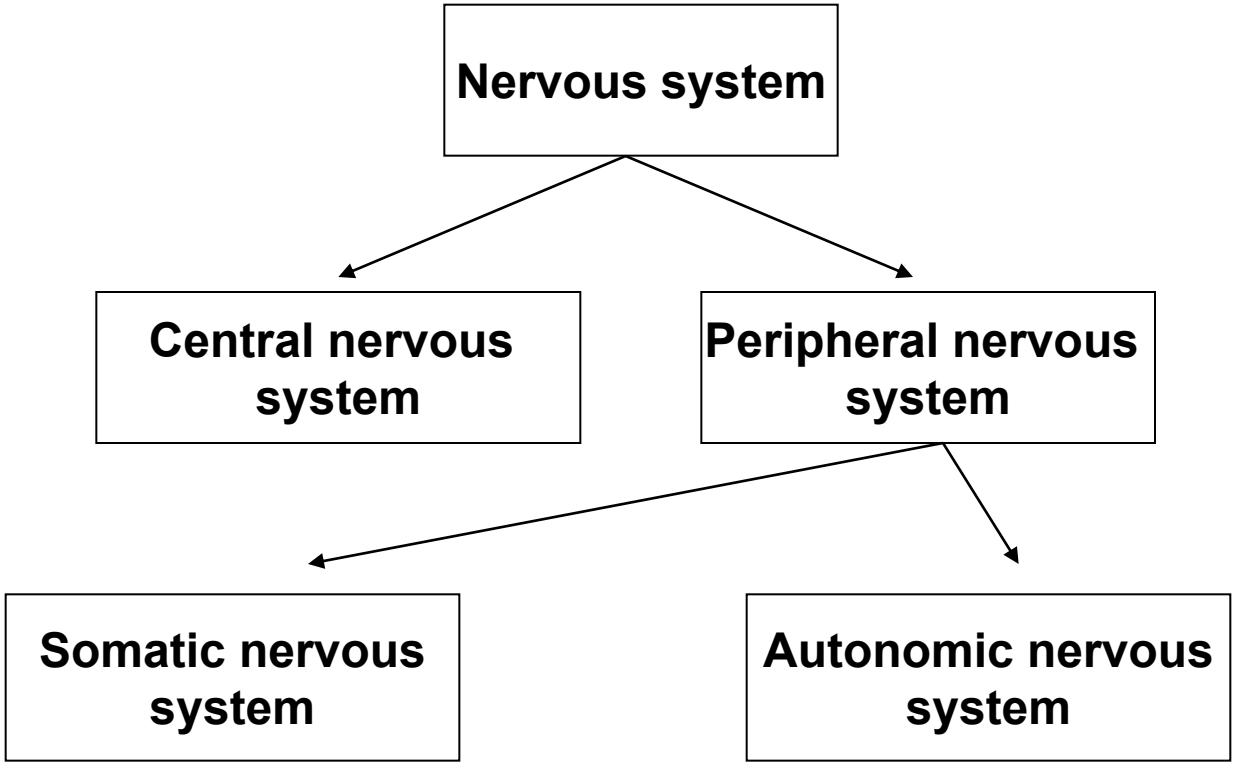
PHARMACOLOGY OF PERIPHERAL NERVOUS SYSTEM

AUTONOMIC NERVOUS SYSTEM


Nervous system
Central nervous system
Peripheral nervous system
Somatic nervous system
Autonomic nervous system

Autonomic nervous system

central part

peripheral part

HYPOTHALAMUS
MEDULLA OBLONG.

afferent system

efferent system

- non - myelinized fibers
- pain perception
- visceral perception

vegetative nerves + ggl.

SYMPATHETIC NERVOUS SYSTEM

PARASYMPATHETIC NERVOUS SYSTEM

Peripheral nervous system:

⇒**autonomic nervous system (ANS)**

⇒**enteric NS**

⇒**somatic efferent (motoric) system**

⇒**senzoric (afferent) fibers**

ANS – mediated the transfer of the impulses between the central nervous system (CNS) and the effector tissues; independent of the control of the will (smooth muscle, myocardium, exocrine glands, etc.), adapts the response of the organism to changes of the external and internal environment

Somatic efferent (motoric) system - converts impulses from the CNS to the will of controlled skeletal muscles

Main functions of ANS

- contractions and relaxations of smooth muscles
- function of all exocrine and some of endocrine glands
- heart functions
- metabolic functions

ANS

Sympathetic

= adrenergnic system

- thoracolumbal s.
- fight or flight
- noradrenaline(NA)
- α a ß receptors

Parasympathetic

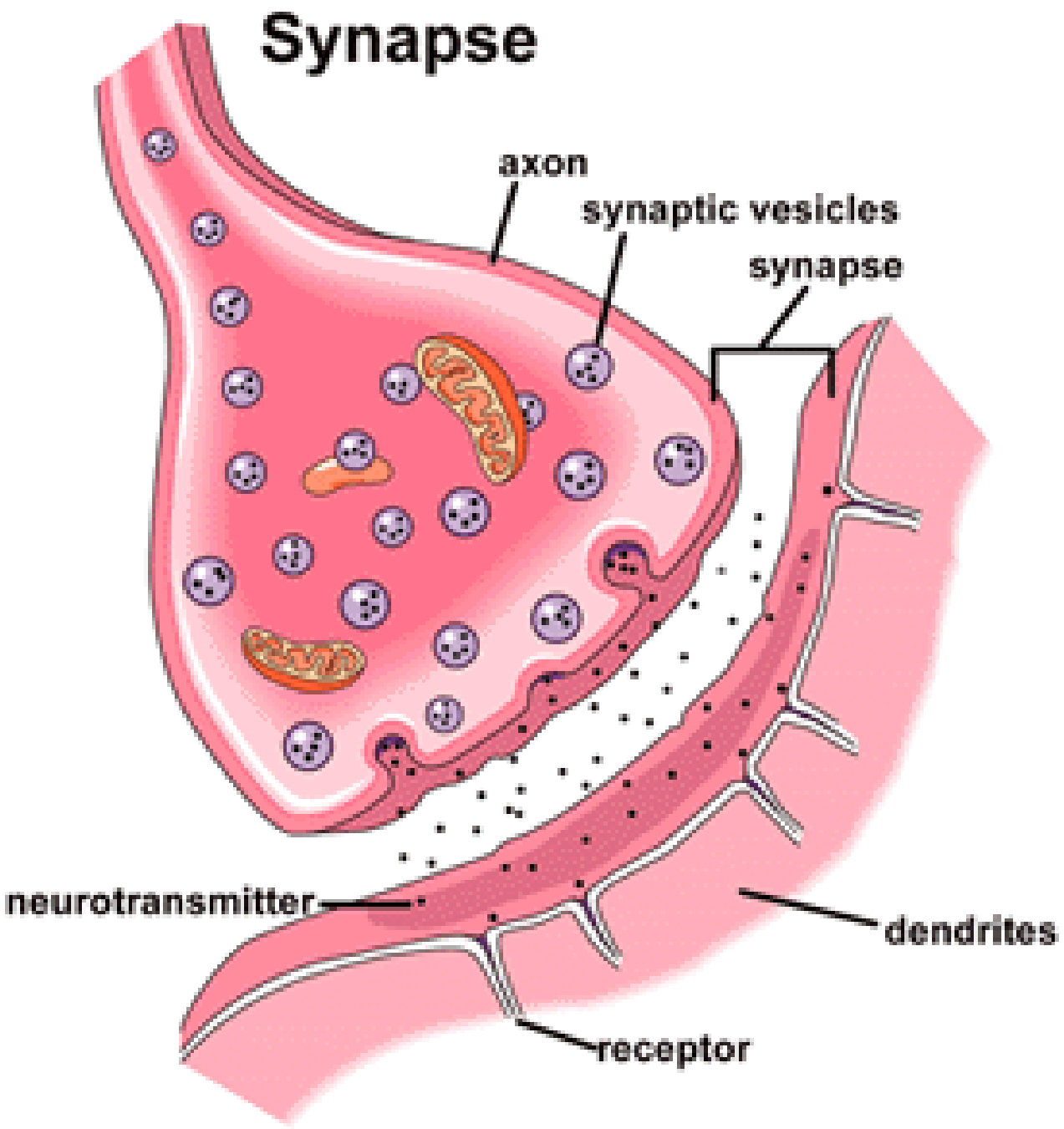
= cholinergnic system

- craniosacral s.
- rest and digest
- acetylcholine
- N a M receptors

Autonomic nervous system

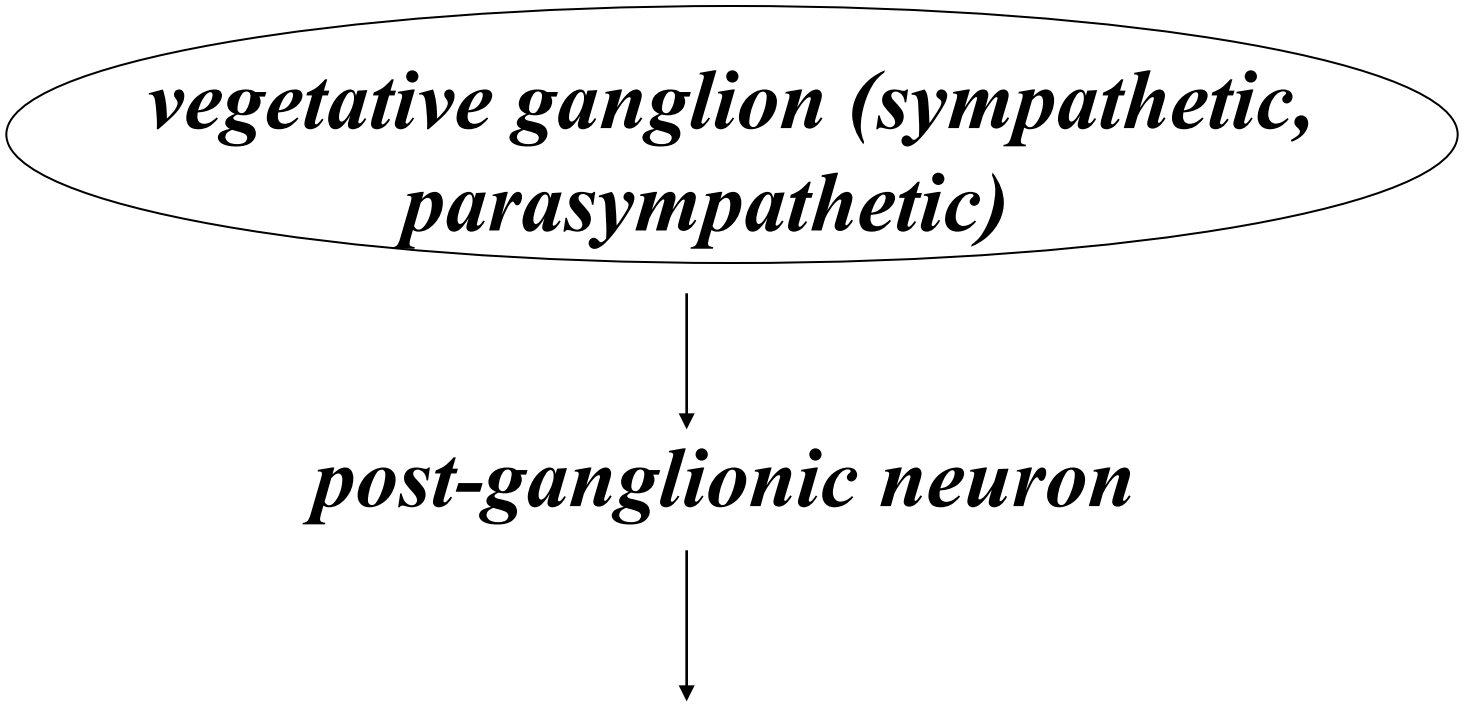
The activity is mutually regulated

- heterotropic interactions
- homotropic interactions
- most of visceral organs is inervated by both S and PS
- opposite activity - bronchi, heart, bladder,,…
- similar action – salivary glands
- only S – blood vessels


Synapse
axon
synaptic vesicles
synapse
neurotransmitter
dendrites
receptor

EFFERENT PART OF ANS:

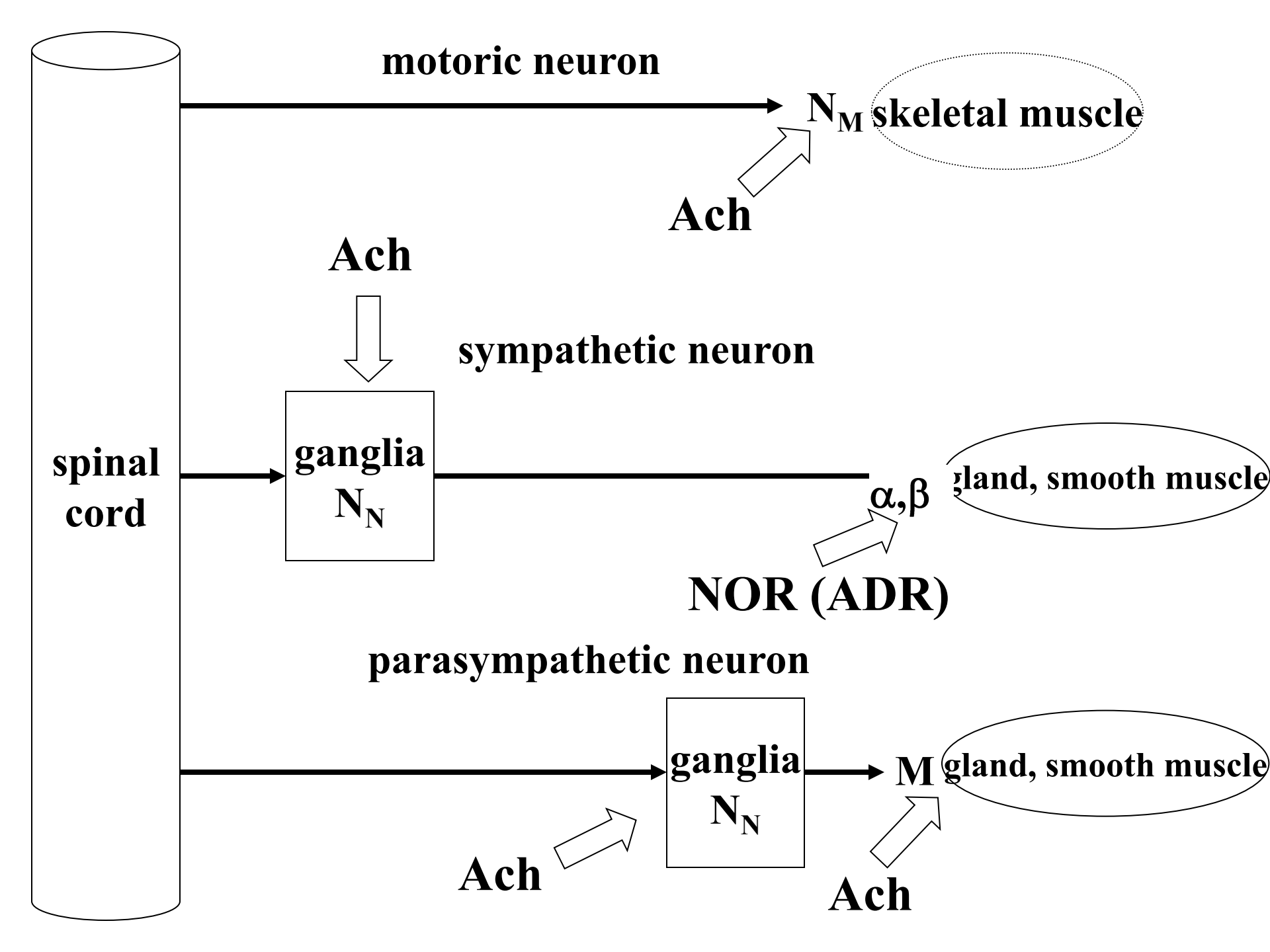
pre-ganglionic neuron



vegetative ganglion (sympathetic, parasympathetic)

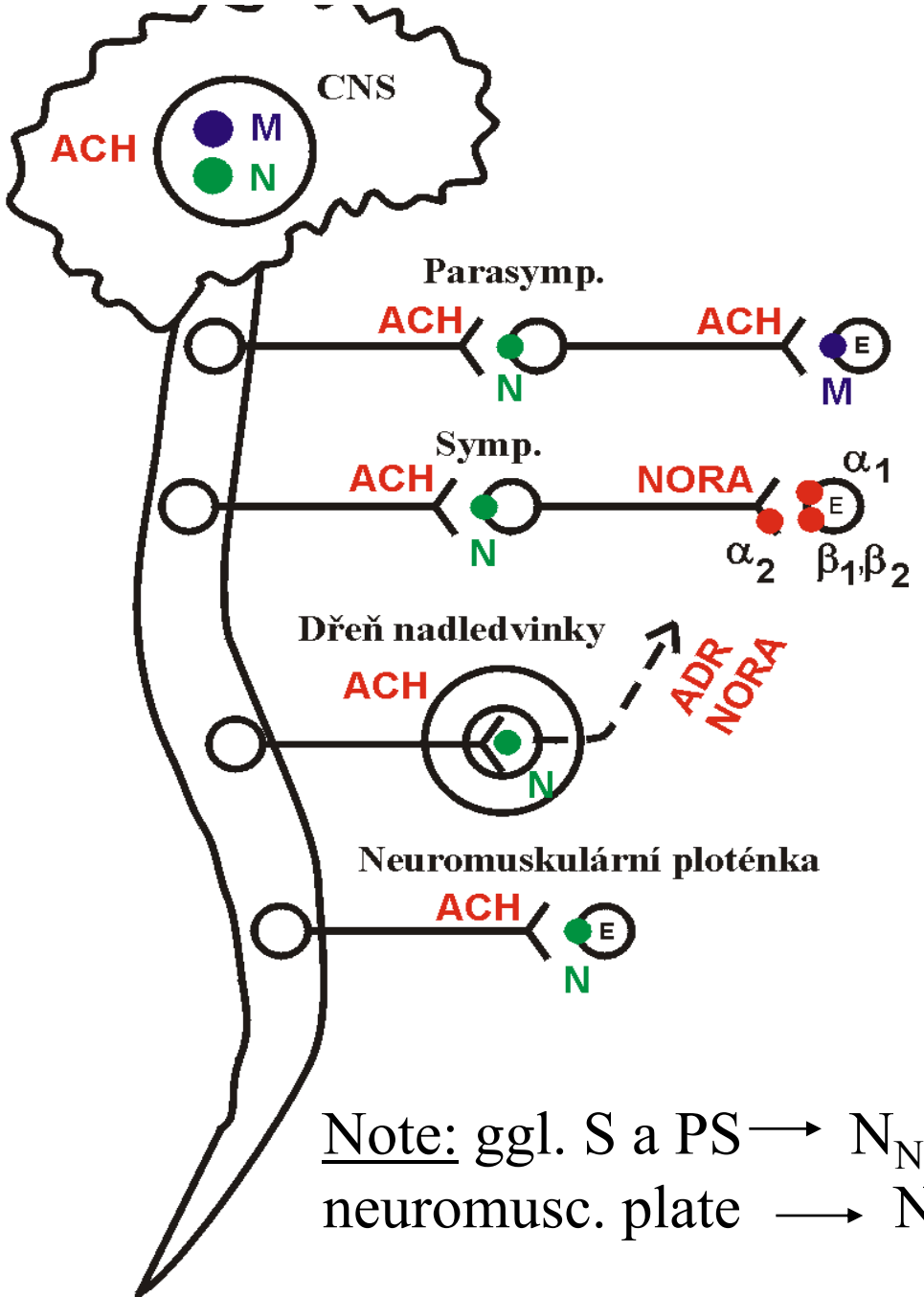
post-ganglionic neuron

EFFECTOR (smooth muscle, myocard, glands,…)


motoric neuron
N_M skeletal muscle
Ach
Ach
sympathetic neuron
spinal cord
ganglia N_N
α,β
gland, smooth muscle
NOR (ADR)
parasympathetic neuron
ganglia N_N
M
gland, smooth muscle
Ach
Ach

Obr. 1

Autonomic nervous system



Note: ggl. S a PS → N_N receptors

neuromusc. plate → N_M receptors

Autonomic acting pharmaceuticals

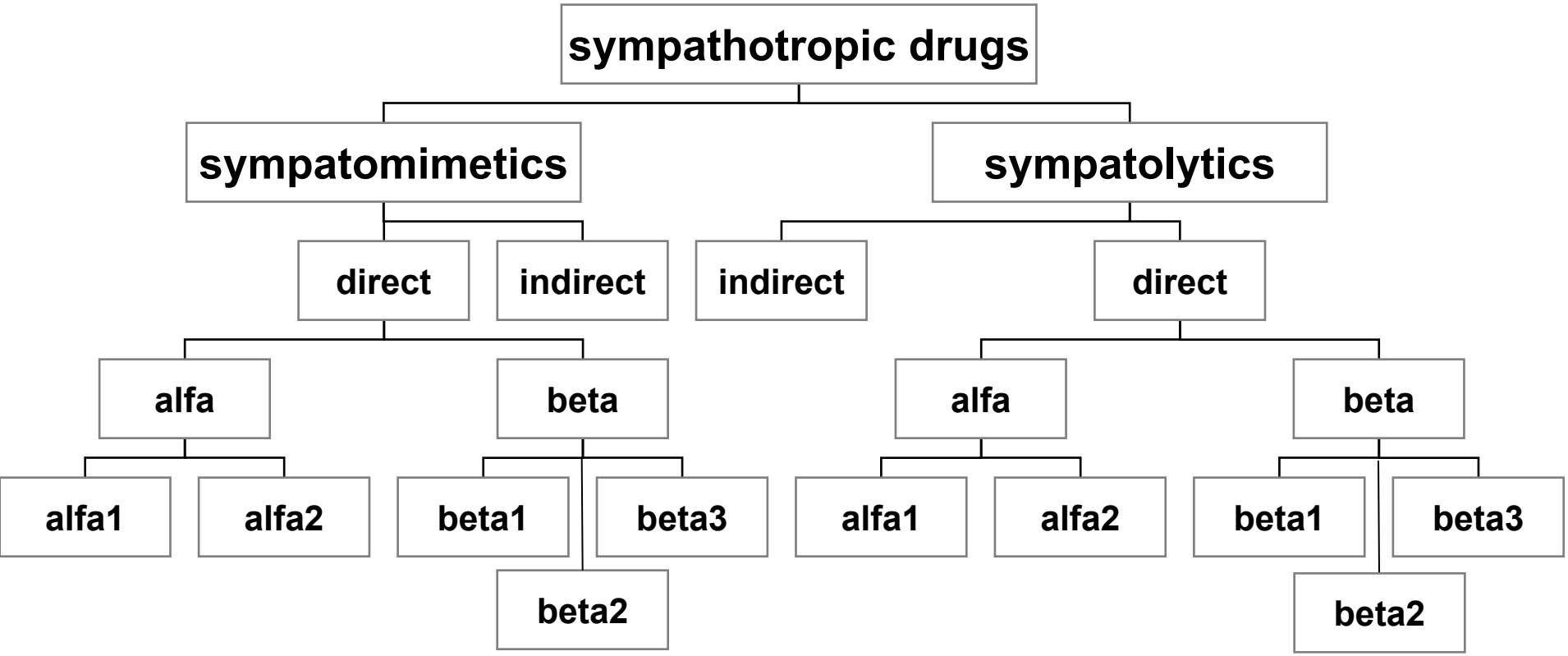
<u>On the basis of mechanism of action - drugs:</u>

1. **binding to the receptors** for Ach or NA:
   a) starting reaction = **agonist - DIRECT MIMETICS**
   b) receptor blockade = **antagonist – DIRECT LYTICS**

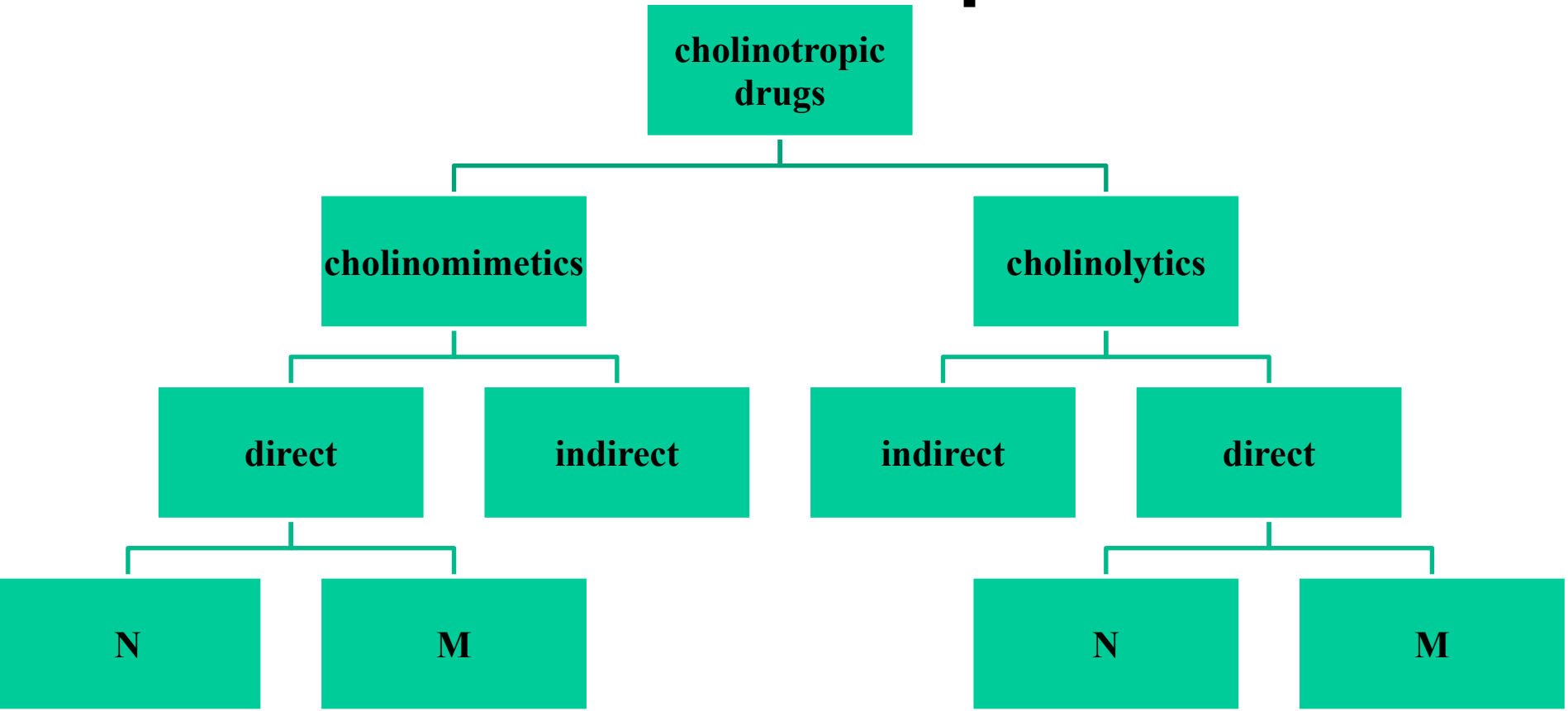
.....

2. **changing the synaptic concentration of NT** – intervene in the fate of the Ach or NA (affect the synthesis, storage, release from nerve endings, inactivation); do not bind directly to receptors on the effector organs
   a) increase of NT effect = **INDIRECT MIMETICS**
   b) decrease of NT effect = **INDIRECT LYTICS**

Vegetative acting drugs
2. sympatotropic



Vegetative acting drugs
2. cholinotropic



Vegetative acting drugs
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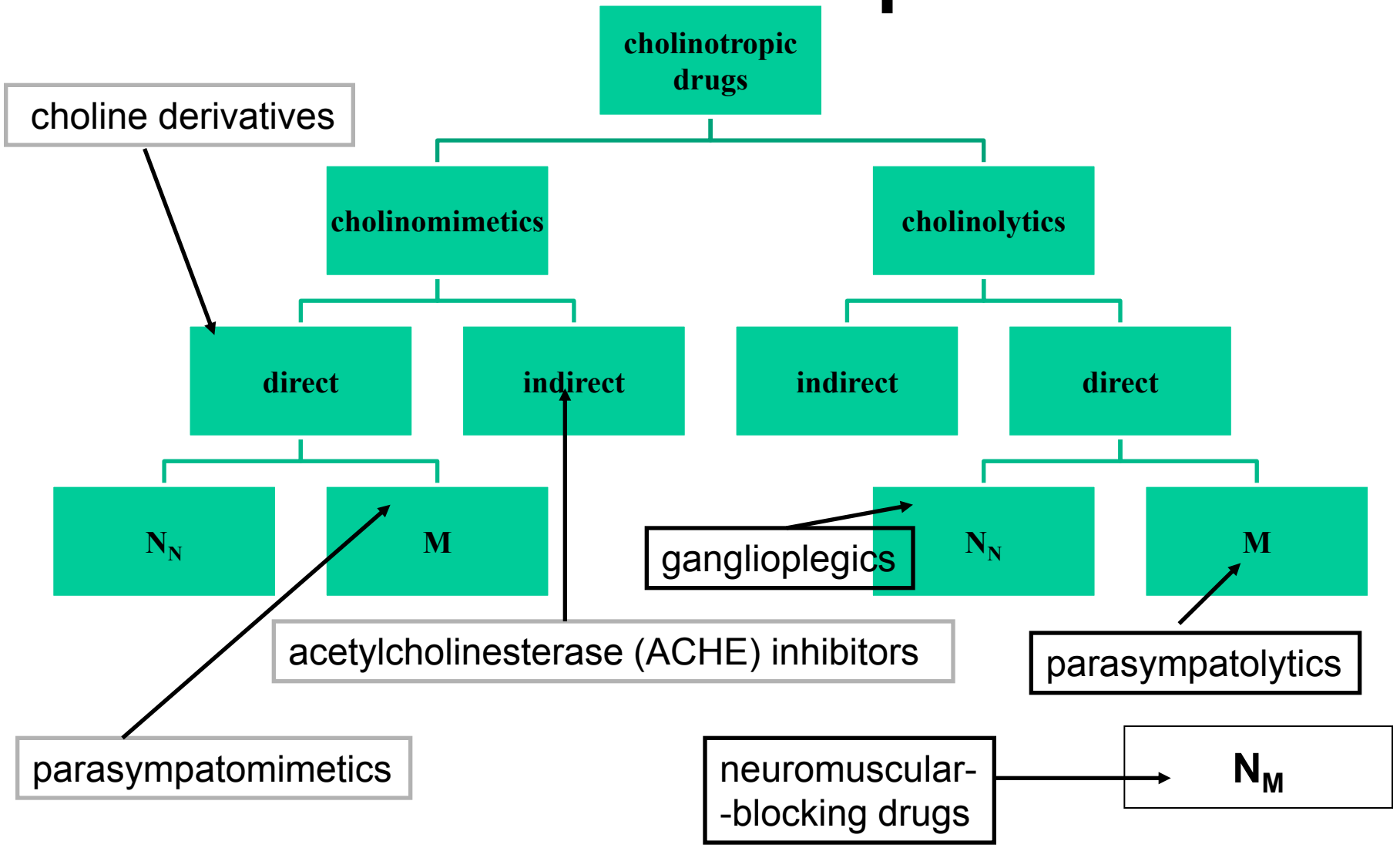
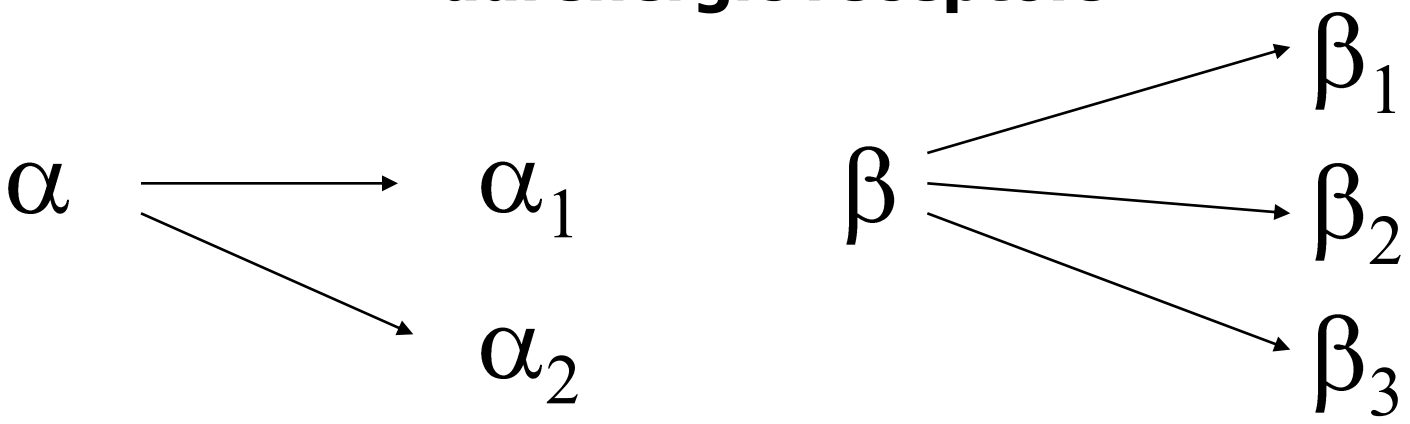


ANS RECEPTORS

adrenergic receptors



cholinergic receptors

NICOTINE: N

- **skeletal muscle N_M**
- **vegetative ganglia N_N**
- **(CNS)**

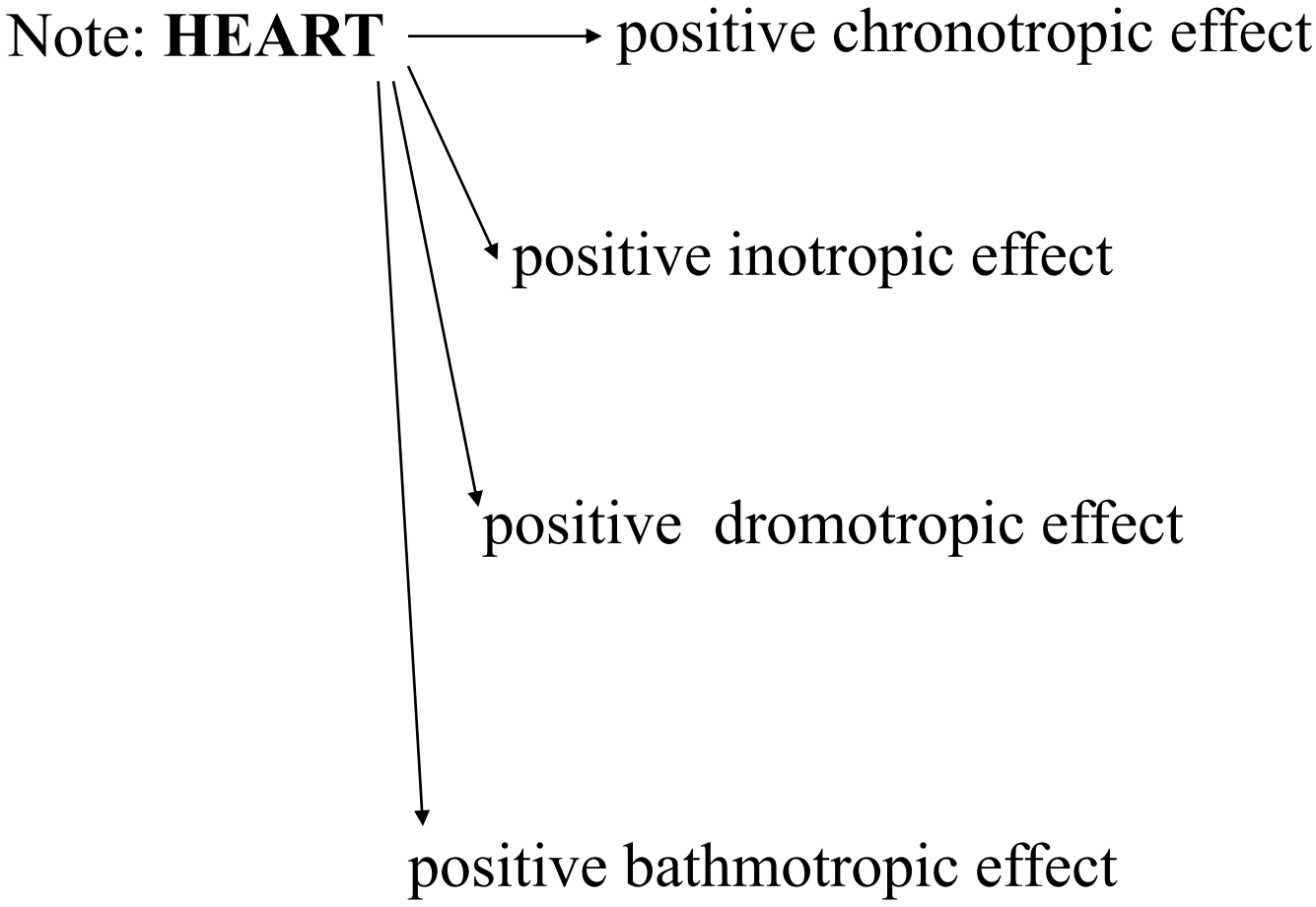
MUSCARINIC:

M_1, M_2, M_3, M_4, M_5

organ	receptor		sympathetic system	parasympathetic system
heart	β_1	M	+ chrono, dromo, bathmo, inotropic	- chrono, dromo bathmo, inotrop.
eye	α_1 β_2	M	mydriasis acomodation into the distance	miosis acom.to close
respiratory tract	(α_1) β_2	M	bronchoconstriction bronchodilatation	bronchoconstriction ↑secretion
blood vessels	α_1 (α_2) β_2	M	vasoconstriction vasoconstr. dilatation (coronary, blood vessels in skeletal muscles)	dilatation

organ	receptor		sympathetic system	parasympathetic system
GIT	α_1 α_2 $\beta_2 > \beta_1$	M M	↓ motility and tone sphincter contraction secretion inhibition	↑ motility sphincter relaxation secretion stimulation ↑ gastr. secretion
urinary bladder	α_1 β_2, β_3	M_3	sphinct. contraction relax. of the bladder wall	sphinct. relaxation contract. of the bladder wall
kidney	$\beta_1 > \beta_2$		↑ renin secretion	
uterus	α_1 β_2		contraction relaxation-tocolysis	

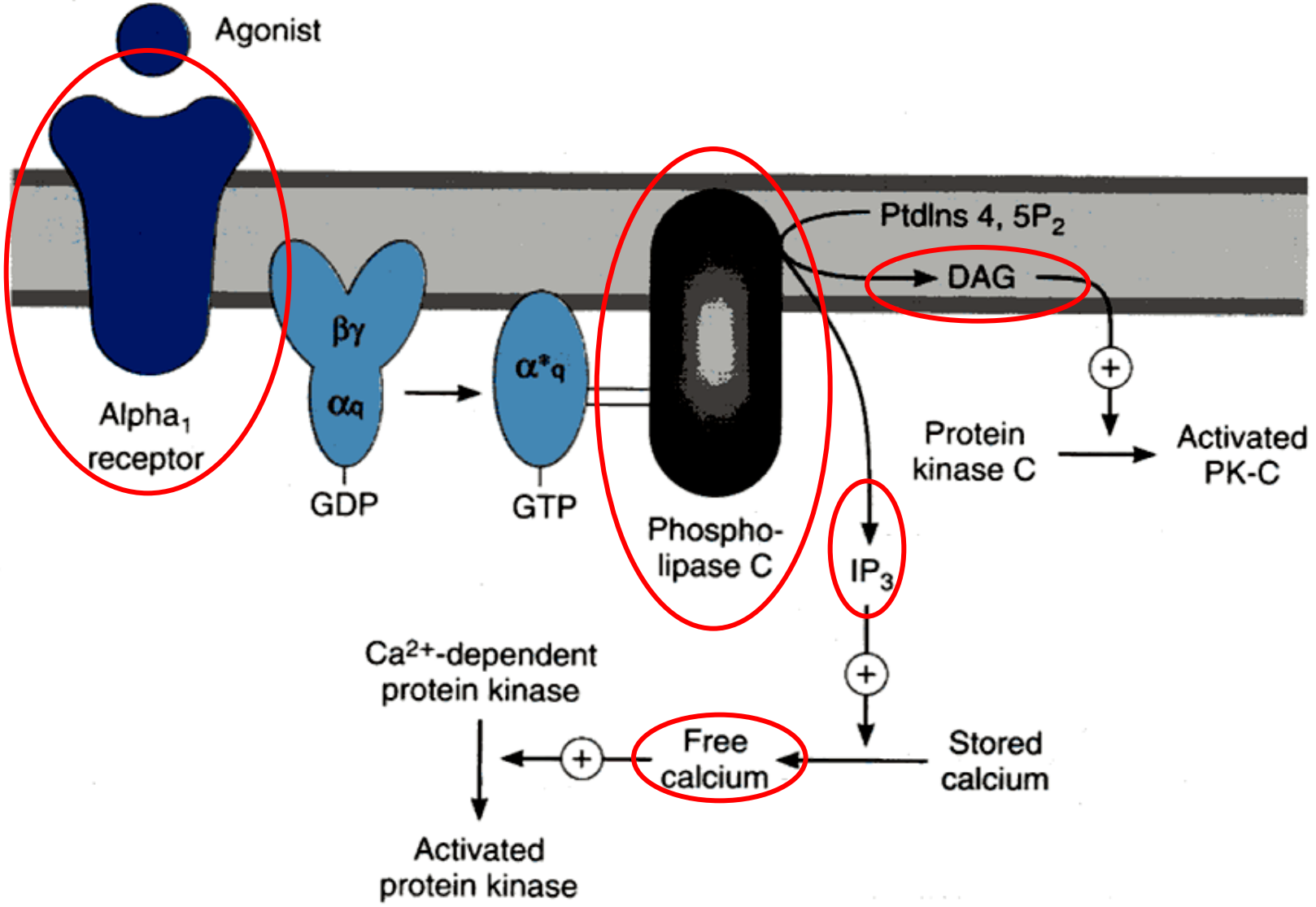
organ	receptor	sympathetic system	parasympathetic system
liver	α_1, β_2	glycogenolysis gluconeogenesis	
pancreas	α_2 β_2	↓insulin secretion ↑insulin secretion	
sexual organs	α_1 M	ejaculation	erection
glands	α_1 M β_2	sparse secretion viscous secretion	sparse significantly increased secretion


Note: **HEART**
positive chronotropic effect
positive inotropic effect
positive dromotropic effect
positive bathmotropic effect

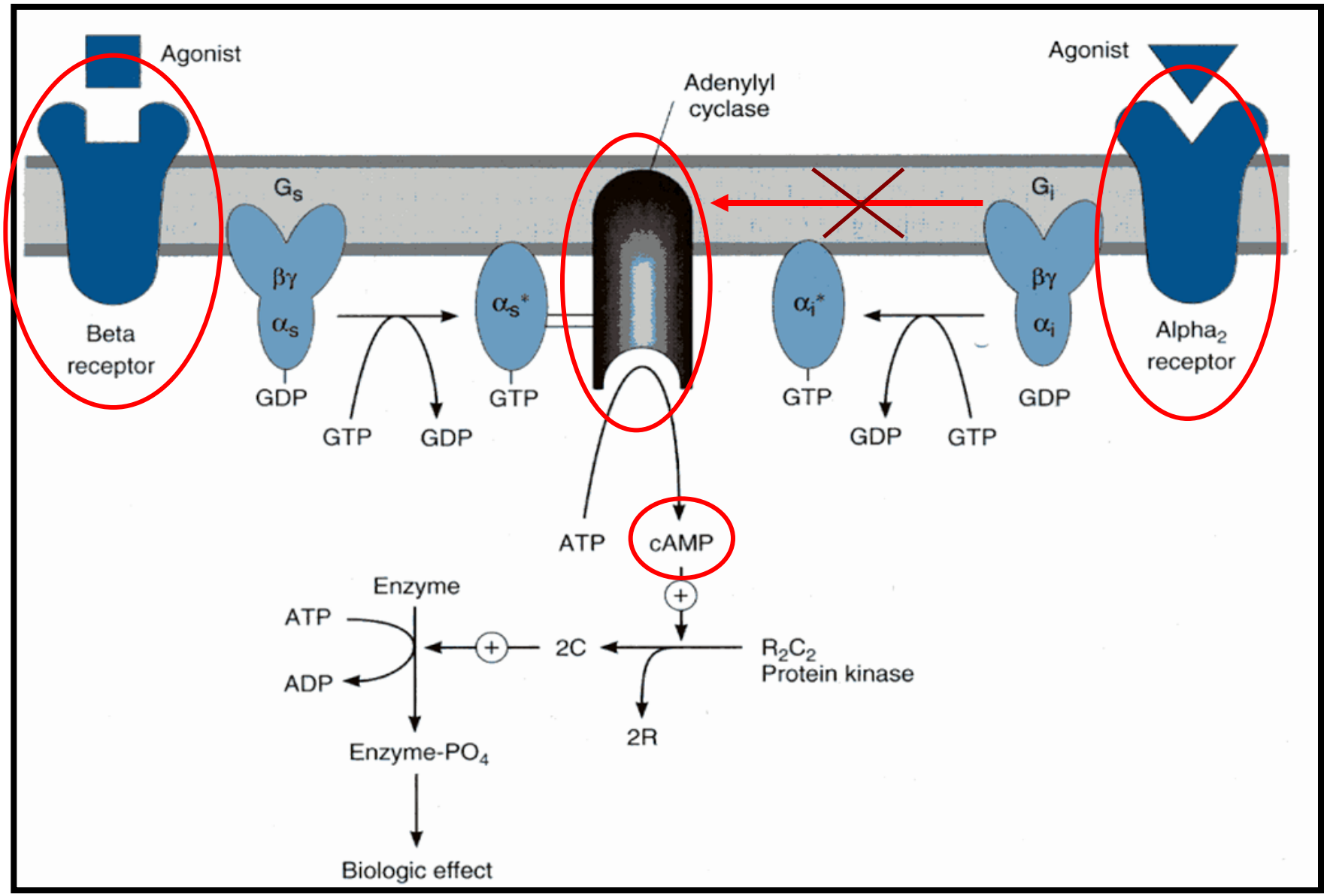
Adrenergic receptors

- metabotropic
- α_1, α_2 a β_1, β_2 a β_3
- stimulated by noradrenaline (norepinephrine)

α_1 receptors:



α_2, β receptors:



Receptor α_1 stimulation:

- ***vasoconstriction*** (skin, mucous membranes, splanchnic area,..)
- ***mydriasis***

  (+ ↓ intraocular pressure)
- ***contraction of pregnant uterus***
- ***ejaculation***
- ***urinary bladder sphincter contraction, GIT sphincter contraction***
- ***glycogenolysis and gluconeogenesis stimulation***
- ***(reduce secretion of bronchial glands)***

Receptor α_2 stimulation:

- **(presynaptic) *increased NA release* (espec. in CNS)**
- ***stimulation of platelet aggregation***
- ***vasoconstriction in local application*, otherwise the influence of stimulation of central receptors to reduce sympathetic tone and BP**
- ***hypotensive effect of central mechanism***
- ***inhibition GIT secretion***
- ***inhibition of lipolysis, increased fat storage***

Receptor β_1 stimulation :

heart:

- ⇧ HR (+ **chronotropic** effect) SA node
- ⇧ automaticity (+ **bathmotropic**) AV node, ventricles
- ⇧ force of heart contraction (**inotropic effect**)
- ⇧ conduction (**dromotropic effect)**
- ⇧ oxygen consumption

ledviny:

- ⇧ renin secretion

Receptor β_2 stimulation:

- ***vasodilatation, espec. in skeletal muscles*** ("preparation for fight or flight"), ⇩ diastol. BP, ***vasodilatation in coronar blood vessels***
- ***bronchodilatation***
- ***relaxation of uterus*** (indic. in impending preterm birth)
- ***intestine wall relaxation***
- ***intestinal passage decrease***
- ***urinary bladder wall relaxation***
- ***glycogenolysis*** - ↑ glycemia, increased insulin secretion
- ***blockade of mast cells degranulation***

Receptor β_3 stimulation:

- ***lipolysis***
- ***urinary bladder wall relaxation (m. detrusor)***

Cholinergic receptors

MUSCARINIC:

M_1(„neural“) – CNS, peripheral neurons,parietal cells of stomach, (glands with external secretion)

M_2 („heart“) - heart (SA, atria, AV, ventricles), (smooth muscle (GIT), neuronal tissue), presynapt. neur.endings

M_3 – glands, blood vessels (smooth muscle, hl. sval, endothelium), smooth muscles: bronchial muscles, GIT, urinary bladder, eye

M_4 – salivary glands, GIT (muscles), eye, CNS

M_5 – lungs, CNS

Cholinergic receptors

- M – metabotropic
- stimulated by acetylcholine
- N – coupled with ion channels
- stimulated by nicotine

Cholinergic receptors

molecular mechanisms of action:

* 1) phospholipase C activation
   2) adenylylcyclase inhibition
   } **M receptors**

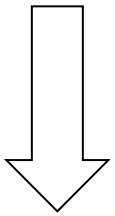
   3) direct openning of ion channels
   } **N recept.**

* **M_1, M_3 receptors**
M_5 → ↑ **PLC** → **IP_3** → ↑ **Ca^{2+}**
DAG

M_2, M_4 receptors → ↓ **AC**

in heart activation of receptor coupled K+ channel, calcium channel inhibition

NICOTINIC RECEPTOR



Pentamer:subunits 2x α and

- β δ γ
- β δ ε

ion channel for **Na^+, K^+ and Ca^{2+}**

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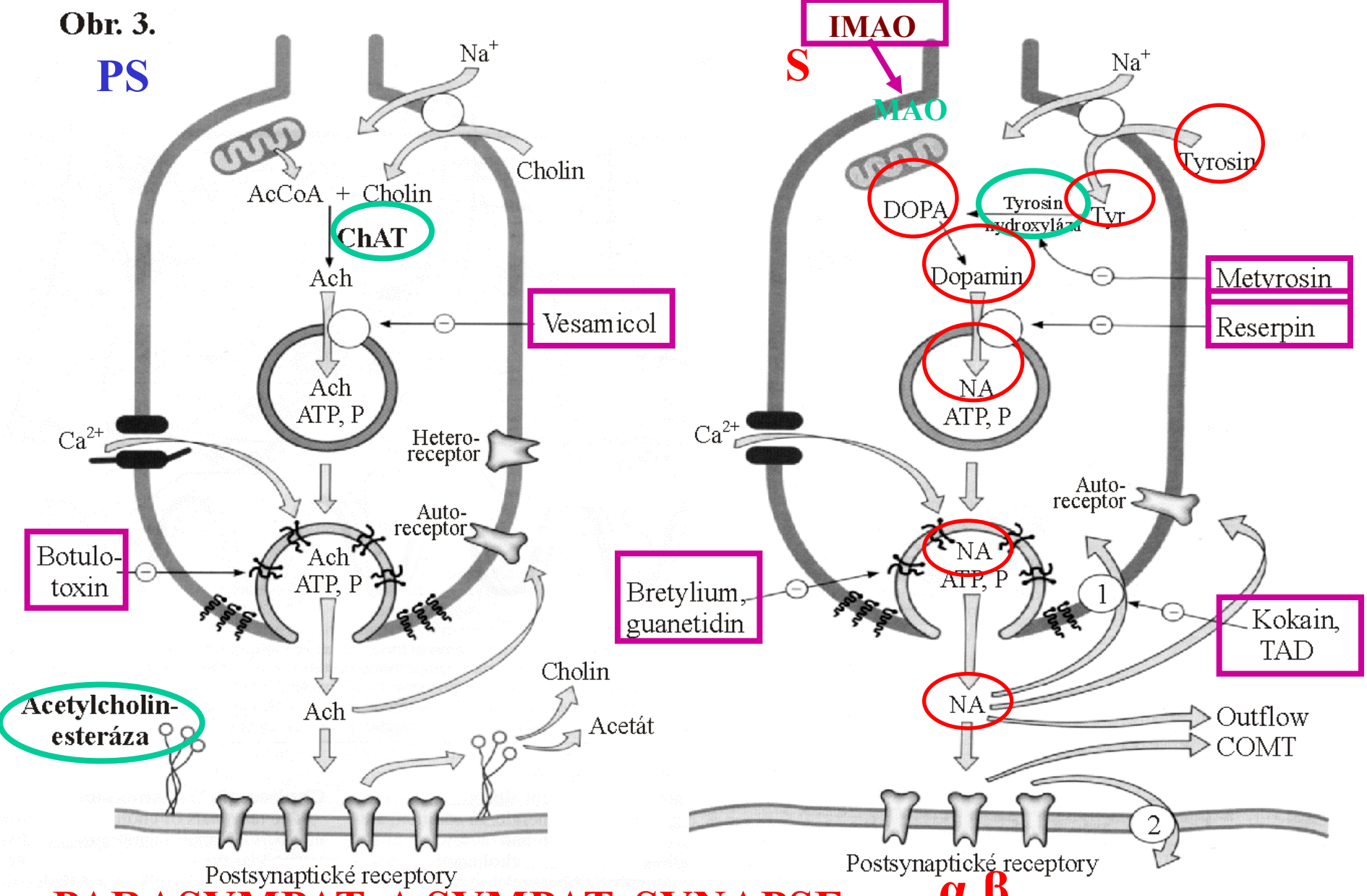
after binding of 2 molecules of Ach to the 2 subunit of the **α**

openning of ion channel – rapid entry of Na^+ into the cell, output of K^+

membrane depolarisation

EXCITATION

Obr. 3.



PARASYMPAT. A SYMPAT. SYNAPSE

Použité zkratky - Ach - acetylcholin, ChAT - cholin acetyltransferáza, AcCoA- acetyl koenzymA, ATP - adenosin trifosfát, P - substance P, NA - noradrenalin, COMT -katechol-O-metyltransferáza, 1 - uptake 1 = reuptake, 2 - uptake 2, TAD - tricyklická antidepresiva