

Autonomic Nervous System

Introduction

The nervous system is divided into:

1- the central nervous system (CNS; the brain and spinal cord)

2- the peripheral nervous system (PNS; neuronal tissues outside the CNS).

The motor (efferent) portion of the nervous system can be divided into two major subdivisions:

autonomic and somatic.

The **autonomic nervous system (ANS)** is largely independent (autonomous) in that its activities are not under direct conscious control.

Autonomic nervous system has 3 subdivisions-

2. Sympathetic nervous system
3. Parasympathetic nervous system
4. Enteric nervous system

Enteric nervous system

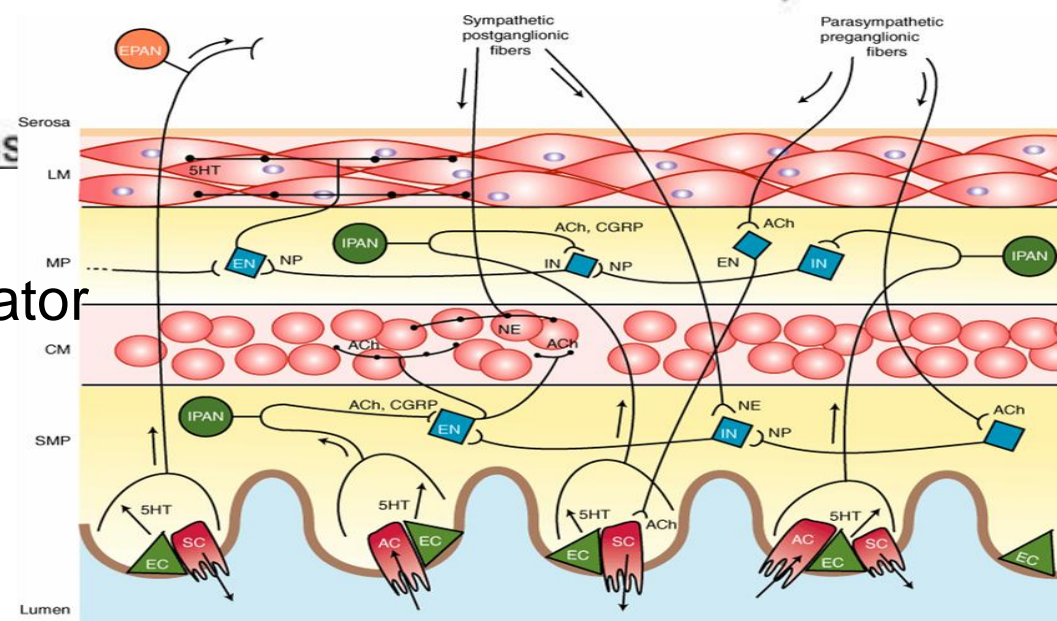
Enteric neurons form plexuses that surround and extend along the length of the gut, including stomach, small and large intestines.

Enteric system activate coordinated contraction of smooth muscles to cause peristaltic constriction of the gut.

Most of enteric nervous system functions independently of higher CNS control.

Many transmitter or neuromodulator substances have been identified in the ENS.

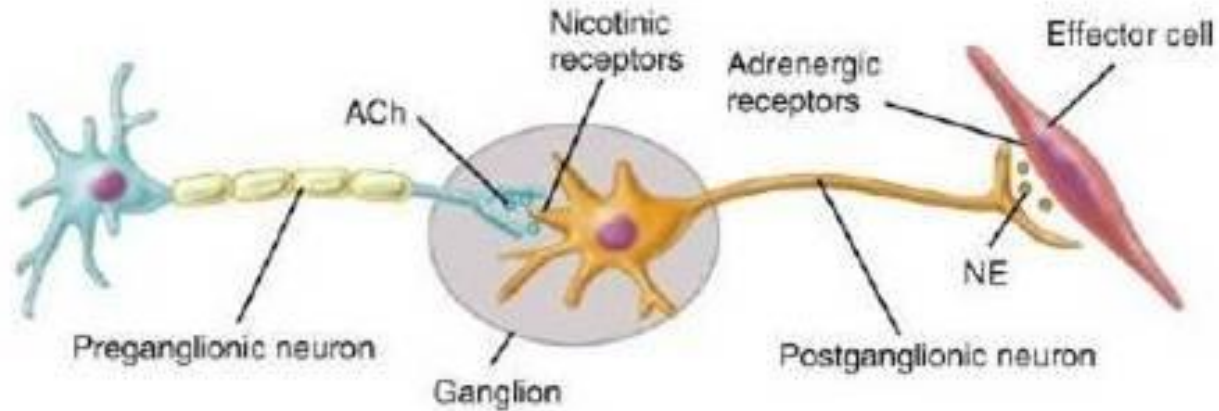
It is modulated by the symp. & parasymp systems.



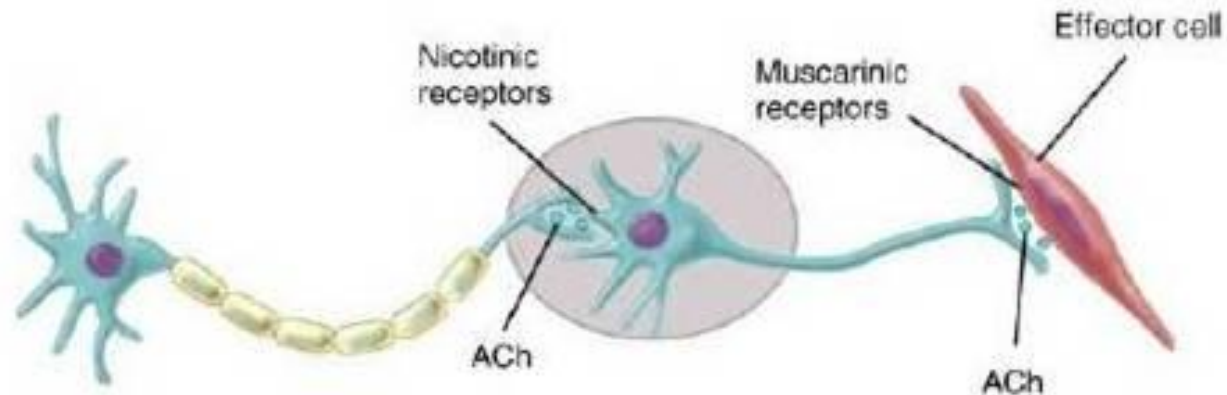
ANS Neurons

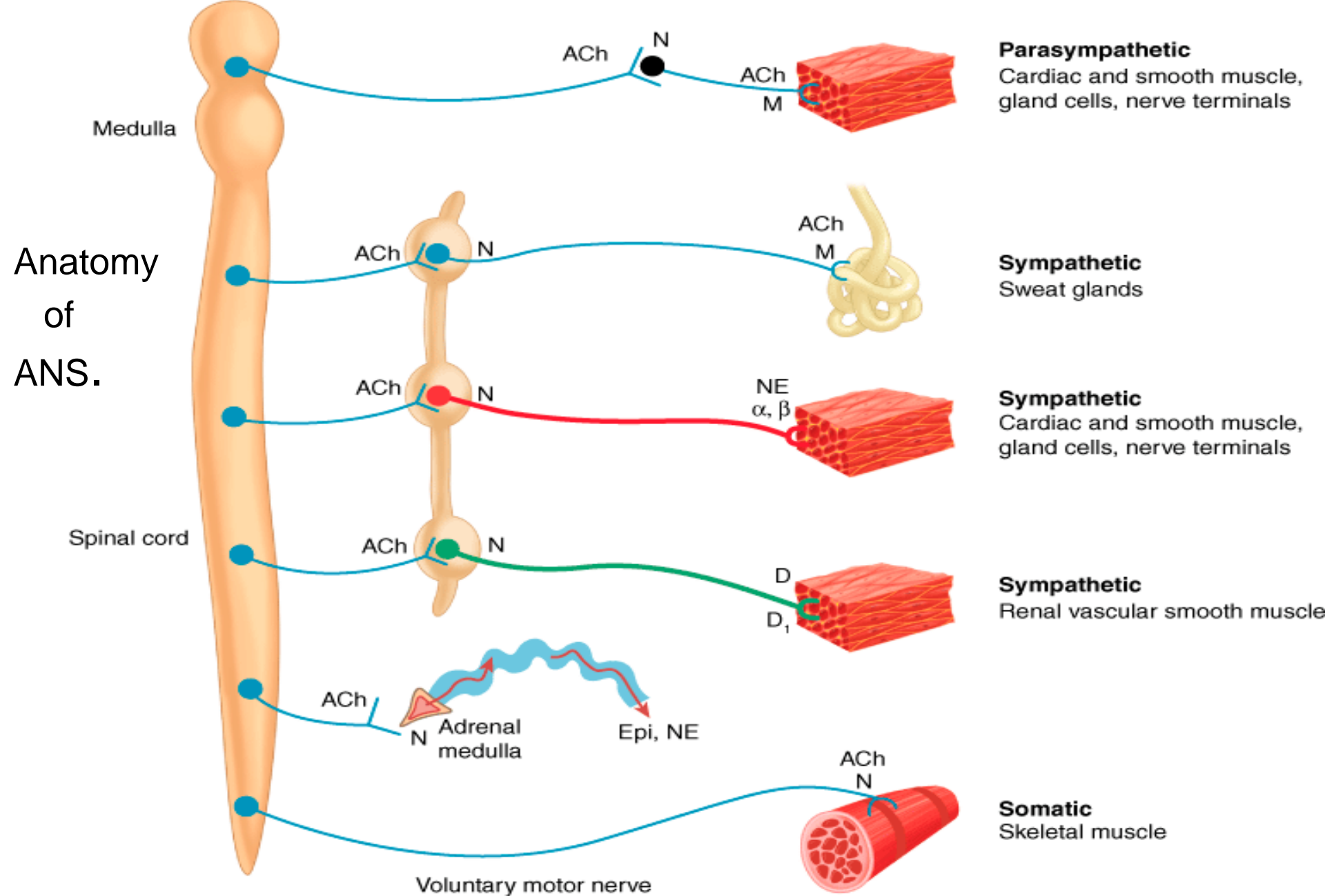
- Classified as either cholinergic or adrenergic neurons based upon the neurotransmitter released

- Adrenergic



- Cholinergic





Parasympathetic cell bodies in brainstem and sacral spinal cord: *craniosacral outflow*.

Parasympathetic Division: Because postganglionic neurons are short (parasymp. ganglia are located near effectors), stimulation involves only one visceral effector (organ)

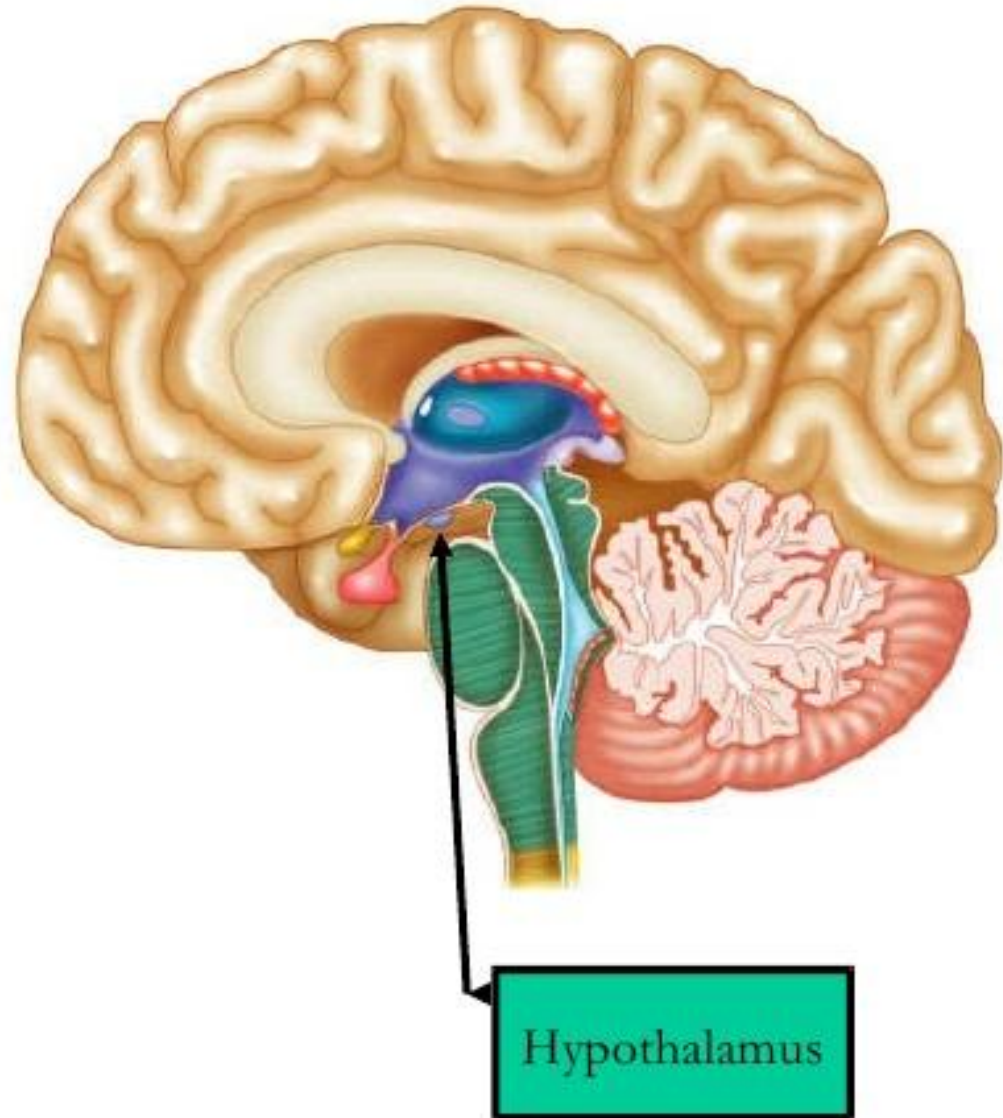
Sympathetic cell bodies located T1-L2 levels: *thoracolumbar outflow*.

One sympathetic preganglionic neuron may have many branches and may synapse with 20+ postganglionic neurons.

Projection of divergence explains why sympathetic responses can affect many effectors at once

Physiological Effects of the ANS

- Some organs have only sympathetic innervation
 - sweat glands, adrenal medulla, arrector pili mm & many blood vessels
 - controlled by regulation of the “tone” of the sympathetic system
- Most body organs receive dual innervation
 - innervation by both sympathetic & parasympathetic
- **Hypothalamus** regulates balance (tone) between sympathetic and parasympathetic activity levels



– Parasympathetic

- S(alivation) L(acrimation) U(rination) D(efecation)
- metabolic “business as usual”
- rest and digest - basic survival functions

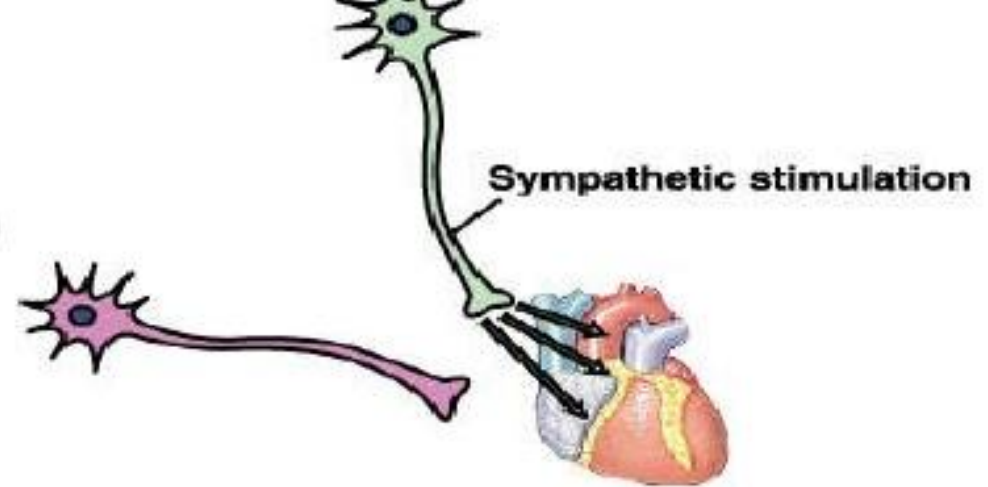
– Sympathetic

- fight or flight = “survival”
- any increase in skeletal muscular activity
 - for these activities - increase heart rate, blood flow, breathing
 - decrease non-survival activities - food digestion, etc.

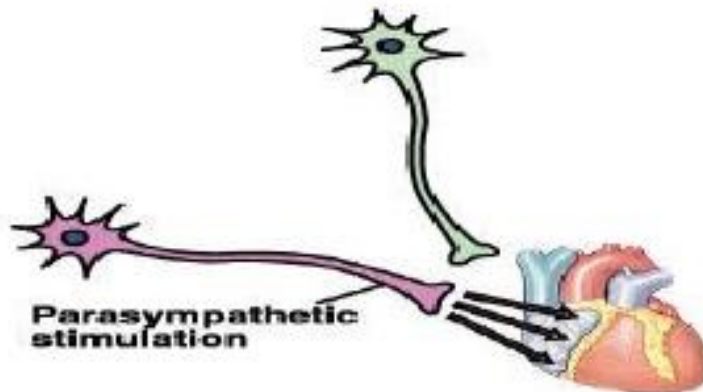
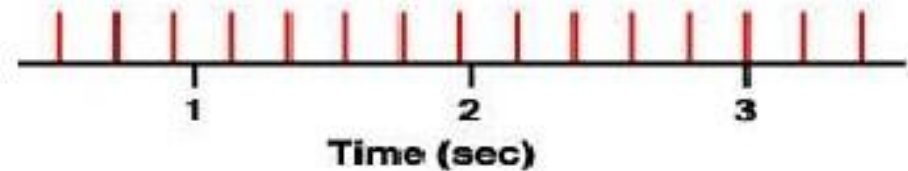
**Sympathetic and parasympathetic systems
have antagonistic effects**

Antagonistic Control

- Most internal organs are innervated by both branches of the ANS which exhibit antagonistic control



Heart rate increases



Heart rate decreases



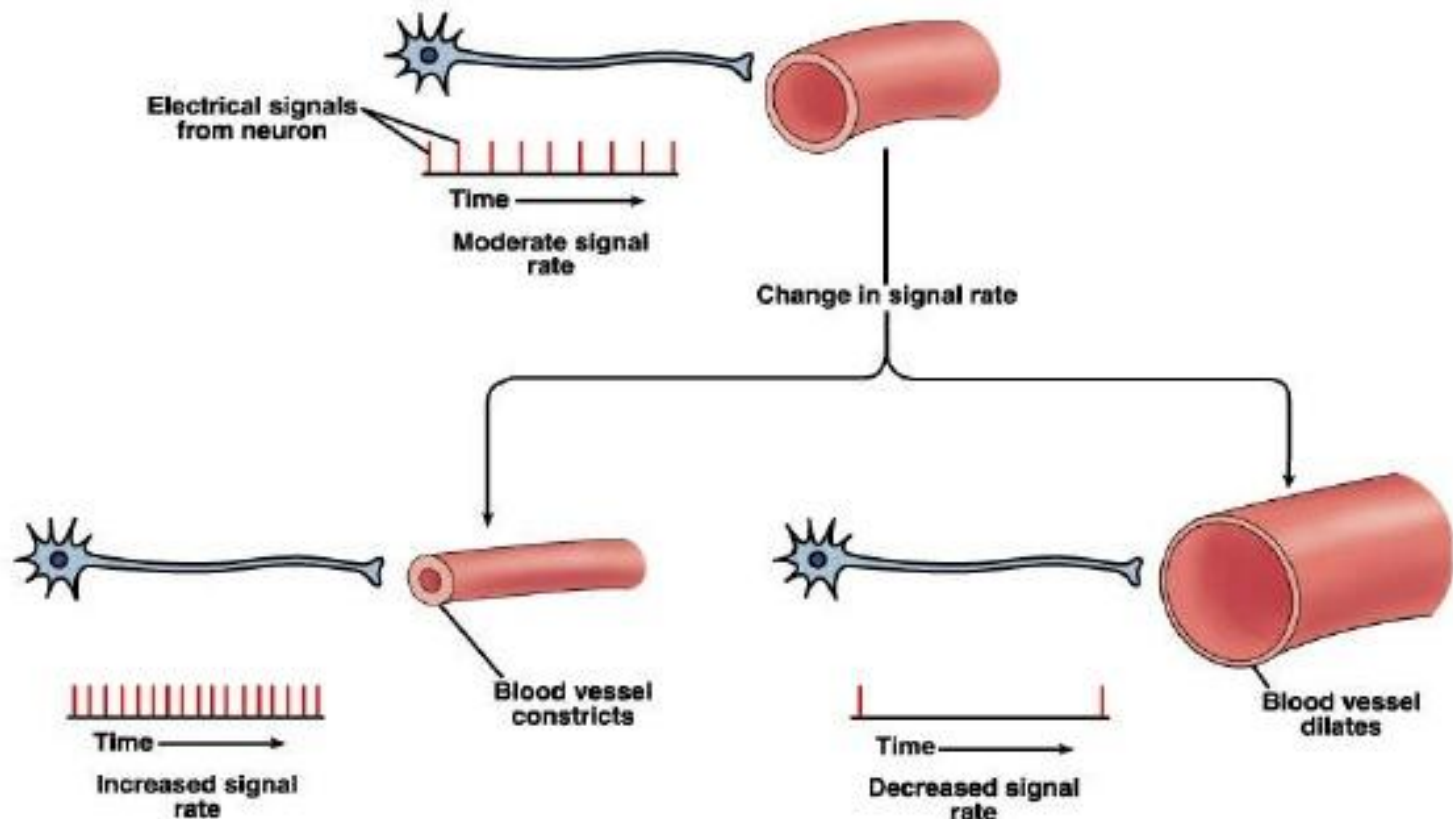
A great example is heart rate. An increase in sympathetic stimulation causes HR to increase whereas an increase in parasympathetic stimulation causes HR to decrease

Exception to the dual innervation rule:

Sweat glands and blood vessel smooth muscle are only innervated by symp and rely strictly on up-down control. Other examples :Adrenal glands, Piloerector muscles of hair

Exception to the antagonism rule:

Symp and parasymp work cooperatively to achieve male sexual function. Parasymp is responsible for erection while symp is responsible to ejaculation. There's similar ANS cooperation in the female sexual response.



Cholinergic transmission

1-Synthesis: choline uptake.

Choline + acetylCo -A +

Choline acetyltransferase.

2-transported to vesicles, by vesicle associated transporter

Stored quantas (up to 50000)

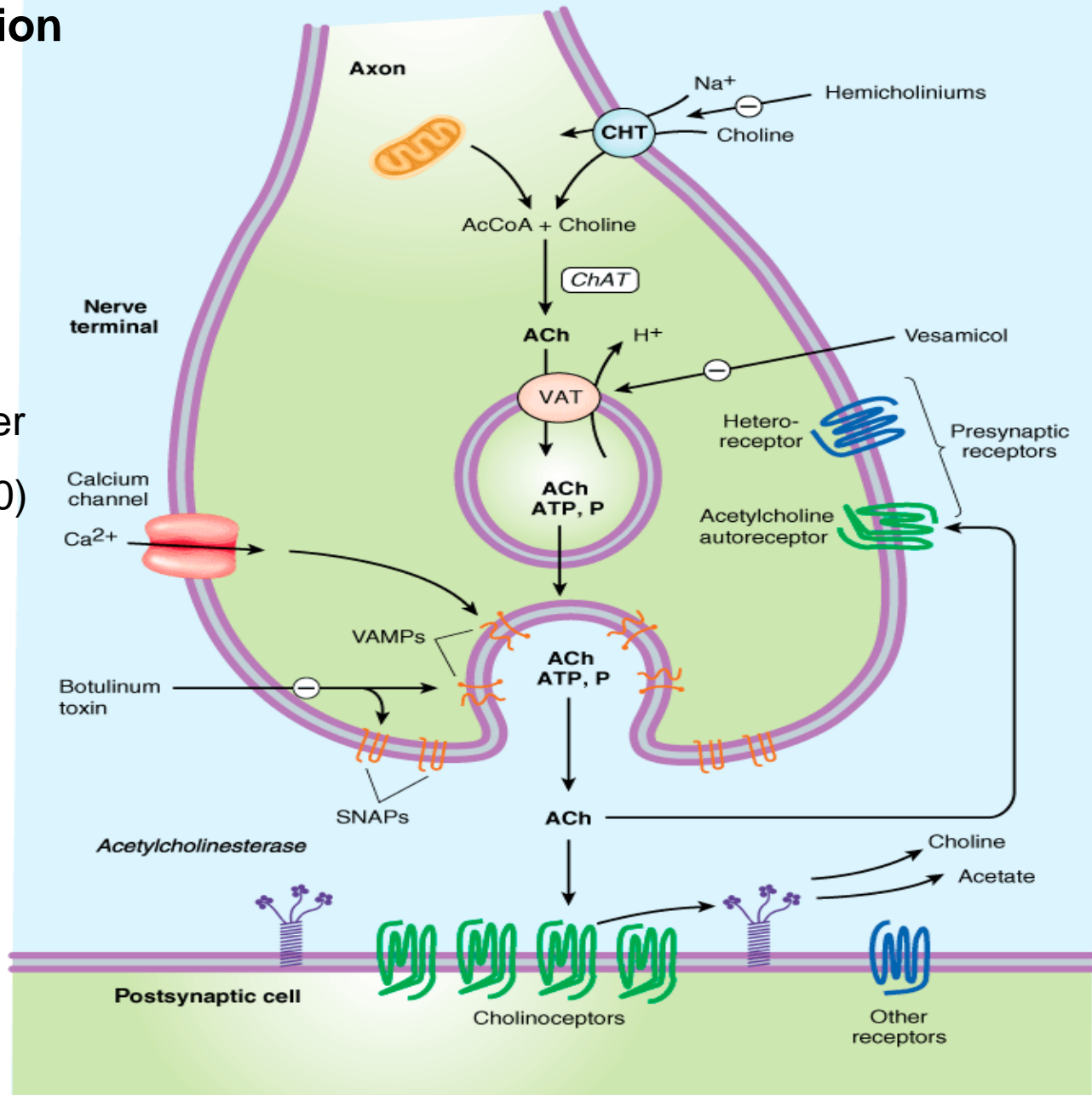
3-Release: exocytosis.

4-Interaction with post synaptic receptors

5- hydrolysis of Ach by Ach.esteras.

Drugs can act on all sites of cholinergic transmission.

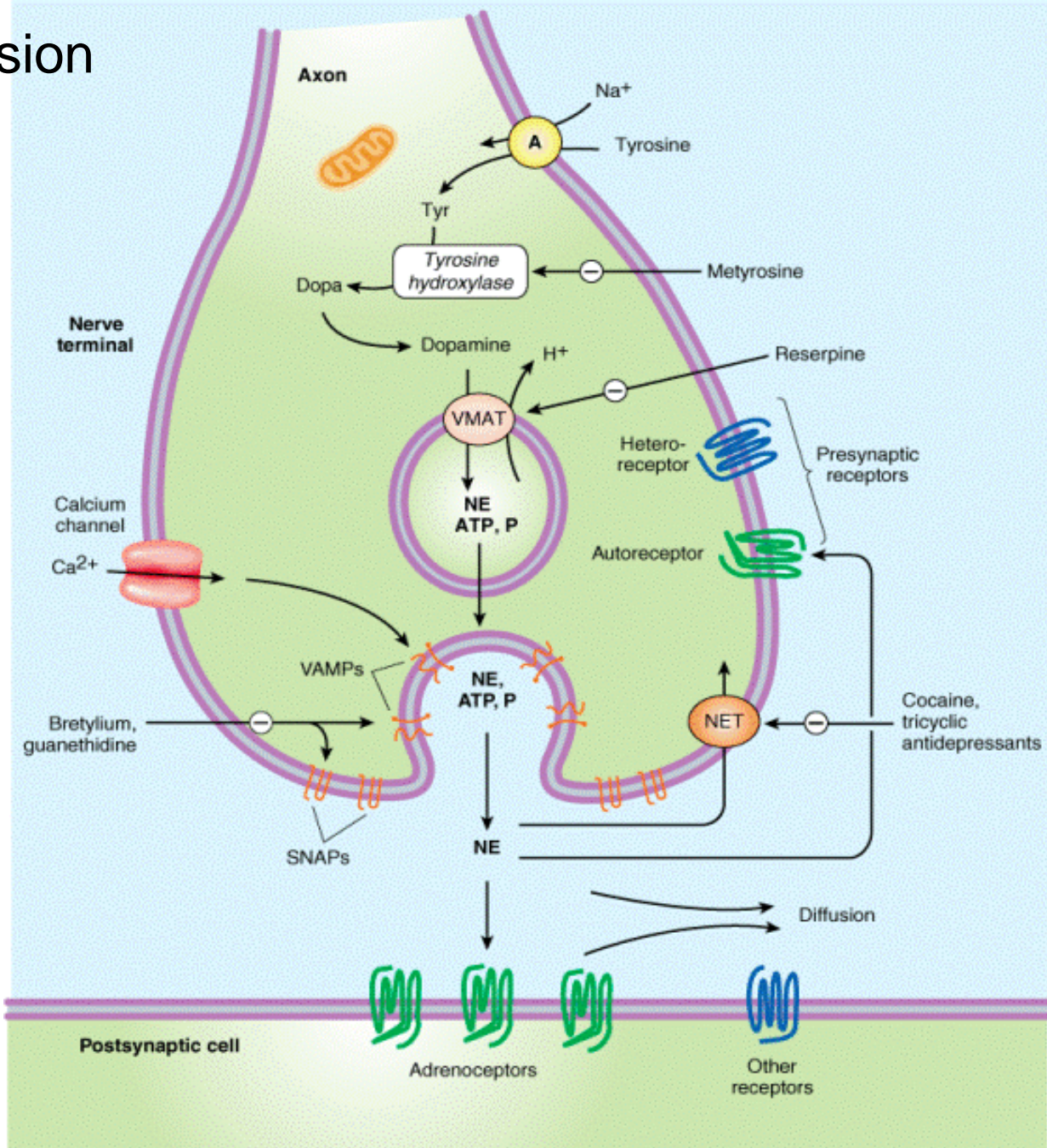
VAMPs: vesicle-associated membrane protein



Adrenergic Transmission

VAT; vesicular
Mono Amine Transporter

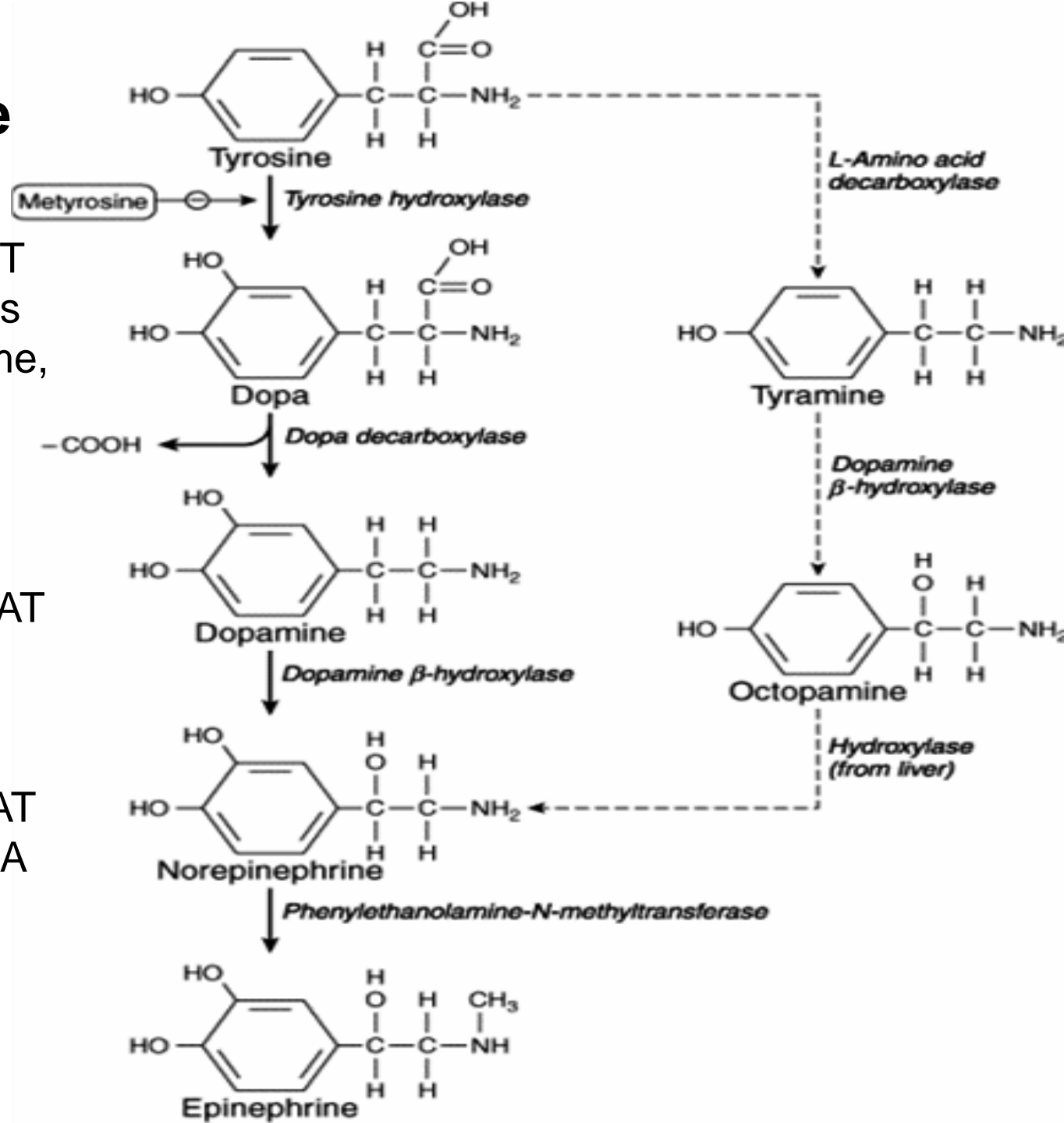
SNAPs: synaptosome –
Associated proteins.



Synthesis of Norepinephrine

Tyrosine uptake by NET
 Tyrosine Hydroxylase is
 The rate-limiting enzyme,
 Subject to end product
 inhibition

DA is transported into
 Storage vesicle by VMAT
 (vesicular monoamine
 transporter)
 and converted to NE
 Reserpine inhibits VMAT
 causing Depletion of CA
 Cocaine & Tricyclic
 antidepressants
 Inhibit NET.



Storage:

NE is stored in vesicles bound to cAMP (4:1) + protein

Release:

1- Calcium dependent exocytosis.

NE + cAMP + protein + Dopamine- β -hydroxylase are released.

Release can be blocked by guanethidine and pretylium.

–Conotoxin GVIA (Toxin of marine snails) blocks Ca channels ω and reduce NE & Ach release.

–Latrotoxin (Black widow spider venom) acts on vesicles α causing explosive release of NE & Ach

2- Calcium independent release.

Tyramine, amphetamine are transported by NET (NE Transporter) into the neuron then transported by VMAT into the vesicles. They displace NE from the vesicular stores, into the cytoplasm. Ne is transported into the synaptic cleft by reverse transport via NET.

They produce an indirect sympathomimetic effect.

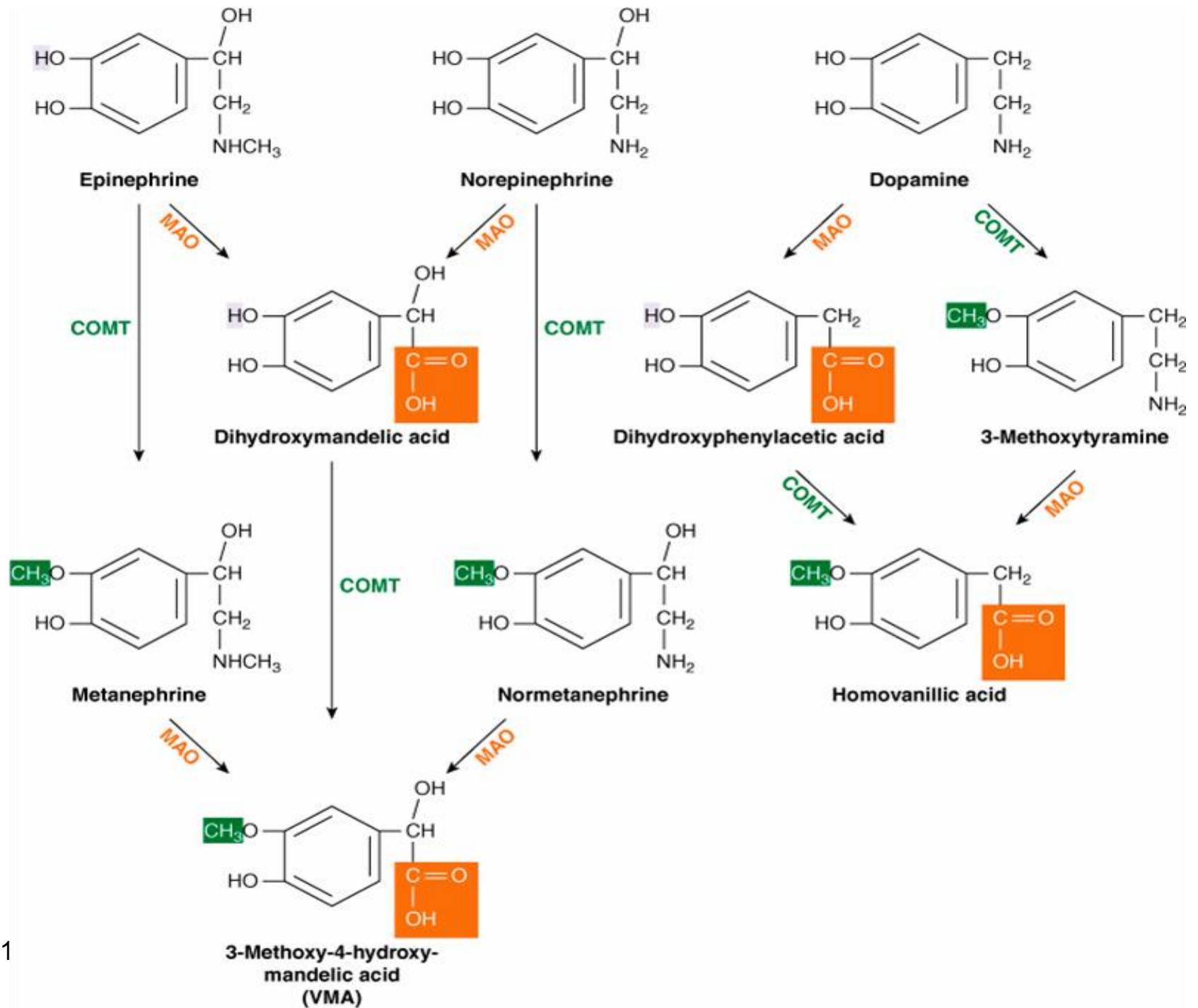
Metabolism of Catecholamines:

NE effects are not terminated by metabolism, but by neuronal reuptake (uptake₁). 80 % of the released NE are transported into the neuron by MAT (Mono amine Transporter).

Monoamine oxidase (MAO) in the mitochondria produces oxidative deamination of mono amines.

Catechol-O-Methyl transferase (COMT) transfers methyl group from S- adenosyl methionine into the OH- group in the meta position of the catechol ring.

VMA is the end product of metabolism, measured in urine for the diagnosis of pheochromocytoma.



Cholinoceptors

Muscarinic M1: CNS neurons, sympathetic postganglionic neurons, some presynaptic sites.

Muscarinic M2: Myocardium, smooth muscle, some presynaptic sites; CNS

Muscarinic M3: Exocrine glands, vessels (smooth muscle and endothelium); CNS

Muscarinic M4: CNS neurons; possibly vagal nerve endings.

Muscarinic M5: Vascular endothelium, especially cerebral vessels; CNS neurons.

Nicotinic NN: Postganglionic neurons, some presynaptic cholinergic terminals.

Nicotinic NM: Skeletal muscle neuromuscular end plates.

Adrenoceptors

Alpha1 (α 1) Postsynaptic, especially smooth muscle. Formation of IP3 and DAG, increased intracellular Ca.

Alpha2 (α 2) Presynaptic adrenergic nerve terminals, platelets, lipocytes, smooth muscle.

Inhibition of adenylyl cyclase, decreased cAMP

Beta1 (β 1) Postsynaptic, heart, lipocytes, brain;, juxtaglomerular apparatus of renal tubules, ciliary body epithelium

Stimulation of adenylyl cyclase, increased cAMP

Beta2 (β 2) Postsynaptic, especially smooth muscle and cardiac muscle. Stimulation of adenylyl cyclase and increased cAMP.

Beta3 (β 3) Postsynaptic effector cells, especially lipocytes; Stimulation of adenylyl cyclase & increased cAMP

Dopamine receptors

D1 (DA 1), D5

Brain; effector tissues, especially smooth muscle of the renal vascular bed.

Stimulation of adenylyl cyclase and increased cAMP

D2 (DA 2) Brain; effector tissues, especially smooth muscle; presynaptic nerve terminals.

Inhibition of adenylyl cyclase; increased potassium conductance.

D3 Brain.

Inhibition of adenylyl cyclase.

D4 Brain, cardiovascular system.

Inhibition of adenylyl cyclase

Dual innervations of most organs by Sym & Parasymp systems.

Sympathetic tone and parasympathetic tone.

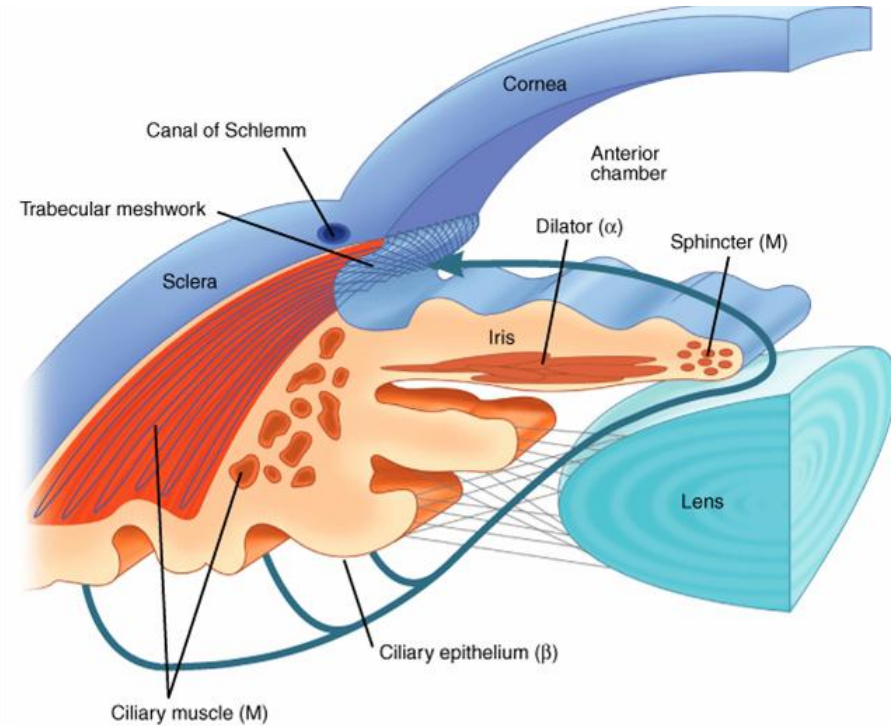
Baro receptor reflex.

Direct Effects of Autonomic *Nerve* Activity

Organ	Sympathetic Activity	Parasympathetic
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Eye, Iris.

radial muscle	Contracts ($\alpha 1$)	mydriasis.
circular muscle.	M3 Contracts	miosis
Ciliary muscle	Contracts M3.	near vision.



Heart

Sinoatrial node	Accelerates $\beta 1$	Decelerates M
Ectopic pacemakers	Accelerates $\beta 1$	

Contractility	Increases $\beta 1$	Decreases (atria) M2
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Blood vessels

Skin, splanchnic vessels	Contracts $\alpha 1$	
Skeletal muscle vessels	Relaxes $\beta 2$	
Endothelium (drug effect)		Releases EDRF (NO) M3, M5

Releases EDRF (NO) M3, M5

Bronchiolar smooth muscle Relaxes β_2 Contracts M3

Gastrointestinal tract

Smooth muscle Walls Relaxes β_2, α_2 Contracts M3

Sphincters Contracts α_1 Relaxes M3

Secretion Increases M3

Genitourinary smooth muscle

Bladder wall Relaxes β_2 Contracts M3

Sphincter Contracts α_1 Relaxes M3

Uterus, pregnant Relaxes β_2

Contracts α Contracts M3

Penis, seminal vesicles Ejaculation α Erection M

Skin

Pilomotor smooth muscle Contracts α

Sweat glands Increase M

Metabolic functions

Liver Glycogenolysis, $\beta_2 \alpha$

Glyconeogenesis $\beta_2 \alpha$

Fat cells Lipolysis β_3

Kidney Renin release β_1