (2). Binding of the alpha G-protein subunit to the enzyme adenylate cyclase (3) activates this enzyme, leading to the production of cyclic AMP (4). Cyclic AMP, in turn, activates protein kinase (5), which can open ion channels (6) and produce other effects.

Sympathetic Receptors

α Receptors:

- NT is NE
- (most common) **α 1 Receptors ⇒Gq ⇒phospholypase C ⇒ Excitation [Ca2+] In↑ ⇒ muscle contraction or secretion by exocytosis.**
- **α 2 Receptors ⇒Gi** ⇒ adenylatecyclase ⇒ cAMP ⇒ **[Ca2+] In ⇒ Inhibition of GI tract and pancreas**

β – Receptors **Clinically more important**

- β_1 ⇒ **Excitation heart ([**E] = [NE])
  - **"β - blockers" = Antagonists** (e.g.: Propranolol)
- β_2 **usually with inhibitory effects: smooth muscle relaxation of some blood vessels and bronchioles** ([E] > [NE])
- β_3 **Adipose; [NE]>[E]**

– **"β -blockers" = Antagonists** (e.g.: Propranolol)

Sympathetic nervous system

- PECULIARITY

  Postganglionic sympathetical fibers of sweat glands secrete Ach.

  Ach interacts to M – ChR in this case, sweat glands increase their activity.

  So these fiber's name is sympathetic cholinergic.

Effects of Sympathetic Division

- *cardiac output increases*
- *SA node*: heart rate (chronotropic) β_1, : ↑*cardiac muscle*: contractility (inotropic) ↑conduction at AV node β_1 : increases
- *vascular smooth muscle:* α1 = contracts; β_2 = relaxes
- *smooth muscles of bronchioles* β_2: relaxes;
- *pupil of eye* α_1: relaxes
- *ciliary muscle* β_2 : relaxes
- *smooth muscles of GI tract* α_2, β_2: relaxes
- *sphincters of GI tract* α_1: contracts
- *glands of GI tract* inhibits

MAIN SYMPATHETIC INFLUENCE ON ORGANS AND TISSUES

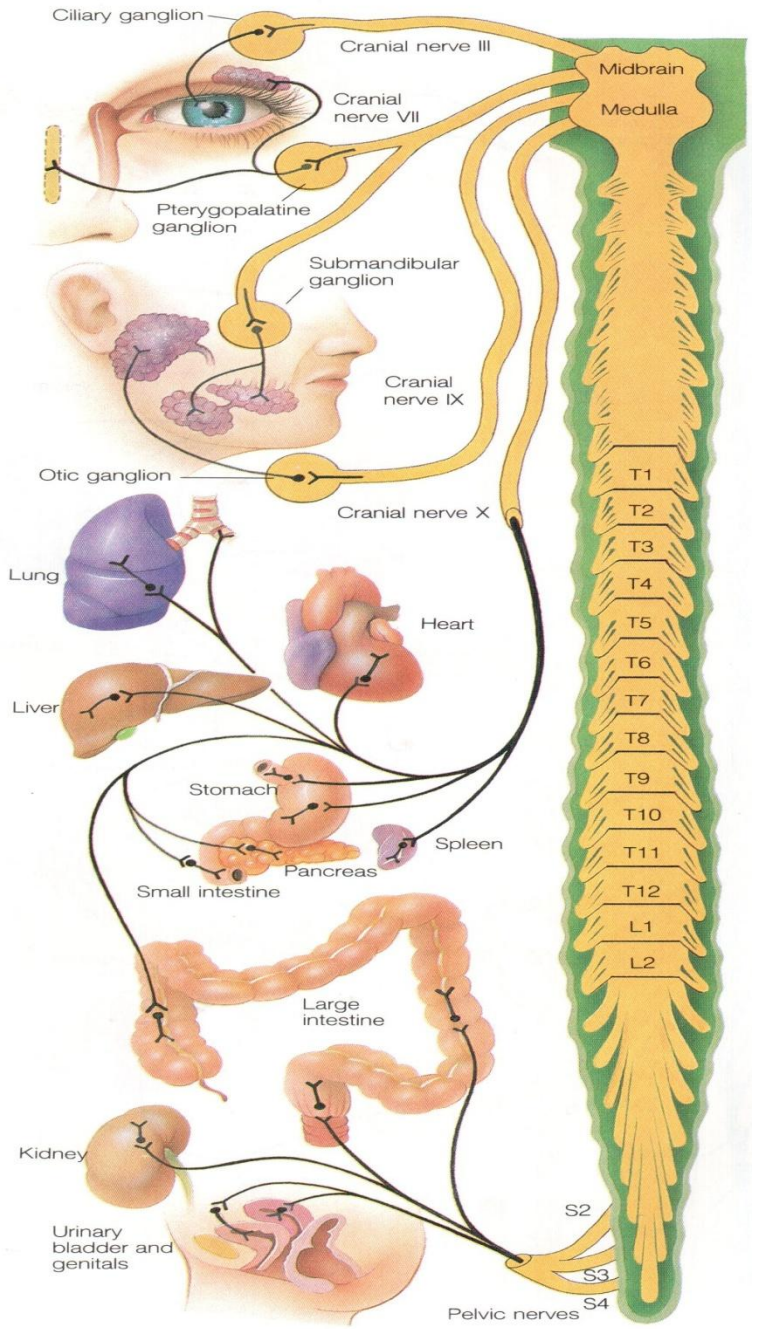
- Energy action :

  - ability to work increases,
  - organism`s life reserve increases
  - ⇑ glycogenolysis, glyconeogenesis, lipolysis
  - ⇑ lungs ventilation
  - blood volume increases in skeletal muscles

- Digestive activity and urinary bladder tonus is decreased

PARASYMPATHETIC NERVOUS SYSTEM

doesn't innervate: skeletal muscles, CNS and bigger part of blood vessels



Parasympathetic Nervous System

PARASYMPATHETIC NERVOUS SYSTEM

- Preganglionic (central) – 1-st neurons :

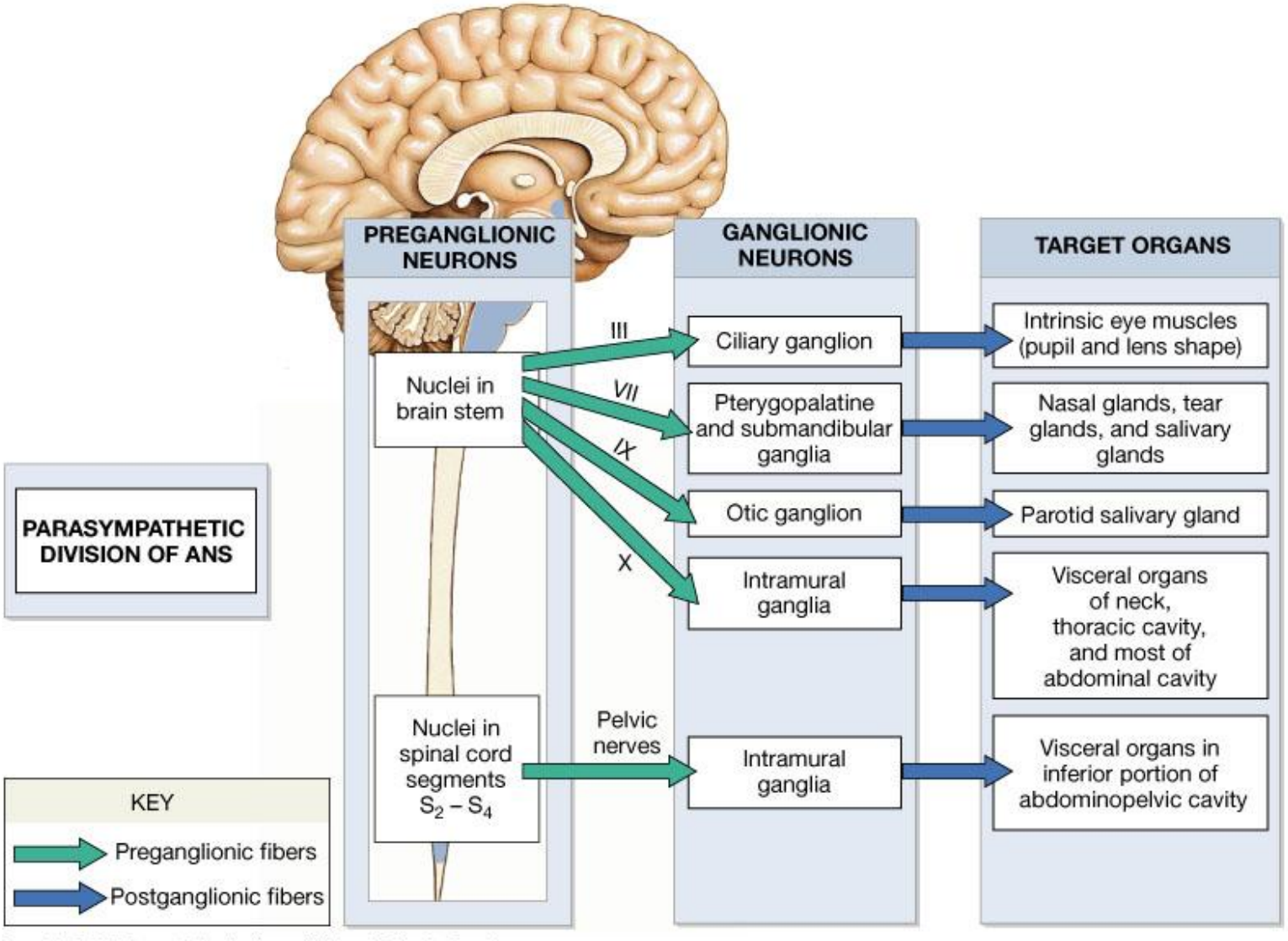
- in mesencephalon part – midbrain – n. oculomotorius (III)

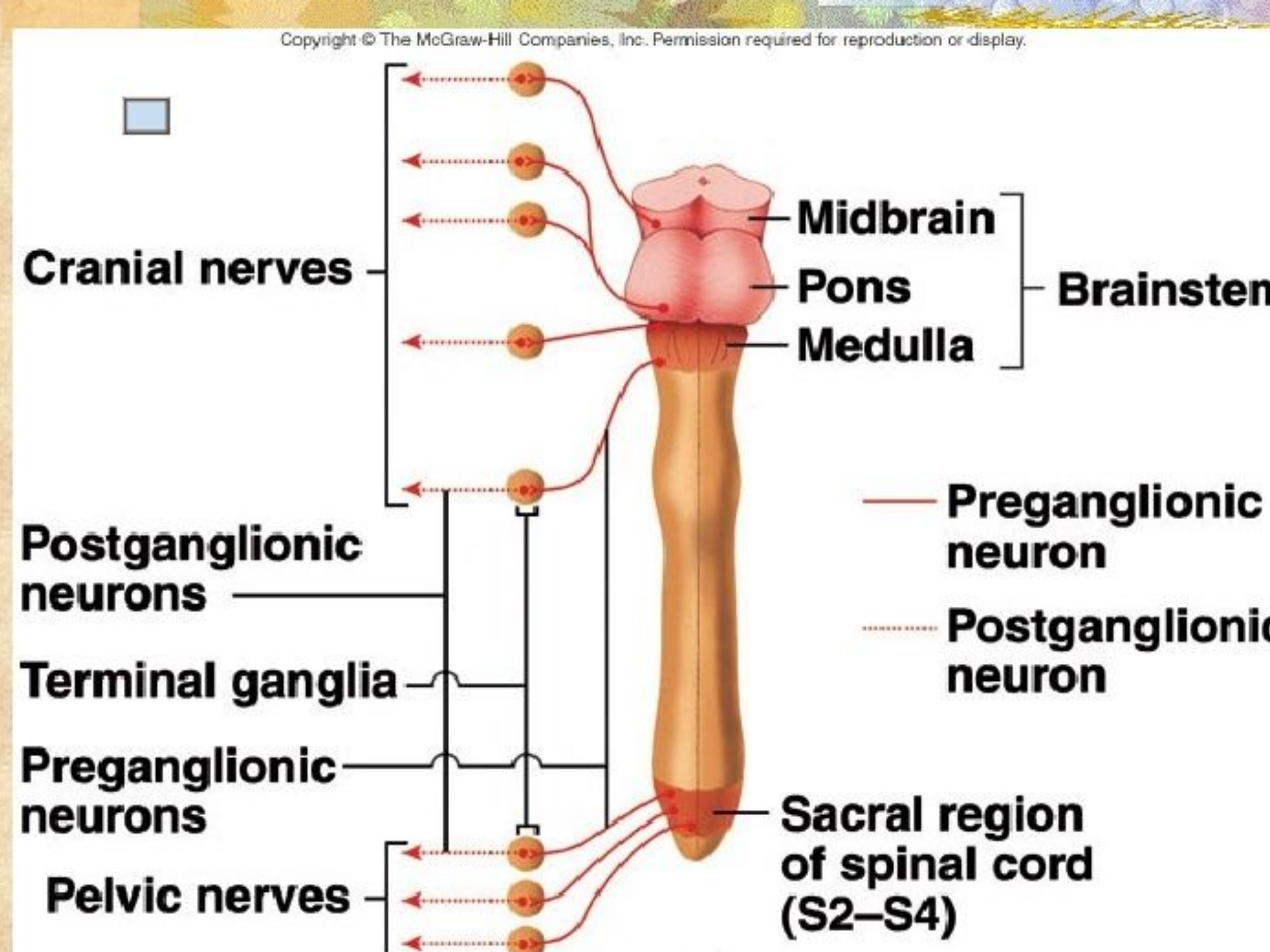
- in medulla oblongata – nucleus VII, IX, X n.

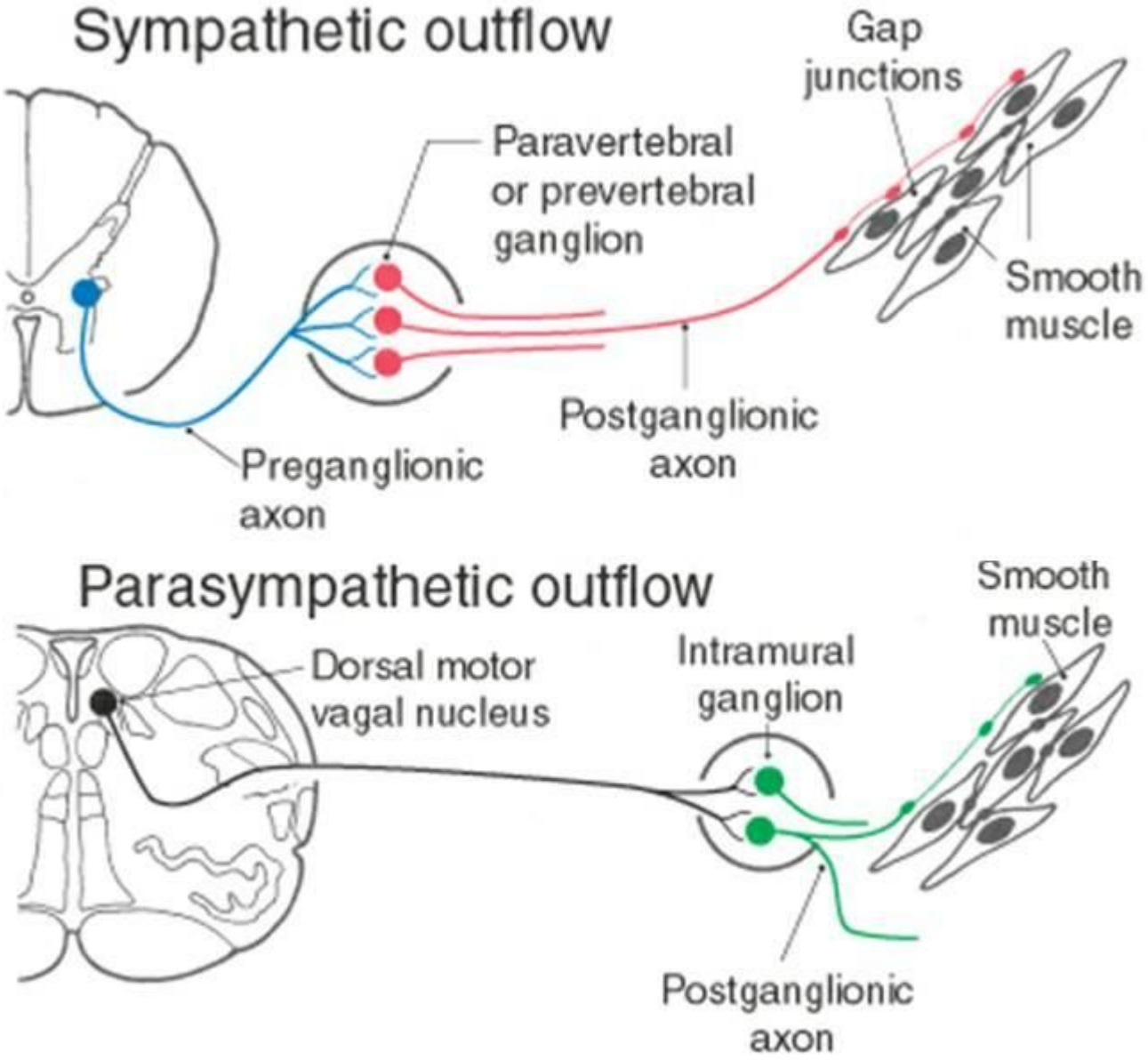
- in sacral part – level of S II-IV

- The fibers of cells in the midbrain and brainstem are in the oculomotor (III), facial (VII), glossopharyngeal (IX), and vagus (X) nerves. They innervate smooth muscles of the eye (III), lacrimal and salivary glands (VII and IX), and smooth muscles of the thoracic and abdominal viscera (X).

The Organization of the Parasympathetic Division of the ANS



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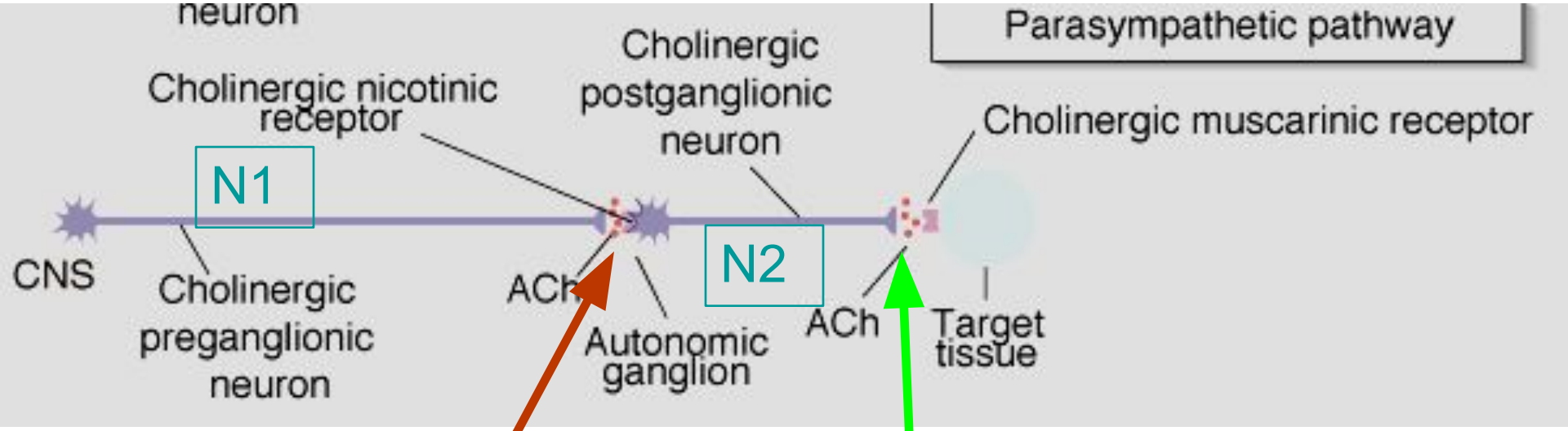
Smooth muscle
Postganglionic axon
Preganglionic axon
Parasympathetic outflow
Smooth muscle
Intramural ganglion
Dorsal motor vagal nucleus
Postganglionic axon

Summary: **Pre- & Postganglionic Parasympathetic Neurons Release ACh**



nicotinic

muscarinic

Receptors

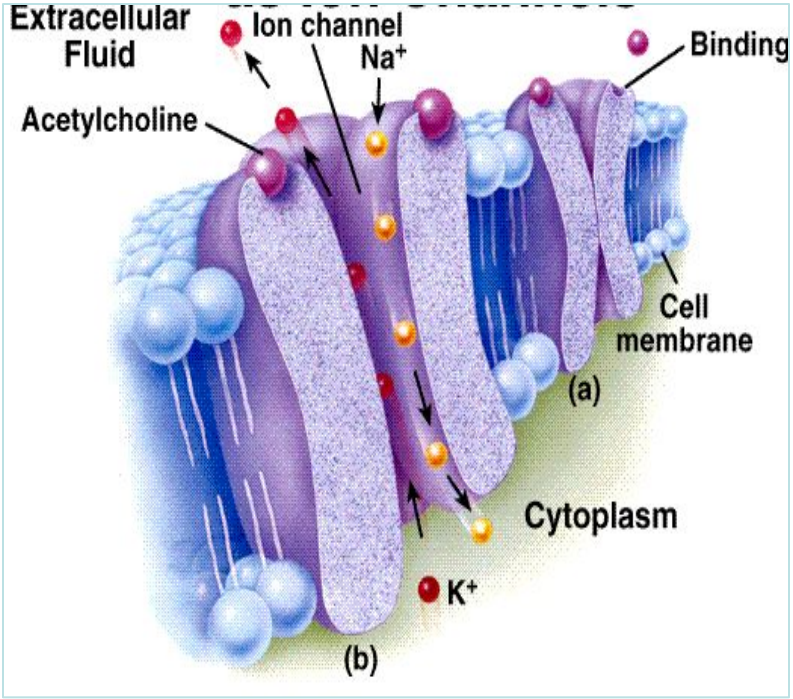
PARASYMPATHETIC NERVOUS SYSTEM

- Main part of preganglionic fibers end in intramural ganglia
- Neurotransmitter of preganglionic neuron is – Ach. Ach interacts to N-cholinereceptors.
- Endings of postganglionic parasympathetic fibers secrete Ach too.
- Ach interact to M-cholinereceptors.

  M-ChR blocks by atropine like substances.

Two Types of Cholinergic Receptors: Nicotinic and Muscarinic

1) Nicotinic cholinergic receptor



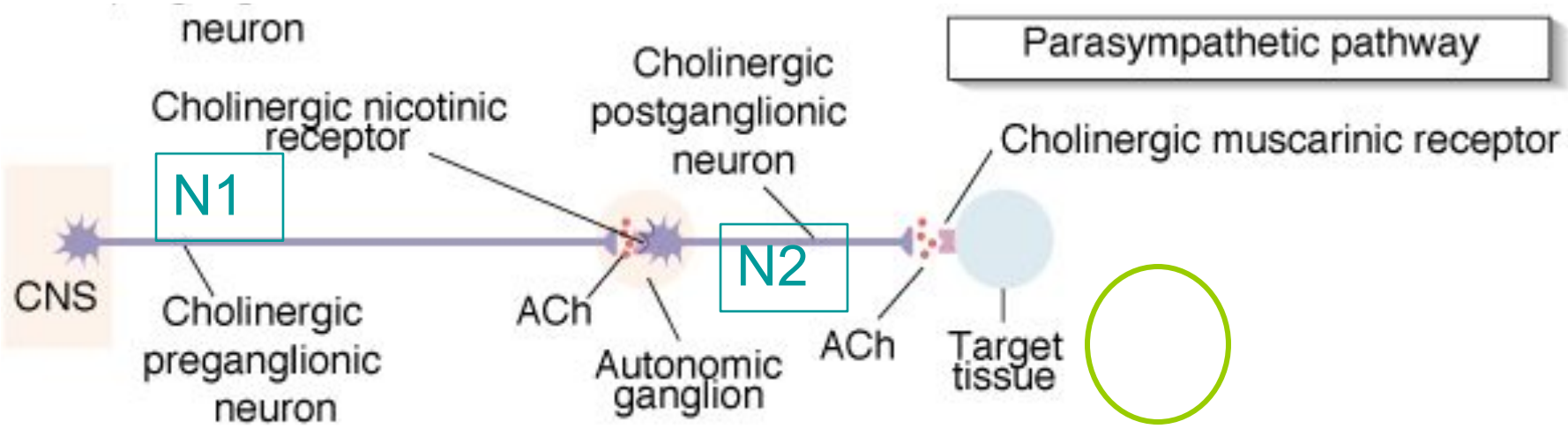
1. Nicotine = agonist
2. In autonomic ganglia & somatic NS
3. Directly opens a Na^+ & K^+ channel: ⇒ ?
4. Curare = antagonist

- When the neurotransmitter, acetylcholine, attaches to the portion of the nicotinic receptor outside of the cell wall, it induces a conformational change that selectively opens up the channel to sodium ions. The resulting influx of positively charged sodium then triggers membrane depolarization.

2) Muscarinic cholinergic receptor

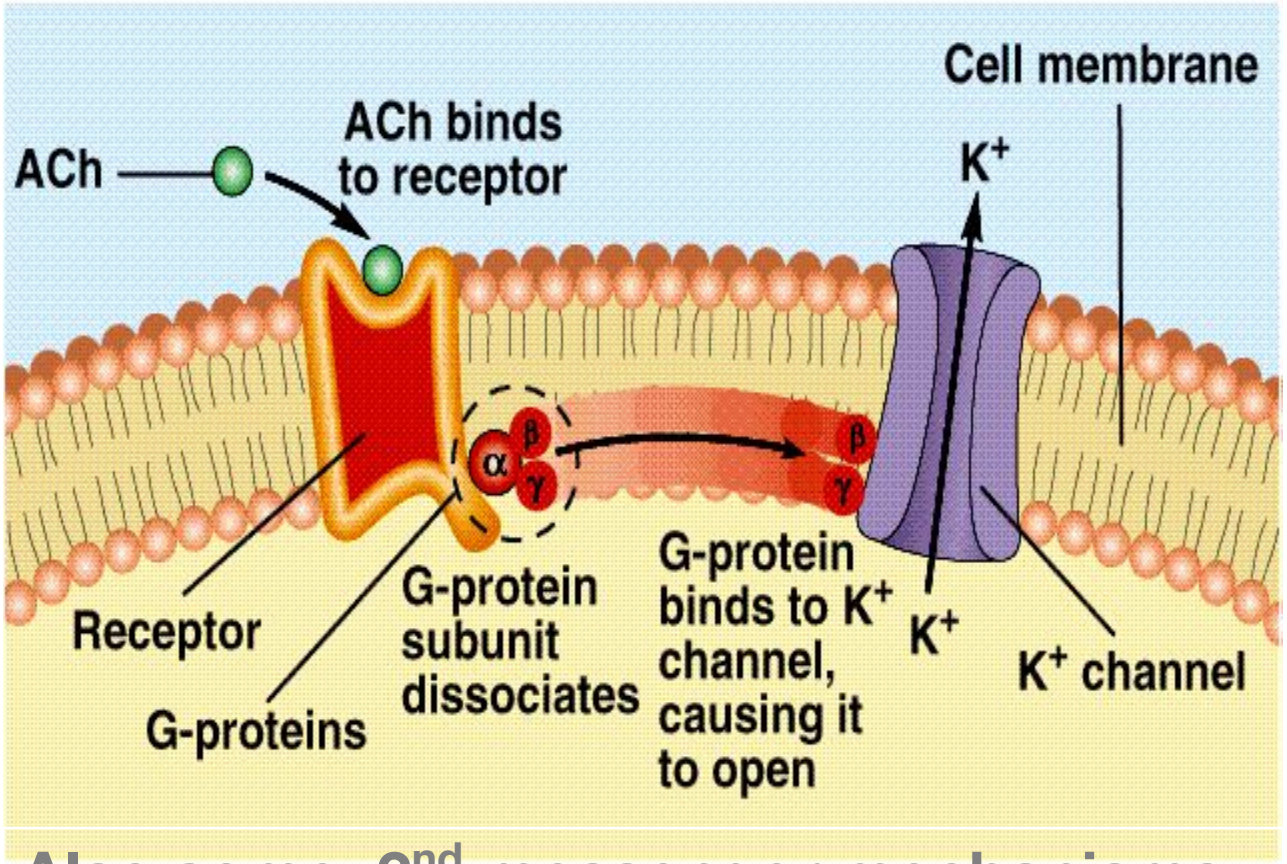
Amanita muscarina

- Muscarine = agonist
- Found in neuro-effector junctions of parasympathetic branch
- G-protein coupled mechanisms
- Atropine = antagonist



Muscarinic ACh are G-protein Mediated

Receptor Mechanism of Sweat Glands:



Also some 2nd messenger mechanisms

There are 5 subtypes of muscarinic receptors:

M1, M3 and **M5** subtypes lead to cellular excitation (stimulant receptors)

M2, M4 subtypes inhibit cellular excitation (inhibitory recepto

Localization of muscarinic receptors:

M_1

On ganglion cells and central neurones, escpecially in cortex, hyppocampus and corpus striatum.
It plays a major role in mediating gastric secretion, relaxation of LES, in learning, memo-

M_2

on effector cells of myocardium and presynaptic membrane (cholinergic nerve ending)

M_3

on smooth musc
of g.i.t., bronch
urogenital syste
on eye muscles
on excretory glar

Molecular mechanism of cholinomimetic action:

Stimulatory action

M1, M3 -receptors (activating)

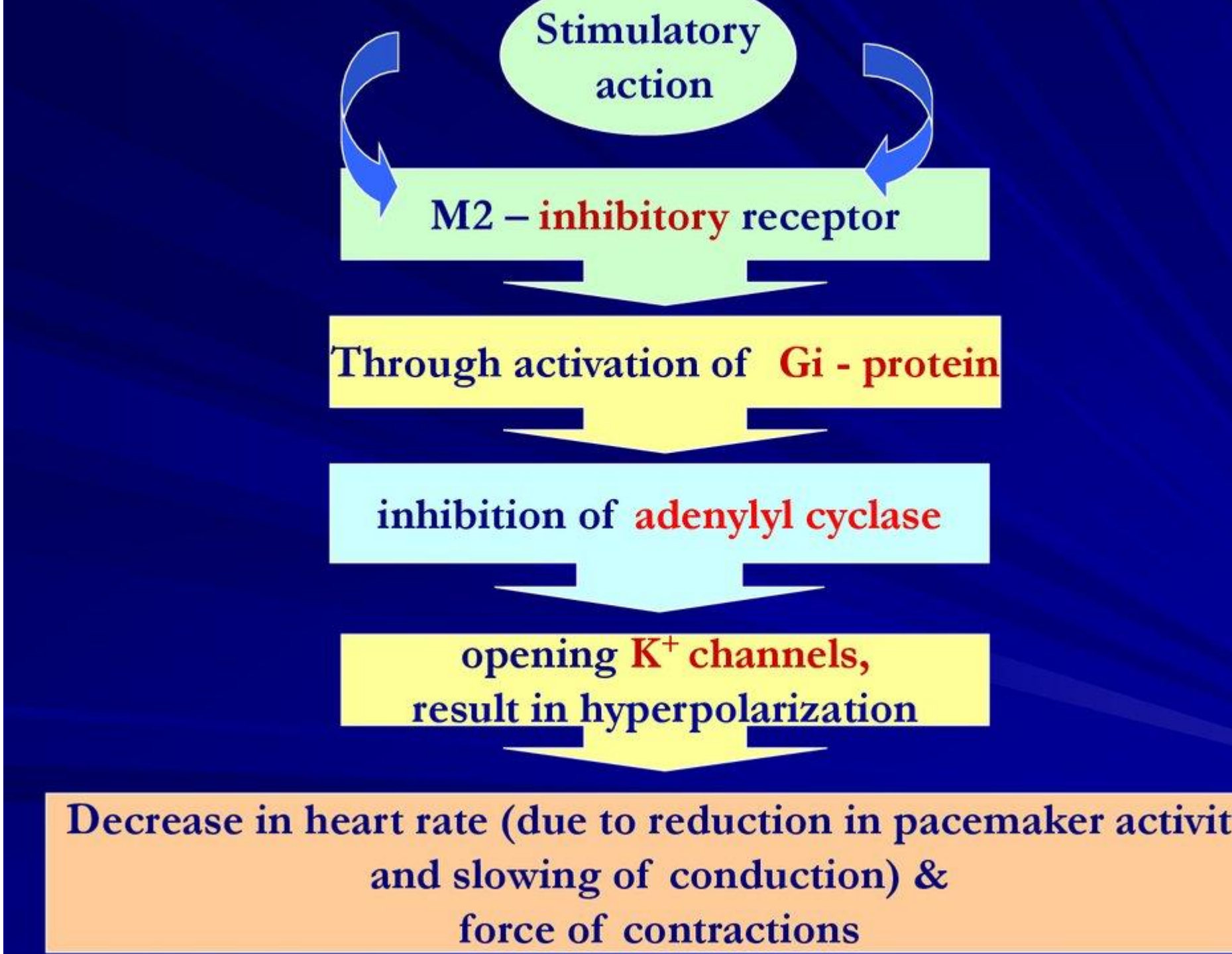
Through Gq prote activate phospholipase "C

hydrolyses phosphatidylinositol -4 bisphosphate (PIP_2)

formation of Diacylglycerol (DAG) Inositol (1,4,5)-triphosphate (IP_3)

influx of Ca^{2+} ions, production of protein kinase C

- depolarization
- Secretion
- Contraction
- Stimulation or inhibition


Stimulatory action
M2 – inhibitory receptor
Through activation of Gi - protein
inhibition of adenylyl cyclase
opening K^+ channels, result in hyperpolarization
Decrease in heart rate (due to reduction in pacemaker activity and slowing of conduction) & force of contractions

Parasympathetic (muscarinic)

- cardiac output M2: decreases
- SA node: heart rate (chronotropic) M2: decreases
- cardiac muscle: contractility (inotropic) M2: decreases (atria only)
- conduction at AV node M2: decreases
- smooth muscles of bronchioles M3: contracts
- pupil of eye M3: contracts
- ciliary muscle M3: contracts
- salivary glands: secretions stimulates watery secretions
- GI tract motility M1, M3: increases
- smooth muscles of GI tract M3: contracts
- sphincters of GI tract M3: relaxes
- glands of GI tract M3: secretes

The ganglion cells of the parasympathetic system are located in or on the wall of the organs supplied or in specific ganglia located near the organs supplied. Hence the postganglionic fibers are short.

- Except for the vagus nerves, the area of distribution of parasympathetic nerves is somewhat limited. The number of synaptic connections is smaller than in the sympathetic division. Accordingly, the effects of the parasympathetic division tend to be local rather than widespread.

MAIN PARASYMPATHETIC INFLUENCE ON ORGANS AND TISSUES

- TROPHIC action :

  - homeostasis restitution
  - ⇑ anabolism level in tissues,
  - ⇑ functional level of internal organs
  - increase blood volume in internal organs vessels

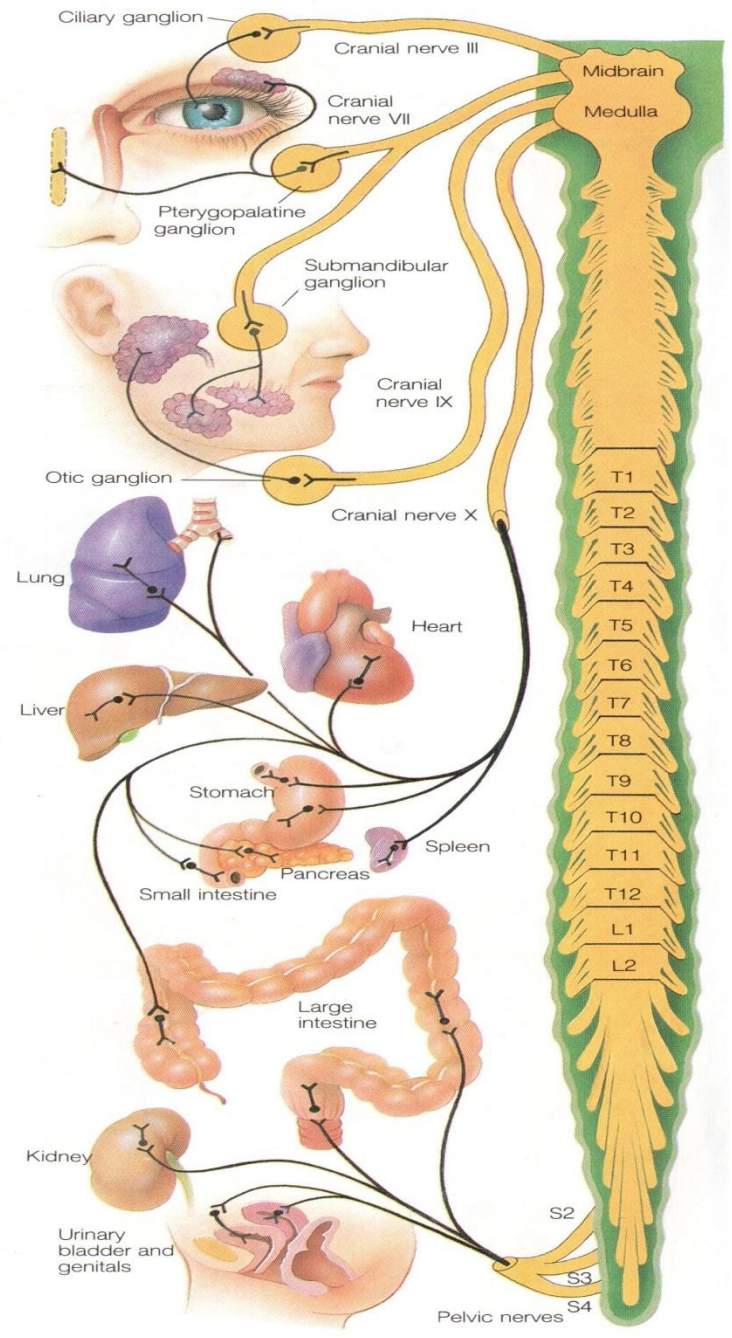
- Decrease of muscle tonus, AP, HR, RR

Parasympathetic activation

- Effects produced by the parasympathetic division
  - relaxation
  - food processing
  - energy absorption

Metasympathetic neural system

forms neurals intramurals plexus in internals organs



Parasympathetic Nervous System

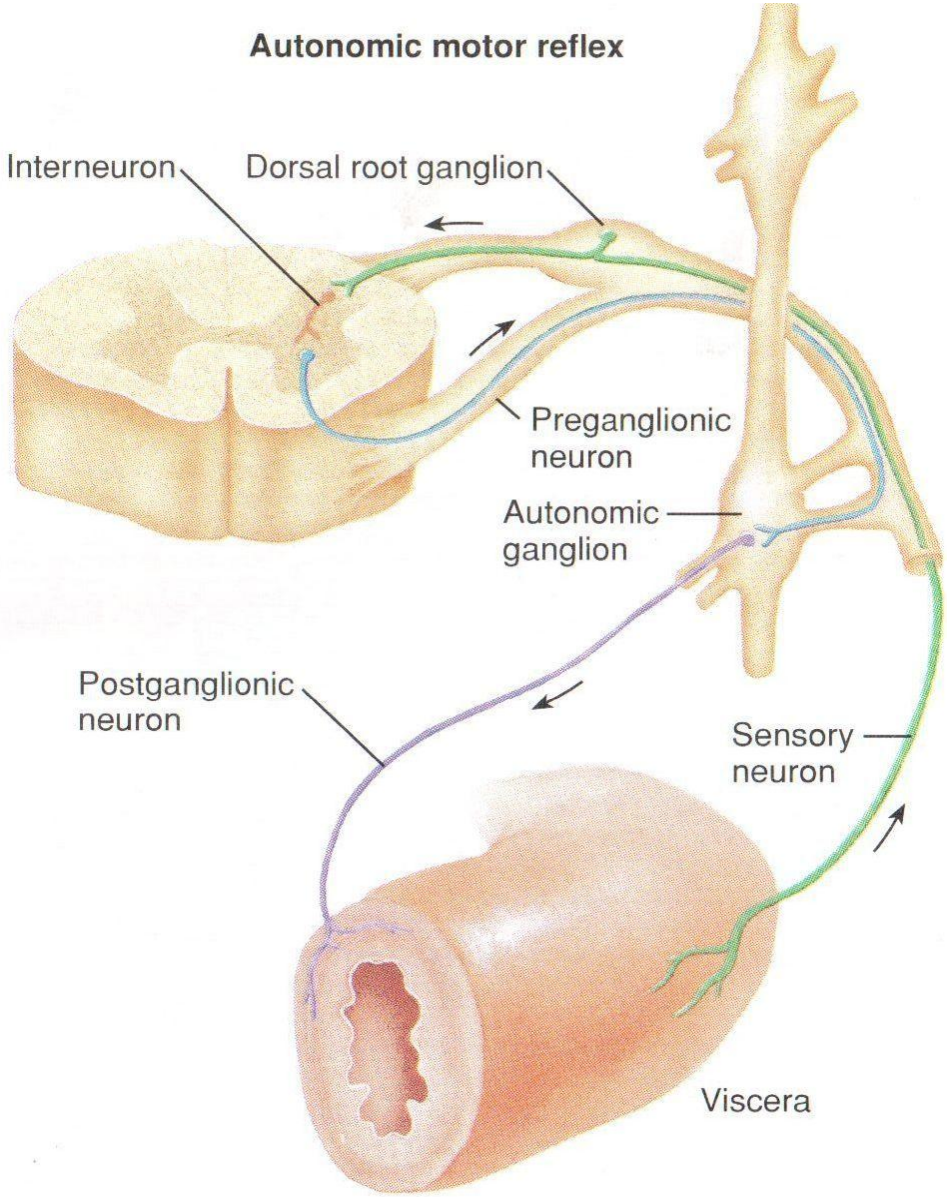
Metasympathetic system

- autonomic neural system of subserous, intramuscular and intramucous plexus of esophagus, stomach, intestine, myocardium and all.
- MNS are composed of motors neurons (Dogel cells I), sensitives neurons (Dogel cells II) and associative neurons (Dogel cells III)
- MNS reflexes have neuronal centers at local level - in intramurals ganglions

Metasympathetic system

- Preganglionic (afferent) fibers terminate in intramurals ganglions.
- P-cells are placed in ganglions of intramuscular and submucous plexus.
- Synapses of intramurals ganglions are blocked by ganglioblockers, but not curare like substanses as neuro-muscular synapses of skeletal muscles
- Endings of postganglionic (efferent) fibers secret ACh, NA, A, purin, serotonin, DOPA, histamine, GABA and all.

ANS reflexes

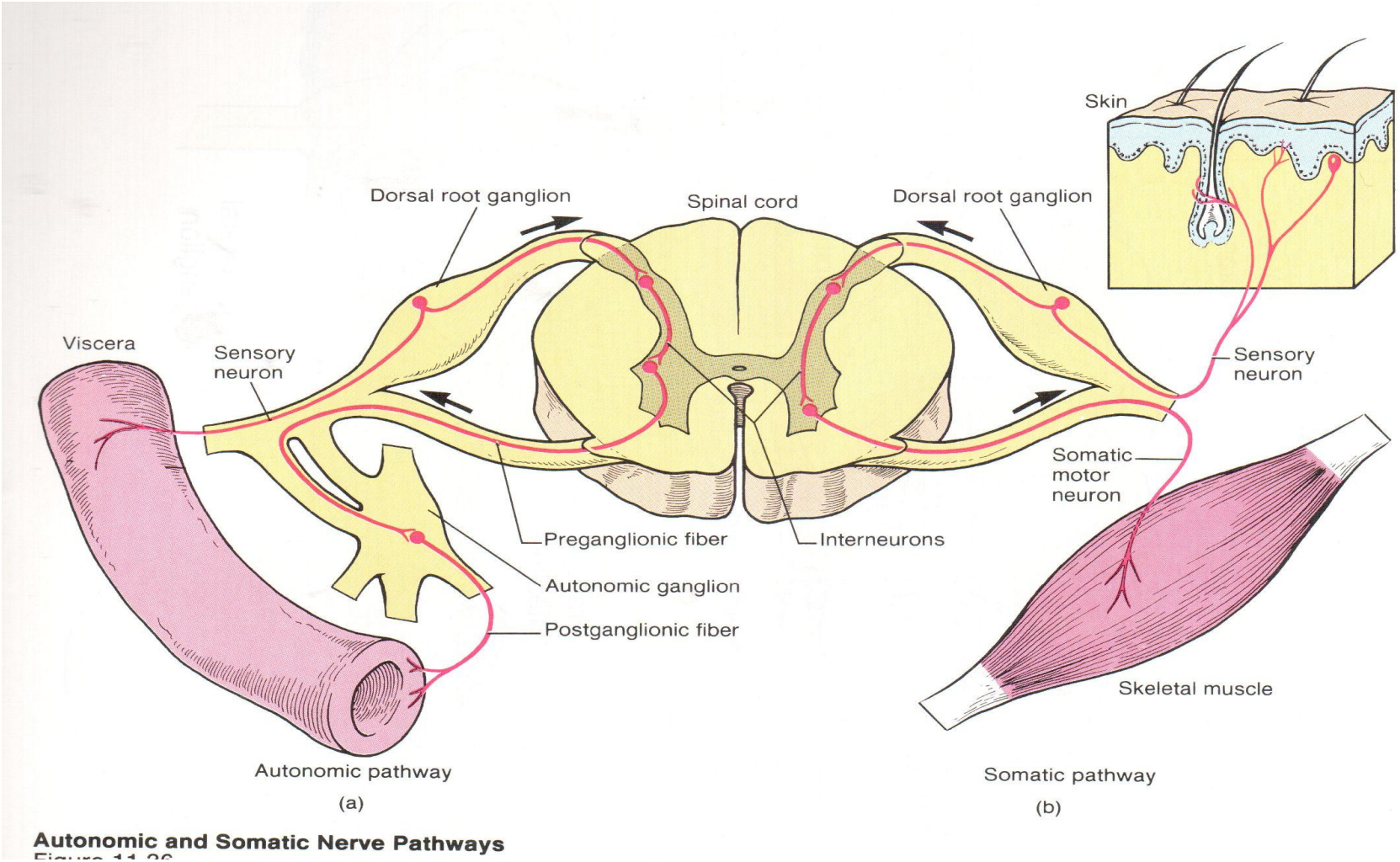


General plan of reflex arc composition :

- **receptors**
- **afferent fibers**
- **central neurons**
- **efferent fibers**
- **working organ**

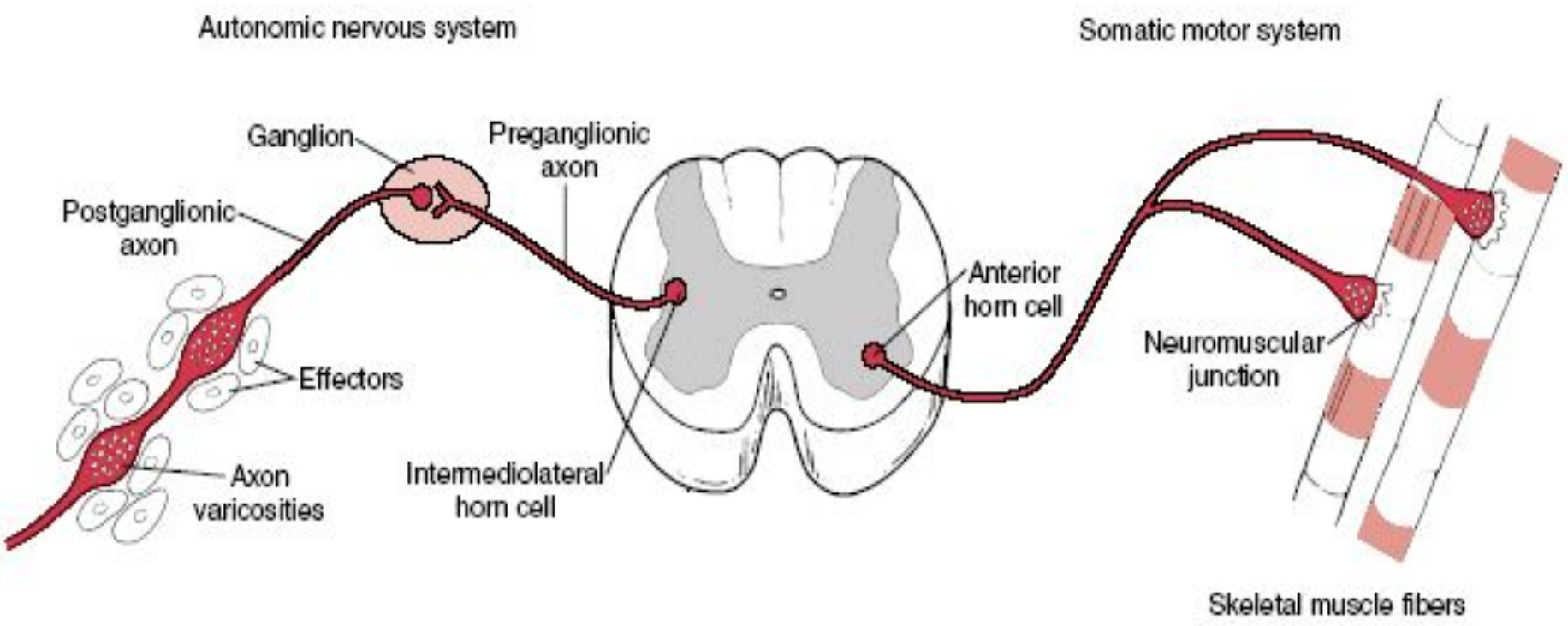
- **Peculiarity of autonomic reflex arc:**
  - **efferent fibers are situated in ganglia out of CNS**

Main differences between somatic and autonomic reflex arcs



Autonomic and Somatic Nerve Pathways

Schematic illustration of the ANS efferent pathway compared with the somatic motor system.



Classification of vegetative reflexes

- **viscero-dermal** reflexes (reflecting zones of stenocardia)
- **Dermatovisceral reflexes** (physio-, reflexotherapy)
- **Viscero-visceral reflex** (gastrocardial reflex)
- **Viscero-motor reflex** (defence, special position of patient)
- **Motor – visceral reflexes** (basis for treatment exercise use)
- **Local** (autonomous) ganglional axon – reflexes :

- internal (centers are situated in intramural ganglions)

- prevertebral (centers are situated in prevertebral ganglions)

- paravertebral (centers are situated in paravertebral ganglions)

Conditional, unconditional; extero-, interoreceptive

ANS NEURONS PECULIARITIES

- Interactivity – unability to exciting under one stimulus action
- High level of additional hyperpolarisation
- Low frequency of impulses generation– no more10-15 / sec
- Stimuli application more than 100 /sec cause full block of vegetative synapse working
- Long duration of synaptic delay– 1.5 – 30.0 msec (in CNS 0.3 – 0.5 msec)
- Long duration of EPSP

ANS FIBRE'S PECULIARITIES -

- Low excitability, long refractority
- Preganglionic fibres have long additional +ve potential
- Postganglionic fibres have long additional –ve potential
- All these fibers have long AP
- All these fibers have big rheobase and chronaxie
- All fibers have small diameter
- Preganglionic fibers – B, postganglionic – C
- Low velocity of impulses conduction
- No segments composition
- Efferent fibers have 2 neurons

PROPERTIES OF THE VEGETATIVE GANGLIAS

- Divergention
- Convergence
- Spatial and temporal summation
- Lability
- Synaptical a delay - 1,5 - 30 msec
- Long after-hyperpolarization
- Transformation of a rhythm

Age changing of ANS

- Influence on organism of PSNS less than SNS during all ages.
- Centers of SNS are activated early in newborn than PSNS. n.Vagus are activated in 2-3 months of life.

- PECULIARITY – SNS are activated in digestive system of newborn after finishing of natural nutrition only.

- Old people have low level SNS and PSNS both. It decrease level of metabolic processes and velocity of adaptation.

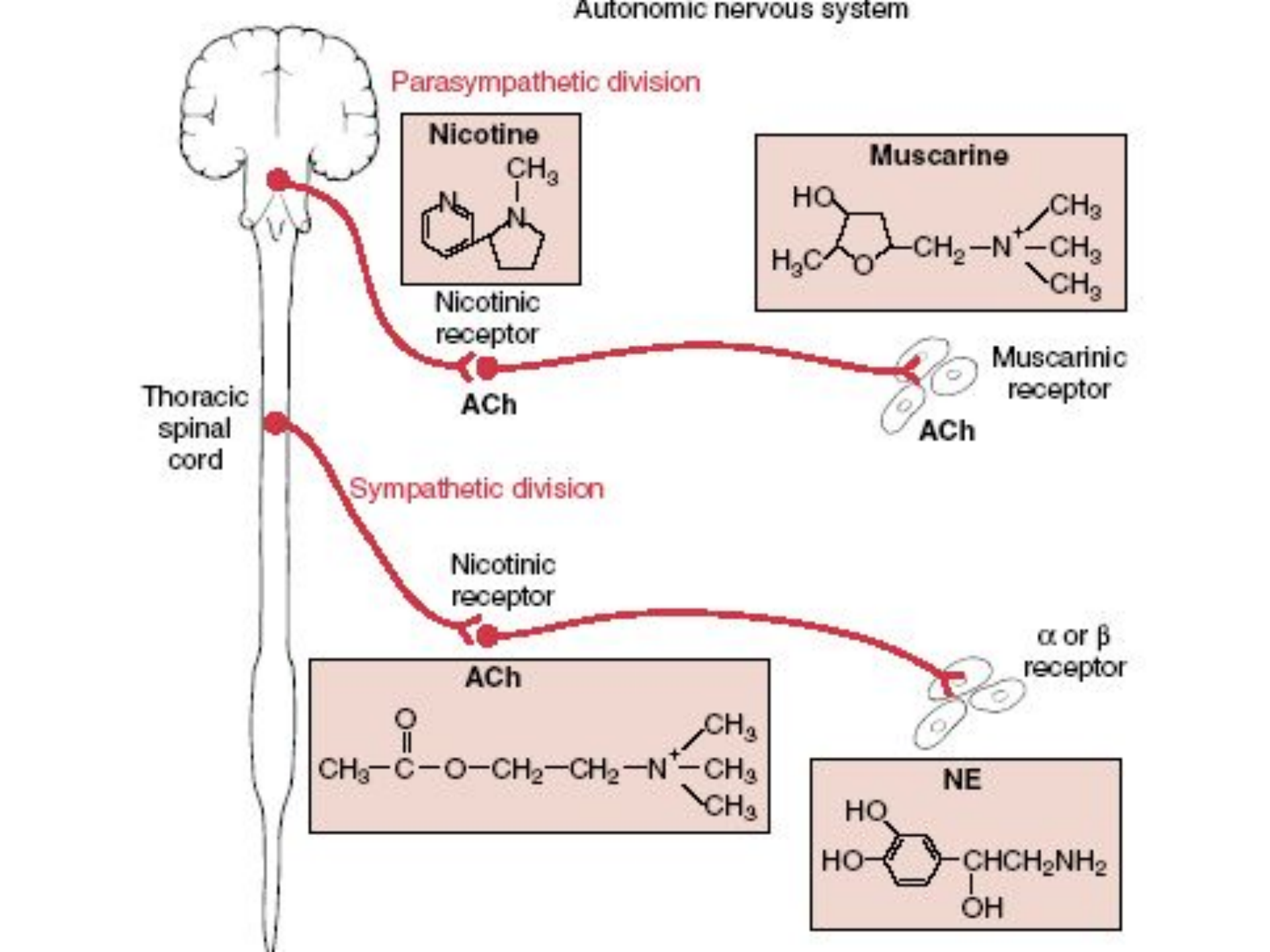
THE STRESS REACTION

- A stressful situation activates three major communication systems in the brain that regulate bodily functions.
- The first of these systems is the voluntary nervous system, which sends messages to muscles so that we may respond to sensory information.
- The second communication system is the autonomic nervous system.
- The brain's third major communication process is the neuroendocrine system, which also maintains the body's internal functioning.

THE STRESS REACTION

When stress occurs, the sympathetic nervous system is triggered. Norepinephrine is released by nerves; epinephrine and norepinephrine is secreted by the adrenal glands. By activating receptors in blood vessels and other structures, these substances ready the heart and working muscles for action.

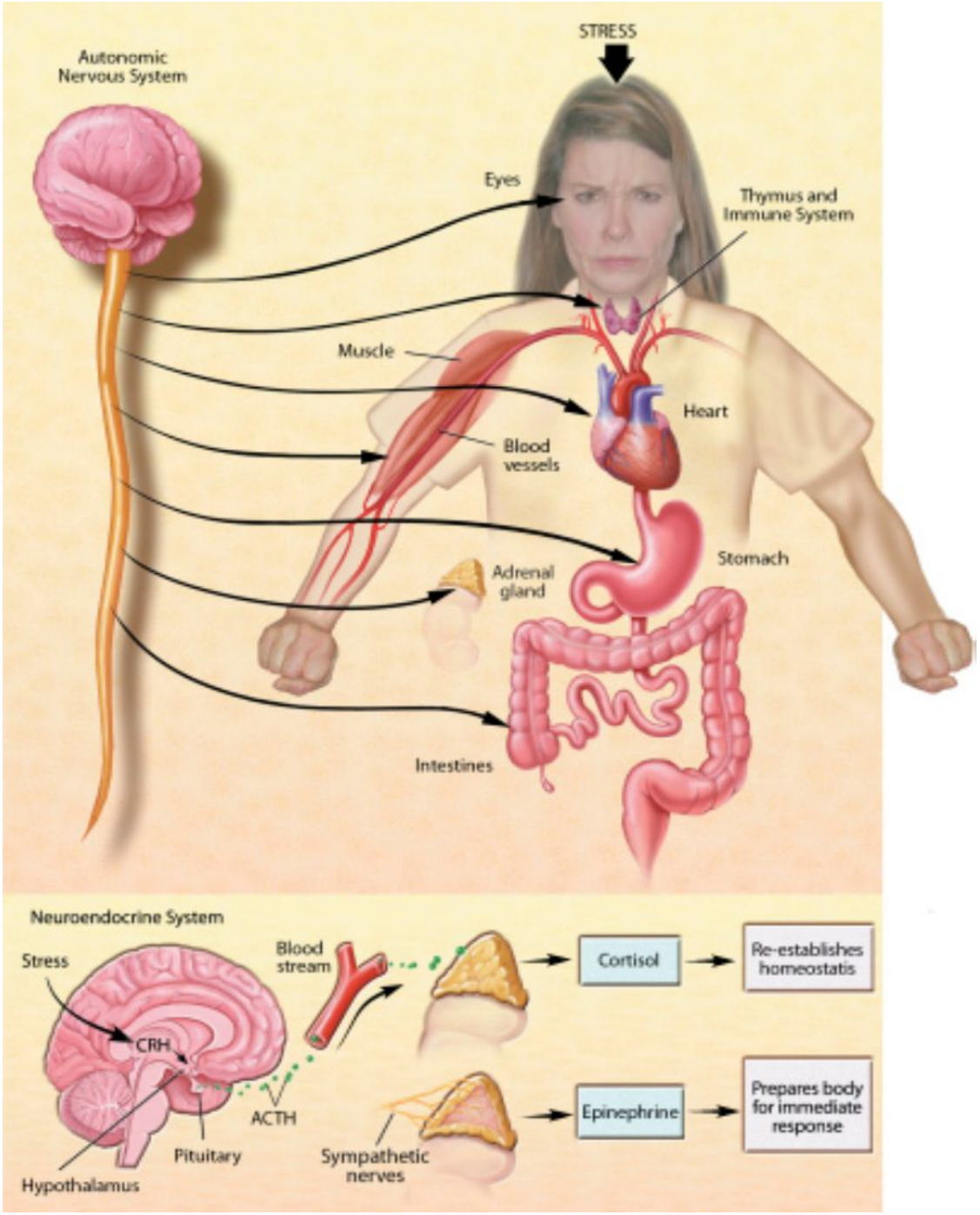
Acetylcholine is released in the parasympathetic nervous system, producing calming effects. The digestive tract is stimulated to digest a meal, the heart rate slows, and the pupils of the eyes become smaller. The neuroendocrine system also maintains the body's normal internal functioning.


Autonomic nervous system
Parasympathetic division
Nicotine
Muscarine
Nicotinic receptor
ACh
Muscarinic receptor
ACh
Thoracic spinal cord
Sympathetic division
Nicotinic receptor
α or β receptor
ACh
NE

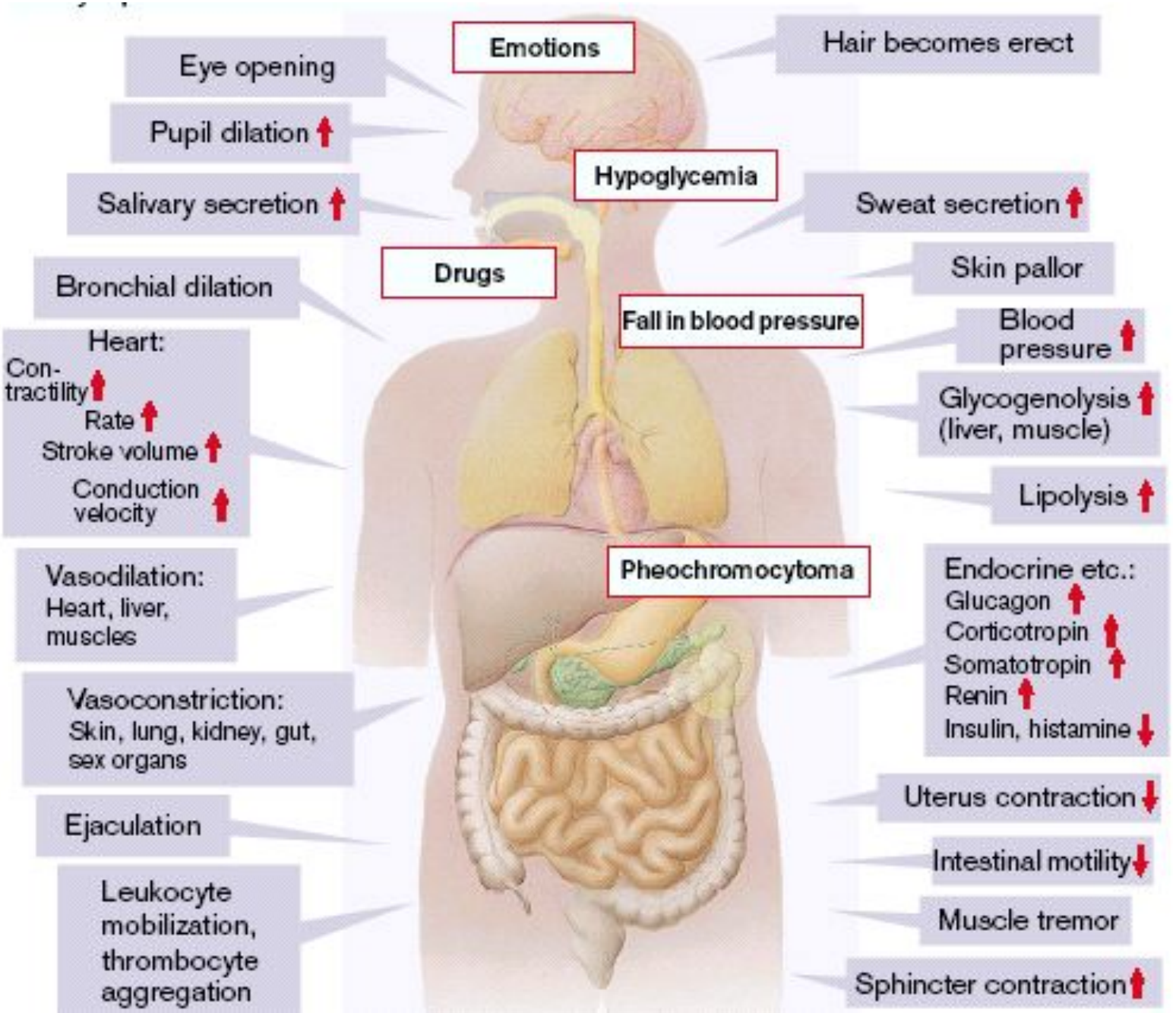
Sympathetic and parasympathetic divisions typically function in opposition to each other. But this opposition is better termed complementary in nature rather than antagonistic. For an analogy, one may think of the sympathetic division as the accelerator and the parasympathetic division as the brake.

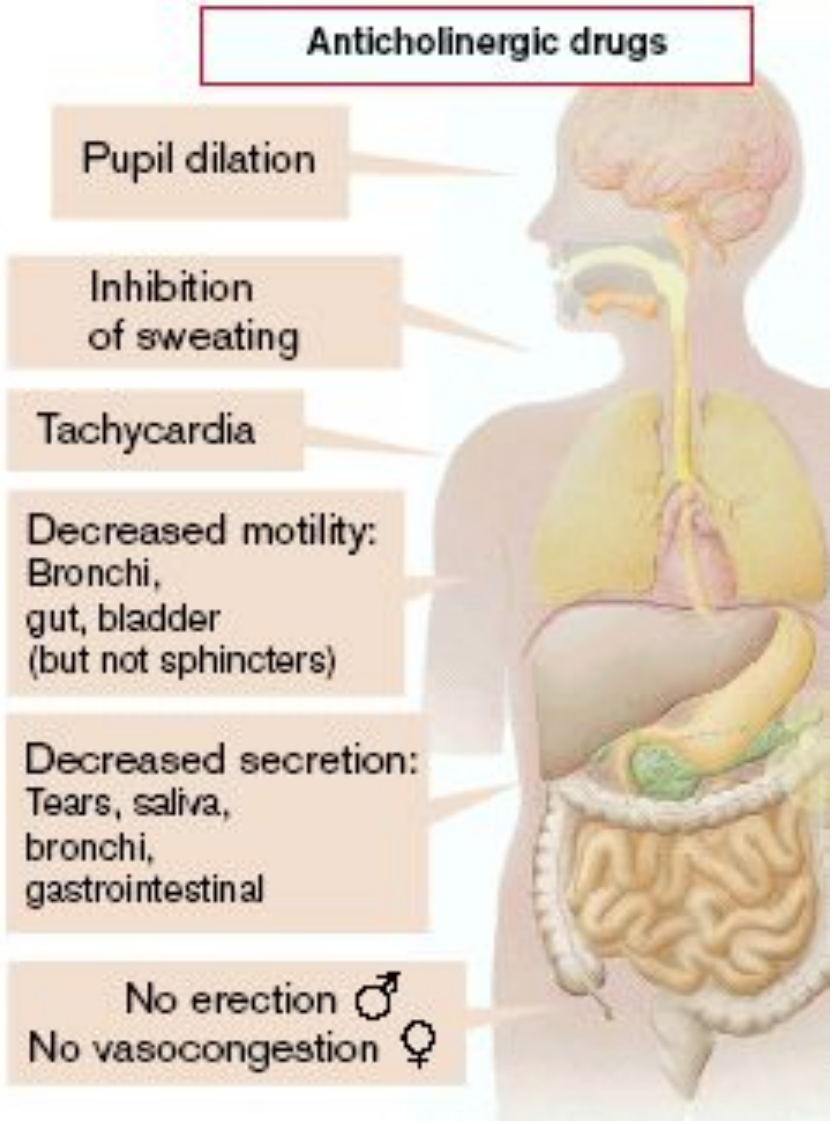
The *sympathetic division* typically functions in actions requiring quick responses.

The *parasympathetic division* functions with actions that do not require immediate reaction. Consider sympathetic as "fight or flight" and parasympathetic as "rest and digest".


STRESS
Autonomic Nervous System
Eyes
Thymus and Immune System
Muscle
Heart
Blood vessels
Stomach
Adrenal gland
Intestines
Neuroendocrine System
Stress
Blood stream
Cortisol
Re-establishes homeostatis
CRH
ACTH
Epinephrine
Prepares body for immediate response
Pituitary
Sympathetic nerves
Hypothalamus

Schematic illustration of sympathetic nerves activation effects

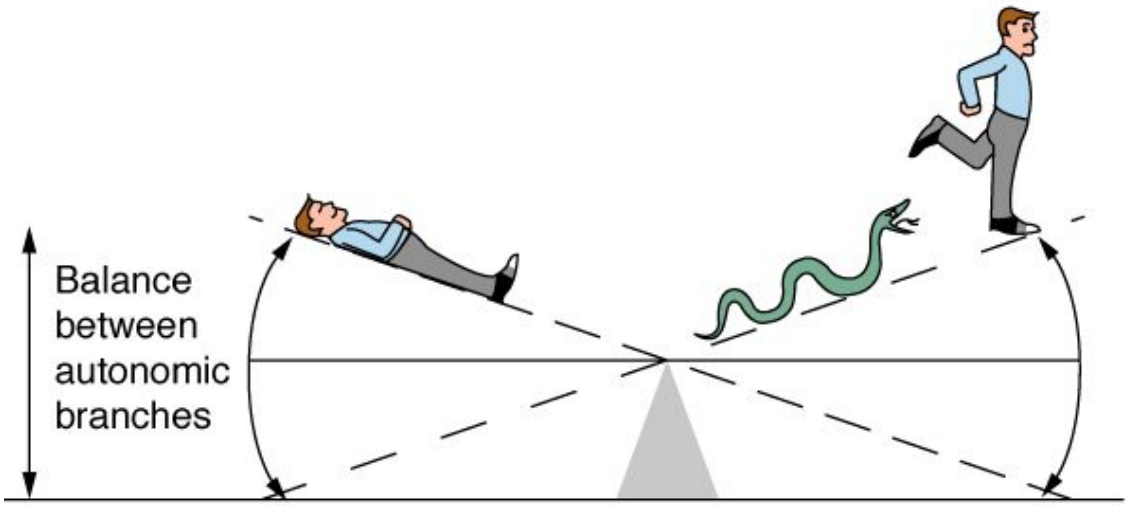




Schematic illustration of effects in case of parasympathetic stimulation loss

Homeostasis and the Autonomic Division

- BP, HR, Resp., H_2O balance, Temp. . .
- **Mostly dual reciprocal innervation**
  - i.e., agonist/antagonist or excitatory/inhibitory
- **Sympathetic:**
  - AKA Thoracolumbar
  - flight-or-fight
- **Parasympathetic:**
  - AKA Craniosacral
  - rest and digest



Responses of Effectors to Parasympathetic and Sympathetic Stimulation

Effector	Parasympathetic	Sympathetic
Eye		
Pupil	Constriction	Dilation (α_1)
Ciliary muscle	Contraction	Relaxation (β_2)
Müller's muscle	None	Contraction (α_1)
Lacrimal gland	Secretion	None
Nasal glands	Secretion	Inhibition (α_1)
Salivary glands	Secretion	Amylase secretion (β)
Skin		
Sweat glands	None	Secretion (cholinergic muscarinic)
Piloerector muscles	None	Contraction (α_1)
Blood vessels		
Skin	None	Constriction (α)
Skeletal muscle	None	Dilation (β_2), Constriction (α)
Viscera	None	Constriction (α_1)
Heart		
Rate	Decrease	Increase (β_1, β_2)
Force	Decrease	Increase (β_1, β_2)

Responses of Effectors to Parasympathetic and Sympathetic Stimulation

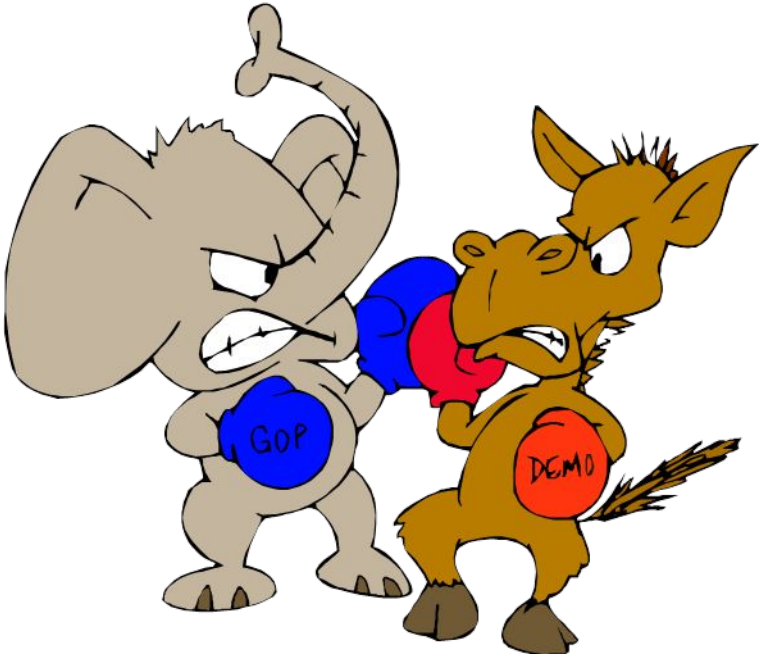
Lungs		
Bronchioles	Constriction	Dilation (β_2)
Glands	Secretion	Decreased (α_1), incr. (β_2) secretion
Gastrointestinal tract		
Wall muscles	Contraction	Relaxation (α, β_2)
Sphincters	Relaxation	Contraction (α_1)
Glands	Secretion	Inhibition
Liver	None	Glycogenolysis and Gluconeogenesis (α_1, β_2)
Pancreas (insulin)	None	Decreased secretion (α_2)
Adrenal medulla	None	Secretion of epinephrine (cholinergic nicotinic)
Urinary system		
Ureter	Relaxation	Contraction (α_1)
Detrusor	Contraction	Relaxation (β_2)
Sphincter	Relaxation	Contraction (α_1)
Reproductive system		
Uterus	Variable	Contraction (α_1)
Genitalia	Erection	Ejaculation/vaginal contraction (α)
Adipose cells	None	Lipolysis (β)

ANS

2 divisions:

Sympathetic

- "Fight or flight"
- "E" division
- Exercise, excitement, emergency, and embarrassment

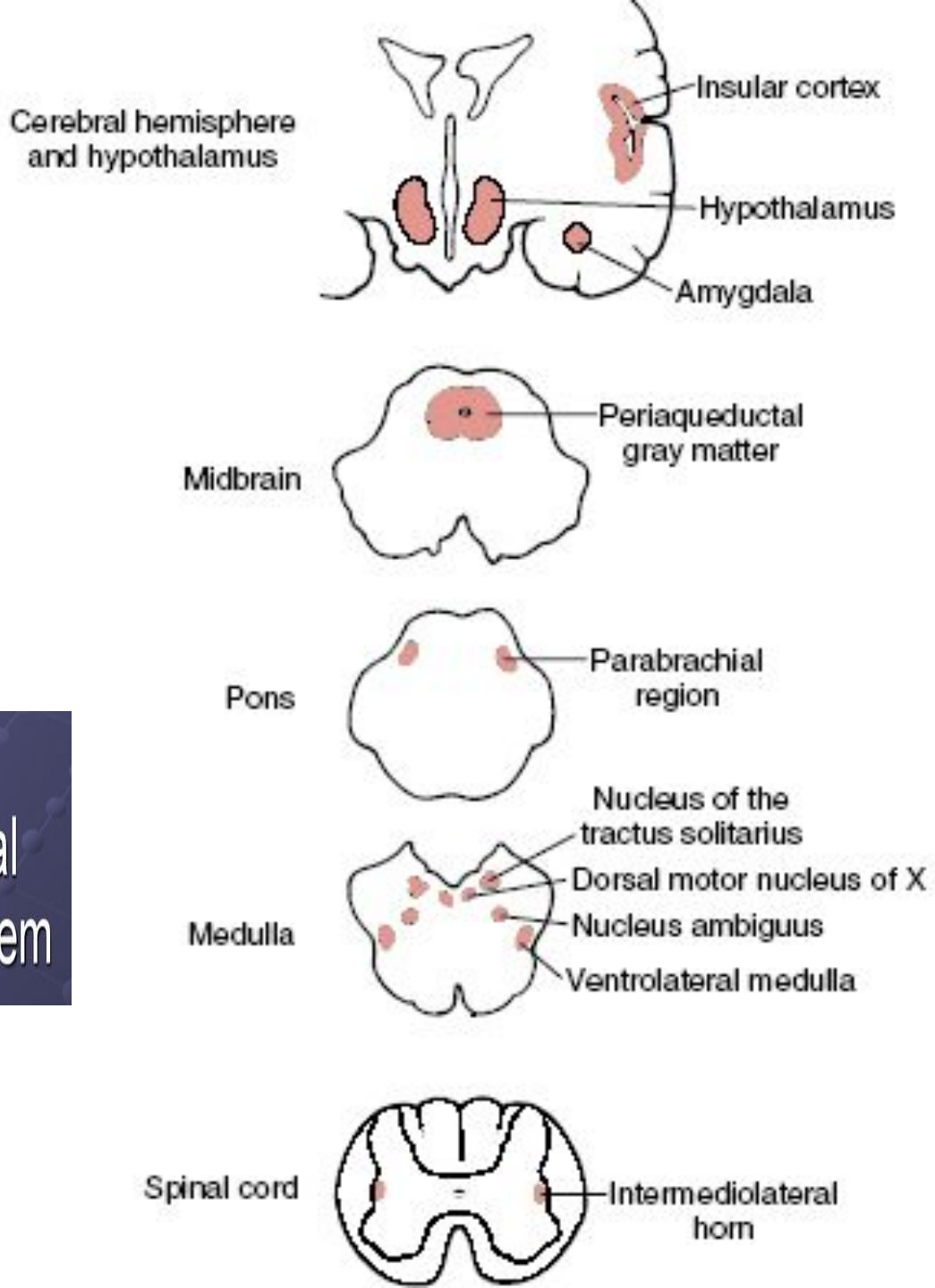


Parasympathetic

- "Rest and digest"
- "D" division
- Digestion, defecation, and diuresis

The central autonomic network

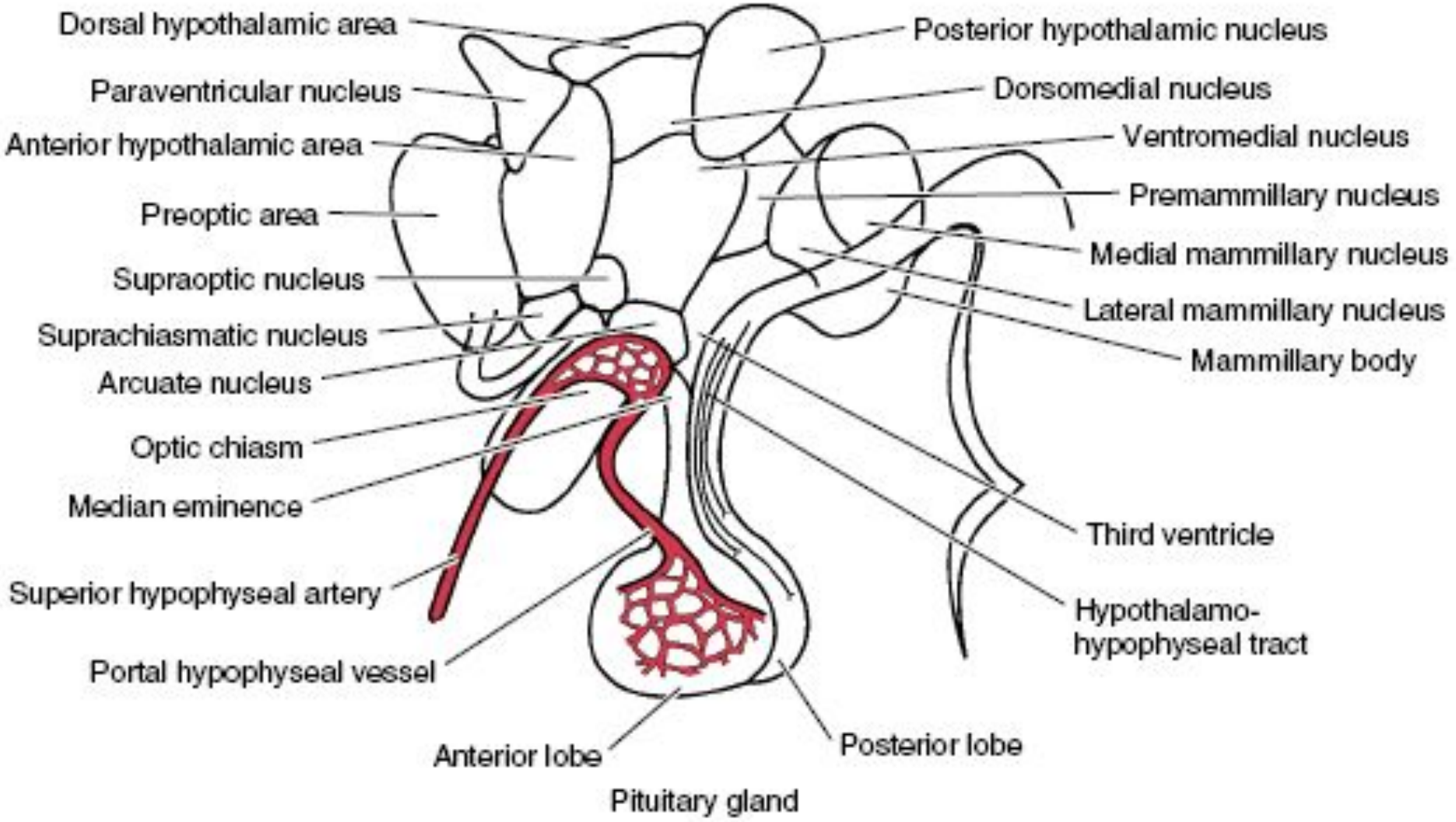
Supersegmentary centers –
hypothalamus, cerebellum, basal ganglias, cortex and limbic system



Although “involuntary”, the autonomic nervous system is regulated by higher centers. The best known of these centers is the **hypothalamus** which has descending projections to cell bodies of the preganglionic neurons. Other areas of the central nervous system affect the activities of the hypothalamus.

Hypothalamus is the important integrative center of vegetative, somatic and endocrinal functions, that is responsible for the complex homeostatic reactions realization and serves as the key structure within the hierarchically organized brain system that regulates visceral functions.

HYPOTHALAMUS and its main nuclei



FUNCTIONS of hypothalamus N1

1. Water and electrolyte balance regulation

(supraoptic and paraventricular nuclei).

2. Secretion of hypothalamic releasing factors

(arcuate and periventricular nuclei and parvocellular cells of the paraventricular nucleus).

3. Temperature regulation

(the anterior and posterior hypothalamic nuclei).

4. Activation of the sympathetic nervous system and adrenal medullary hormone secretion

(the dorsal and posterior hypothalamus).

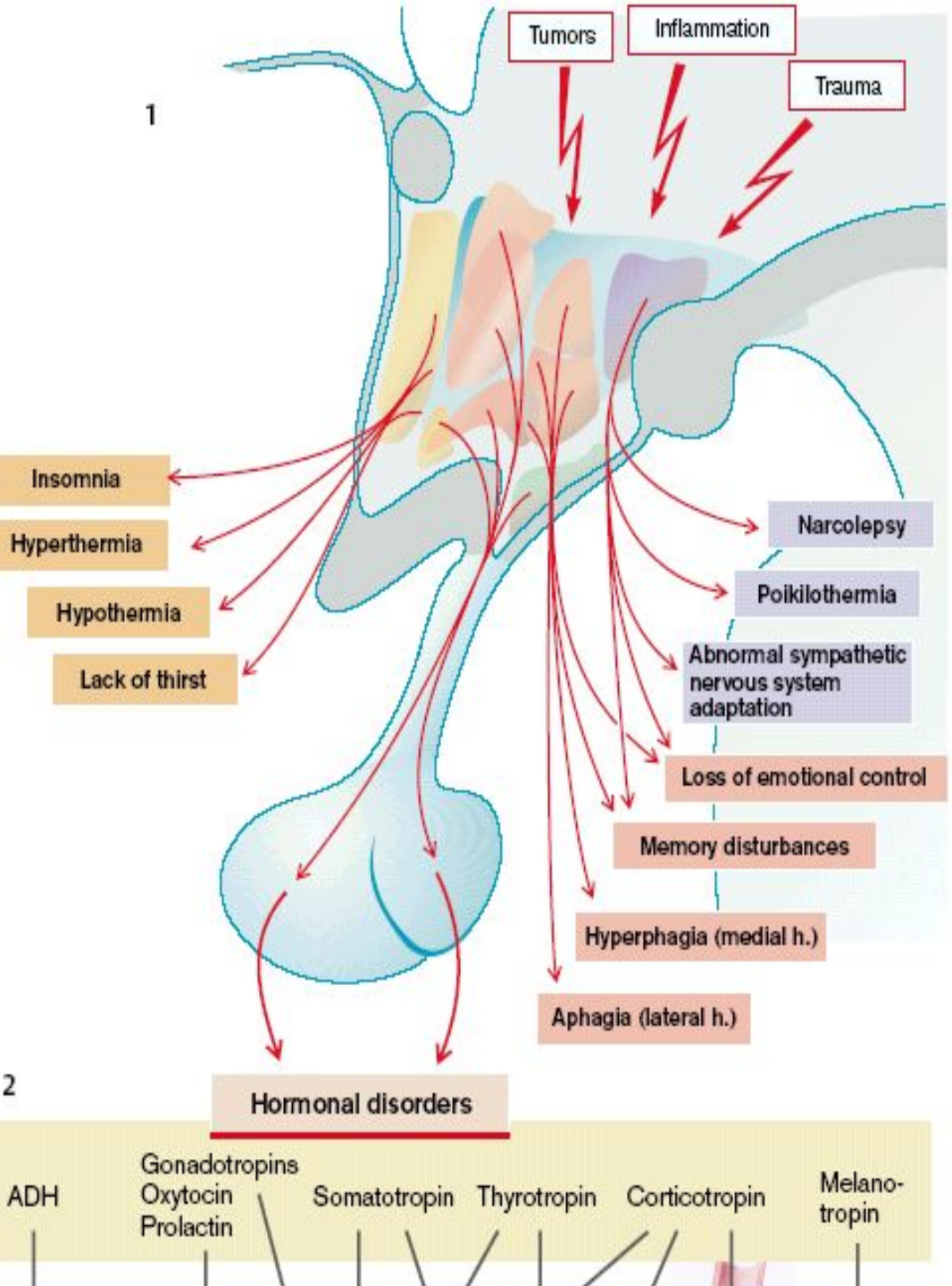
FUNCTIONS of hypothalamus N2

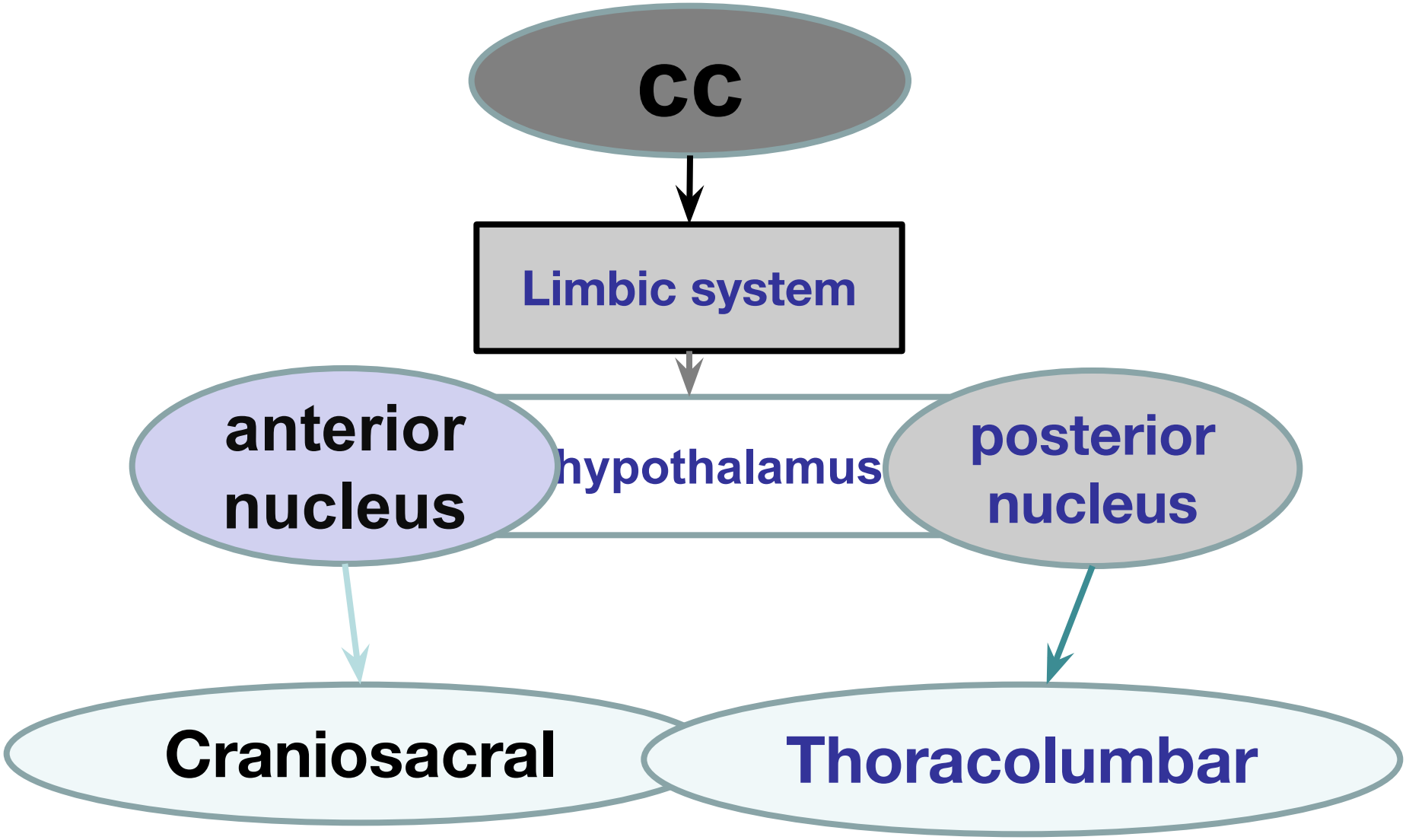
5. Thirst and drinking regulation
(lateral hypothalamus).

6. Hunger, satiety and the regulation of eating behavior
(the arcuate nucleus, ventromedial nucleus, and lateral hypothalamic area).

7. Regulation of sexual behavior
(the anterior and preoptic hypothalamic areas).

8. Regulation of circadian rhythms.
Sleep-wakefullness cycle
(the suprachiasmatic nucleus of hypothalamus).


1
Tumors
Inflammation
Trauma
Insomnia
Hyperthermia
Hypothermia
Lack of thirst
Narcolepsy
Poikilothermia
Abnormal sympathetic nervous system adaptation
Loss of emotional control
Memory disturbances
Hyperphagia (medial h.)
Aphagia (lateral h.)
2
Hormonal disorders
ADH
Gonadotropins
Oxytocin
Prolactin
Somatotropin
Thyrotropin
Corticotropin
Melano-
tropin


cc
Limbic system
anterior nucleus
hypothalamus
posterior nucleus
Craniosacral
Thoracolumbar


THANKS FOR
ATTENTION !