Synapses and Neurotransmitters

Communication Between Neurons

- **Synapse: A specialized site of contact, and transmission of information between a neuron and an effector cell**

Anterior Motor Neuron

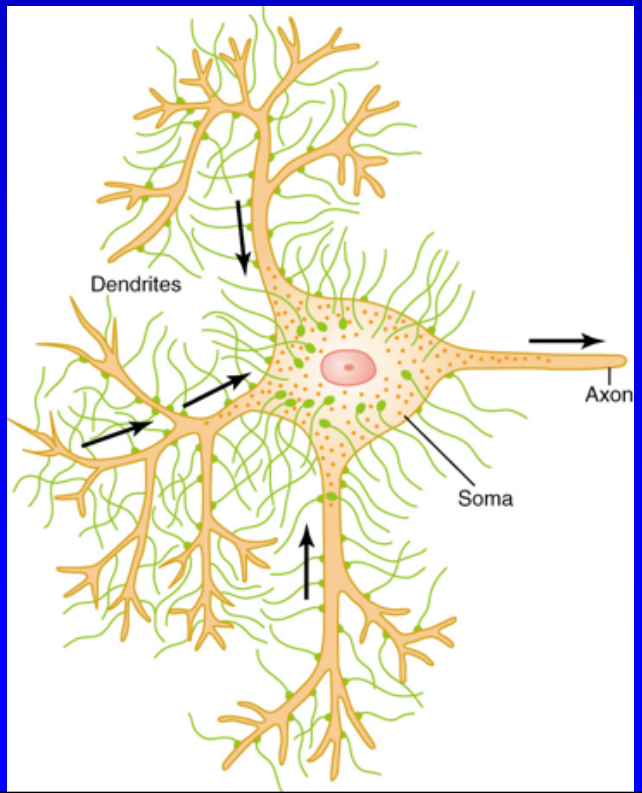
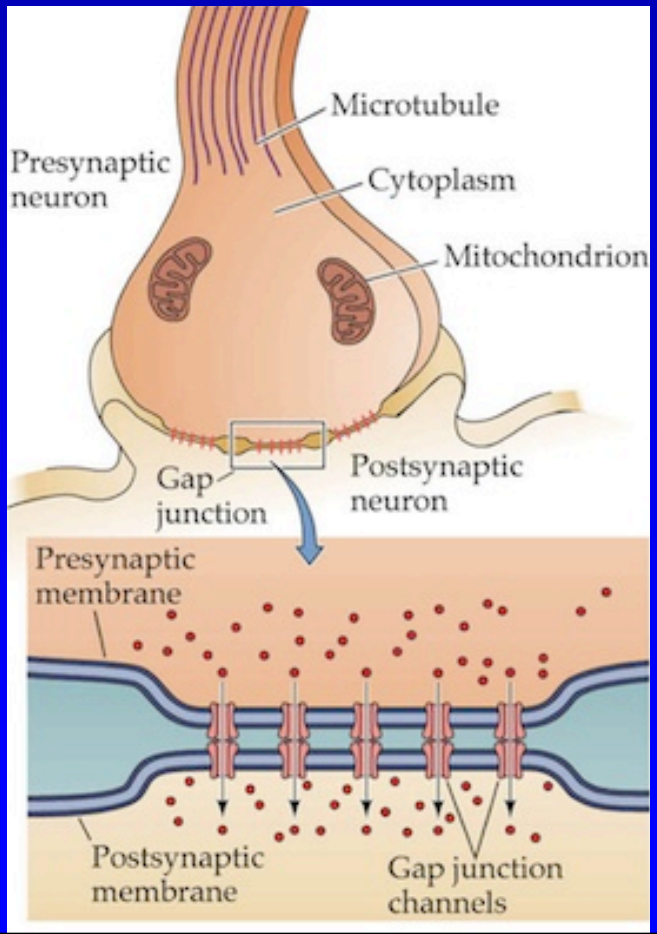


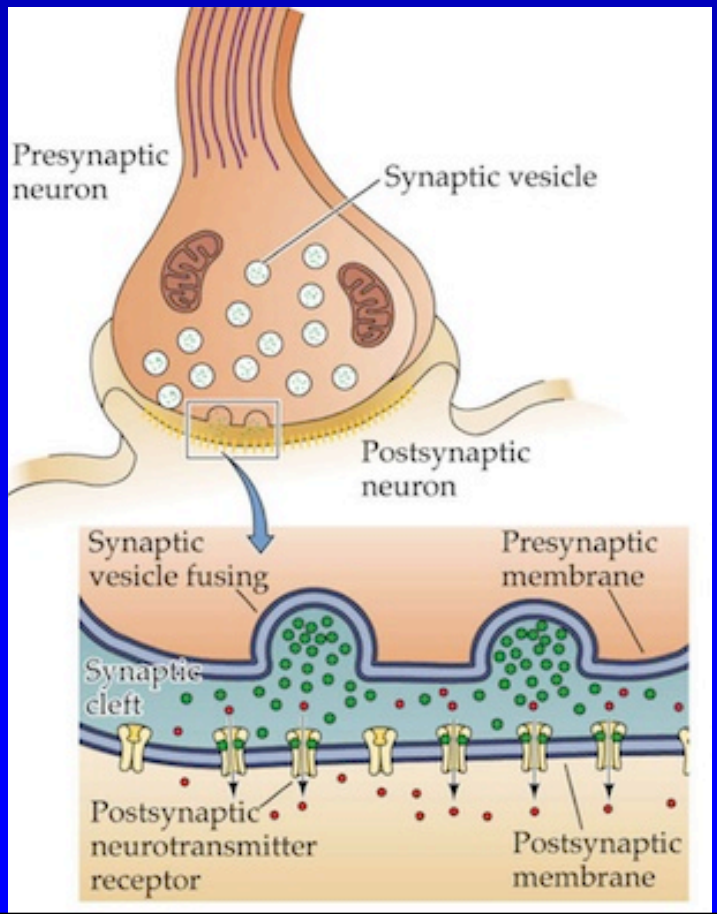
Figure 45-5

Communication Between Neurons

- Electrical synapse

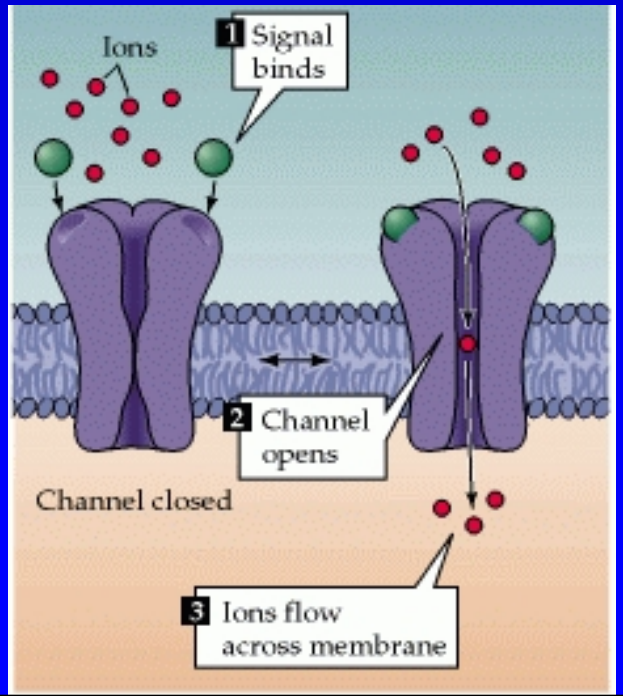


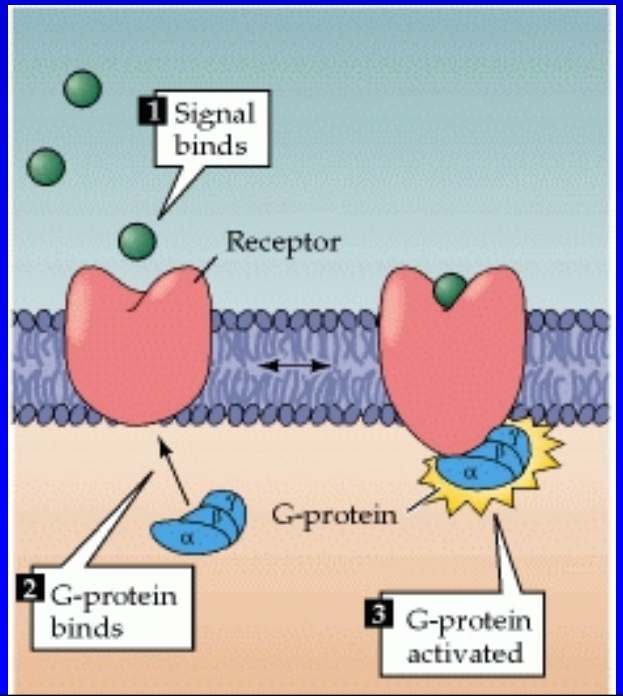
Chemical synapse



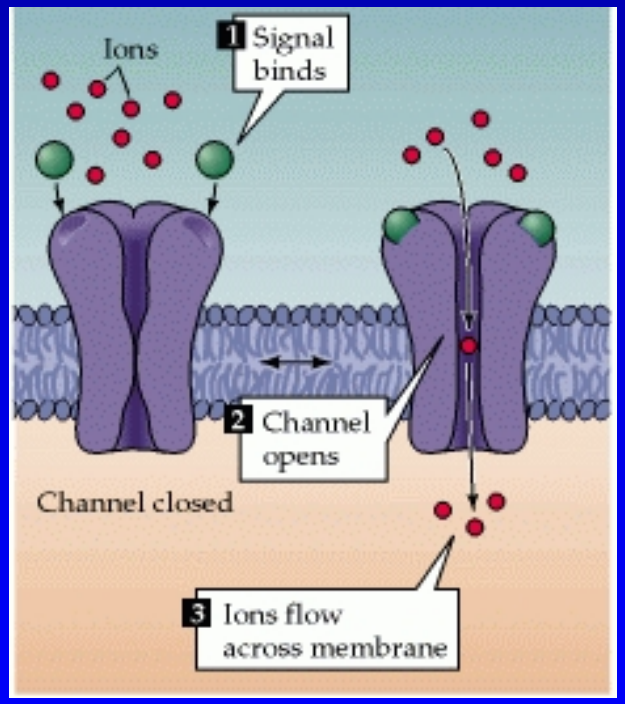
Action of Neurotransmitter on Postsynaptic Neuron

- Two types of receptors
  - Ion channels receptors **Ionotropic**
  - Second messenger receptors **Metatropic**





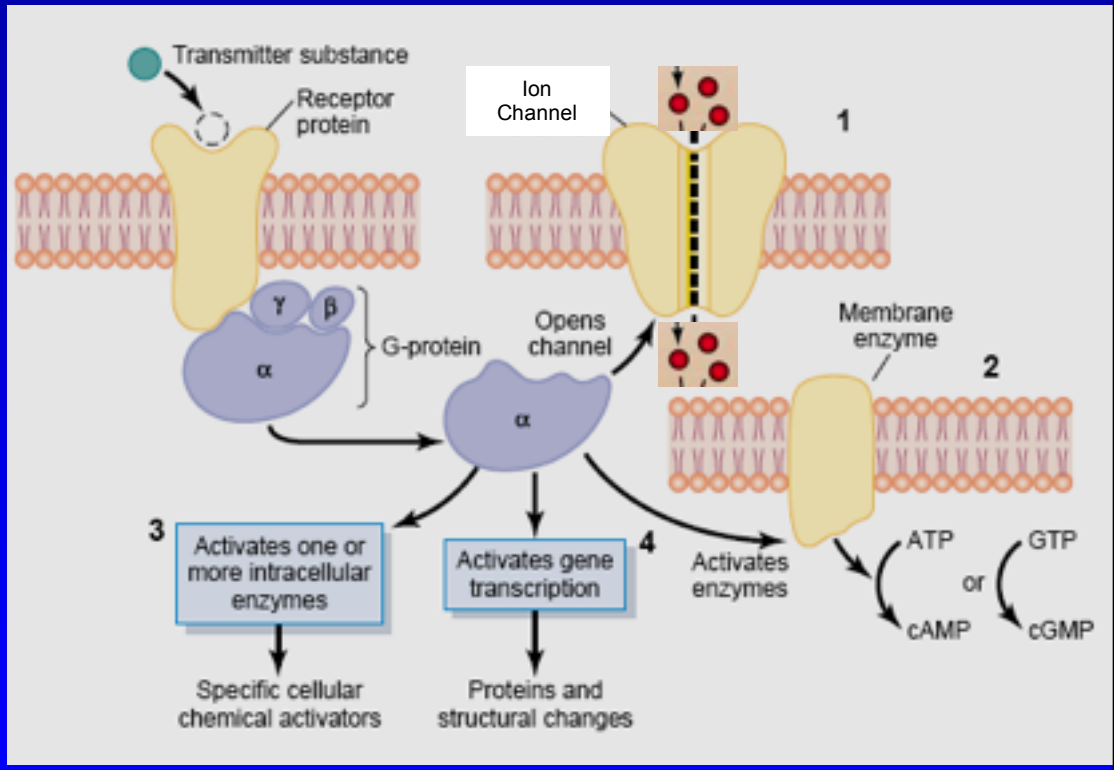
Ion Channels receptors



- transmitters that open sodium channels excite the postsynaptic neuron.
- transmitters that open chloride channels inhibit the postsynaptic neuron.
- transmitters that open potassium channels inhibit the postsynaptic neuron.

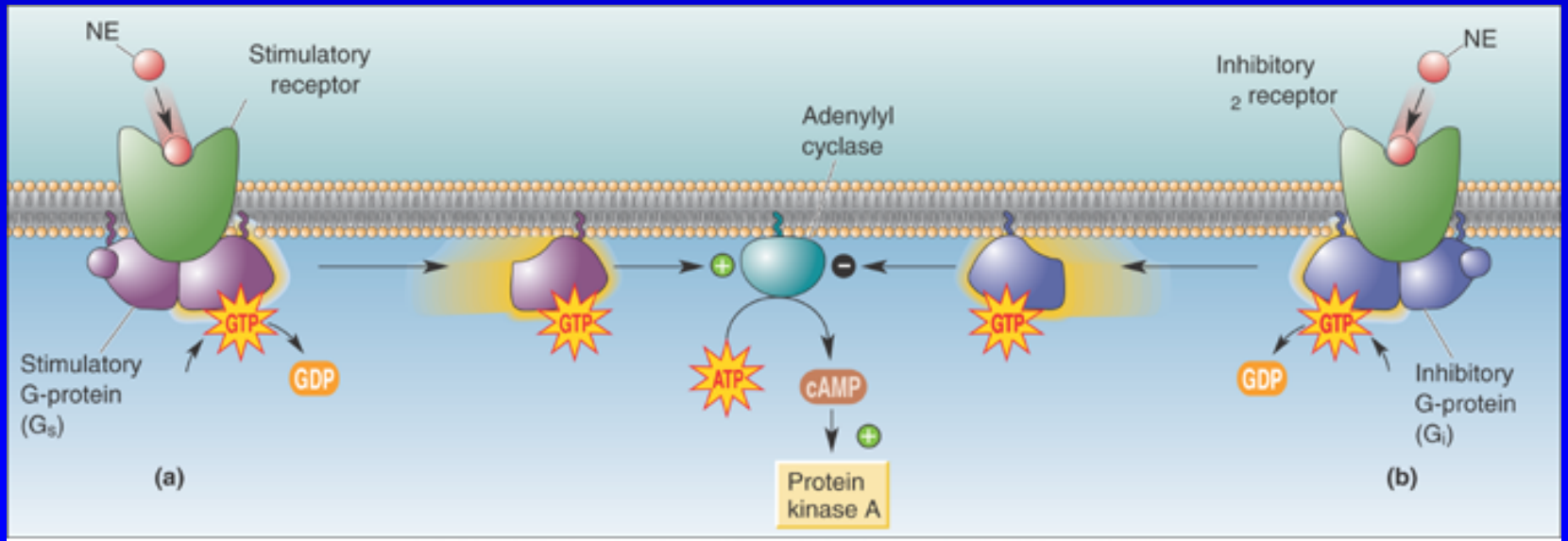
Seconded messenger receptors (as example G-protein)

1. *Opening specific ion channels*
2. *Activation of cAMP or cGMP*
3. *Activation of one or more intracellular enzymes*
4. *Activation of gene transcription.*



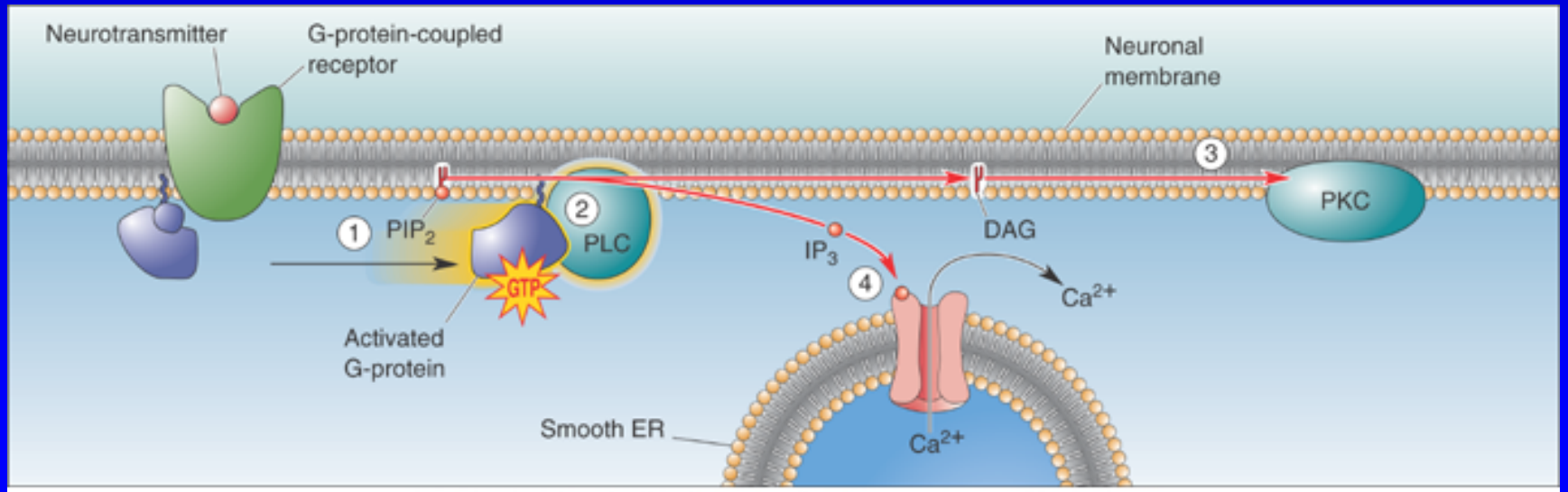
G-Protein-Coupled Receptors and Effectors

- GPCR Effector Systems (Cont'd)
  - Push-pull method (e.g., different G proteins for stimulating or inhibiting adenylyl cyclase)



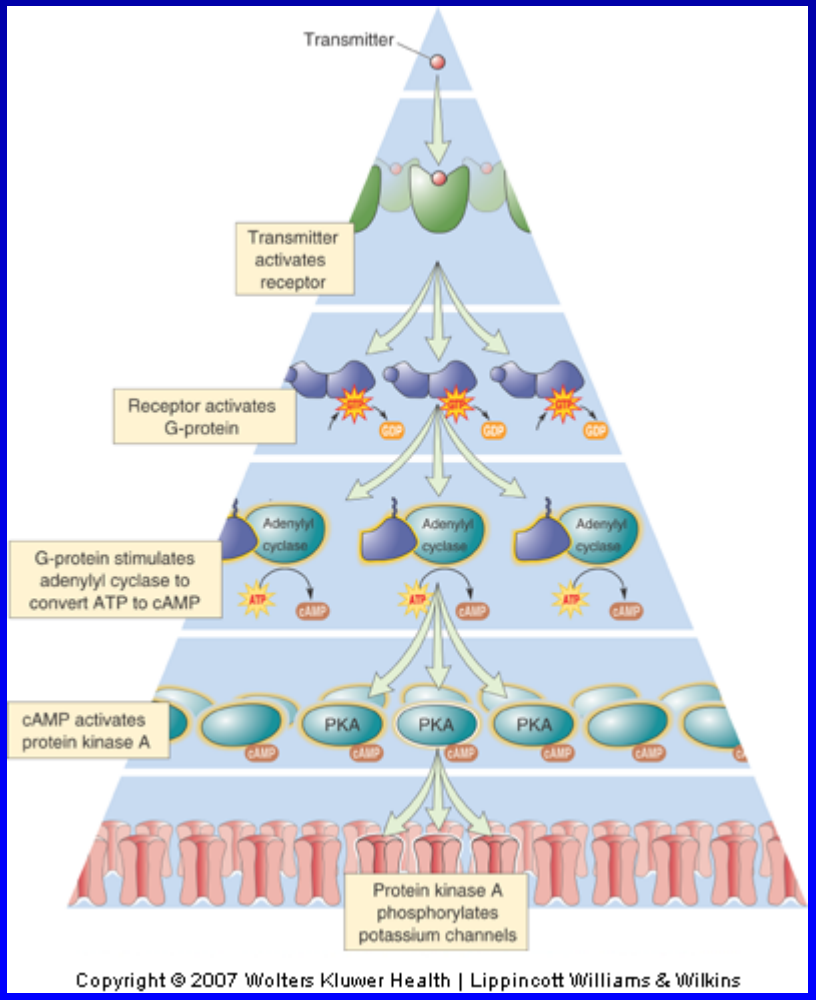
G-Protein-Coupled Receptors and Effectors

- GPCR Effector Systems (Cont'd)
  - Some cascades split
    - G-protein activates PLC→ generates DAG and IP3→ activate different effectors



G-Protein-Coupled Receptors and Effectors

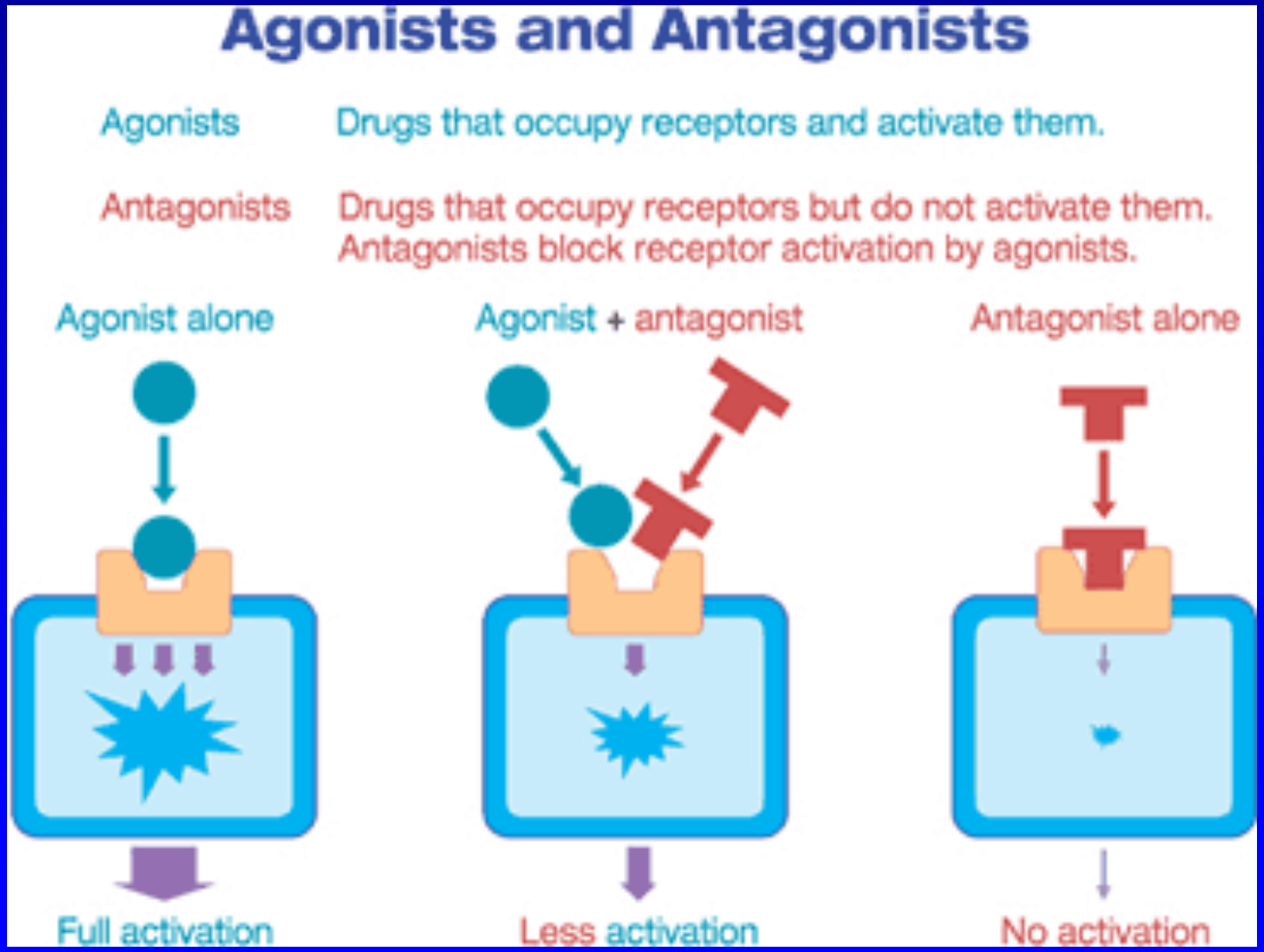
- GPCR Effector Systems (Cont'd)
  - Signal amplification



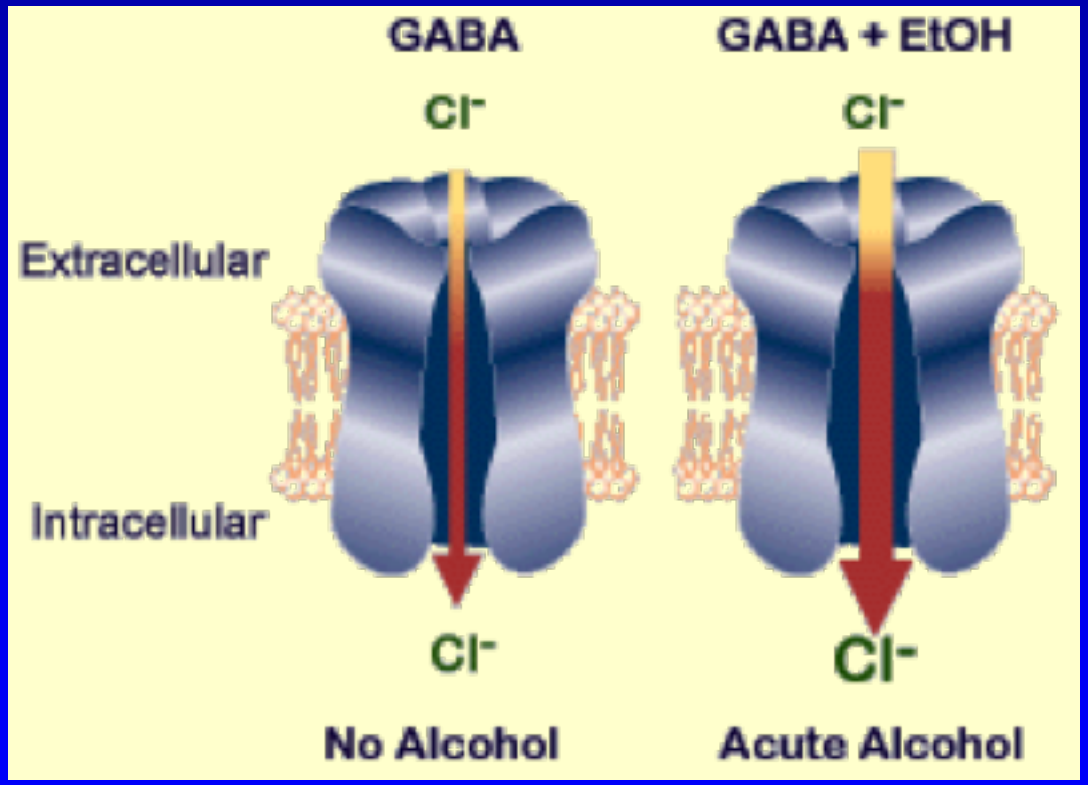
Drugs and the Synapse
1) at the receptor

- The study of the influence of various kinds of drugs has provided us with knowledge about many aspects of neural communication at the synaptic level.
- Drugs either facilitate or inhibit activity at the synapse.
  - Antagonistic drugs block the effects of neurotransmitters (e.g., novacaine, caffeine).
  - Agonist drugs mimic or increase the effects of neurotransmitters (e.g., receptors in the brain respond to heroin, LSD and cocaine)
  - Allosteric modulation

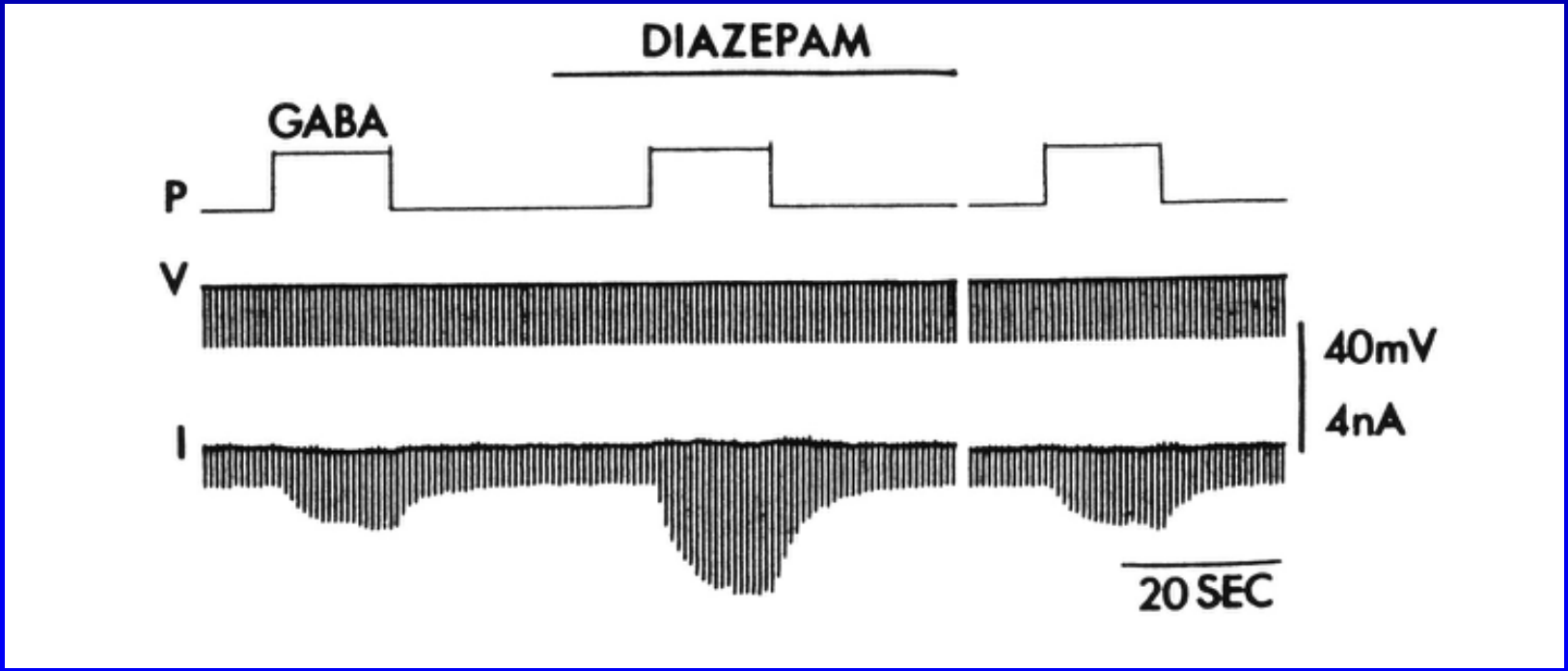
Agonists and Antagonists



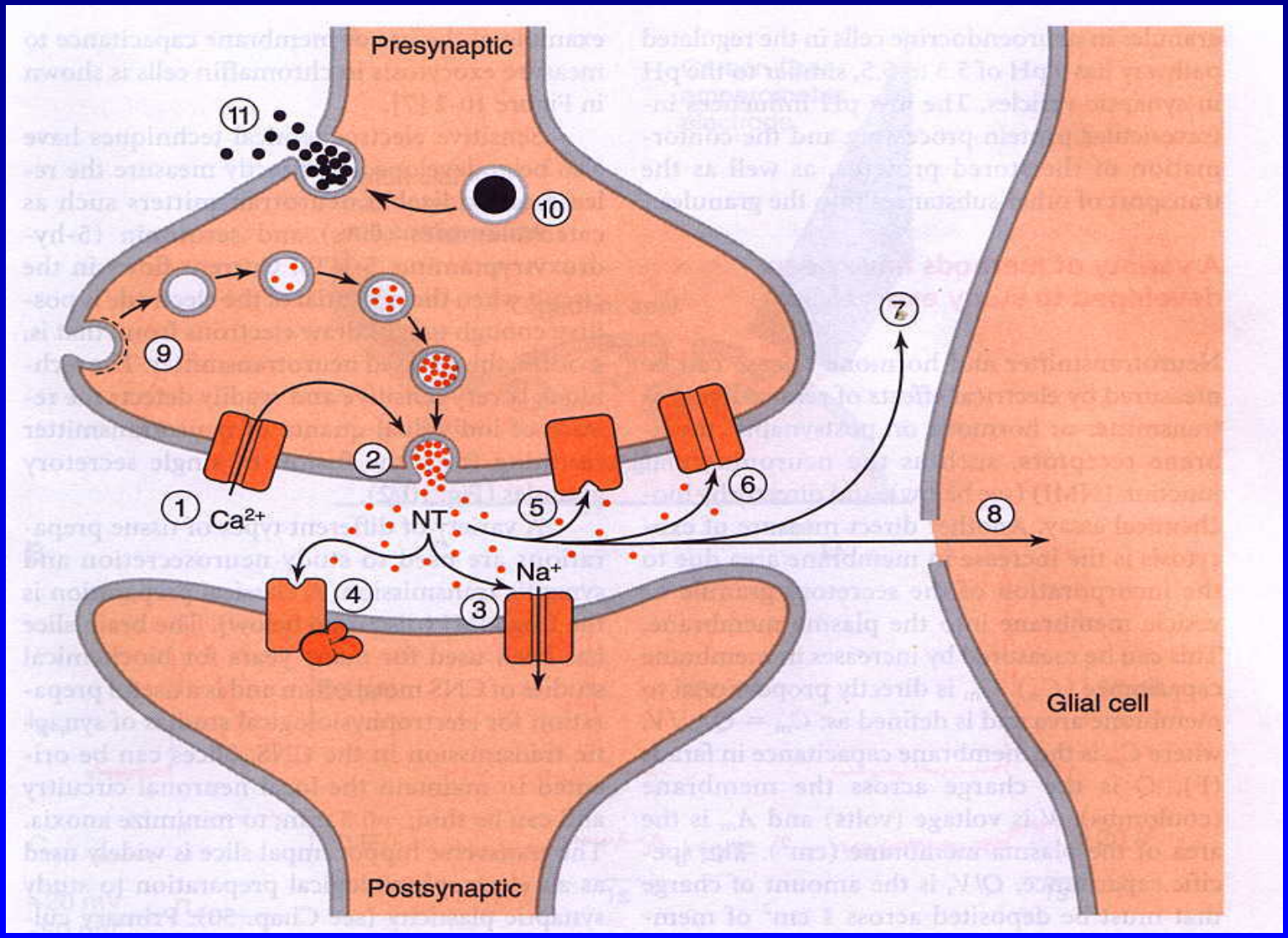
Allosteric modulation



Benzodiazepines potentiate GABA-induced responses



Synaptic Transmission



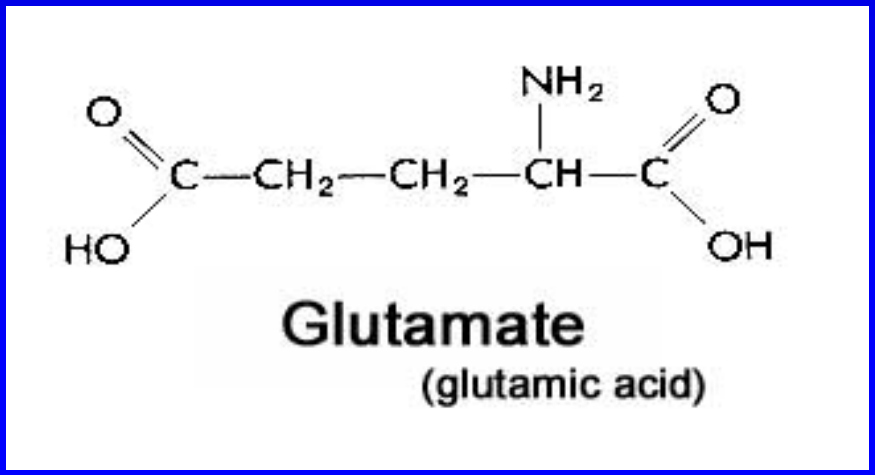
Drugs and the Synapse
2) alter various stages of synaptic processing.

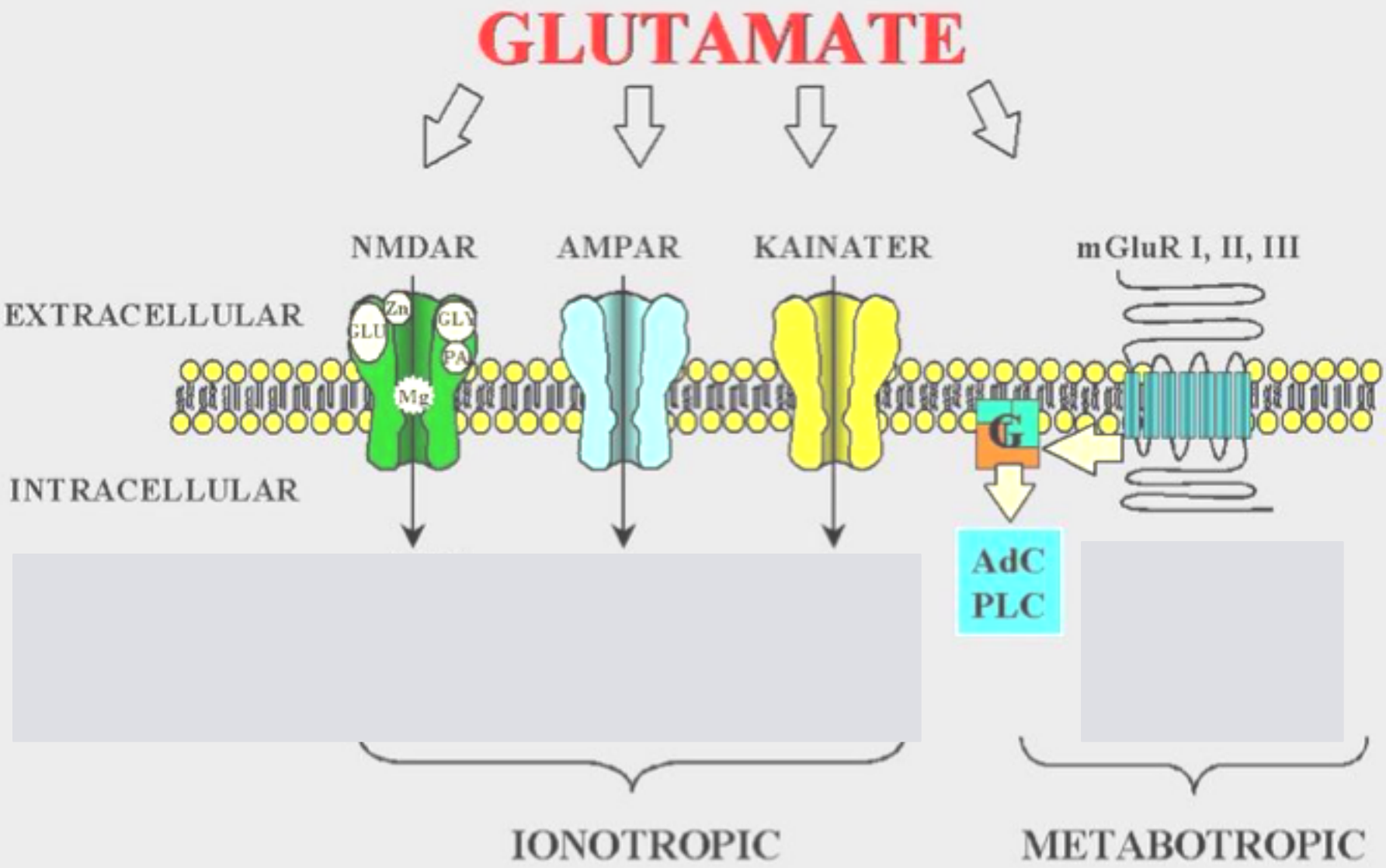
- Drugs work by doing one or more of the following to neurotransmitters:
  1. Increasing the synthesis.
  2. Causing vesicles to leak.
  3. Increasing release.
  4. Decreasing reuptake.
  5. Blocking the breakdown into inactive chemical.
  6. Directly stimulating or blocking postsynaptic receptors.

Fast Neurotransmitteres

Glutamate (L-glutamic acid)

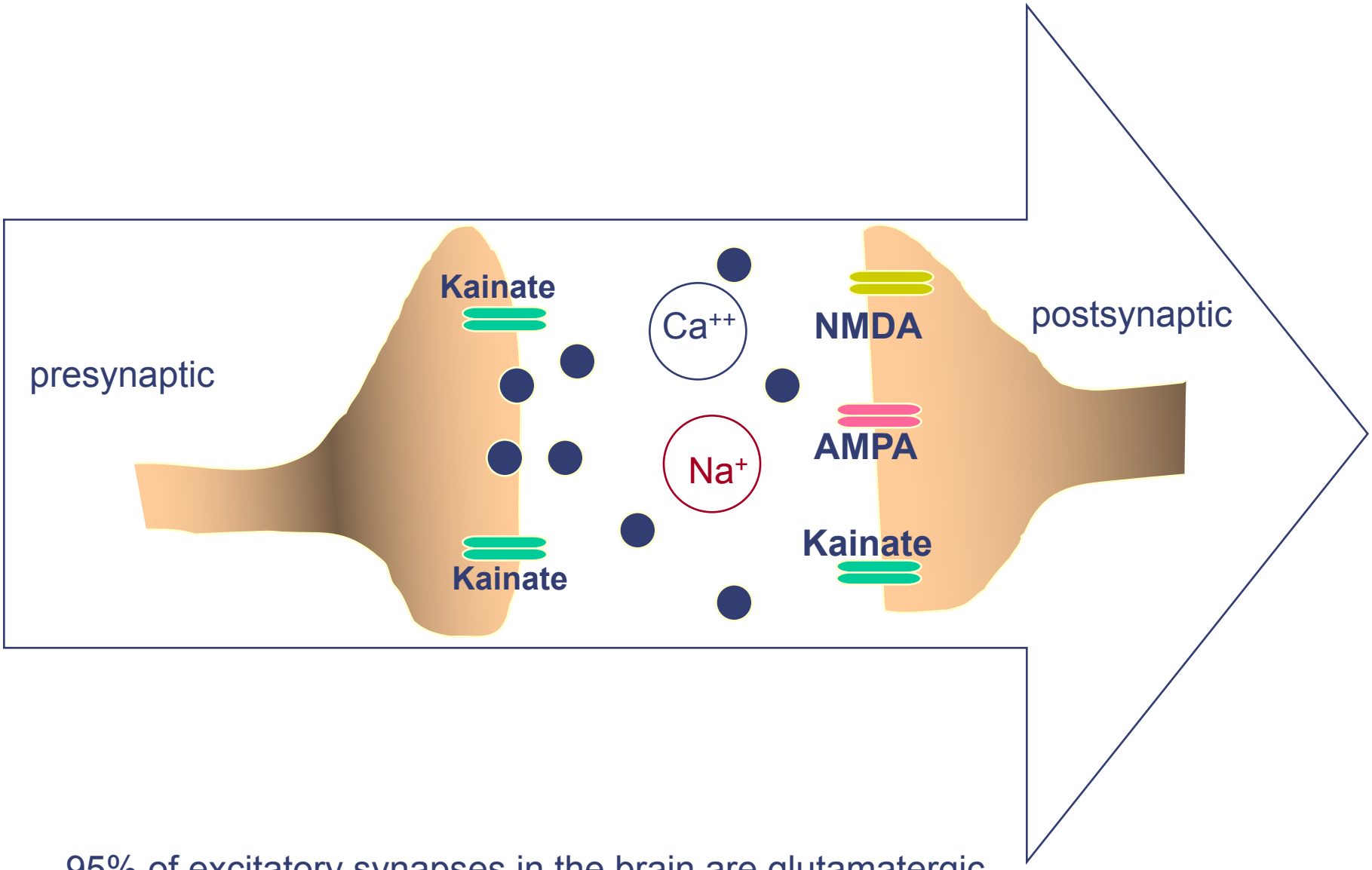
- Main excitatory neurotransmitter in the mammalian CNS
- 95% of excitatory synapses in the brain are glutamatergic
- Precursor for the GABA (major inhibitory neurotransmitter)



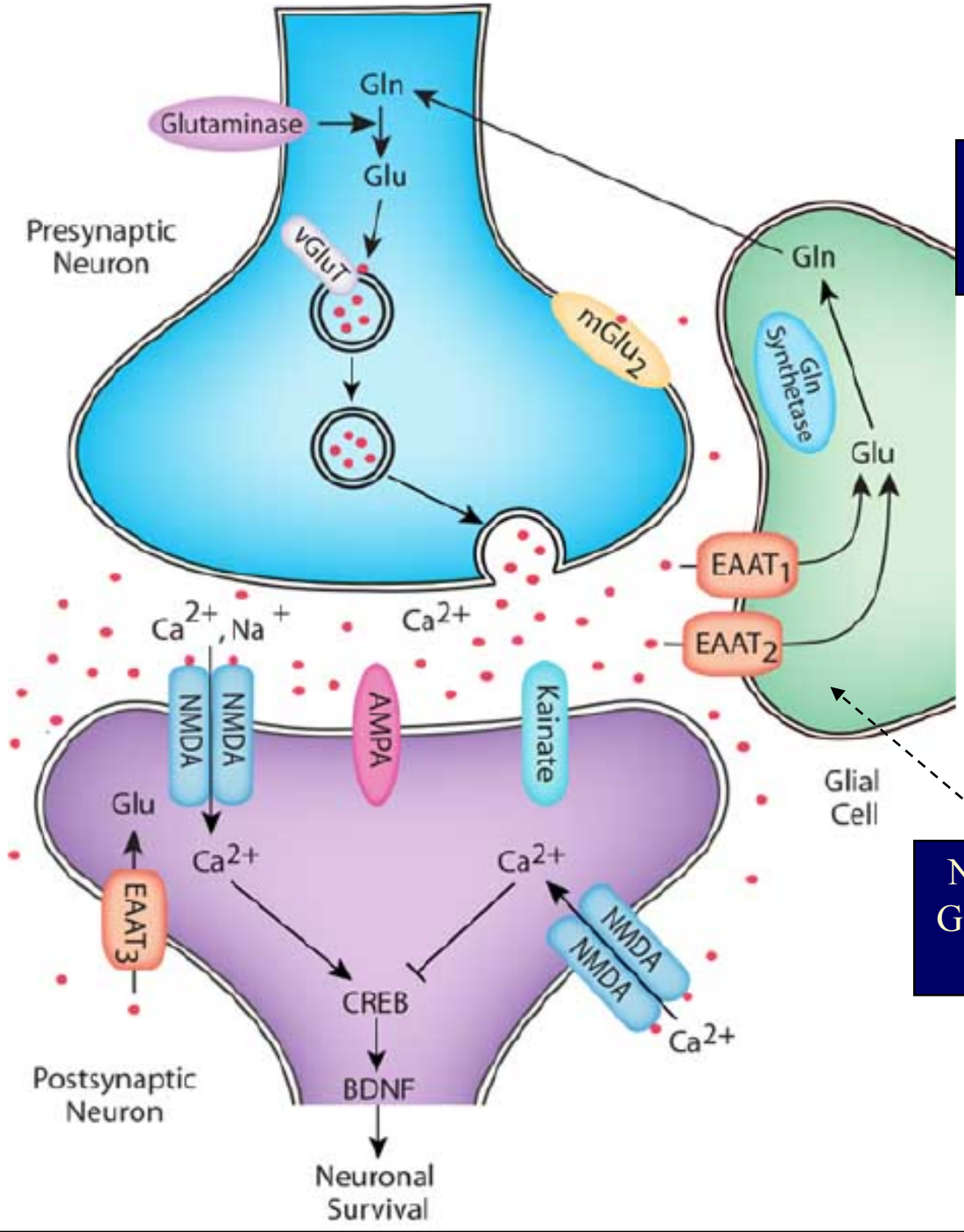


Fast synaptic transmission

Slow synaptic transmission



95% of excitatory synapses in the brain are glutamatergic



Interconversion of glutamate to glutamine

Note – significant Glu uptake (mainly astrocytes)

Glutamate and CNS disorders

1) Stroke

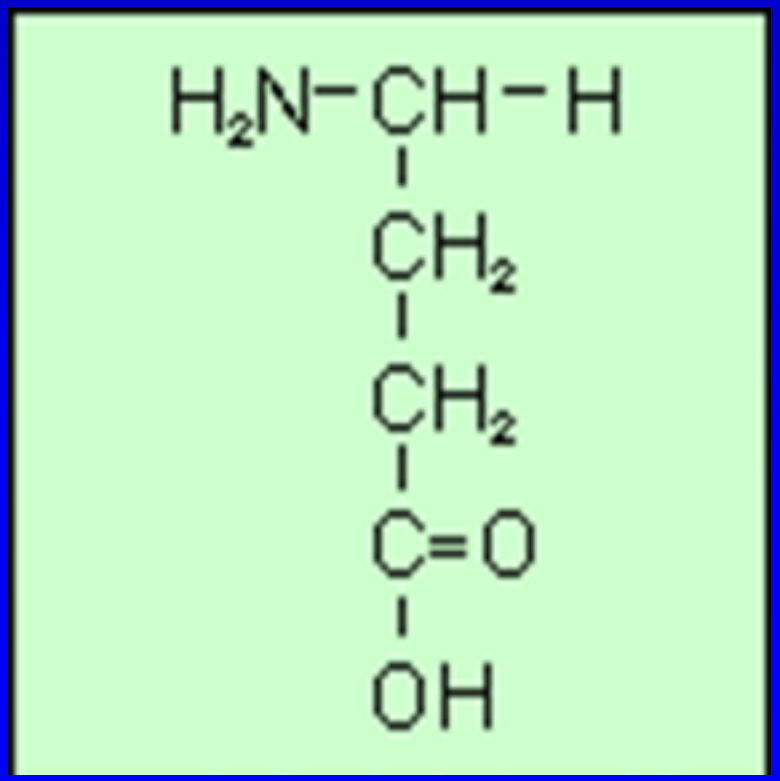
Ischemia → no ATP → increase Glutamate

→ Over activation NMDA R & AMPA R → increase Ca+ → cell death

2) dysfunction of glutamatergic transmission may also involve in schizophrenia-like symptoms, cognitive dysfunction, Depression and memory impairment

GABA

- Main inhibitory neurotransmitter in the mammalian CNS



GABA

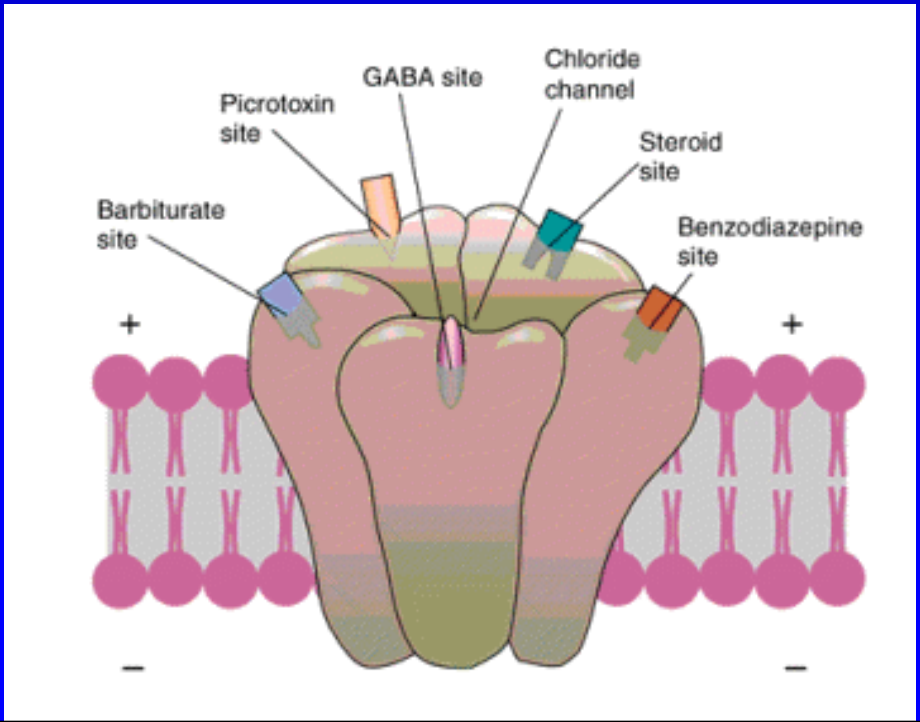
- Main inhibitory neurotransmitter in the mammalian CNS

Ionotropic
$GABA_A$
Heterooligomeric protein complex that consists of several binding sites coupled to an integral **Cl^- channel**

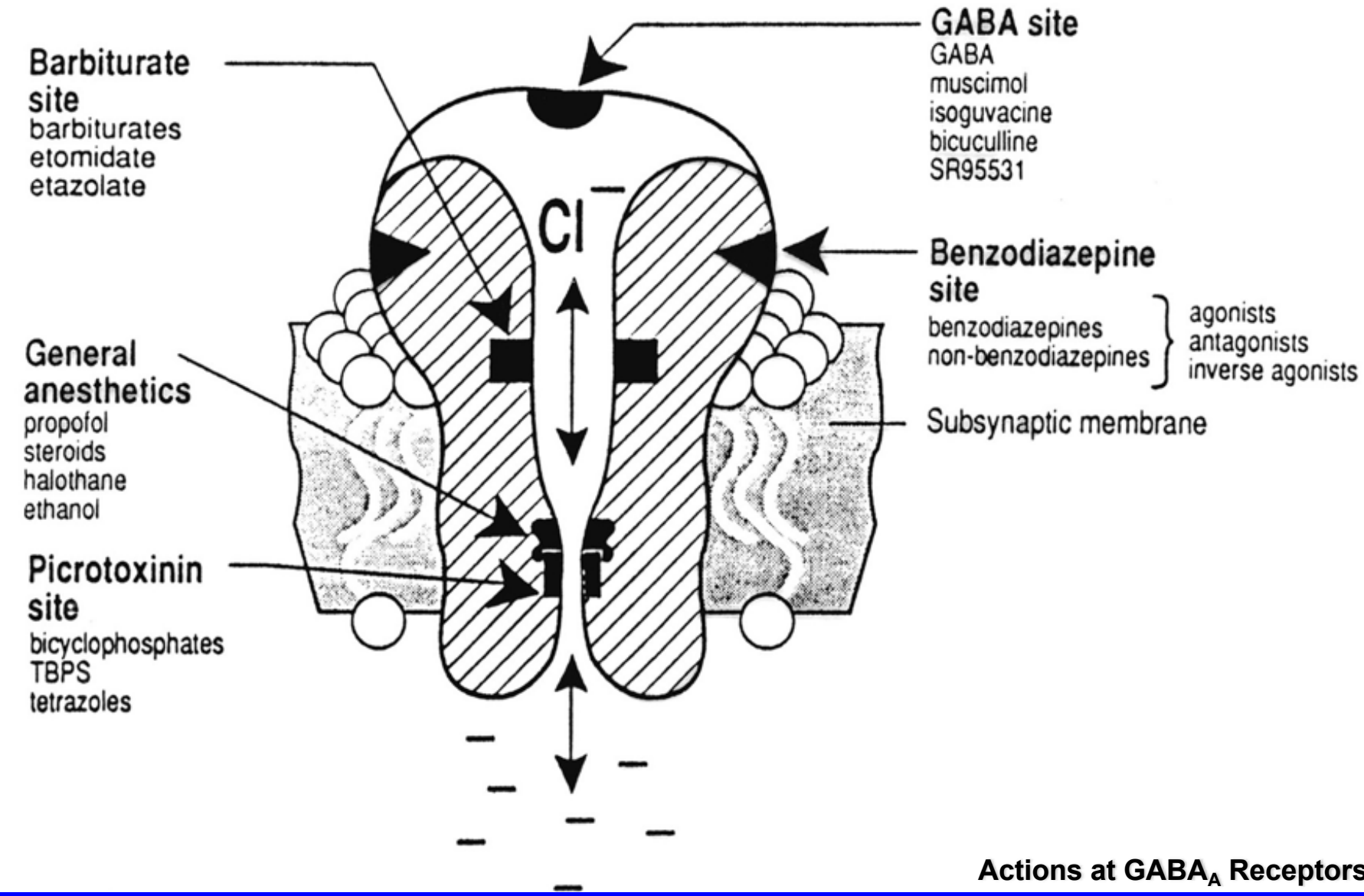
Metabotropic
$GABA_B$
G - protein coupled receptor, seven transmembrane domain protein

GABA-A- ionotropic receptor

- An integral chloride channel activated by competitive agonists: GABA and muscimol
- Blocked by convulsant bicuculine (competitive antagonist) and picrotoxin (noncompetitive antagonist)
- Allosterically modulated by benzodiazepines and barbiturates, which potentiate the effect of GABA



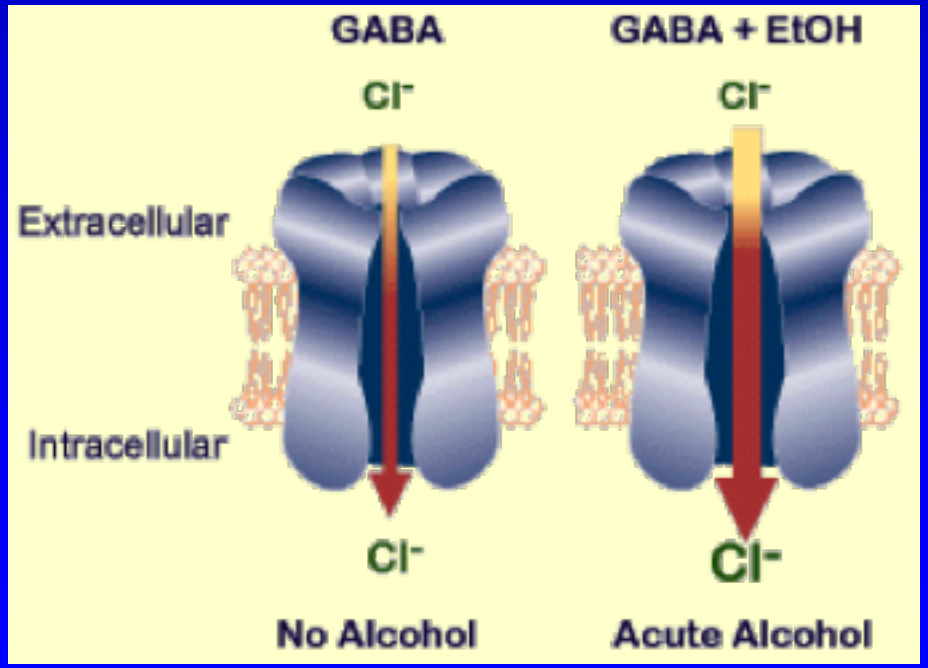
$GABA_A$ receptor



Actions at $GABA_A$ Receptors

$GABA_A$ and ethanol

- Ethanol facilitates GABA ability to activate the receptor and prolongs the time that the Cl^- channel remains open



GABA

Synthesis

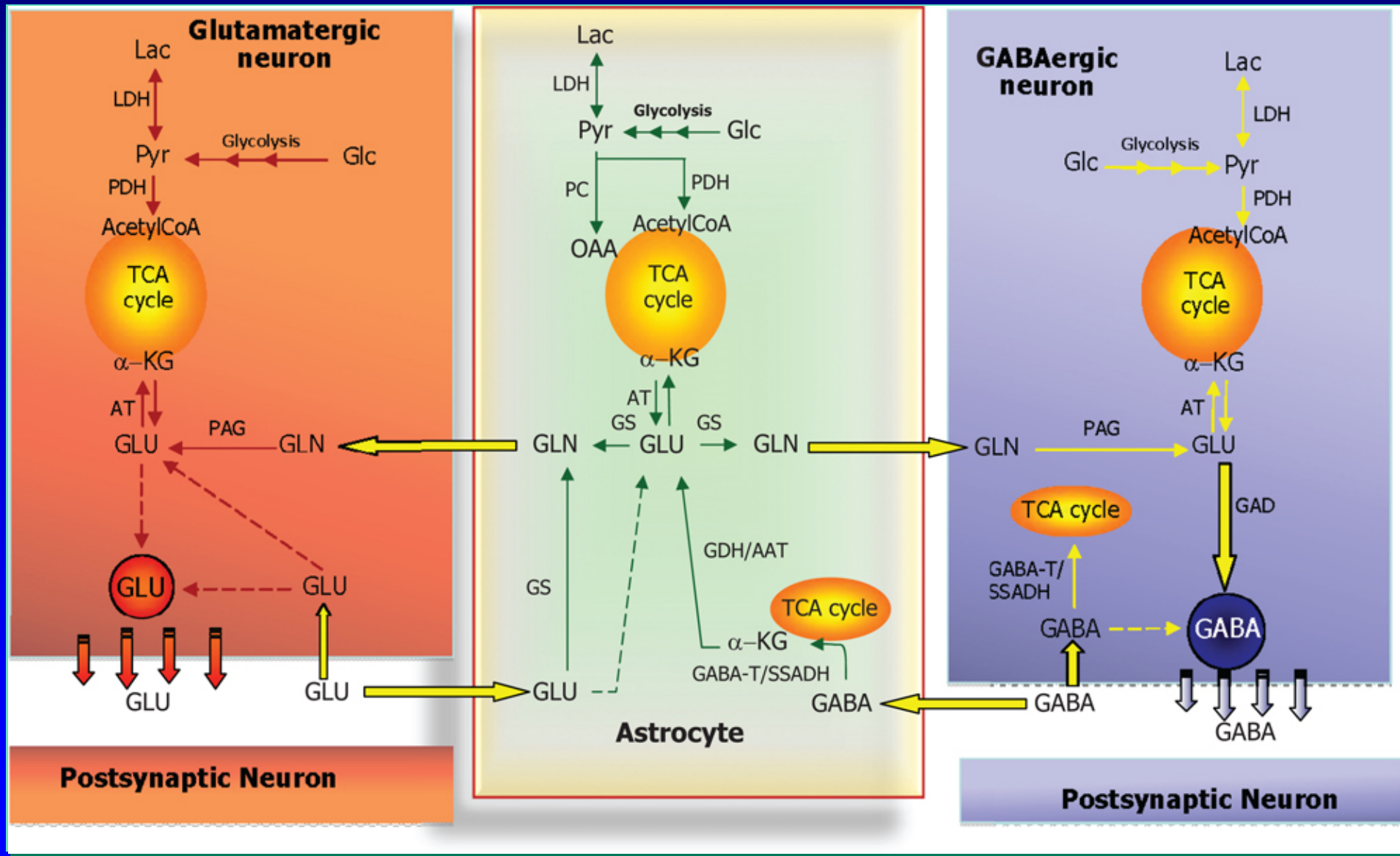
GABA is formed by the α-decarboxylation of glutamate in the reaction catalyzed by GAD (glutamic acid decarboxylase)

GABA

Degradation

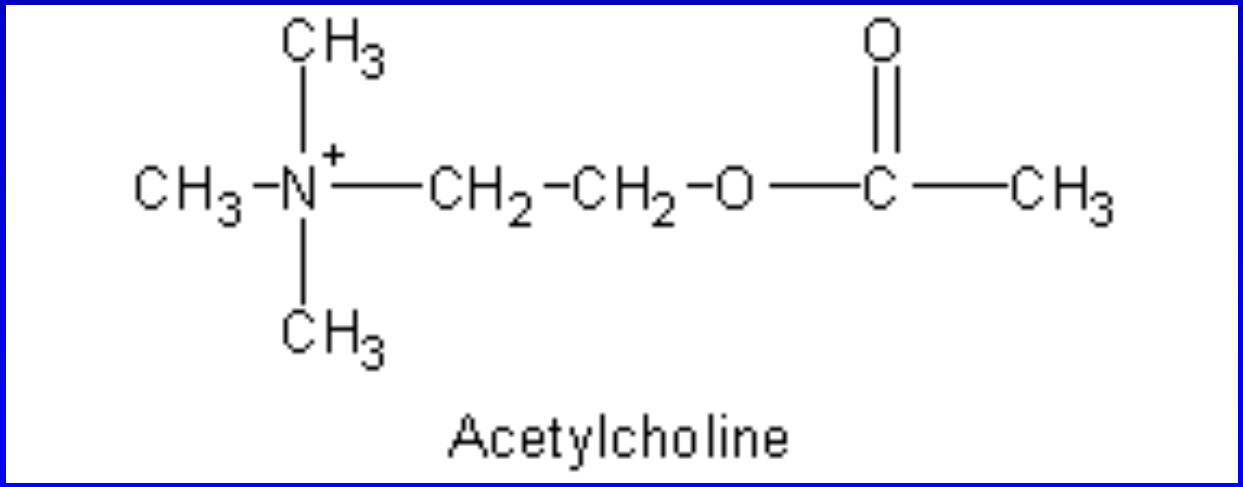
GABA —*GABA-T*→ succinic semialdehyde

GABA is catabolized into the succinic semialdehade
in the reaction catalyzed by **GABA-T** (***GABA-Transaminase***)


Glutamatergic neuron
Lac
LDH
Pyr
Glycolysis
Glc
PDH
AcetylCoA
TCA cycle
α–KG
AT
GLU
PAG
GLN
GLU
GLU
GLU
Postsynaptic Neuron
Lac
LDH
Pyr
Glycolysis
Glc
PC
PDH
AcetylCoA
OAA
TCA cycle
α–KG
AT
GS
GS
GLN
GLU
GLN
GS
GDH/AAT
TCA cycle
α–KG
GABA-T/SSADH
GLU
GABA
Astrocyte
GABAergic neuron
Lac
LDH
Glc
Glycolysis
Pyr
PDH
AcetylCoA
TCA cycle
α–KG
AT
GLN
PAG
GLU
TCA cycle
GAD
GABA-T/ SSADH
GABA
GABA
GABA
Postsynaptic Neuron

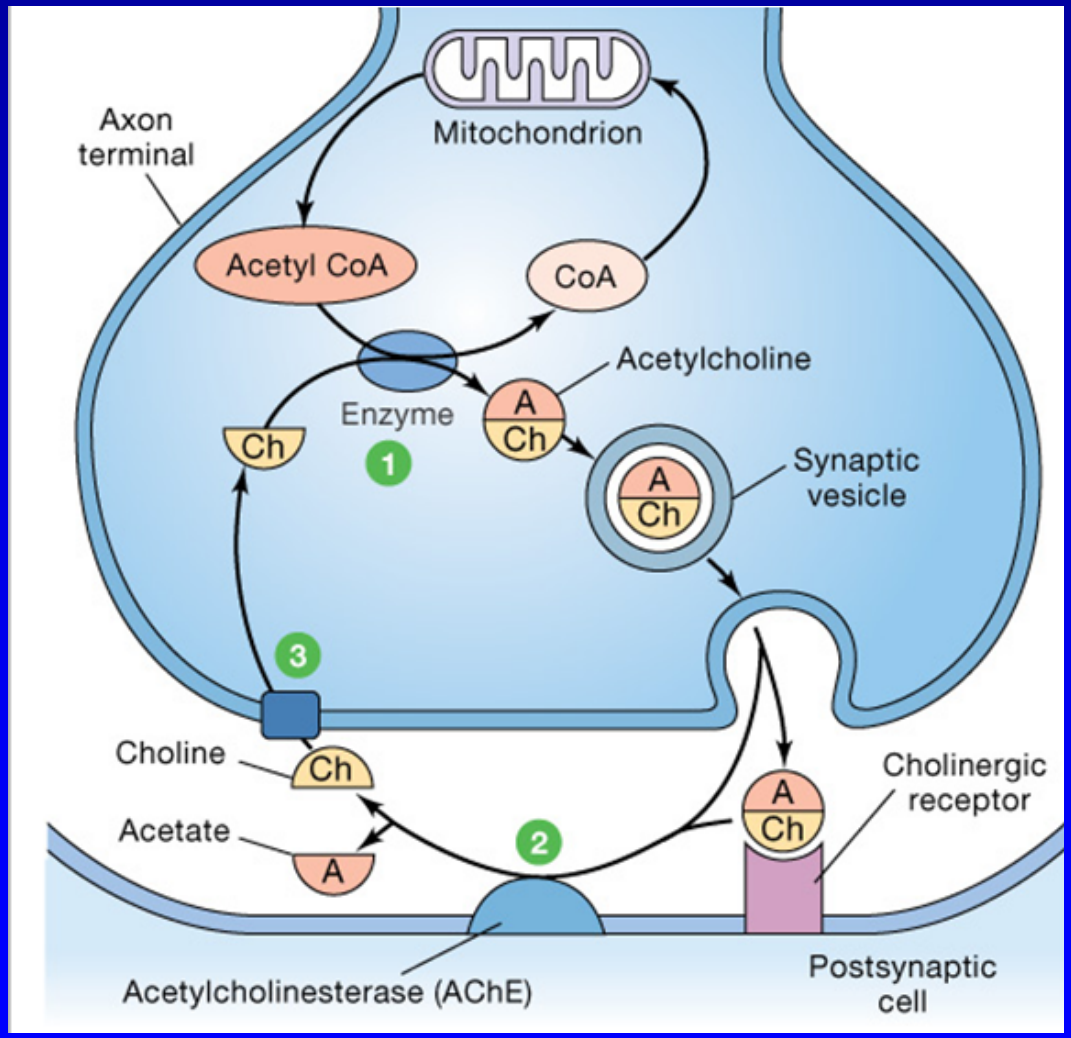
Neuromodulators

Acetylcholine

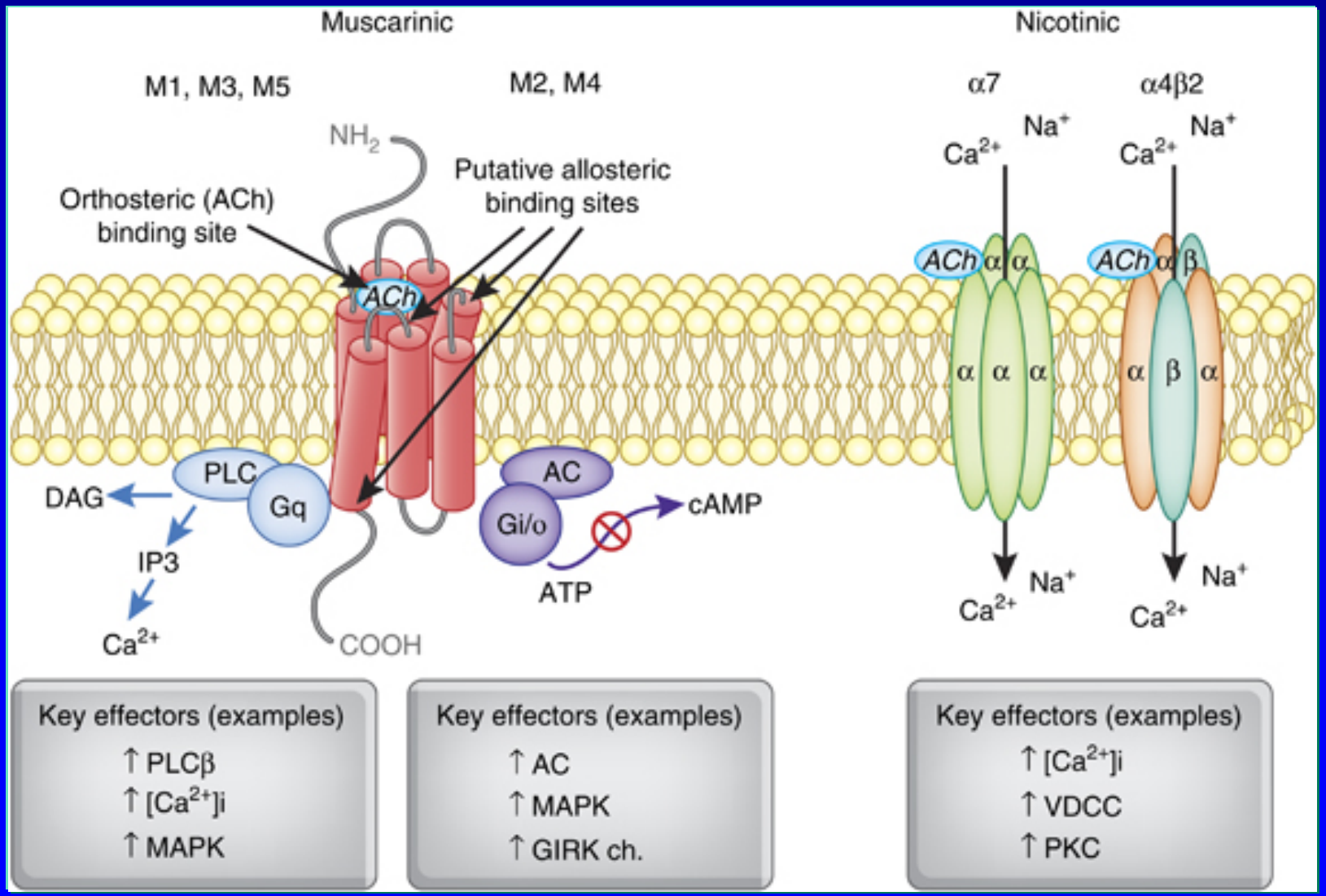


Choline + Acetyl CoA $\xrightarrow{\text{ChAT}}$ Acetyl choline + CoA

Acetylcholine synapse

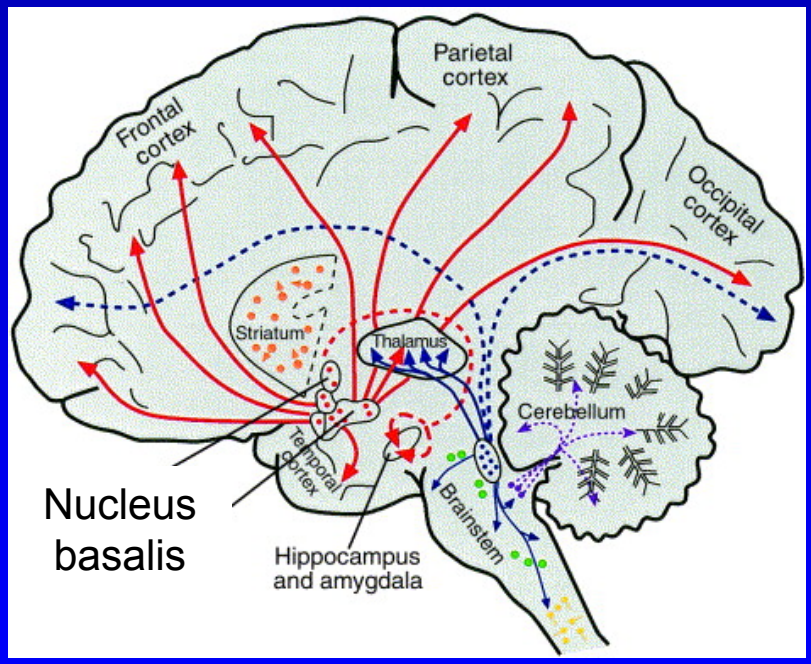


Acetylcholine receptors



Acetylcholine Pathway

- arousal and reward
- enhancement of sensory perceptions
- sustaining attention



Alzheimer's disease – loss of cholinergic cells in nucleus basalis