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 CNS can be divided into two major subdivisions:

Autonomic and **Somatic**.

The **autonomic nervous system (ANS)** is largely independent (autonomous), 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.

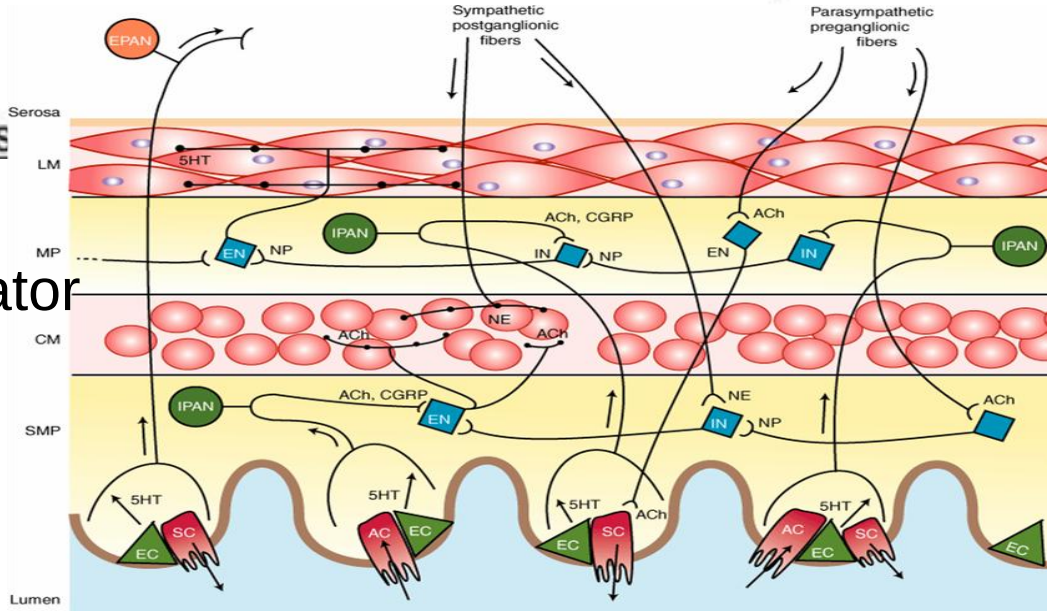
Enteric system activate coordinated contraction of smooth muscles to cause peristaltic constriction of the gut.

Most of enteric nervous system functions

independently of higher CNS control.

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

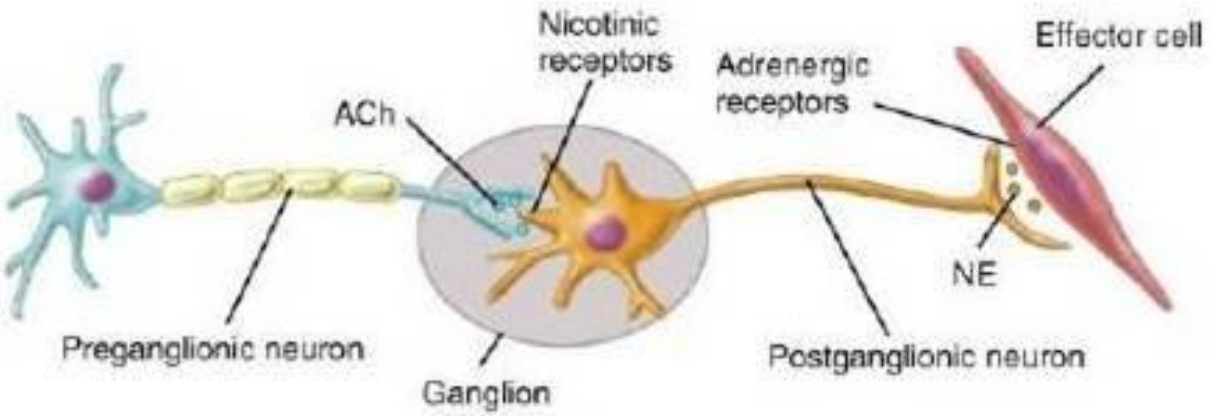
It is modulated by the symp. & parasymp systems.



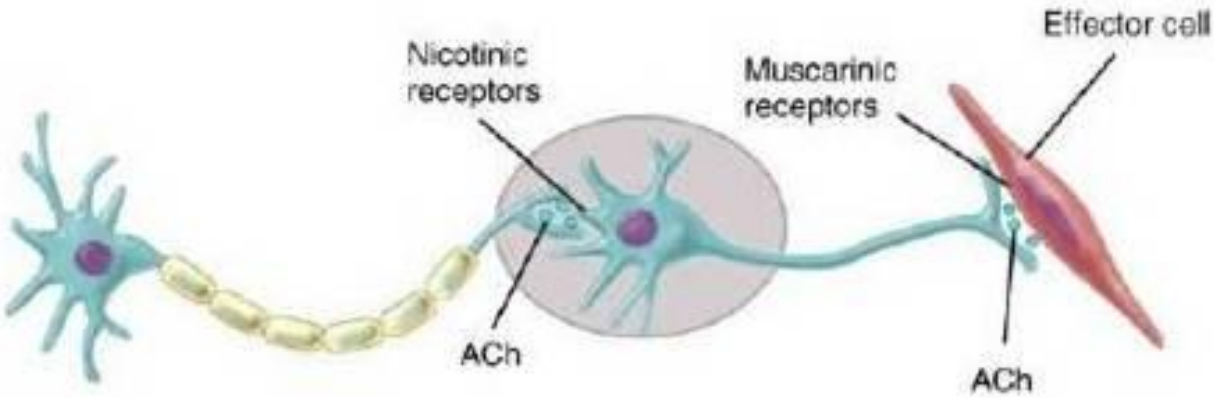
ANS Neurons

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

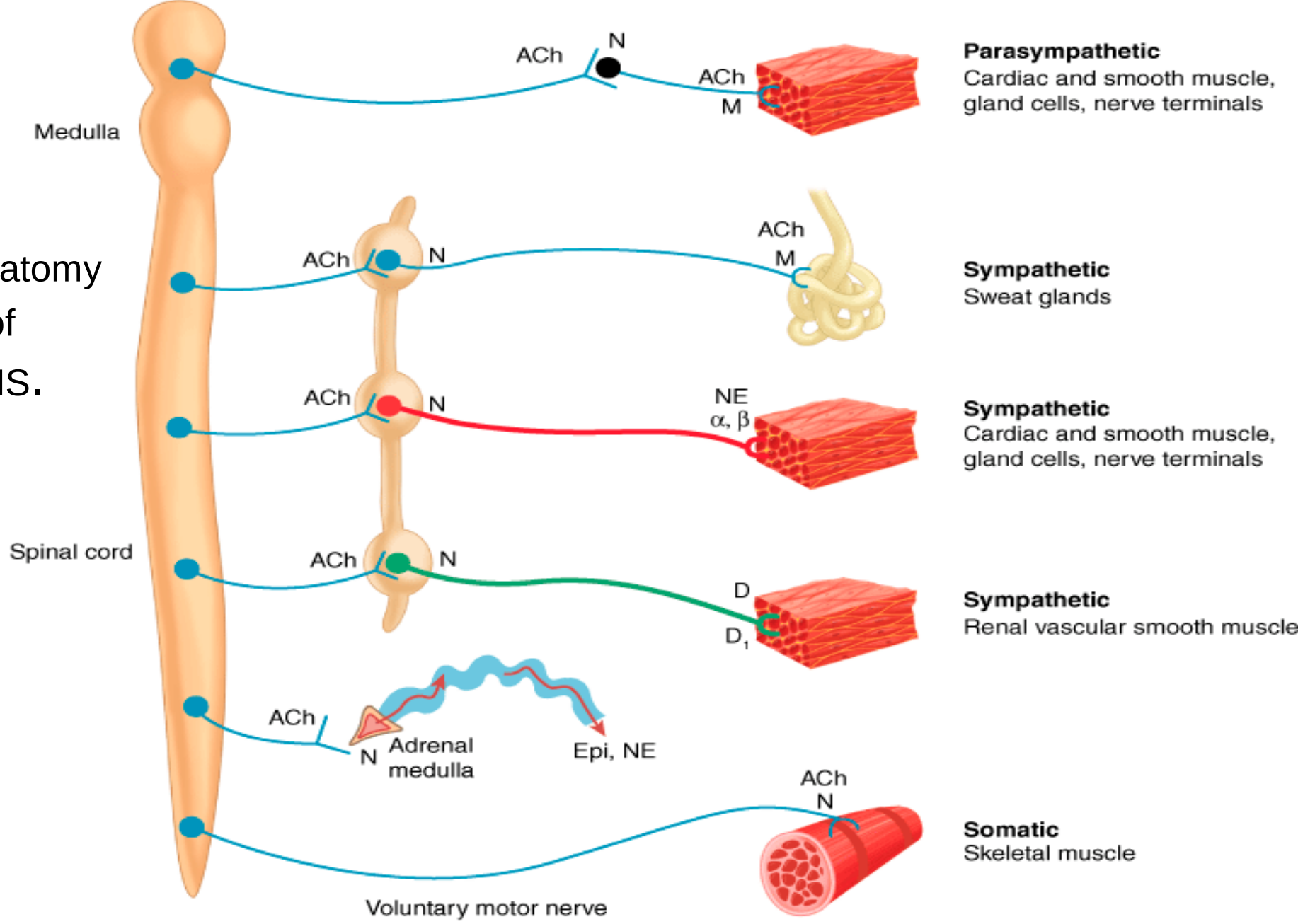
- Adrenergic



- Cholinergic



Anatomy of ANS.



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

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

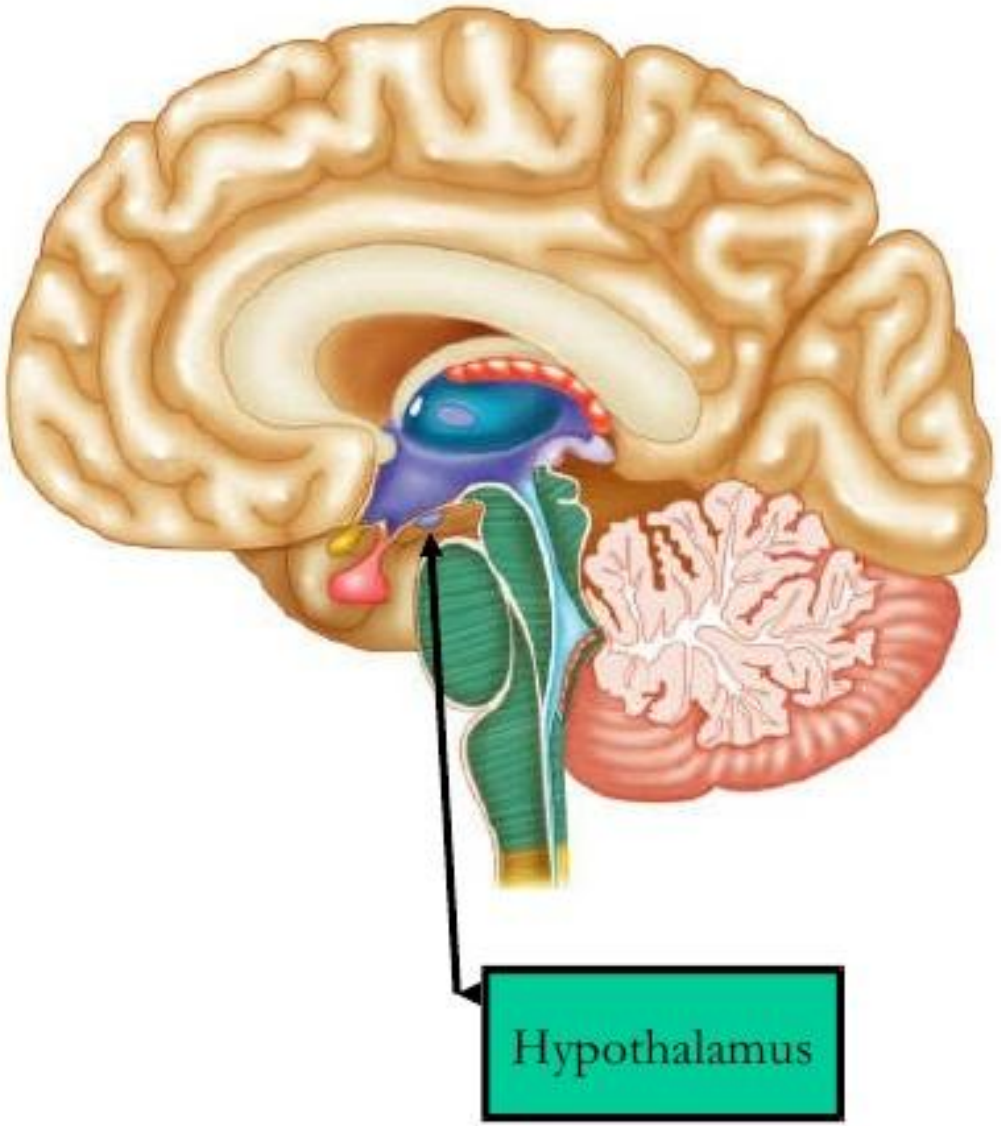
Sympathetic cell bodies located T1-L2 levels: ***thoracolumbar outflow****.*

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

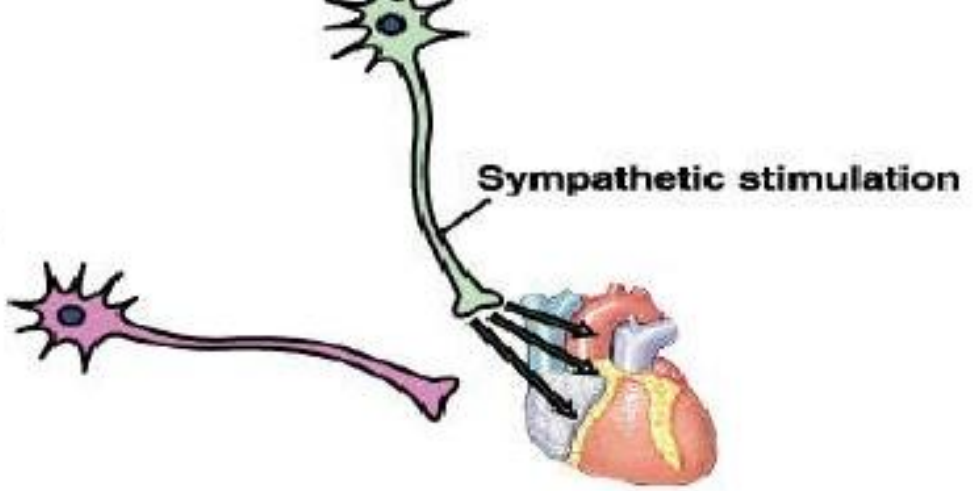
    for these activities - increase heart rate, blood flow, breathing

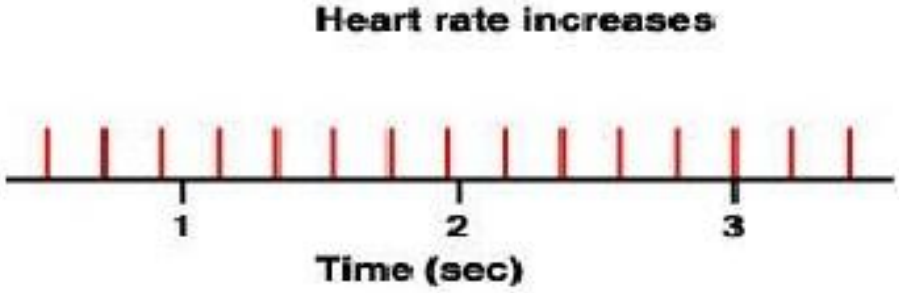
    decrease non-survival activities - food digestion, etc.

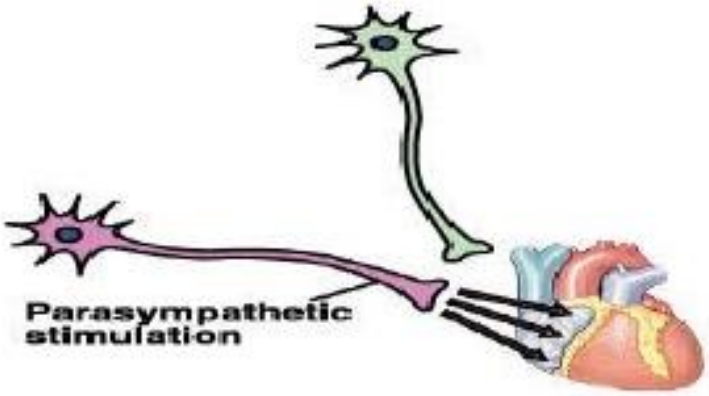
Sympathetic and parasympathetic systems have antagonistic effects

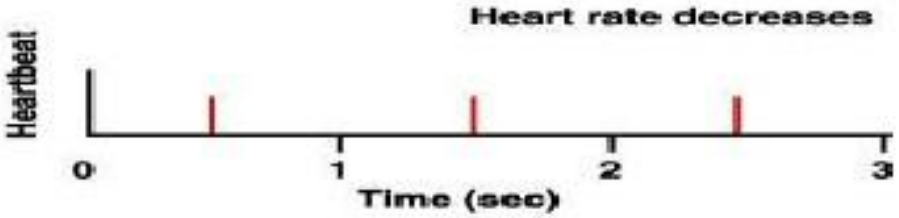
Antagonistic Control

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









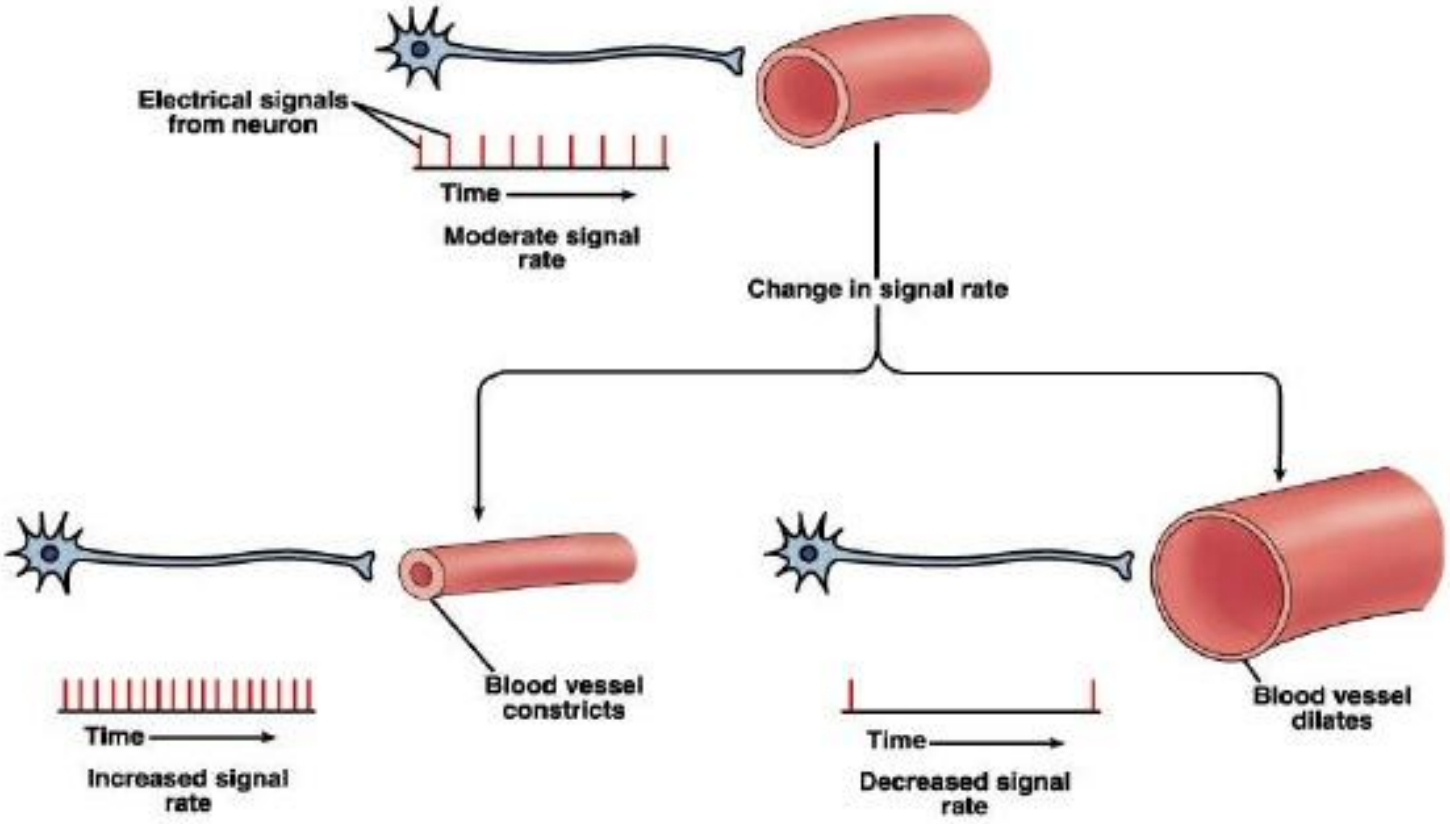
A great example is heart rate. An increase in sympathetic stimulation causes HR to increase whereas an increase in parasympathetic stimulation causes HR to decrease

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)

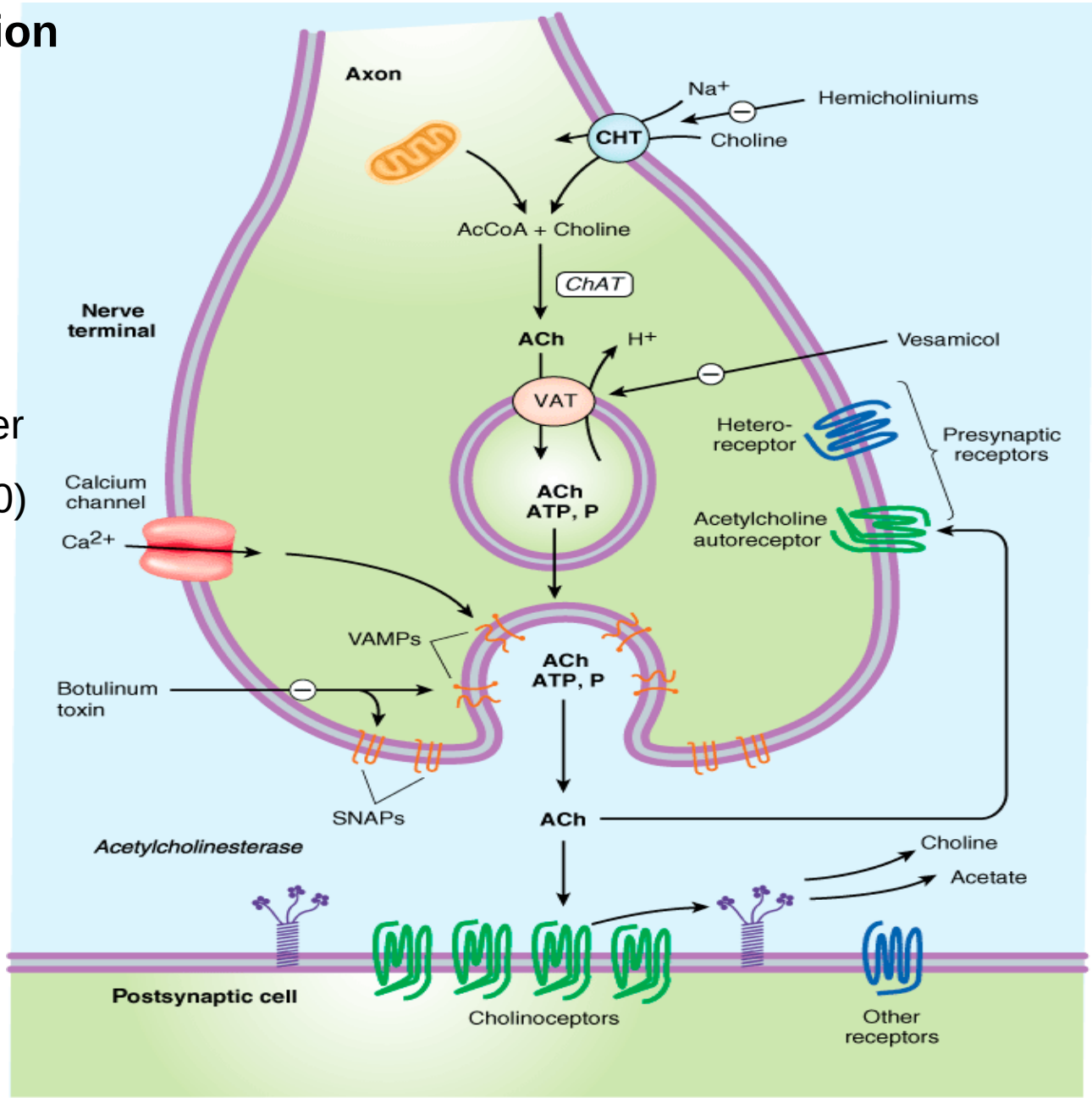
3-Release: exocytosis.

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

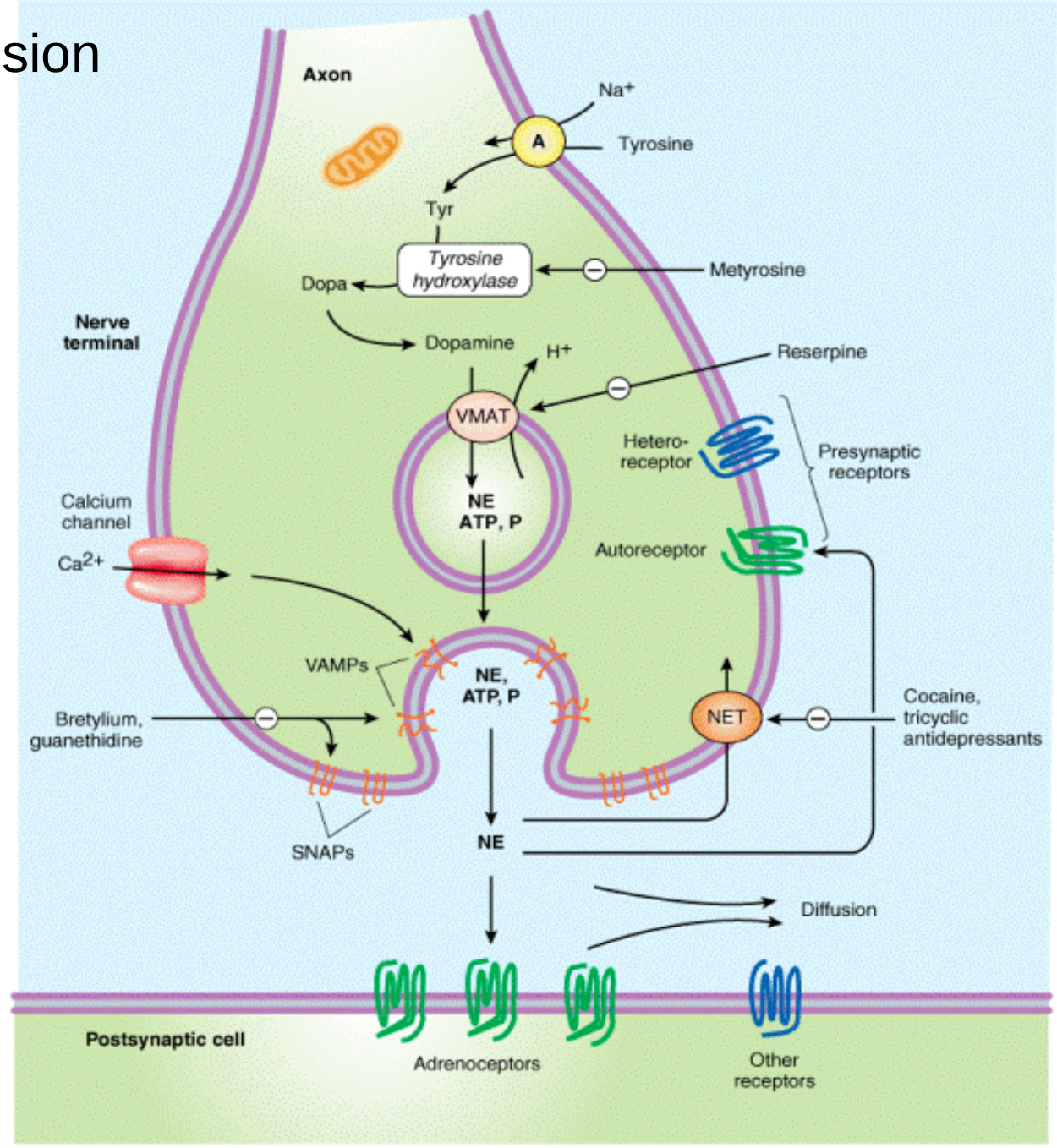


Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 11th Edition:* http://www.accessmedicine.com

Adrenergic Transmission

VAT; vesicular
Mono Amine Transporter

SNAPs: synaptosome – Associated proteins.



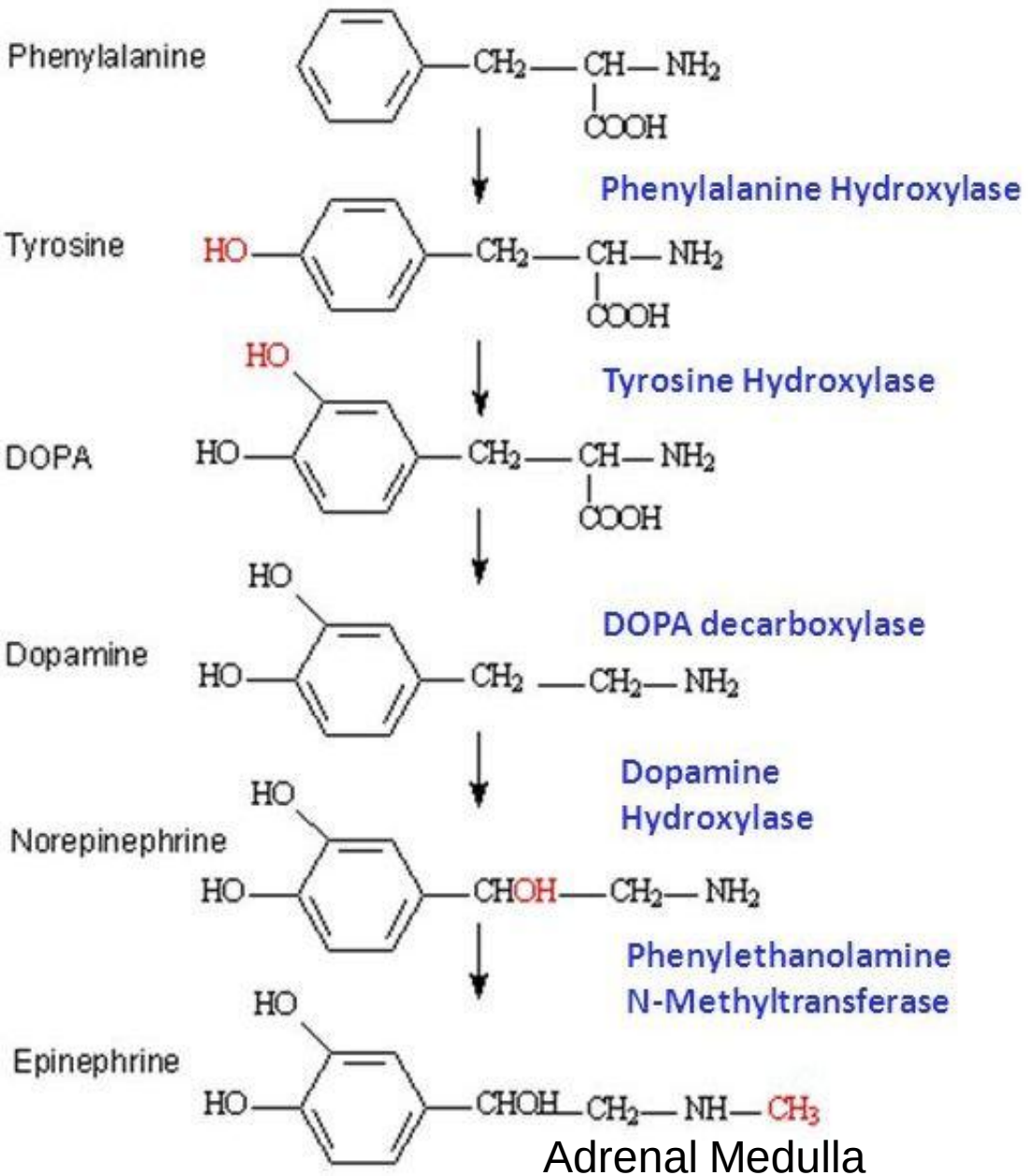
Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 12th Edition*: http://www.accessmedicine.com

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- hydroxylaes are released.

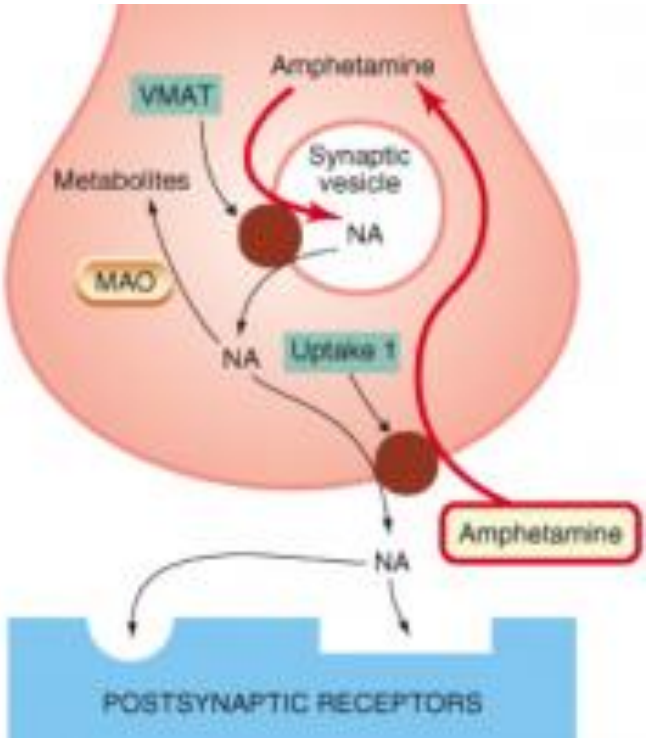
Release can be blocked by guanethidine and pretylium.

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

–Latrotoxin (Black widow spider venom) acts on α vesicles 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 displaces 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:

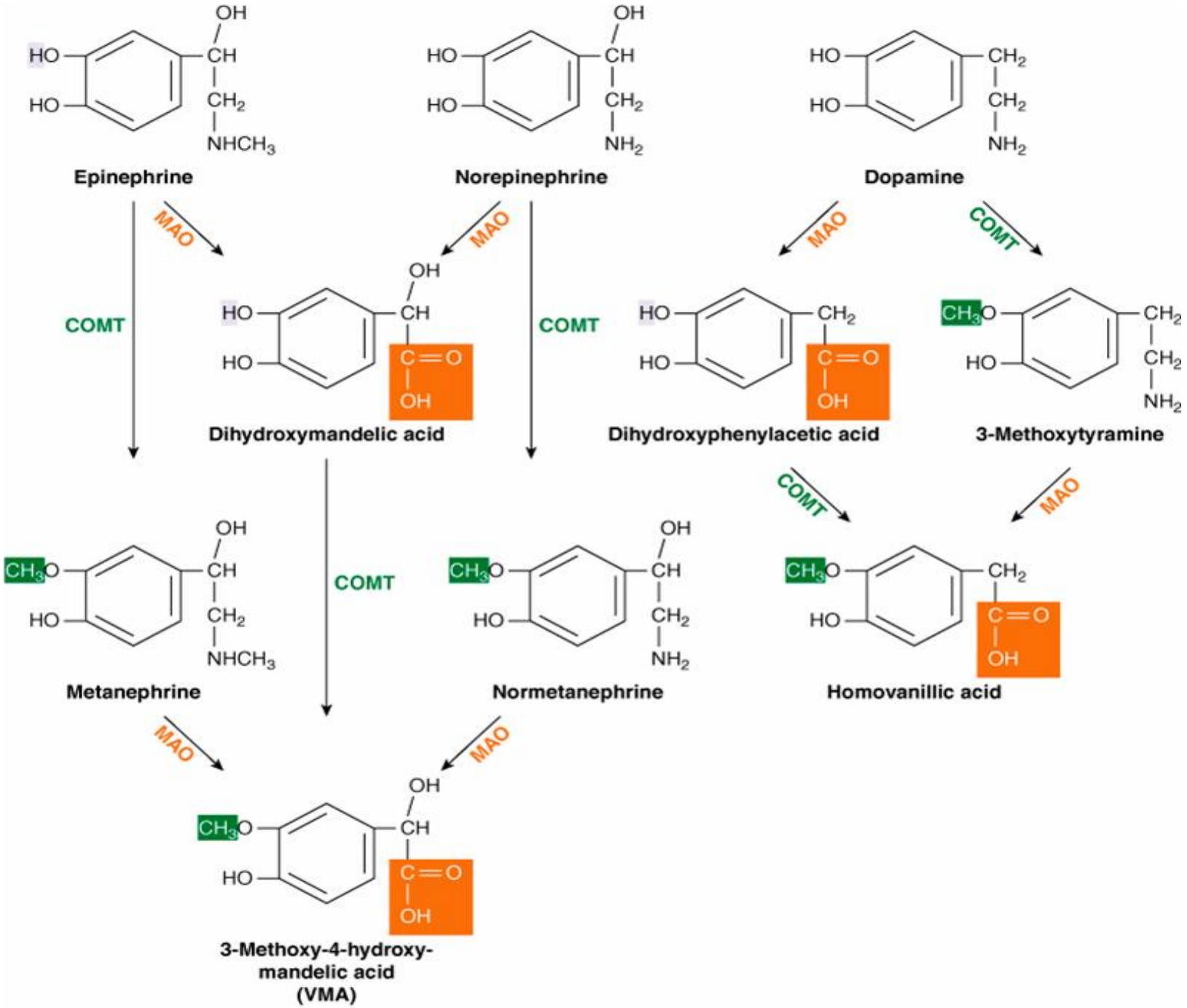
NE effects are not terminated by metabolism, but by neuronal reuptake (uptake1).

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.


Epinephrine
Norepinephrine
Dopamine
MAO
COMT
Dihydroxymandelic acid
Dihydroxyphenylacetic acid
3-Methoxytyramine
Metanephrine
Normetanephrine
Homovanillic acid
3-Methoxy-4-hydroxy-
mandelic acid
(VMA)

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.

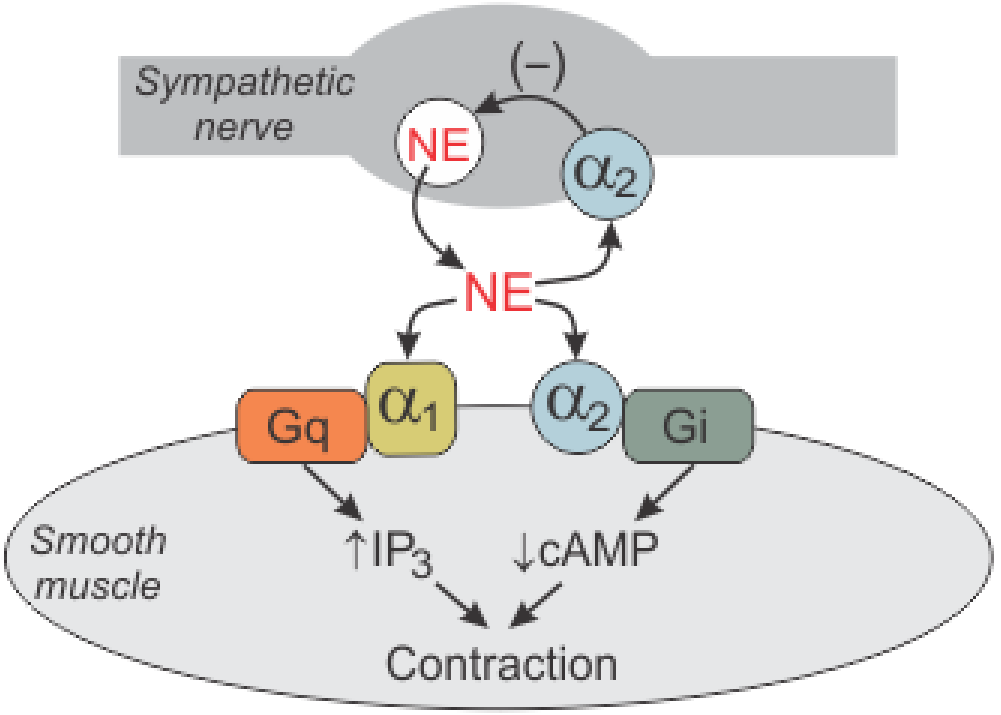
Muscarinic M5: Vascular endothelium, especially cerebral vessels; CNS neurons.

Nicotinic NN: Postganglionic neurons, some presynaptic cholinergic terminals.

Nicotinic NM: Skeletal muscle neuromuscular end plates.

Adrenoceptors

Alpha1 (α)1



Postsynaptic, especially smooth muscle.

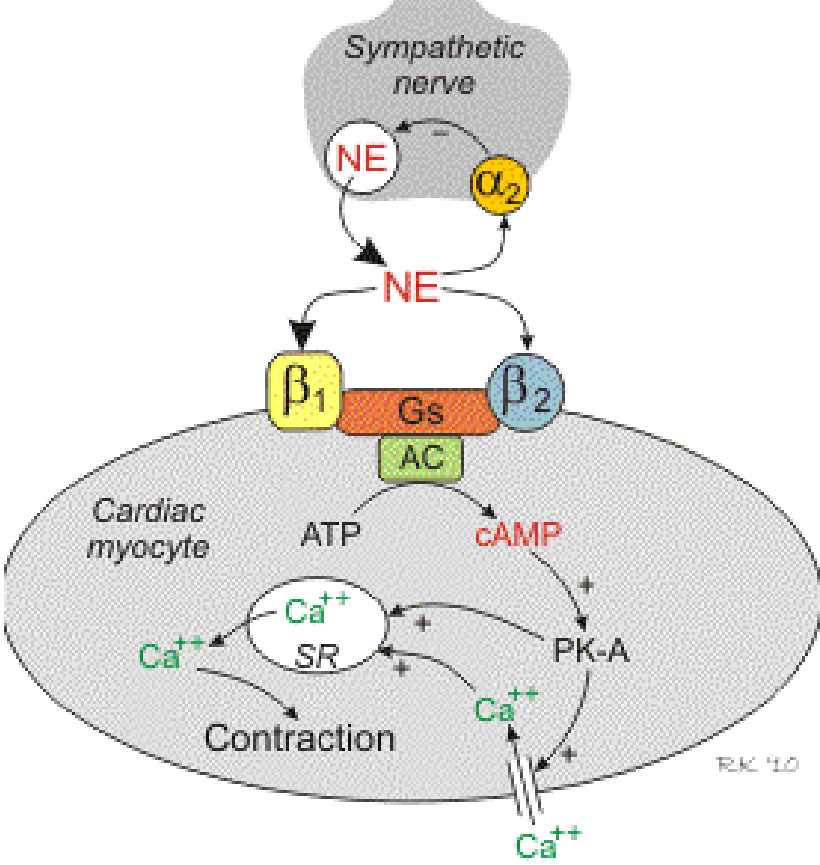
Formation of IP3 and DAG, increased intracellular Ca producing smooth muscle contraction.

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

Inhibits NE release.

Inhibition of adenylyl cyclase, decreased cAMP

Beta1 (β1)
Heart, lipocytes, brain;, juxtaglomerular apparatus of renal tubules.
Stimulation of adenylyl cyclase, increased cAMP



Beta2 (β2) smooth muscle & cardiac muscle.
Stimulation of adenylyl cyclase and increased cAMP.

Beta3 (β3) lipocytes; Stimulation of adenylyl cyclase & increased cAMP

Dopamine receptors

D1 (DA 1), D5

Brain, especially smooth muscle of the renal vascular bed.

Stimulation of adenylyl cyclase and increased cAMP

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

Inhibition of adenylyl cyclase; increased potassium conductance.

D3 Brain.

Inhibition of adenylyl cyclase.

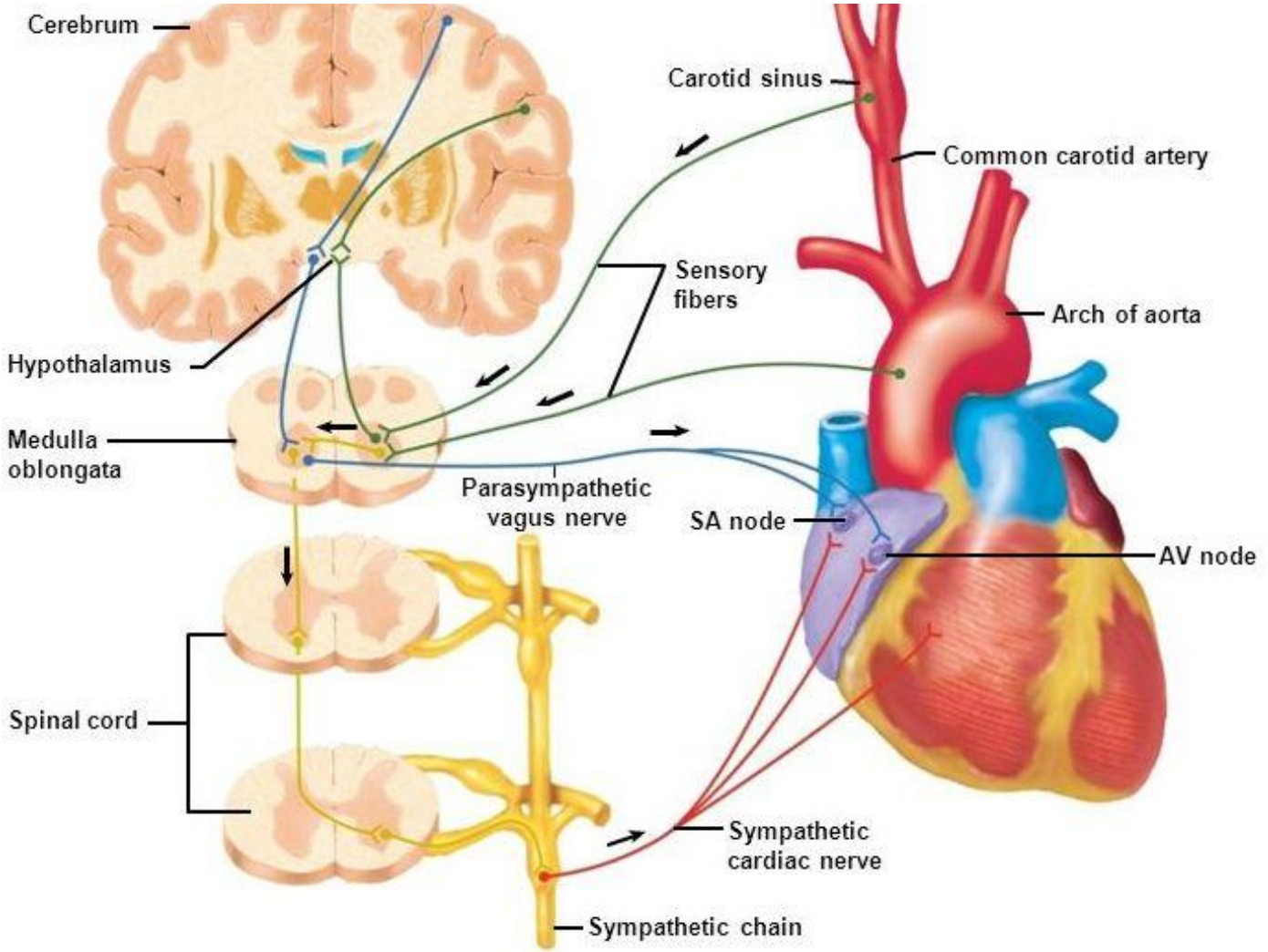
D4 Brain, cardiovascular system.

Inhibition of adenylyl cyclase

Dual innervations of most organs by Sym & Parasym sytems.

Sympathetic tone and parasympathetic tone.

Baro receptor reflex.



Direct Effects of Autonomic *Nerve* Activity

Organ **Sympathetic Activity** **Parasympathetic**

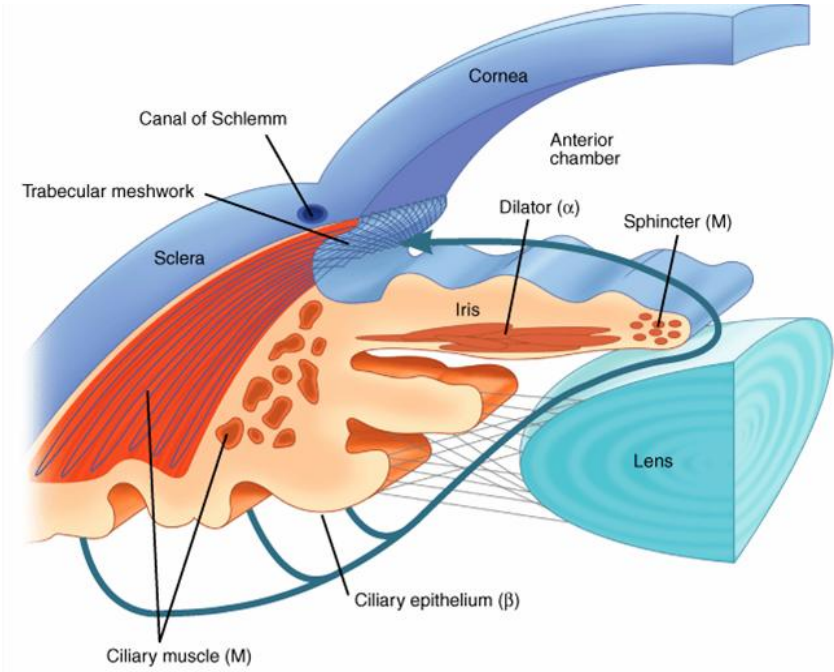
Eye, Iris.

radial muscle Contracts (α1) mydriasis.

circular muscle. M3 Contracts miosis

Ciliary muscle Contracts M3.

near vision.



Heart

Sinoatrial node Accelerates β1 Decelerates M2

Ectopic pacemakers Accelerates β1

Contractility Increases β1 Decreases

(atria) M2

Blood vessels

Skin, splanchnic vessels Contracts α1

Skeletal muscle vessels Relaxes β2

Endothelium (drug effect) Releases EDRF (NO) M3, M5 5

Bronchiolar smooth muscle	Relaxes	β2	Contracts	M3
Gastrointestinal tract				
Smooth muscle Walls	Relaxes	β2, α2	Contracts	M3
Sphincters	Contracts	α1	Relaxes	M3
Secretion			Increases	M3
Genitourinary smooth muscle				
Bladder wall	Relaxes	β2	Contracts	M3
Sphincter	Contracts	α1	Relaxes	M3
Uterus, pregnant	Relaxes	β2		
	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,		β2 α	
	Glyconeogenolysis		β2 α	
Fat cells	Lipolysis		β3	
Kidney	Renin release		β1	