Topics discussed in this lecture:

1) Introduction:
a) definition / b) General functions of ANS/ c) Characteristics of ANS/ d) Physiological anatomy
2) Sympathetic nervous system
a) Anatomy/ b) Effector functions
3) Parasympathetic nervous system
a) Anatomy/ b) Effector functions
4) Organization of the autonomic neuroeffector junction

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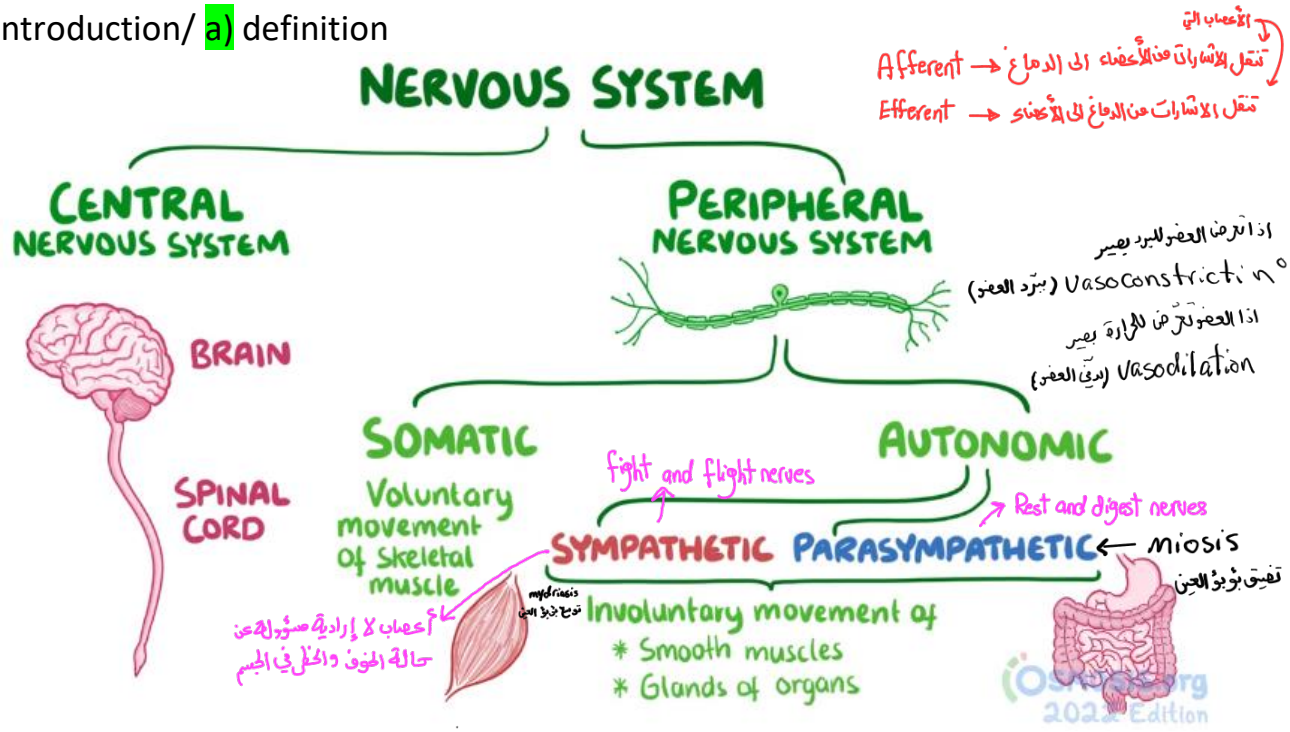
1) Introduction/ a) definition



Autonomic nervous system (ANS): This nervous division is anatomically distinct from the motor somatic nervous system, which innervates skeletal muscle. This group of efferent paths originates from the central nervous system and innervates heart, smooth muscle, glandular tissue and enteric nervous system. ANS has two subdivisions, sympathetic and parasympathetic

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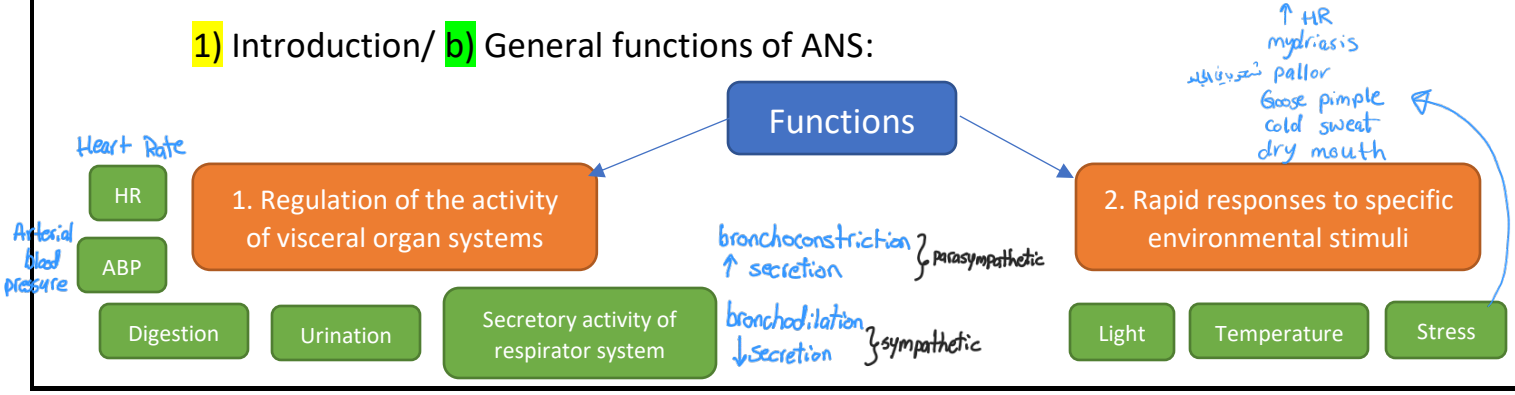
1) Introduction/ b) General functions of ANS:



B1. Regulation of the activity of visceral organ systems:

→ examples of functions under ANS control include:

- heart rate
- arterial blood pressure
- digestion, intestinal motility, secretions (these functions are controlled in conjunction with hormones).
- emptying of urinary bladder
- secretory activity of respiratory tract and airways resistance (by regulation of diameter of bronchioles).

→ By regulation of these functions, ANS plays an important role in maintaining constancy of internal environment (homeostasis).

B2. Rapid responses to specific environmental stimuli, these include:

- Light: constriction of the pupil to bright light (miosis), and dilation of pupil to low light (mydriases).
- Temperature: cutaneous vasodilation and sweating in a warm environment, and vasoconstriction in cold.
- Stress: The ANS (mainly the sympathetic and the adrenal medulla) mediates the immediate response (fight or flight response) to threatening stimuli. This involves a series of well coordinated responses to meet the metabolic demands for severe physical exertion. The features of this response include:

• increase heart rate and force of contraction.
• Widely dilated pupils.
• Pallor (pale of fear) as blood is directed to the skeletal muscle.(In "fight and flight" reactions the blood circulation is redistributed *higher amount of blood is directed to muscles, lower amount is directed to unnecessary tissues in the response such as the skin and GI tract (vasodilation(توسع الأوعية الدموية)for muscles blood vessels and vasoconstriction(تضيق الأوعية الدموية)for unnecessary tissues' vessels)*.
• Goose pimple: a state of the skin caused by cold, fear, or excitement, in which small bumps appear on the surface as the hairs become erect; goosebumps *it is caused by the contraction of smooth muscle cells found in the root of the hair*.
• Cold sweat. (it is cold because of the low amount of blood that is delivered to the skin)
• Dry mouth.*decreased secretion of salivary glands because u are reducing the blood flow*

* On the other hand during ordinary situation the parasympathetic division conserves and restores , it :

• Slow heartbeat
• Decreases respiratory rate
• Stimulates digestion
• Removes waste
• Store energy

palpitation خفقان في القلب

1) Introduction / c) Characteristics of ANS

Characteristics of autonomic responses:

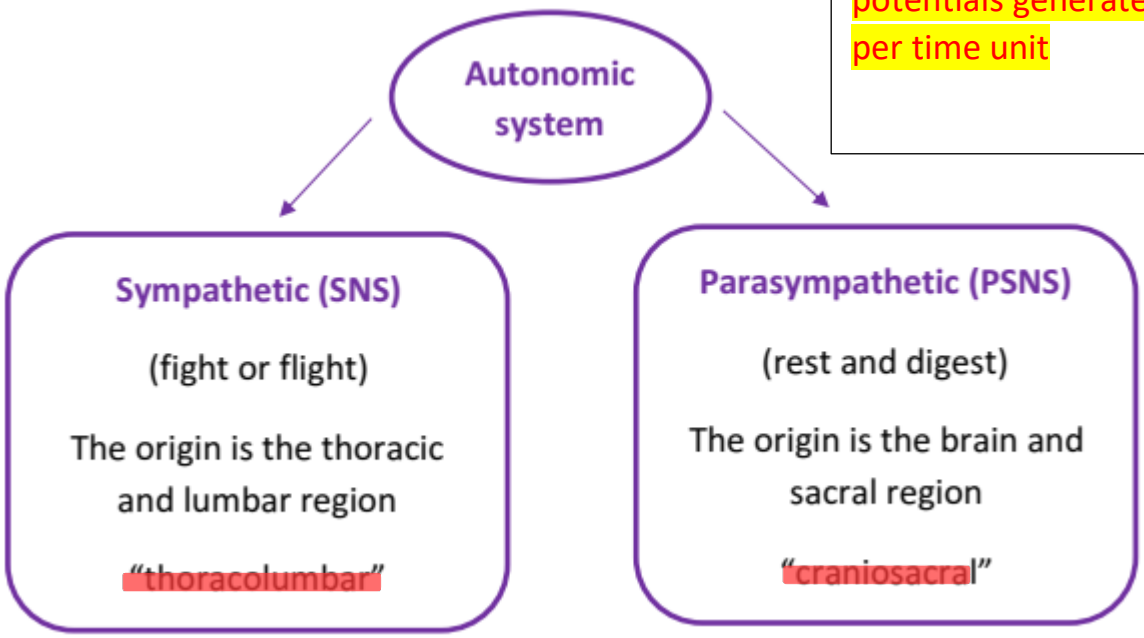
C1. Speed of onset: ANS can produce dramatic changes in the level of activity of organs they innervate within seconds. Changes in heart rate, sweating, goose pimples, and rise or fall in blood pressure can take place within few seconds (3-5 sec).

C2. Automatic nature: regulation of visceral functions occurs without conscious control. Some functions are brought under voluntary control such as urination and defecation through the participation of voluntary muscles. The impulses in ANS to target organs are set up reflexively in response to specific type of sensory information. The reflex responses are sensitive to emotional states of the body. Stress, excitements, euphoria, fear, anxiety or anger can influence reflexes and induce a variety of symptoms, such as sweating, palpitation, or digestive disturbances.

C3. Tonic activity: The ANS fires continuous impulses to target organs at very low rate. The basal rate of firing is called "sympathetic tone" and "parasympathetic tone". These tones establish basal rate of contractile activity in smooth muscle cells, and secretory activity of glandular tissues. The activity of these effector cells can be changed as a result of an increase or a decrease in the activity of any divisions of the ANS.

Tonic activity= the number of action potentials generated per time unit

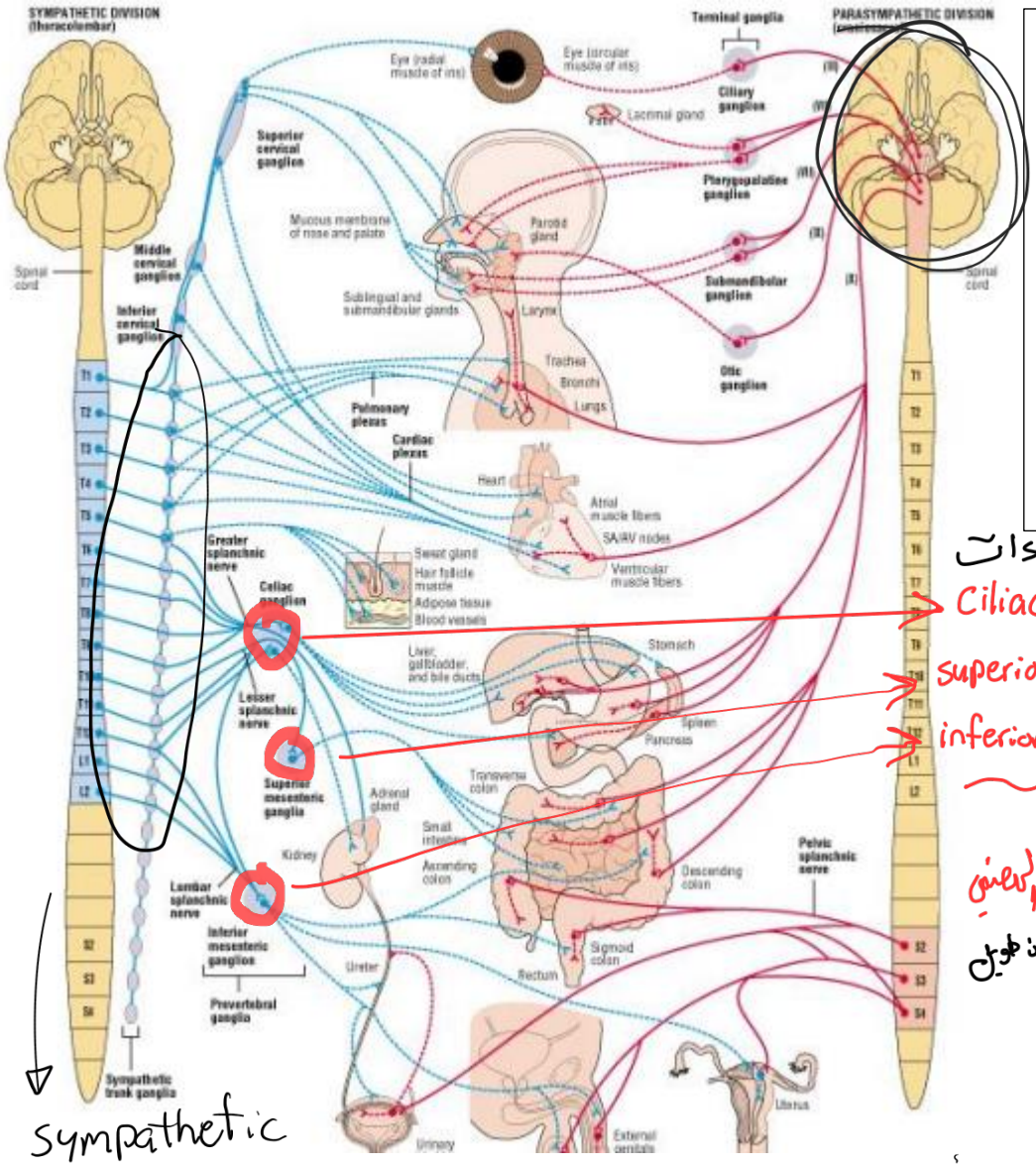
1) Introduction / d) Physiological anatomy



Two neurons carry impulses of the ANS from the CNS to the effector organs. The first is known as preganglionic neuron, the cell body is located in the CNS (in appropriate nucleus in the brain or in the lateral gray of the spinal cord). The fibres of preganglionic are small and myelinated, and usually end within a ganglion where they synapse with the second neuron called postsynaptic neuron. The second neuron (postsynaptic) carries impulses to target organ.

(T1-L2) → Sympathetic

Cranium + (S2-S4) → parasympathetic



We can notice that preganglionic

Fibers in sympathetic are short while in parasympathetic they are long. and postganglionic fibers are long in sympathetic while in parasympathetic they are short.

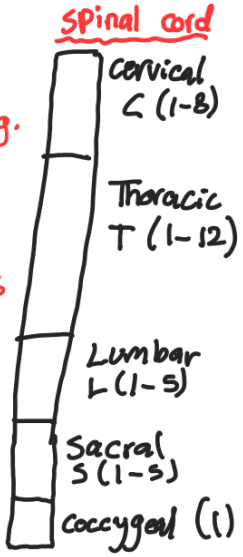
استثناءات

Ciliac ganglione

superior mesentric g.

inferior mesentric g.

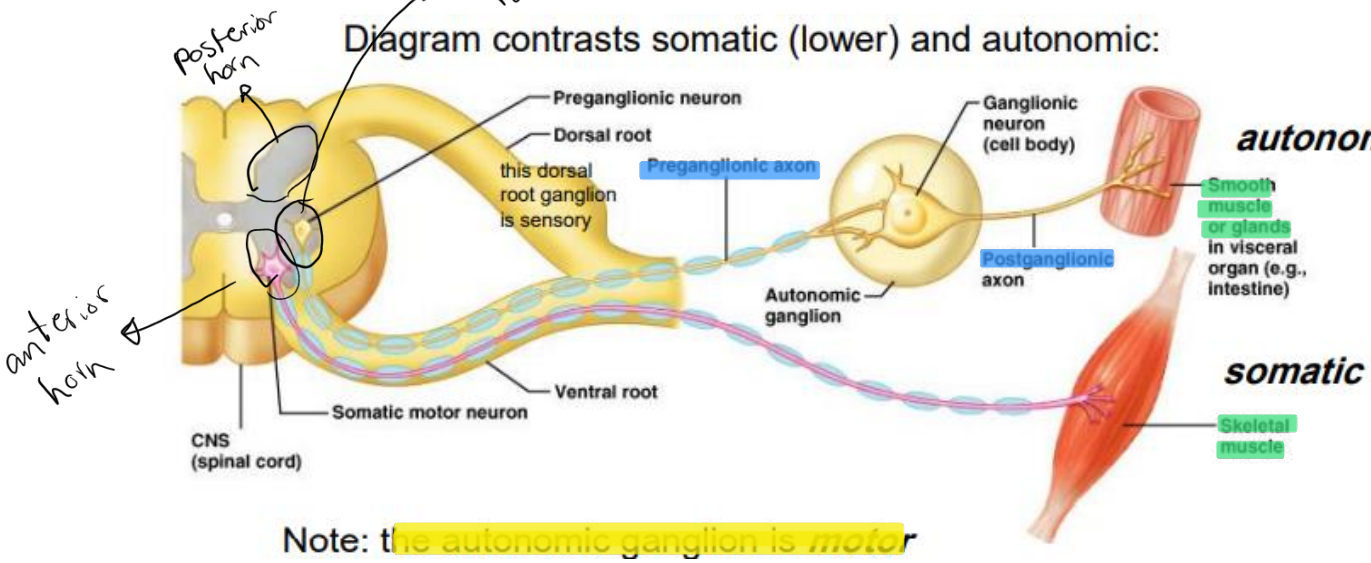
كلهم رايحين للجهاز الهضمي وفيهم الpre بكون طويل



sympathetic chain

* الأعصاب الخارجة من الحبل الشوكي تخرج من ال lateral horn

lateral horn

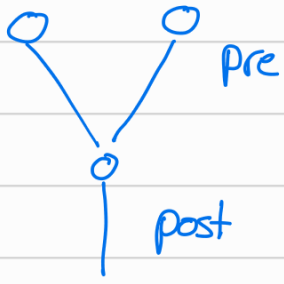


Note: the autonomic ganglion is *motor*

* Both sympathetic and parasy. consists of 2 nerves but somatic nerves are one nerve يبدأ من العمود الفقري ثم للعضلة مباشرة

Sympathetic chain → تكون على يمين و يسار الحبل الشوكي
وهي عبارة عن ganglions بصير عندها ال synapse تبع ال sympathetic

بتوزّع (Diverge)



بتجمّع (converge)

حالة واحدة خاصة:

بيطلع قصد presynaptic بعد posts. ، متى حدث هيك؟
لما يروح sympathetic nerve على ال Adrenal Gland (above the kidney)

* جزء من الغدة الكظرية هو عبارة (بتعدّل postsynaptic neuron) ، اسمه ال Medulla ← بيفرز نفس المواد اللي تفرزها ال posts. neurons تبع ال sympathetic

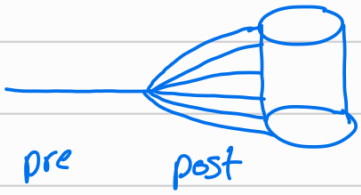
أي ال presy. راحت على ال postsy. يروح للغدة الكظرية ، بل الغدة نفسها تعمل كـ postsy. و تطلّع نفس المواد التي تطلّعها ال postganglionic ، ولكن بدل أن تفرزهذه المواد الى عضوين ، تفرزها الى الدم (وهذا هو الفرق).

* الخلايا اللي تفرز هذه المواد في ال adrenal medulla اسمها Chromaffin cells

parasympathetic

pre : long
post : short
so the ganglion is almost inside the organ or near to it

* الأعصاب اللي تطلع من الدماغ عددها 12
الاعصاب إلي الهم علاقة فيهم جال parasy. هذه الأعصاب رقم: 3 7 9 10
10 Vagus nerve العصب التائه



أما من ال sacral بيطلع S3, S4 وأحيانًا S2, S5 أيضًا

- فرق: لا يحتوي converge و diverge حتى على عصب واحد pre وعصب واحد post
أحيانًا خط واحد pre و 2 post

حتى نقل جميع أجزاء العضلة الملساء و تعمل bronchoconstriction or brochodilation in both sympathetic and parasy.

* The effect of the ANS may be stimulation or inhibition for the organ (gland).

In general, parasympathetic → stimulates secretion from glands

sympathetic → inhibits secretion from glands except in sweat glands

This depends on:

1) Type of neurotransmitters
2) Type of receptors
3) Intracellular changes.

← تقريبًا جميع الأعضاء تُغذى من para sym. و sym. في نفس الوقت

يوجد 3 أعضاء تُغذى من ال SNS فقط، وهي:-

1) Sweat glands
2) Skin
3) Blood vessels (Vasoconstriction)

لأن الأدوية الدموية التي محتاجين نفتح بها الدم بشكل كبير من الأدوية الدموية الرايحة الى العضلات (ميكانيك و القلب) فنعيس لها Vasodilation لأنها تميل الى أن ترتخي ولين يستجيب ال PSNS

Effects of SNS:

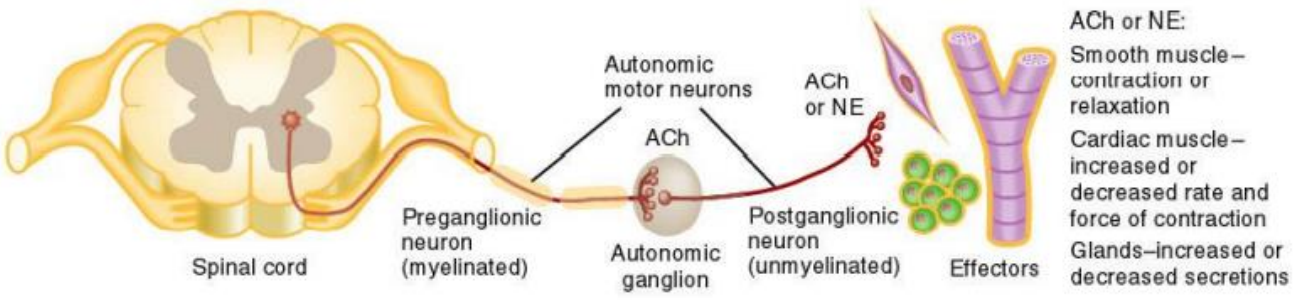
1) ↑ BP
2) ↓ Body temperature (Vasoconstriction)
3) ↑ HR
4) ↑ Cardiac output كمية الدم الخارجة من القلب خلال دقيقة
5) Bronchodilation (in respiratory system)
6) motility inhibition (in digestive system - GI
   secretion inhibition
7) lypolysis (breaking down lipids to produce energy)
8) mobilization of carbohydrates (Glucose)
9) ↑ metabolic rate
10) Mydriasis

Effects of PSNS:

1) ↑ motility, ↑ secretion (in digestive system - GI)
2) ↑ secretions in glands
3) ↓ HR
4) ↓ Cardiac output
5) pupil Miosis
6) ↑ micturition (in GUS) يعني التبول في الجهاز البولي التناسلي
7) ↑ accomidation of lens التعاجات العدسة من أجل رؤية الأشياء القريبة

Note:

- The parasympathetic, in contrast to sympathetic system is viewed as regulator of activities involved in replenishment of energy supply and general maintenance of the organism. The control provided by parasympathetic system is discrete and selectively directed to individual organs.
- SNS is acting over the cardiac muscle to increase the force of contraction while the PSNS has no effect on the force of contraction, it is acting only on the conductive tissue not the cardiac muscles itself.



(b) Autonomic nervous system

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2) Sympathetic nervous system/ a) Anatomy

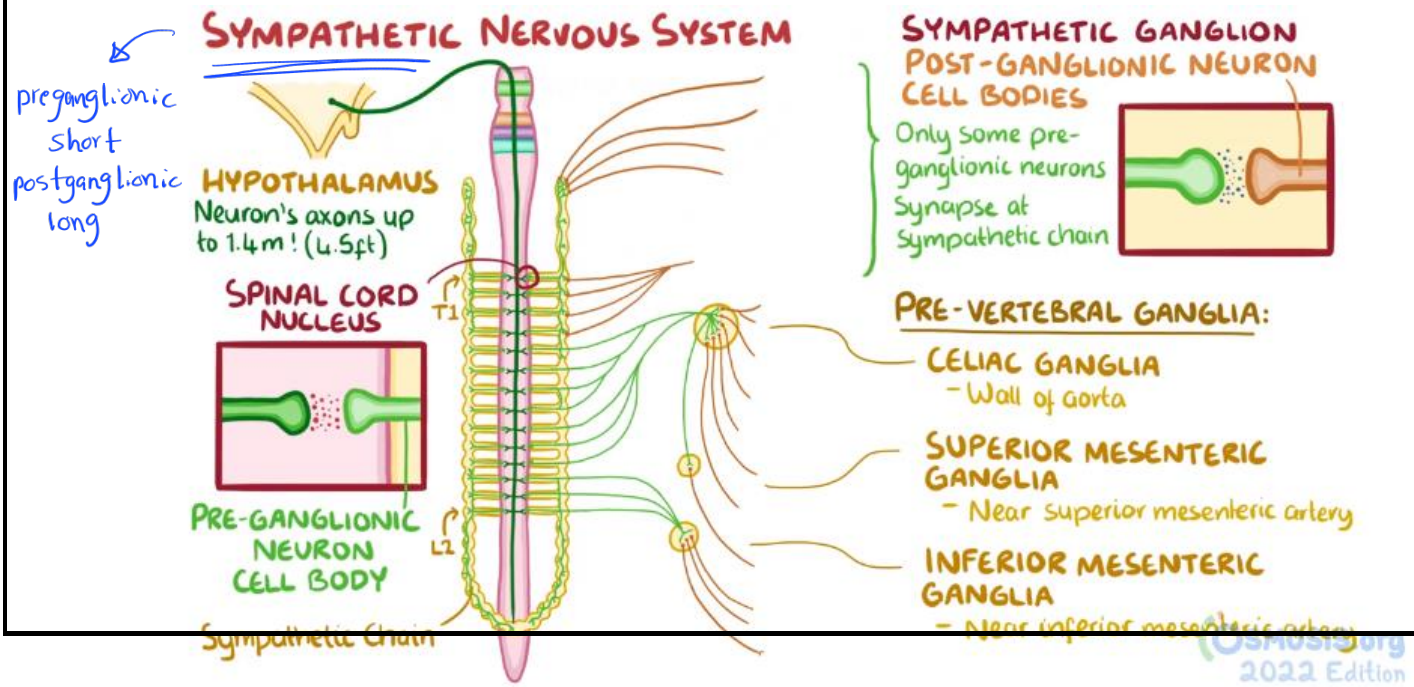
The cell bodies of preganglionic neurons lie in lateral gray of spinal cord at segmental levels of T1 through L3. Axons leaves spinal cord via ventral roots, then leave ventral root via white rami communicans to enter a vertebral ganglion of the sympathetic chain at the same segmental level. The preganglionic axon then can:

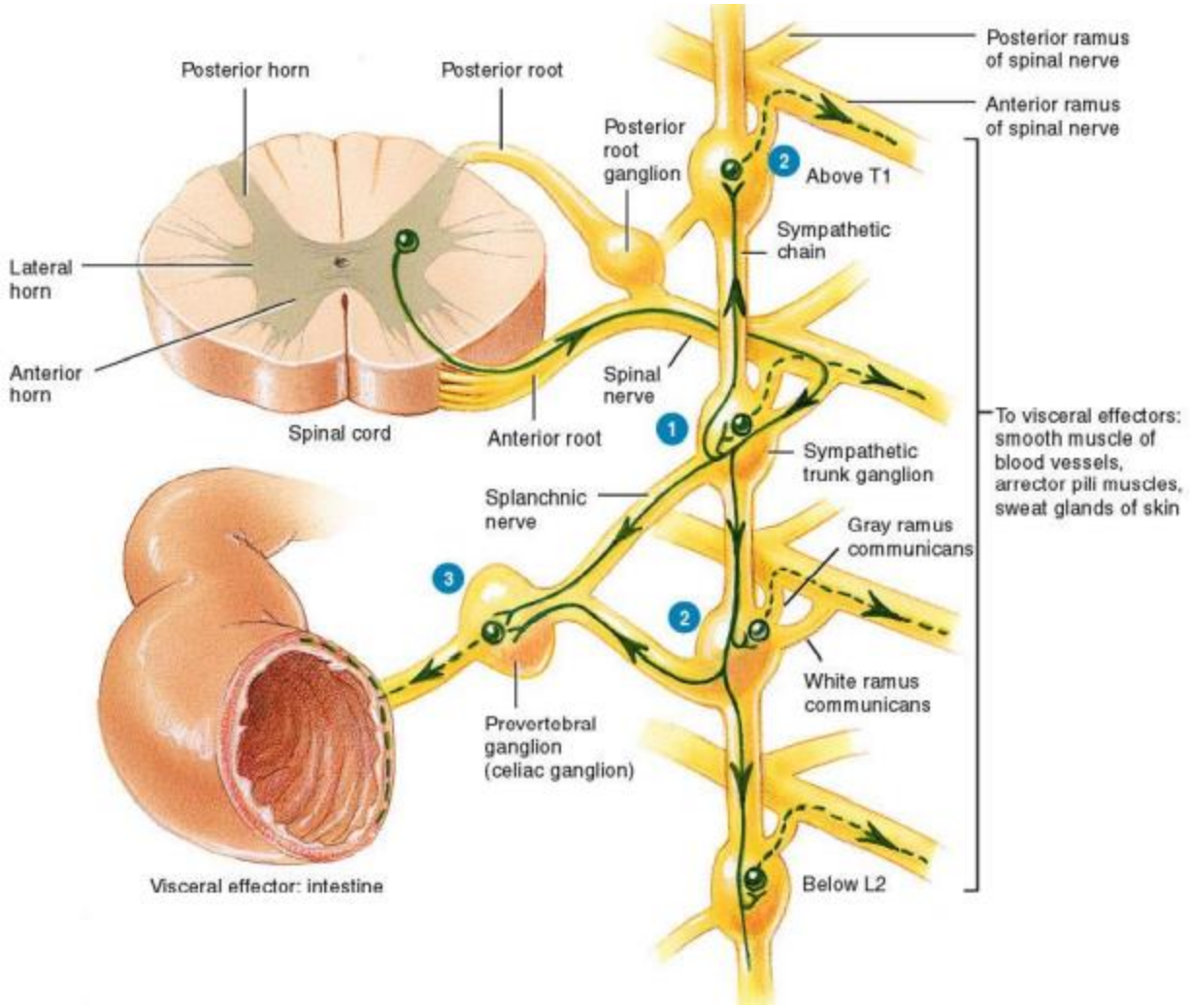
A1- Synapse with postganglionic cells at the same segmental level.

A2- Turn cranial or caudal and synapse with sympathetic postganglionic neuron at higher or lower segmental level. Synapse may occur at more than one postganglionic neuron. After synapse with neurons at paravertebral ganglia (beside the vertebral column), axons of second neurons leave ganglia via gray rami communicans to return to the corresponding spinal nerve.

A3- Some preganglionic fibers that enter ganglia pass without any synapse at the paravertebral ganglia and continue to some ganglia located in the abdomen known as prevertebral ganglia (Far away from the vertebral column), where they have the synapse with the second neuron. There are three unpaired prevertebral ganglia: celiac, superior mesenteric and inferior mesenteric ganglia

A4- Some preganglionic fibers pass without synapse in paravertebral ganglia and celiac ganglion. These fibers continue to adrenal gland where they synapse onto chromaffin cells. These cells liberate epinephrine into blood stream. (Dr. mohammed didn't focus on it)





→ Individual postsynaptic neuron in vertebral ganglia can receive signals from many preganglionic fibers (convergence) and one preganglionic neuron can relay impulse to many postganglionic neurons at different segmental levels (divergence). This organization of the sympathetic system induces widespread effects on target cells innervated by sympathetic postganglionic fibers.

2) Sympathetic nervous system/ b) Effector functions

→ Sympathetic system innervates widely distributed tissues. These include, sweat glands, smooth muscle cells of blood vessels supplying skeletal muscle, skin, etc, smooth muscle cells of hair follicles. This innervation is consistent with diffuse projections of the sympathetic postganglionic fibers that originate in vertebral ganglia and distribute with the spinal nerves.

→ In human, the previously mentioned target tissues do not have any parasympathetic innervation. Thus, the sympathetic which has excitatory effects on these tissues regulates:

- Blood pressure (blood vessels supplying skeletal muscle are major players). In addition to that the effect on heart also contributes in regulation of blood pressure.
- Body temperature by sympathetic effects on cutaneous blood vessels + sweat glands.

→ In addition to its effect on widely distributed tissues, sympathetic system is involved in handling stress responses (fight or flight reaction). Together with adrenal gland, the sympathetic system is designed to promote the production of energy for muscular work and to shut down organs which have nonessential functions in reaction to stressful situations. These effects on the following systems include:

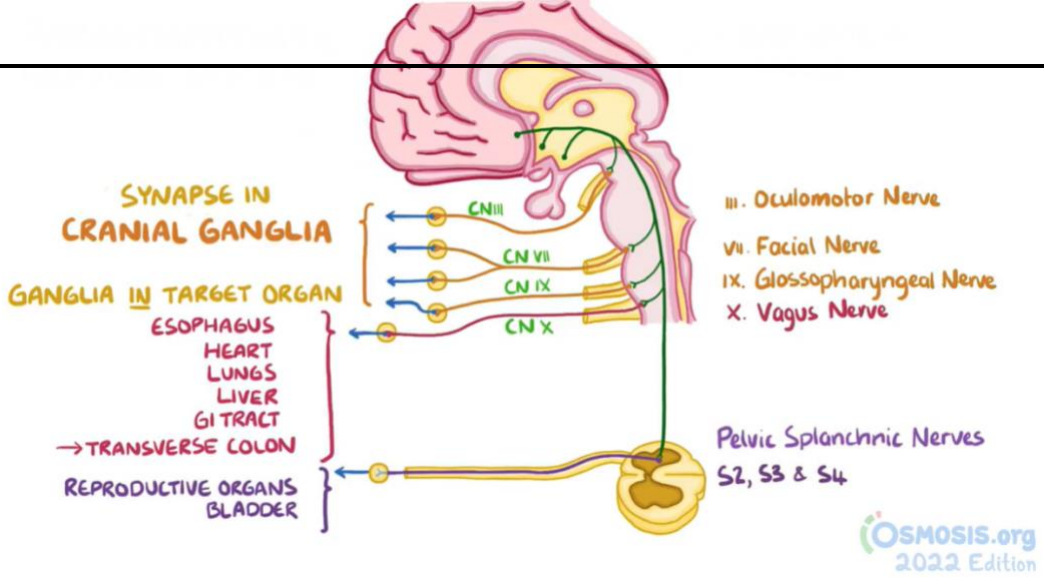
- Cardiovascular system: effects on vessels will result in redistribution of blood by enhancing blood flow to skeletal muscle and reducing blood flow to skin and mesentery.
- Effects on heart: increasing cardiac output (volume of blood pumped per minute).*it is acting over the cardiac muscle to increase the force of contraction*.
- Respiratory system: causes relaxation of bronchial muscle which result in bronchodilation. *more airflow for the lungs and better oxygenation for the blood*.
- Digestive system: inhibition of motility and secretion.
- Metabolic effects:

♣ Mobilization of glucose. ♣ Increased lipolysis. ♣ Increased metabolic rate

3) Parasympathetic nervous system / a) Anatomy

Parasympathetic nervous system: The preganglionic fibers arise in appropriate cranial nuclei and in segments S3 and S4 (sometimes S2, S5 also). These fibers leave the CNS in the III, VII, IX, and X (vagus) nerves for fibers of cranial origin and in pelvic nerve for fibers of sacral origin. The preganglionic fibers are long and go all the way to the effector organ where they synapse with the second postganglionic neuron located within the tissue of the effector organ or to a ganglion located very close to the effector organ. The axons of postsynaptic neurons are short.

Synaptic organization of parasympathetic nervous system: In parasympathetic there is no or little branching of preganglionic fibers (divergence). The ratio of pre to post ganglionic neurons is 1:1 or 1:2. As a result of this arrangement, the parasympathetic actions tend to be more discrete and confined to the innervated organ.



3) Parasympathetic nervous system / b) Effector functions

Overall, the parasympathetic, in contrast to sympathetic system is viewed as regulator of activities involved in replenishment (تجديد) of energy supply and general maintenance of the organism. The control provided by parasympathetic system is discrete and selectively directed to individual organs. The types of actions produced by parasympathetic stimulation include:

- Gastrointestinal system: increases motility and secretory activity.
- Glands: increases secretory activity (but remember sweat glands are under sympathetic control).
- Heart: decrease rate of contraction (bradycardia).

It has no effect on the force of contraction, it is acting only on the conductive tissue not the cardiac muscle itself

- Pupil: control pupil diameter by papillary light reflex (miosis) (regulates the amount of light falling on retina).
- Accommodation of the lens for near vision.
- Voiding the urinary bladder (micturition).

4) Organization of the autonomic neuroeffector junction

The terminals of autonomic nerve fibers are unlike terminals of the somatic motor fibers (skeletal neuromuscular junction). The autonomic terminals are highly branched forming extensive network of fibers beaded with small swellings or varicosities. These varicosities are sites from where transmitter is released.

The receptors on effector cells are scattered widely over the innervated organ. Unlike skeletal muscle, there is no specialized receptive region at the effector cell. The effect of ANS on these cells can be stimulatory or inhibitory. This effect depends on transmitter type, receptor subtype and changes in functional proteins induced in cell by binding of transmitter to its receptor.

- The first nerve in sympathetic and parasympathetic secrets Acetylcholine and affects Nicotinic receptors on the second nerve - (pregan.)

- In sympathetic, the second nerve secrets Norepinephrin or Epinephrin + Norepinephrin (in adrenal medulla to the blood). (postgan.)

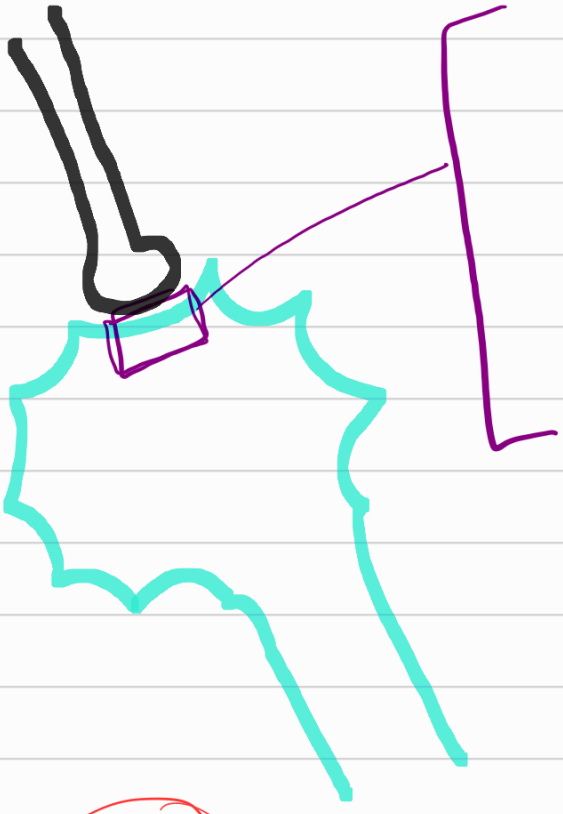
* ال sympathetic اللي رايحين للعدد الوحيدين اللي بيفرزوا (on the effector organ) Acetycholine.

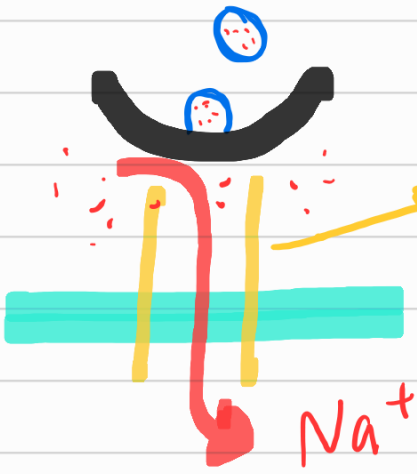
* In parasympathetic, the (pre) and (post) secrete acetycholine.

adrenergic receptors < α (1,2) / β (1,2,3) : (sympathetic) norepinephrine ال Receptors اللي بتأثر عليهم ال * (on the organ)

Muscarinic receptors (M1 - M5) : acetylcholine ال Receptors اللي بتأثر عليهم ال * (on the organ)

- بينما ال Nicotinic Receptors هي ال Receptors اللي على ال postsynaptic neuron

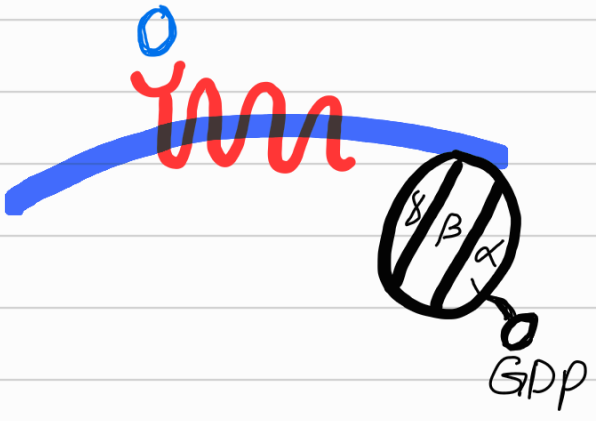




Nicotine Receptor
(Na^+ channel)

أول ما يرتبط الـ acetylcholine
يفتح الـ Nicotine receptor ويدخل
Na^+ لداخل الـ neuron ← Epsp

Muscarinic Receptors M(1-5)
(G protein coupled receptors)



α (S, I, q)

α(S) ينشط الأدينيل سيكليز
adenylyl cyclase
المسؤول عن تحويل
ATP → cAmp
protein kinase A ← ينشط
phosphorylates some compound مما يحفز استجابة الخلية

α(I) inhibites adenylyl cyclase

α(q) ينشط الفوسفوليبيز سي
phospholipase c (PLC)
يعطي البيبز
PIP2 → DAG + IP_3

M(1,3,5) → activators
يرتبط بـ $G_{protein}$ ، α_q

M2 → inhibitory (on heart)
يرتبط بـ $G_{protein}$ ← α_i

تنشيل الـ M2 على القلب عن طريق الـ parasympathetic
رح تفتح k+ channels مما يقلل الـ AP وتقل الـ
HR وبالتالي depolarization

* ال muscarinic receptors وال Nicotine receptors اللتين بيشتغلوا بفعل ال acetylcholine

* Atropine inhibits the muscarinic receptors

Muscarine → (يشتغل) Muscarinic receptors (Bradycardia)
Atropine → inhibits Muscarinic receptors (Tachycardia) } عكس التأثير بكل حالة
Nicotine → (يشتغل) Nicotine receptors

Bradycardia ↓ 60-100 ↑ Tachycardia

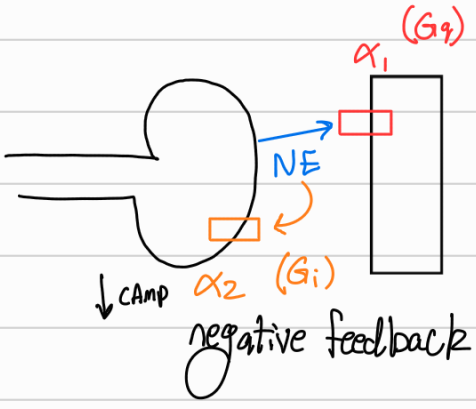
Adrenergic Receptors

Epi / NE (Chatecolamins)

α 1,2
β 1,2,3

α_1 : smooth muscles (except) smooth muscles on bronchi (موجودة بكل)
effect of NE = effect of Epi
G protein coupled receptor - $\alpha(q)$ (IP_3 ↑ Ca^{++})

α_2 : postsynaptic SNS / ↓ cAmp / G_I



β_3 : موجود فقط على الأنسجة الدهنية ومسؤول عن عملية كسر الدهون

(**) β_1 , β_2 → more sensitive than α

(***) Heart → sympathetic β_1 , parasympathetic M_2 (Muscarinic type 2)

β_1 : ↑ HR / ↑ cardiac output

β_2 : Smooth muscles (all including bronchi)
Epi ↑ > NE ↓
G protein - G_S ↑ cAmp

(*) β blockers (anti-arythmic drugs) → inhibit (β_1)

(*) Salbutamol (β_2 - Agonists) → activates (β_2)

Effects of the two branches of the ANS

Organ	Sympathetic Effect	Parasympathetic Effect
Pupil	dilation	constriction
Lens	Far focus (lower curvature)	Near focus (increased curvature)
Salivary Gland secretion	High in viscosity	serous
Heart	Increased rate and pressure	Lower rate and pressure
Lungs	Dilation of respiratory passages	Constriction of respiratory passages
Gastrointestinal	Decreased motility	Increased motility
Kidneys	Decreased filtration rate	Increased filtration rate
Male genitalia	Ejaculation	Erection
Vascular smooth muscle	Variable depending on the neurotransmitter	Relaxation
Sweat glands	Increased activity	No innervation
Arteries to skeletal muscle	dilation	No innervation
Veins	Variable depending on the neurotransmitter	No innervation

→ Adrenergic receptors

(α_1) - produce excitation (contraction or constriction)
- Gq proteins → stimulation of PLC and increase in IP3 and intracellular Ca^{++}.

(α_2) - produce inhibition (relaxation or dilation)
- Gi proteins → ↓cAmp

(β_1) - produce excitation (↑HR , ↑ conduction velocity , ↑ contracility)
- G_S proteins → ↑ cAmp
* sensitive to Epi and NE

(β_2) - produce relaxation (dilation of vascular smooth muscle, dilation of bronchiols, relaxation of the bladder wall)
- G_S proteins → ↑ cAmp.

Characteristic	Sympathetic	Parasympathetic	Somatic*
Origin of preganglionic nerve	Nuclei of spinal cord segments T1–T12; L1–L3 (thoracolumbar)	Nuclei of cranial nerves III, VII, IX, and X; spinal cord segments S2–S4 (craniosacral)	
Length of preganglionic nerve axon	Short	Long	
Neurotransmitter in ganglion	ACh	ACh	
Receptor type in ganglion	Nicotinic	Nicotinic	
Length of postganglionic nerve axon	Long	Short	
Effector organs	Smooth and cardiac muscle; glands	Smooth and cardiac muscle; glands	Skeletal muscle
Neurotransmitter in effector organs	Norepinephrine (except sweat glands, which use ACh)	ACh	ACh (synapse is neuromuscular junction)
Receptor types in effector organs	α_1, α_2, β_1, and β_2	Muscarinic	Nicotinic

Receptor	Location	G Protein	Mechanism
Adrenergic			
α_1	Smooth muscle	G_q	↑ IP_3/Ca^{2+}
α_2	Gastrointestinal tract	G_i	↓ cAMP
β_1	Heart	G_s	↑ cAMP
β_2	Smooth muscle	G_s	↑ cAMP
Cholinergic			
N_M (N_1)	Skeletal muscle	—	Opening Na^+/K^+ channels
N_N (N_2)	Autonomic ganglia	—	Opening Na^+/K^+ channels
M_1	CNS	G_q	↑ IP_3/Ca^{2+}
M_2	Heart	G_i	↓ cAMP
M_3	Glands, smooth muscle	G_q	↑ IP_3/Ca^{2+}

Organ	Sympathetic Action	Sympathetic Receptor	Parasympathetic Action	Parasympathetic Receptor
Heart	↑ heart rate	β_1	↓ heart rate	M_2
	↑ contractility	β_1	↓ contractility (atria)	M_2
	↑ AV node conduction	β_1	↓ AV node conduction	M_2
Vascular smooth muscle	Constricts blood vessels in skin; splanchnic	α_1	—	
	Dilates blood vessels in skeletal muscle	β_2	—	
Gastrointestinal tract	↓ motility	α_2, β_2	↑ motility	M_3
	Constricts sphincters	α_1	Relaxes sphincters	M_3
Bronchioles	Dilates bronchiolar smooth muscle	β_2	Constricts bronchiolar smooth muscle	M_3
Male sex organs	Ejaculation	α	Erection	M
Bladder	Relaxes bladder wall	β_2	Contracts bladder wall	M_3
	Constricts sphincter	α_1	Relaxes sphincter	M_3
Sweat glands	↑ sweating	M (sympathetic cholinergic)	—	
Eye				
Radial muscle, iris	Dilates pupil (mydriasis)	α_1	—	
Circular sphincter muscle, iris	—		Constricts pupil (miosis)	M
Ciliary muscle	Dilates (far vision)	β	Contracts (near vision)	M
Kidney	↑ renin secretion	β_1	—	
Fat cells	↑ lipolysis	β_1	—	