

# **Autonomic Nervous System**

**Introduction**

2018 - 2019

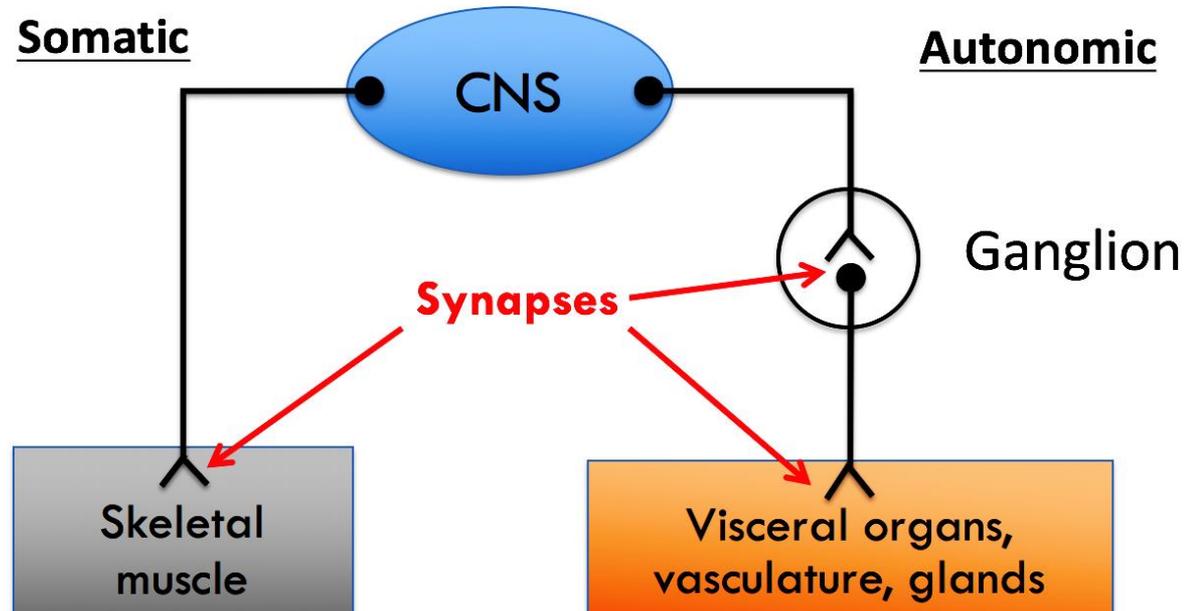
The nervous system is divided into:

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.



Autonomic nervous system has **3 subdivisions-**

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

## Enteric nervous system

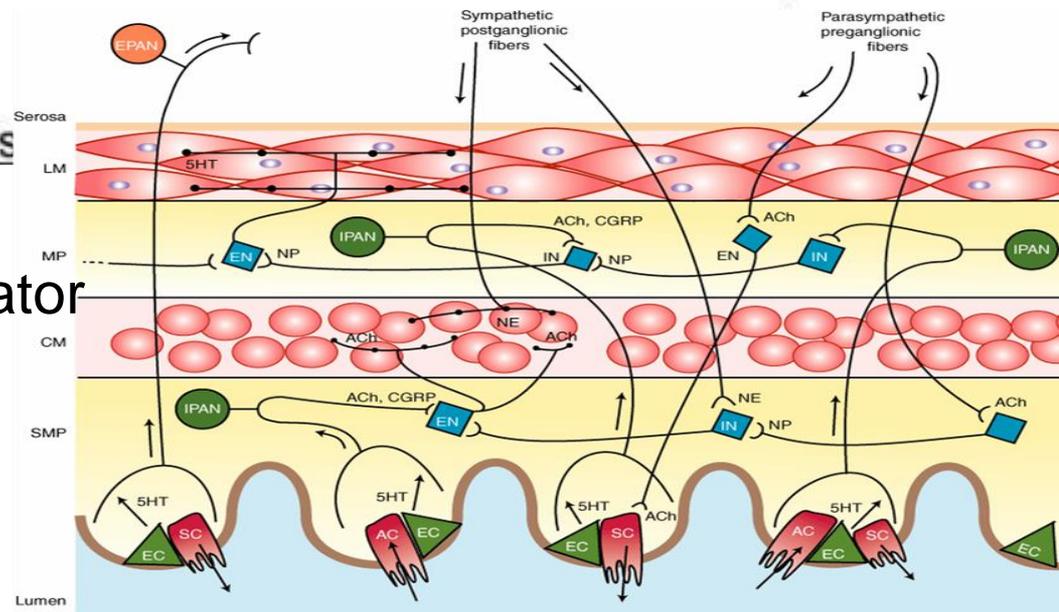
Enteric neurons form plexuses that surround and extend along the length of the gut, including stomach, small and large intestines.

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.

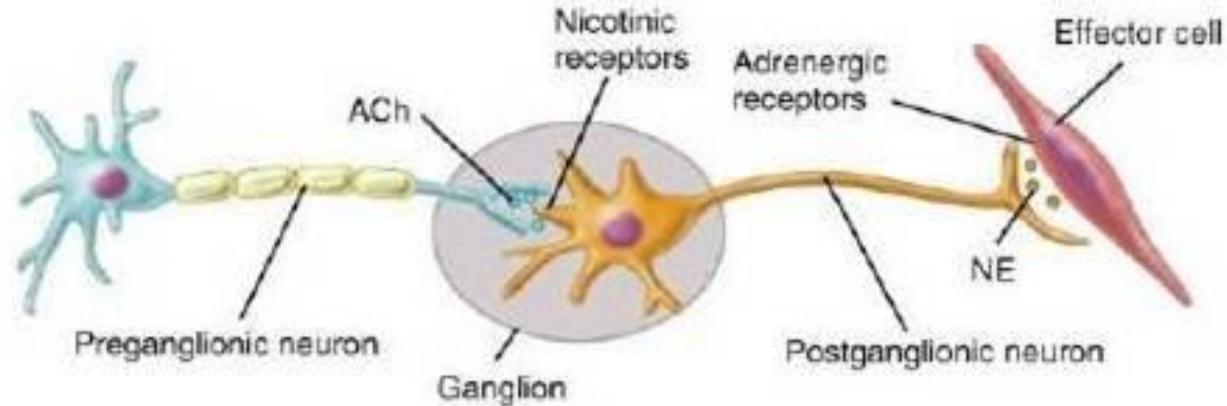
It is modulated by the symp. & parasymp systems.



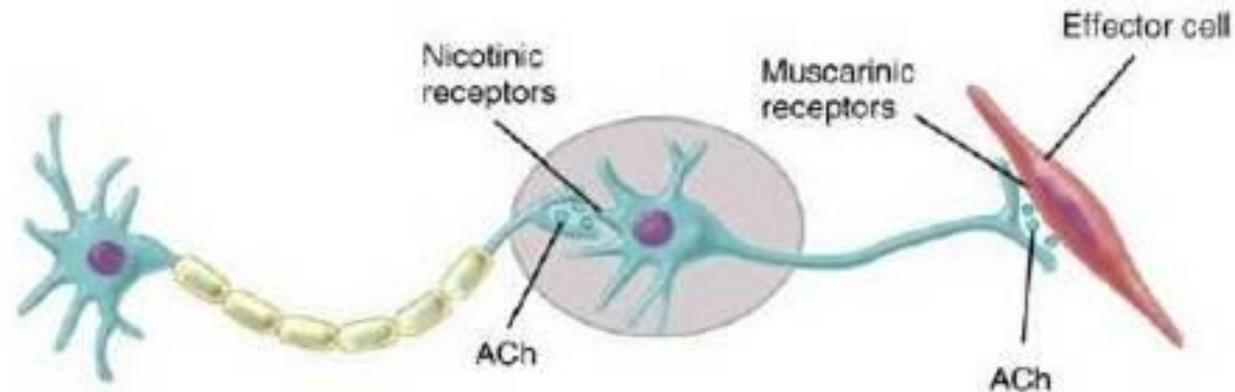
# ANS Neurons

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

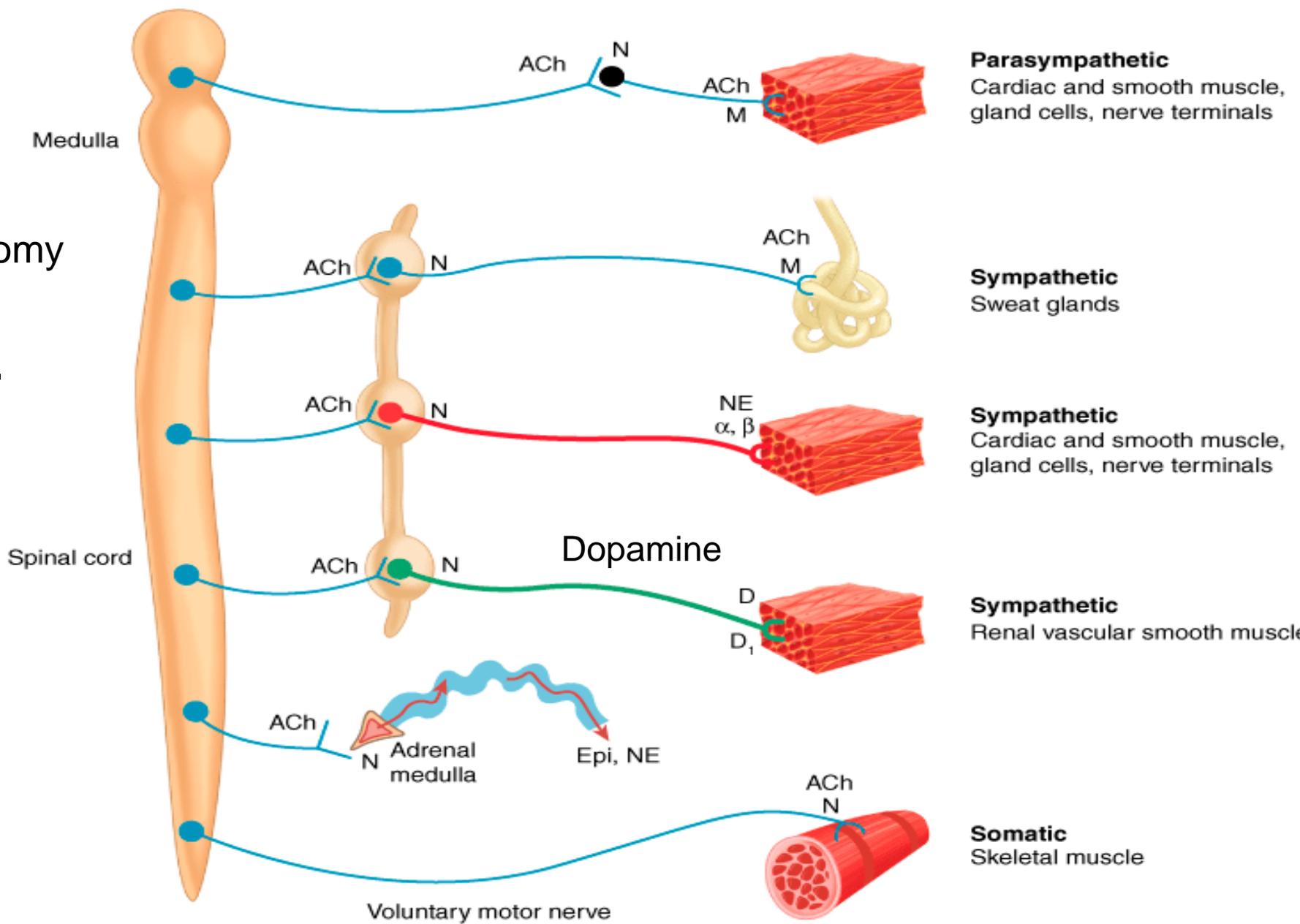
- Adrenergic



- Cholinergic



# Anatomy of ANS.



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

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# Parasympathetic cell bodies in brainstem

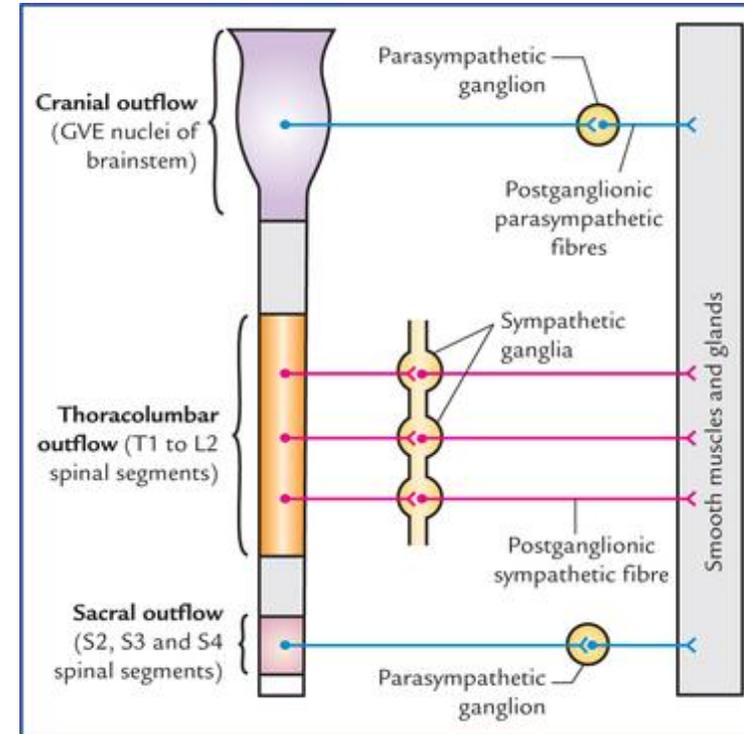
& sacral spinal cord: ***craniosacral outflow.***

**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.***

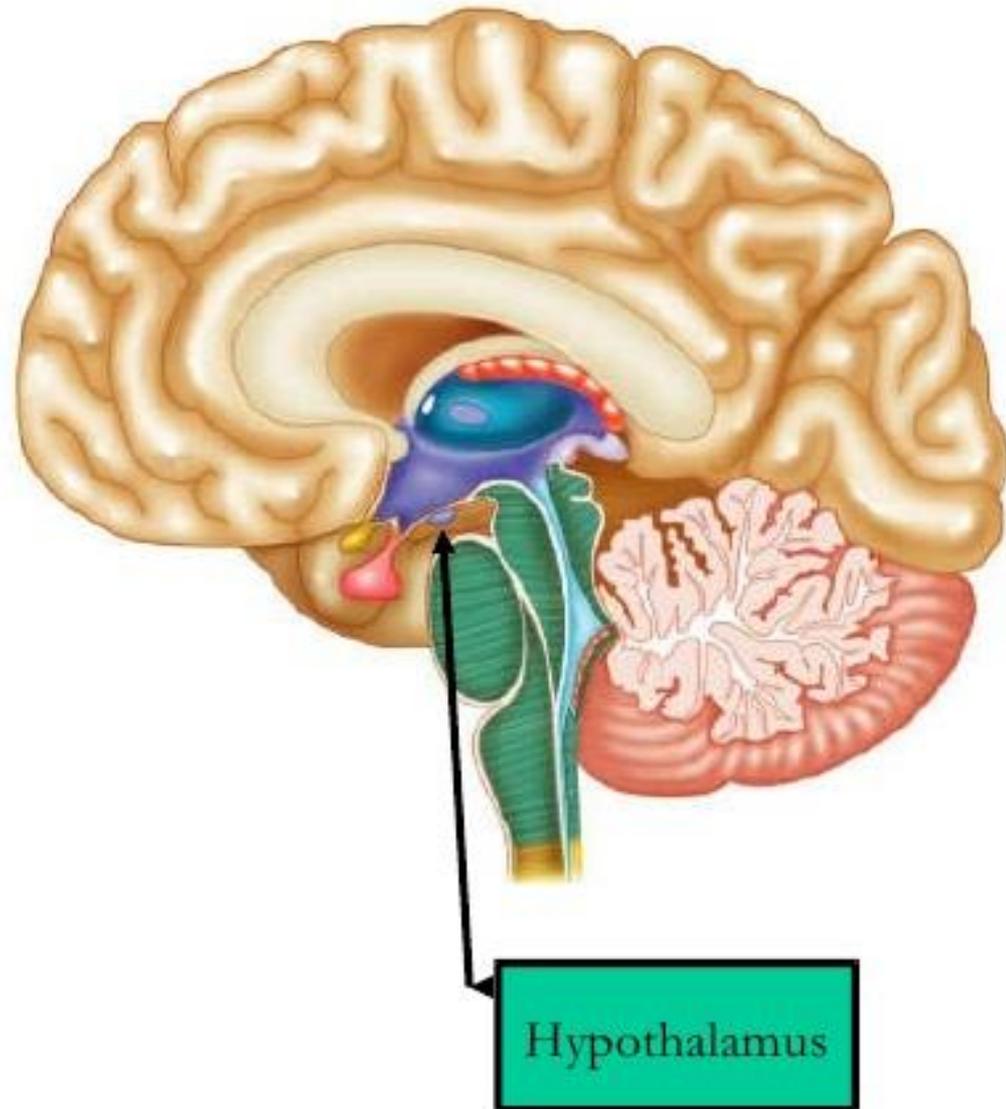
One sympathetic preganglionic neuron may have many branches and may synapse with 20+ postganglionic neurons.

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

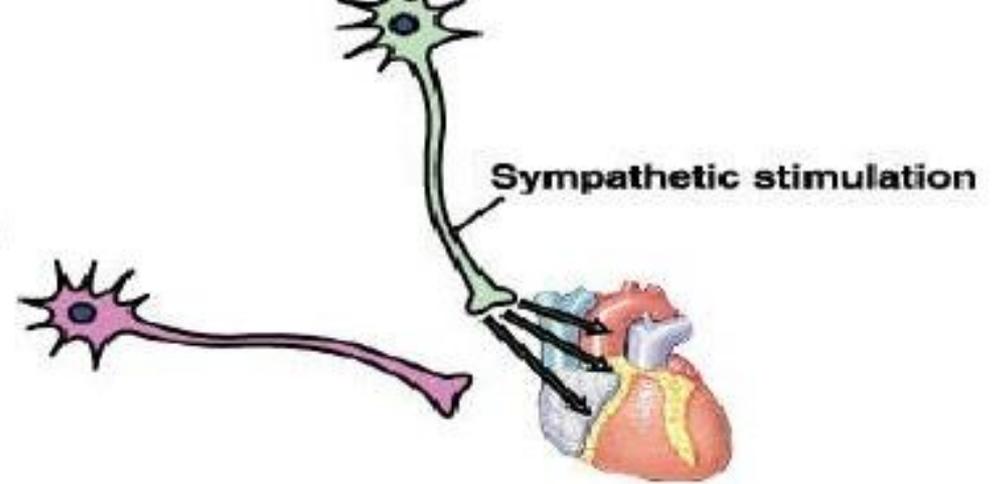
## – Sympathetic

- 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.

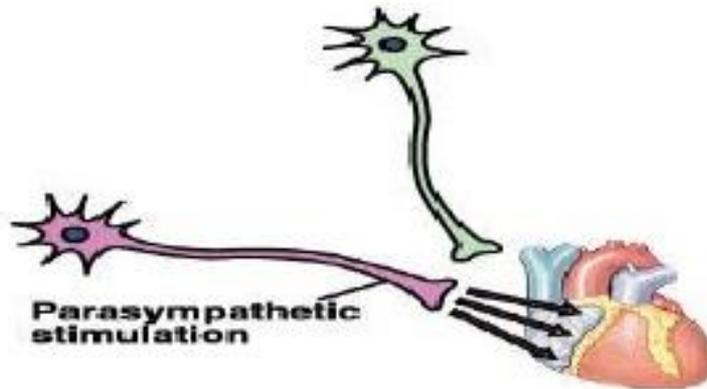
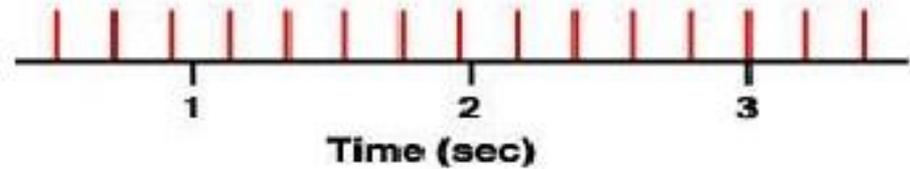
**Sympathetic and parasympathetic systems  
have antagonistic effects**

# Antagonistic Control

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



Heart rate increases



Heart rate decreases



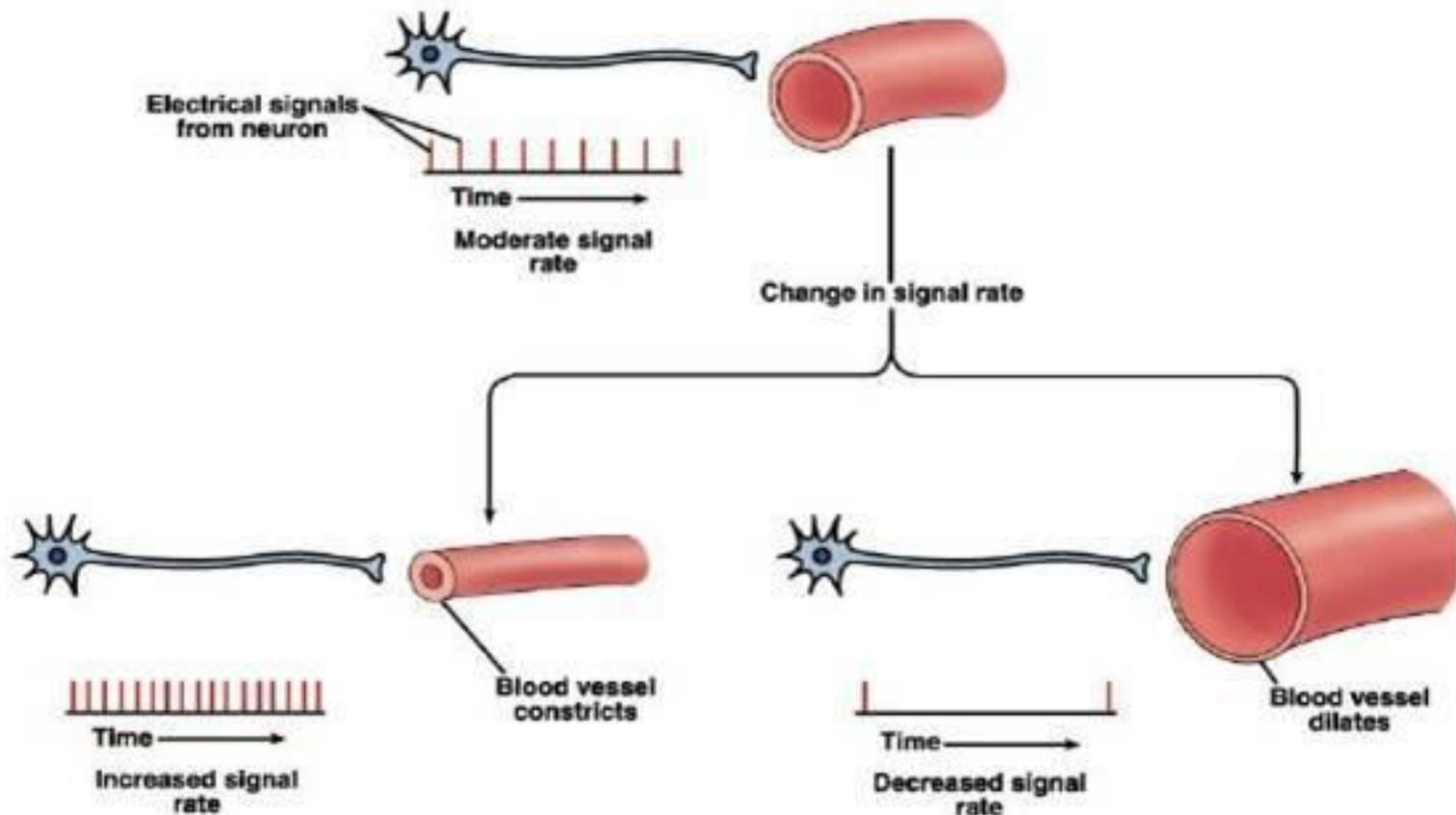
A great example is heart rate. An increase in sympathetic stimulation causes HR to increase whereas an increase in parasympathetic stimulation causes HR to decrease

### 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)

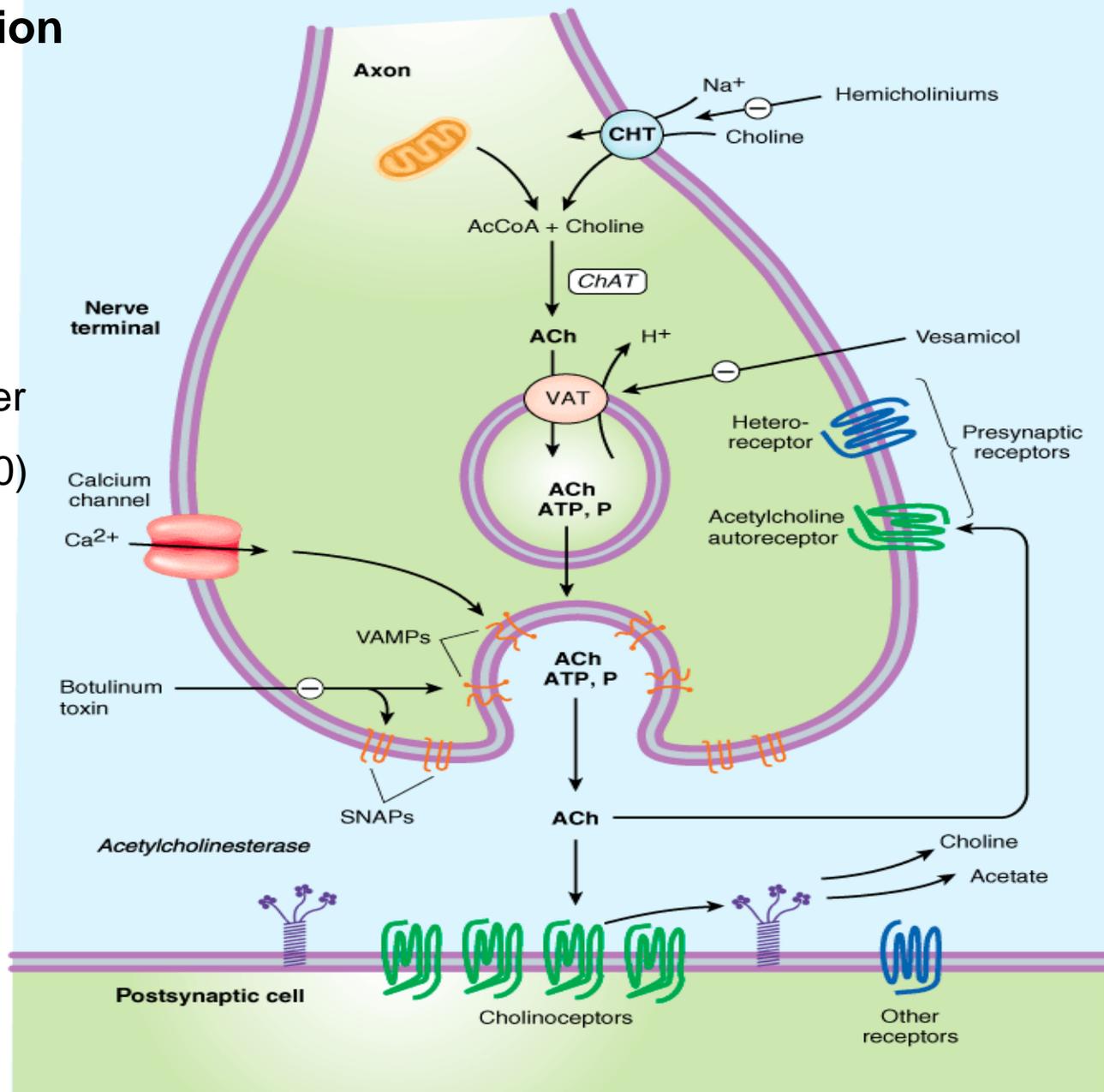
3-Release: exocytosis.

4-Interaction with post synaptic receptors

5- hydrolysis of Ach by Ach.esteras.

Drugs can act on all sites of cholinergic transmission.

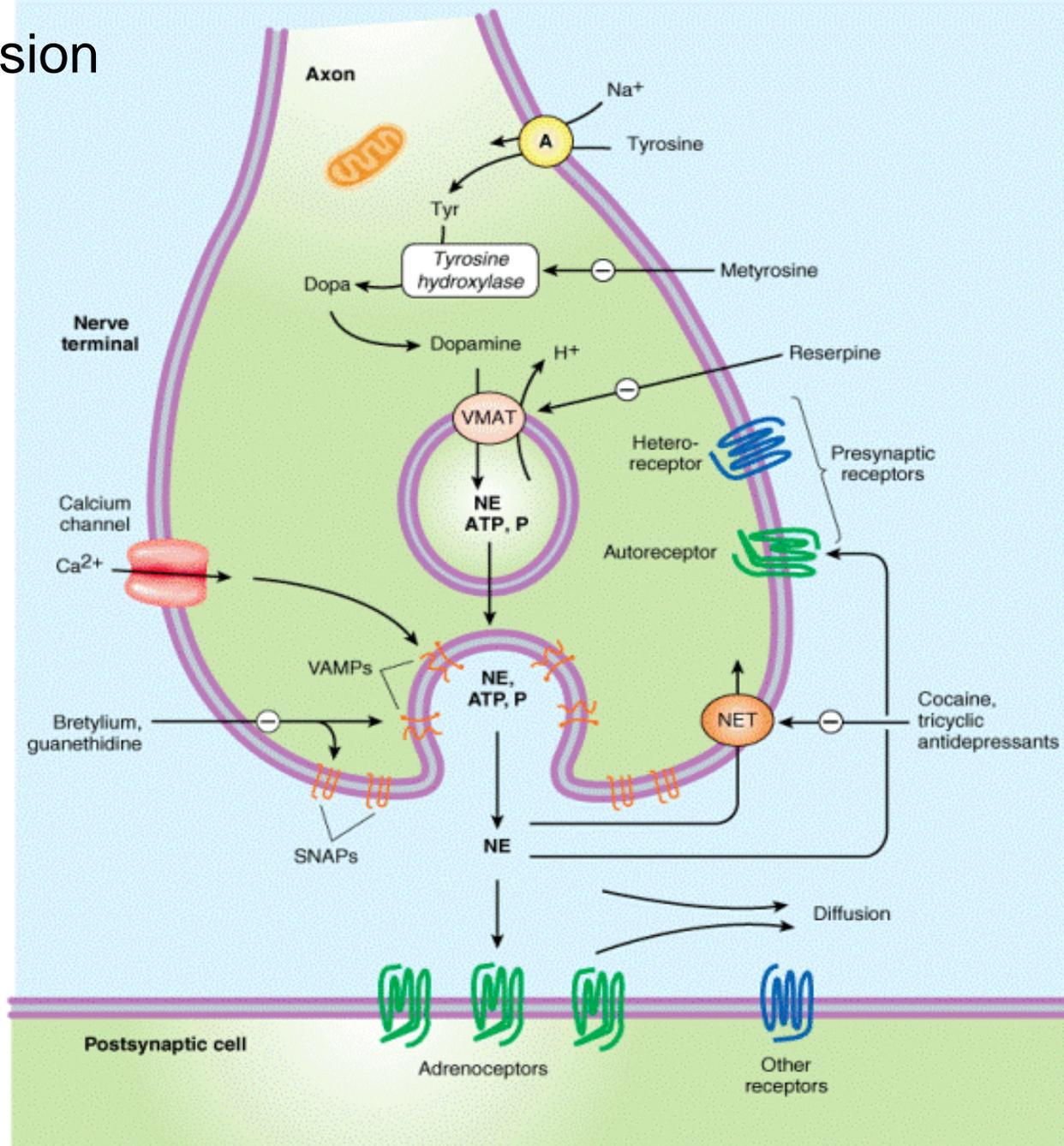
**VAMPs: vesicle** detaicossa-  
nietorp enarbmem



# Adrenergic Transmission

VAT; vesicular  
Mono Amine Transporter

SNAPs: synaptosome –  
Associated proteins.

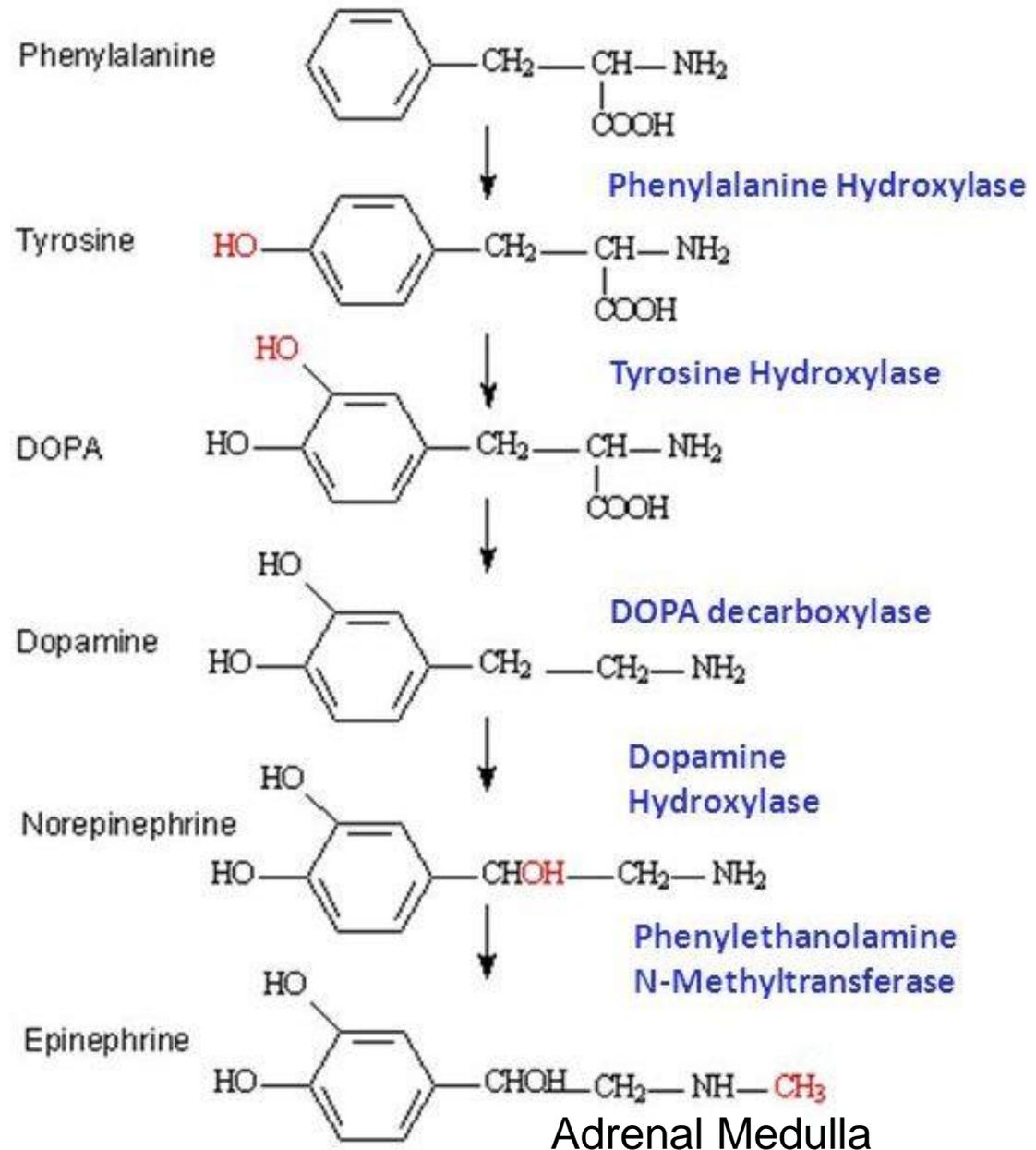


# Synthesis of Norepinephrine

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

DA is transported into  
Storage vesicle by VMAT1  
(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:

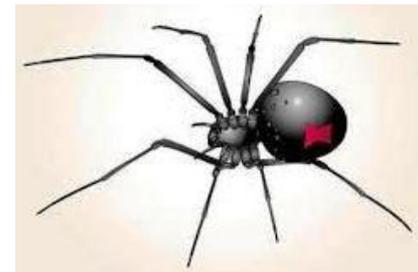
## 1- Calcium dependent exocytosis.

NE + cAMP + protein + Dopamine- $\beta$ -hydroxylase are released.

Release can be blocked by guanethidine and pretylium.

$\omega$ -Conotoxin GVIA, Toxin of marine snails blocks Ca channels & reduce NE & Ach release.

$\alpha$ -Latrotoxin (Black widow spider venom) acts on vesicles causing explosive release of NE & Ach.



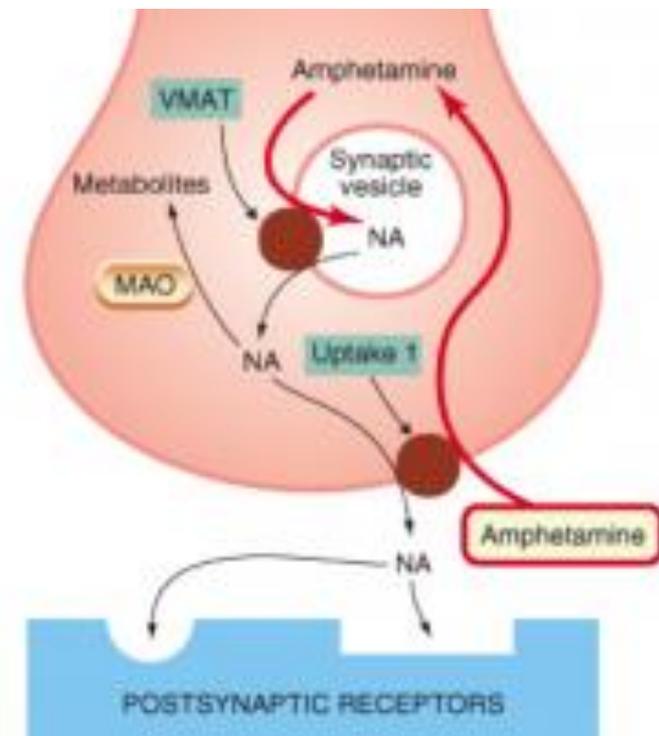
## 2- Calcium independent release.

Tyramine, amphetamine are transported by NET (NE Transporter) into the neuron then transported by VMAT into the vesicles.

They displace NE from the vesicular stores, into the cytoplasm.

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

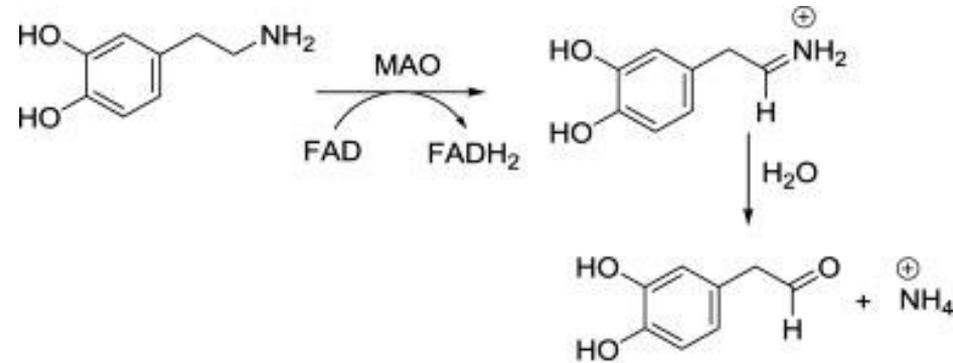
They **produce an indirect sympathomimetic effect**



# Metabolism of Catecholamines:

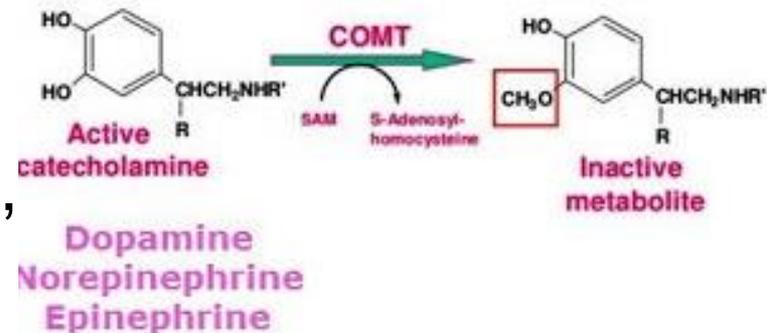
NE effects are terminated by neuronal reuptake (uptake<sub>1</sub>). 80% of the released NE are transported into the neuron by MAT (Mono amine Transporter).

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

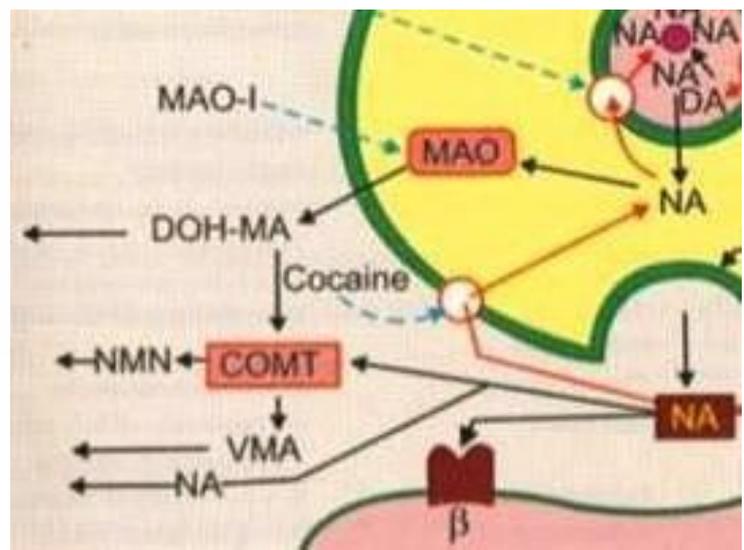
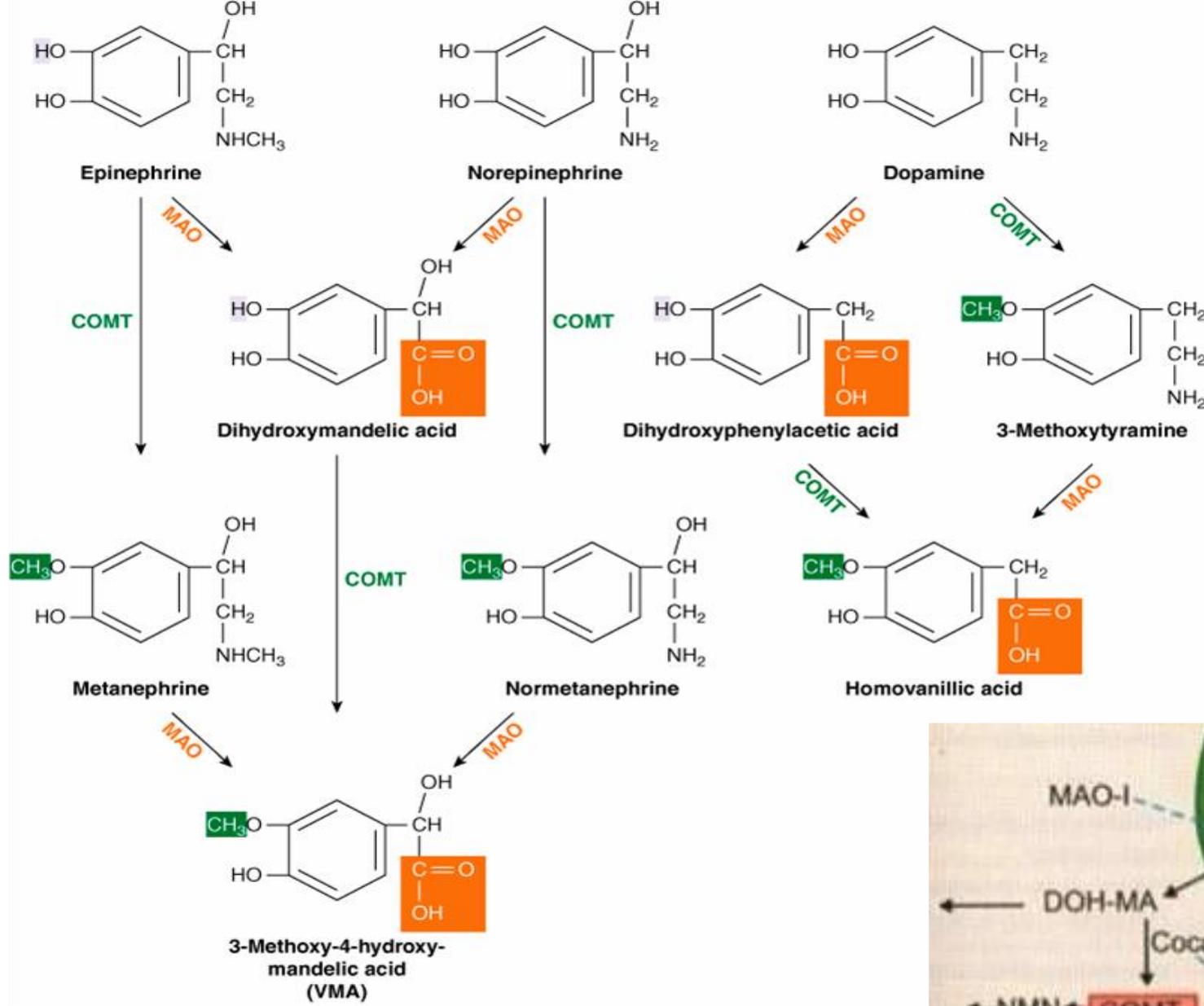


**Catechol-O-Methyl transferase (COMT)** transfers methyl group from S-adenosyl methionine into the OH-group in the meta position of the catechol ring.

## Catechol-O-Methyl Transferase (COMT)



**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 ( $\alpha$ )1

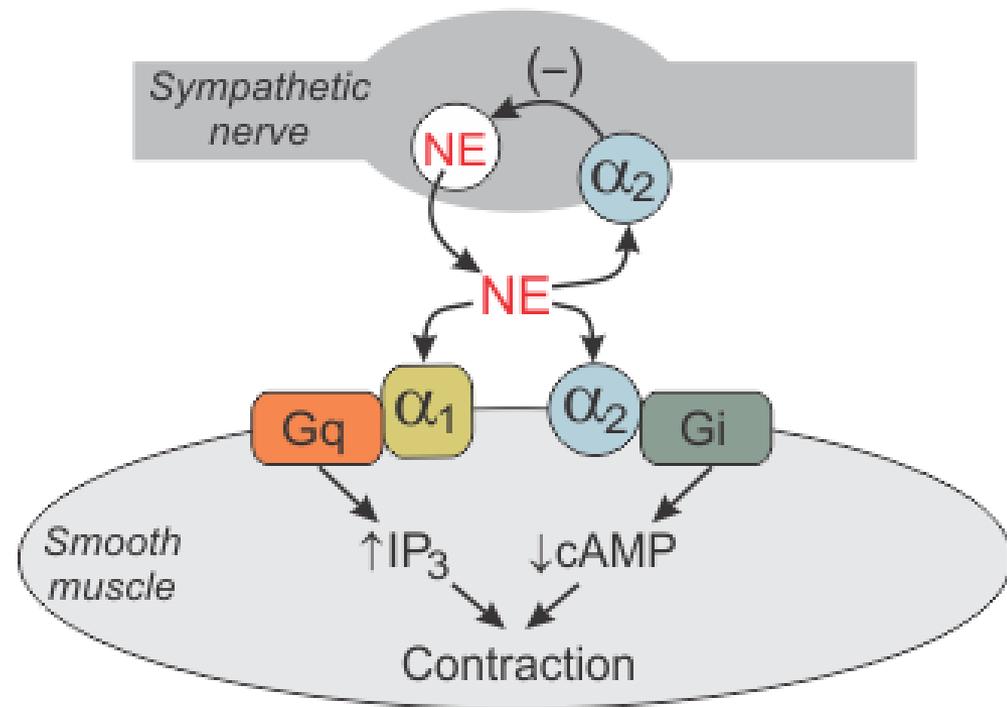
Postsynaptic, especially smooth muscle.

Formation of IP<sub>3</sub> and DAG, increased intracellular Ca producing smooth muscle contraction.

**Alpha2 ( $\alpha$ )2** Presynaptic adrenergic nerve terminals, platelets, lipocytes, smooth muscle.

Inhibits NE release.

Inhibition of adenylyl cyclase, decreased cAMP



## Beta1 ( $\beta_1$ )

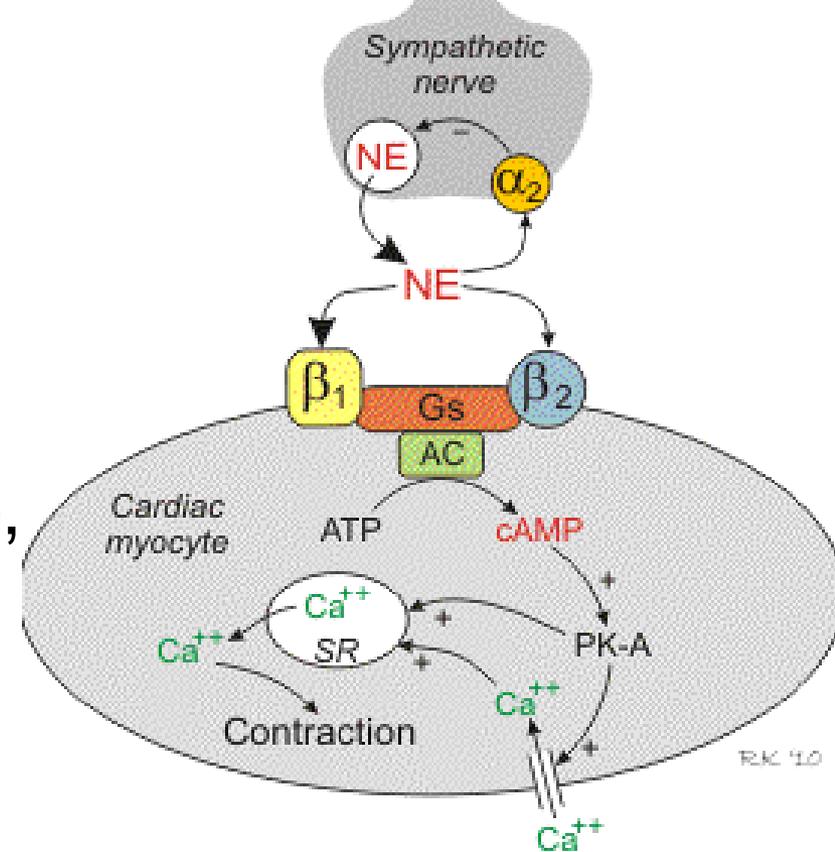
Heart, lipocytes, brain; juxtaglomerular apparatus of renal tubules.

Stimulation of adenylyl cyclase, increased cAMP

**Beta2 ( $\beta_2$ )** smooth muscle & cardiac muscle.

Stimulation of adenylyl cyclase and increased cAMP.

**Beta3 ( $\beta_3$ )** 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.

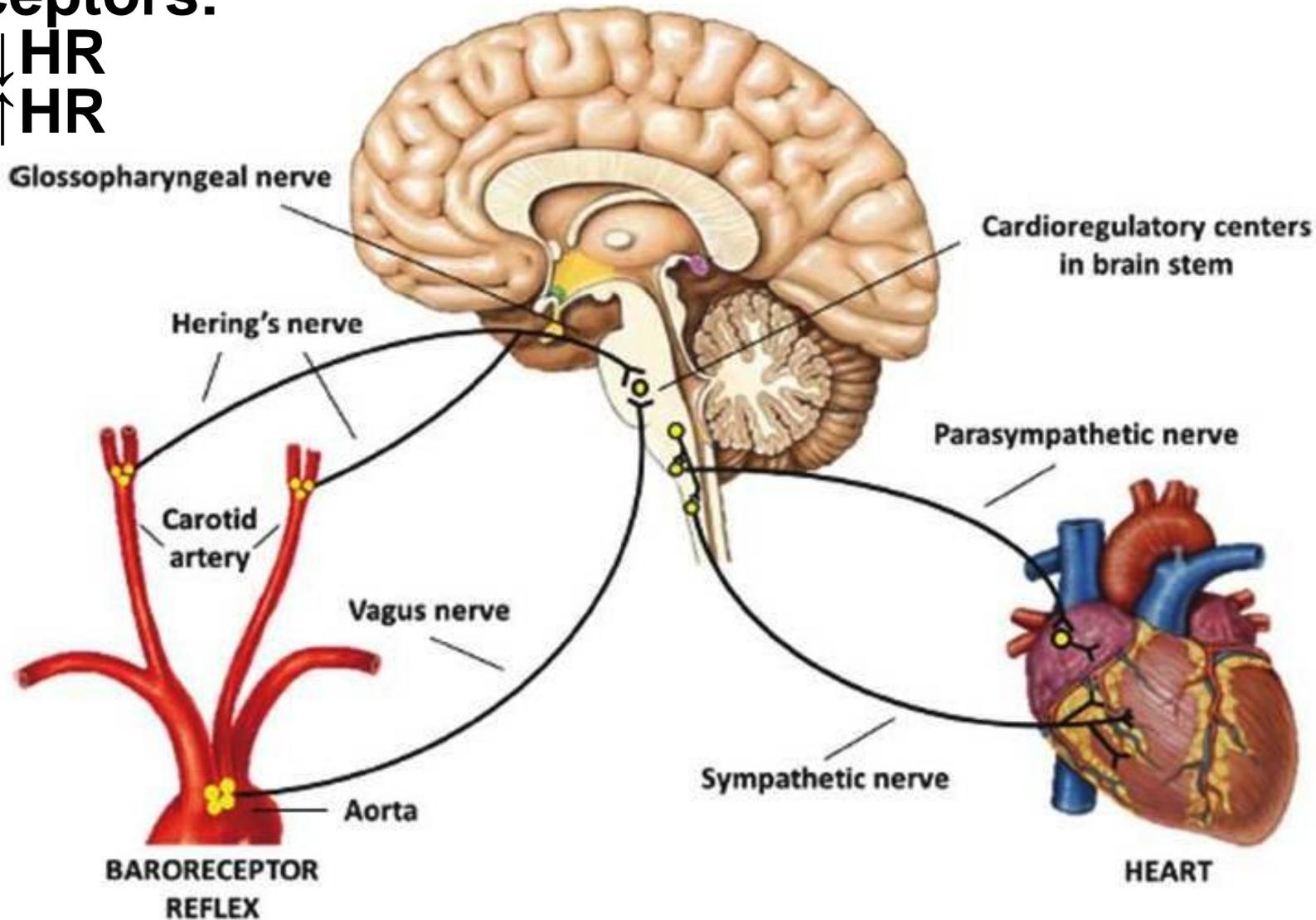
**D4** Brain, cardiovascular system.

Inhibition of adenylyl cyclase

# Dual innervations of most organs by Sympathetic & Parasympathetic systems.

## Baroreceptors:

↑ BP → ↓ HR  
↓ BP → ↑ HR



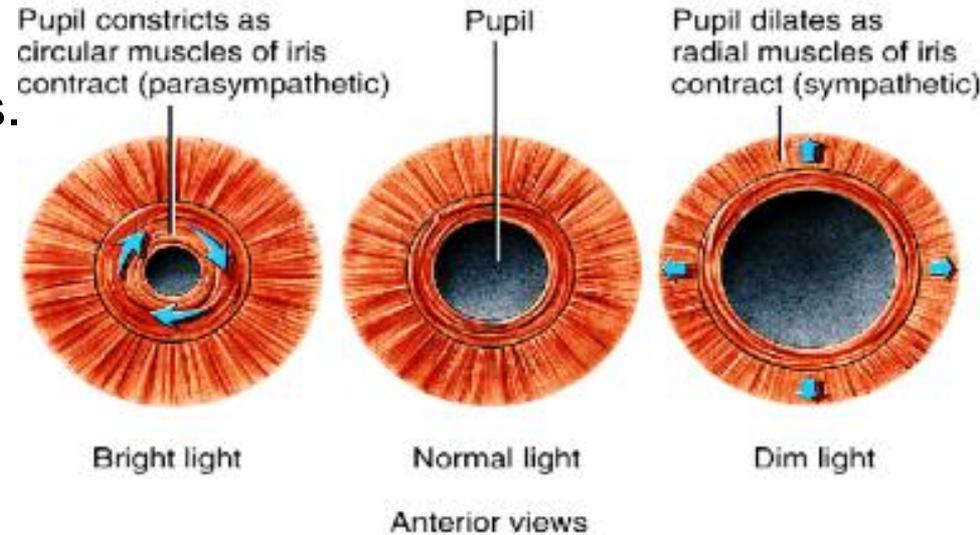
# Direct Effects of Autonomic *Nerve* Activity

Organ	Sympathetic	Parasympathetic
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## Eye, Iris.

radial muscle	$\alpha 1$ mydriasis	M3 miosis.
circular muscle.		

Ciliary muscle	M3 Contracts.	near vision.
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## Heart

Sinoatrial node	$\blacktriangle$ HR $\beta 1$	$\blacktriangledown$ HR	M2
Ectopic pacemakers	Accelerates	$\beta 1$	
Contractility	$\blacktriangle$ $\beta 1$	$\blacktriangledown$ (atria)	M2

## Blood vessels

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

**Bronchiolar smooth muscle** Relaxes  $\beta_2$  Contracts M3

**Gastrointestinal tract**

Smooth muscle Walls Relaxes  $\beta_2, \alpha_2$  Contracts M3  
 Sphincters Contracts  $\alpha_1$  Relaxes M3  
 Secretion Increases M3

**Genitourinary smooth muscle**

Bladder wall Relaxes  $\beta_2$  Contracts M3  
 Sphincter Contracts  $\alpha_1$  Relaxes M3  
 Uterus, pregnant Relaxes  $\beta_2$   
 Contracts  $\alpha$  Contracts M3  
 Penis, seminal vesicles Ejaculation  $\alpha$  Erection M

**Skin**

Pilomotor smooth muscle Contracts  $\alpha$   
 Sweat glands Increase M

**Metabolic functions**

Liver Glycogenolysis,  $\beta_2 \alpha$   
 Glyconeogenesis  $\beta_2 \alpha$   
 Fat cells Lipolysis  $\beta_3$   
 Kidney Renin release  $\beta_1$

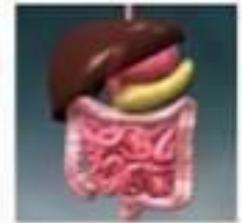
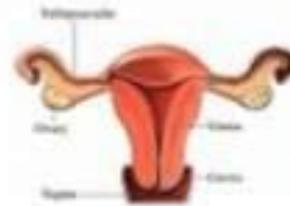
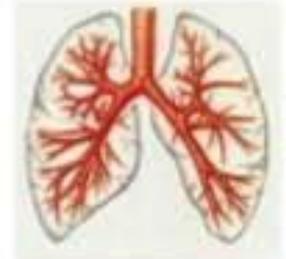
# Action on **alpha**-adrenoceptors

- **Arterioles and veins ( $\alpha_1$ ):** contraction and rise in BP
- **Eye ( $\alpha_1$ ):** decreased aqueous secretion and mydriasis
- **GIT ( $\alpha_1$ ):** contraction of sphincters
- **Bladder trigone ( $\alpha_1$ ):** contraction
- **Uterus ( $\alpha_1$ ):** contraction
- **Insulin secretion ( $\alpha_2$ ):** inhibited
- **Male sex organs:** ejaculation
- **Salivary glands ( $\alpha_1$ ):** **Viscous saliva secretion**



# Action on **beta**-adrenoceptors

- **Arterioles and veins ( $\beta_2$ ):** dilation and fall in BP
- **Heart ( $\beta_1$ ):** increased heart rate, force, and conduction velocity
- **Lung ( $\beta_2$ ):** bronchodilation
- **Eye ( $\beta_2$ ):** enhanced aqueous secretion
- **GIT ( $\beta_2$ ):** intestinal relaxation
- **Bladder detrusor ( $\beta_2$ ):** relaxation
- **Uterus ( $\beta_2$ ):** relaxation
- **Liver ( $\beta_2$ ):** glycogenolysis
- **Insulin and glucagon secretion ( $\beta_2$ ):** augr
- **Fat ( $\beta_3$ ):** lipolysis
- **Kidney ( $\beta_1$ ):** renin release



**Augmentation**

