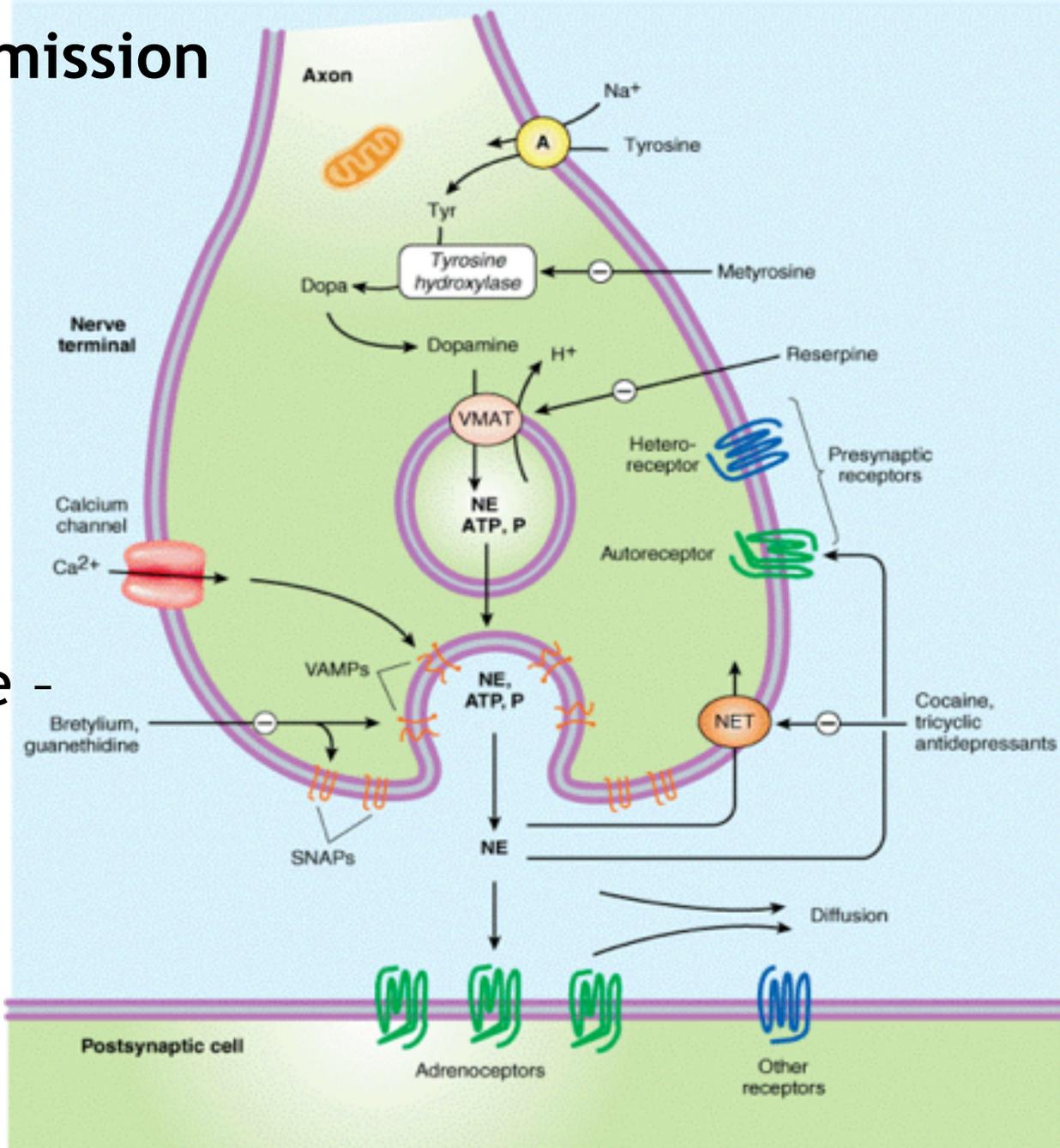


ANS Introduction 2

Adrenergic Transmission

VAT; vesicular
Mono Amine
Transporter

SNAPs: synaptosome
Associated proteins.



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

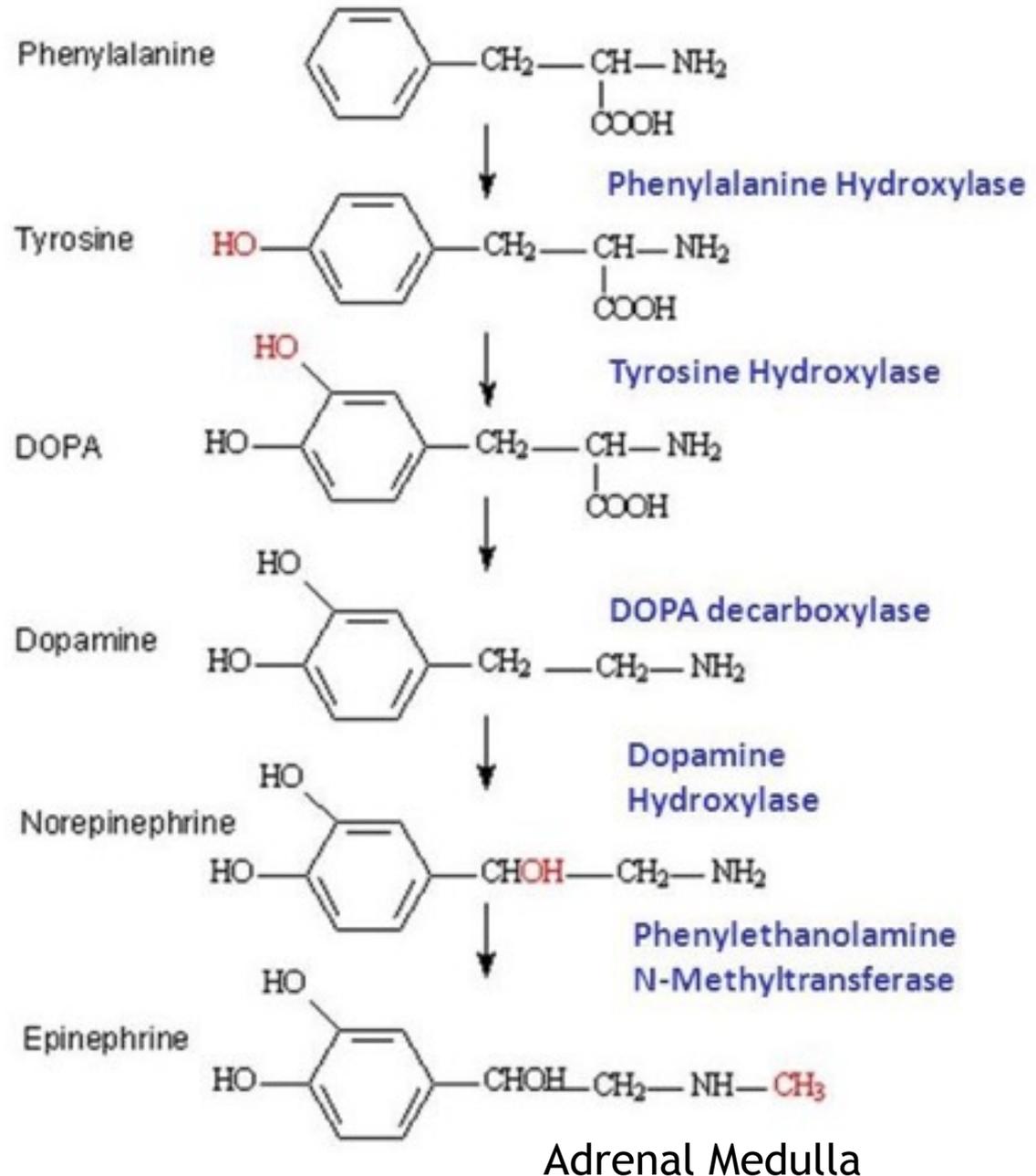
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Synthesis of Norepinephrine

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.



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.

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.

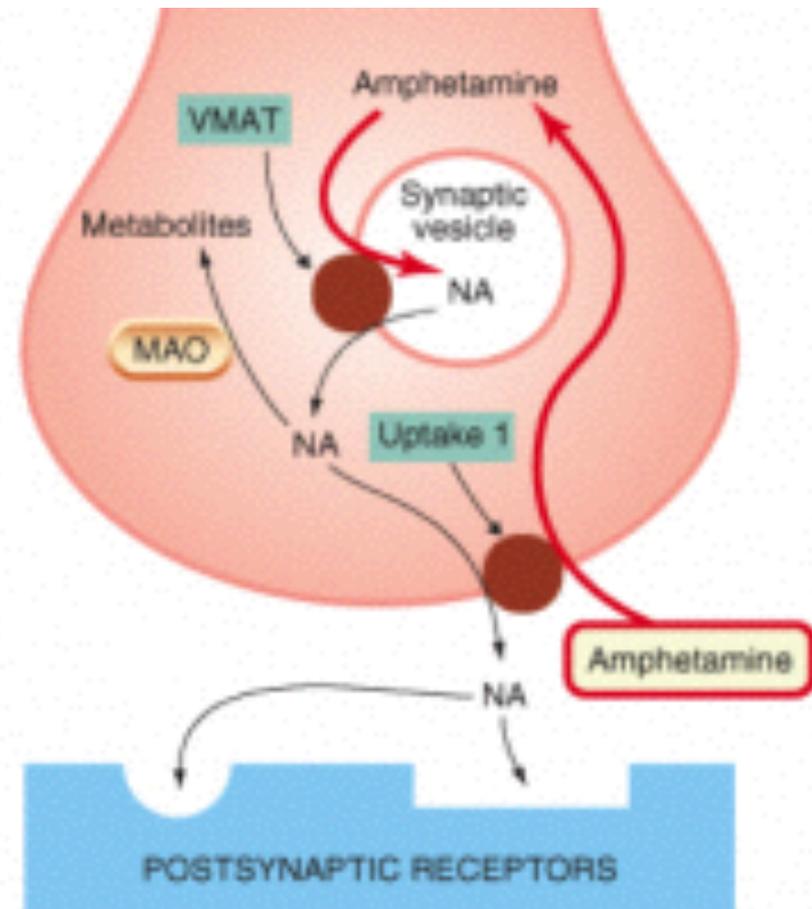


2- Calcium independent release

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



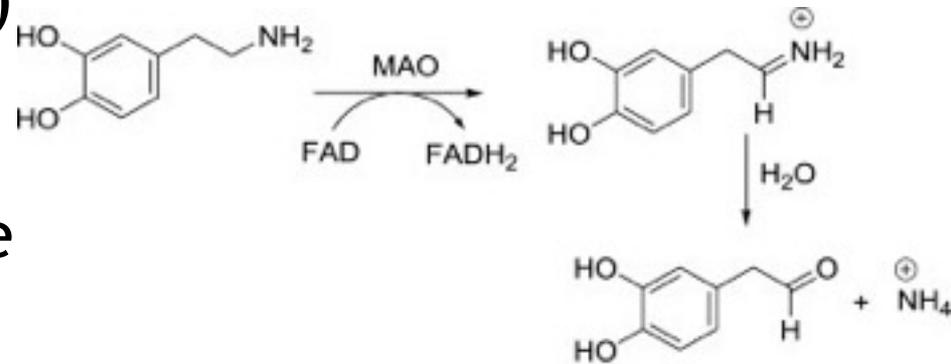
Metabolism of Catecholamines:

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

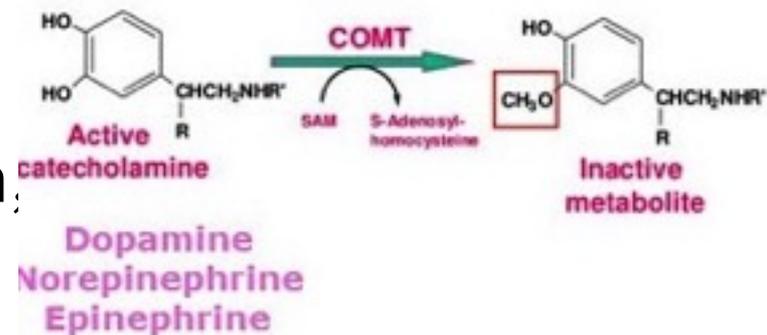
Monoamine oxidase (MAO) in mitochondria produces oxidative deamination of mono amines.

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.



Catechol-O-Methyl Transferase (COMT)



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)

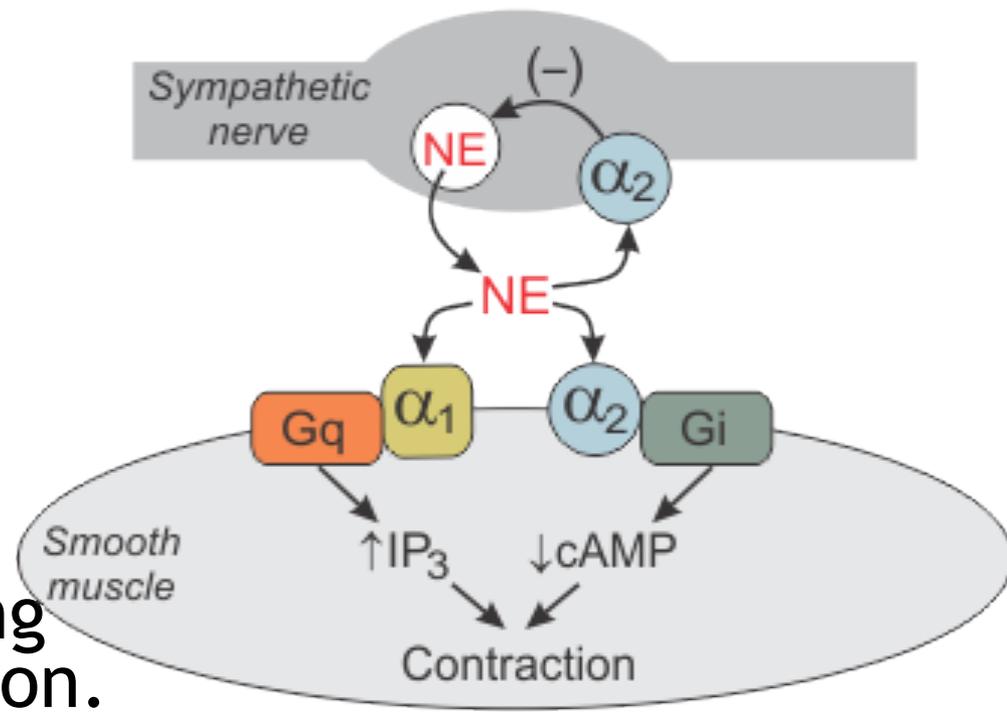
Postsynaptic, especially smooth muscle.

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

Alpha2 (α 2)

Presynaptic adrenergic nerve terminals, platelets, lipocytes, smooth muscle.
Inhibits NE release.

Inhibition of adenylyl cyclase, decreased cAMP



Beta1 (β_1)

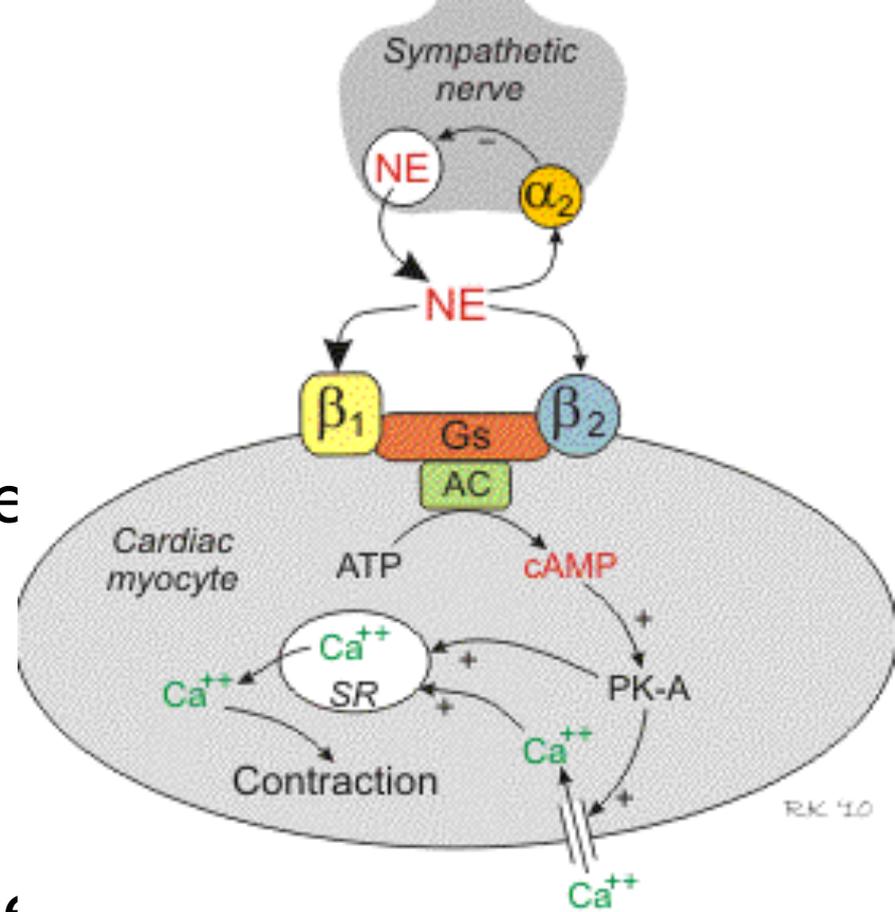
Heart, lipocytes, brain; juxtaglomerular apparatus of renal tubules.

Stimulation of adenylyl cyclase increased cAMP

Beta2 (β_2) smooth muscle & cardiac muscle.

Stimulation of adenylyl cyclase and increased cAMP.

Beta3 (β_3) lipocytes; Stimulation of adenylyl cyclase & increased cAMP



Dopamine receptors

D1 (DA 1, D5)

Brain, especially smooth muscle of the renal vascular bed.

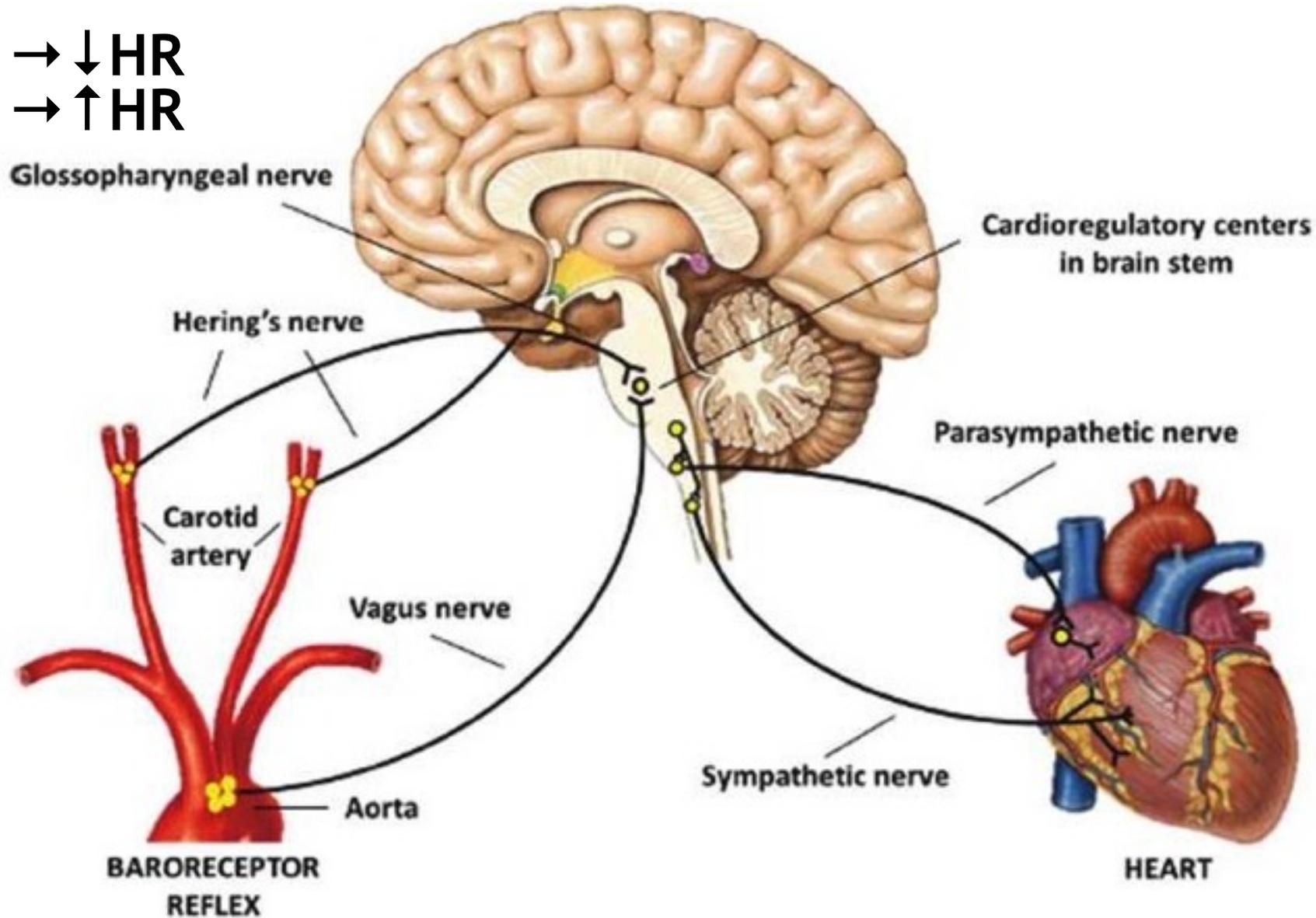
Stimulation of adenylyl cyclase and increased cAMP.

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

Inhibition of adenylyl cyclase; increased potassium conductance.

Baroreceptors:

\uparrow BP \rightarrow \downarrow HR
 \downarrow BP \rightarrow \uparrow 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.		

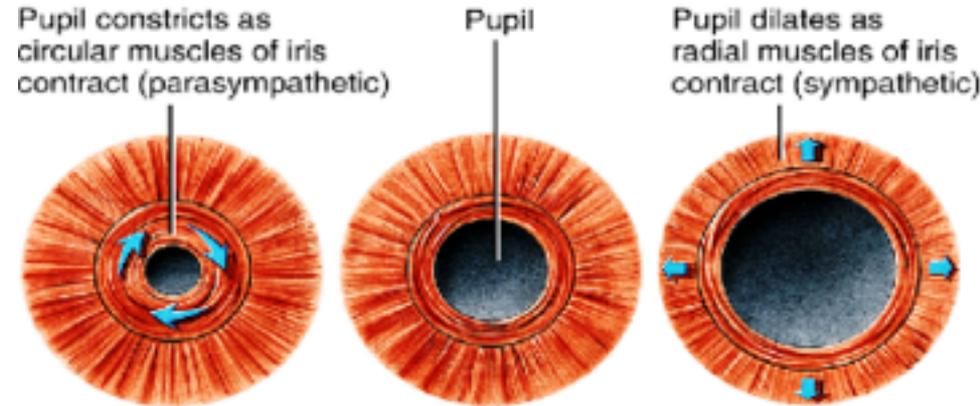
Ciliary muscle	M3 Contracts.	near vision.
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Heart

Sinoatrial node	▲ HR $\beta 1$	▼ HR M2
Ectopic pacemakers	Accelerates $\beta 1$	
Contractility	▲ $\beta 1$	

Blood vessels

Skin, splanchnic vessels	Contracts $\alpha 1$
Skeletal muscle vessels	Relaxes $\beta 2$
Releases (NO)	



Bright light

Normal light

Dim light

Anterior views

▼ (α1), M2

Endothelium (drug effect) M3, M5

