

Section X

The nervous system

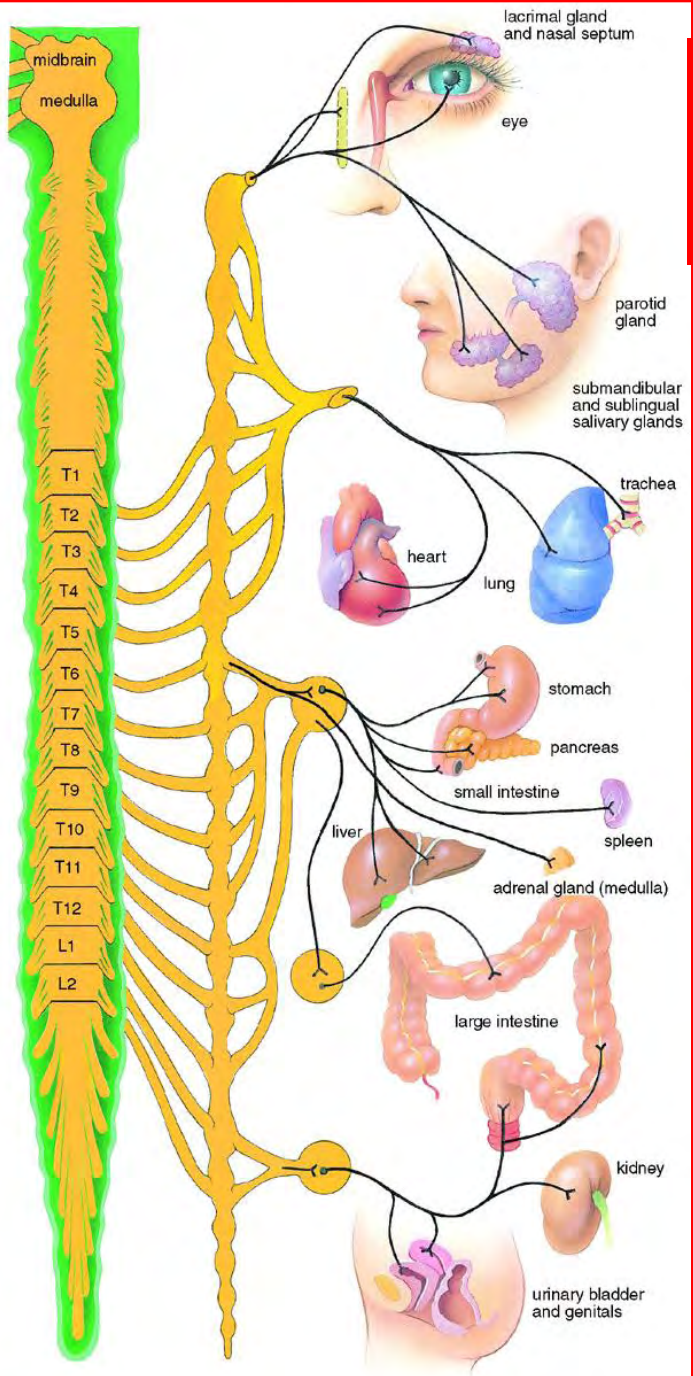
Chapter 5

Drugs Affecting the Nervous System

Part 1

The Efferent Nervous System

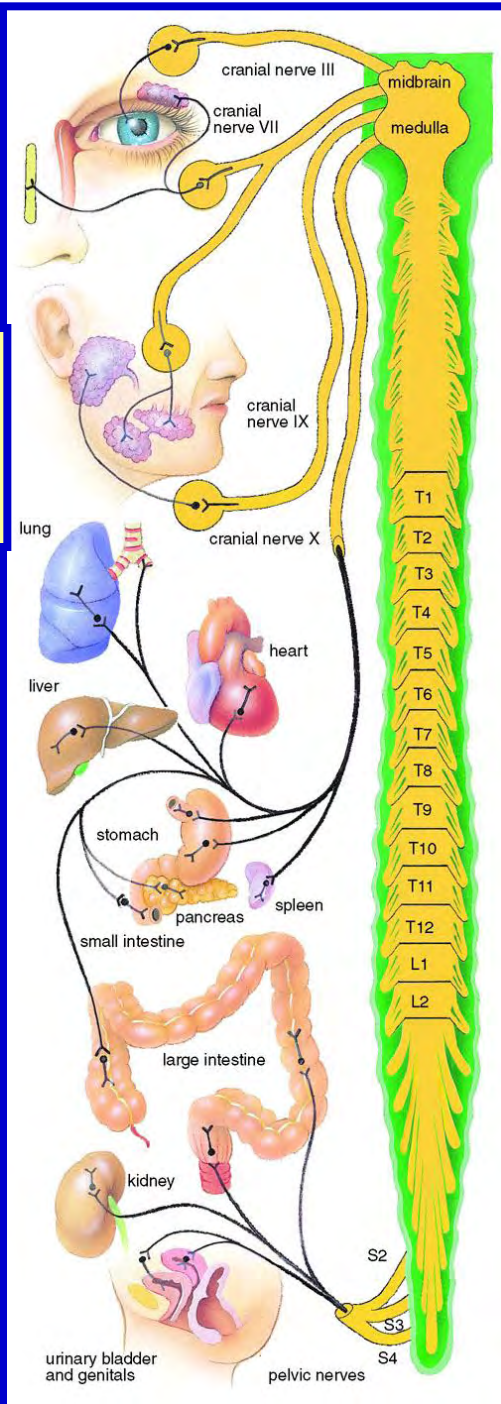
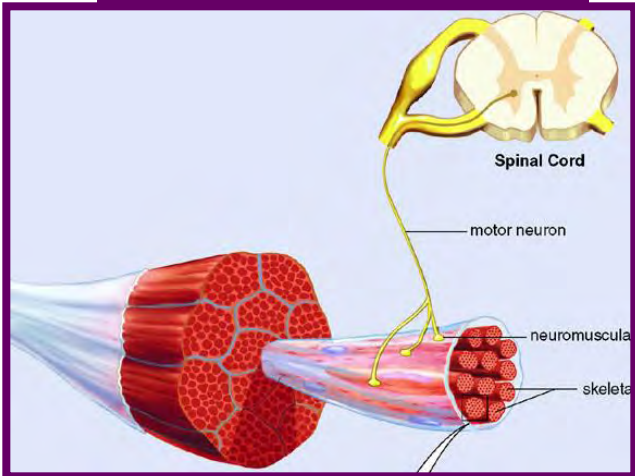
**Neurotransmitters and receptors
Drug actions and classification**

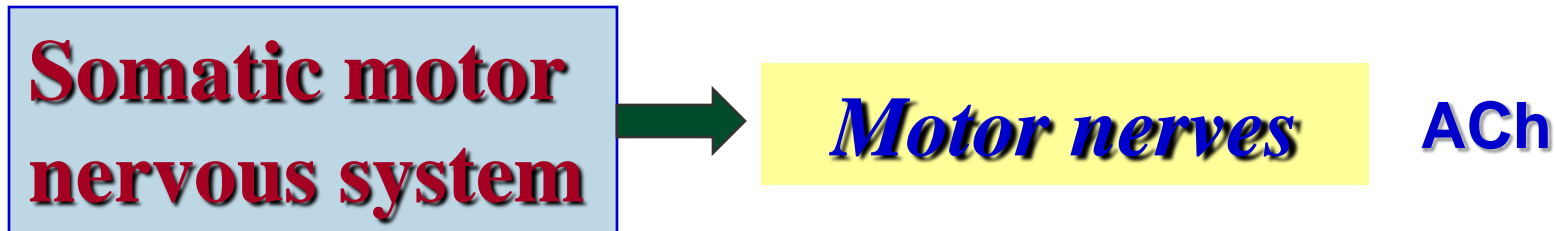
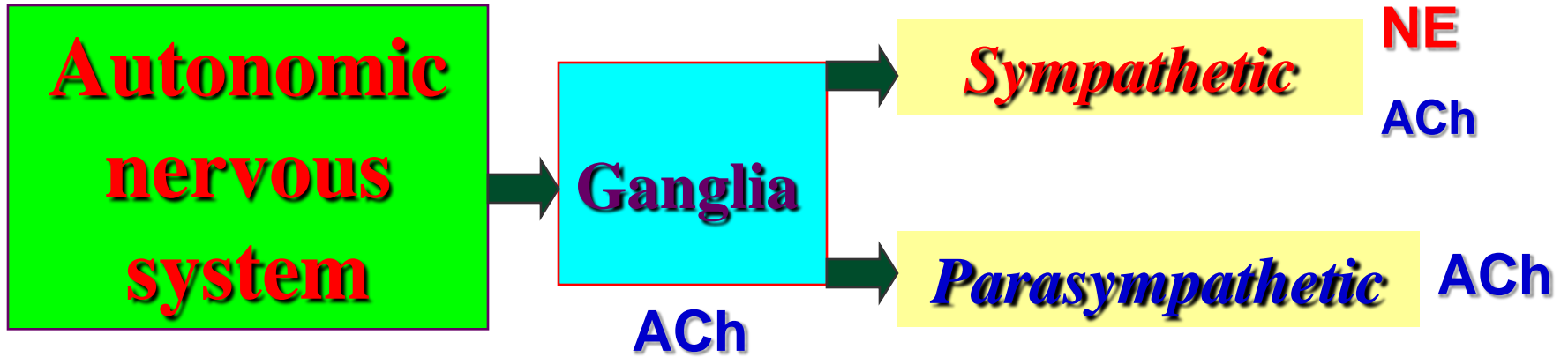


**Sympathetic
nerves**

**Parasympathetic
nerves**

Motor nerve





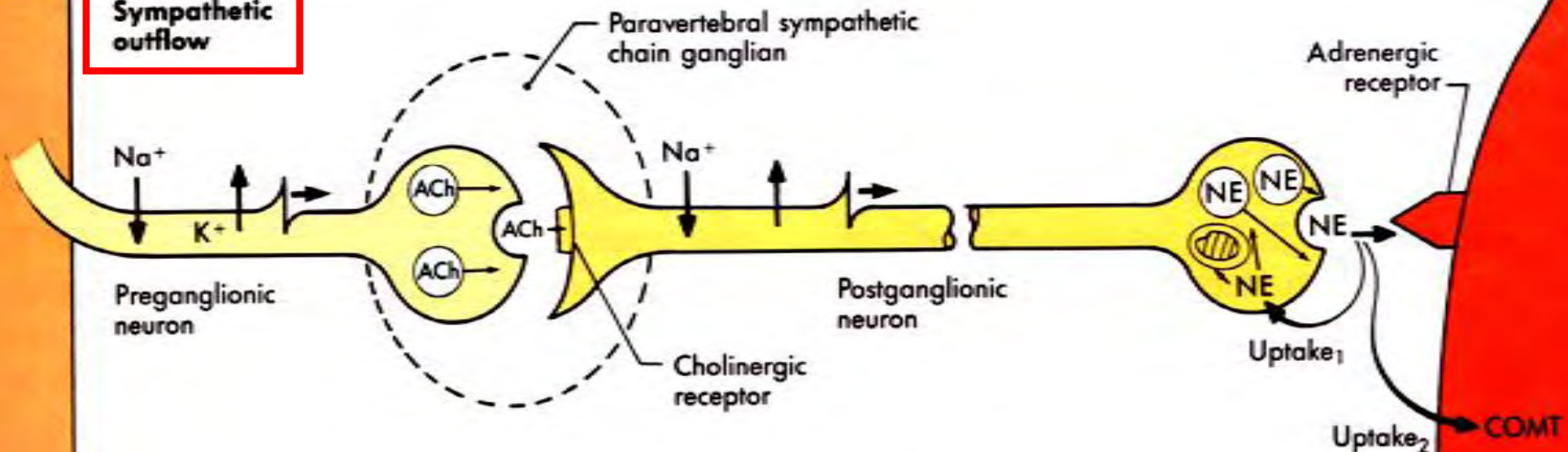
Overview of efferent nervous system

Chemical transmission via synapse

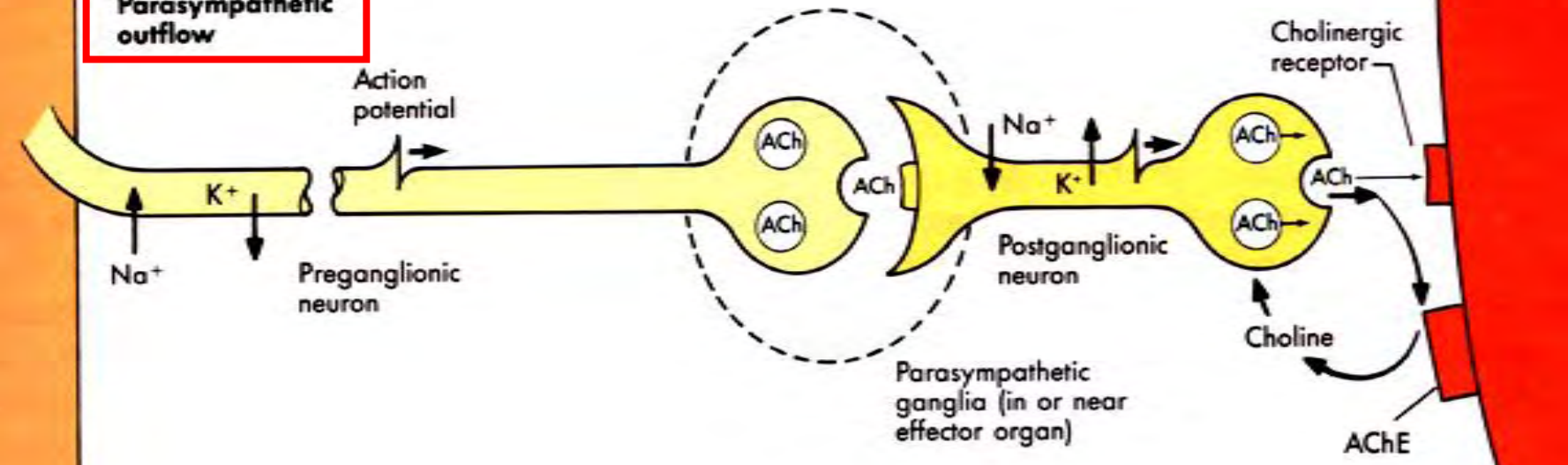
Spinal cord

Effector organ

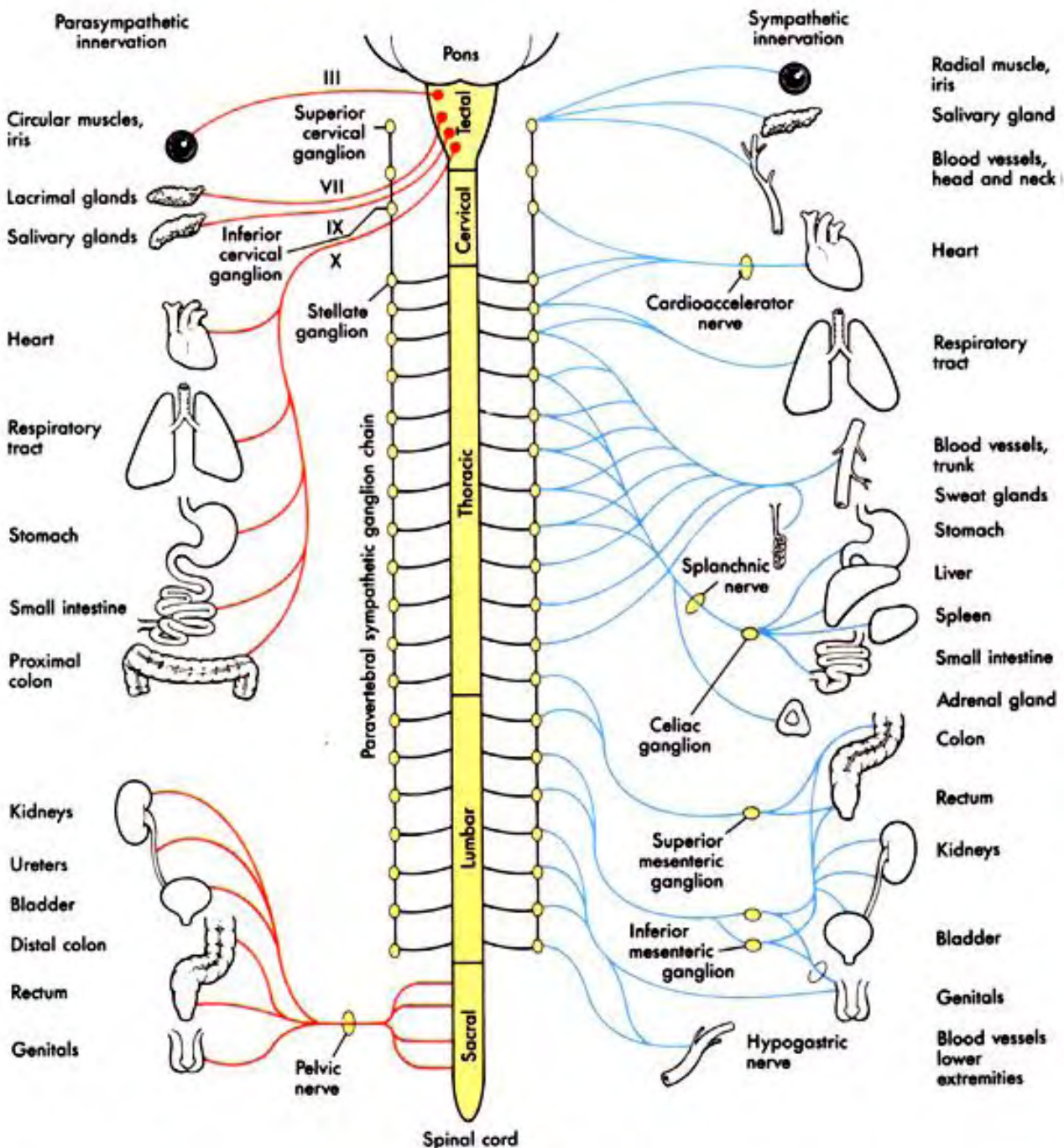
Sympathetic outflow



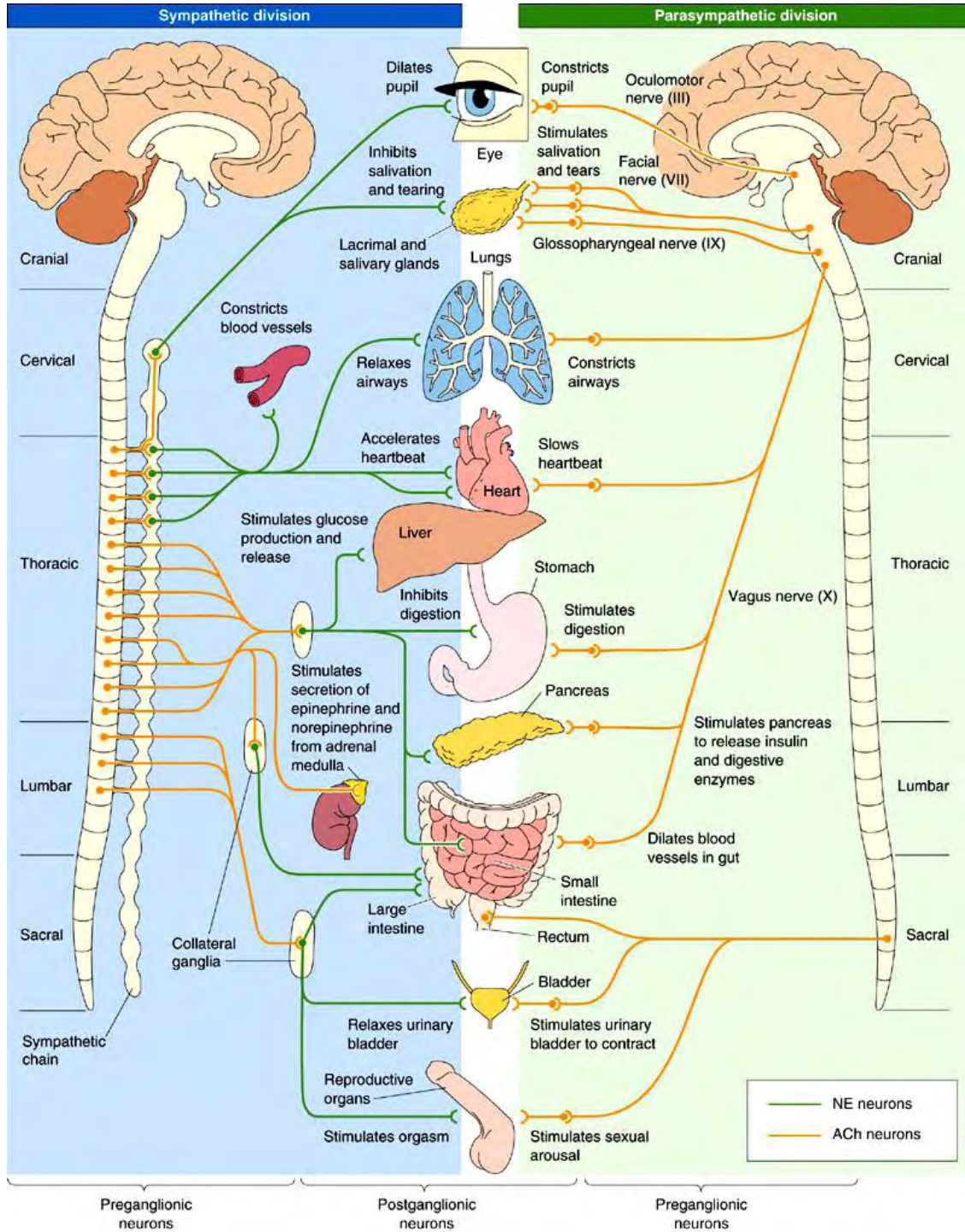
Parasympathetic outflow



Autonomic nervous system

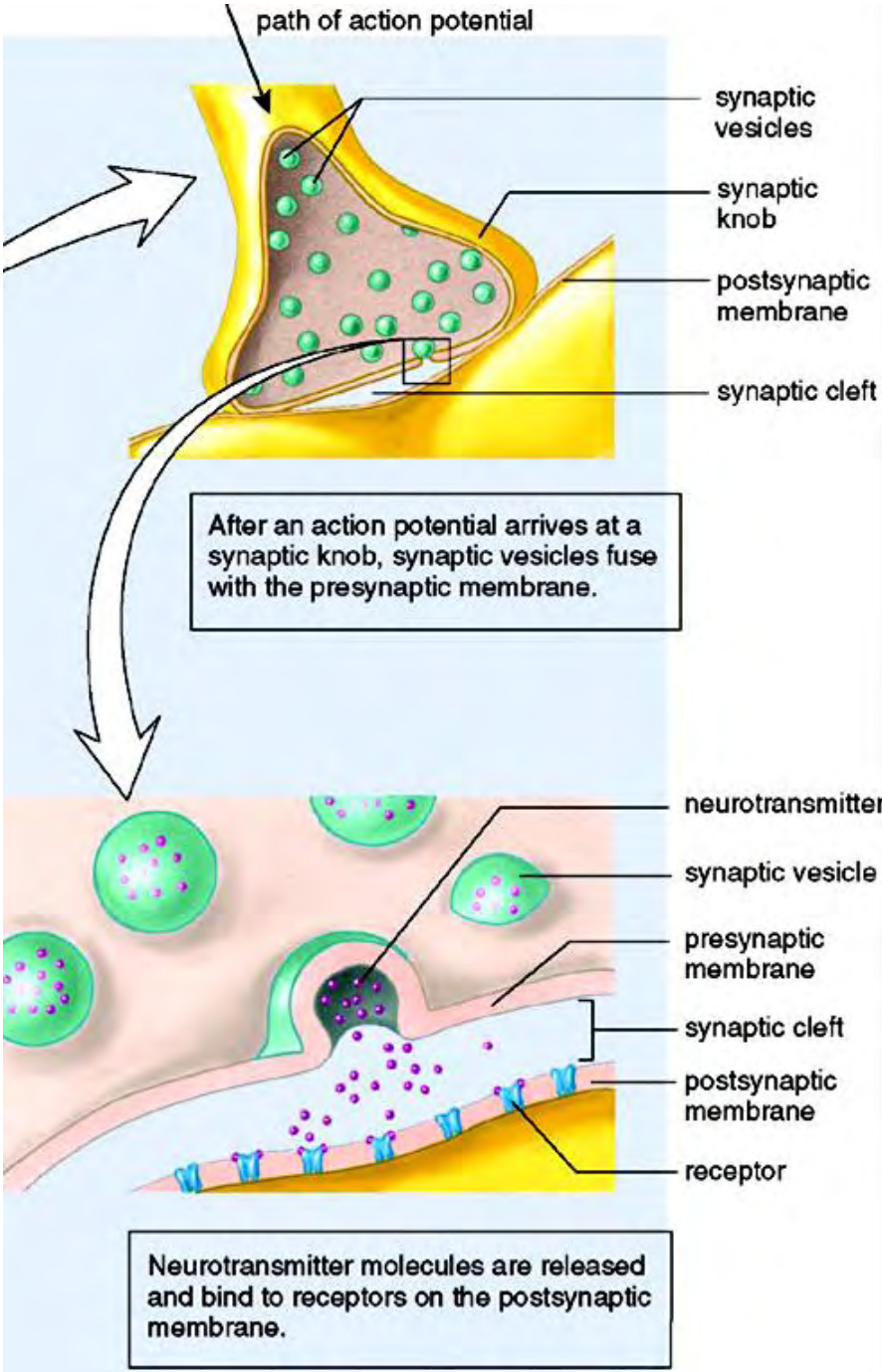


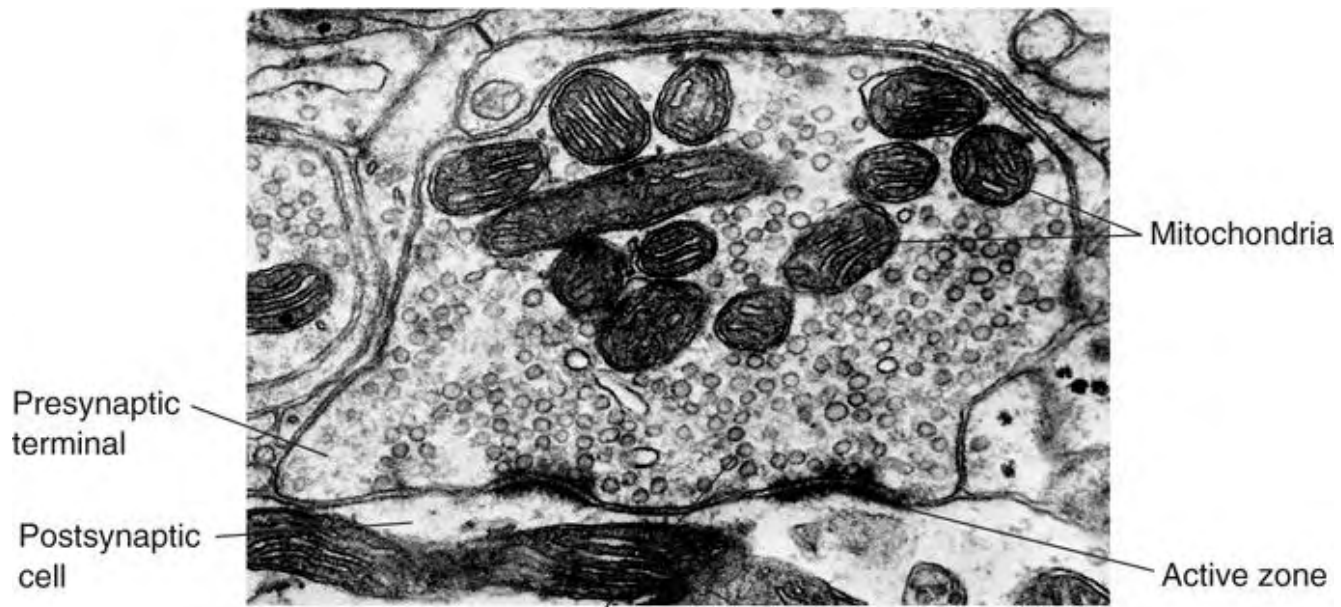
***Overview of
autonomic
nervous system***



***Overview of
autonomic
nervous system***

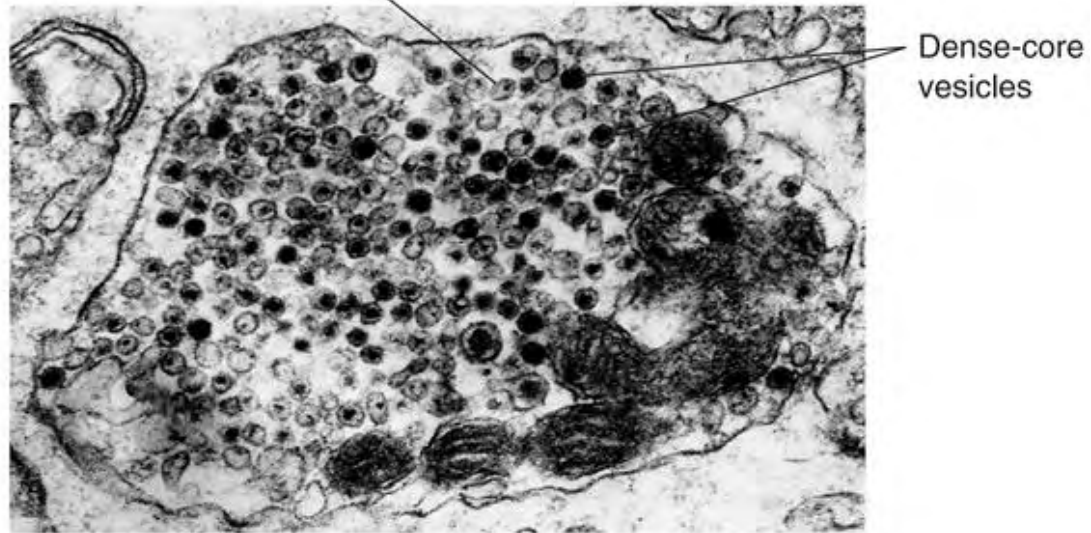
Synapse





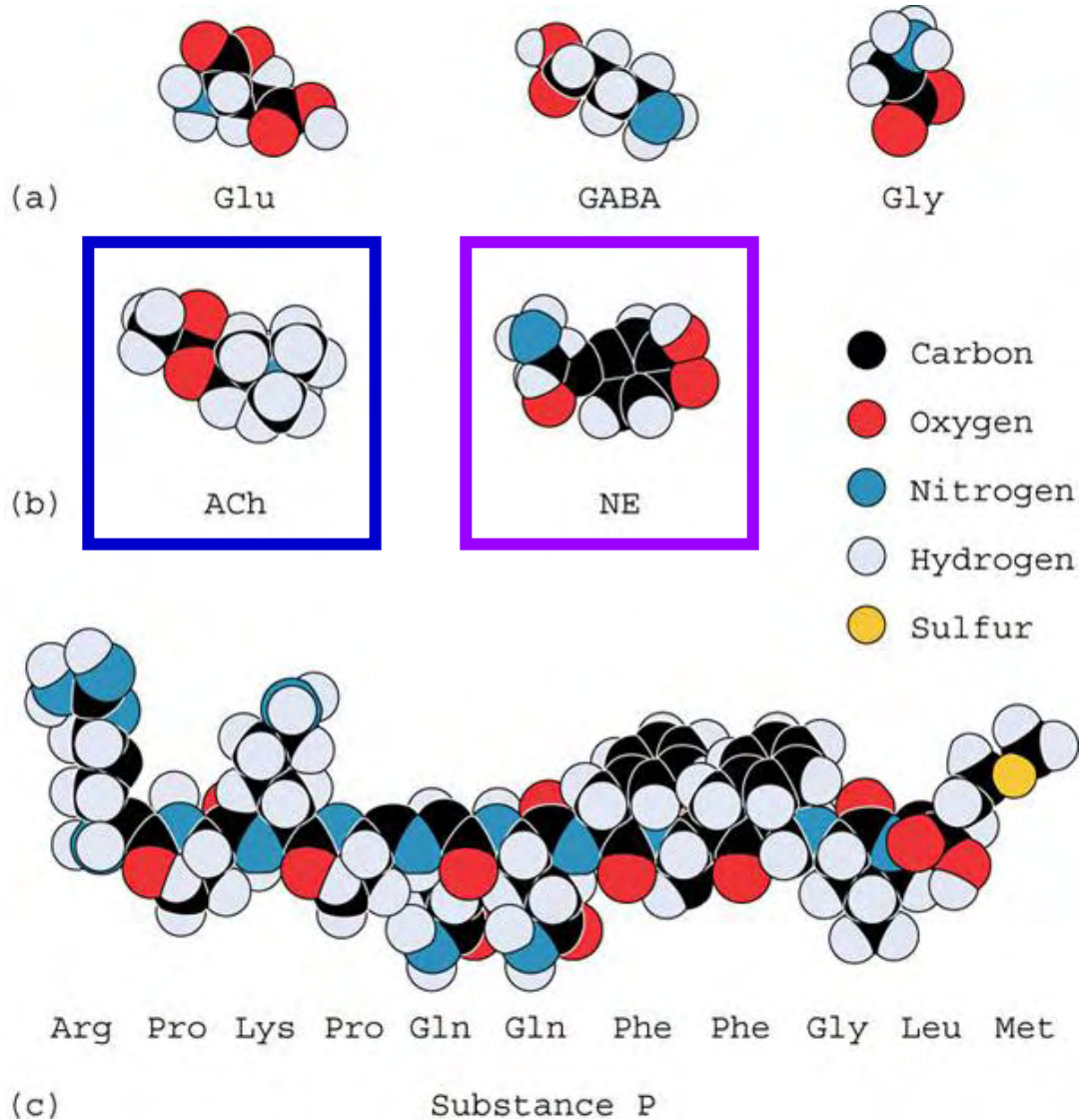
(a)

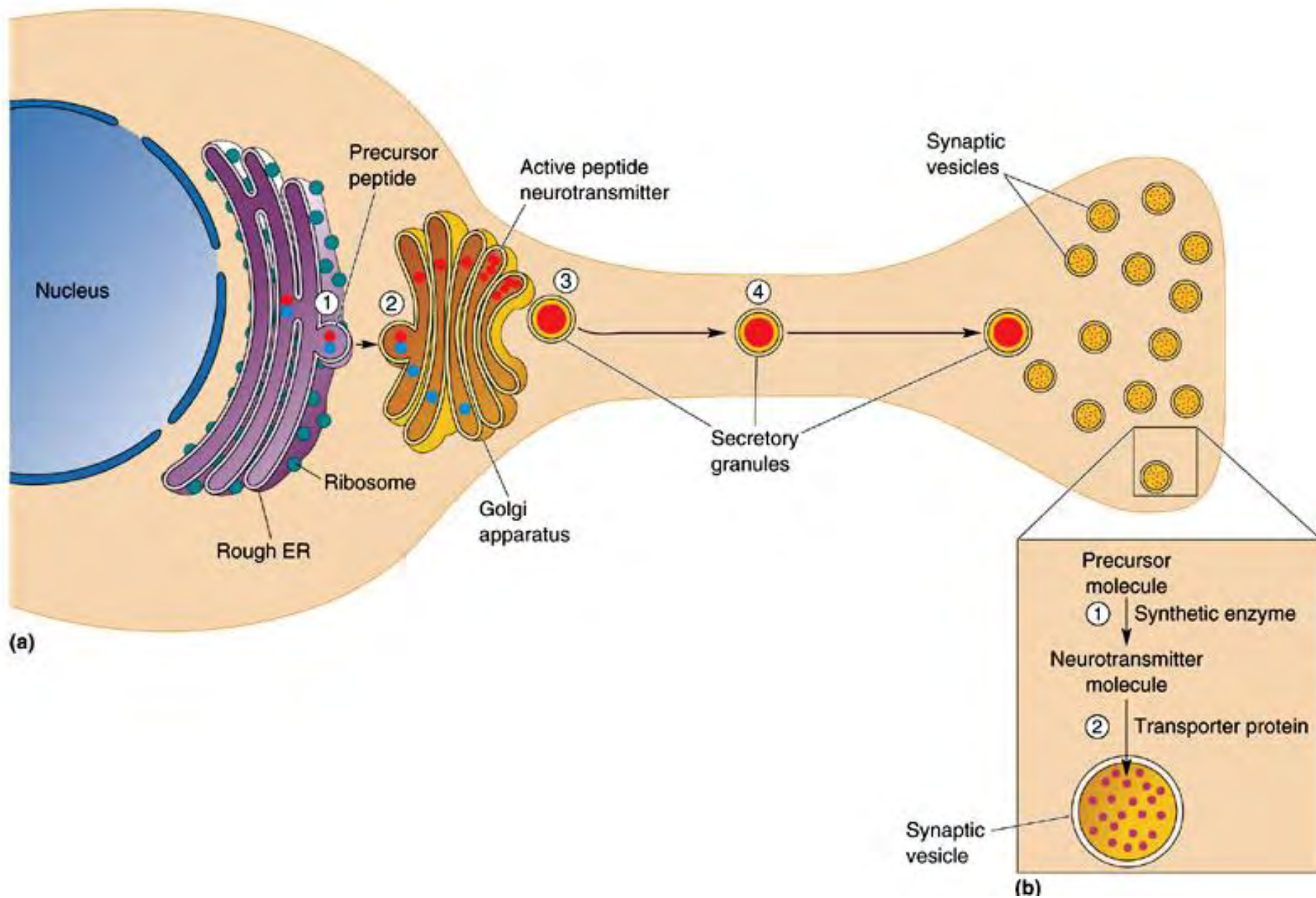
Vesicles



(b)

Neurotransmitters





(a)

(b)

Receptors

Neurotransmitter:

ACh

Agonists:

Nicotine

Muscarine

Antagonists:

Curare

Atropine

Cholinoceptors

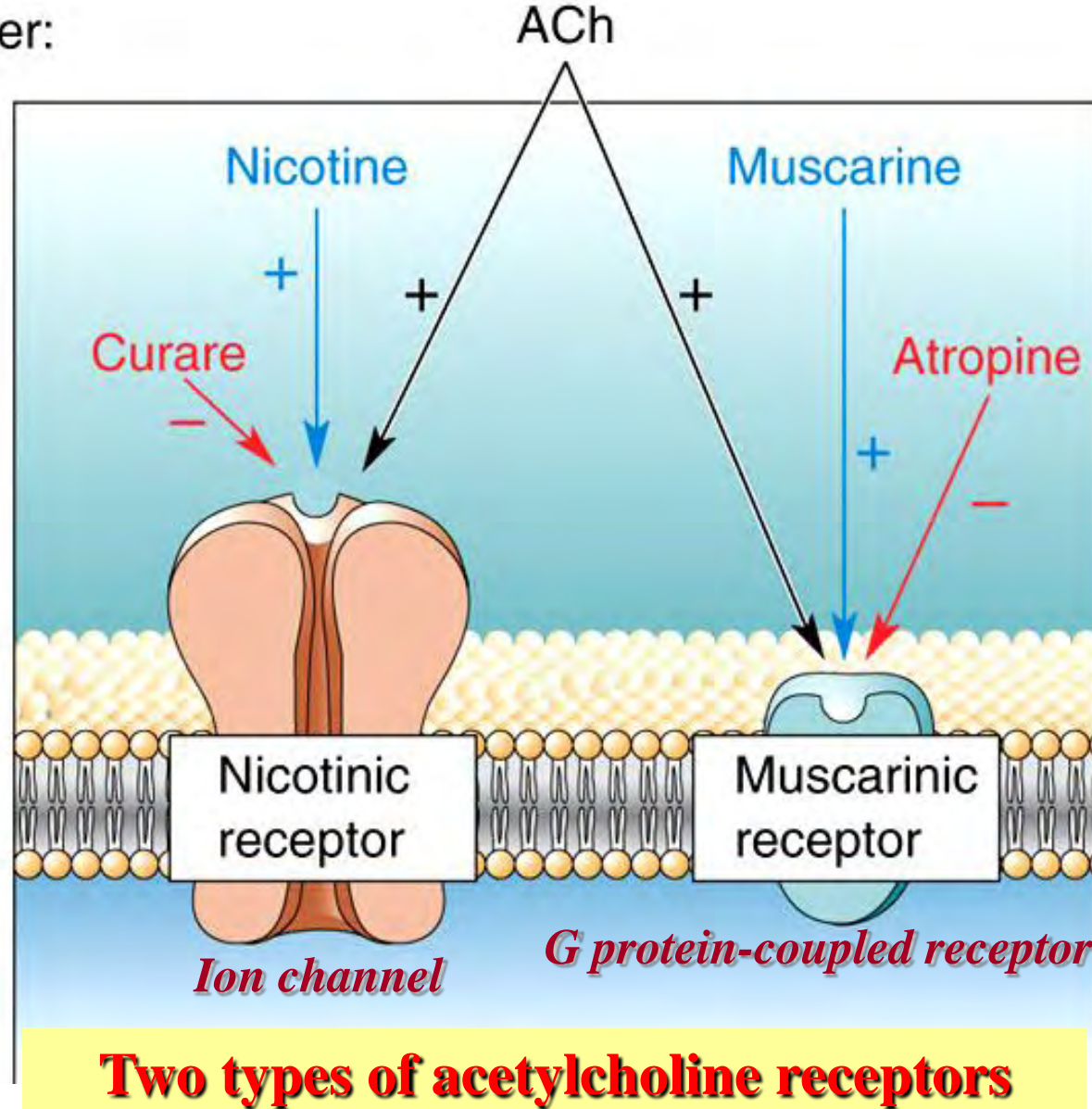
Receptors:

Nicotinic receptor

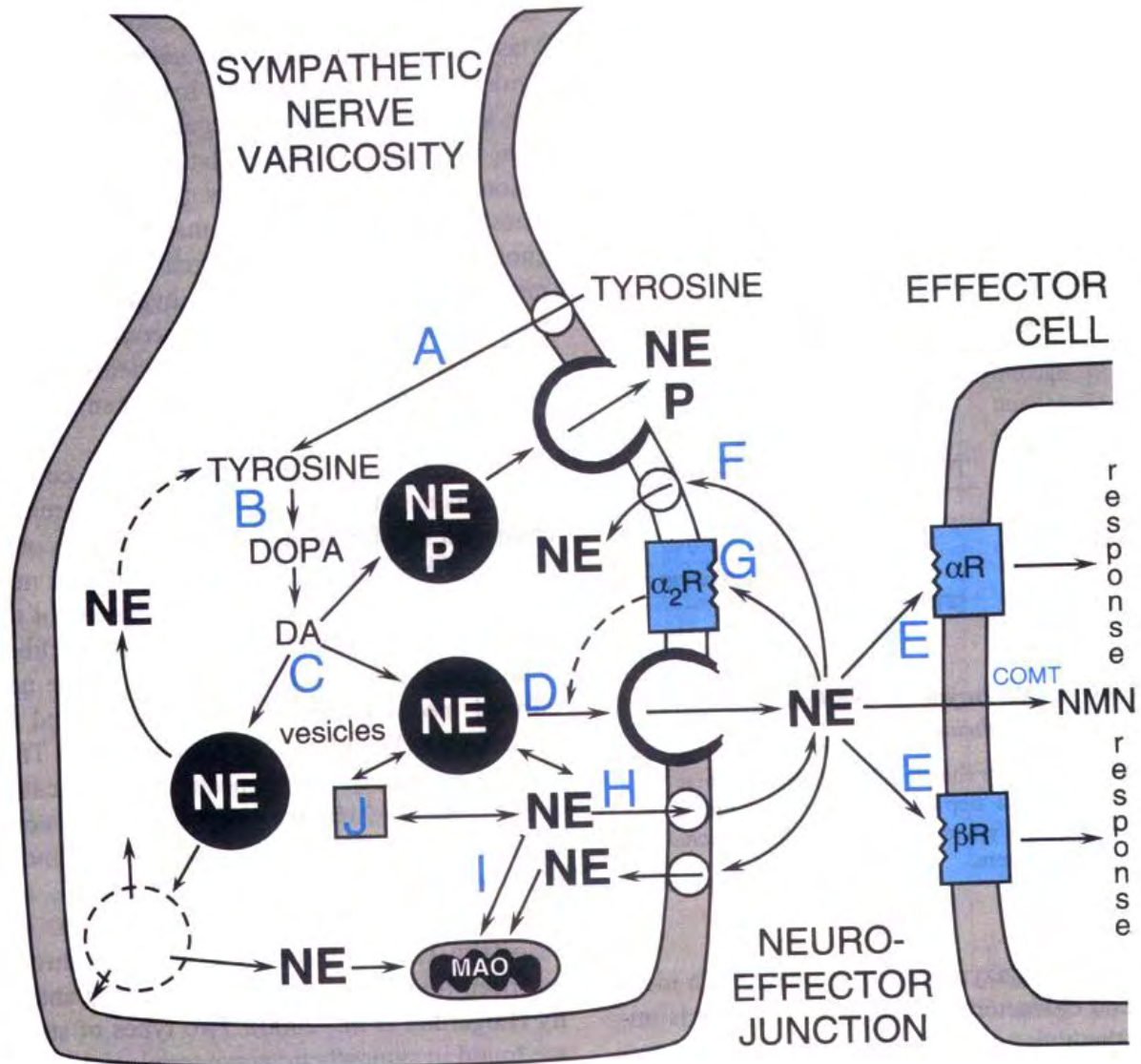
Muscarinic receptor

Ion channel

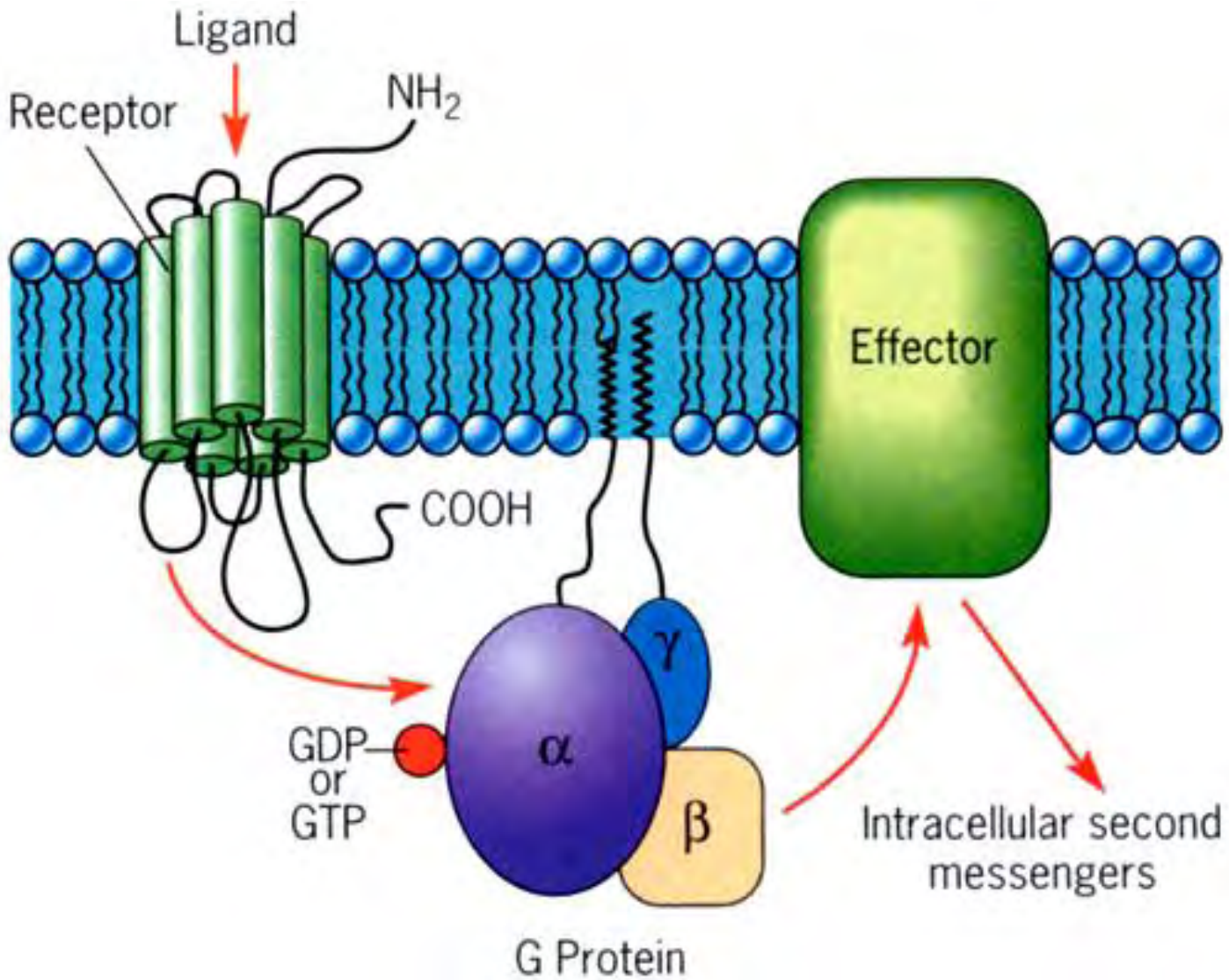
G protein-coupled receptor



Two types of acetylcholine receptors



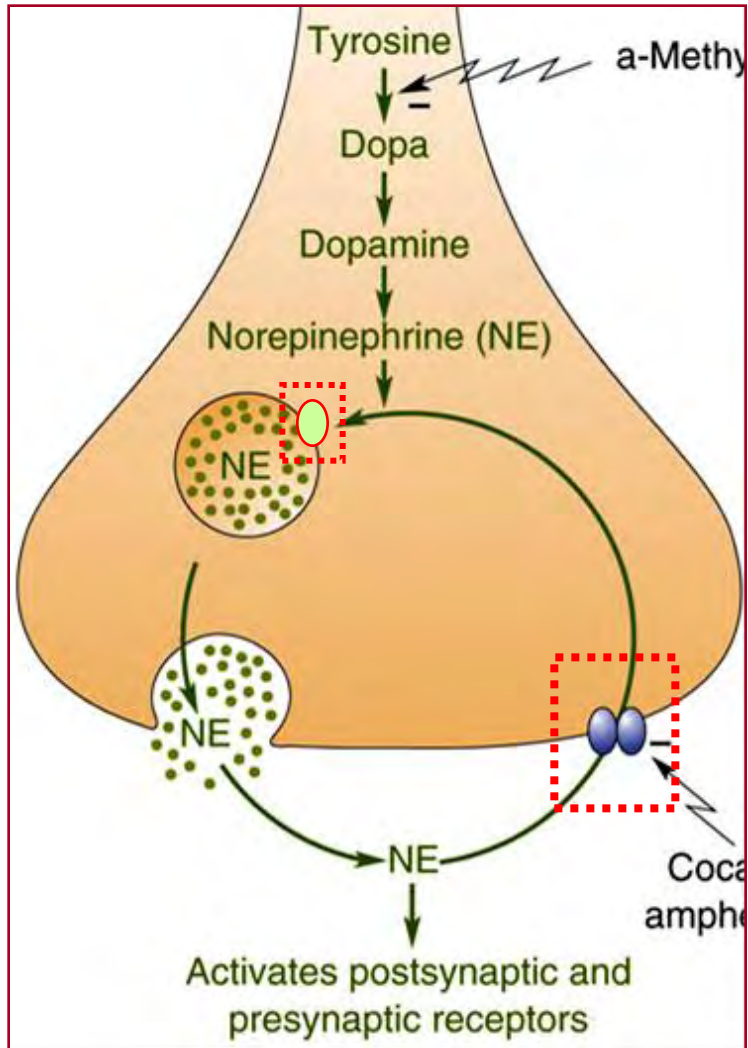
Adrenoceptors: G protein-coupled receptors



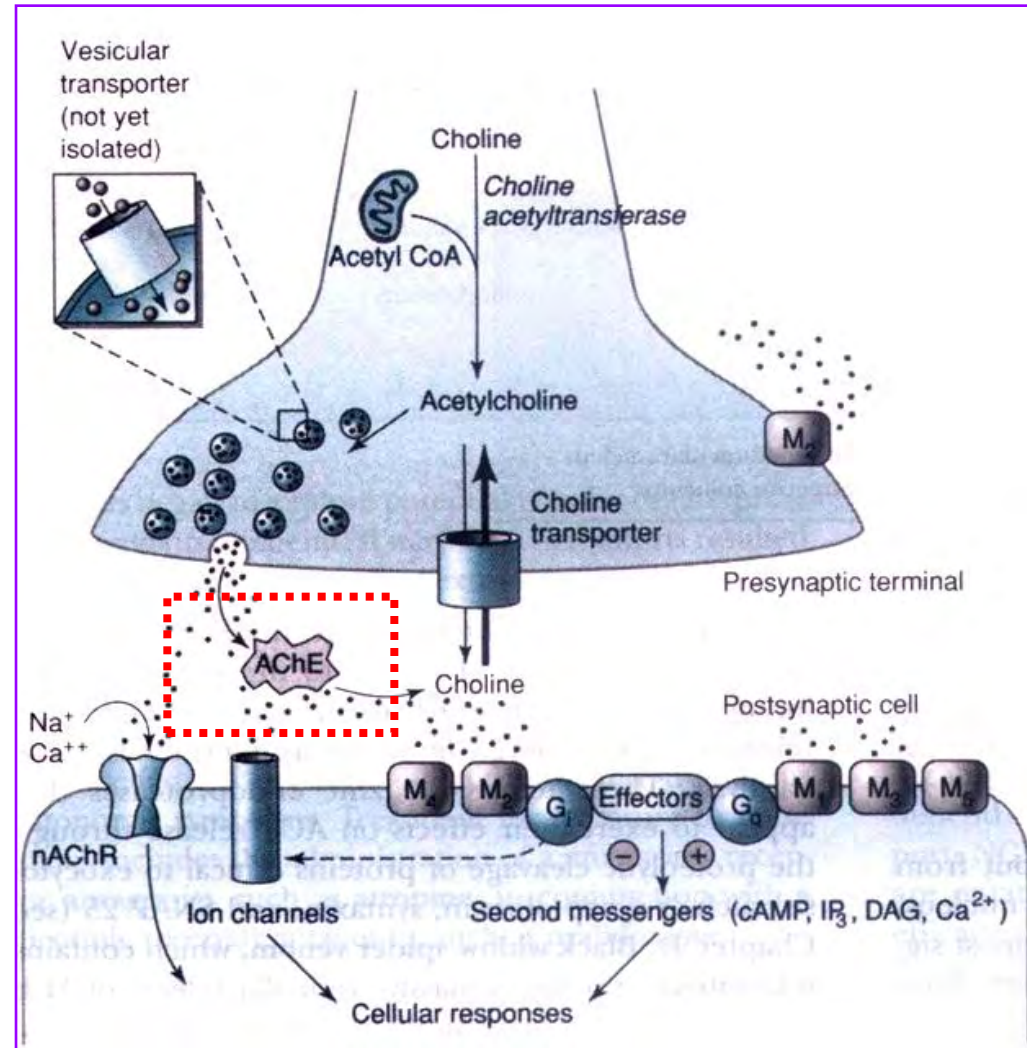
G protein-coupled receptor

Termination of neurotransmitter actions

Neurotransmitter transporters



Enzymatic degradation: acetylcholinesterase



1 *Transmitters and Receptors*

- **1.1 *Transmitters***

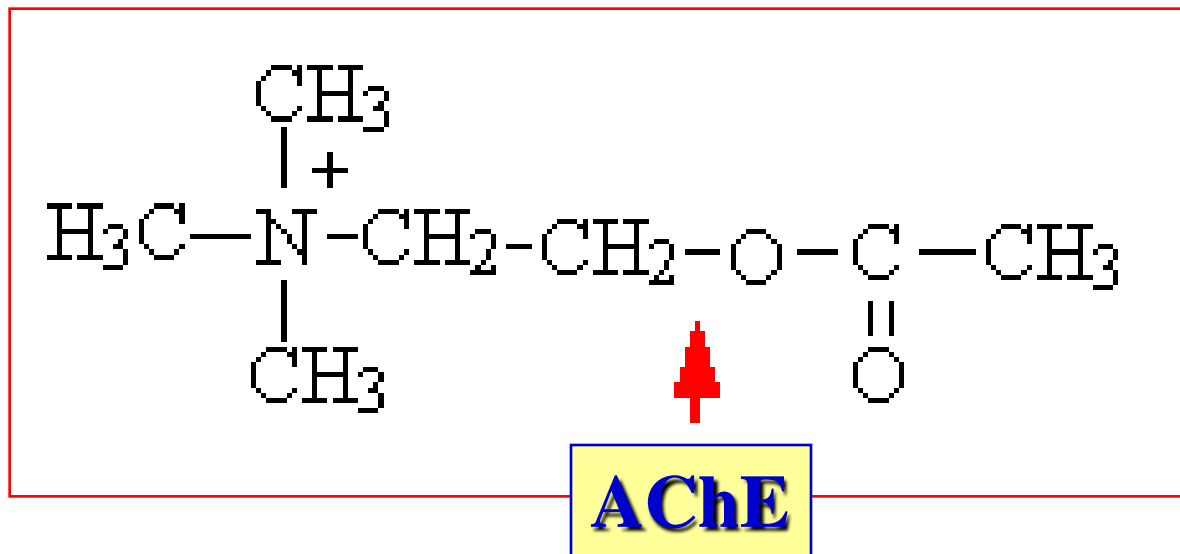
- **(1) Acetylcholine (ACh)**

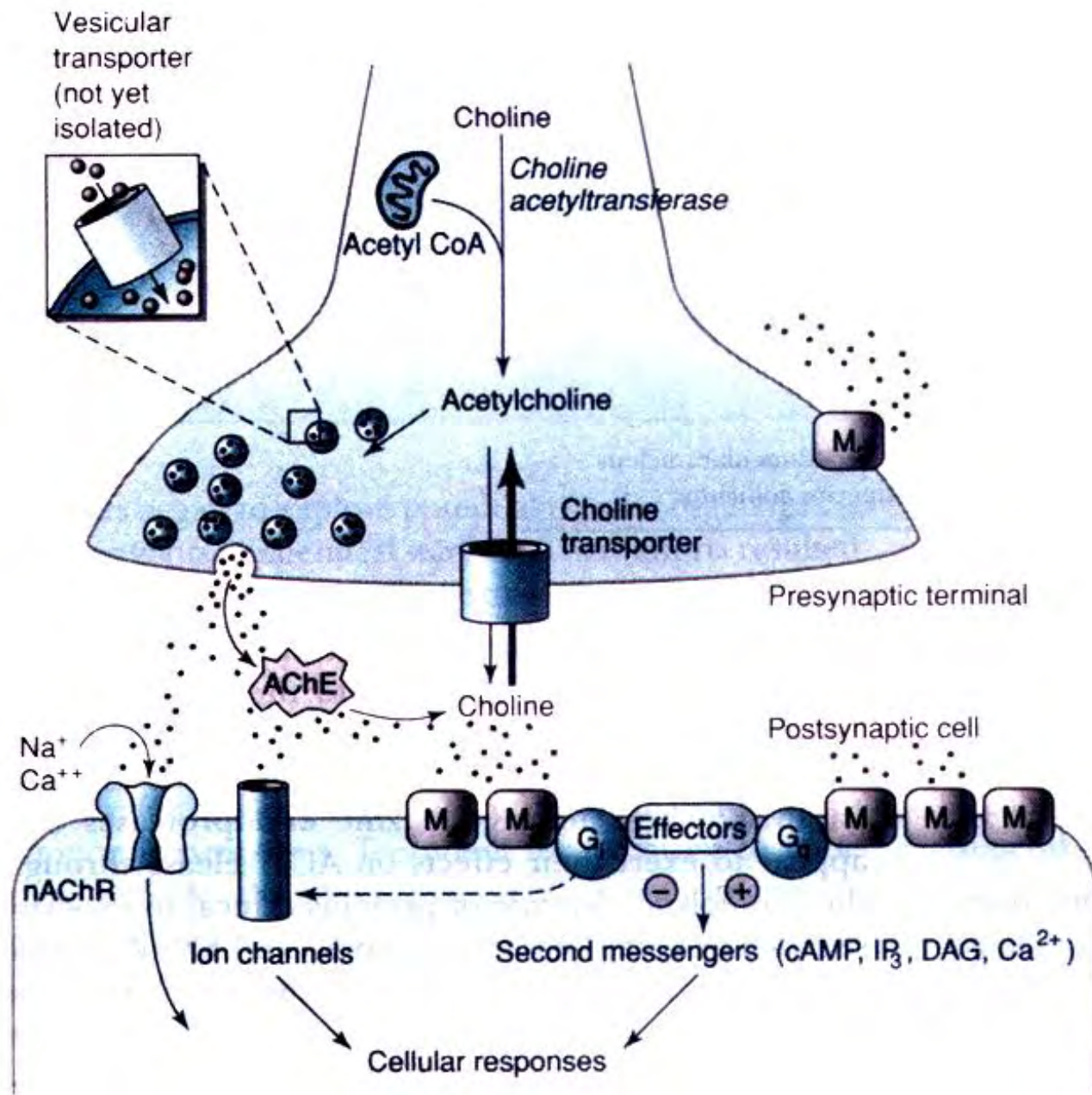
- ***Cholinergic nerves***

- **a. pre-ganglionic fibers of sympathetic and parasympathetic nerves**
- **b. post-ganglionic fibers of parasympathetic, and part of sympathetic nerves**
- **c. motor nerves**

A *Transmitters and Receptors*

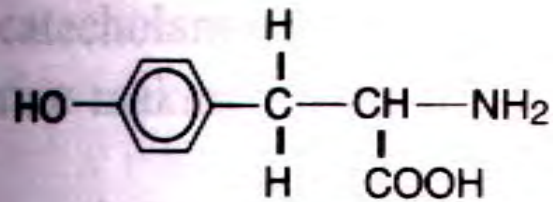
- *Acetylcholinesterase (AChE)*
- **Terminating ACh effects**





A *Transmitters and Receptors*

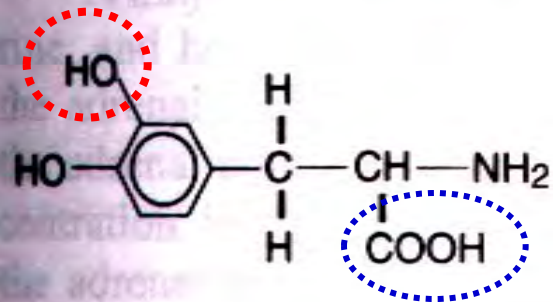
- (2) Norepinephrine (NE)
- *or* noradrenaline (NA)
- *Adrenergic nerves*
- **most of post-ganglionic fibers of sympathetic nerves**



TYROSINE

tyrosine-3-monooxygenase
(tyrosine hydroxylase)

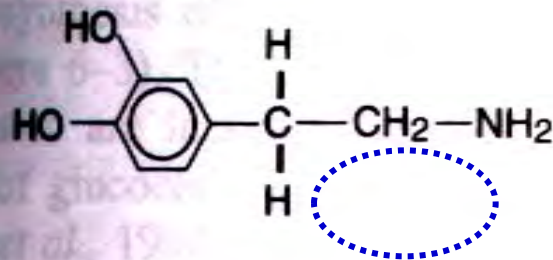
tetrahydrobiopterin



DOPA

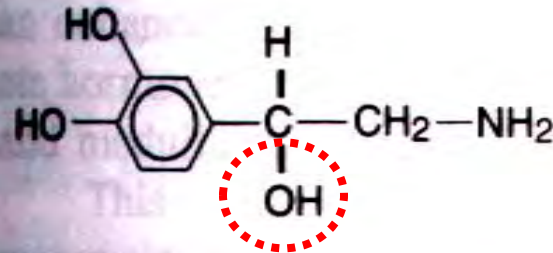
aromatic L-amino acid
decarboxylase

pyridoxal phosphate



DOPAMINE

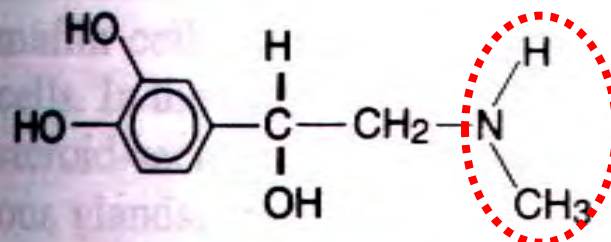
dopamine β -hydroxylase
ascorbate



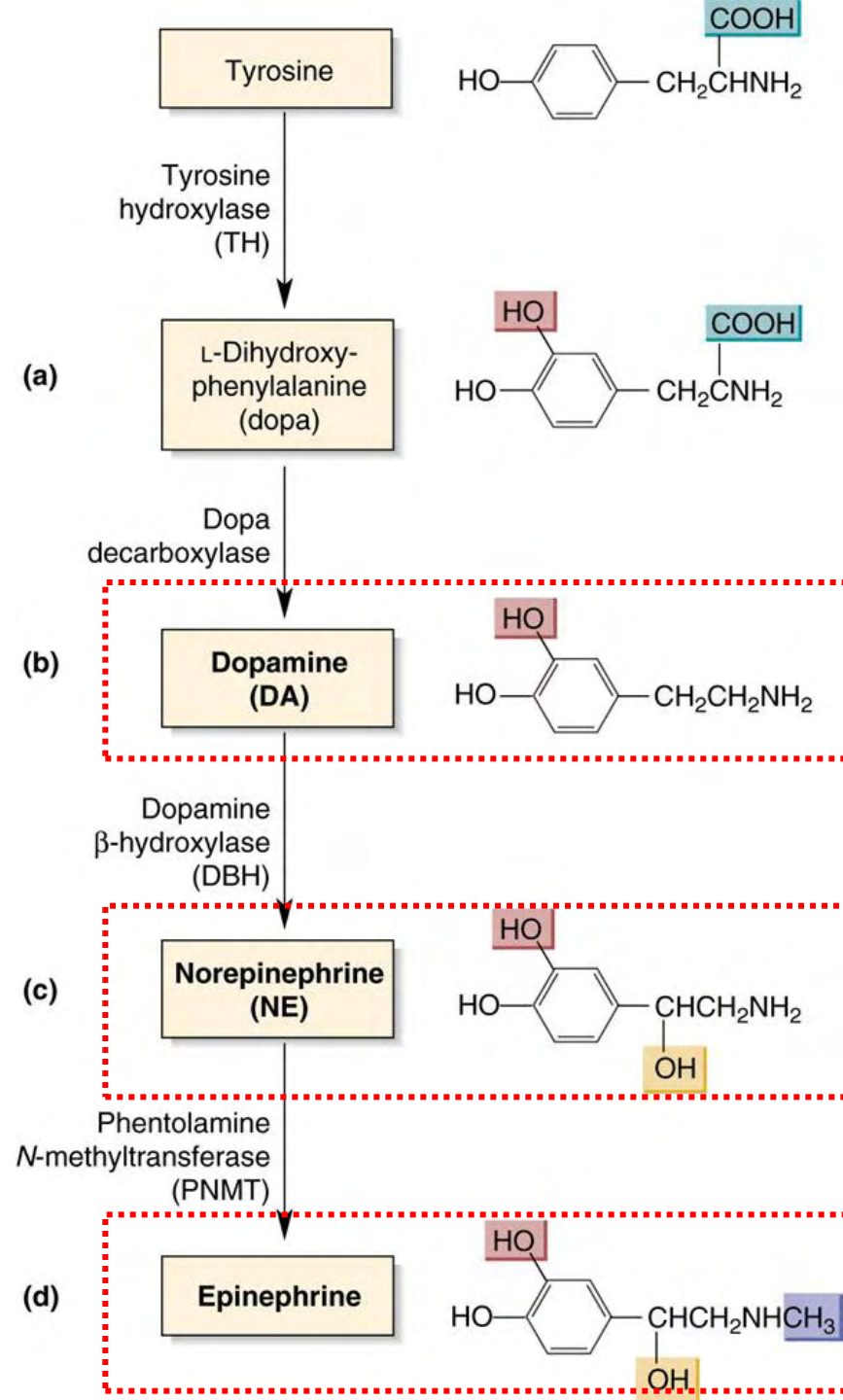
NOREPINEPHRINE

phenylethanolamine-
N-methyltransferase

S-adenosylmethionine

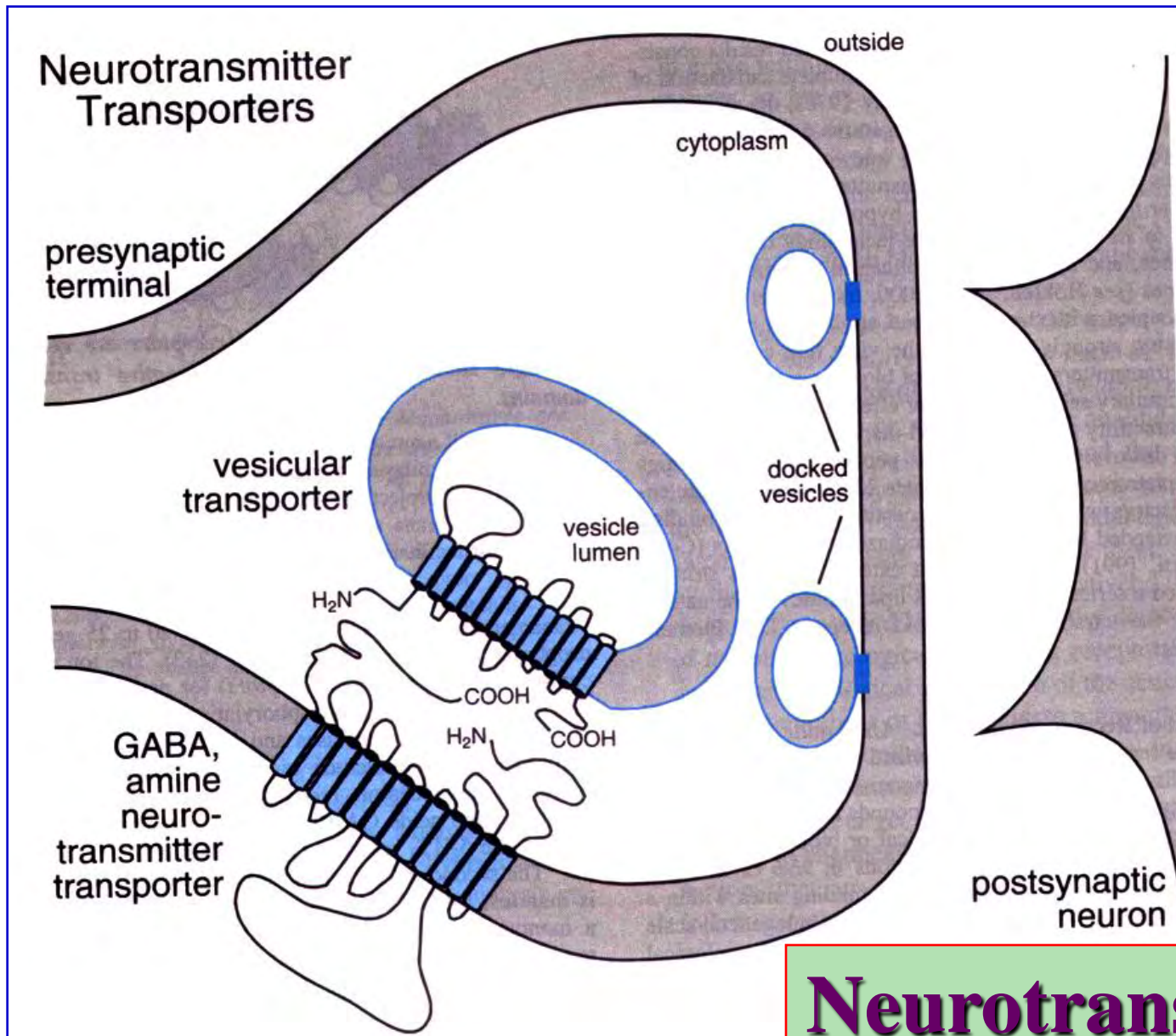


EPINEPHRINE

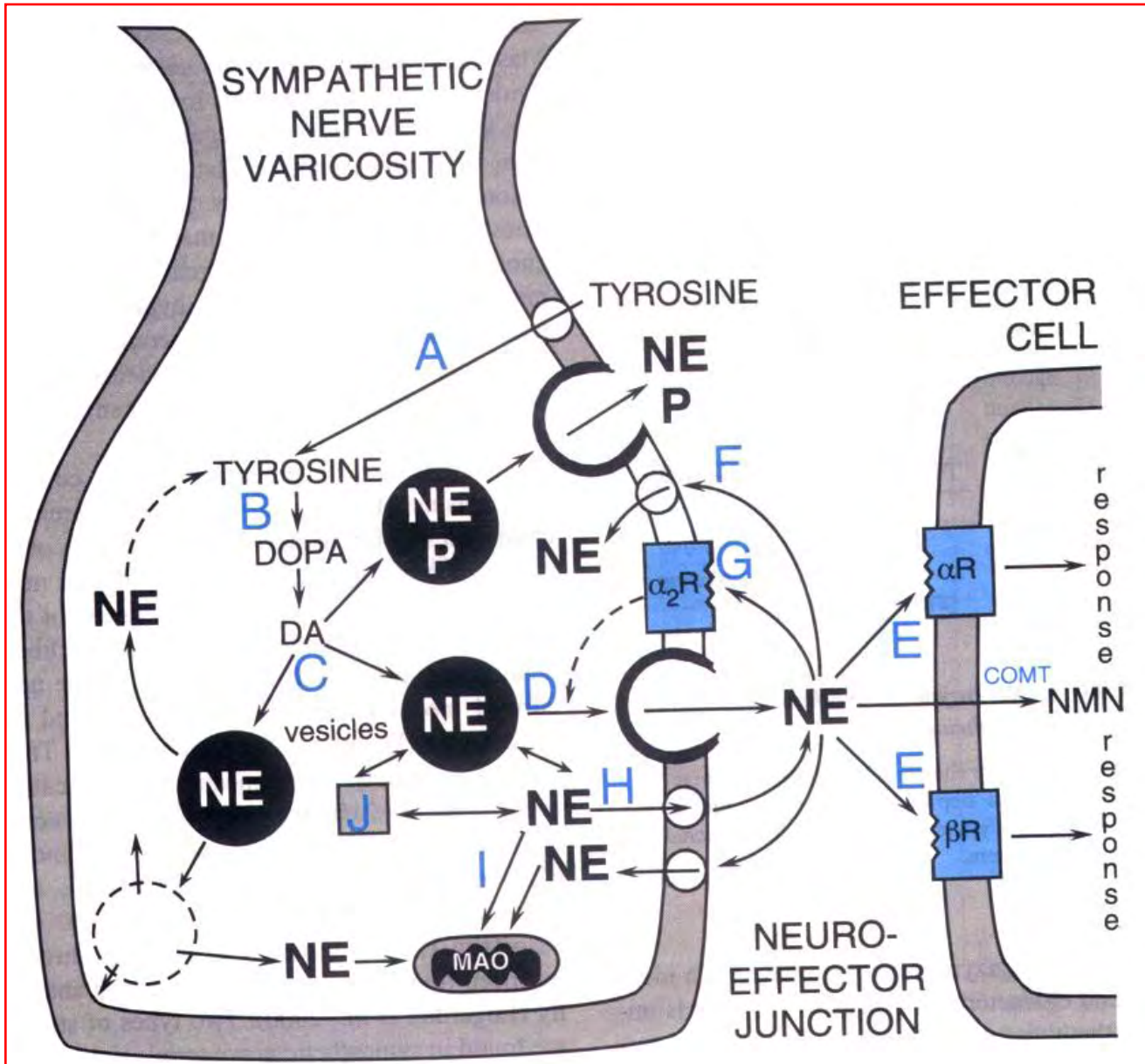


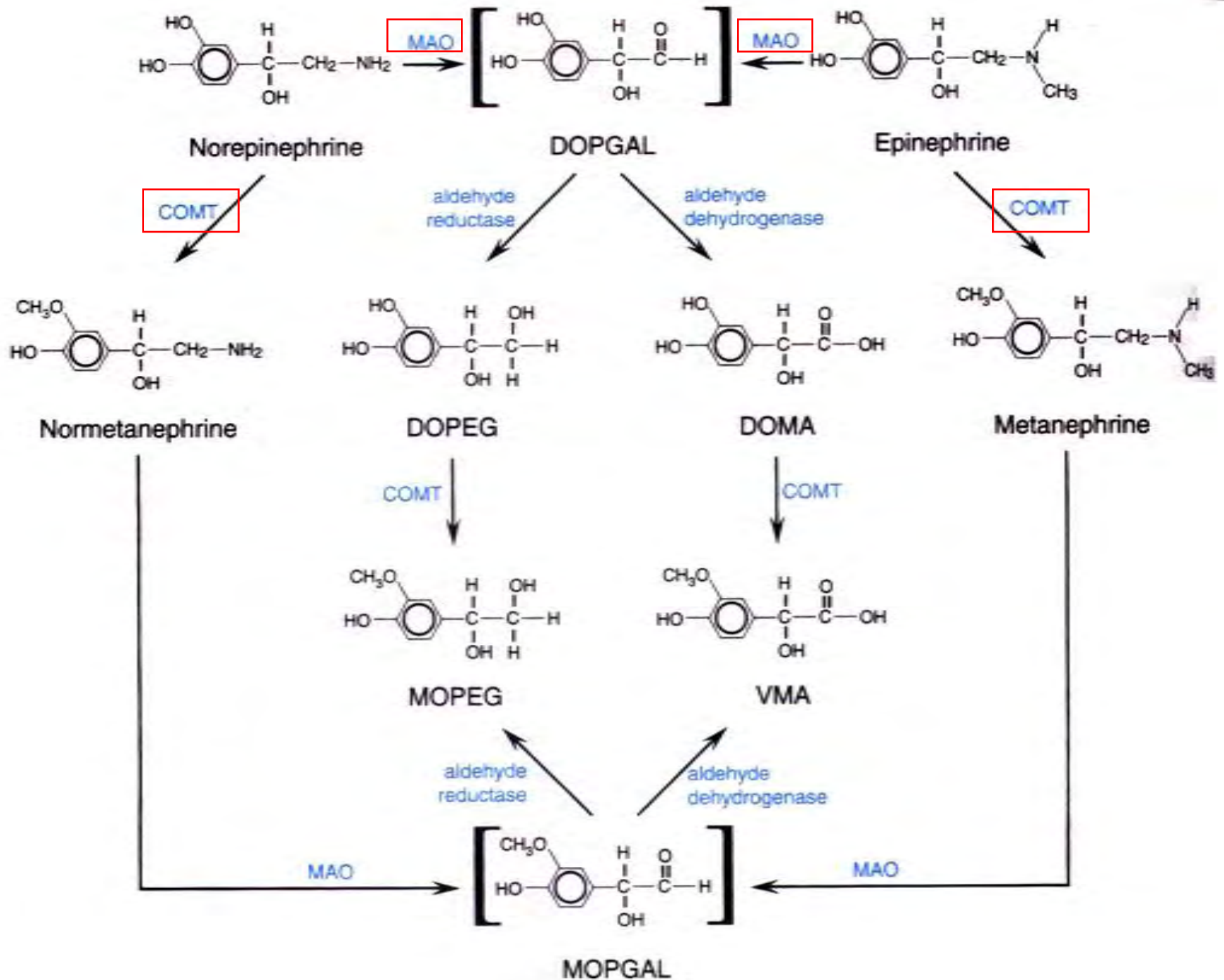
A *Transmitters and Receptors*

- *Termination of norepinephrine effects*
- **Uptake**
 - **neurotransmitter transporters**
 - uptake 1: neuronal uptake
 - uptake 2: non-neuronal uptake
- **Enzymatic degradation**
 - monoamine oxidase (MAO)
 - catechol-*O*-methyltransferase (COMT)



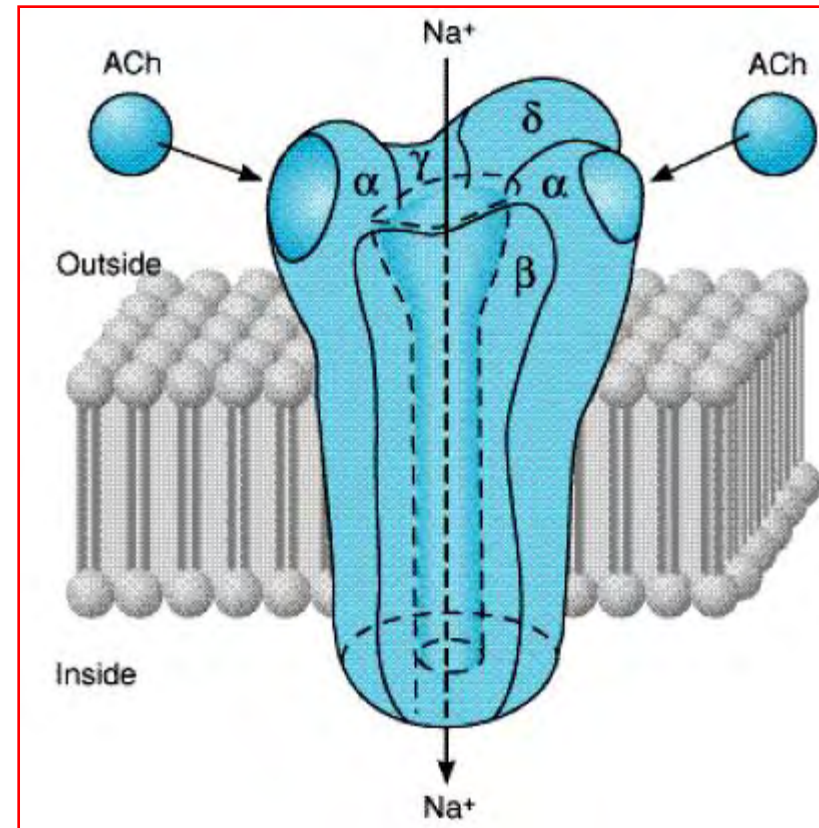
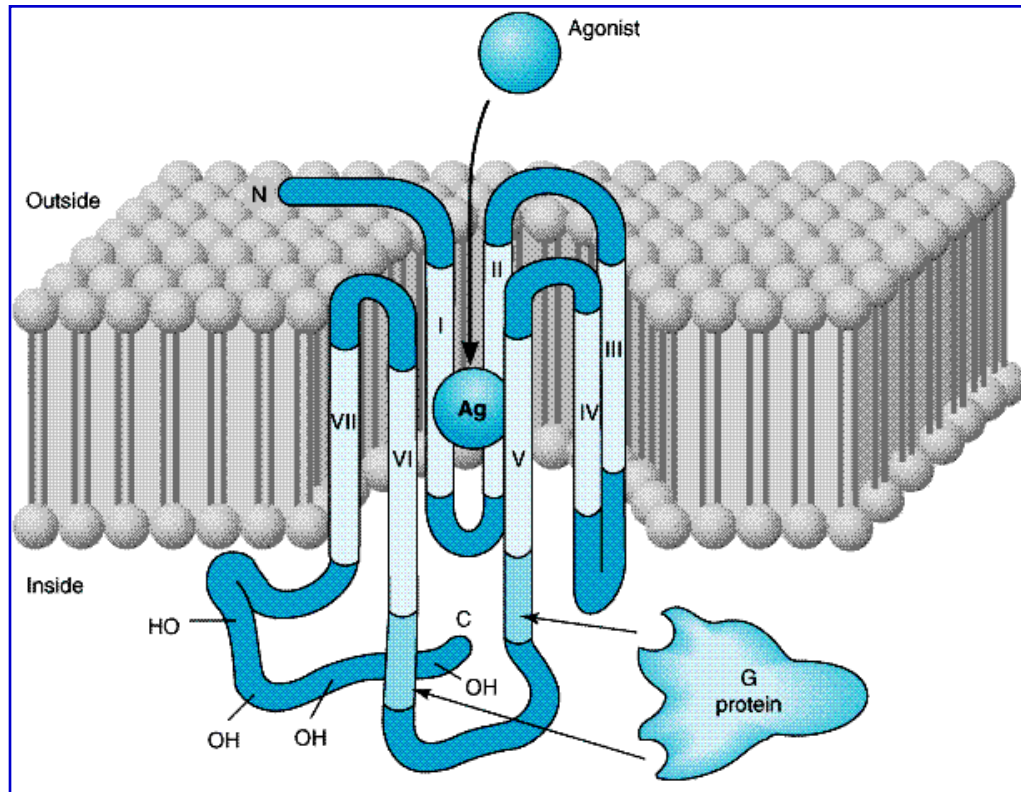
Neurotransmitter transporters





A *Transmitters and Receptors*

- *2 Receptors*
- **2.1 Acetylcholine receptors**
- (cholinoceptors, cholinergic receptors)
- *Muscarinic receptors (M receptors)*
- *Nicotinic receptors (N receptors)*



Mucarinic receptors:

***7-transmembrane G
protein-coupled receptor***

Nicotinic receptors:

***ligand-gated ion
channel***

A *Transmitters and Receptors*

- *Mucarinic receptors*
- **Depression of the heart:** heart rate, conduction
- **Contraction of smooth muscles:**
 - **sensitive:** GI tract, bronchial, urinary bladder
 - **insensitive:** uterine, blood vessels
- **Exocrine glands:** **sensitive:** sweat, tears, salivary
 - **insensitive:** GI tract
- **Eye:** **miosis:** contraction of sphincter muscle of iris
 - **contraction for near vision:** contraction of ciliary muscle

A *Transmitters and Receptors*

- **Nicotinic receptors**
- **N_N receptors (N_1 receptors)**
- **Sympathetic and parasympathetic ganglia**
- **Adrenal medulla**
- **N_M receptors (N_2 receptors)**
- **Contraction of skeletal muscles**

A *Transmitters and Receptors*

- **2.2 Adrenoceptors (adrenergic receptors)**
- **α receptors**
- **α_1 receptors:**
 - contraction of vascular smooth muscles: **BP \uparrow**
 - contraction of radial muscle of iris: **mydriasis**
- **α_2 receptors:** CNS, presynaptic membranes of adrenergic nerves: **vasodilatation**

B *Transmitters and Receptors*

- **β receptors**
- **β_1 receptors:** contractility, automaticity, conduction, oxygen-consumption, cardiac output: heart stimulation
- **β_2 receptors:** relaxation of bronchial smooth muscles

B *Drug actions and classification*

- *1. Mechanisms of drug actions*
- **1.1 Direct actions on the receptors**
 - **Agonists**
 - **Antagonists**

B *Drug actions and classification*

- **1.2 Indirect actions *via* affecting transmitters**
- **(1) Synthesis:** L-dopa 左旋多巴
- **(2) Inactivation:** **AChEI**, MAOI
- **(3) Release:** neostigmine 新斯的明, ephedrine 麻黄碱, amphetamine 苯丙胺
- **(4) Transport and storage:** imipramine 丙咪嗪, reserpine 利血平 (利舍平)

B *Drug actions and classification*

■ 1.3 Mimetics and antagonists

■ (1) Mimetics

■ **direct-acting:** receptor agonists

■ **indirect-acting:** increasing amounts and/or effects of transmitters

■ (2) Antagonists

■ **direct-acting:** receptor antagonists

■ **indirect-acting:** decreasing amounts and/or effects of transmitters

B *Drug actions and classification*

■ *2. Drug classification*

■ **2.1 Cholinomimetics**

■ **(1) Cholinoceptor agonists**

- **M, N receptor agonists: carbachol** 卡巴胆碱
- **M receptor agonists: pilocarpine** 毛果芸香碱
- **N receptor agonists: nicotine** 烟碱

■ **(2) Cholinesterase inhibitors (Anticholinesterases)**

- **Reversible: neostigmine** 新斯的明
- **Irreversible: organophosphates** 有机磷酸酯类

B *Drug actions and classification*

- **2.2 Cholinergic antagonists**

- **(1) Cholinoceptor antagonists**

- **M cholinoceptor antagonists**

- **non-selective: atropine** 阿托品

- **M₁ cholinoceptor-selective: pirenzepine**

- **pirenzepine** 哌仑西平

B *Drug actions and classification*

- **N cholinceptor antagonists**
- **N_N cholinceptor antagonists: mecamylamine**
 - 美加明
- **N_M cholinceptor antagonists: succinylcholine**
 - 琥珀胆碱
- **(2) Cholinesterase reactivators**
- **pralidoxime iodide 碘解磷定**

B *Drug actions and classification*

■ 2.3 Adrenoceptor agonists

■ (1) α receptor agonists

- $\alpha_1\alpha_2$ receptor agonists: norepinephrine 去甲肾上腺素
- α_1 receptor agonists: phenylephrine 去氧肾上腺素
- α_2 receptor agonists: clonidine 可乐定

■ (2) α, β receptor agonists

- epinephrine, adrenaline 肾上腺素

B *Drug actions and classification*

- **(3) β receptor agonists:**
- **$\beta_1\beta_2$ receptor agonists: isoproterenol**
 - 异丙肾上腺素
- **β_1 receptor agonists: dobutamine 多巴酚丁胺**
- **β_2 receptor agonists: salbutamol 沙丁胺醇**

B *Drug actions and classification*

- **2.4 Adrenoceptor antagonists**
- **(1) α receptor antagonists**
- **$\alpha_1\alpha_2$ receptor antagonists:**
 - **short-acting:** phentolamine 酚妥拉明
 - **long-acting:** phenoxybenzamine 酚苄明
- **α_1 receptor antagonists:** prazosin 哌唑嗪
- **α_2 receptor antagonists:** yohimbine 育亨宾

B *Drug actions and classification*

- (2) β receptor antagonists
 - $\beta_1\beta_2$ receptor antagonists: propranolol 普萘洛尔
 - β_1 receptor antagonists: atenolol 阿替洛尔
 - β_2 receptor antagonists: butoxamine 布他沙明

- (3) α, β receptor antagonists
 - labetalol 拉贝洛尔