PSYCH 260

Neurochemistry I

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Prelude (4:44)

https://www.youtube.com/watch?v=f8FAJXPBdOg

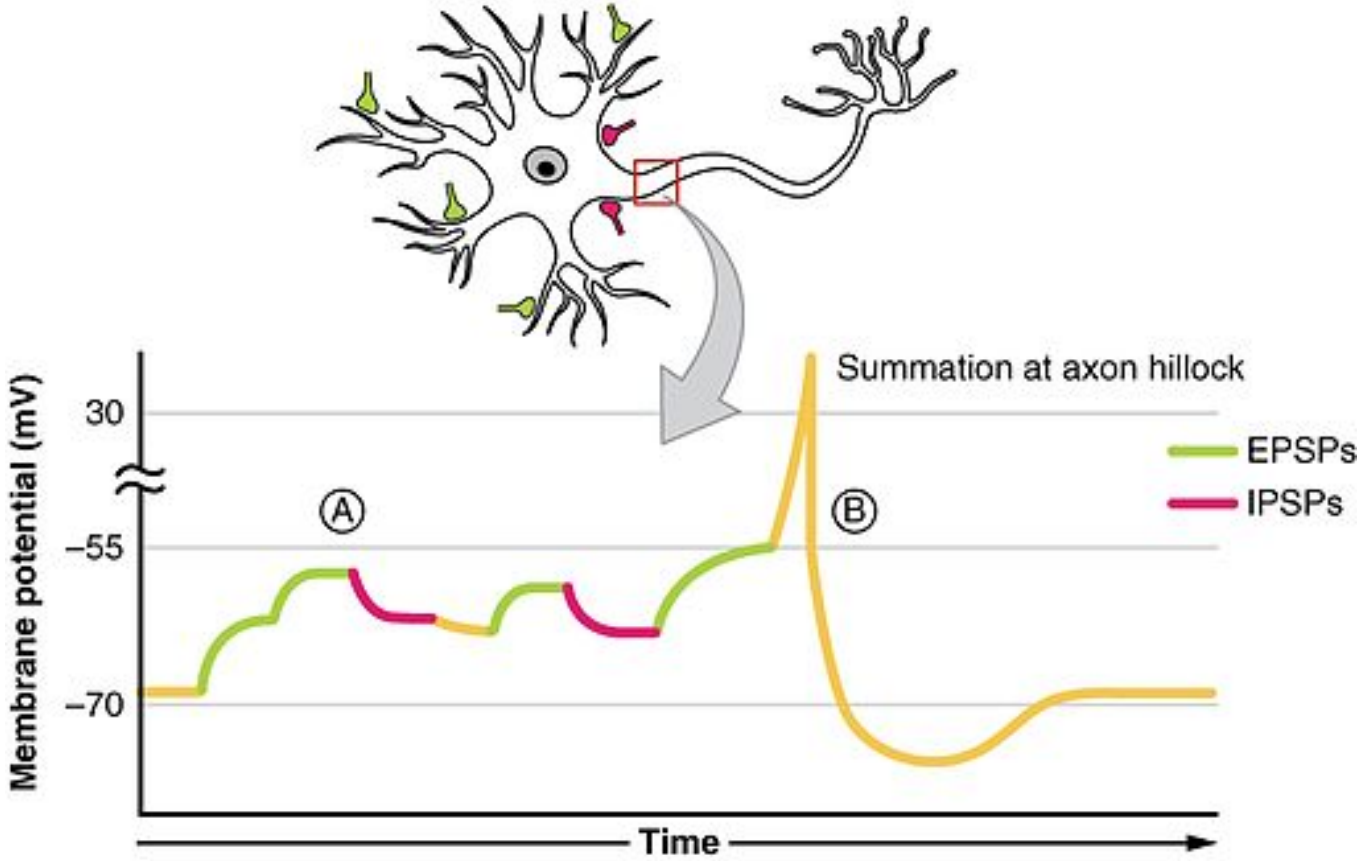
Today's Topics

- How neurons talk to one another
- Synaptic communication

In the beginning

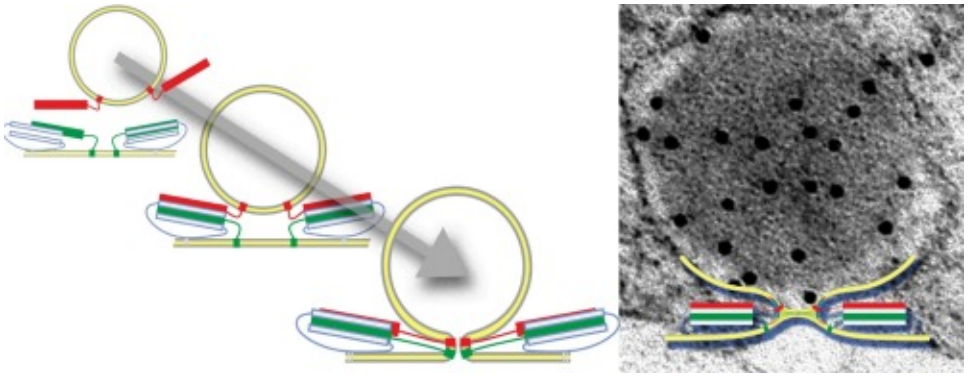
- Soma receives input from dendrites
- Axon hillock sums/integrates
- If sum > threshold, AP “fires”

Illustration of summation

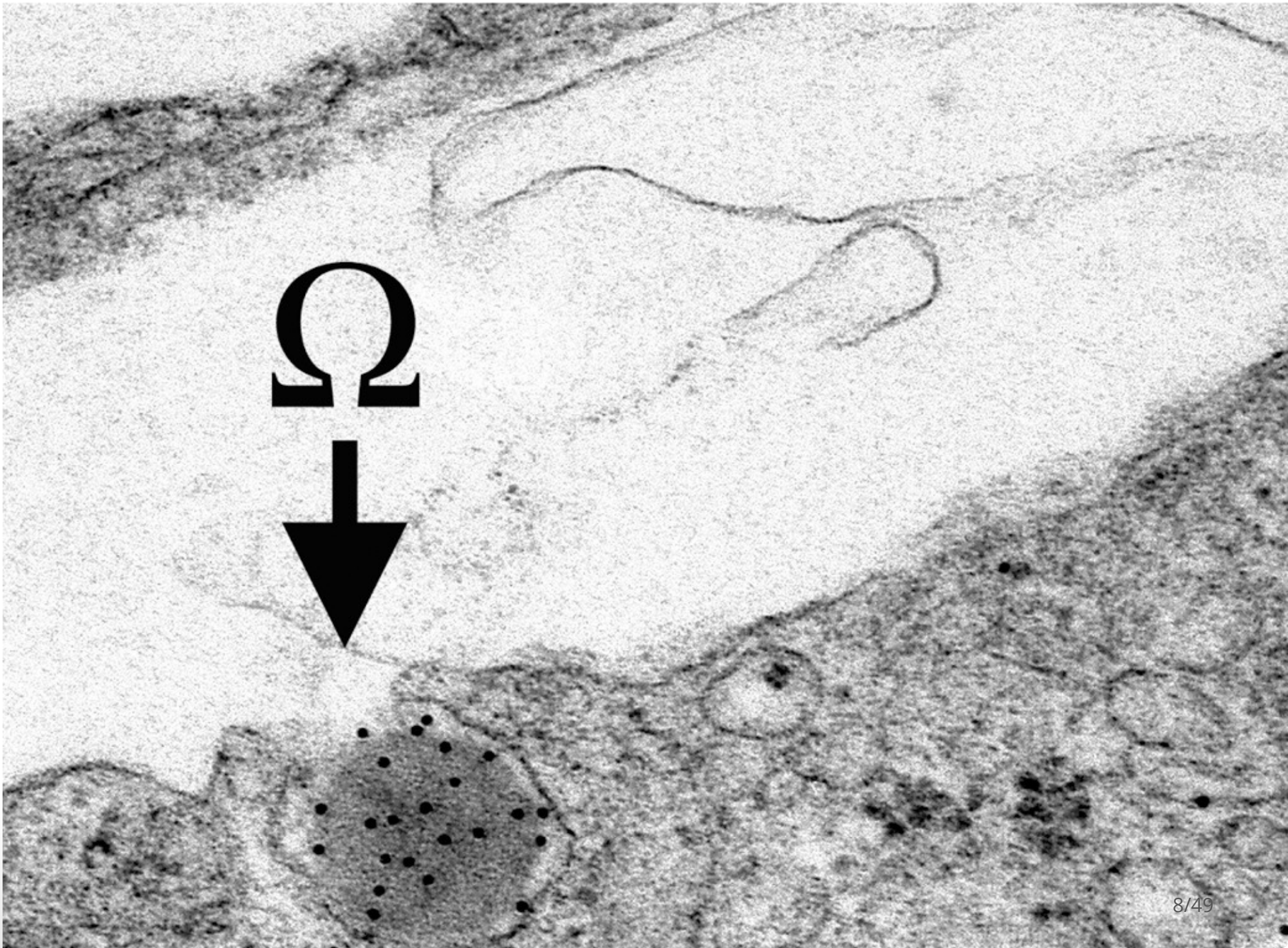


Steps in synaptic transmission

- Rapid change in voltage triggers neurotransmitter (NT) release
- *Voltage-gated calcium Ca++ channels* open
- Ca++ causes *synaptic vesicles* to bind with presynaptic membrane, merge,
- NTs released via *exocytosis*
- NTs diffuse across *synaptic cleft*



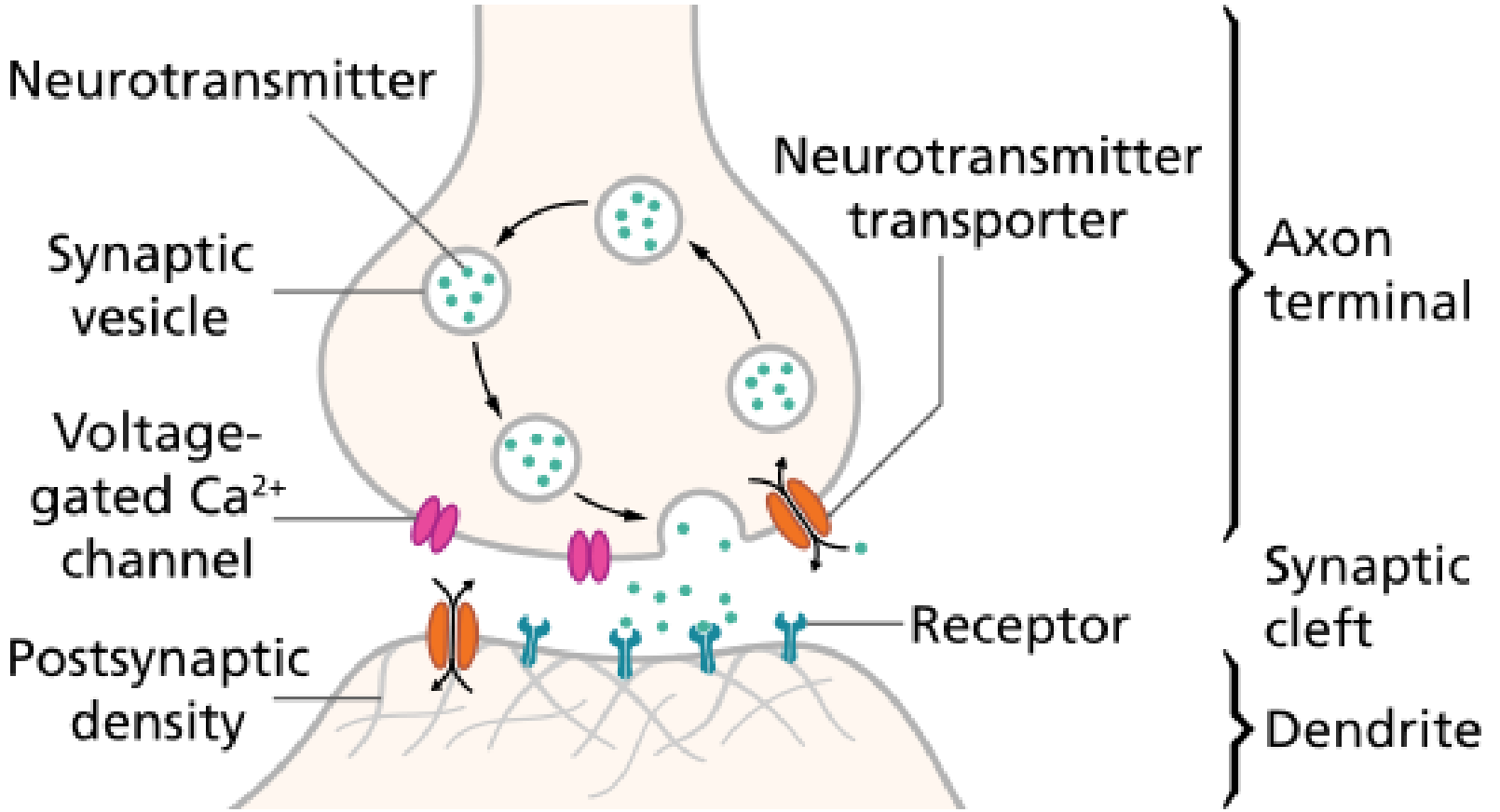
(Hastoy, Clark, Rorsman, & Lang, 2017)


Ω

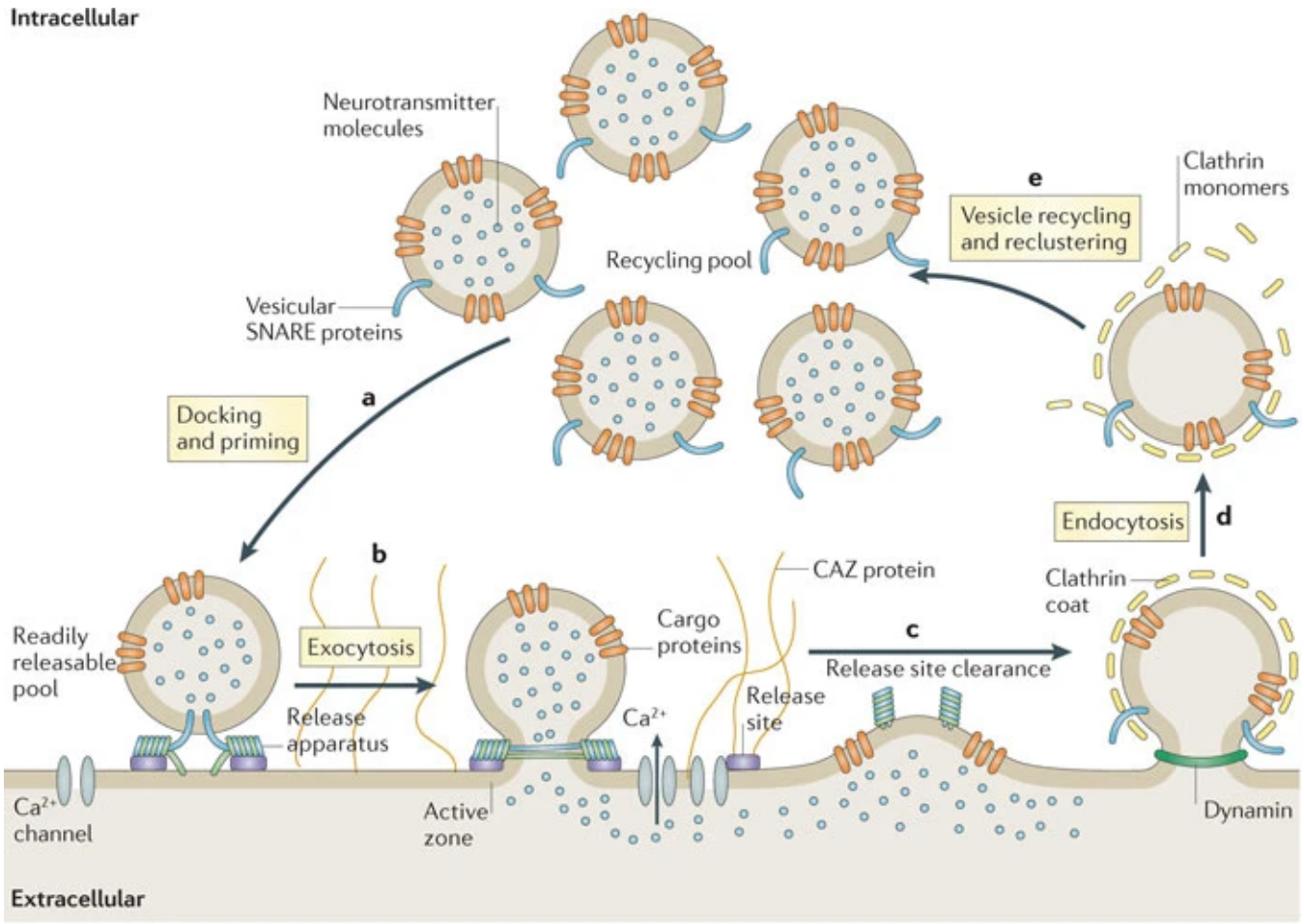
Steps in synaptic transmission

- NTs bind with *receptors* on *postsynaptic membrane*
- Receptors respond
- NTs unbind, are inactivated

Synaptic transmission



Exocytosis



(Haucke, Neher, & Sigrist, 2011)

Why do NTs move from presynaptic terminal toward postsynaptic cell?

- Electrostatic force pulls them
- Force of diffusion

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Relative sizes

- Neural membrane ~8 nm
- Synaptic vesicles ~40-60 or ~90-120 nm
- Synaptic cleft ~20-50 nm
- Cleft small relative to vesicles

Postsynaptic receptor types

- *Ionotropic* (receptor + ion channel)
  - Ligand-gated
  - Open/close ion channel
  - Ions flow in/out depending on membrane voltage and ion type
  - Fast-responding (< 2 ms), but short-duration effects (< 100 ms)

Postsynaptic receptor types

- *Metabotropic* (receptor only, no attached ion channels
  - Trigger G-proteins attached to receptor
  - G-proteins activate 2nd messengers
  - 2nd messengers open/close adjacent channels, change metabolism
  - Slower, but longer-lasting effects

Receptor types

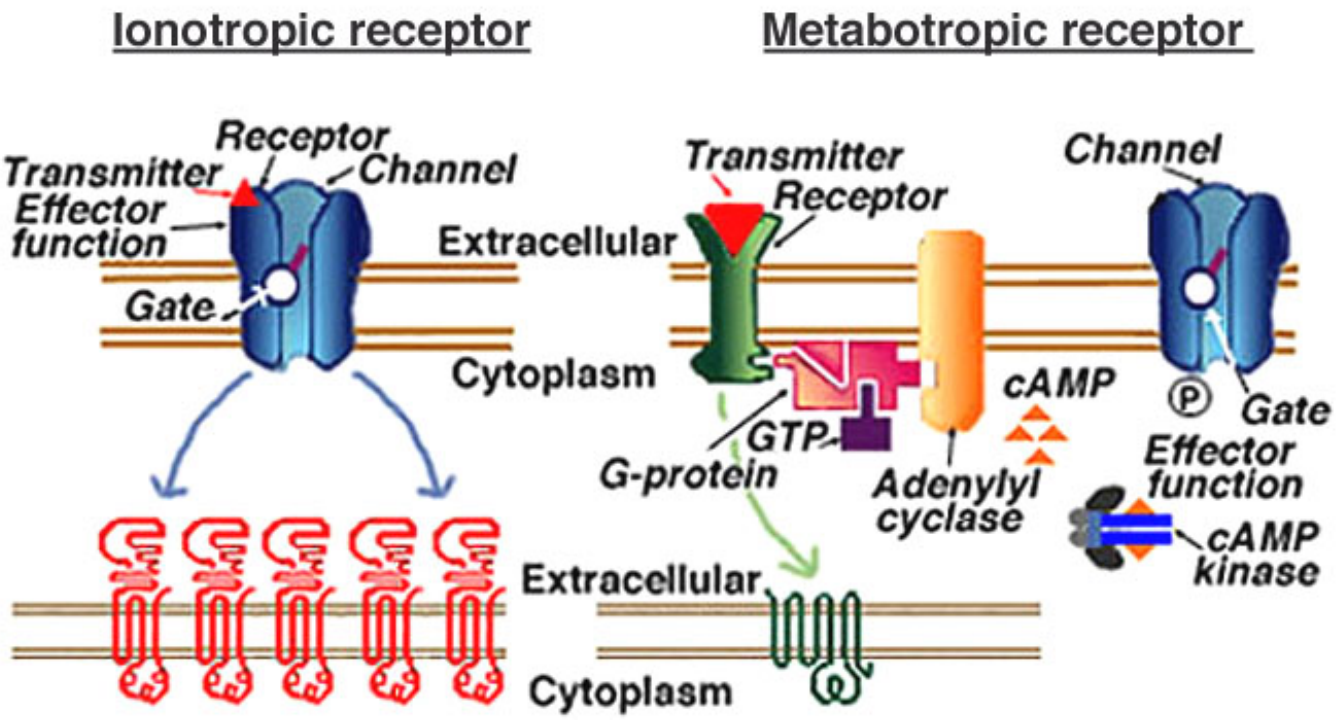

Fig. 5a. Ionotropic receptors and their associated ion channels form one complex (top). Each iGluR is formed from the co-assembly of multiple (4-5) subunits (From Kandel et al., 1991).

Fig. 5b. Metabotropic receptors are coupled to their associated ion channels by a second messenger cascade (top). Each mGluR is composed of one polypeptide, which is coupled to a G-protein (from Kandel et al., 1991).

Receptors generate *postsynaptic potentials (PSPs)*

- Small voltage changes
- Amplitude scales with # of receptors activated
-

receptors activated ~ # of vesicles released

Postsynpatic potential types

- *Excitatory PSPs (EPSPs)*
  - Depolarize neuron (make more +)
  - Move membrane potential closer to threshold
- *Inhibitory (IPSPs)*
  - Hyperpolarize neuron (make more -)
  - Move membrane potential away from threshold

Mechanisms of NT inactivation

- *Buffering*
  - e.g., glutamate into astrocytes (Anderson & Swanson, 2000)
- *Reuptake* via *transporters*
  - molecules in membrane that move NTs inside
  - e.g., serotonin via serotonin transporter (SERT)
- *Enzymatic* degradation
  - e.g., Acetylcholinesterase (AChE) degrades acetylcholine (ACh)

Questions to ponder

- Why must NTs be inactivated?

Questions to ponder

- Why must NTs be inactivated?
  - Keeps messages discrete, localized in time and space

What sort of PSP would *opening* a Na+ channel produce?

- Excitatory PSP, Na+ flows in
- Excitatory PSP, Na+ flows out
- Inhibitory PSP, Na+ flows in
- Inhibitory PSP, Na+ flows out

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- Excitatory PSP, Na+ flows in
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- Inhibitory PSP, Na+ flows in
- Inhibitory PSP, Na+ flows out

What sort of PSP would *opening* a Cl- channel produce?

Remember [Cl-out]>>[Cl-in]; Assume resting potential ~60 mV

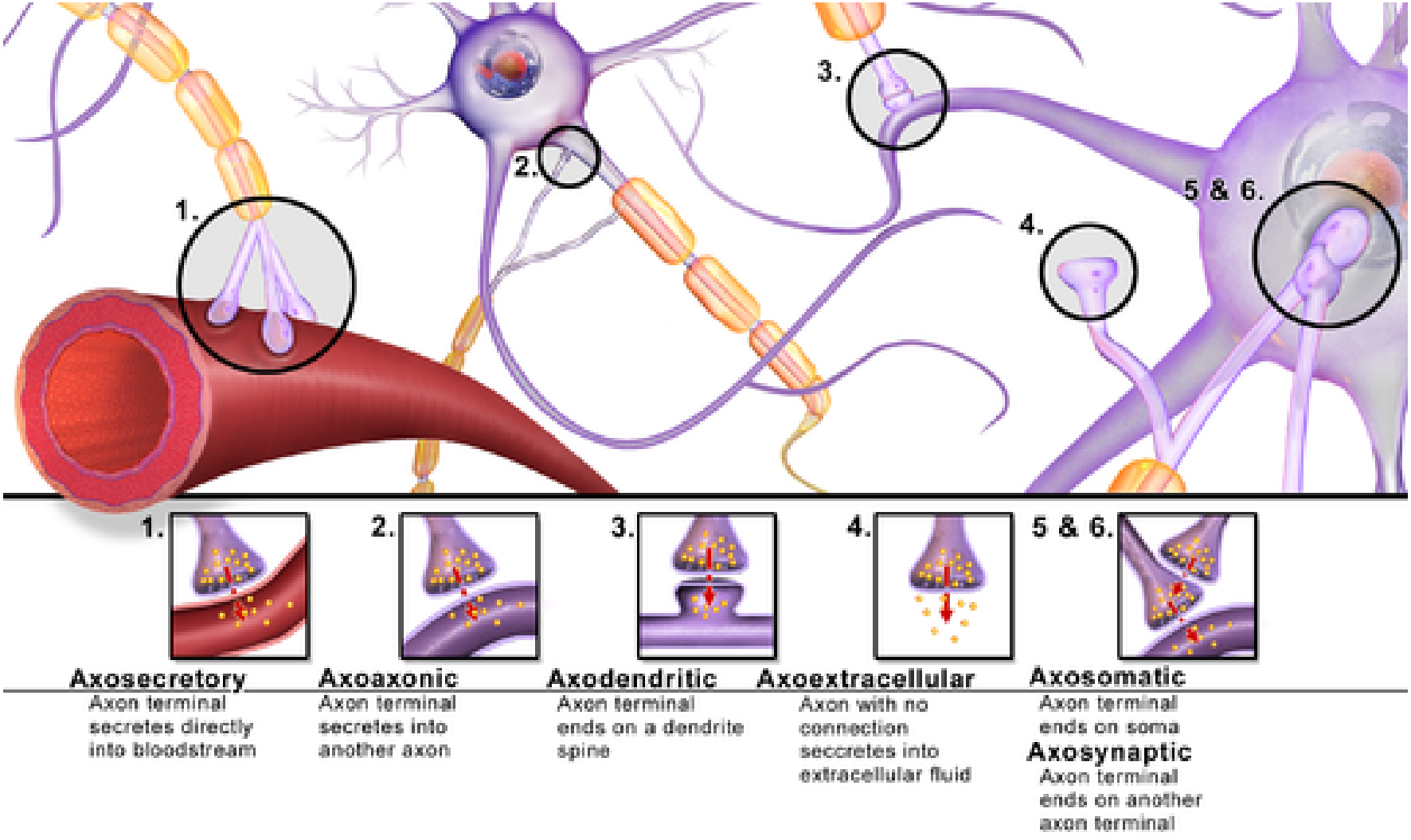
- Excitatory PSP, Cl- flows in
- Excitatory PSP, Cl- flows out
- Inhibitory PSP, Cl- flows in
- Inhibitory PSP, Cl- flows out

What sort of PSP would *opening* a Cl- channel produce?

Remember [Cl-out]>>[Cl-in]; Assume resting potential ~60 mV

- Excitatory PSP, Cl- flows in
- Excitatory PSP, Cl- flows out
- Inhibitory PSP, Cl- flows in
- Inhibitory PSP, Cl- flows out

Types of synapses



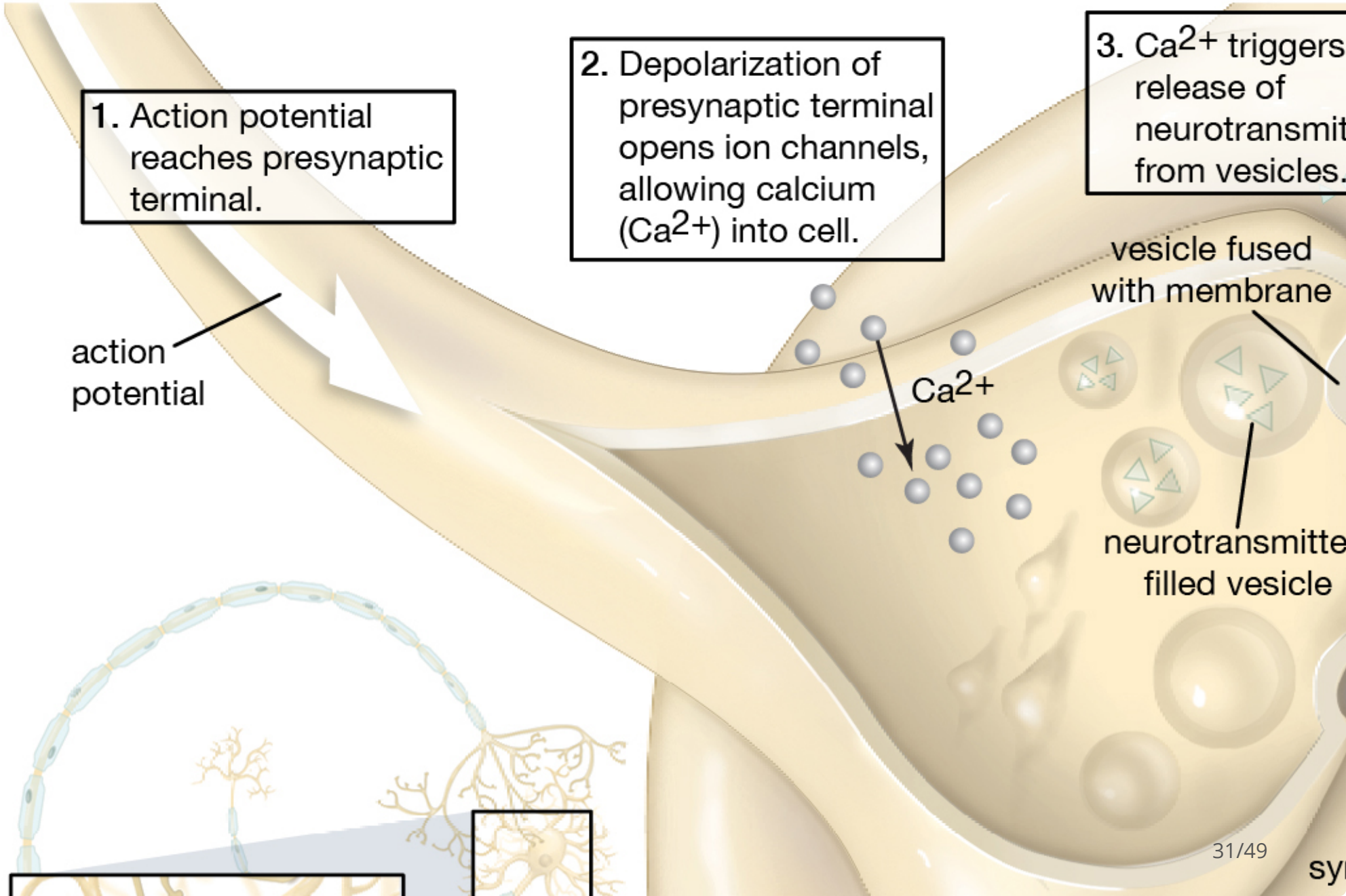
Types of synapses

- Axodendritic (axon to dendrite)
- Axosomatic (axon to soma)
- Axoaxonic (axon to axon)
- Axosecretory (axon to bloodstream)

Synapses on

- dendrites
  - usually excitatory
- cell bodies
  - usually inhibitory
- axons
  - usually modulatory (change p(fire))

Summary of chemical communication

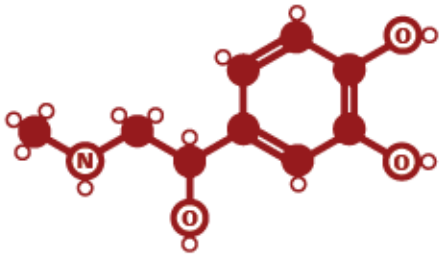


Neurotransmitters

THE STRUCTURES OF NEUROTRANSM

STRUCTURE KEY: Carbon atom · Hydrogen atom · Oxygen atom · Nitrogen atom

ADRENALINE
Fight or flight neurotransmitter



Produced in stressful or exciting situations. Increases heart rate & blood flow, leading to a physical boost & heightened awareness.

NORADRENALINE
Concentration neurotransmitter

Affects attention & responding actions in the brain, & involved in fight or flight response. Contracts blood vessels, increasing blood flow.

DOPAMINE
Pleasure neurotransmitter

Feelings of pleasure, and also addiction, movement, and motivation. People repeat behaviours that lead to dopamine release.

GABA
Calming neurotransmitter

ACETYLCHOLINE
Learning neurotransmitter

GLUTAMATE
Memory neurotransmitter

What are they?

- Chemicals produced by neurons
- Released by neurons
- Bound by neurons and other cells
- Send messages (have physiological effect on target cells)
- Inactivated after release

Neurotransmiters

Family	Neurotansmitter
Amino acids	Glutamate (Glu)
	Gamma aminobutyric acid (GABA)
	Glycine
	Aspartate

Glutamate

- Primary excitatory NT in CNS (~ 1/2 all synapses)
- Role in learning (via NMDA receptor)
- Transporters on neurons and glia (astrocytes and oligodendrocytes)
- Linked to umami (savory) taste sensation, think monosodium glutamate (MSG)
- Dysregulation in schizophrenia (McCutcheon, Krystal, & Howes, 2020), mood disorders (Małgorzata, Paweł, Iwona, Brzostek, & Andrzej, 2020)

Glutamate

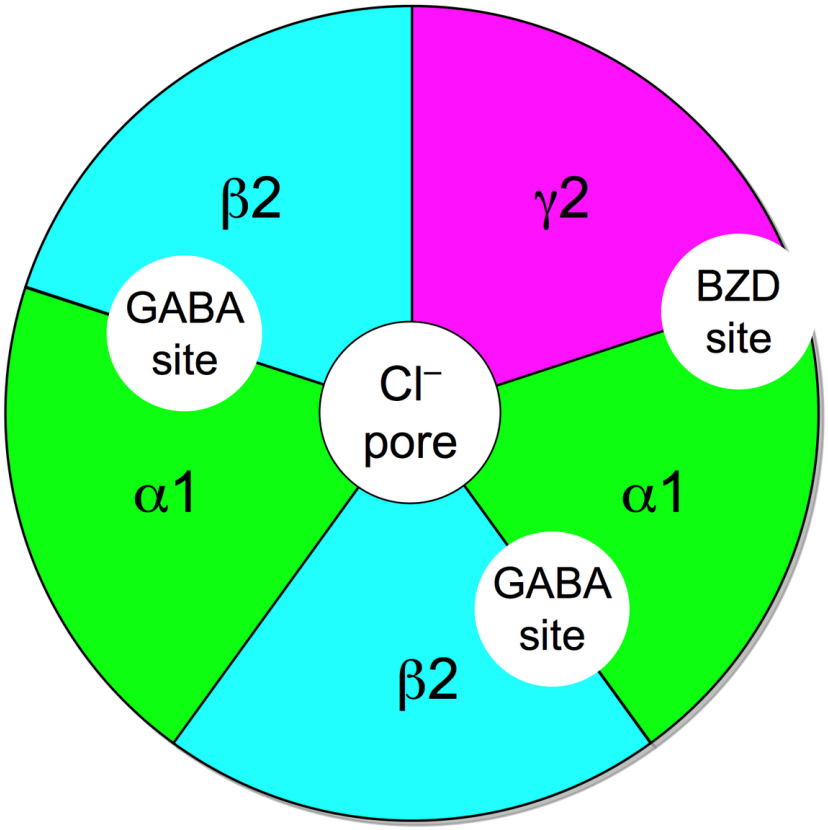
Type	Receptor	Esp Permeable to
Ionotropic	**AMPA**	Na+, K+
	Kainate	
	NMDA	Ca++
Metabotropic	mGlu	

γ-aminobutyric Acid (GABA)

- Primary inhibitory NT in CNS
- Excitatory in developing CNS, [Cl-] in >> [Cl-] out
- Binding sites for benzodiazepines (e.g., Valium), barbiturates, ethanol, etc.
- Synthesized from glutamate
- Inactivated by transporters

Type	Receptor	Esp Permeable to
Ionotropic	GABA-A	Cl-
Metabotropic	GABA-B	K+

GABA



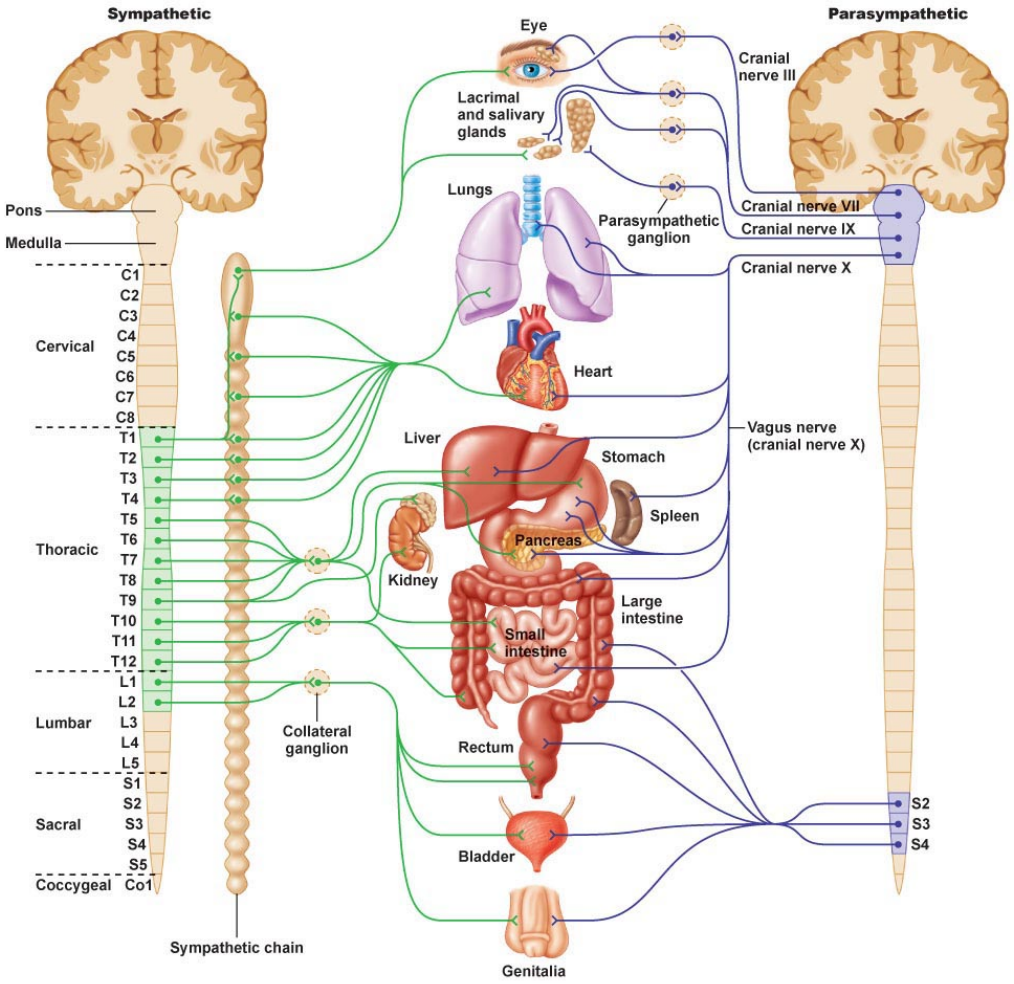
Other amino acid NTs

- *Glycine*
  - Spinal cord interneurons
  - Also inhibitory
- *Aspartate*
  - Like Glu, stimulates NMDA receptor

Acetylcholine (ACh)

- Primary NT of CNS output
- Somatic nervous system (neuromuscular junction)
- Autonomic nervous system
    - Sympathetic branch: preganglionic neuron
    - Parasympathetic branch: pre/postganglionic
- Inactivation by acetylcholinesterase (AChE)

ACh anatomy



http://myzone.hrvfitltd.netdna-cdn.com/wp-content/uploads/2014/09/Image-1.jpg

Acetylcholine

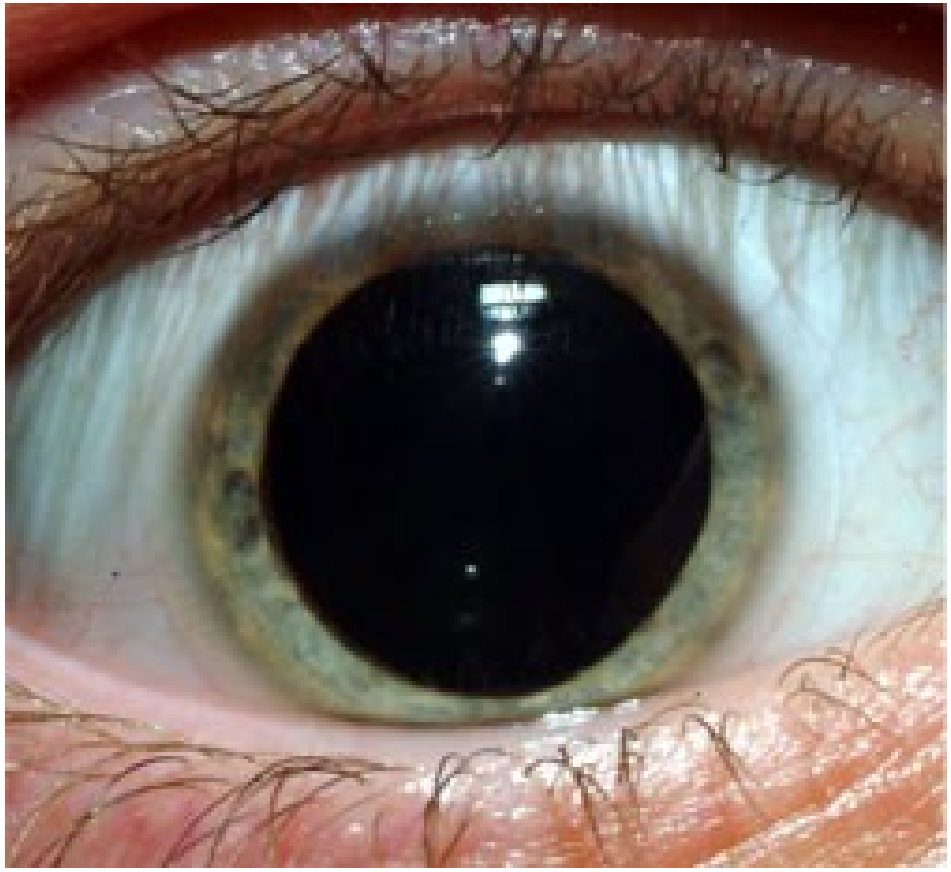
Type	Receptor	Esp Permeable to	Blocked by
Ionotropic	**Nicotinic (nAChR)**	Na+, K+	e.g., Curare
Metabotropic	**Muscarinic (mAChR)**	K+	e.g., Atropine

Curare

http://www.general-anaesthesia.com/images/indian-curare.jpg

Atropine

- aka, nightshade or belladonna



https://aapos.org/glossary/dilating-eye-drops

How to stop your prey

Substance	Effect
Japanese pufferfish toxin	Blocks voltage-gated Na+ channels
Black widow spider venom	Accelerates presynaptic ACh release
Botulinum toxin (BoTox)	Prevents ACh vesicles from binding presynaptically
Sarin nerve gas	Impedes ACh breakdown by AChE
Pesticides	Impede AChE
Tetanus toxin	Blocks release of GABA, glycine

Next time…

- More on NTs!

References

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