2.3 NEUROTRASMETTITORI

- **Recettori ionotropi e metabotropi**
- **Principali neurotrasmettitori**
- **Glutammato e suoi recettori**
- **GABA e suoi recettori**
- **Catecolamine e loro recettori**
- **Neurotrasmettitori e recettori del SNA**
- **Patologie della sinapsi chimica**

- i neurotrasmettitori liberati per esocitosi dalla cellula presinaptica si legano ai recettori sulla cellula postsinaptica e attivano (o chiudono) canali ionici

- i recettori postsinaptici:
  - ***riconoscono*** il neurotrasmettitore (formano un complesso)
  - si ***attivano*** (complesso attivato)
  - ***conducono*** ioni oppure ***attivano*** una ***G proteina*** che attiva ***2i messaggeri*** che agiscono sui rispettivi ***effettori***

- si dividono in due classi principali: ***ionotropi*** e ***metabotropi***

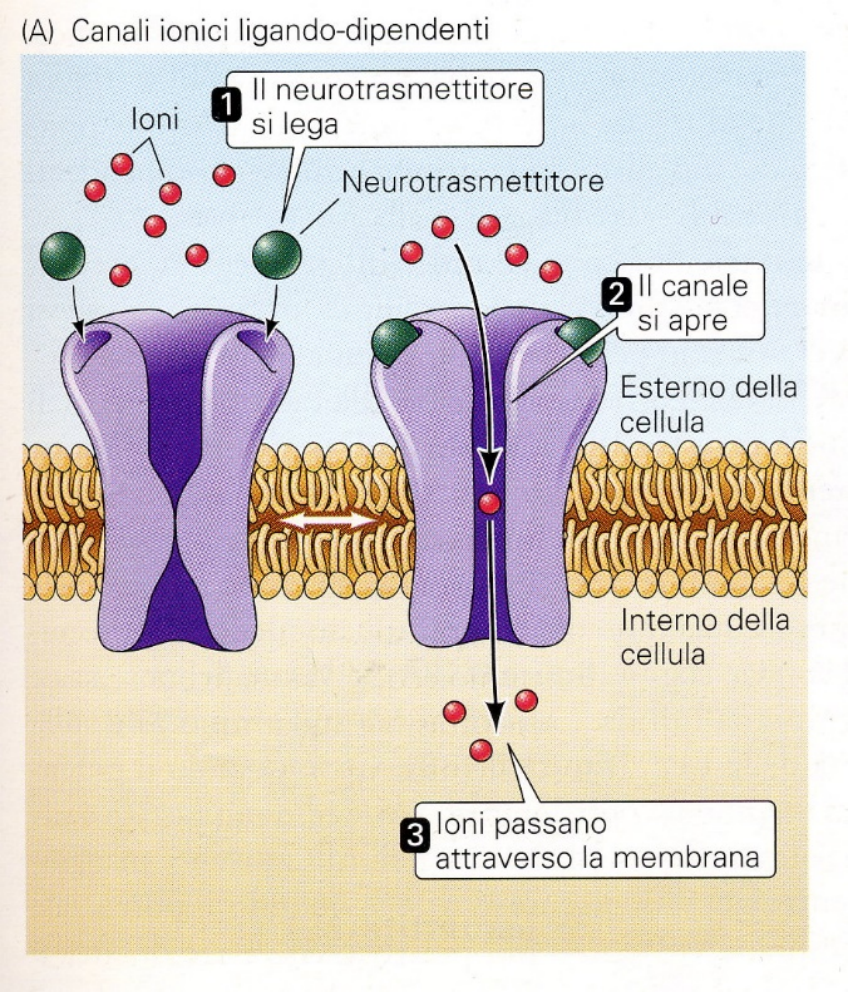
• Recettori ionotropi

il recettore ionotropo ***è un canale ionico 'ligando-dipendente'***

sono recettori ionotropi:

nAChR
$GABA_A$
glicina
NMDA
AMPA
kainato

apertura rapida (ms)

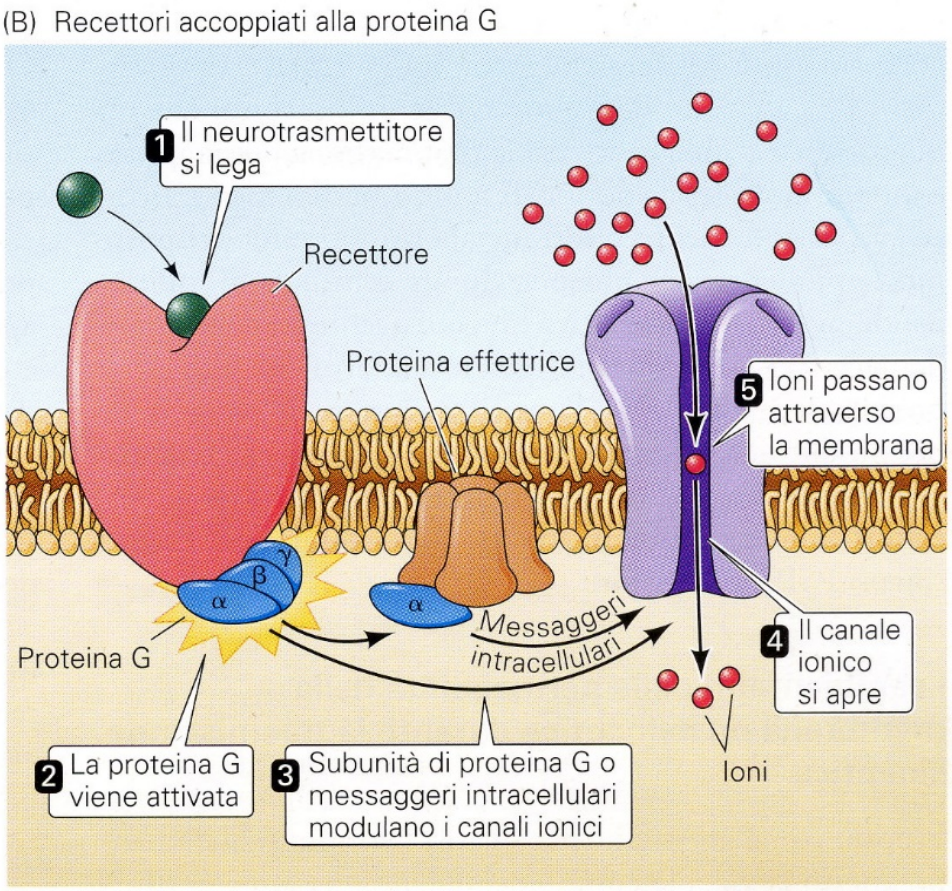


• Recettori metabotropi

- il recettore metabotropo ***non è un canale***. E' una proteina con ***7 α–eliche*** transmembranali, che interagisce con una proteina G che a sua volta attiva altri effettori (canali e/o secondi messaggeri)
- sono recettori metabotropi:

mAChR
$GABA_B$
glutamatergici
α, e β–adrenergici
neuropeptidergici
dopaminergici
serotoninergici
purinergici

- azione lenta (100 ms-100 s)
  - apre o chiude un canale del Na^+, K^+ o Ca^{2+}

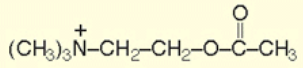


- La proteina G, attivata dal recettore, ***apre*** (o *chiude*) ***direttamente*** i canali ionici
- La proteina G, attivata dal recettore, ***attiva*** (o *inibisce*) ***enzimi*** che producono ***2i messaggeri*** che, a loro volta aprono o chiudono ***canali ionici***

Neurotrasmettitori a basso peso molecolare

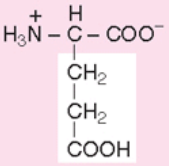
NEUROTRASMETTITORI A BASSO PESO MOLECOLARE

Aceticolina

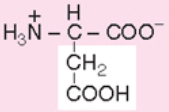


AMINOACIDI

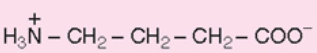
Glutammato



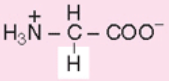
Aspartato



GABA

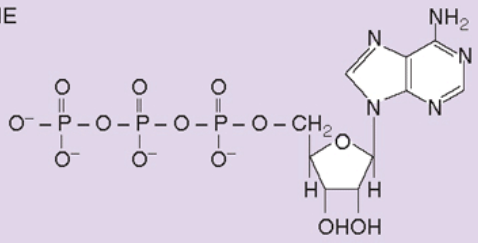


Glicina



PURINE

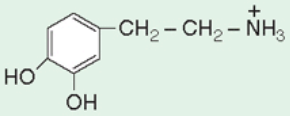
ATP



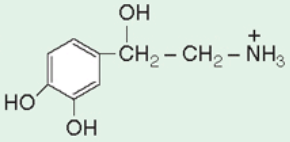
AMMINE BIOGENE

CATECOLAMMINE

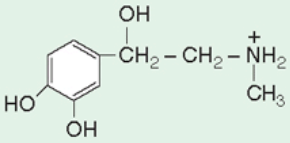
Dopamina



Noradrenalina

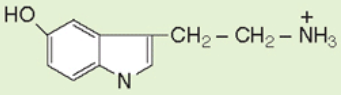


Adrenalina



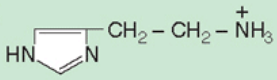
INDOLAMINA

Serotonina (5-HT)



IMIDAZOLAMMINA

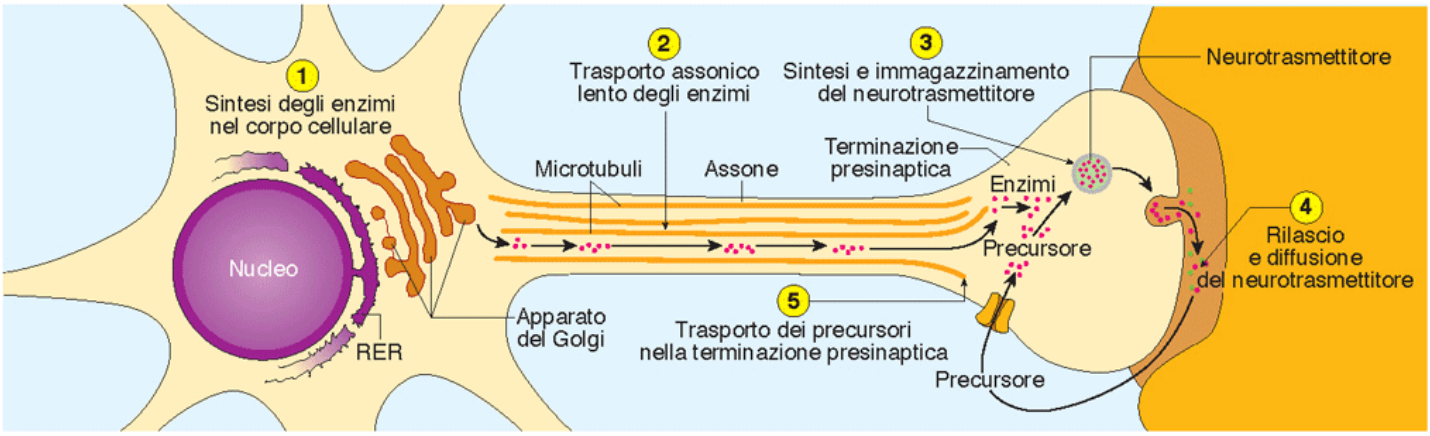
Istamina

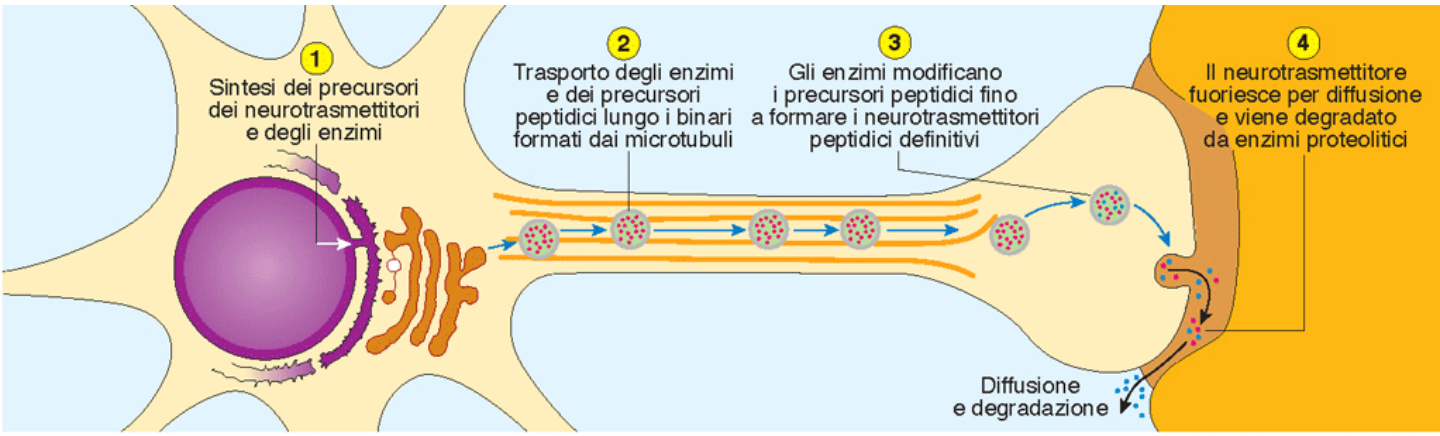


PRINCIPALI NEUROTRASMETTITORI PEPTIDICI

NEUROPEPTIDI	Aminoacidi
Leu-encefalina	5
Met-encefalina	5
α-Endorfina	16
β-Endorfina	30
Sostanza P	11
Somatostatina 14	14
Ormone rilasciante la tireotropina (TRH)	3
Ormone rilasciante l'ormone luteinizzante (LHRH)	10
Angiotensina II	8
Vasopressina	9
Ossitocina	9
Colecistochinina octapeptide (CCK-8)	8
Peptide intestinale vasoattivo (VIP)	27
Neuropeptide Y	36
Neurotensina	12
Bombesina (BBS-14)	14

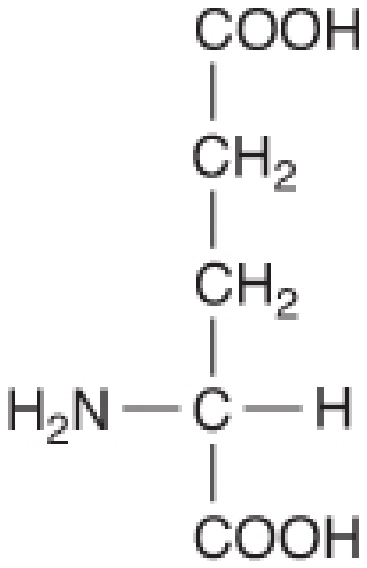
Differenze di sintesi e trasporto tra i piccoli neurotrasmettitori ed i trasmettitori peptidici



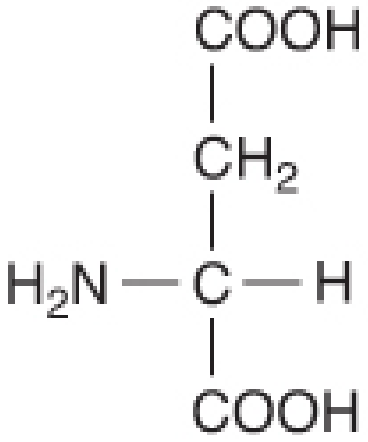


- **Glutammato e suoi recettori**

GLUTAMMATO:
è il principale neurotrasmettitore eccitatorio del sistema nervoso centrale



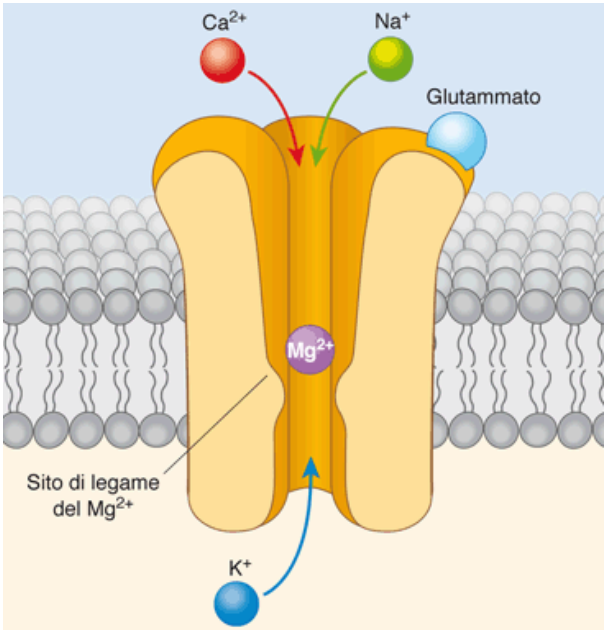
Glutammato



Aspartato

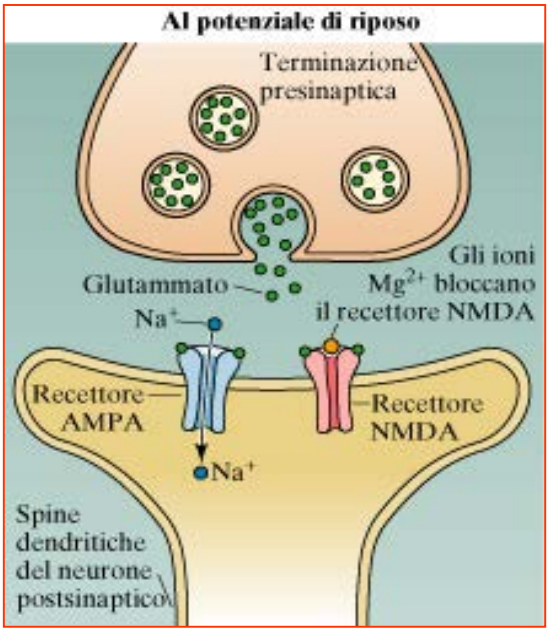
(a) Neurotrasmettitori aminoacidici eccitatori

RECETTORI IONOTROPI DEL GLUTAMMATO

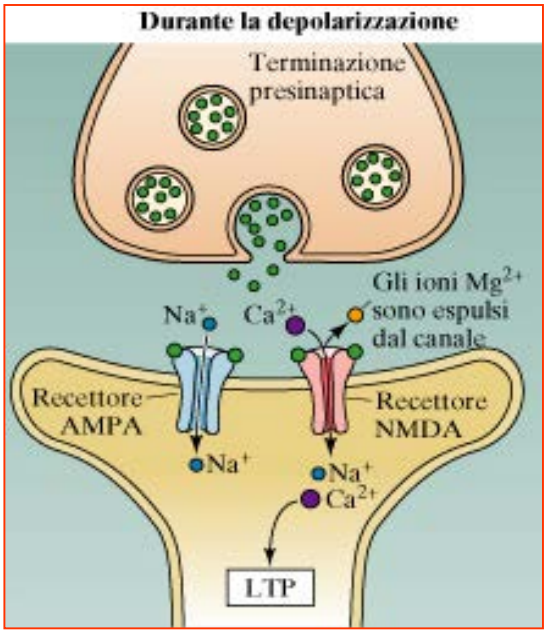


RECETTORI NMDA DEL GLUTAMMATO

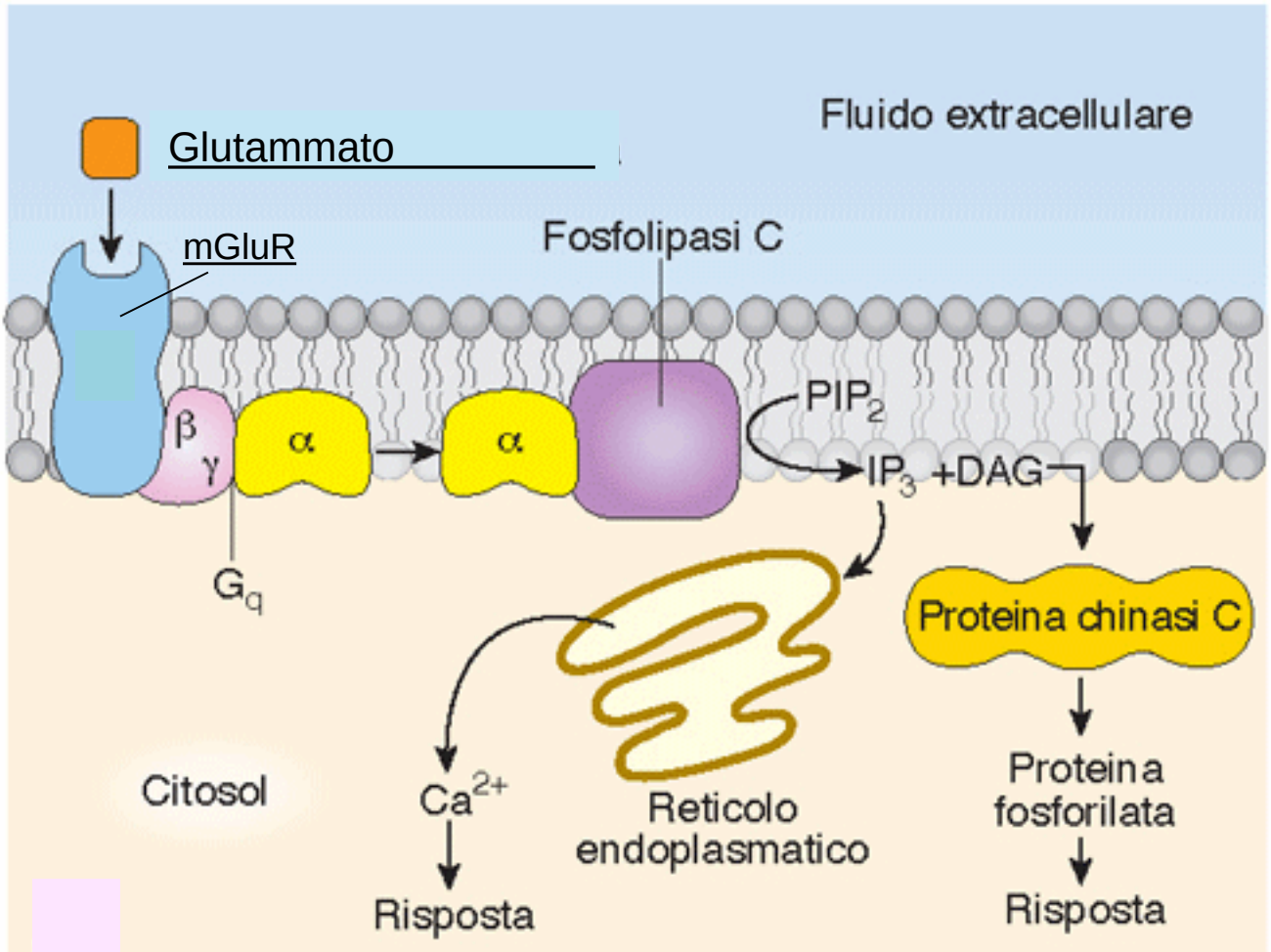
Recettori AMPA



Recettori NMDA



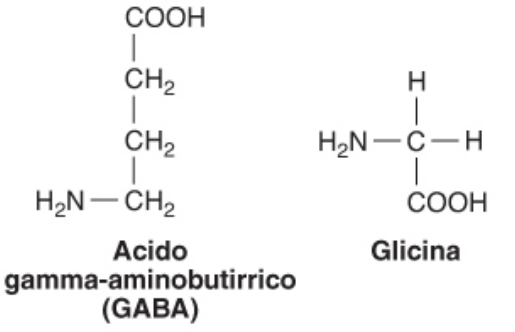
RECETTORI METABOTROPI DEL GLUTAMMATO



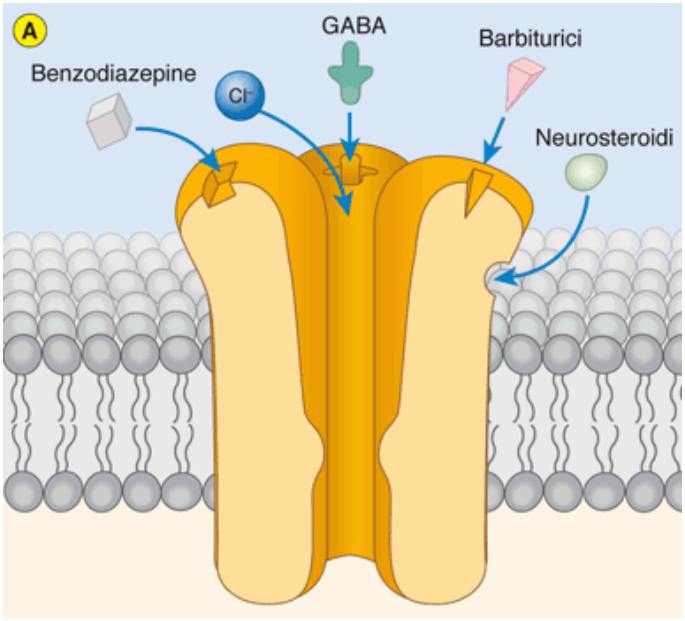
• il glutammato si lega anche agli ***mGluR1*** causando:

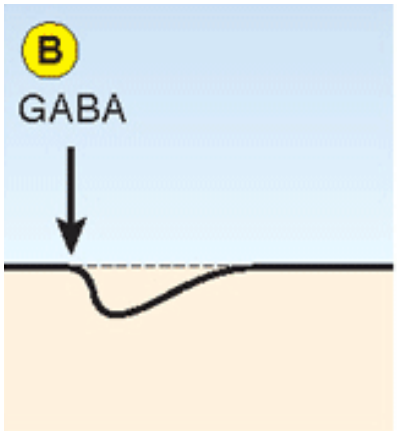
- attivazione di una proteina ***Gq***
- attivazione della ***PLC*** (fosfolipasi C)
- formazione di 2 messaggeri:
  inositolo trifosfato (***IP_3***) (intracellulare)
  diacil-glicerolo (***DAG***) (attiva la ***PKC***)
- l'***IP_3*** apre canali del Ca^{2+} a livello del reticolo endoplasmatico con conseguente aumento del Ca^{2+} intracellulare

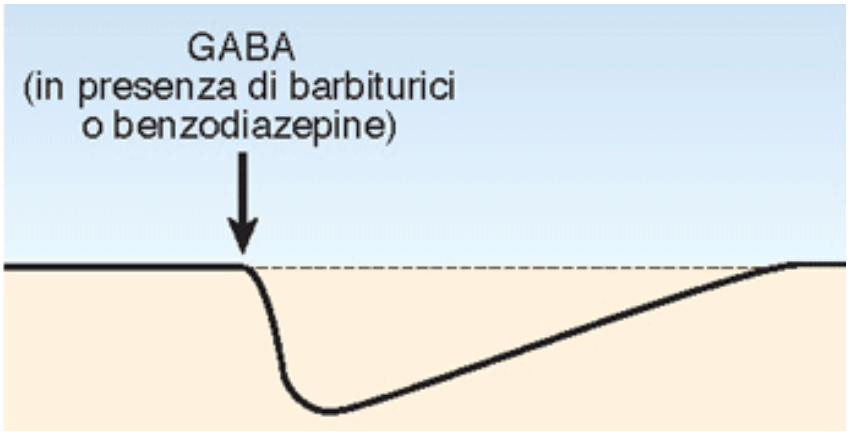
- **GABA e suoi recettori**

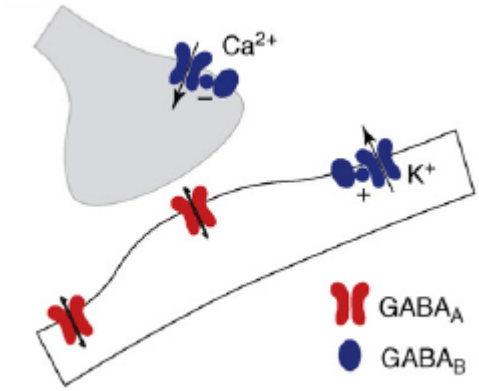


(b) Neurotrasmettitori aminoacidici inibitori









The $GABA_A$ receptors directly control the gating of ion channels permeable to chloride and bicarbonate ions. They cluster at synaptic release sites, where they produce synaptic conductances with fast rise and decay kinetics and mediate phasic inhibition.

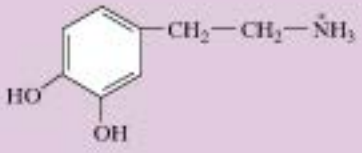
$GABA_B$ receptors are located both pre- and postsynaptically, where their major respective roles appear to be in regulating transmitter release by inhibiting Ca^{2+} channels, and mediating slow inhibitory conductances lasting hundreds of milliseconds through the activation of inwardly rectifying K^+ channels

• CATECOLAMINE e recettori

AMMINE BIOGENE

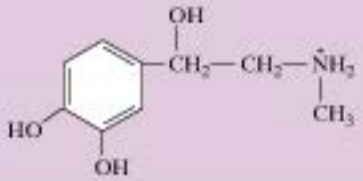
CATECOLAMINE

Dopamina



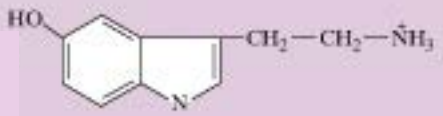
Noradrenalina

Adrenalina



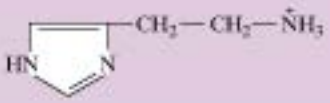
INDOLAMMINA

Serotonina (5-HT)



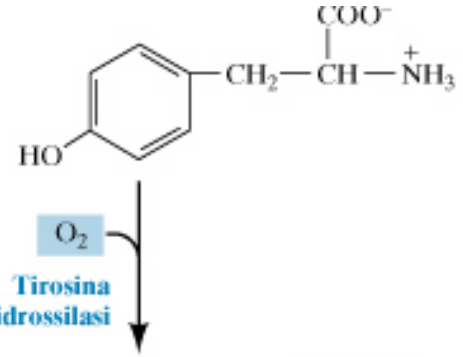
IMIDAZOLAMMINA

Istamina

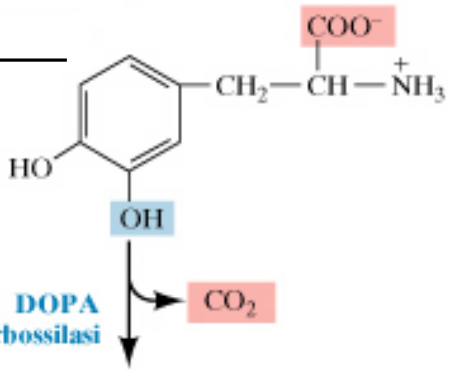


Tirosina

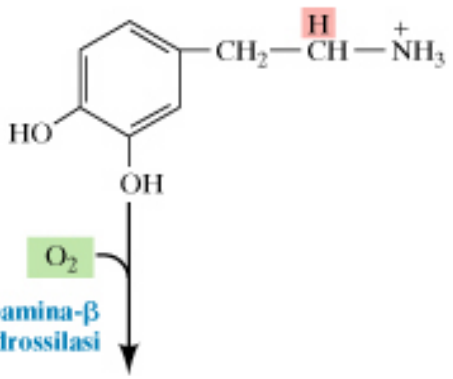
Tirosina



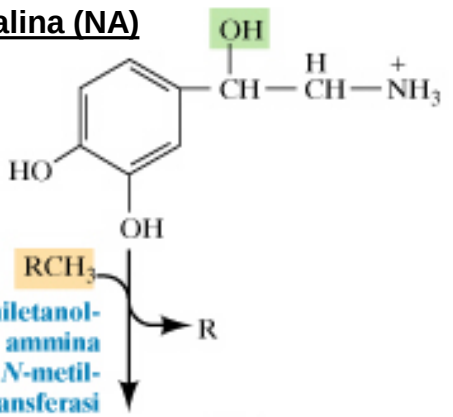
DOPA



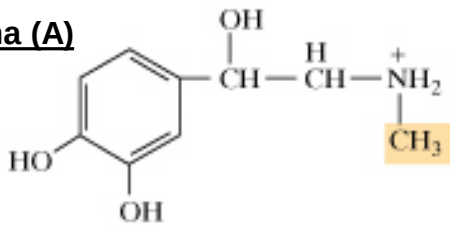
Dopamina



Noradrenalina (NA)

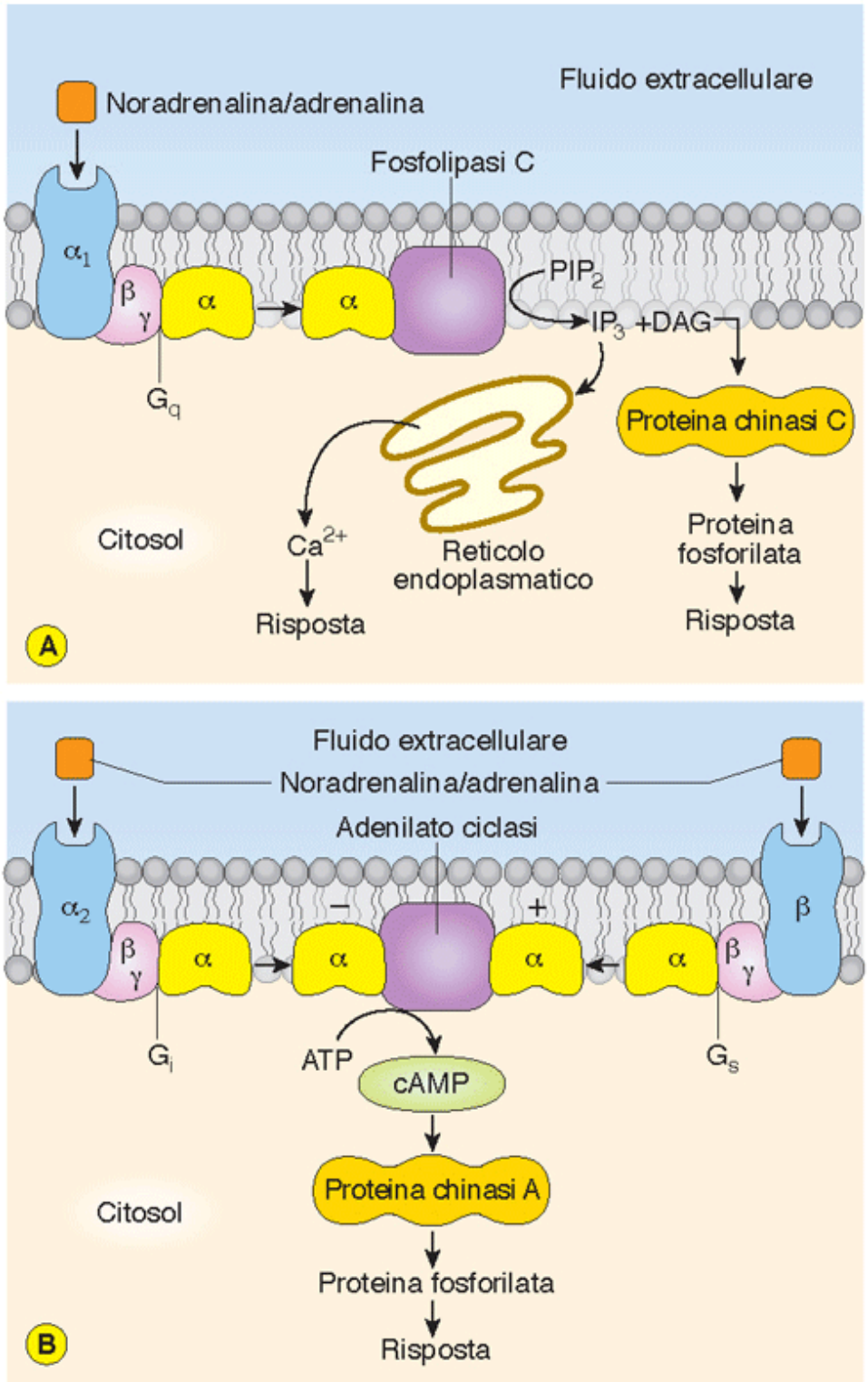


Adrenalina (A)

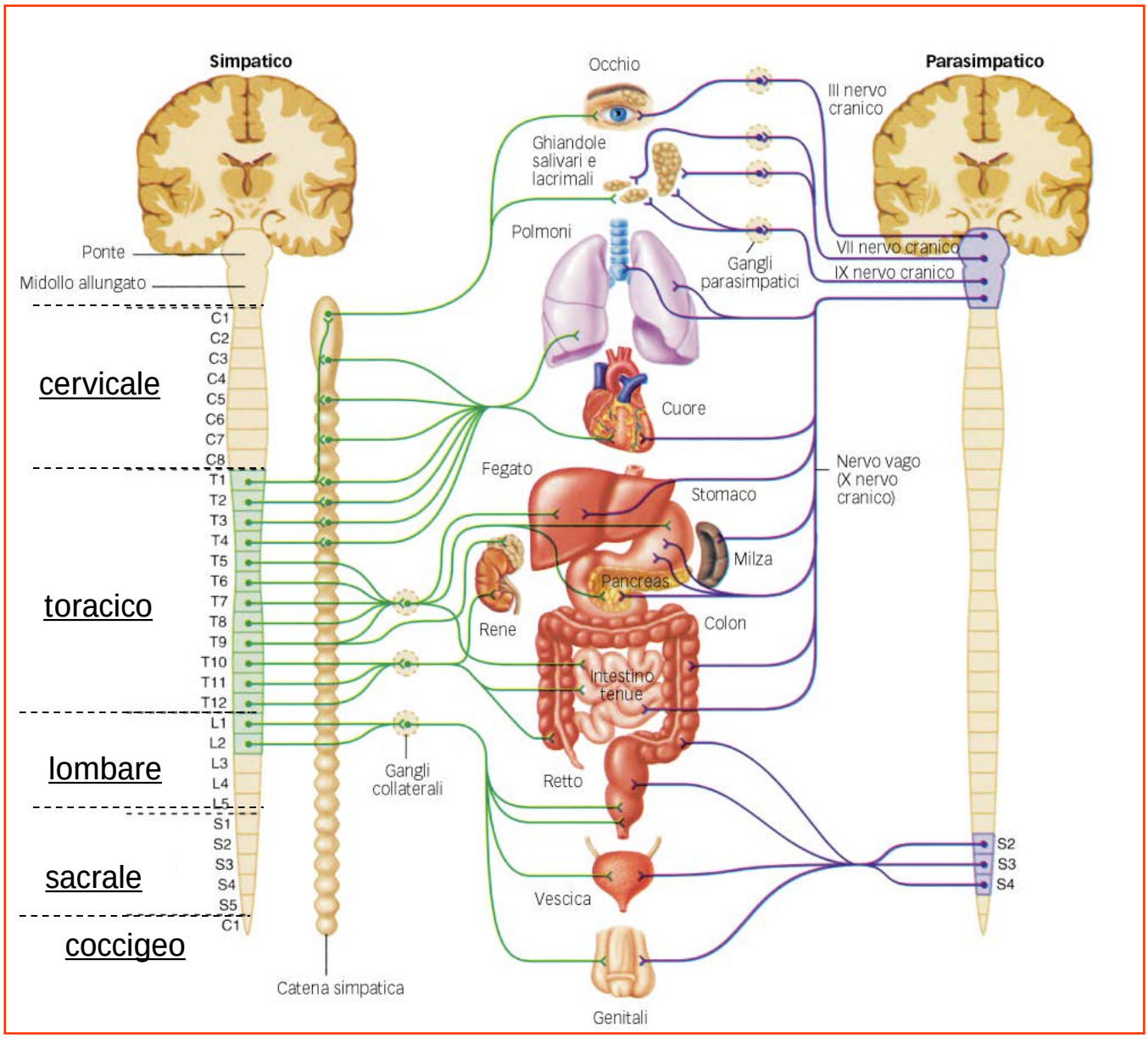


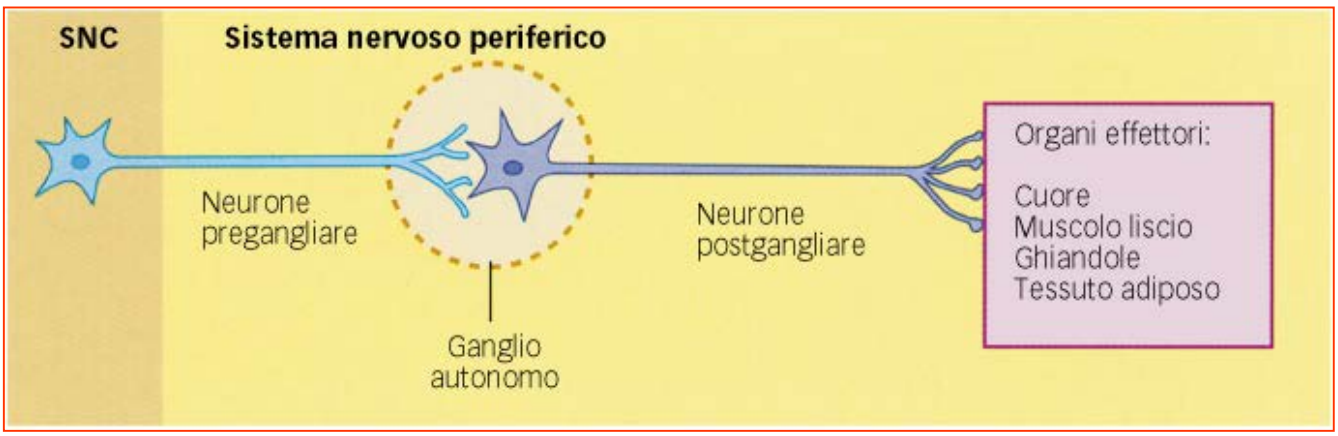
I recettori α-AR e β-AR

- i ***recettori adrenergici*** attivati dalla ***A*** e ***NA*** sono ***metabotropi***
- sono divisi in due classi: ***α*** (α_1, α_2) e ***β*** (β_1, β_2, β_3). Indicati come ***α-AR*** e ***β-AR***
- possono attivare sia la via dell'***IP_3*** che quella del ***cAMP/PKA***



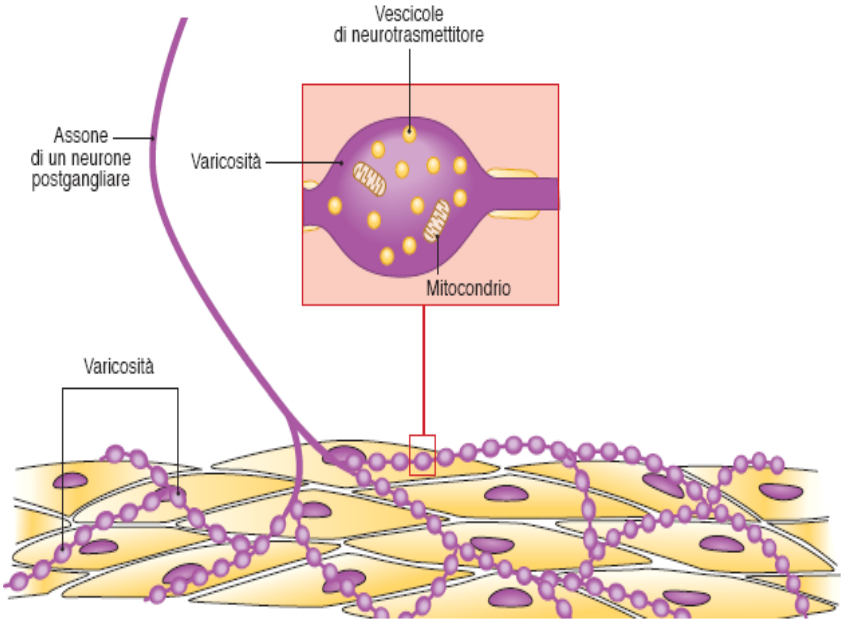
• Neurotrasmettitori e recettori del SNA



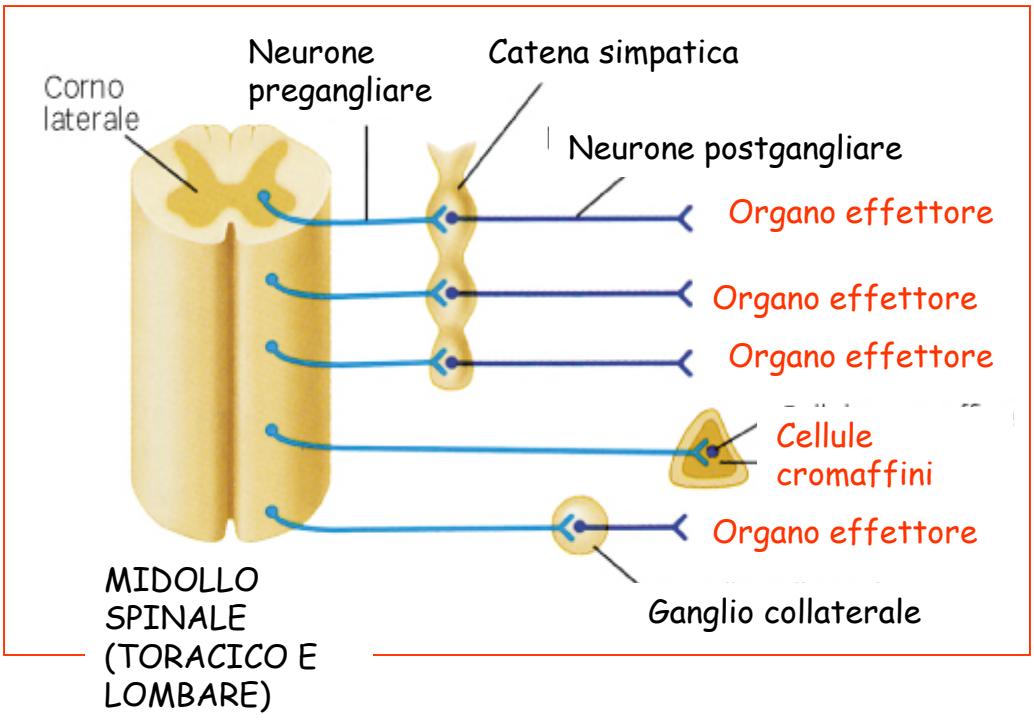


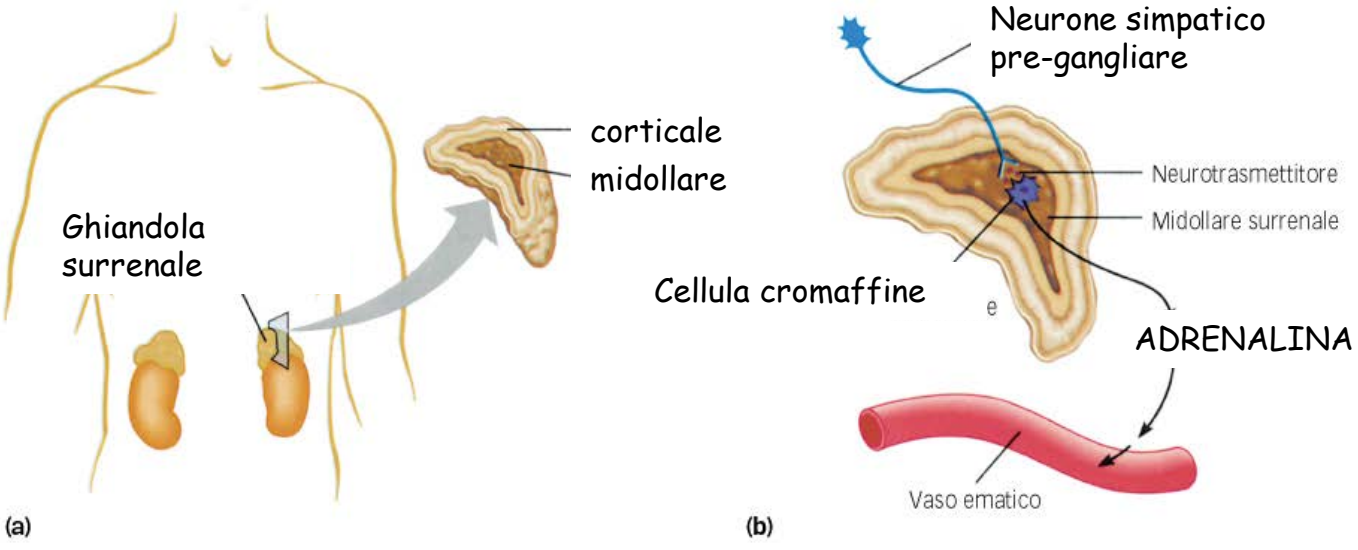
Struttura della giunzione neuro-effettrice del SNA

- diversa struttura della sinapsi del SNA rispetto al SNC
- le fibre postgangliari autonome (*amieliniche*) presentano numerose *varicosità*, contenenti vescicole di neurotrasmettitore
- NA per il simpatico ed ACh per il parasimpatico

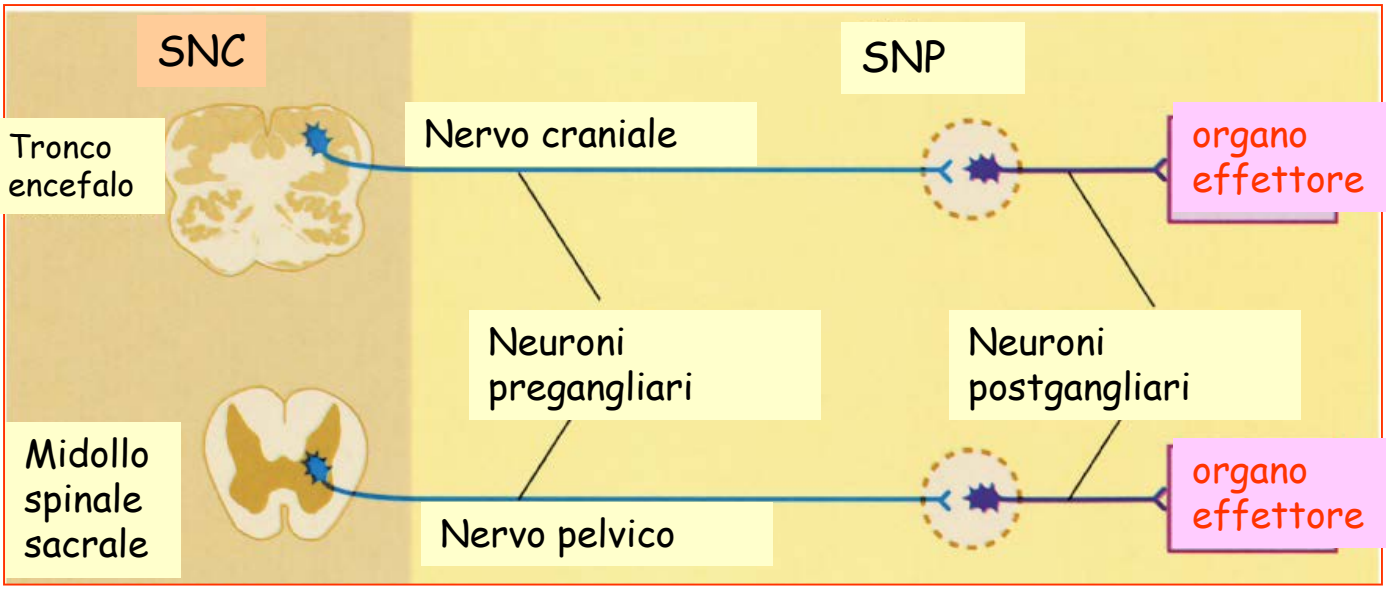


Neuroni pregangliari e postgangliari del sistema nervoso SIMPATICO

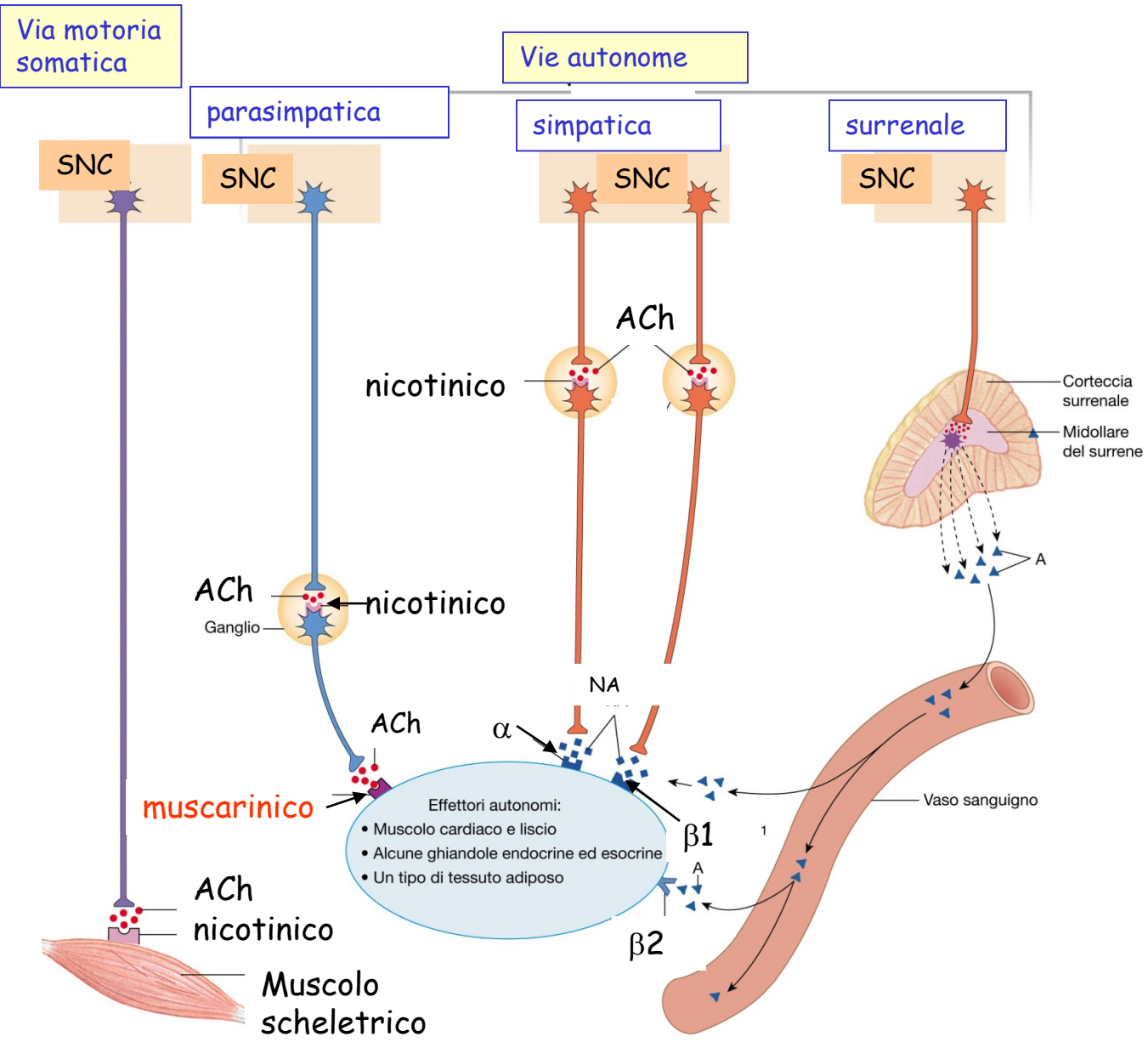




Neuroni pregangliari e postgangliari del sistema nervoso PARASIMPATICO

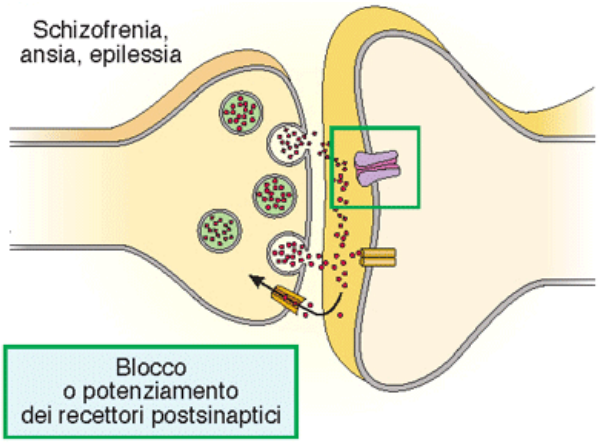


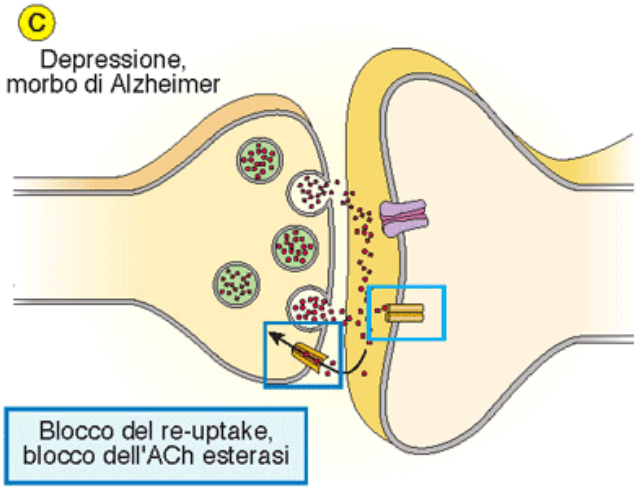
Le vie efferenti del sistema nervoso



• Patologie della sinapsi chimica

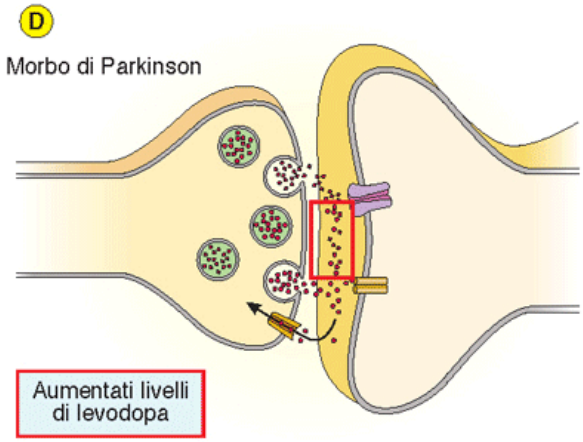
Schizofrenia: eccessivo rilascio di dopamina. (bloccanti recettore).





Depressione: deficienza serotonina e noradrenalina.
Fluoxetina: inibisce il reuptake.

Alzheimer: perdita neuroni colinergici e recettori nicotinici.
Anti-aceticolinesterasi.



Parkinson: perdita neuroni dopaminergici della sostanza Nigra.
L-dopa: precursore dopamina.