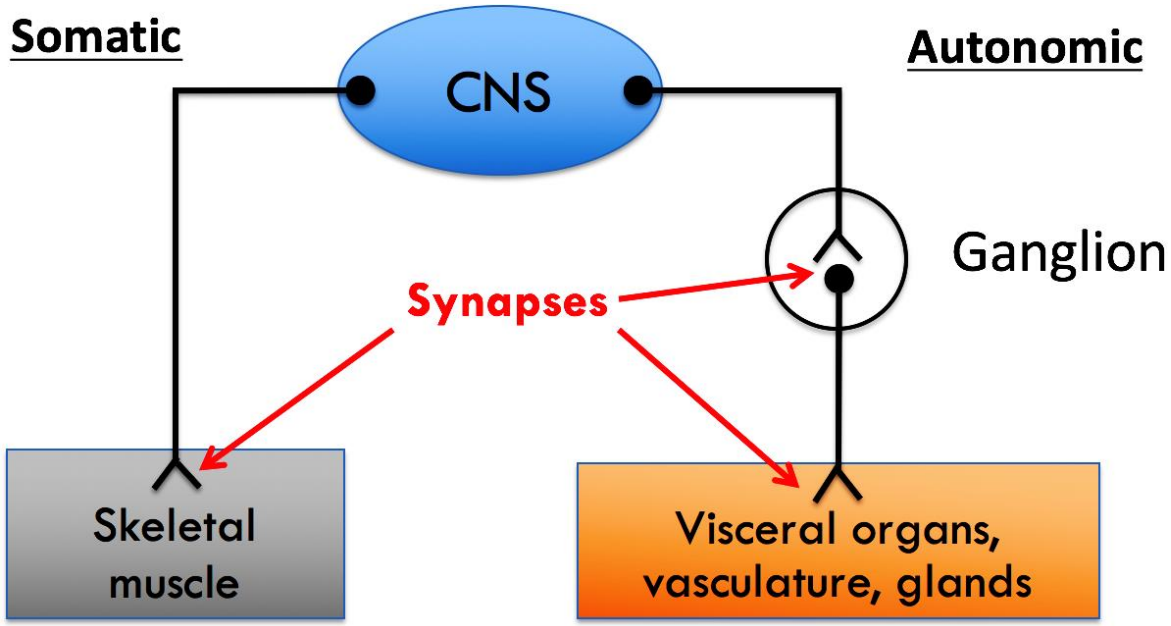
# Autonomic Nervous System

## Introduction

2020

The nervous system is divided into:
1- CNS; the brain and spinal cord
2- The peripheral nervous system
The motor (efferent) portion of CNS can be divided into: **Autonomic** and **Somatic**.
The **autonomic nervous system (ANS)** is largely independent (autonomous), its activities are not under direct conscious control.



The Autonomic nervous system has 3 subdivisions:

1. The sympathetic nervous system
2. The parasympathetic nervous system
3. The enteric nervous system.

The **enteric nervous system** (ENS) is one of the main divisions of the autonomic **nervous system** (ANS) and consists of a mesh-like **system** of neurons that governs the function of the gastrointestinal tract.

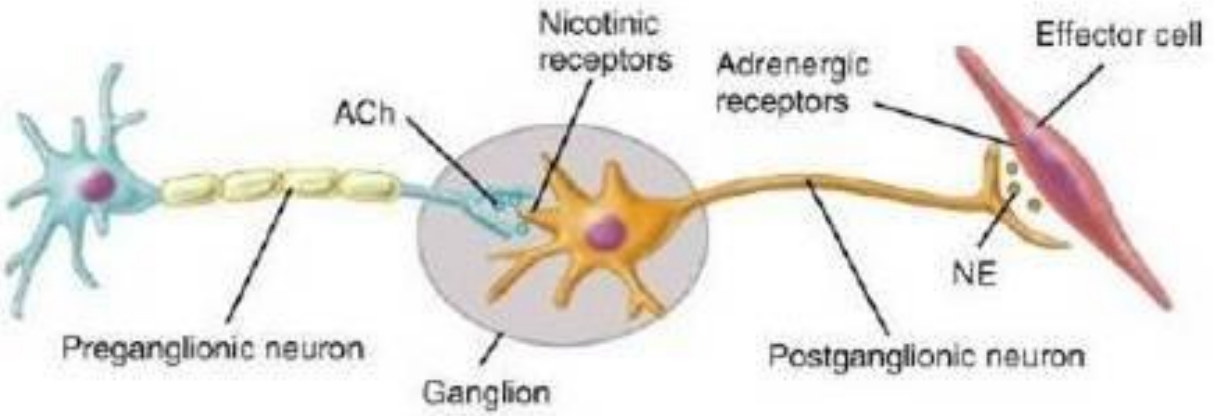
Many transmitter & neuromodulator substances have been identified in the ENS.

It is modulated by the sympathetic & parasympathetic systems

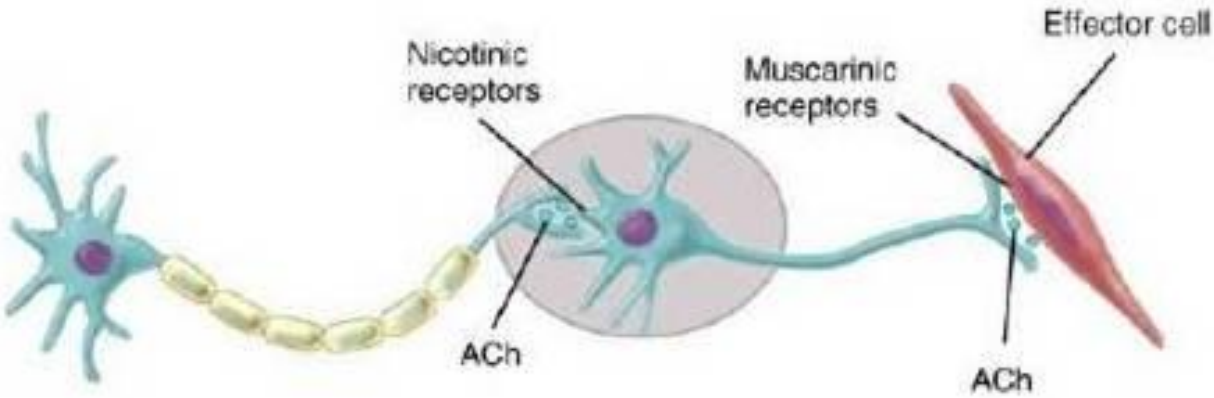
# ANS Neurons

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

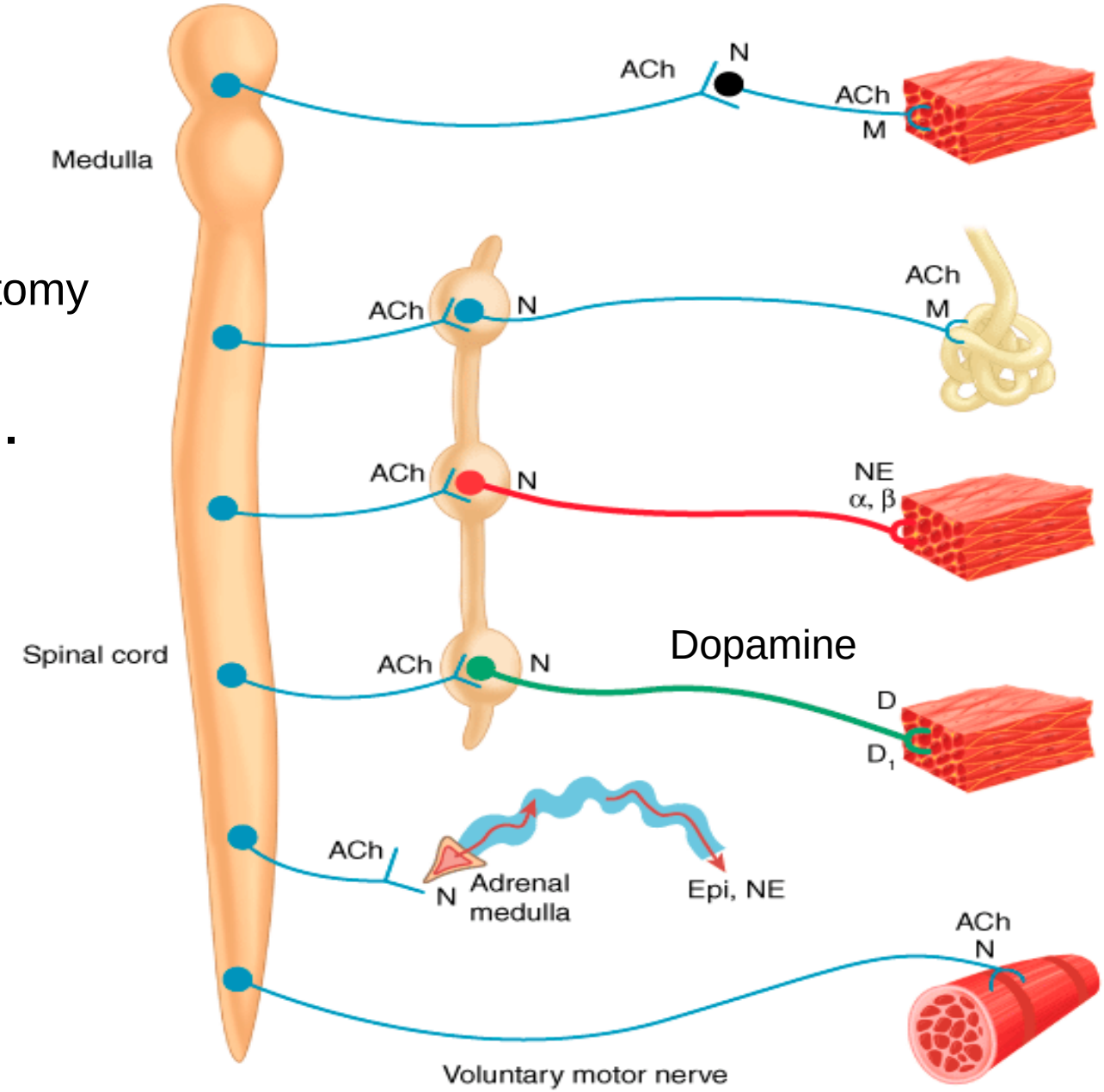
- Adrenergic




- Cholinergic



Anatomy of ANS.



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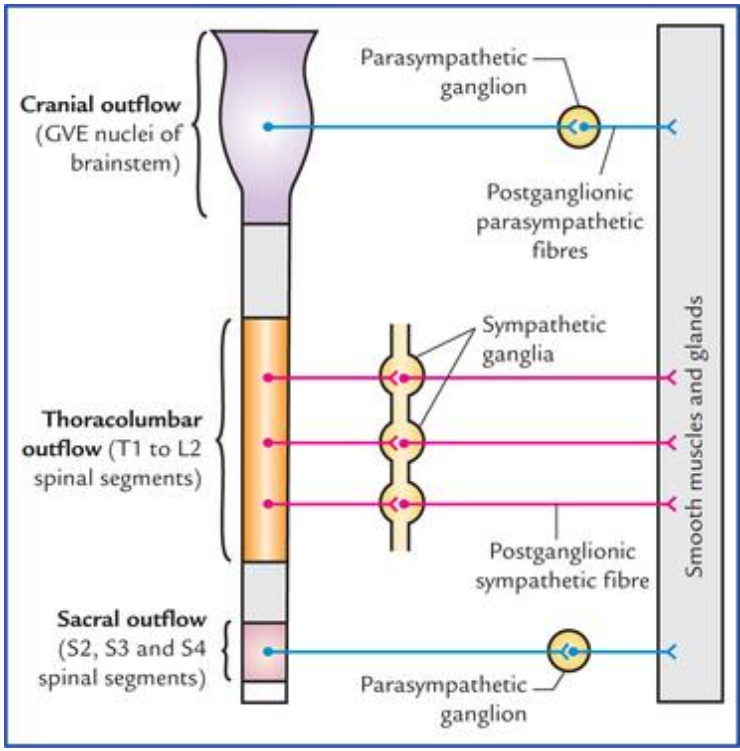
**Parasympathetic** cell bodies in brainstem & sacral spinal cord: ***craniosacral outflow.***




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

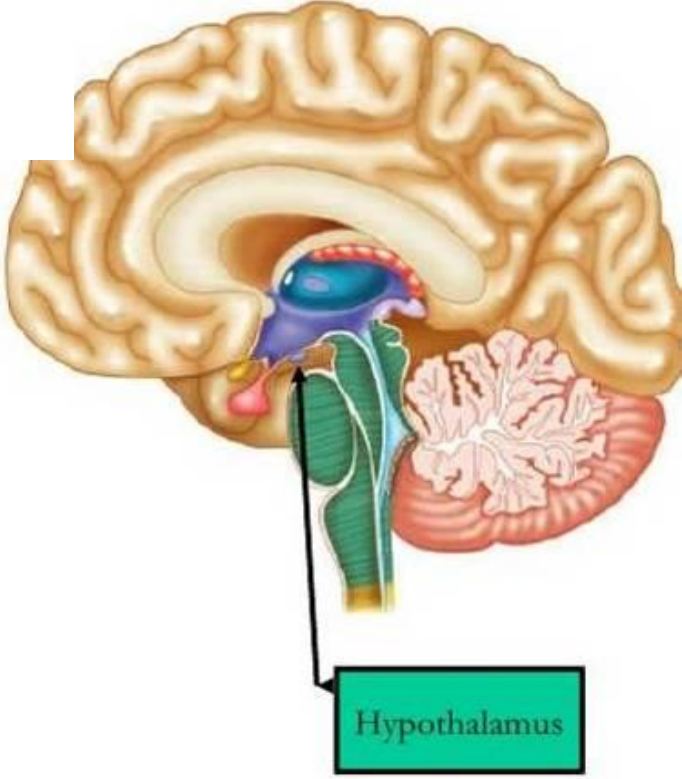
Sympathetic cell bodies located T1-L2 levels: ***thoracolumbar outflow.***

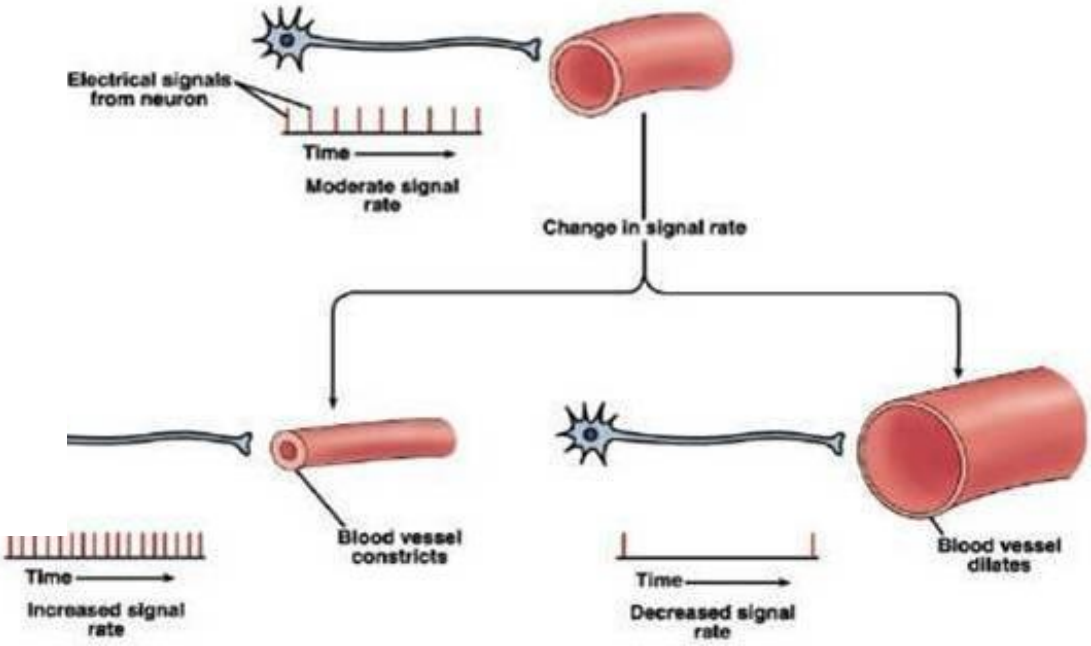
One sympathetic preganglionic neuron may have many branches and may synapse with 20+ postganglionic neurons.

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

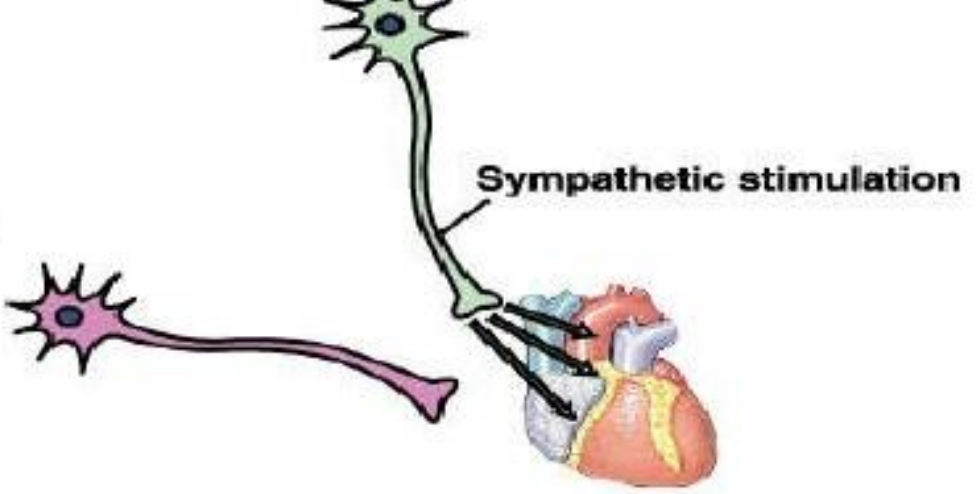
    for these activities - increase heart rate, blood flow, breathing

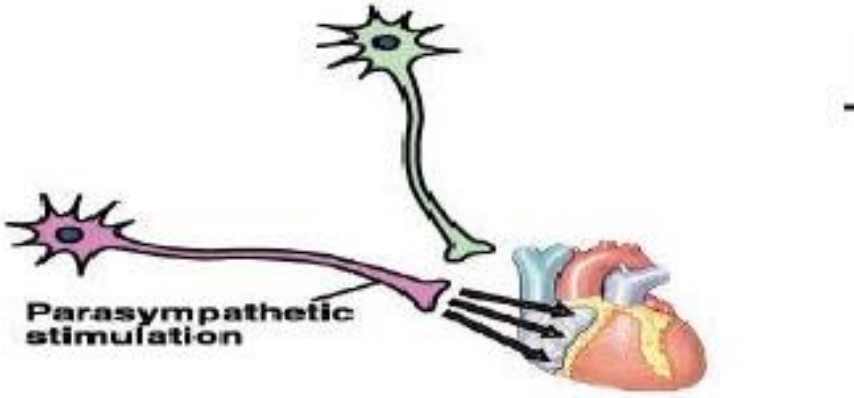
    decrease non-survival activities - food digestion, etc.

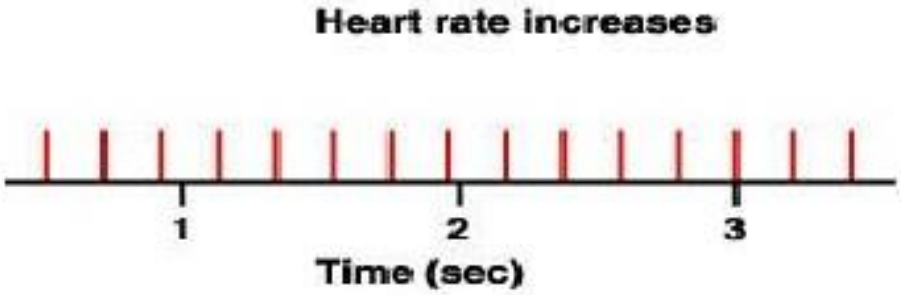
**Sympathetic and parasympathetic systems have antagonistic effects**

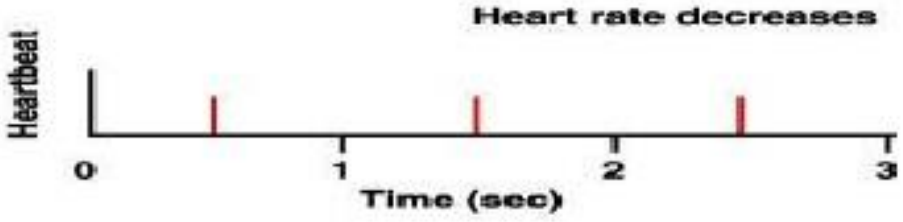
# Antagonistic Control

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



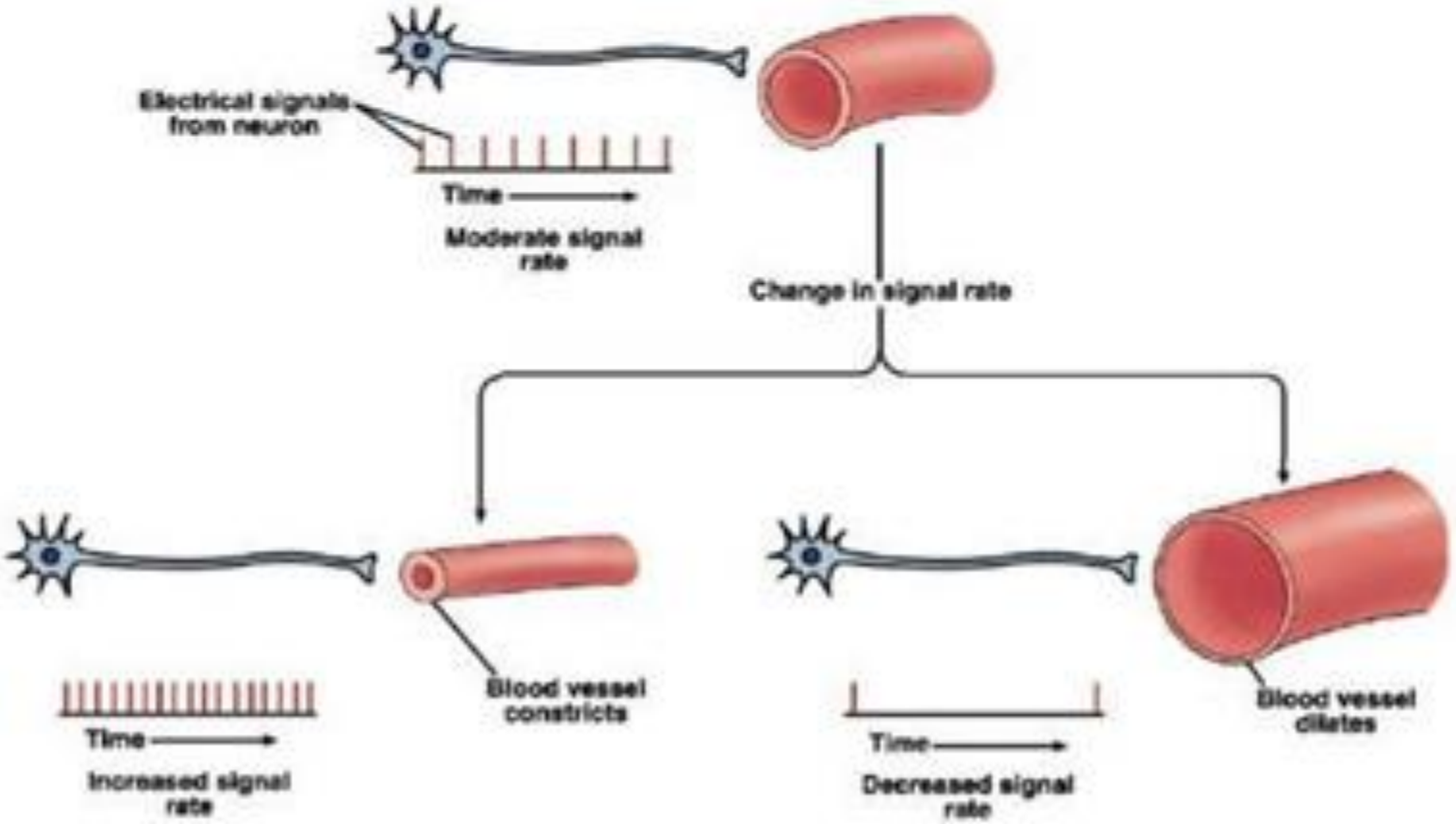

A great example is heart rate. An increase in sympathetic stimulation causes HR to increase whereas an increase in parasympathetic stimulation causes HR to decrease

**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)

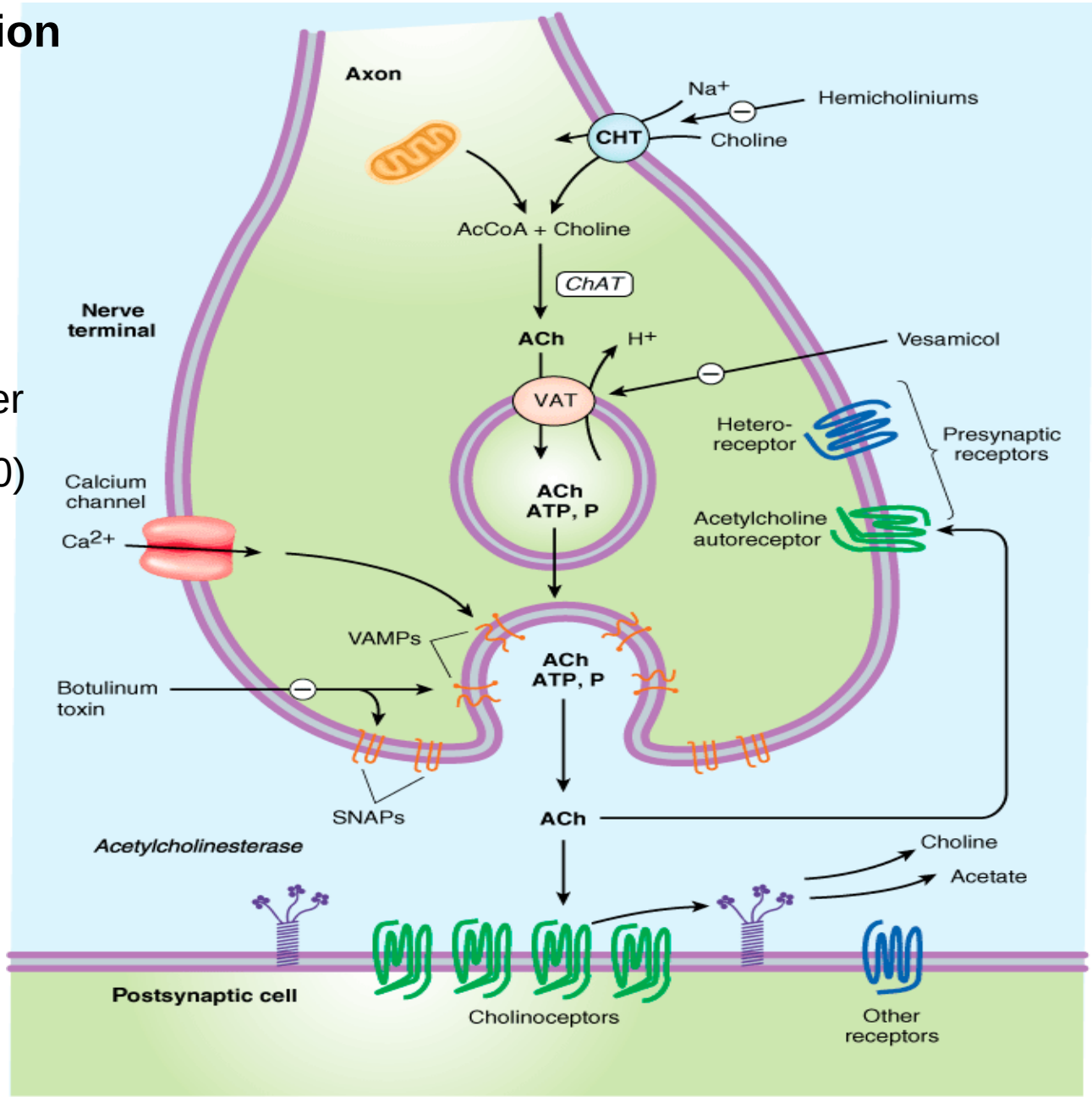
3-Release: exocytosis.

4-Interaction with post synaptic receptors

5- hydrolysis of Ach by Ach.esteras.

Drugs can act on all sites of cholinergic transmission.

***VAMPS:vesicle*** detaicossa-nietorp enarbmem

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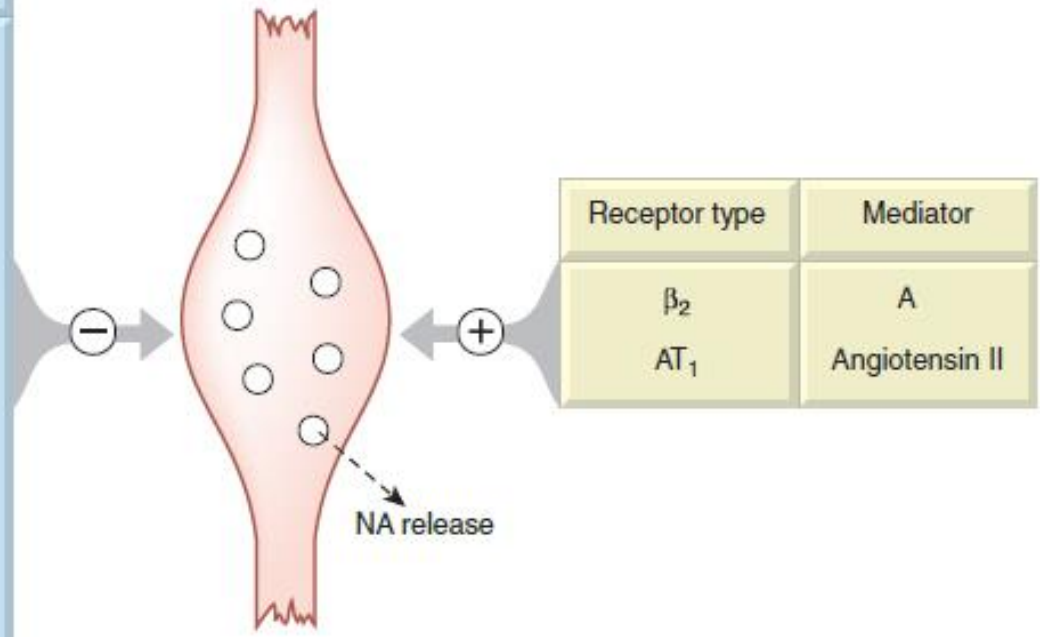
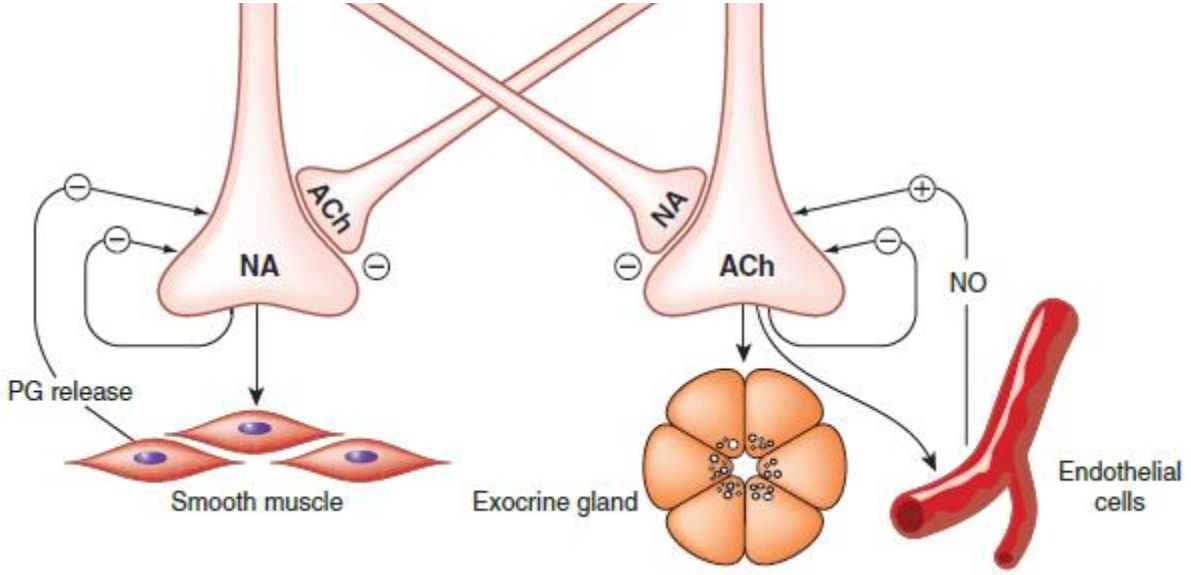
# Presynaptic receptors

| Mediator | Receptor type |
|---|---|
| ACh | Musc. |
| NA/A | $\alpha_2$ |
| 5-HT | 5-HT$_1$ |
| Adenosine | $A_1$ |
| PGE | EP |
| Histamine | $H_2$ |
| Enkephalin | $\mu$, $\delta$ |
| Dopamine | $D_2$ |
| ATP | P2X / P2Y |
| Endocannabinoids | $CB_1$ |

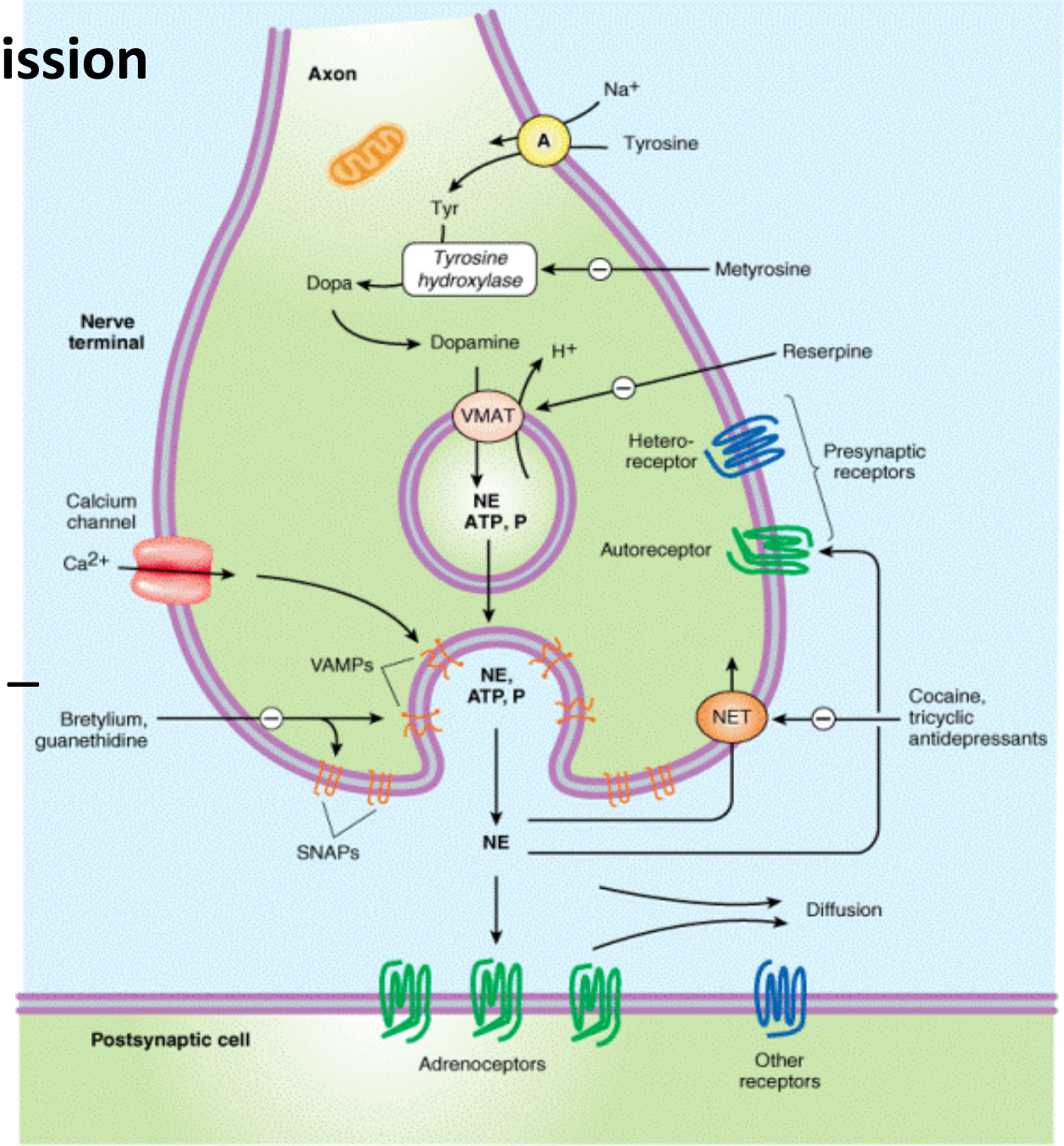


# Adrenergic Transmission

VAT; vesicular Mono Amine Transporter

SNAPs: synaptosome – Associated proteins.

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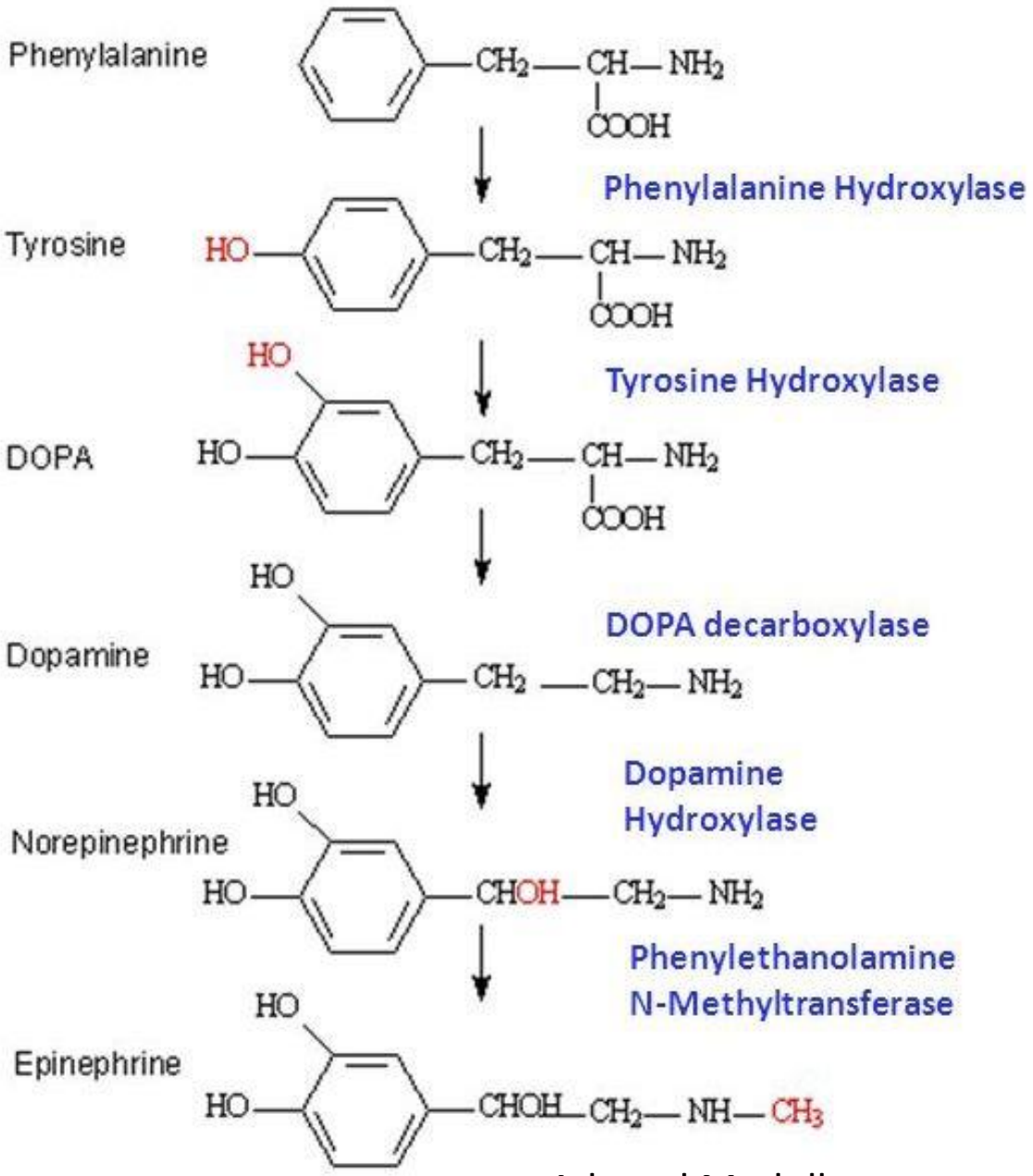
# Synthesis of Norepinephrine

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.




Adrenal Medulla

**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.

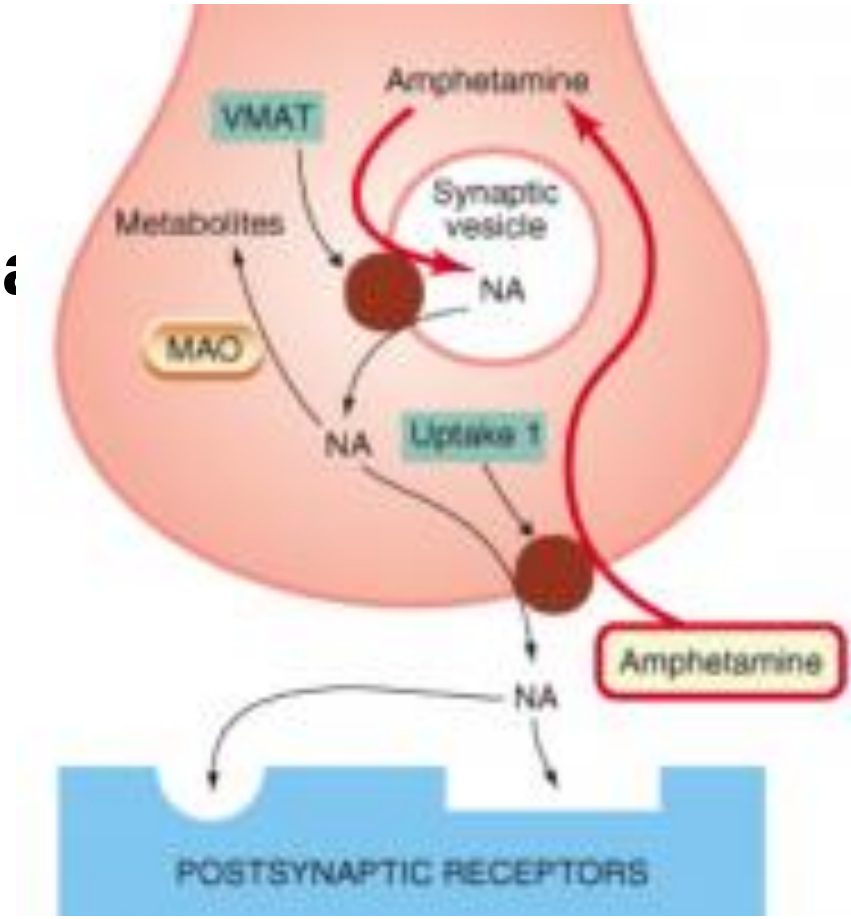
Release can be blocked by guanethidine and pretylium.

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

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

## 2- Calcium independent relea

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.

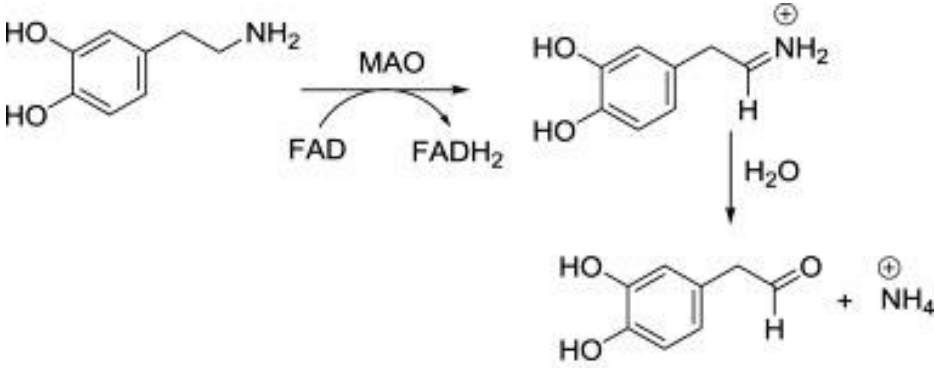



Ne is transported into the synaptic cleft by reverse transport via NET.

They **produce an indirect sympathomimetic effect**

# Metabolism of Catecholamines:

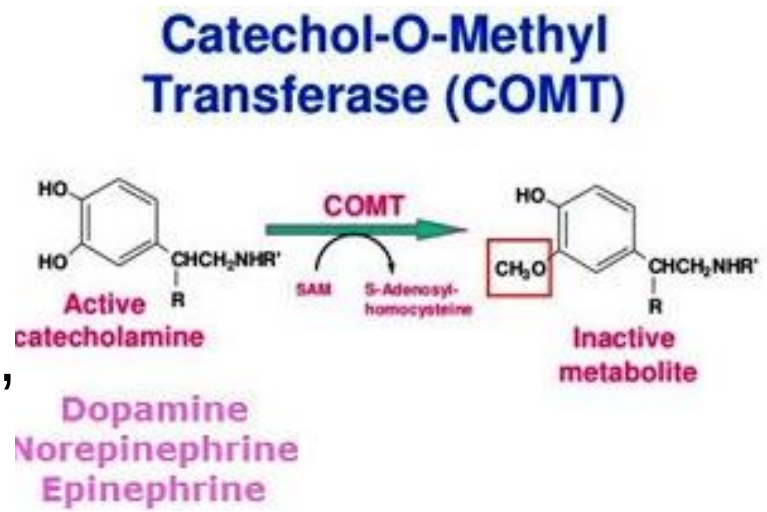
NE effects are terminated by neuronal reuptake (uptake1). 80% of the released NE are transported into the neuron by MAT (Mono amine Transporter).




**Monoamine oxidase (MAO)** in 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.

**Muscarinic M5:** CNS neurons.

**Nicotinic NN:** Postganglionic neurons, some presynaptic cholinergic terminals.

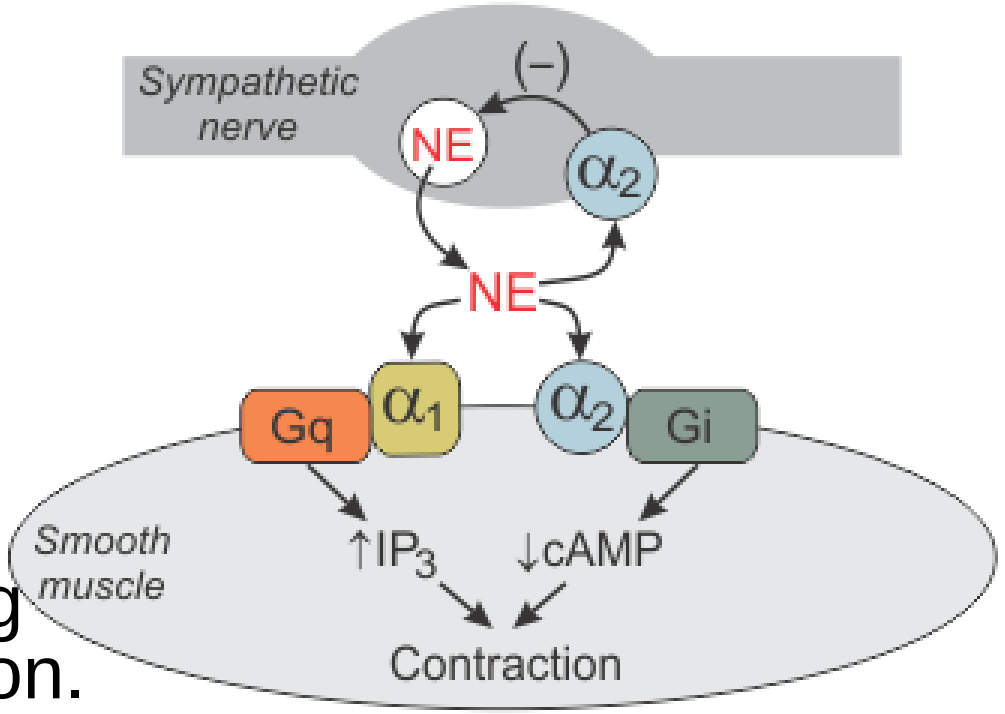
**Nicotinic NM:** Skeletal muscle neuromuscular end plates.

**Adrenoceptors**

**Alpha1 (α)**1

Postsynaptic, especially smooth muscle.

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



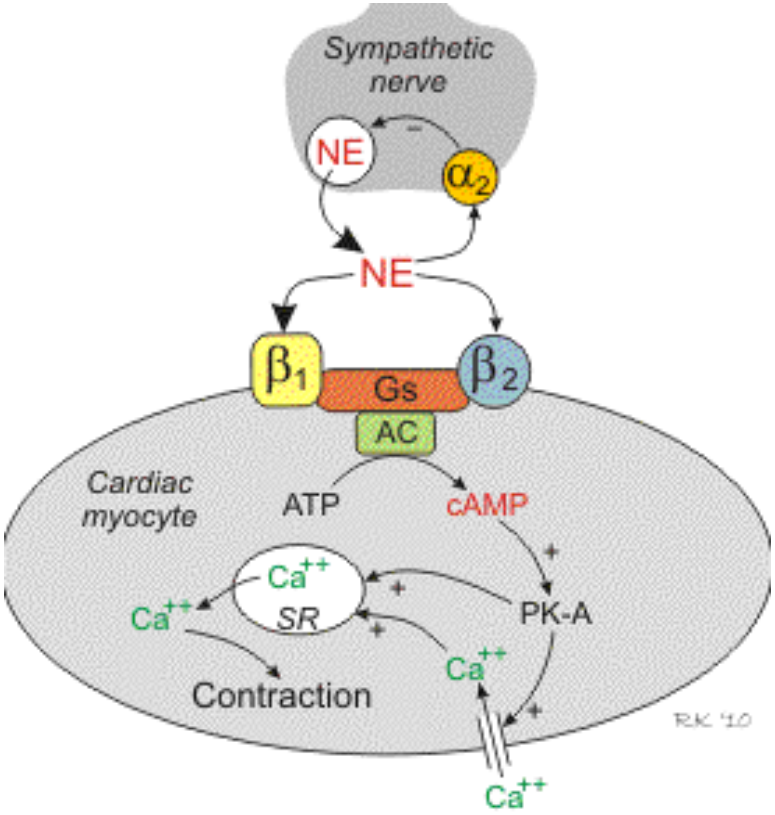

**Alpha2 (α)**

**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.

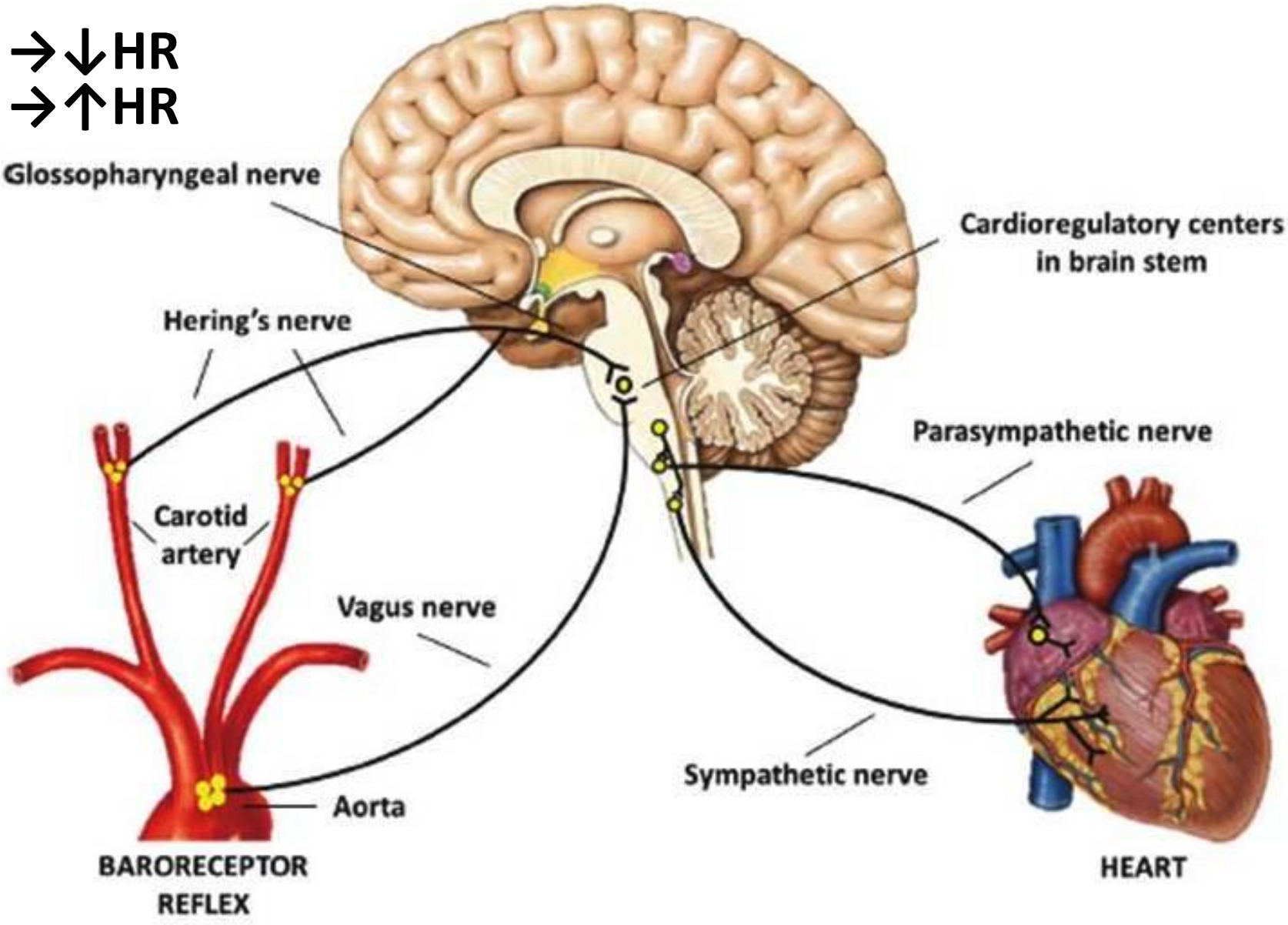
Stimulation of adenylyl cyclase and increased cAMP.

**D2 (DA 2, D3, D4)** Brain, especially smooth muscle; presynaptic nerve terminals (D2).

Inhibition of adenylyl cyclase; increased potassium conductance.

## Baroreceptors:

↑ BP →↓HR
↓ BP →↑HR

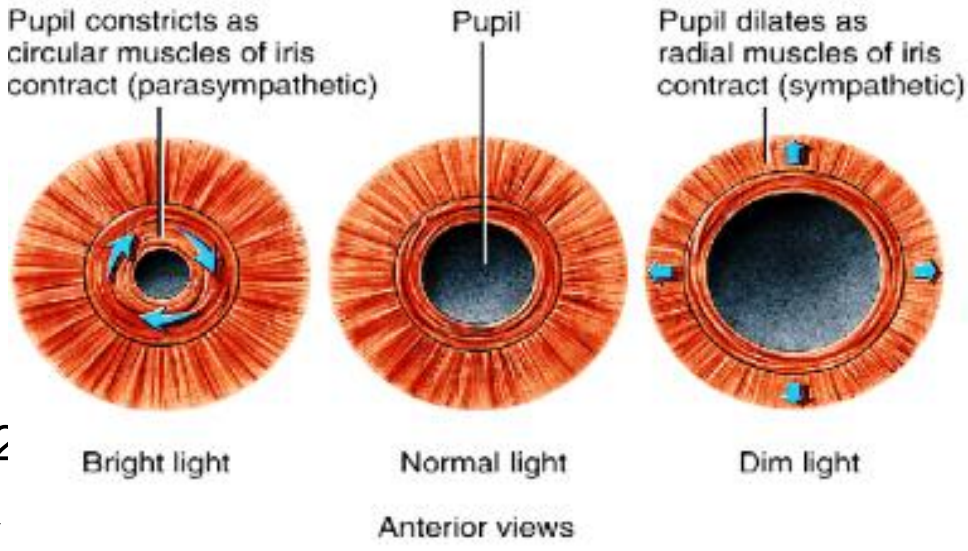


# Direct Effects of Autonomic *Nerve* Activity

**Organ Sympathetic Parasympathetic**

**Eye, Iris.**
radial muscle α1 mydriasis M3 miosis.
circular muscle.

Ciliary muscle M3 Contracts.
near vision.




**Heart**
Sinoatrial node ▲HR β1 ▼ HR M2
Ectopic pacemakers Accelerates β1
Contractility ▲ β1 ▼

**Blood vessels**
Skin, splanchnic vessels Contracts α1
Skeletal muscle vessels Relaxes β2 Endothelium (drug effect) M3, M5 Releases (**NO**)

| | | | | |
|---|---|---|---|---|
| **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 | |
| | Gluconeogenesis | | β2 α | |
| Fat cells | Lipolysis | | β3 | |
| **Kidney** | Renin release | | β1 | |