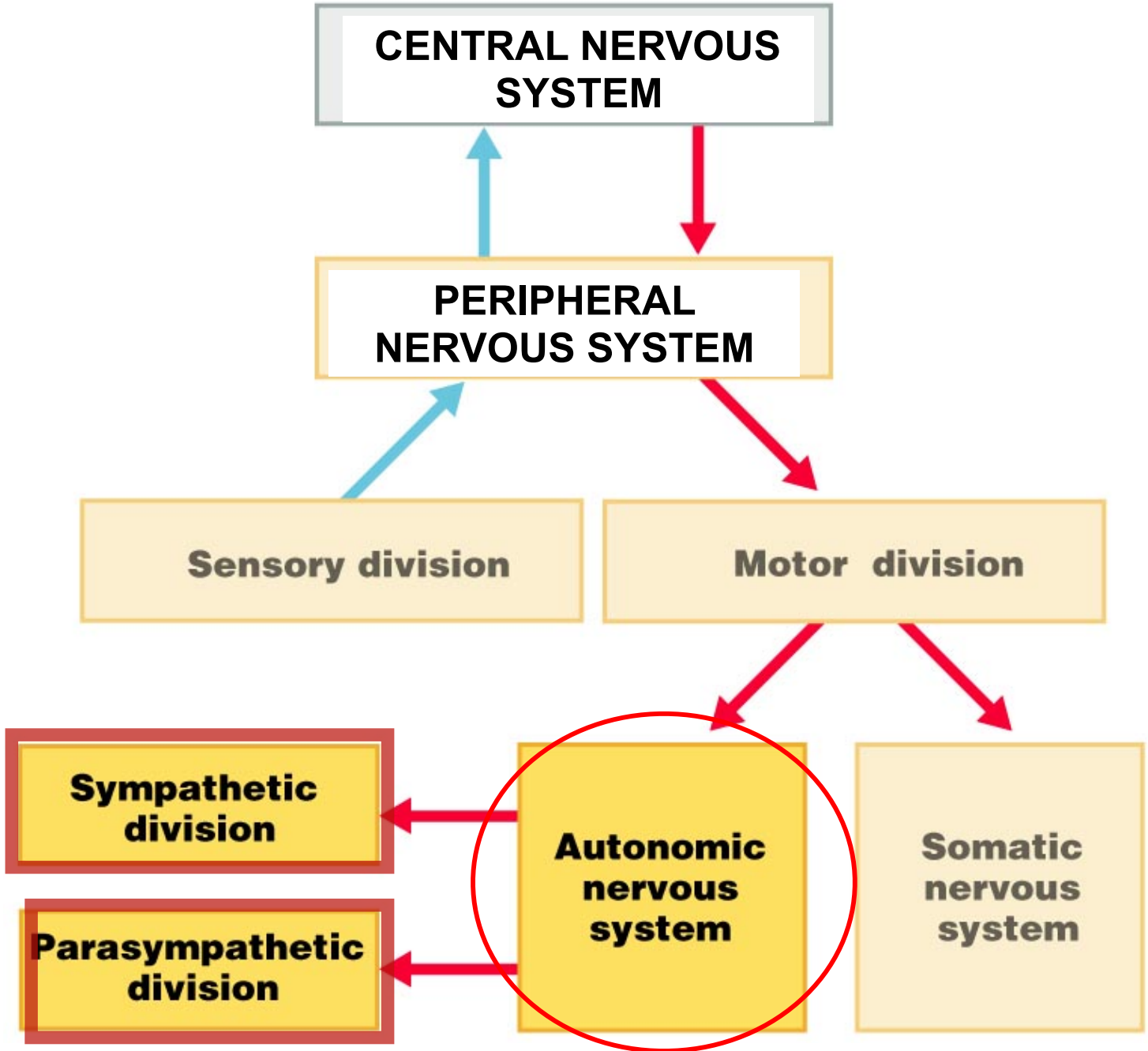
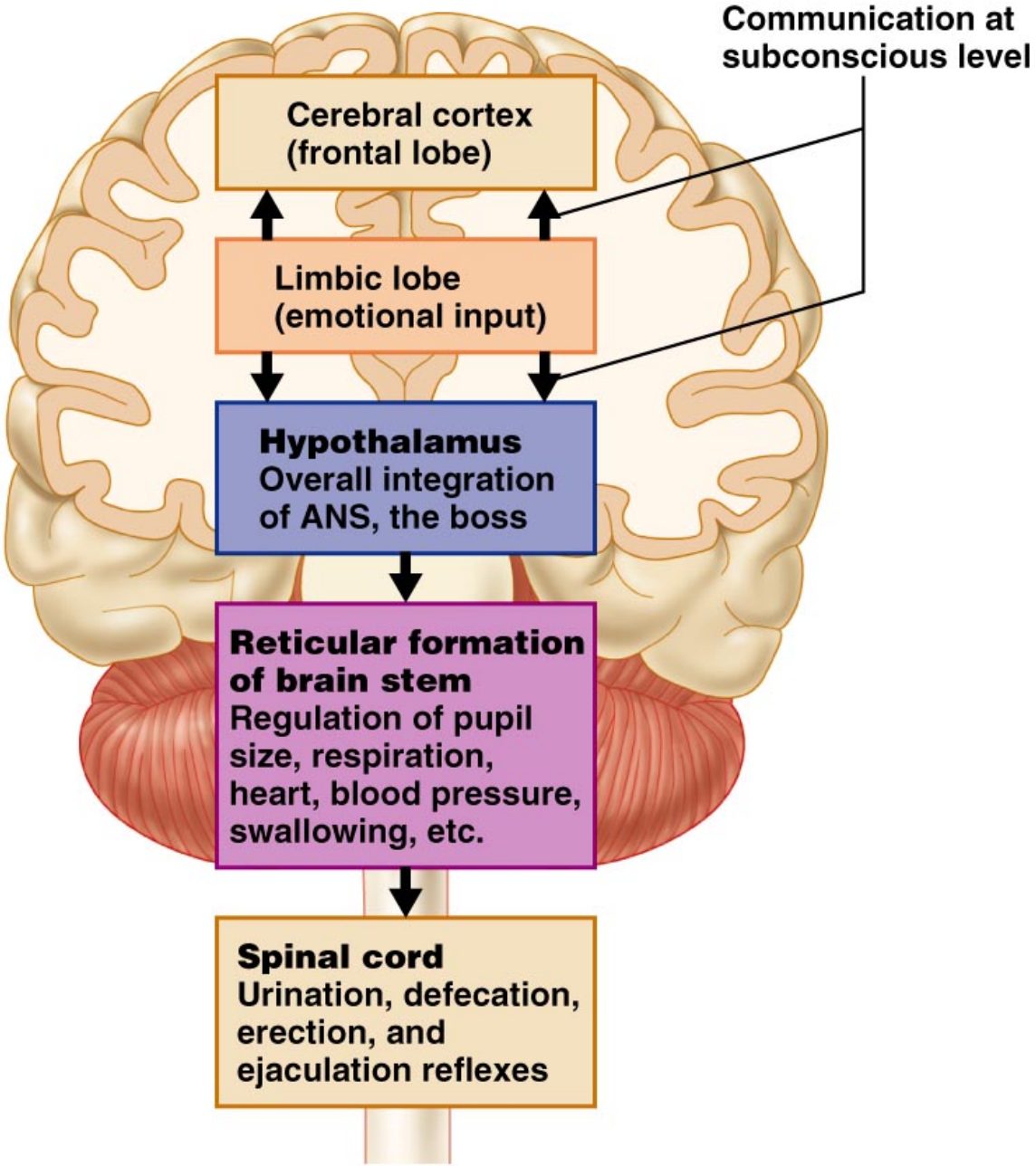
AUTONOMIC NERVOUS SYSTEM

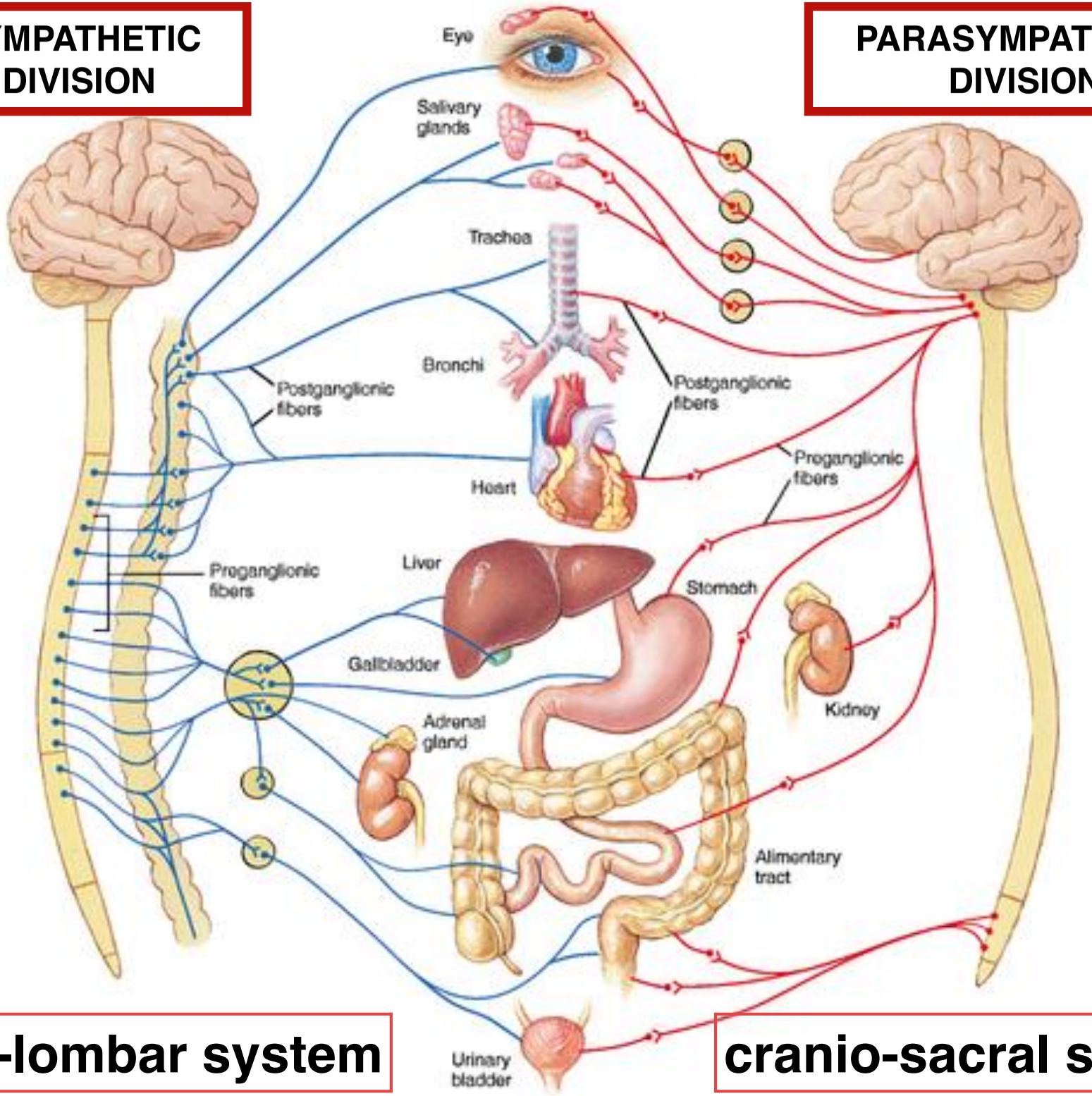


The Autonomic Nervous System (ANS) is under control of the Central Nervous System (CNS)



SYMPATHETIC DIVISION

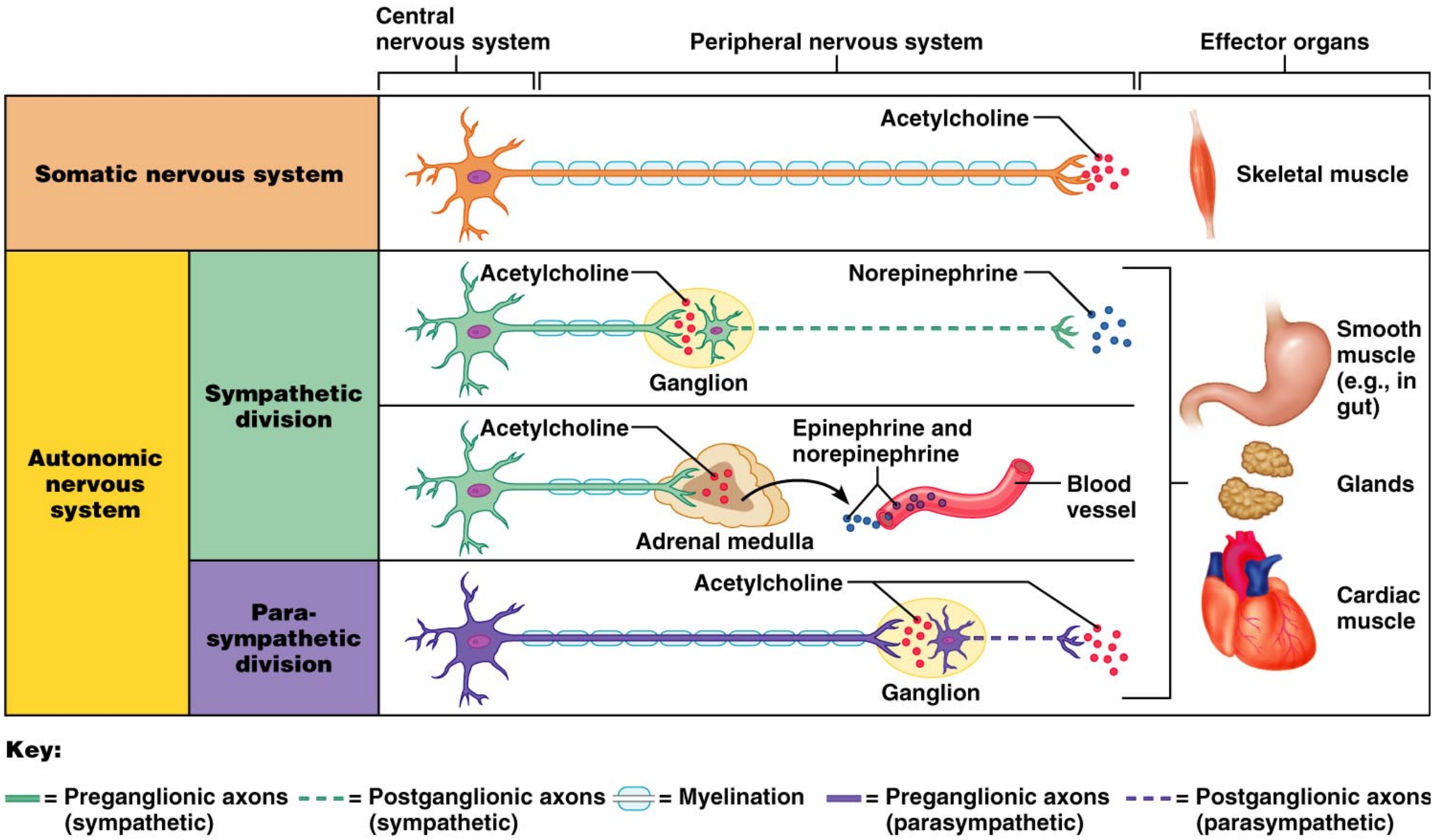
PARASYMPATHETIC DIVISION

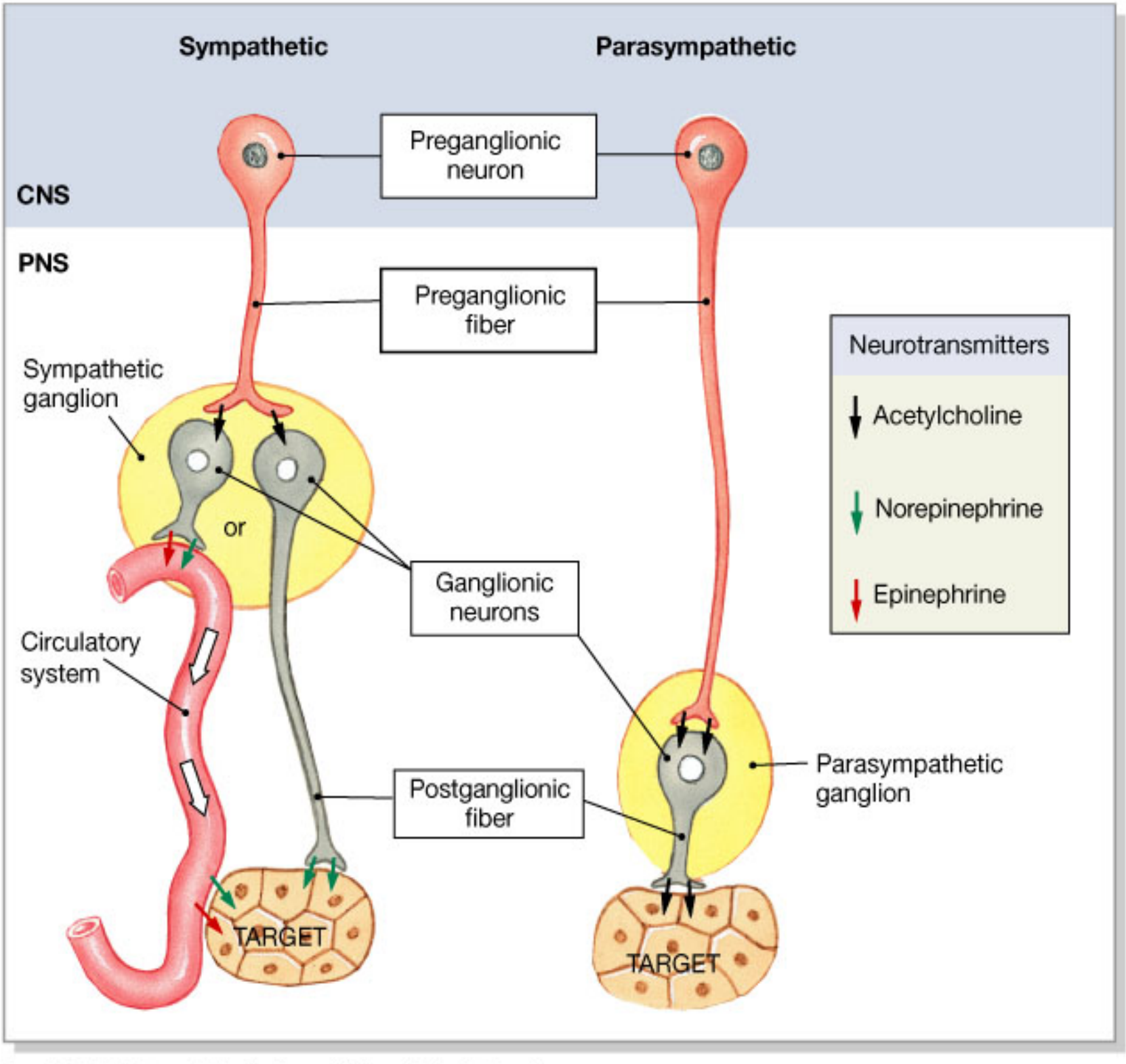


toraco-lombar system

cranio-sacral system

Autonomic Nervous System fibers



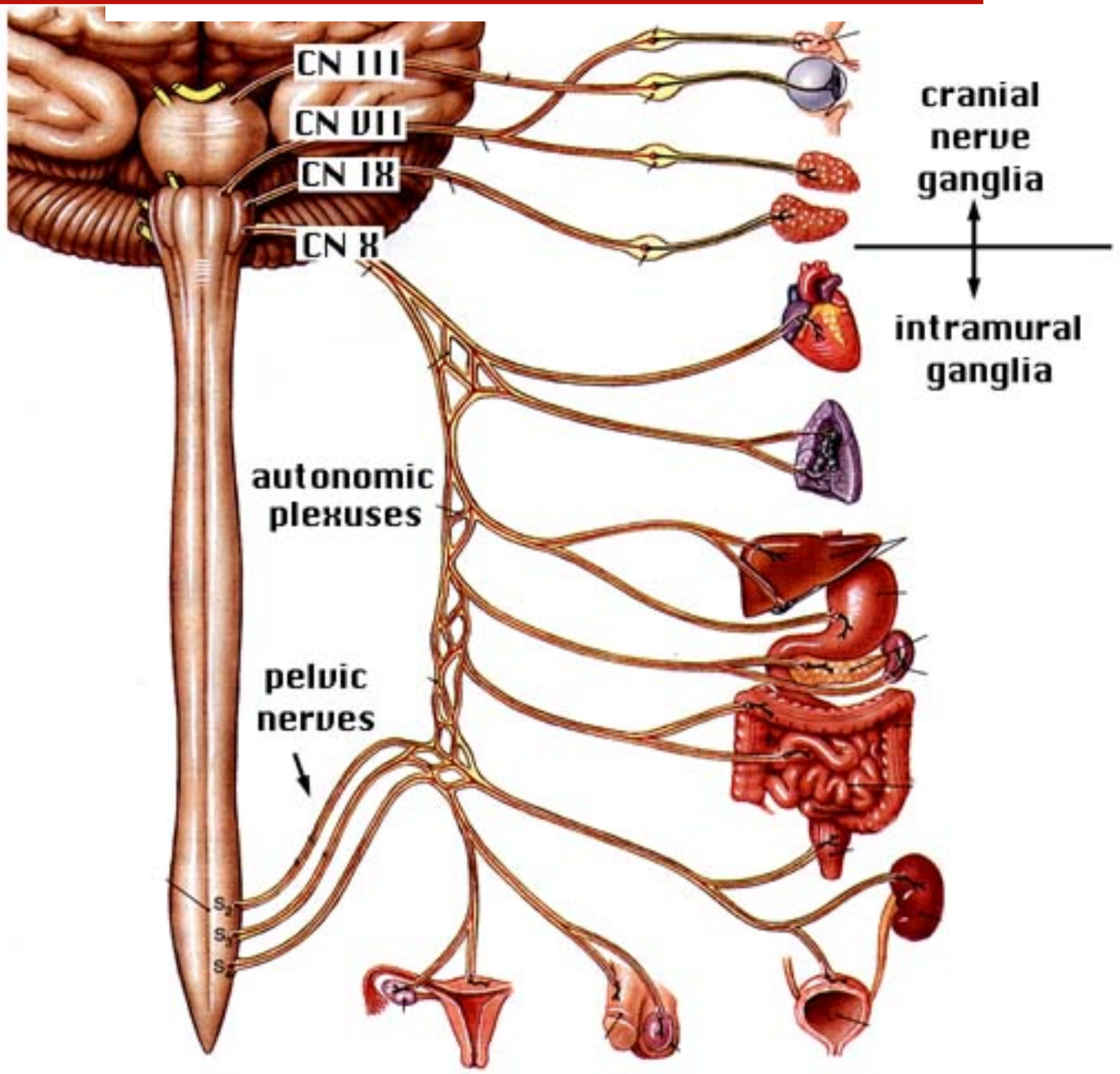

Sympathetic
Parasympathetic
CNS
PNS
Preganglionic neuron
Preganglionic fiber
Sympathetic ganglion
or
Ganglionic neurons
Circulatory system
Postganglionic fiber
Parasympathetic ganglion
TARGET
TARGET
Neurotransmitters
Acetylcholine
Norepinephrine
Epinephrine

PNS vs SNS

The parasympathetic nervous system (PNS) controls homeostasis of the body at rest and is responsible for the "rest and digest" function

The sympathetic nervous system (SNS) controls the body's responses to a perceived threat and is responsible for the "fight or flight" response

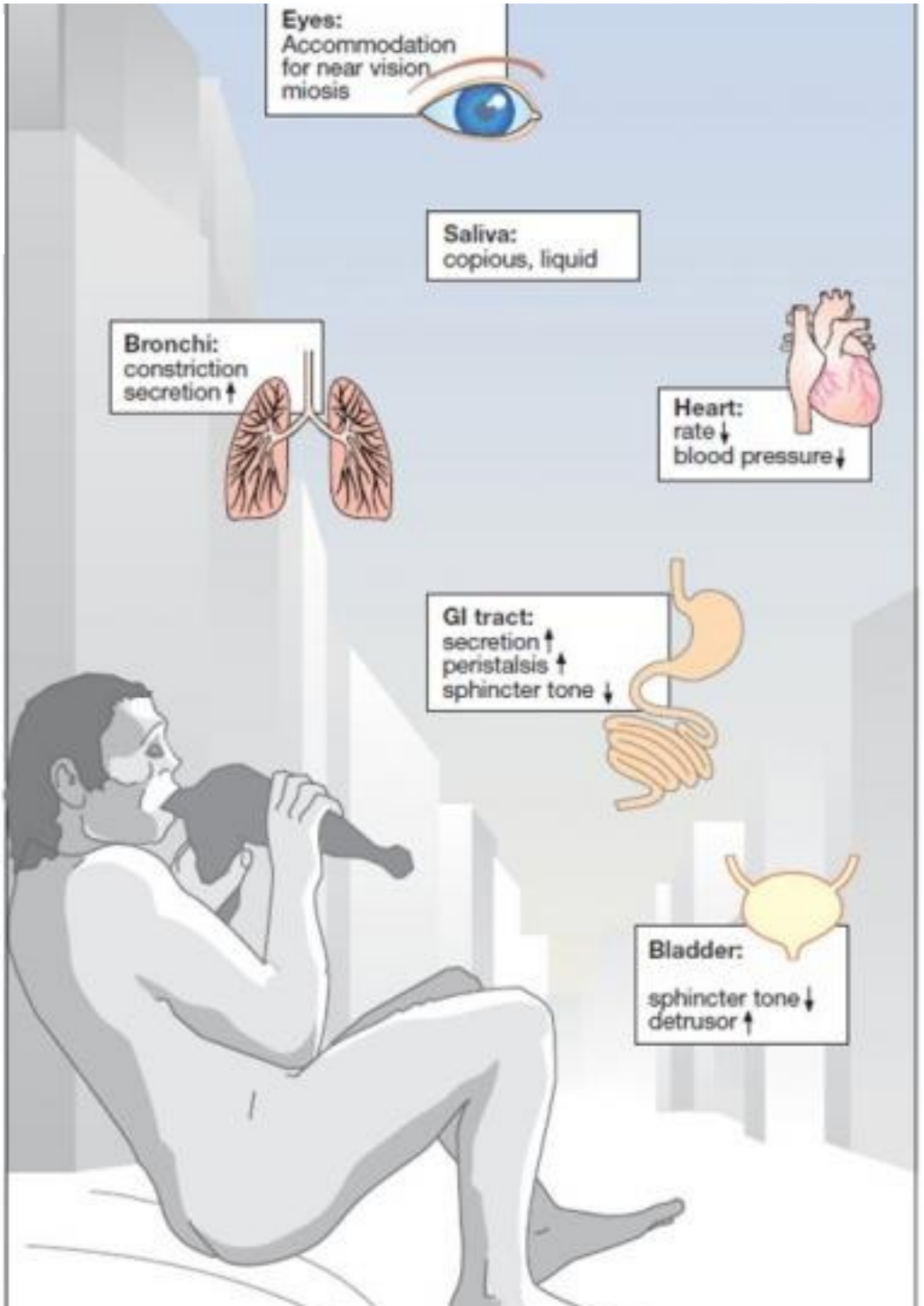
PARASYMPATHETIC DIVISION



"rest and digest" functions:

Eyes:
Accommodation for near vision
Miosis

Bronchi:
Constriction
Increased secretion



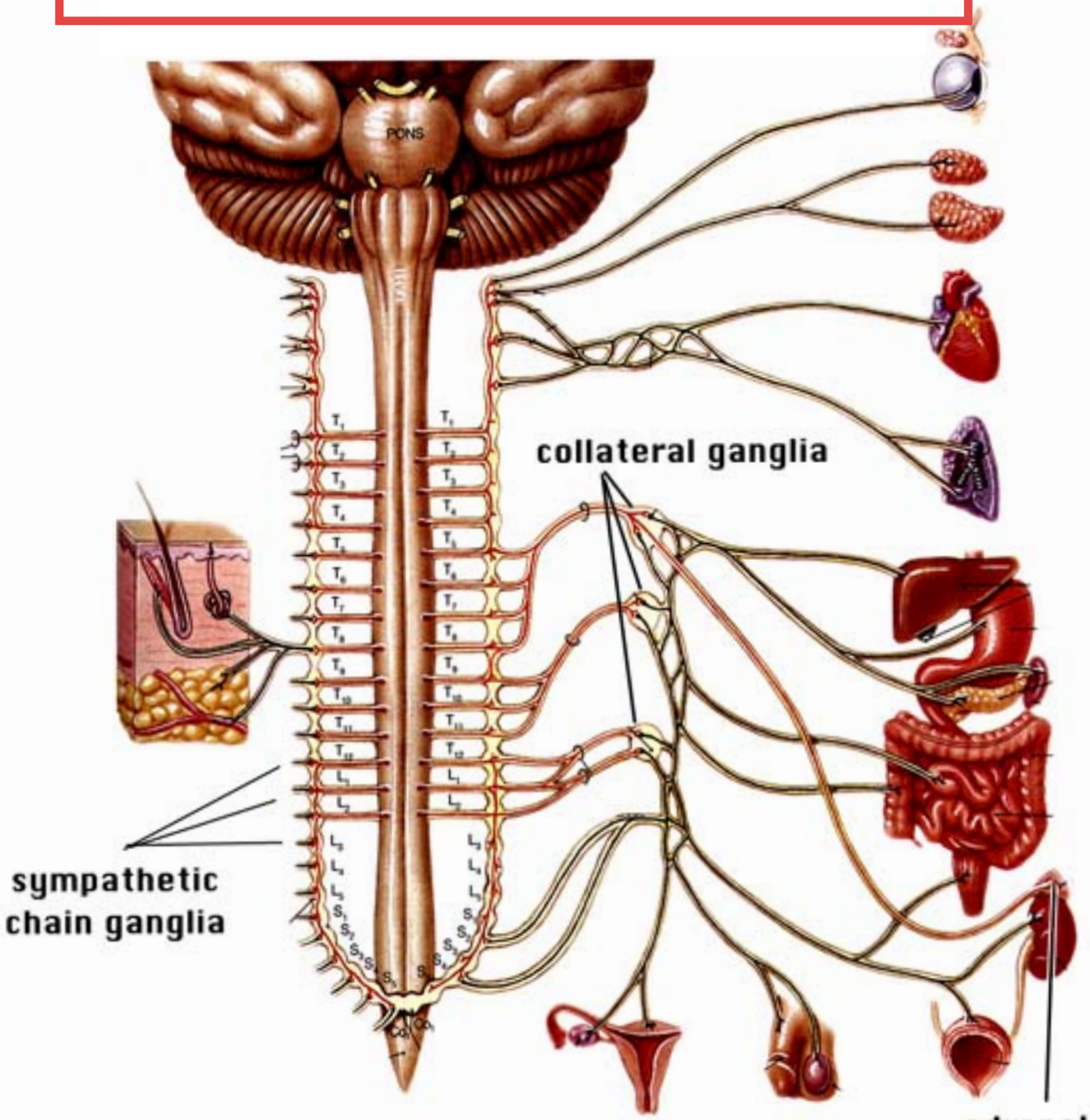
Saliva:
Copious, liquid

Heart:
Decreased rate
Decreased blood pressure

Gastro-intestinal tract:
Increased secretion
Increased peristalsis
Decreased sphincter tone

Bladder:
Increased detrusor tone
Decreased sphincter tone

SYMPATHETIC DIVISION



Modified from Fig. 17-5, Prentice Hall, Martini/Timmons 1997

SNC:
Increased drive and alertness

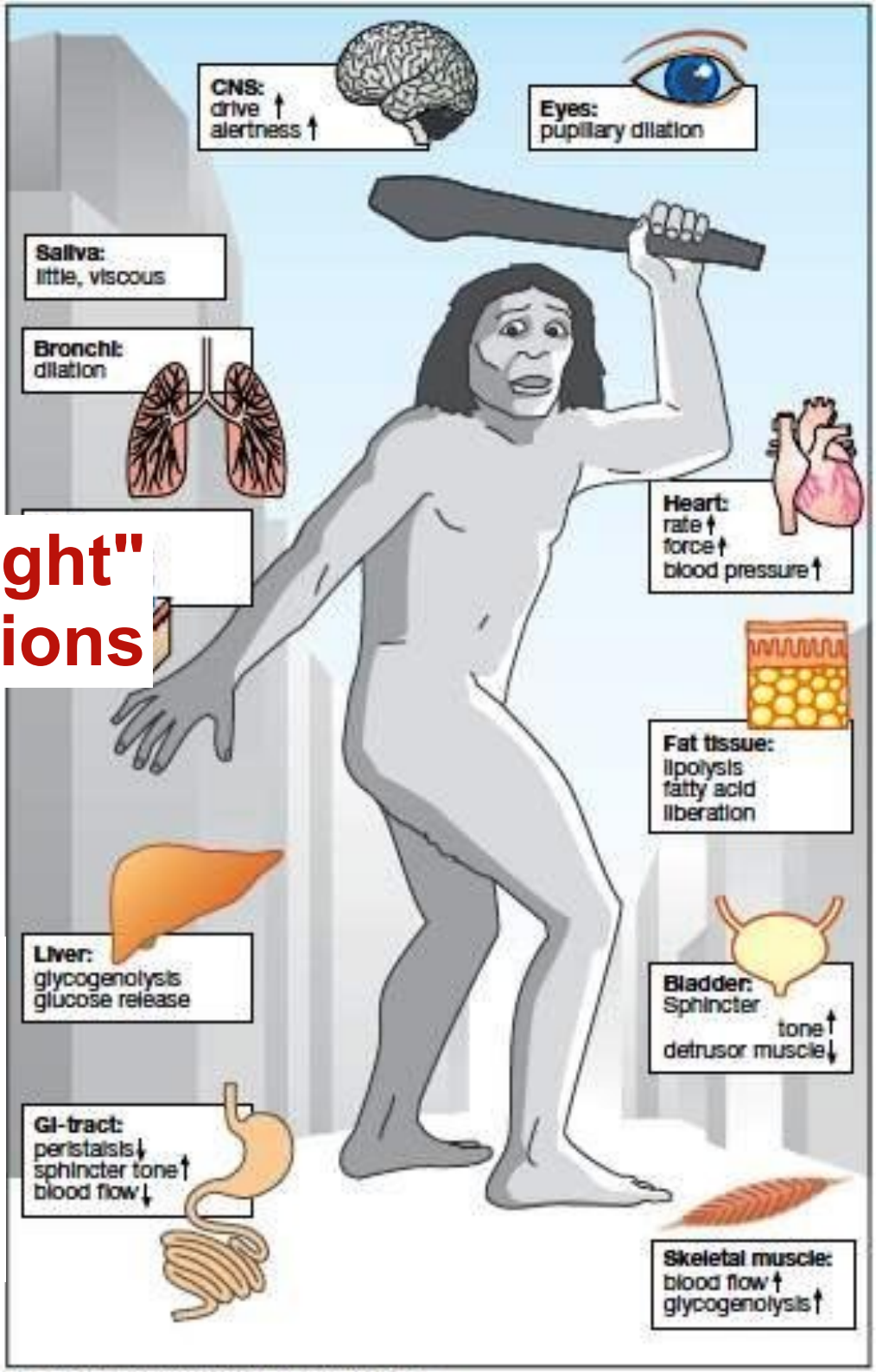
Saliva:
Little, viscous

Bronchi:
Dilatation

"Fight or flight" functions

Liver:
Glycogenolysis
Glucose release

Gastrointestinal tract:
Decreased peristalsis
Increased sphincter tone
Decreased blood flow



Eyes:
Pupillary dilation

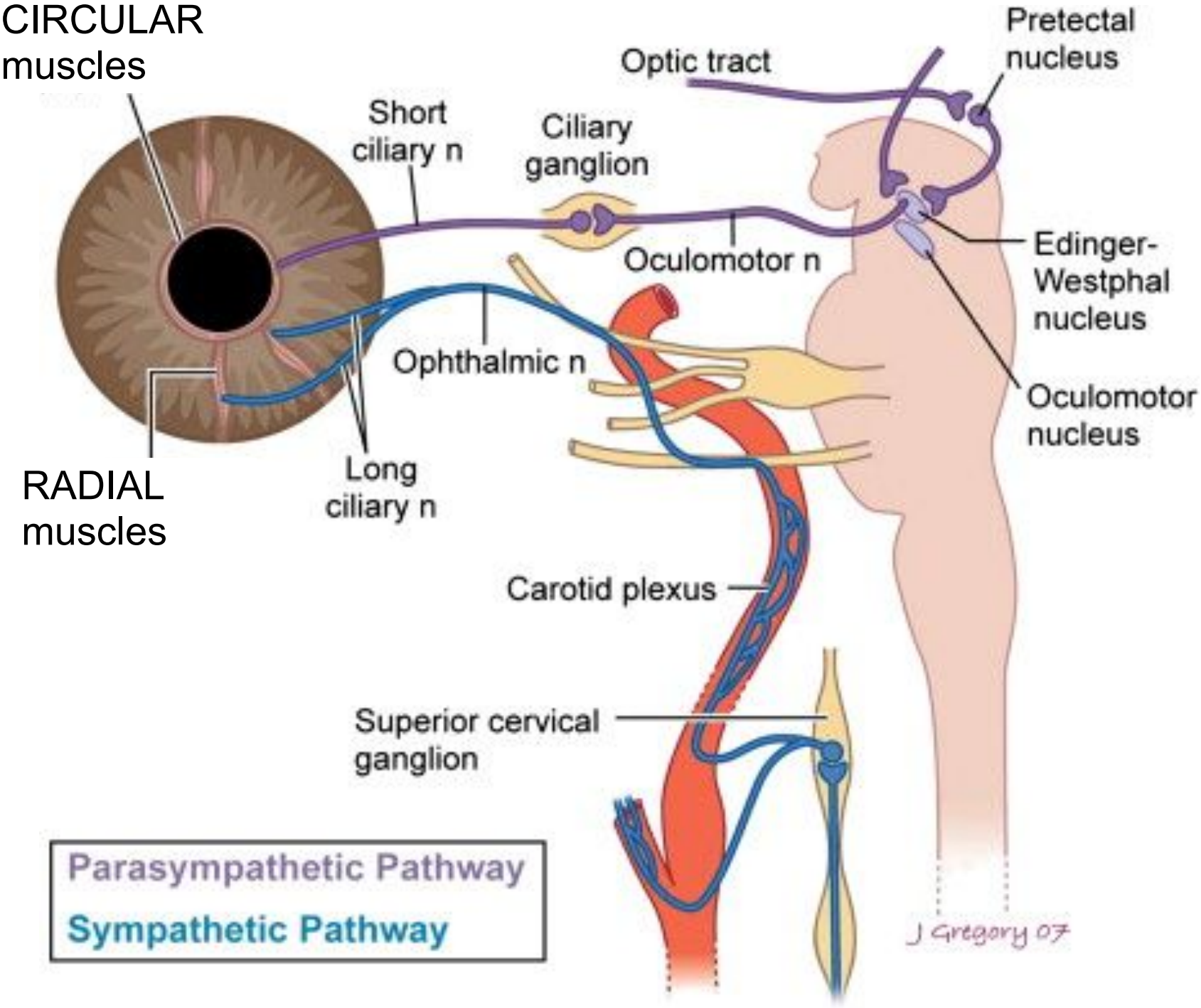
Heart:
Increased rate
Increased force
Increased blood pressure

Fat tissue:
Lipolysis
Fatty acids liberation

Bladder:
Decreased detrusor tone
Increased sphincter tone

Skeletal muscle:
Increased blood flow
Increased glycogenolysis

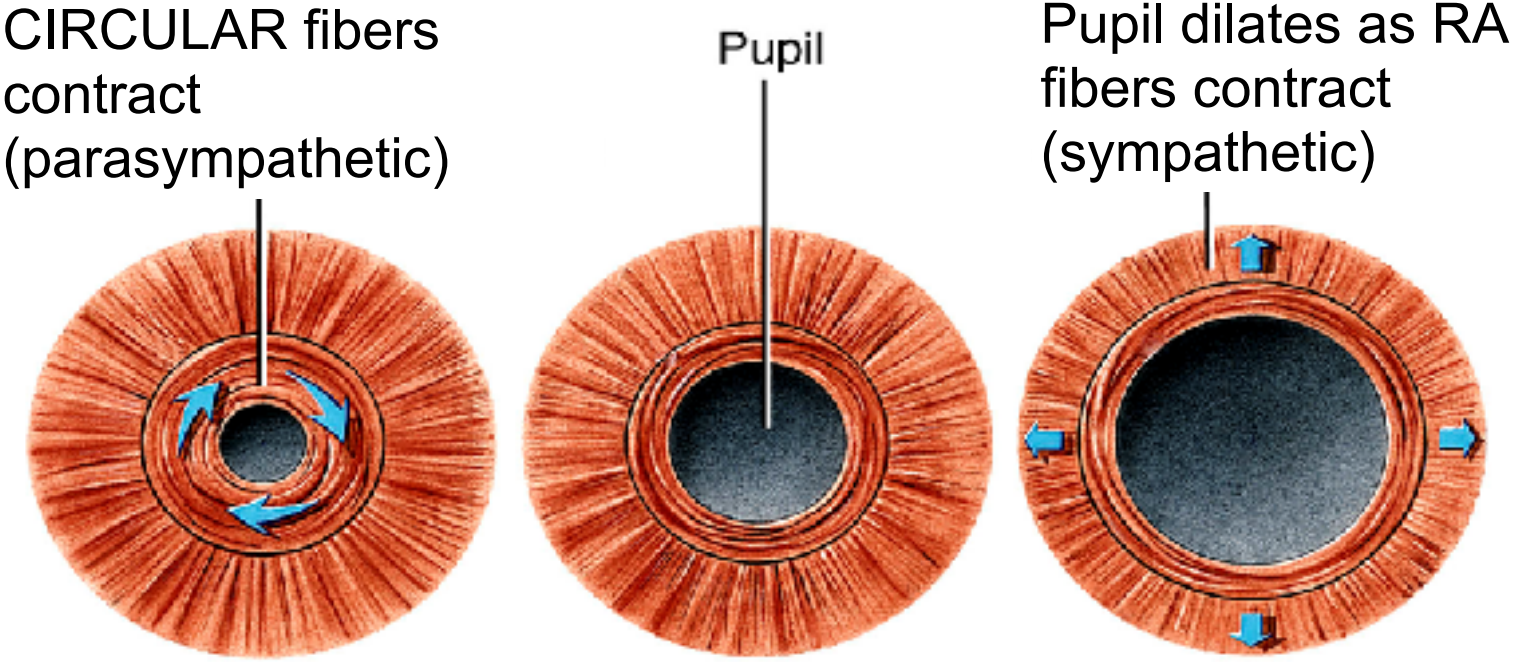
CIRCULAR muscles



RADIAL muscles

The circular and radial muscles control the size of the pupil

Pupil constricts as CIRCULAR fibers contract (parasympathetic)

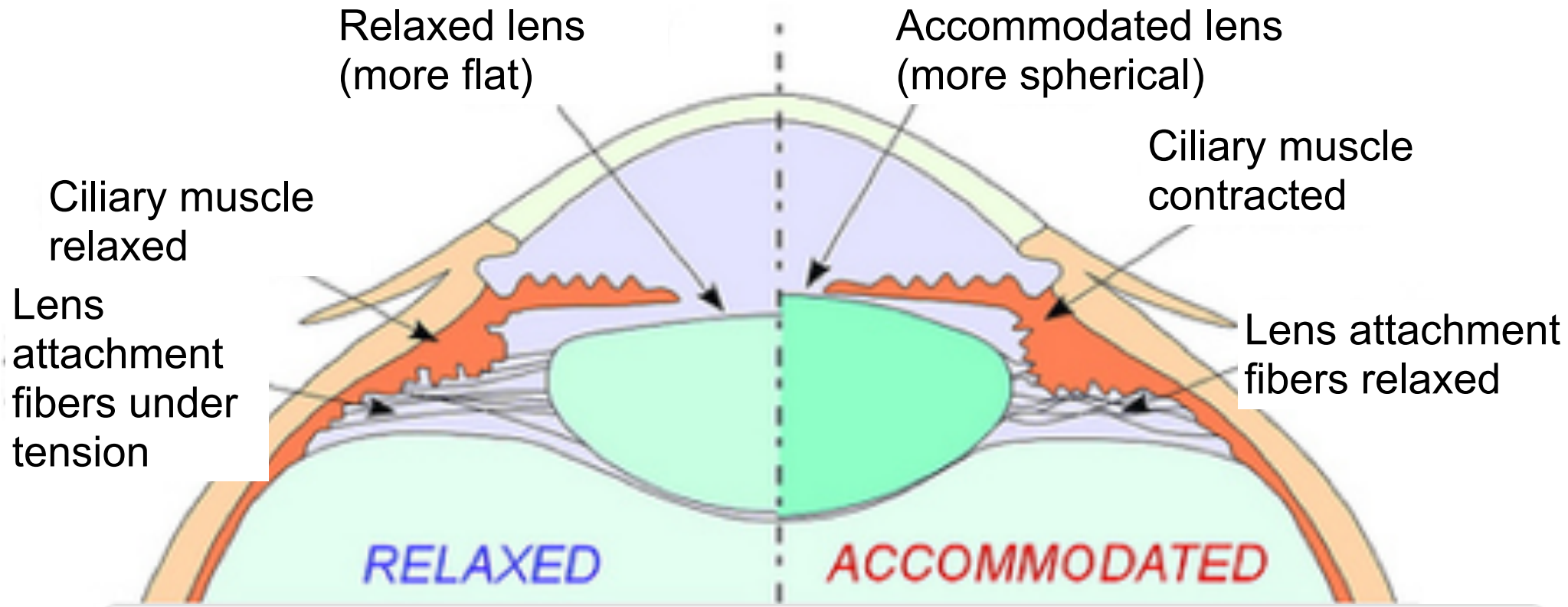


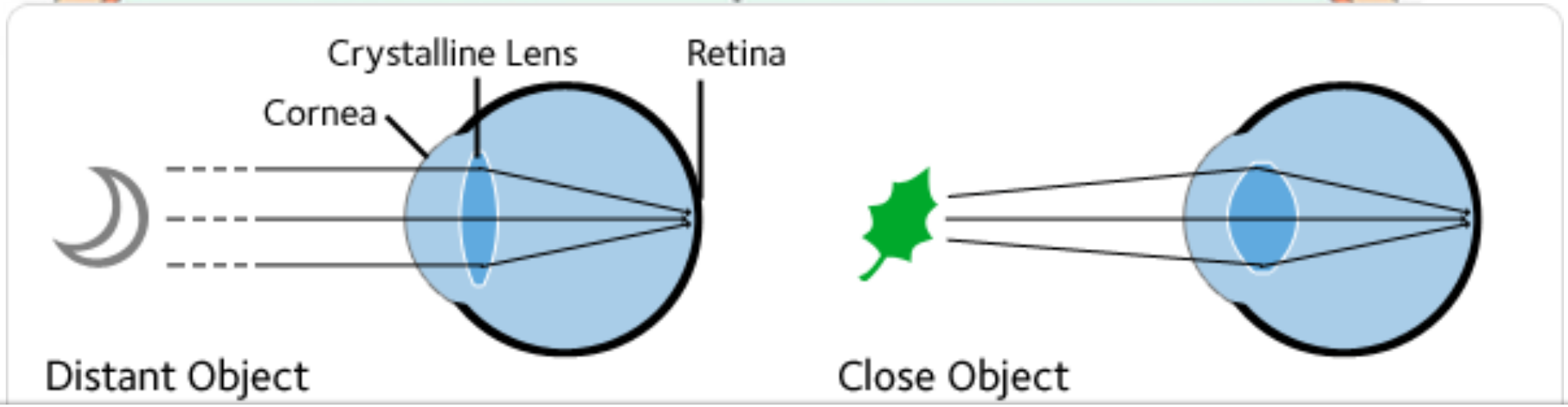
Pupil dilates as RADIAL fibers contract (sympathetic)

Miosis

Midriasis

The ciliary muscles control the shape of the lens



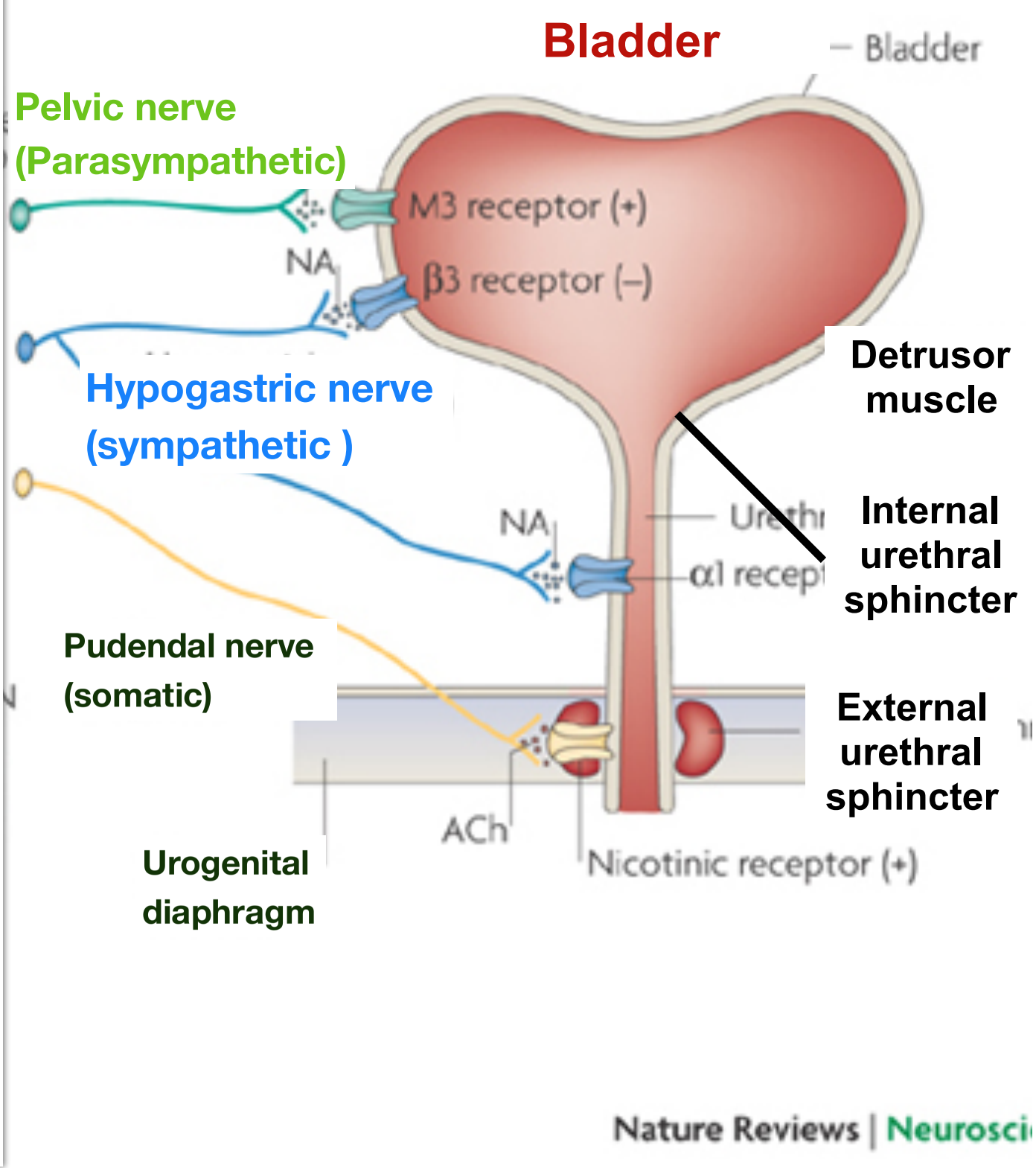


Sympathetic system

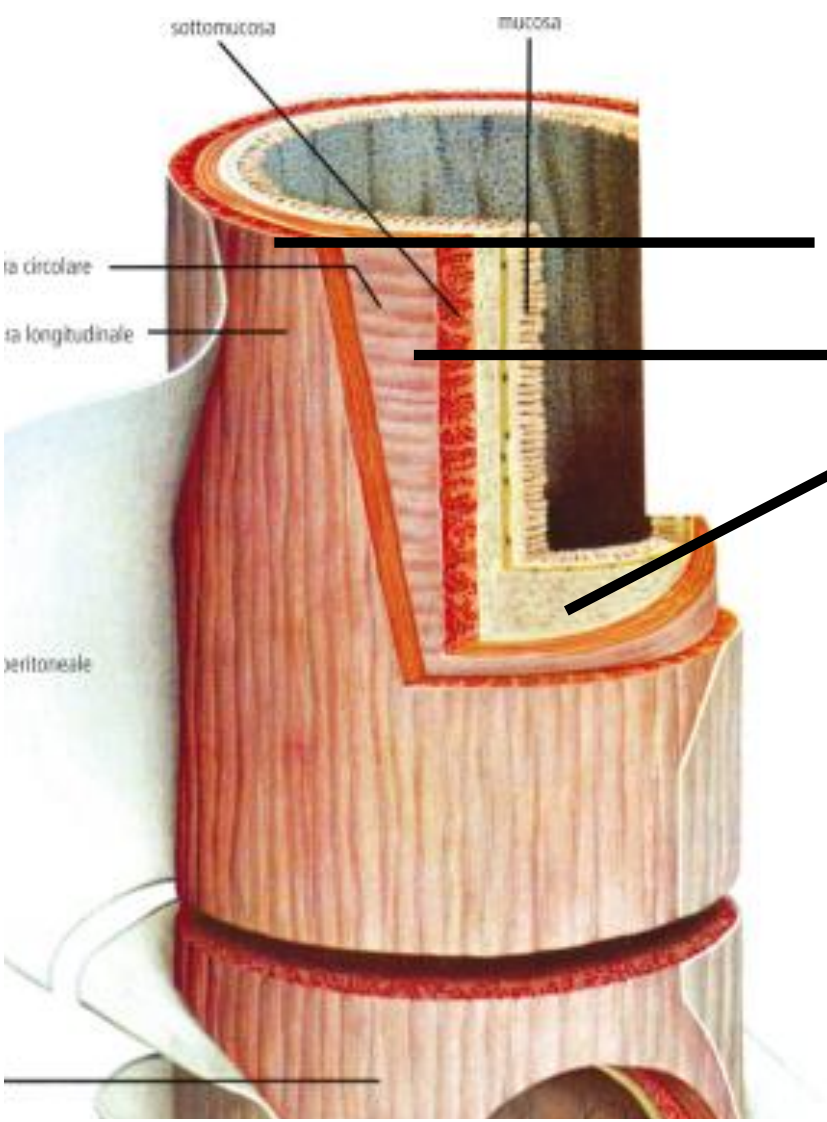
Parasympathetic system

Parasympathetic system:
Detrusor muscle contracts

Sympathetic system:
Detrusor muscle relax
Internal urethral sphincter contracts



Intestinal tract



Longitudinal muscle

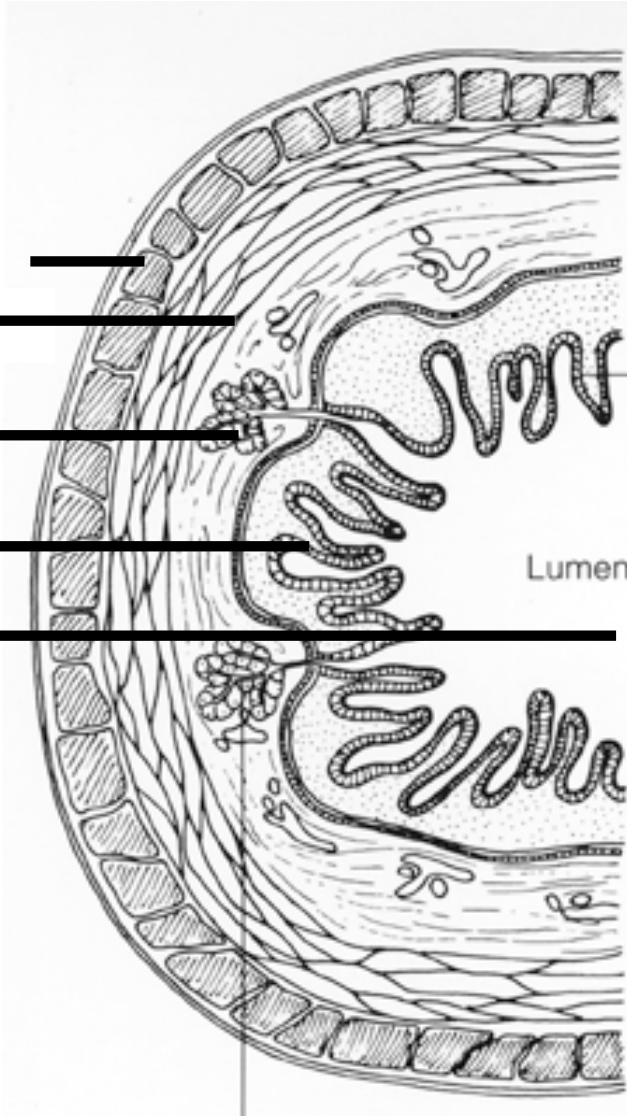
Circular muscle

Submucosa

Gland

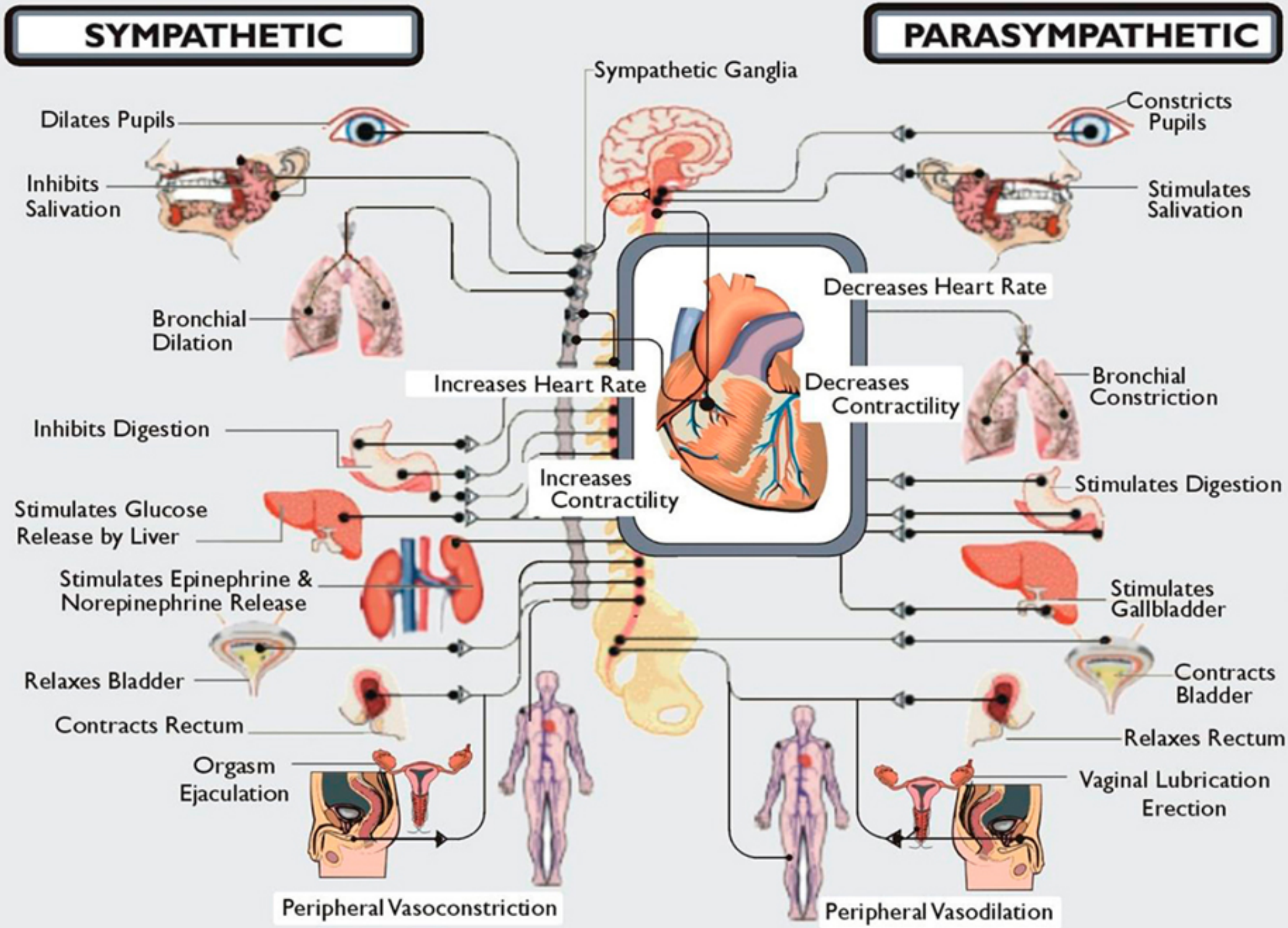
Epithelium

Lumen

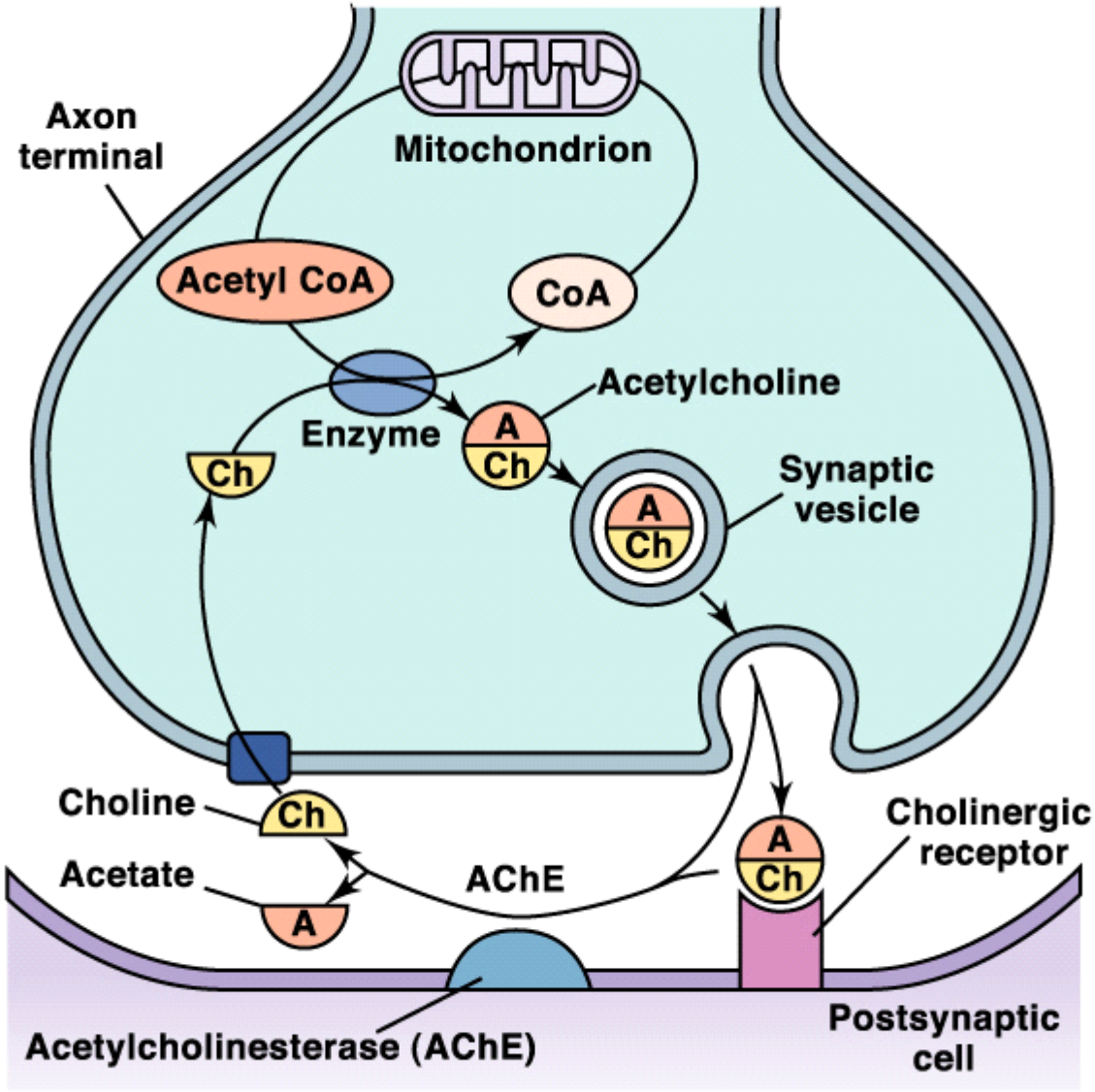


Sympathetic system:
Decreased peristalsis
Increased sphincter tone

Parasympathetic system:
Increased peristalsis
Decreased sphincter tone


SYMPATHETIC
PARASYMPATHETIC
Sympathetic Ganglia
Dilates Pupils
Inhibits Salivation
Bronchial Dilation
Increases Heart Rate
Inhibits Digestion
Stimulates Glucose Release by Liver
Stimulates Epinephrine & Norepinephrine Release
Relaxes Bladder
Contracts Rectum
Orgasm Ejaculation
Peripheral Vasoconstriction
Increases Contractility
Constricts Pupils
Stimulates Salivation
Decreases Heart Rate
Decreases Contractility
Bronchial Constriction
Stimulates Digestion
Stimulates Gallbladder
Contracts Bladder
Relaxes Rectum
Vaginal Lubrication Erection
Peripheral Vasodilation

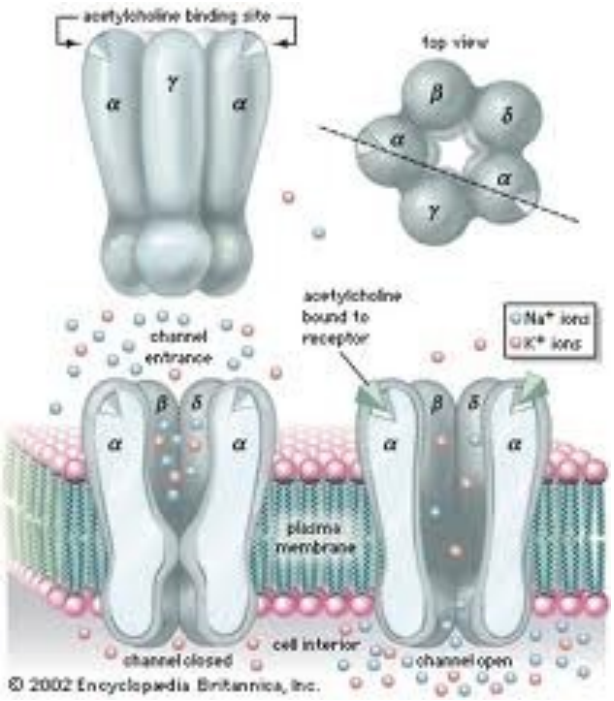
CHOLINERGIC TRANSMISSION
ACETYLCHOLINE SYNTHESIS AND DEGRADATION

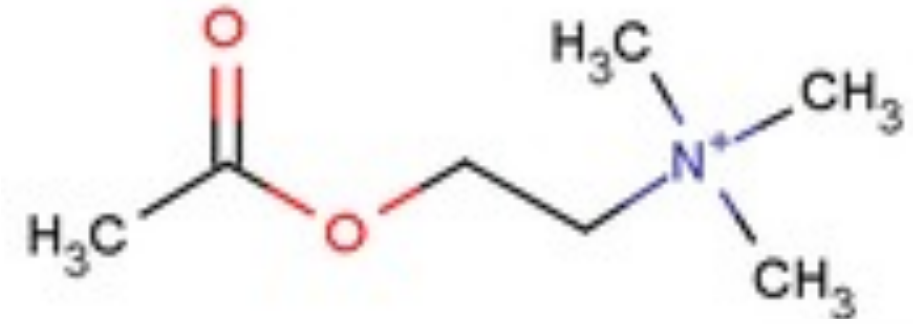


ACETYLCHOLINE RECEPTORS
(Dale, 1914)

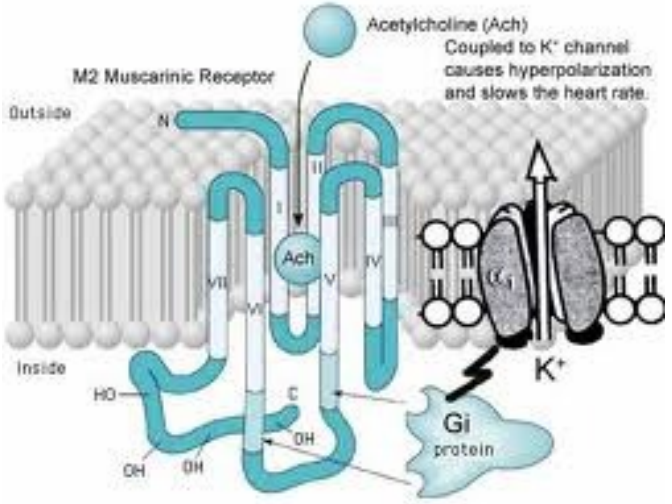
NICOTINIC
ionotropic

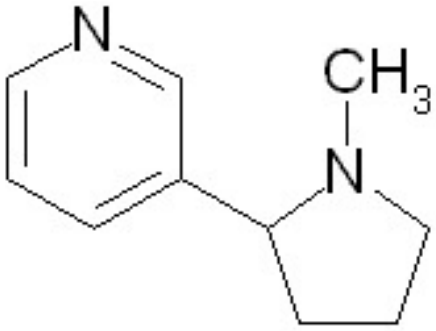
MUSCARINIC
metabotropic



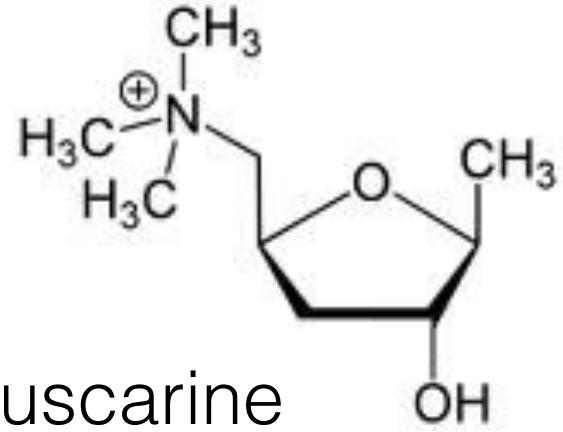


Acetylcholine





Nicotine



Muscarine

NICOTINIC RECEPTOR CLASSIFICATION

SUBTYPE	MAIN LOCALIZATION	MEMBRANE RESPONSE
Muscle type **(alpha1)2-beta1-delta-epsilon**	Skeletal neuromuscular junction (mainly post-synaptic)	Excitatory
Ganglion type **(alpha3)2-(beta2)3**	Autonomic ganglia (mainly post-synaptic)	Excitatory
CNS type **(alpha4)2-(beta2)3** **(alpha7)5**	Many brain regions: pre- and post-synaptic	Excitatory

NICOTINIC RECEPTOR CLASSIFICATION

SUBTYPE	AGONISTS	CLINICAL USE
Muscle type (alpha1)2-beta1-delta-epsilon	Acetylcholine Carbachol Succinylcholine Suxamethonium	None None Paralysis during anasthesia (short acting)
Ganglion type (alpha3)2-(beta2)3	Acetylcholine Carbachol Nicotine Epibatidine	None None Smoke cessation None
CNS type (alpha4)2-(beta2)3 (alpha7)5	Nicotine Epibatidine Acetylcholine Varenicline	None None None Smoke cessation

NICOTINIC RECEPTOR CLASSIFICATION

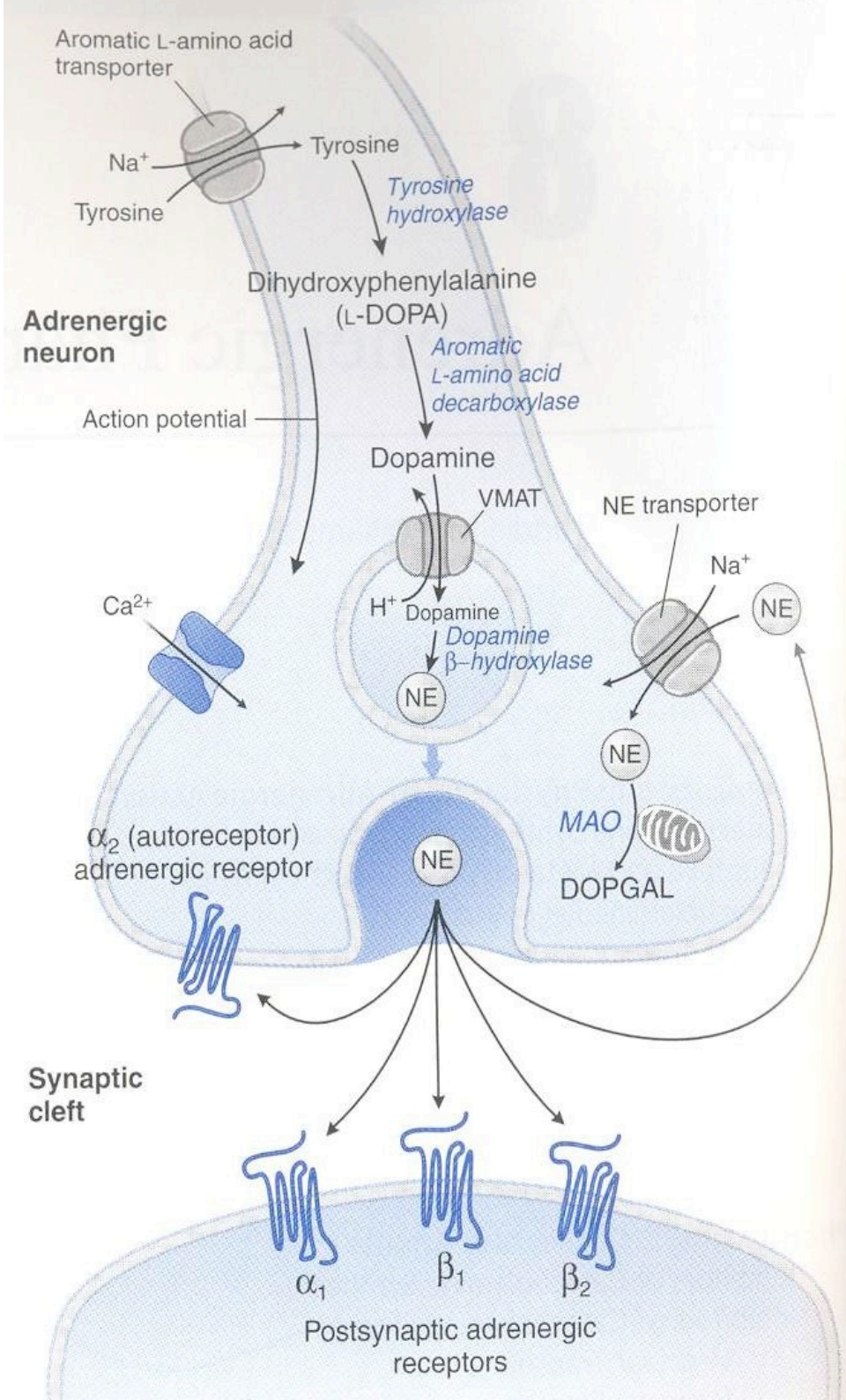
SUBTYPE	ANTAGONISTS	CLINICAL USE
Muscle type (alpha1)2-beta1-delta-epsilon	Tubocurarine Pancuronium Atracurium Vecuronium	Paralysis during anaesthesia
Ganglion type (alpha3)2-(beta2)3	Mecamylamine Trimetaphan Hexamethonium	Obsolete anti-hypertensive drug
CNS type (alpha4)2-(beta2)3 (alpha7)5	Mecamylamine Methylaconitine Alpha-bungarotoxin Alpha-conotoxin	Crosses the BBB (antagonizes nicotine CNS effects) None

MUSCARINIC RECEPTOR CLASSIFICATION		
SUBTYPE	**MAIN LOCATION**	**FUNCTIONAL RESPONSE**
M1 ("neural)	Cerebral cortex Autonomic ganglia	CNS excitation Gastric secretion
M2 ("cardiac")	Heart: atria CNS	Cardiac inhibition (bradicardia) Neural inhibition
M3 ("Glandular - Smooth muscle")	Exocrine glands: gastric, salivary, etc Smooth muscle: GI tract, eye, airways, bladder Blood vessel (endothelium)	Gastric, salivary secretion Contraction, ocular accomodation Vasodilatation (NO-mediated)
M4	CNS	Enhanced locomotion
M5	CNS (very localized expression)	Not known

MUSCARINIC RECEPTOR CLASSIFICATION		
SUBTYPE	**AGONISTS**	**CLINICAL USE**
M1 ("neural)	NON-SELECTIVE: Acetylcholine Carbachol Pilocarpine Bethanechol	- - Glaucoma Treatment of bladder and gastrointestinal hypotonia
M2 ("cardiac")	Not known	
M3 ("Glandular - Smooth muscle")	SELECTIVE: Cevimeline	Sjögren'syndrome (to increase salivary and lacrimal secretion)
M4	Not known	Not known
M5	Not known	Not known

MUSCARINIC RECEPTOR CLASSIFICATION		
SUBTYPE	**ANTAGONISTS**	**CLINICAL USE**
M1 ("neural)	NON-SELECTIVE: Atropine Oxibutynin Ipatropium SELECTIVE: Pirenzepine	Ophthalmic (midriasis and paralisis of accomodation) Prevention of motion sickness COPD and Asthma Anaesthetic premedication Inhibition of gastric secretion
M2 ("cardiac")	Gallamine	
M3 ("Glandular - Smooth	SELECTIVE Darifenacin	Urinary incontinence
M4	Not known	
M5	Not known	

ADRENERGIC TRANSMISSION NORADRENALINE SYNTHESIS AND DEGRADATION



ADRENERGIC RECEPTOR CLASSIFICATION

The main pharmacological classification into alfa (α) and beta (β) was originally based on order of potency of agonists:

alfa (α): Epinephrine = NE > dopamine > isoproterenol
beta (β): Isoproterenol > Epineprine > NE > dopamine

Epinephrine and Norepinephrine show relatively little receptor **selectivity**

	α_1	α_2	β_1	β_2	DA
Norepinephrine	+++	+++	+	-	-
Epinephrine	+++	++	+++	++	-
Dopamine	++	+	++	+++	+++
Dobutamine	+	-	+++	+	-
Isoproterenol	-	-	++	++	-

ADRENERGIC RECEPTOR CLASSIFICATION

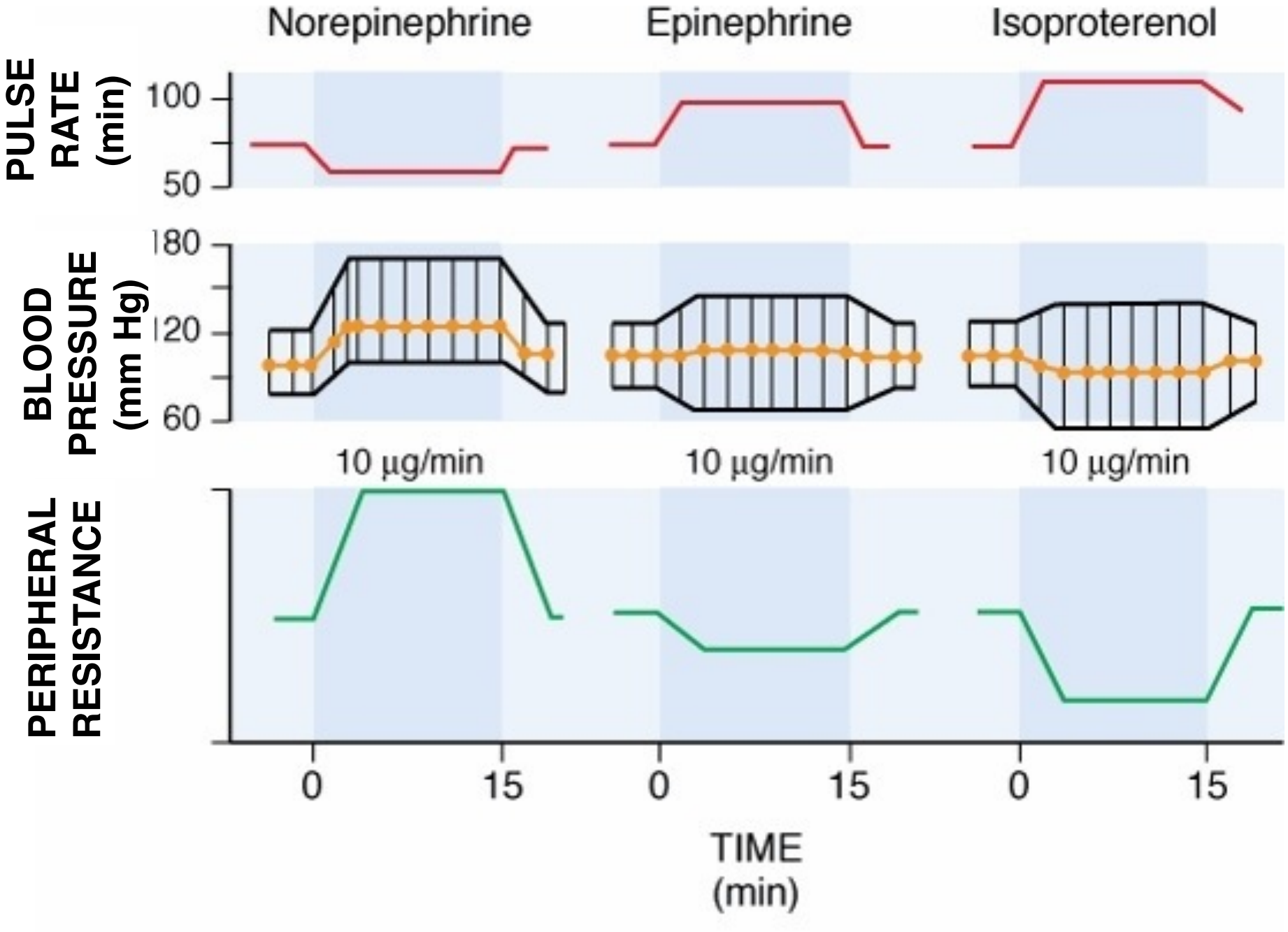
SUBTYPE	MAIN LOCATION	FUNCTIONAL RESPONSE
Alpha 1	**Blood vessels**	Contraction
	GI tract	Relaxation
	GI sphincters	Contraction
	Bladder sphincter	Contraction
	Iris	Contraction (midriasis)
Alpha 2	**Presynaptic brain stem** **Presynaptic nerve terminals**	Inhibition of sympathetic outflow Decreased release of neurotransmitters

ADRENERGIC RECEPTOR		
SUBTYPE	**AGONISTS**	**CLINICAL USES**
Alpha 1	Phenylephrine Methoxamine	Nasal decongestion
Alpha 2	Clonidine	Hypertension
	ANTAGONISTS	**CLINICAL USES**
Alpha 1	Prazosin Doxazocin Tamsulosin	Hypertension Benign prostatic hypertophy
Alpha 2	Yohimbine	No clinical use

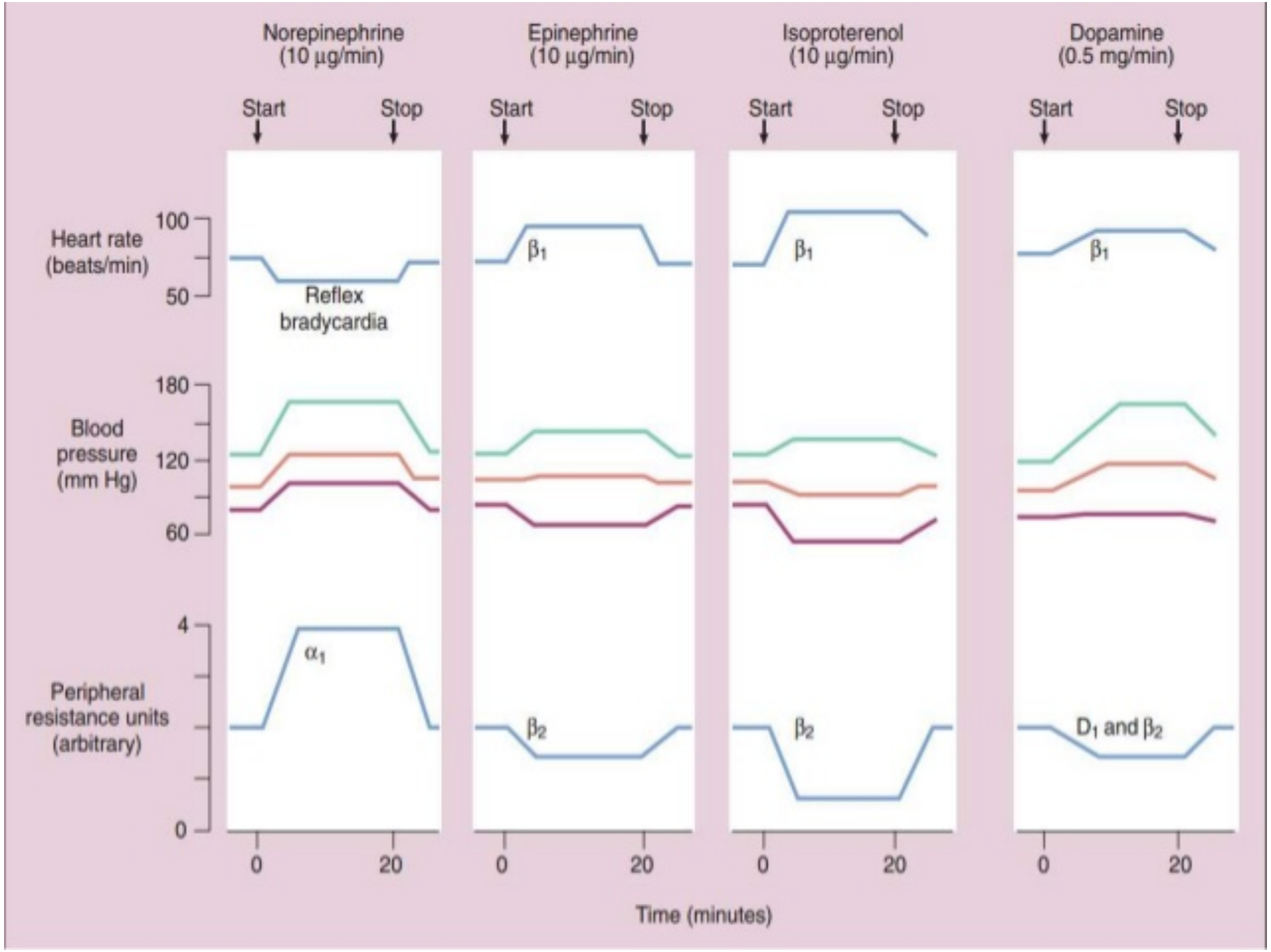
ADRENERGIC RECEPTOR CLASSIFICATION		
SUBTYPE	**MAIN LOCATION**	**FUNCTIONAL RESPONSE**
Beta 1	**Heart**	Increase rate and force of contraction
	Kidney (iuxtaglomerular apparatus)	Renine release
Beta 2	**Smooth muscle:** bronchi, blood vessel	Dilate
	ciliary, GI tract, bladder detrusor	Relax
	Skeletal muscle	Increase mass, tremor
	Liver	Glycogenolysis
Beta 3	Fat tissue	Lipolysis, thermogenesis

ADRENERGIC RECEPTOR		
SUBTYPE	**AGONISTS**	**CLINICAL USES**
Beta 1	Dobutamine	Cardiogenic shock
Beta 2	Salbutamol Terbutaline Formoterol	Asthma
Beta 3	Mirabegron	Symptoms of overactive bladder

ADRENERGIC RECEPTOR		
SUBTYPE	**ANTAGONISTS**	**CLINICAL USES**
Beta 1	Propranolol Alprenolol Metoprolol Nevibolol	Angina pectoris Hypertension Cardiac dysrhytmias (Anxiety, tremor)
Beta 2	Butoxamine	None
Beta 3		

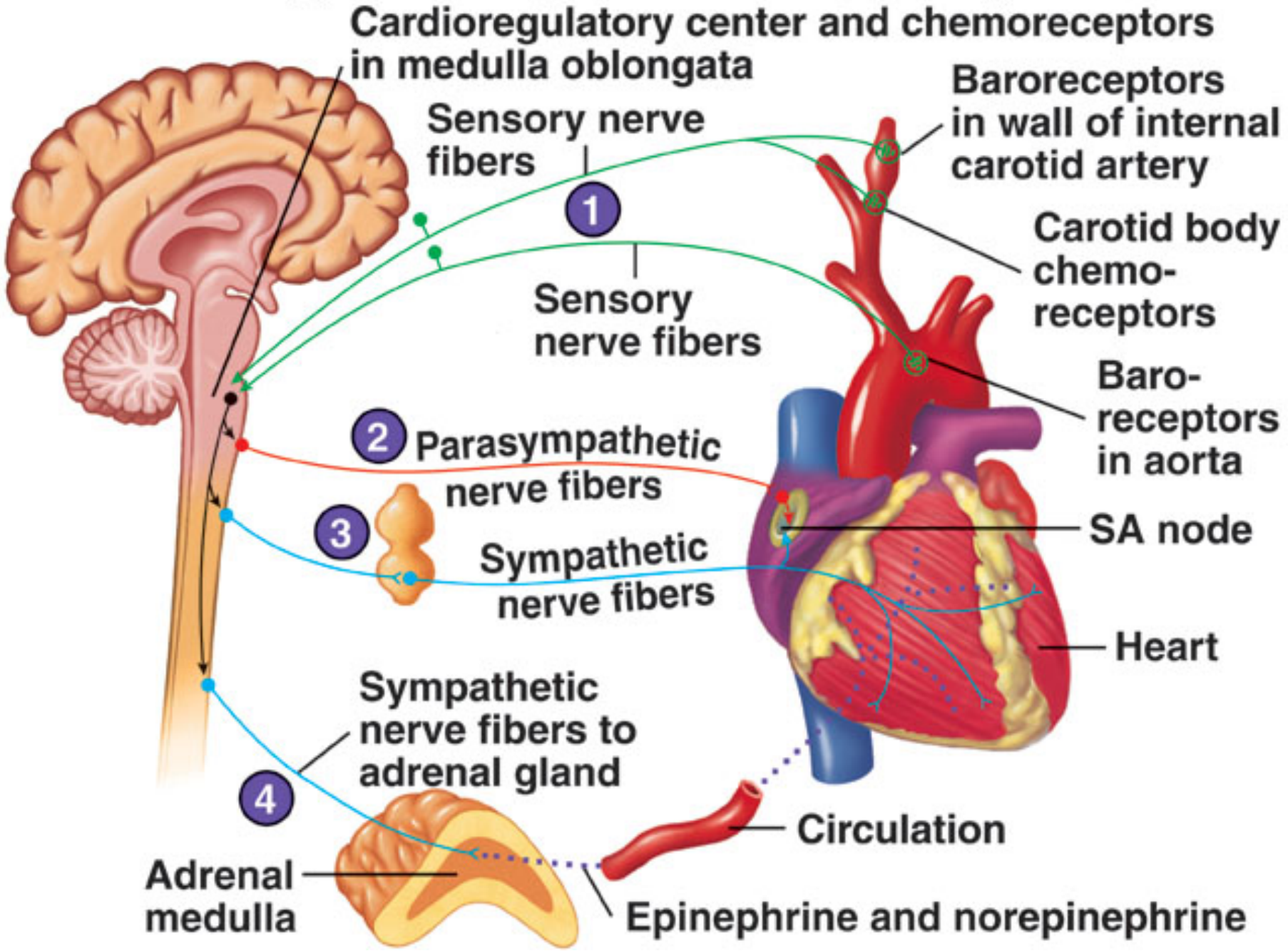


Effect of intravenous infusion of Norepinephrine, Epinephrine or Isoproterenol in human beings

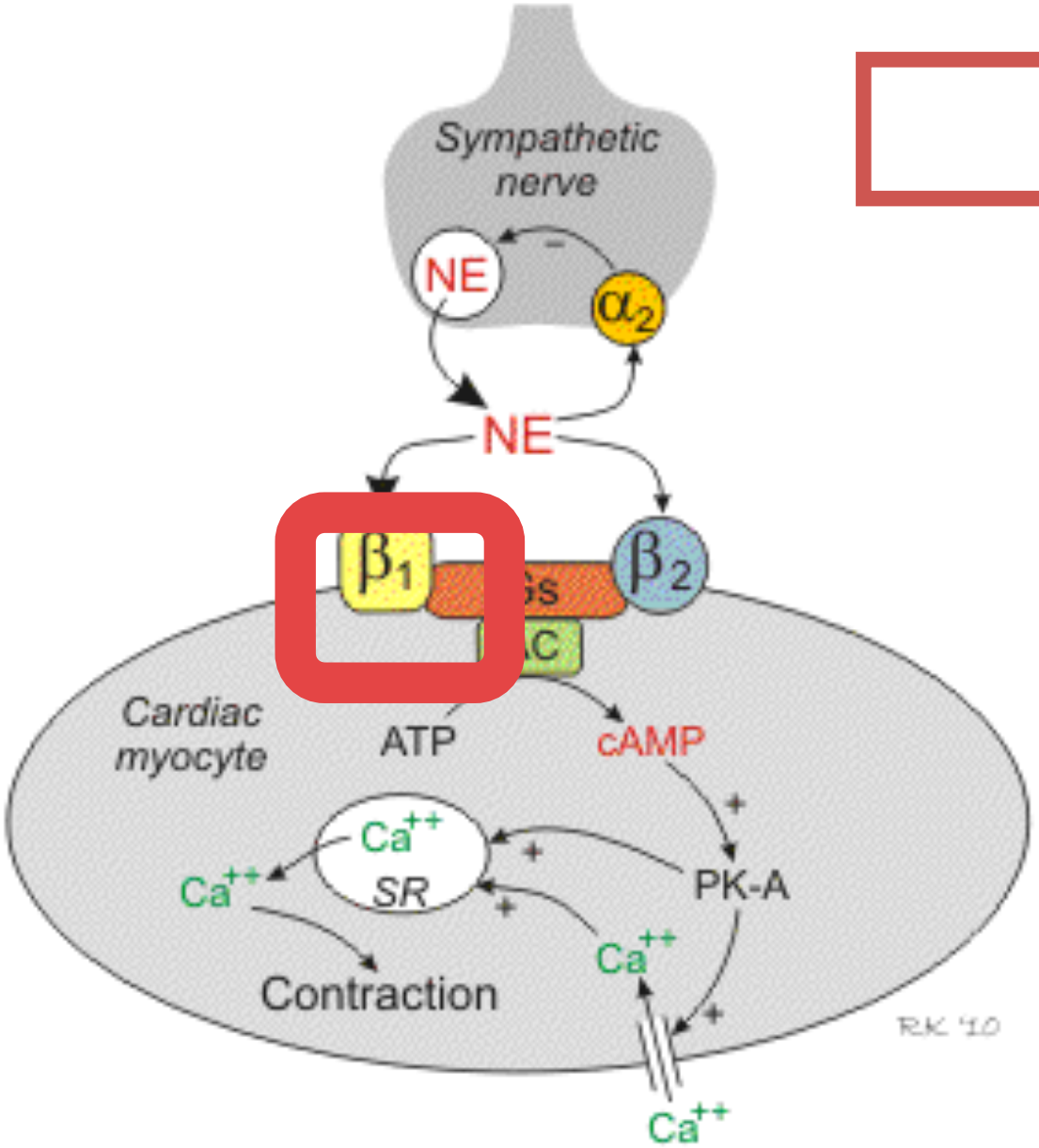


Effect of intravenous infusion of Norepinephrine, Epinephrine or Isoproterenol in human beings

BAROCEPTOR, CHEMOCEPTOR AND CARDIOVASCULAR REGULATION



HEART

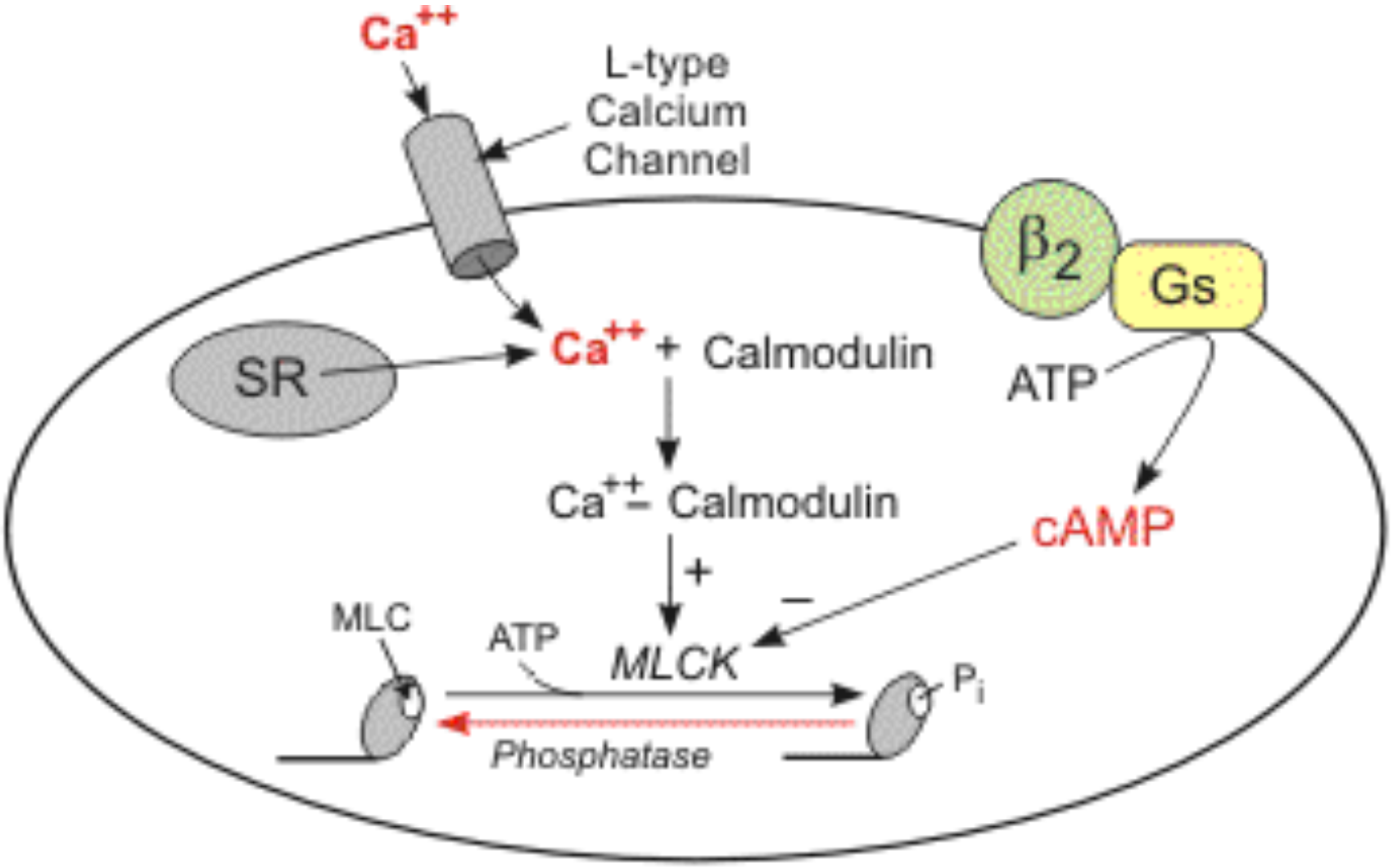


PHOSPHORYLATION OF L-TYPE CALCIUM CHANNELS

INCREASE OF CICR (CALCIUM INDUCED CALCIUM RELEASE)

----> POSITIVE INOTROPIC

VASAL SMOOTH MUSCLE



INHIBITION OF MLCK (MYOSIN LIGHT CHAIN KINASE) -----> VASODILATATION