DEBRE MARKOS UNIVERSTY SCHOOL OF MEDICINE DEPARTMENT OF MEDICAL PHYSIOLOY

AUTONOMIC NERVOUS SYSTEM

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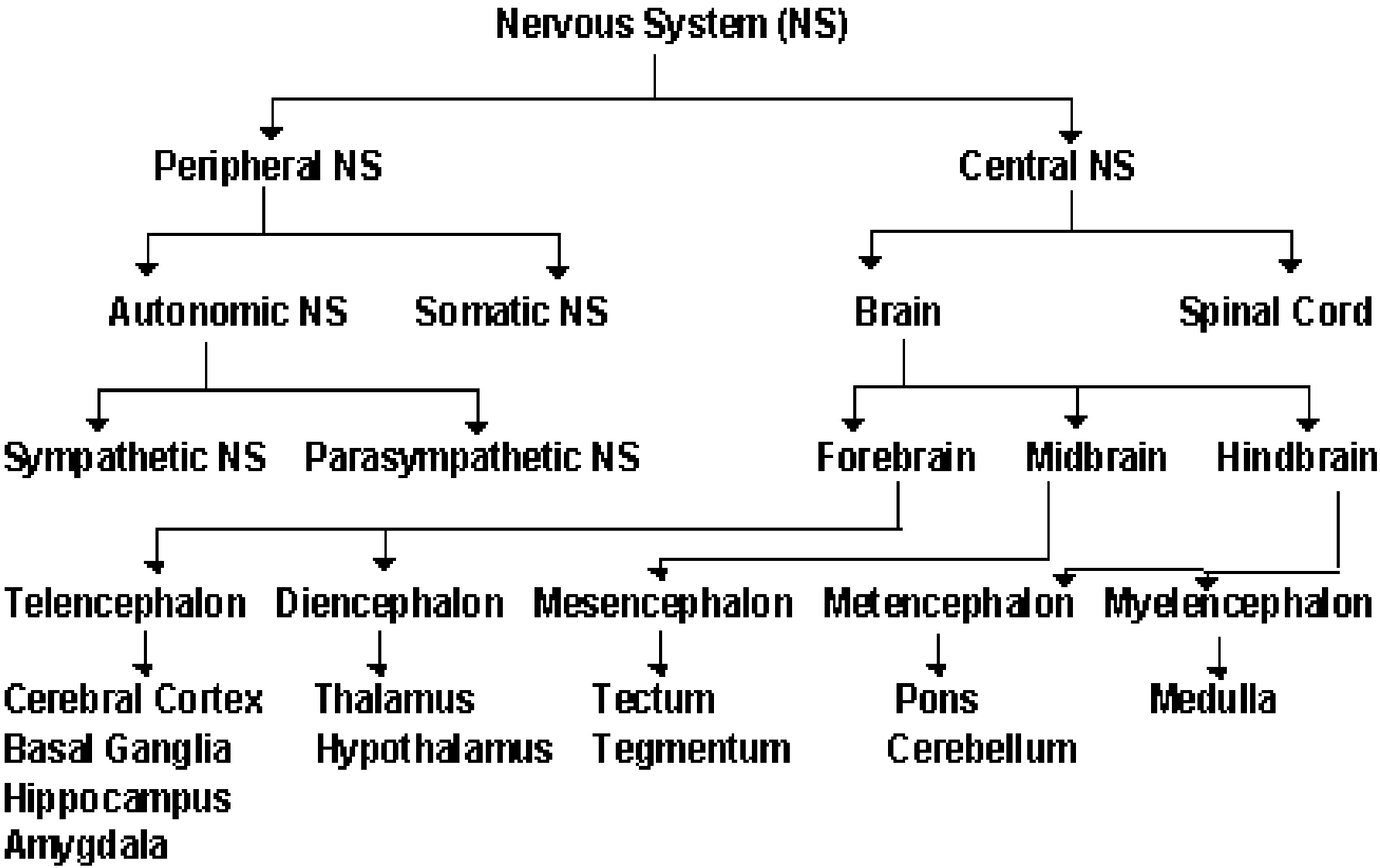
Organization of the Nervous System



Organization of the Nervous System cont'd….

1. **Central Nervous System-CNS**

   - The brain + the spinal cord
     - The center of integration and control

2. **Peripheral Nervous System -PNS**

   - The nervous system outside of the brain and spinal cord
   - Consists of:

     -31 pairs of spinal nerves

     -12 pairs of cranial nerves

   - Carry info to and from the spinal cord

Organization of the NS cont'd….

- PNS Can be divided further into:
  - Somatic nervous system –SoNS
  - Autonomic nervous system –ANS
- Divisions of the ANS
    - o Sympathetic nervous system-SyNS
    - o Parasympathetic nervous system-PaNS
    - o Enteric nervous system-ENS

Somatic motor nervous system

- The somatic portion of the efferent division of the PNS is all the nerve fibres going from the CNS to the skeletal muscle cells.
- The cell bodies of these neurons are located in groups in the gray matter of the spinal cord (AHC).
- Their large diameter, myelinated axons leave the CNS and pass without any synapses to skeletal-muscle cells (intrafusal and extrafusal fibers).
- Release NT called acetylcholine.
- somatic neurons leads to contraction of the innervated skeletal-muscle cells, these neurons are called **motor neurons**

COMPARISON OF SoNS Vs ANS

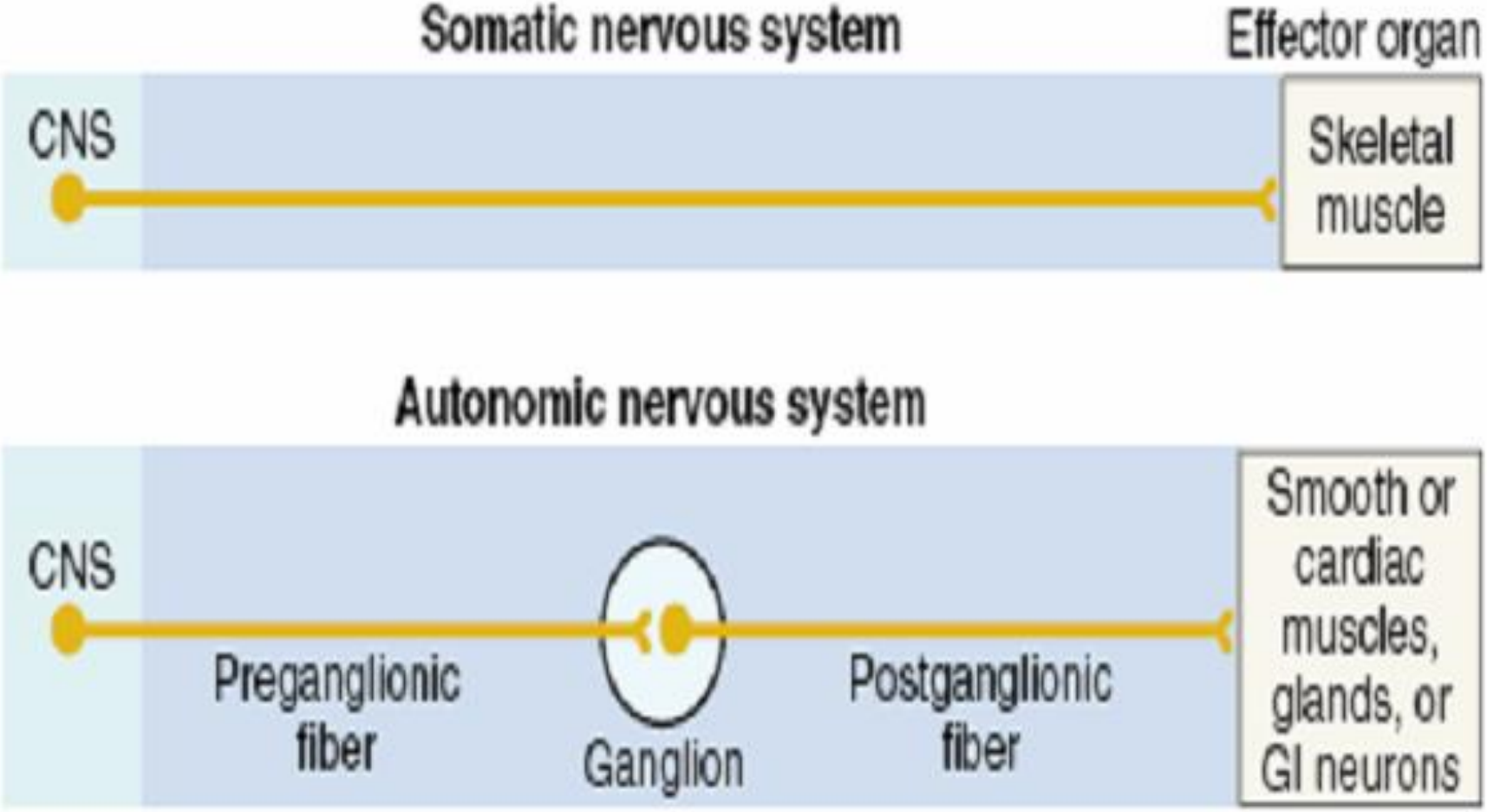
SoNS

1. Controls voluntary activities such as contraction of the **muscle**.
2. Nerve fibres are originated from the **anterior horn of the grey matter (GM)** of the spinal cord.
3. The motor nerve contains **single, long, thick and myelinated axon.**
4. The NT is always **Ach** and the receptor is always **NR**

   -Always excitatory

ANS

1. Controls **involuntary** activities such as **CVS, GIT, glands function**
2. Nerve fibres are originated from the **lateral horn of the GM** of the spinal cord.
3. Autonomic fibres contain **two neurons (pre-&post-ganglionic neurons)**
4. The NTs are both **Ach** and **nor epinephrine** and the receptors are **adrenergic** and **cholinergic**



Efferent division of the peripheral nervous system.

Overall plan of the somatic and autonomic nervous systems.

The Cranial Nerves

- Are components of the PNS
- There are 12 pairs of cranial nerves
- Each of them are designated by the Roman numbers (I-XII)
- Some are mixed nerves (sensory, motor, autonomic)
- Three of them are pure sensory nerves (I,II,VIII)
- Four of them has autonomes (III,VII,IX,X)
- Four of them are pure motor (IV,VI,XI,XII)

Cranial nerves (I-VI)

Nerve	Name	Sensory	Motor	Autonomic Parasympathetic
I	Olfactory	Smell		
II	Optic	vision		
III	Oculomotor		4 Extrinsic Eye muscles causes upward mov't of the eye ball	Pupillary constriction Accommodation Focusing
IV	Trochlear		1 Extrinsic Eye muscle (Sup. Oblique)	
V	Trigeminal	Somatic senses (Face, tongue), corneal sensitivity	Chewing	
VI	Abducens		1 Extrinsic Eye muscle (Lateral rectus)	

Cranial nerves (VII-XII)

Nerve	Name	Sensory	Motor	Autonomic Parasympathetic
VII	Facial	Taste	Muscles of facial expression	Salivary glands Tear glands
VIII	Auditory (Vestibulo cochlear)	Hearing.& Balance		
IX	Glossopharyn geal	Taste Blood gases	Swallowing Gagging	Salivary glands
X	Vagus	Blood pressure Blood gases Taste	Speech Swallowing Gagging	Many visceral organs (heart, gut, lungs)
XI	Spinal accessory		Neck muscles: Sternocleidomastoid Trapezius	
XII	Hypoglossal		Tongue muscles (Speech)	

Cranial nerves cont'd….

Cranial Nerves Mediate 5 Special Senses: Smell, Vision, Hearing, Taste, Equilibrium

- Smell: CN-I (Olfactory)
- Vision: CN- II (Optic)
- Hearing: CN-VIII (Cochlear division)
- Equilibrium: CN-VIII (vestibular division)
- Taste: CNs -VII, IX, X (minor) (Facial, Glossopharyngeal, Vagus)

Most of the Nerves Carry Somatic (Skin & Muscle) Sense

- The trigeminal (V) is the sensory nerve for the face & corneal sensitivity.

Three Nerves Are Concerned With Eyeball Movements

- Oculomotor (III): superior rectus, medial rectus, inferior rectus, inferior oblique
- Trochlear (IV): superior oblique
- Abducens (VI): lateral rectus

Cranial nerves Cont'd…

Cranial Nerves Innervate Skeletal Muscles….

- The Facial nerve (VII) controls **muscles of facial expression**
- The Spinal accessory (XI) stimulates the **trapezius and sternocleidomastoid** muscles
- **Chewing muscles (masseter, temporalis)** are innervated by the Trigeminal (V)
- Speech muscles **(larynx)** are under the control of the Vagus (X)
- The Hypoglossal (XII) moves the **tongue**

Cranial Nerves cont'd…

Four of the CNs Carry Parasympathetic Fibres

- Oculomotor (III): innervates **iris constrictor** (causes pupil constriction); also controls **ciliary muscle** (focuses the lens)
- Facial (VII) and Glossopharyngeal (IX): stimulate **salivary glands** to secrete
- Vagus (X): the major nerve of the parasympathetic system: goes to most visceral organs **(heart, lungs, kidneys, liver, stomach, intestines)**

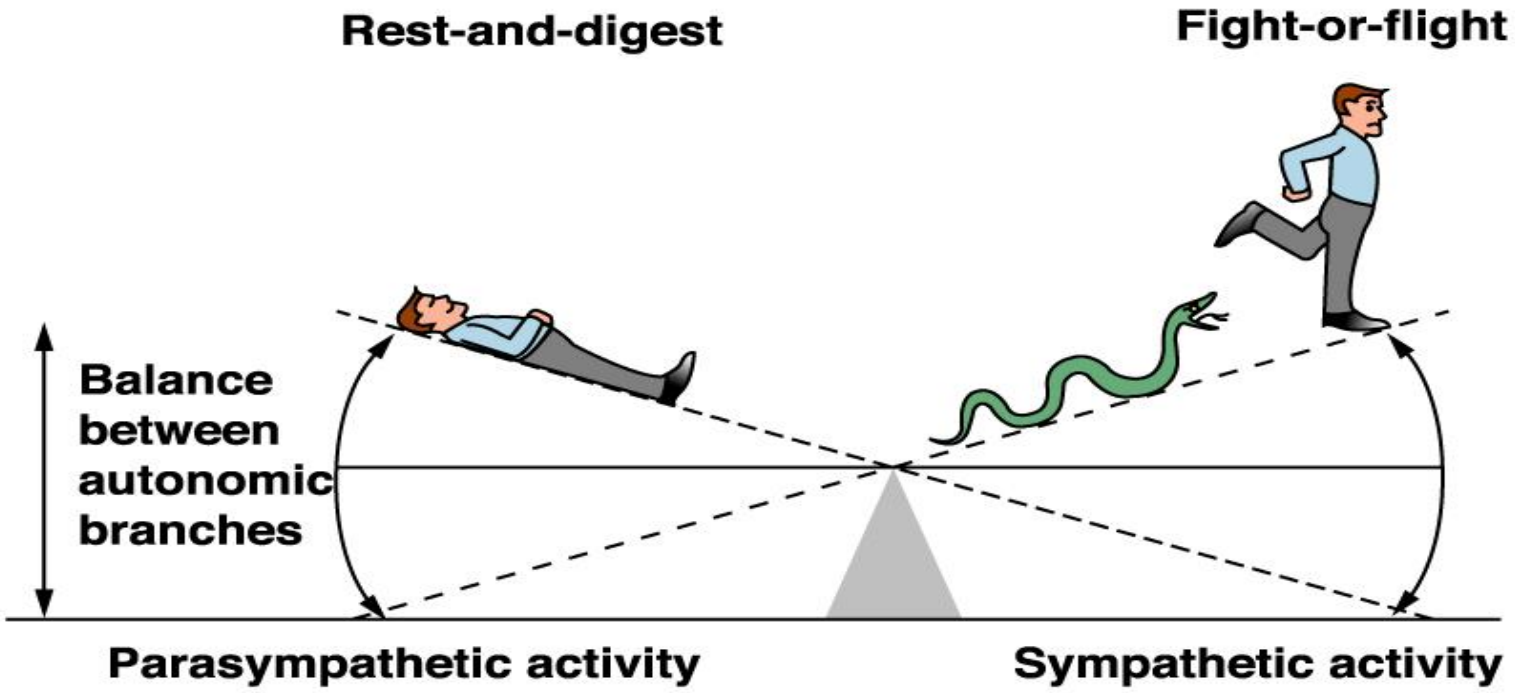
Cranial nerves cont'd…

Damage to Cranial Nerves Medical Problems

- **Anosmia** (loss of smell): sometimes caused by fractures which damage the **cribiform plate**. This damages the **Olfactory nerve** as it passes through this plate.
- **Bell's Palsy**: paralysis of the muscles of facial expression on one side. Caused by inflammation of the **Facial nerve**.
- **Tic douloureux**: severe facial pain caused by inflammation of the trigeminal nerve.
- **Blindness**: caused by damage to **optic nerve**. Degree of blindness depends upon the location of the damage.

Autonomic Nervous System

- Sympathetic Nervous System
  - "Fight or Flight"
- Parasympathetic Nervous System
  - "Rest and Digest".
  - The efferent innervation of all tissues other than skeletal muscle
  - A special case occurs in the gastrointestinal tract, where autonomic neurons innervate a nerve network in the wall of the intestinal tract.



Dual innervation

- Innervation by both PaNS and syNS
- Most body structures receive dual innervations
- Purpose: For better control
- The following structures do not receive dual innervation:

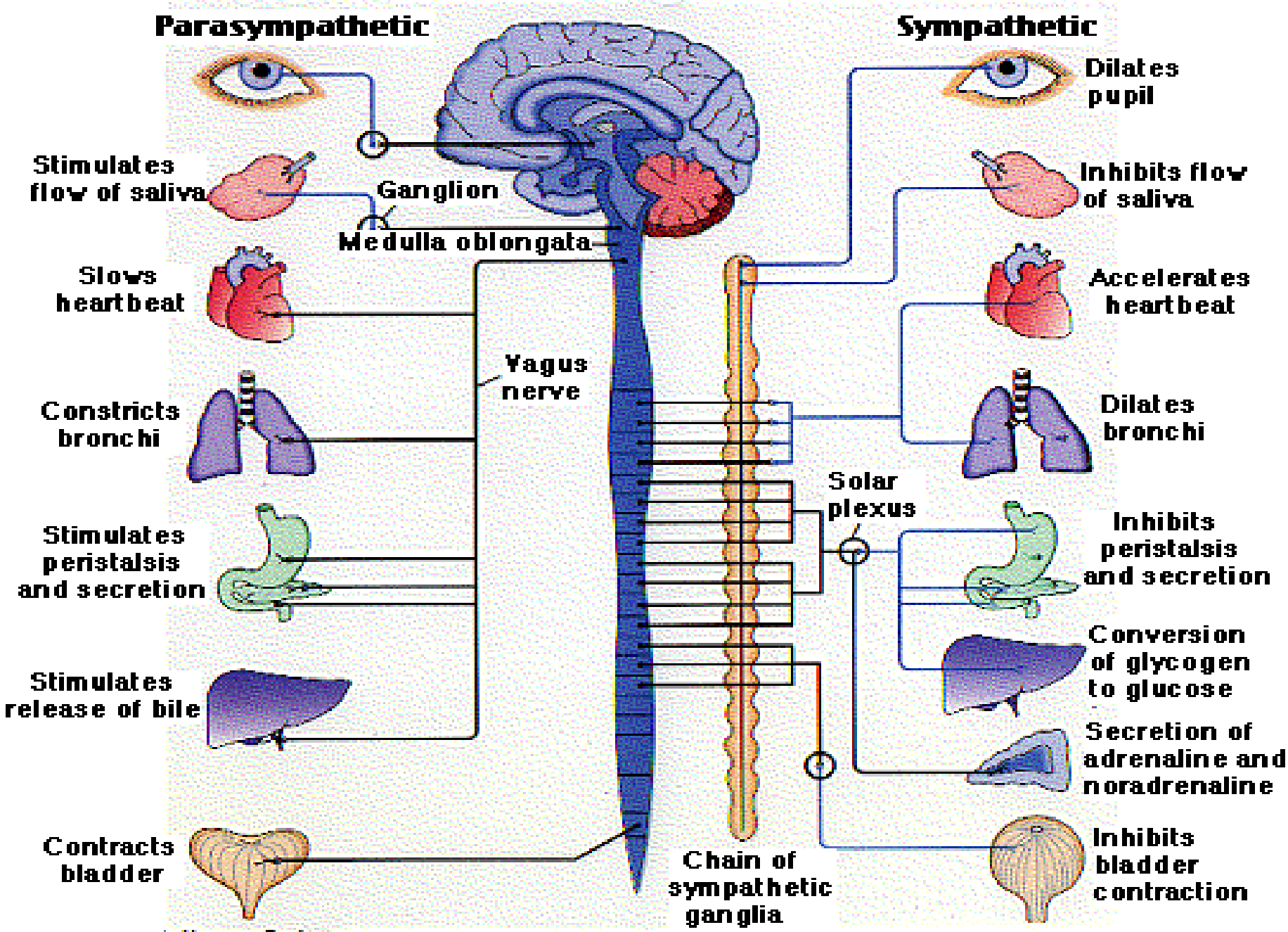
  →The sweat glands

  → Adrenal medulla

  → Blood vessels

  → Skin piloerectors

Effects of Autonomic innervation



Some Effects of Autonomic Nervous System Activity

Effector Organ	Receptor Type*	Sympathetic Effect	Parasympathetic Effect†
Eyes			
Iris muscles	Alpha	Contracts radial muscle (widens pupil)	Contracts sphincter muscle (makes pupil smaller)
Ciliary muscle	Beta	Relaxes (flattens lens for far vision)	Contracts (allows lens to become more convex for near vision)
Heart			
SA node	Beta	Increases heart rate	Decreases heart rate
Atria	Beta	Increases contractility	Decreases contractility
AV node	Beta	Increases conduction velocity	Decreases conduction velocity
Ventricles	Beta	Increases contractility	Decreases contractility slightly
Arterioles			
Coronary	Alpha	Constricts	—
	Beta	Dilates	
Skin	Alpha	Constricts	—‡
Skeletal muscle	Alpha	Constricts	—
	Beta	Dilates	
Abdominal viscera	Alpha	Constricts	—
	Beta	Dilates	
Salivary glands	Alpha	Constricts	Dilates
Veins	Alpha	Constricts	—
	Beta	Dilates	
Lungs			
Bronchial muscle	Beta	Relaxes	Contracts
Bronchial glands	Alpha	Inhibits secretion	Stimulates secretion
	Beta	Stimulates secretion	

Stomach			
Motility, tone	Alpha and Beta	Decreases	Increases
Sphincters	Alpha	Contracts	Relaxes
Secretion		Inhibits (?)	Stimulates
Intestine			
Motility	Alpha and Beta	Decreases	Increases
Sphincters	Alpha	Contracts (usually)	Relaxes (usually)
Secretion	Alpha	Inhibits	Stimulates
Gallbladder	Beta	Relaxes	Contracts
Liver	Alpha and Beta	Glycogenolysis and gluconeogenesis	—
Pancreas			
Exocrine glands	Alpha	Inhibits secretion	Stimulates secretion
Endocrine glands	Alpha	Inhibits secretion	—
	Beta	Stimulates secretion	

Effector Organ	Sympathetic Receptor Type*	Sympathetic Effect	Parasympathetic Effect†
Fat cells	Alpha and Beta	Increases fat breakdown	—
Kidneys	Beta	Increases renin secretion	—
Urinary bladder			
Bladder wall	Beta	Relaxes	Contracts
Sphincter	Alpha	Contracts	Relaxes
Uterus	Alpha	Contracts in pregnancy	Variable
	Beta	Relaxes	
Reproductive tract (male)	Alpha	Ejaculation	Erection
Skin			
Muscles causing hair erection	Alpha	Contracts	—
Sweat glands	Alpha	Localized secretion	Generalized secretion
Lacrimal glands	Alpha	Secretion	Secretion

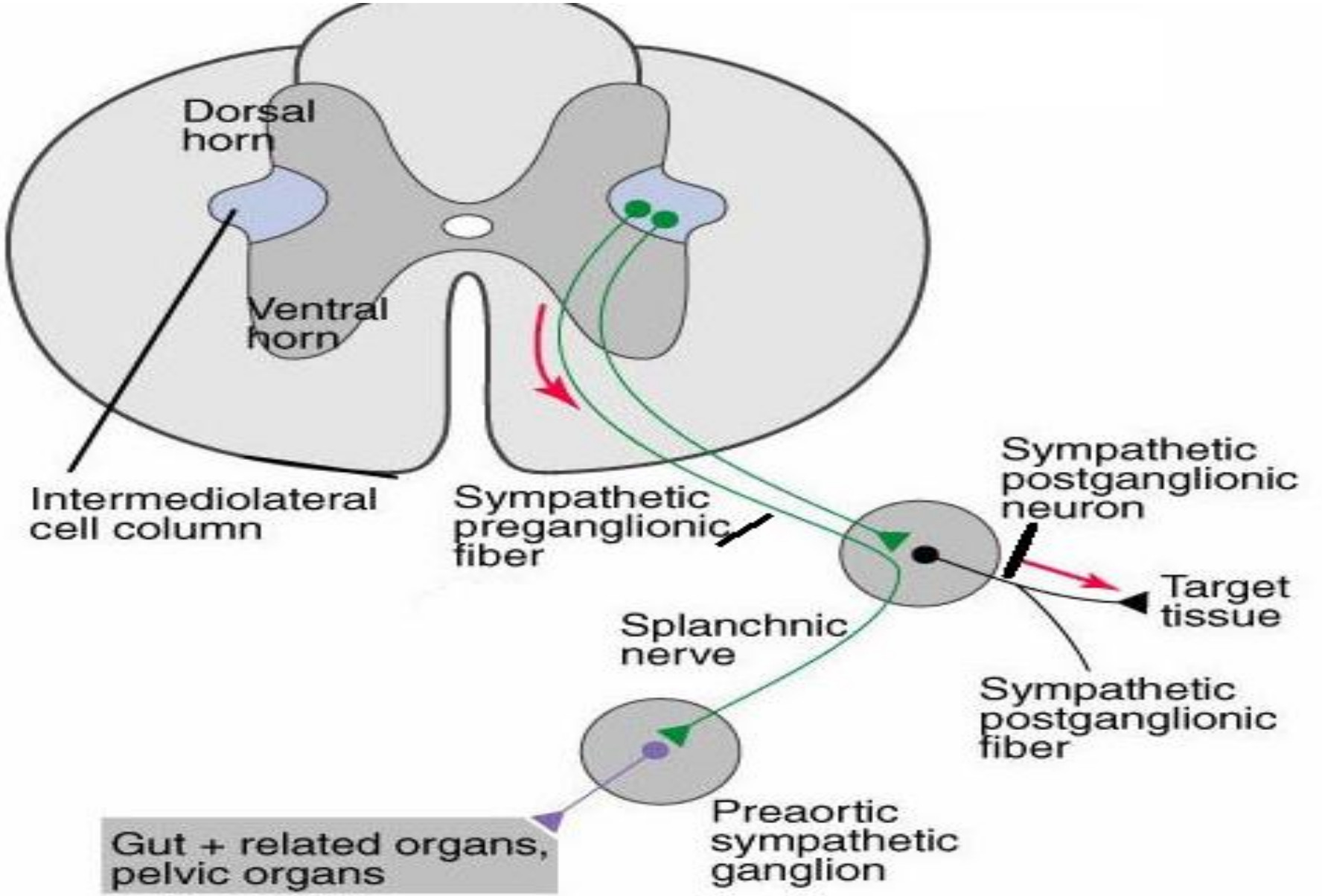
Sympathetic Division: (Thoracolumbar out flow)

- Originates in lateral horns of T_1-T_{12} and L_1-L_2 region of spinal cord
- Components of the Sympathetic neurons
  - Cell bodies of preganglionic motor neurons are located in the thoracic and lumbar part of the spinal cord
  - Preganglionic axons synapse in lateral/collateral ganglia, which are located near the spinal cord far away from the organs being innervated (short preganglionic neurons)
  - Sympathetic postganglionic axons travel from the lateral/collateral ganglia to the target organs
    - ✓Contains long postganglionic neurons

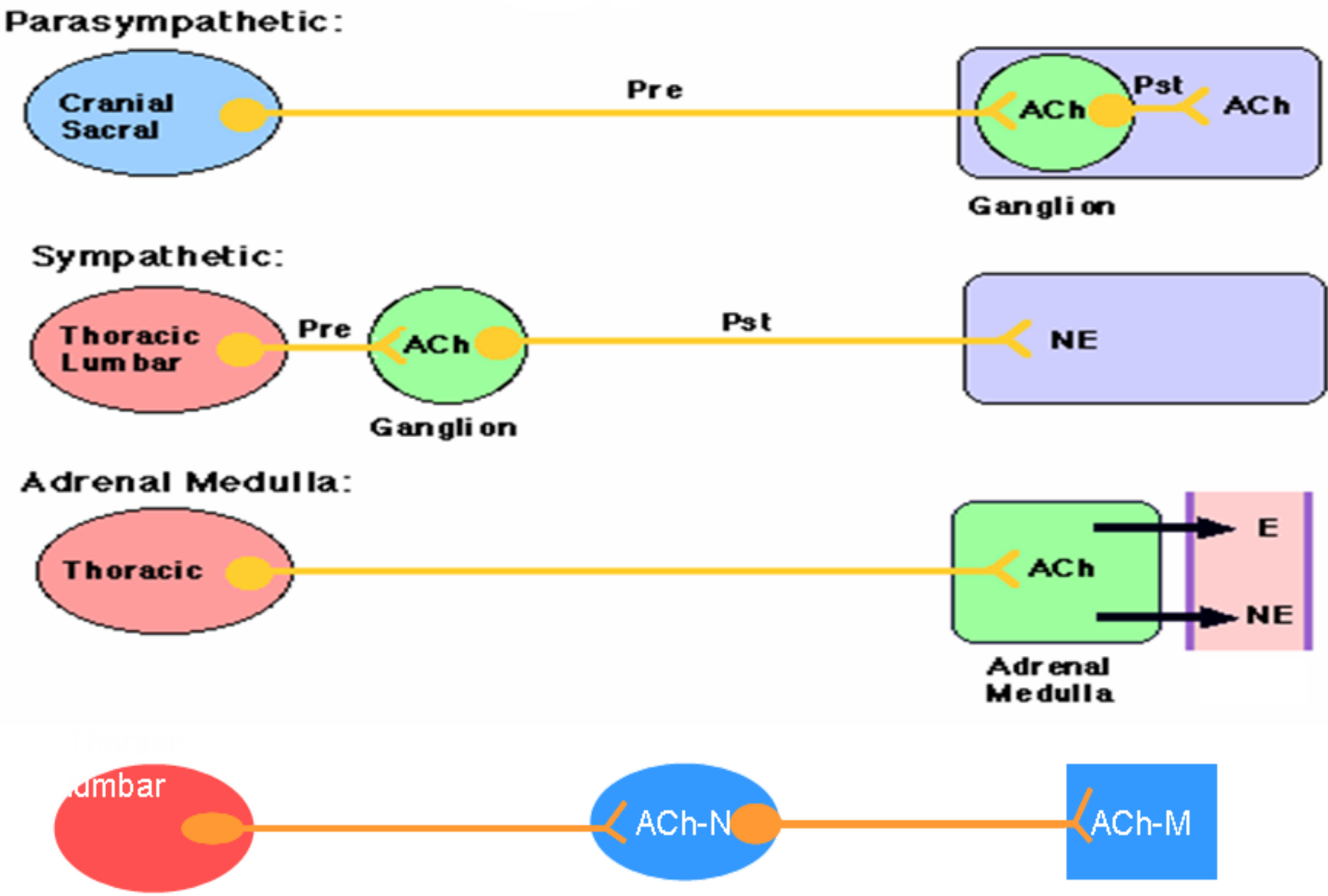
Functions of the SyNS

- Sympathetic - largely fight or flight responses
- Works with adrenal medulla –epinephrine
- Increases MR
- Increases CO during exercise and excitements
- Generally excitatory to almost all body parts except for the GIT.
- Has rather inhibitory effects on the GIT

Sympathetic Division



Neuronal organizations of the ANS



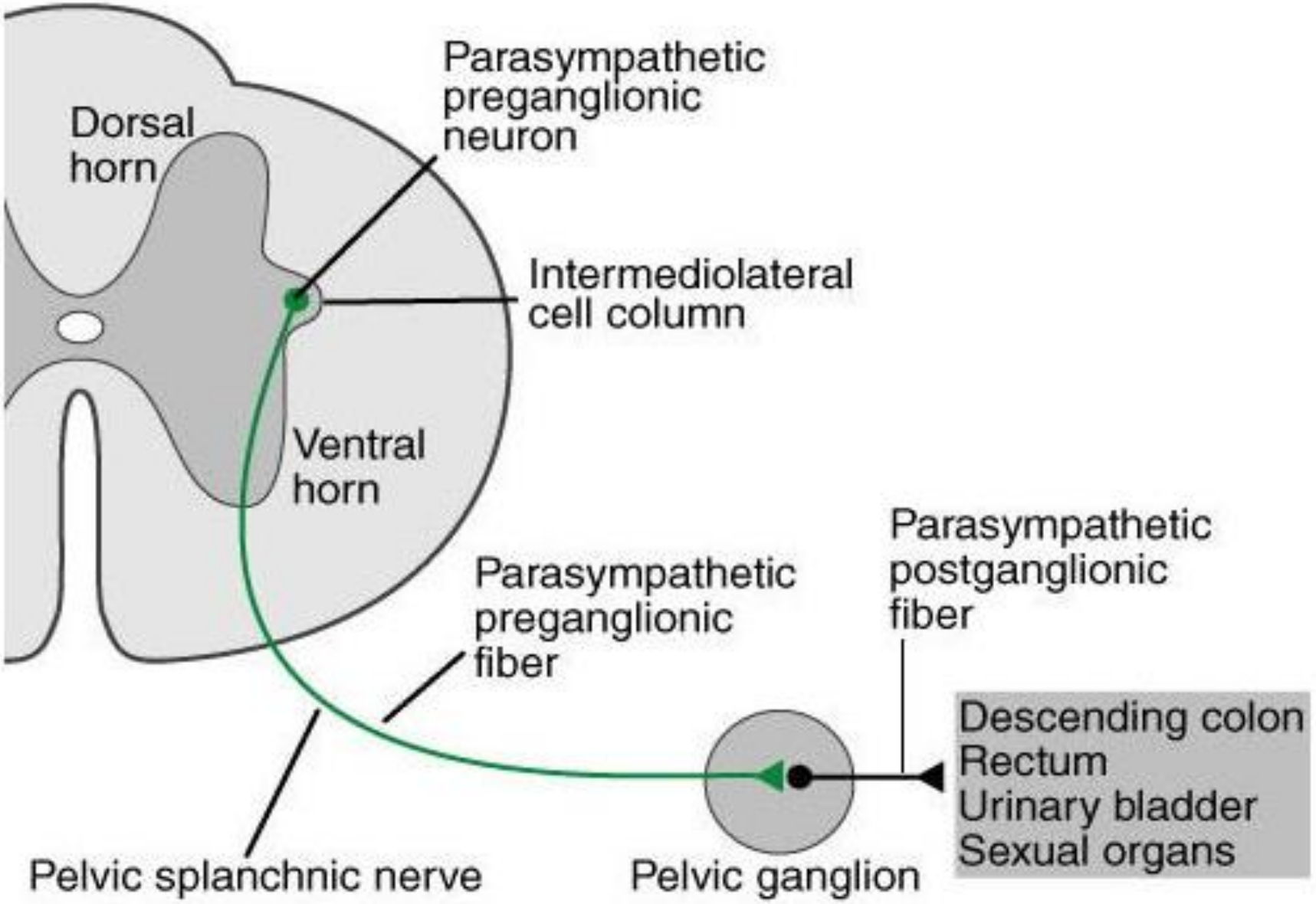
Parasympathetic Division: (Craniosacral)

- Originates from cranial and sacral regions.
- Cranial components are part of CN III (Oculomotor), VII (Facial), IX (Glossopharyngeal), and X (Vagus)
- Sacral components are from S_2 - S_4 segments of the spinal nerves.

Organization of the parasympathetic neurons

1. Cell bodies of preganglionic motor neurons located in certain nuclei of cranial nerves and in the sacral part of the spinal cord
2. Preganglionic axons synapse in terminal ganglia which are located close to or on the organ being innervated
3. Contains long preganglionic neurons
4. Parasympathetic postganglionic axons travel from the terminal ganglia to the target organ
5. Contains short postganglionic cholinergic neurons

Parasympathetic Division



Function

Regulation of digestion, defecation and micturition

- Conservation of **energy, anabolic**, **maintains** a **homeostatic environment** ”resting and digesting" system
- No mass discharge, discrete activities
- There is tonic impulse discharge to the heart
- Parasympathetic neurons in general have **inhibitory effect on almost all body tissues** except in the **GIT.**
- **They have rather excitatory effects on the GIT.**

Properties of pre- and post -ganglionic neurons

- All preganglionic neurons are cholinergic neurons. They secrete acetylcholine and are excitatory
- Sympathetic post ganglionic neurons are adrenergic with few exceptions. They secrete nor epinephrine and are either excitatory or inhibitory.
- Parasympathetic post ganglionic neurons are cholinergic. They secrete acetylcholine and are either excitatory or inhibitory.

Receptors in the autonomic nervous system

- Two principal receptors of acetylcholine (Cholinergic receptors)
  a. Nicotinic receptors
  b. Muscarinic receptors
- Acetylcholine activates both receptors.

Properties of pre- and post -ganglionic neurons…

- Muscarinic receptors are found on all effector cells stimulated by postganglionic cholinergic neurons of both PaNS and SyNS.
- Nicotinic receptors are found between pre- and post ganglionic neurons (ganglia) of both PaNS and SyNS. Also found at many non-autonomic nerves e.g., NMJ
- **Adrenergic receptors**

  a. Alpha receptors –subtypes include $alpha_1$ and $alpha_2$

  b. Beta receptors- subtypes include $beta_1$, $beta_2$ and $beta_3$

Autonomic ganglia

- Ganglion (ganglia = pl) is a collection of cell bodies outside the CNS
- Nucleus (nuclei = pl) is a collection of cell bodies within the CNS

Types of the autonomic ganglia

1. Lateral (paravertebral) ganglia
   - Are sympathetic ganglia
   - Form sympathetic chains on both sides of the vertebral column
2. Collateral (prevertebral) ganglia
   - Are also sympathetic ganglia
   - Located in midway b/n the **cord** and the **viscera**
   - *those are celiac g., superior mesenteric G. and inferior MG*
3. Terminal ganglia: a parasympathetic ganglia, located near/within the organ that they innervate.

Function of the autonomic ganglia

1. Relay stations
2. Expansion centres
3. Distribution centres

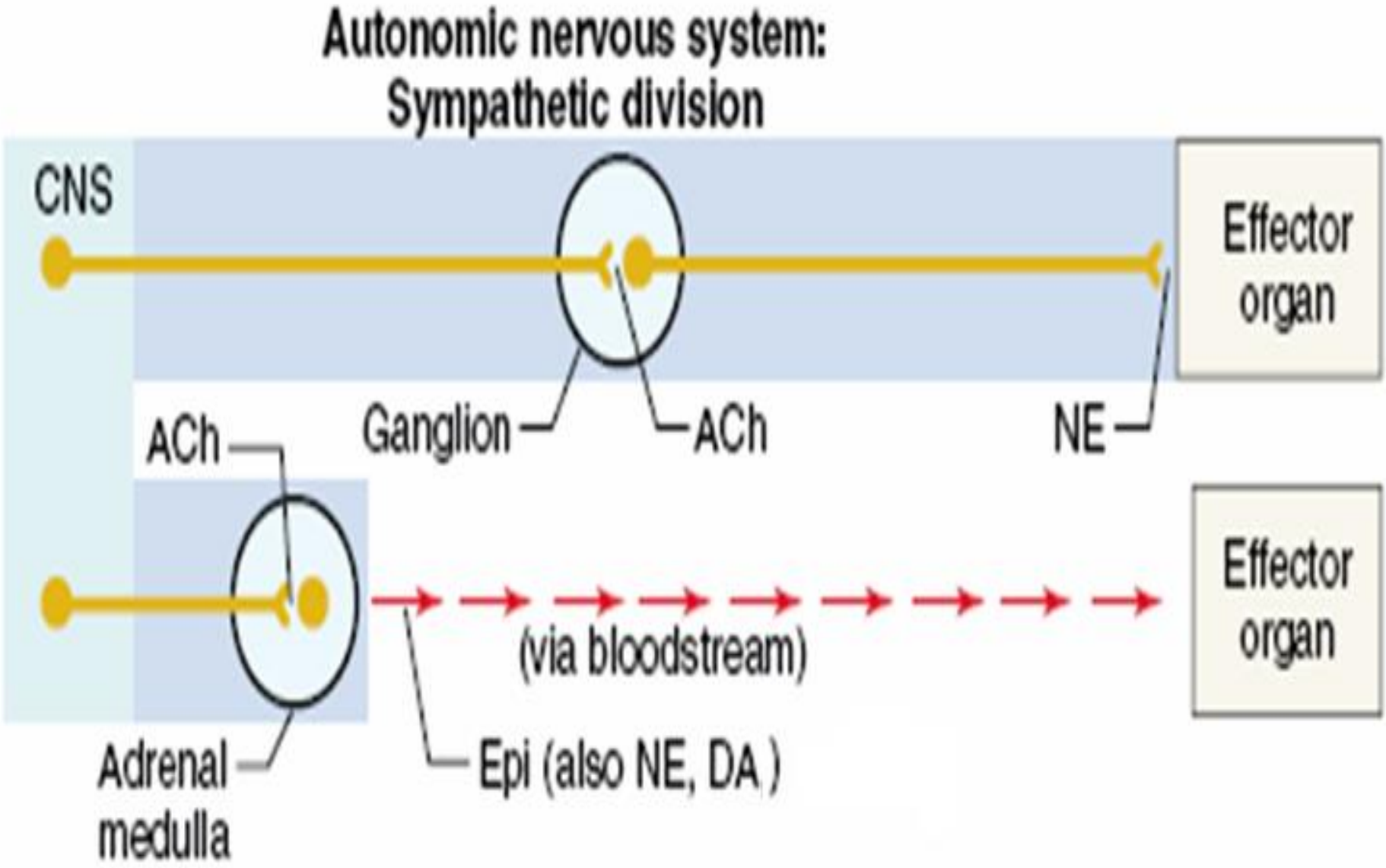
ANS Neurotransmitters

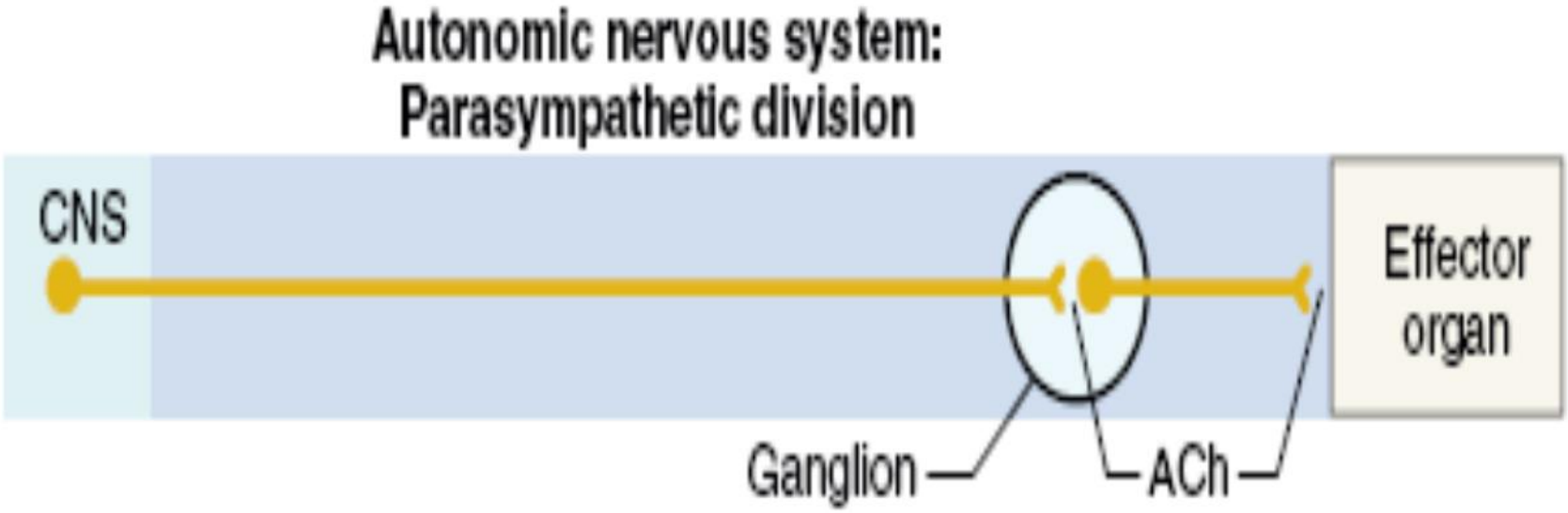
- Two neurotransmitters are used in the ANS.
  - acetylcholine (ACh)
  - nor epinephrine (NE)
- Neurotransmitters are released by the preganglionic cell or postganglionic cells.
- Bind to specific receptors in the postsynaptic cell membrane.
- Binding has either an **excitatory** or an **inhibitory** effect on the effectors, depending on the specific receptor.

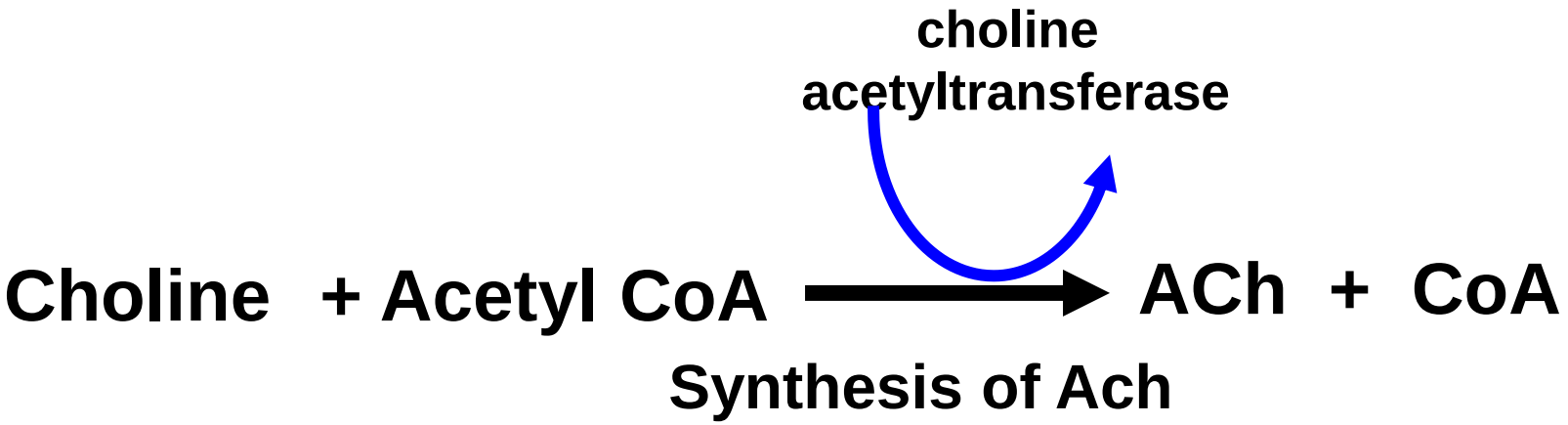
ANS Neurotransmitters

- Both preganglionic and postganglionic neurons in the parasympathetic division release **acetylcholine** and thus are called **cholinergic.**
- The preganglionic axon and a few postganglionic neurons in the sympathetic **division** are also **cholinergic.**
- Most of the postganglionic neurons of the sympathetic division release **nor epinephrine** and are called **adrenergic.**

ANS Neurotransmitters







Synthesis of Ach

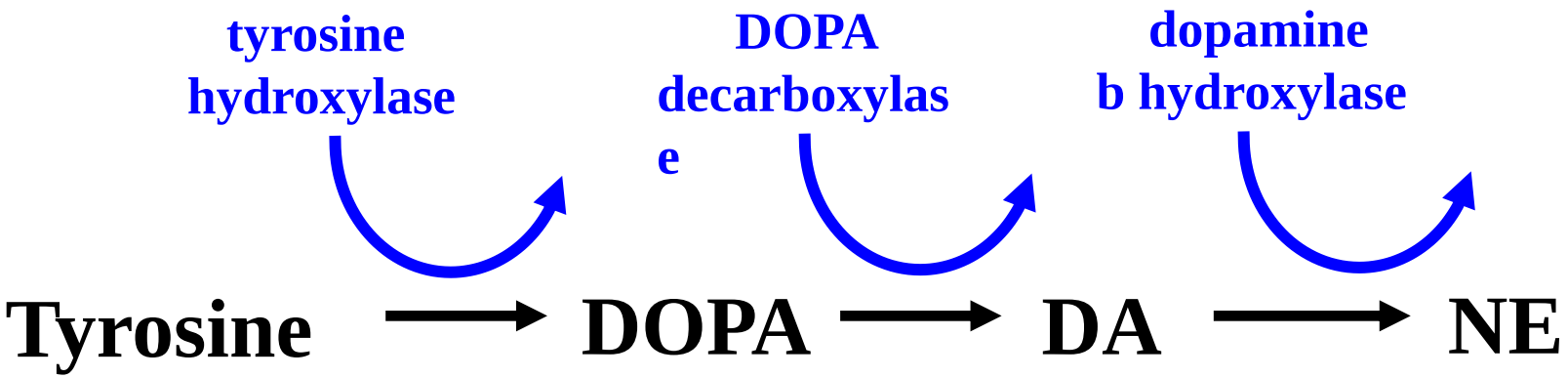
Autonomic Receptors

Receptor Name	Typical Locations	Result of Ligand Binding
Cholinoceptors		
Muscarinic M_1	CNS neurons, sympathetic postganglionic neurons	Formation of IP_3 and DAG, increased intracellular Ca2+
Muscarinic M_2	Myocardium, smooth muscle, CNS neurons	Opening of K+ channels, inhibition of adenylyl cyclase
Muscarinic M_3	Exocrine glands, vessels (smooth muscle and endothelium); CNS neurons	Like M_1 receptor-ligand binding
Muscarinic M_4	CNS neurons; possibly vagal nerve endings	Like M_2 receptor-ligand binding
Muscarinic M_5	Vascular endothelium, especially cerebral vessels; CNS neurons	Like M_1 receptor-ligand binding
Nicotinic N_N	Postganglionic neurons, some presynaptic cholinergic terminals	Opening of Na^+, K^+ channels, depolarization
Nicotinic N_M	Skeletal muscle neuromuscular endplates	Opening of Na^+, K^+ channels, depolarization

Autonomic Receptor

RECEPTOR TYPE	Typical Locations	Result of Ligand Binding
Adrenoceptors		
$Alpha_1$	Postsynaptic effector cells, especially smooth muscle	Formation of IP_3 and DAG, increased intracellular calcium
$Alpha_2$	Presynaptic adrenergic nerve terminals, platelets, lipocytes, smooth muscle	Inhibition of adenylyl cyclase, decreased cAMP
$Beta_1$	Postsynaptic effector cells, especially heart, lipocytes, brain	Stimulation of adenylyl cyclase, increased cAMP
$Beta_2$	Postsynaptic effector cells, especially smooth muscle and cardiac muscle	Stimulation of adenylyl cyclase and increased cAMP.
$Beta_3$	Postsynaptic effector cells, especially lipocytes; heart	Stimulation of adenylyl cyclase and increased cAMP

Norepinephrine Synthesis



- DA=Dopamine

Autonomic reflexes

- A reflex is a fast and involuntary response to a stimulus
- A reflex action consists of an action that is signalled to CNS and a reaction sent by the CNS
- Any reflex is transmitted through a reflex arc
- A reflex arc of any reflex has 5-components

1. A receptor that detects changes and under takes transduction
2. Afferent (sensory) pathway-Conducts AP to CNS
3. Integrating centre (spinal cord, brain)
4. Efferent (motor) pathway-Conducts AP to effectors
5. Effector organs (Cardia muscles, smooth muscles and glands)

Representative autonomic reflexes

- The baroreceptor reflex
- The chemoreceptor reflex
- Defecation reflex
- Micturition reflex
- Smooth muscle contractions
- Cardiac muscle contractions
- Secretion by glands
- Alteration of heart rate
- Changes in respiratory rate and depth
- Regulation of digestive system activities
- Alteration of pupil diameter

Pharmacology of the ANS

- Sympathomimetic drugs act on adrenergic effector organs.

  Epinephrine

  Nor epinephrine

  Methoxamine

- Drugs that stimulate specific adrenergic receptors but not others

  Phenylephrine

  Isoprotrenol

  Albuferol

- Drugs that cause release of catcholamines from the nerve endings.

  Ephedrine

  Tyramine

  Cathinon/cathin

  Amphetamine

Pharmacology of the ANS

Drugs that block adrenergic activity are:

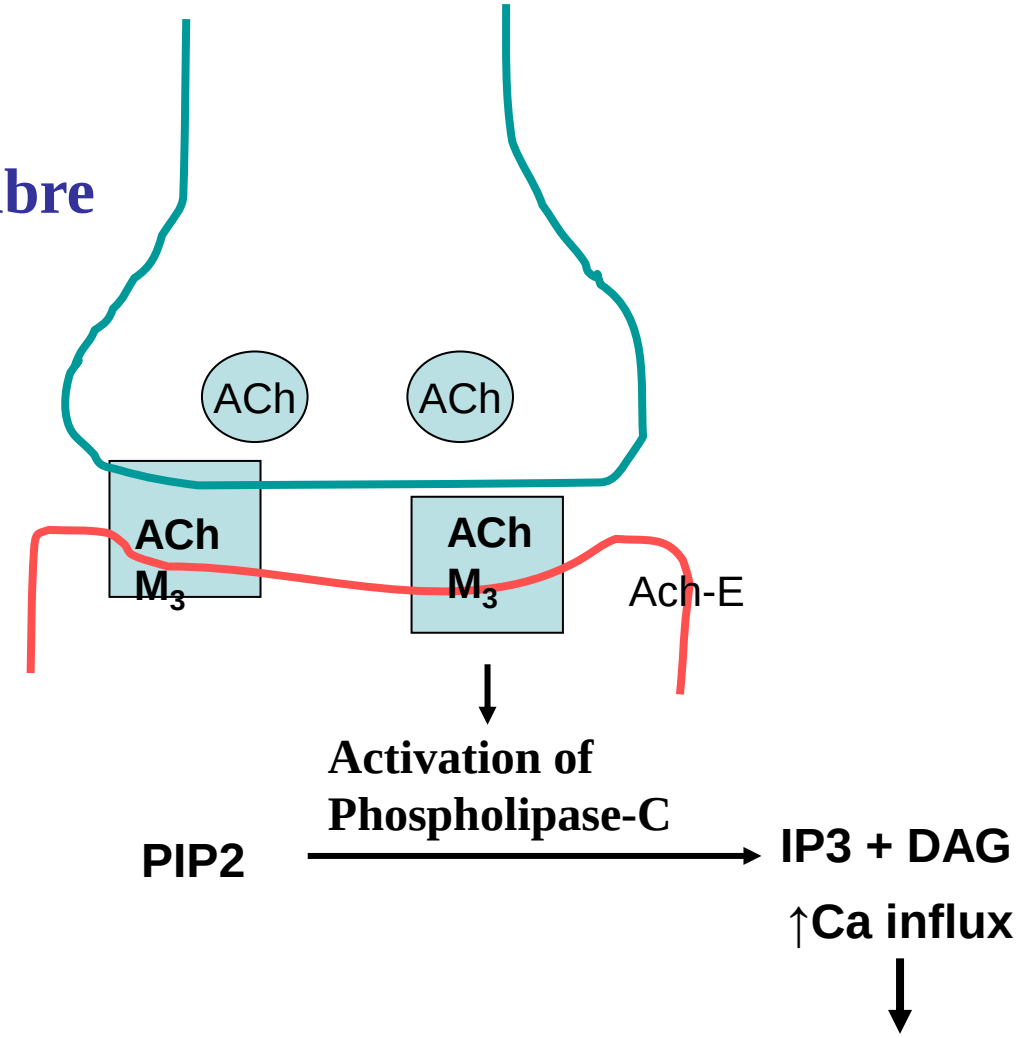
1. Synthesis and storage of NE can be prevented by:
   - Reserpine
2. Release NE can be blocked by
   - Guanethidine
3. Alpha receptors can be blocked by:
   - Phenoxybenzamine
   - Phentolamine
4. Drugs Blocking $beta_1$ and $beta_2$ receptors
   - Propranolol
   - Metoprolol
5. Drugs that block nerve impulse transmission through autonomic ganglia of both PaNS and SyNS
   - Hexamethonium

Pharmacology of the ANS

- Parasympathomimetic Drugs
  - Pilocarpine
  - Methacholine
- Parasympathetic potentiating effect Anti-cholenstrase drugs
  - Neostegmine
  - Physostigmine
  - Ambenonium
  - Malathion
- Cholinergic blockers at the effector organs
  - Atropine
  - Homatropine
  - Hyosin/scopolamine
- Drugs that stimulate autonomic post-ganglionic neurons
  - Acetylcholine
  - Nicotine

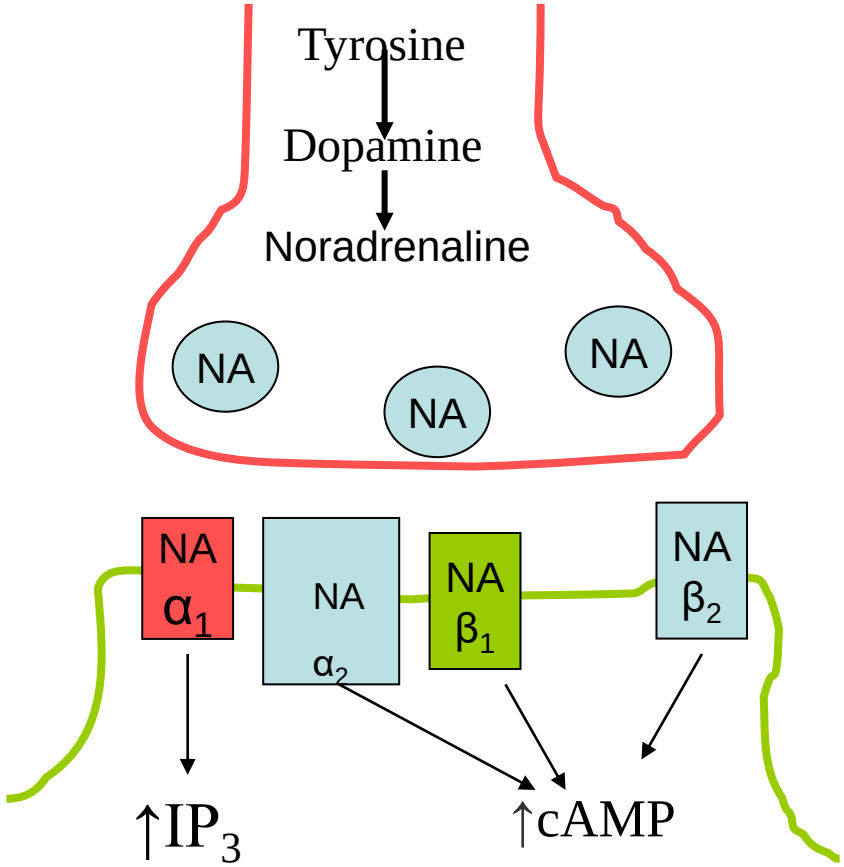
Mechanism of action of ACh

A Cholinergic fibre



- M_3 in the bronchial SM and in the GIT
- M2 in the heart and BVs Inhibition of cAMP production, activation of K+ channels

Mechanism of action of Catecholamines



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