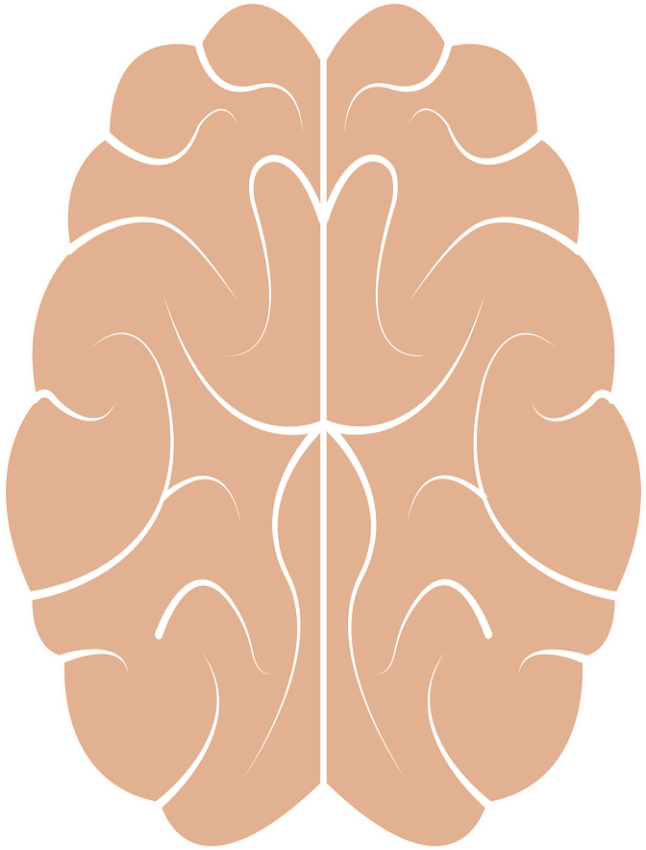

Physiology

Done By:

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Autonomic Nervous System

Ref: **Textbook of Medical Physiology,** Guyton, 13th ed.: 773-784. 12th ed: 729-738, 11th ed. P748-760, and

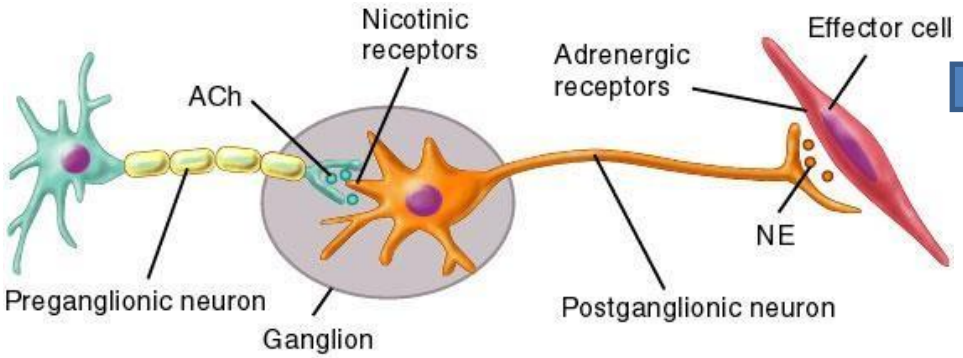
10th ed. p697-708.

MOLECULAR BASIS OF PHYSIOLOGICAL ACTIONS OF THE ANS

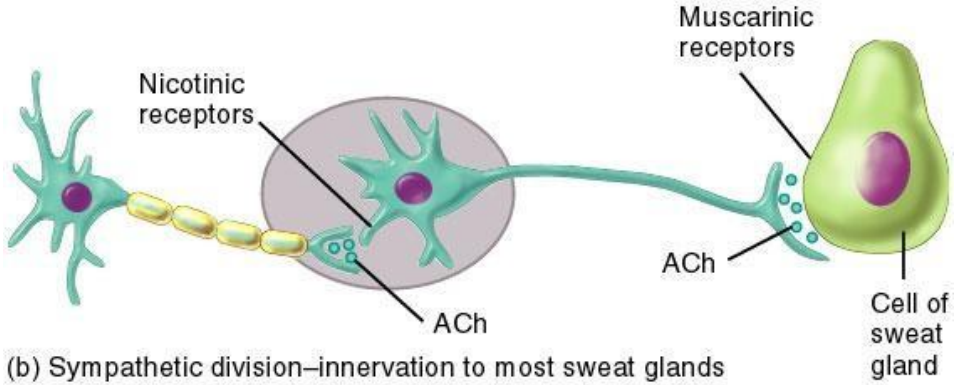
CNS = central nervous system
NT = neurotransmitter

We are aware that we have 2 neurons forming the axe from the origin of **CNS** either from the spinal cord for the sympathetic or from the cranial-sacral for the parasympathetic

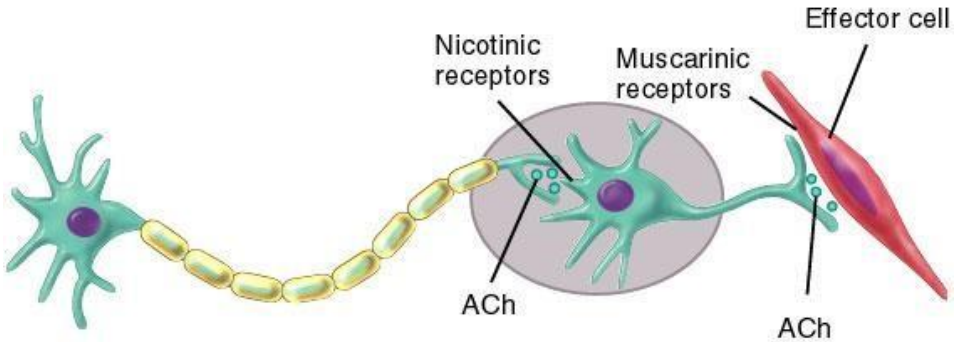
In the first neurons of the both divisions (sympathetic and parasympathetic) they are releasing acetylcholine as **NT**
Then acetylcholine is acting synapse with the second neuron located in the ganglia
After that the second neuron releasing epinephrine of the sympathetic divisions
and acetylcholine of the parasympathetic division



(a) Sympathetic division–innervation to most effector tissues



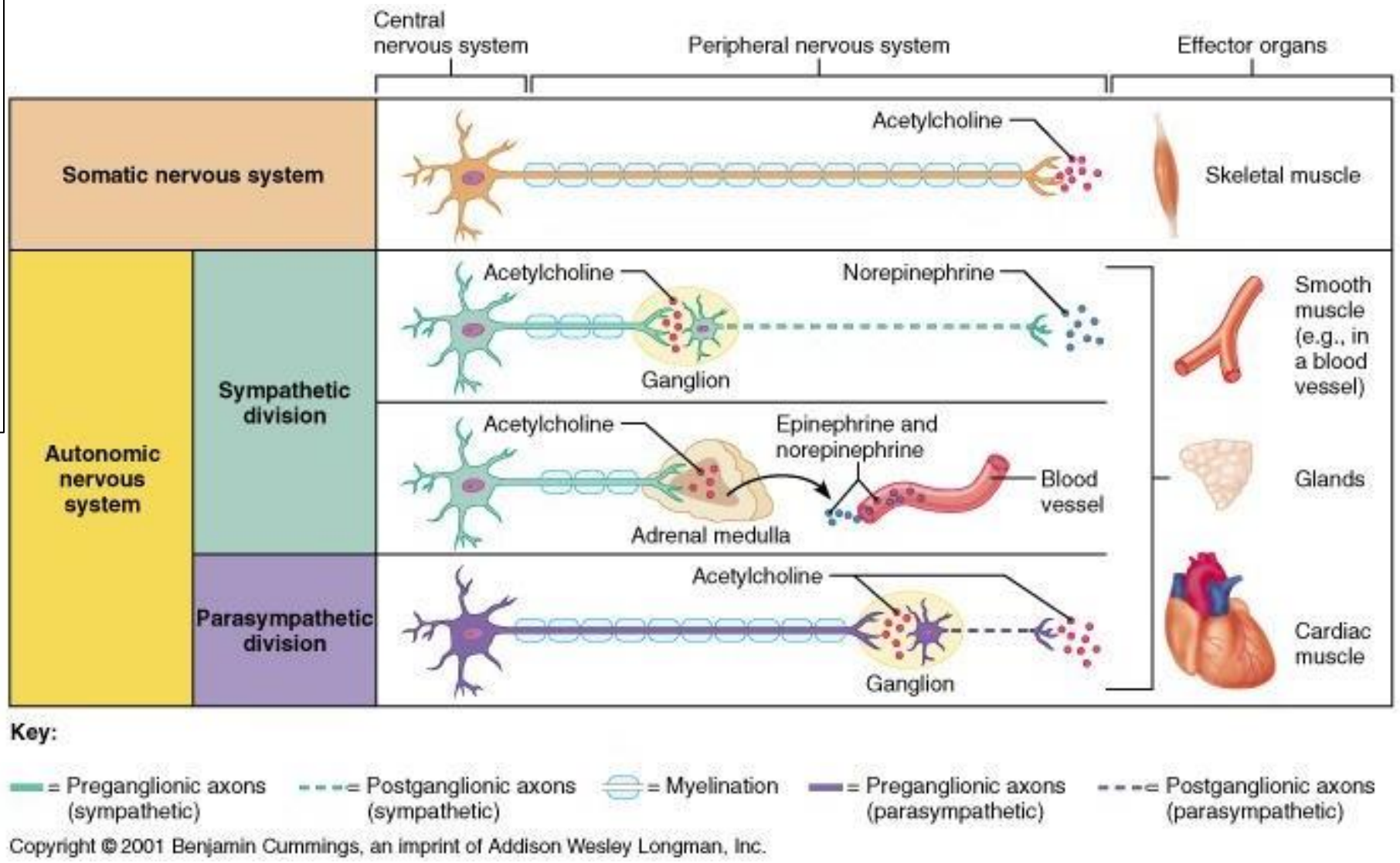
(b) Sympathetic division–innervation to most sweat glands



(c) Parasympathetic division

NOTICE: We have an exception for **sympathetic fibers** that innervate *sweat glands* and *pile erector muscles*, so they are divisions of the sympathetic but they are releasing acetylcholine as **NT**

Remember:
when we talked about the adrenal medulla we said we have fibers that are sympathetic belonging to the 1st neuron and they are innervating the suprarenal gland and the type of **NT** that is released is acetylcholine



The types of neurotransmitters that are released by the 1st or the 2nd neurons.

The neurotransmitters are acting at a certain receptor located in the target

EXAMPLE: At the ganglia, we have fibers of the 1st neuron synapsing with 2nd neuron, so the preganglionic fibers are releasing acetylcholine so we have to stimulate the 2nd neuron by signal transduction mechanism

–Neurotransmitters

- **At ganglion**: preganglionic neurons of both sympathetic and parasympathetic release **acetylcholine** (Ach).
- **Effector organs:**

  - parasympathetic fibers release **acetylcholine**

  - Sympathetic: **norepinephrine**.
- **An exception** for sympathetic nerves to **sweat glands**, which release **acetylcholine** (Ach).

What type of signal transduction mechanism will be used in this ganglia?

Simply these receptors once they are activated by ligand which acetylcholine causing the activation of sodium channels to generate an action potential at the postsynaptic membrane and 2nd neuron and get action potential at 2nd neuron
SO the receptor for the acetylcholine in the ganglia is called **Nicotinic**

NOTE: They can be stimulated by Nicotine

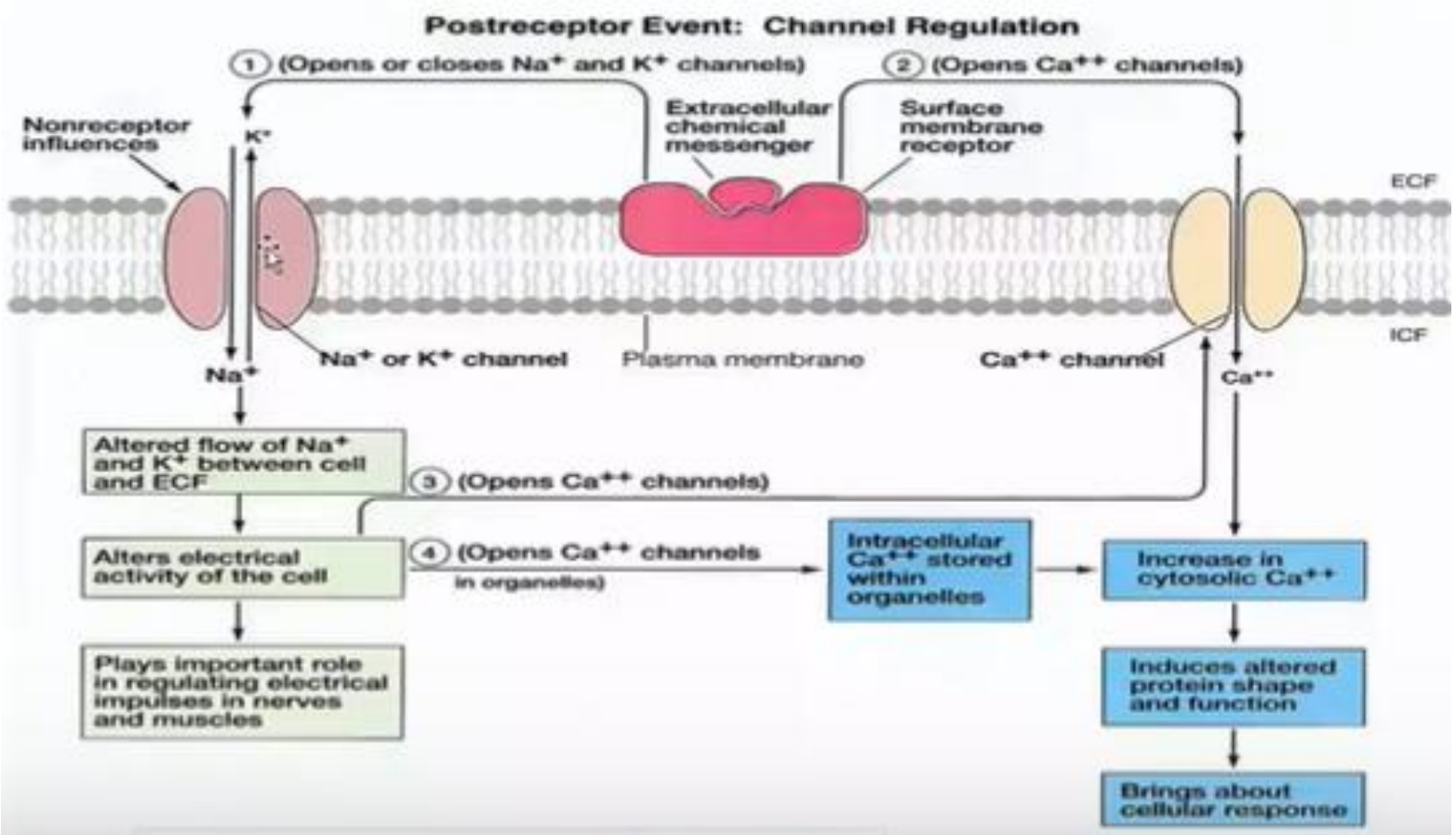
Receptors and Signal transduction mechanisms

-**At ganglia**: sympathetic and parasympathetic have **nicotinic** receptors at the post synaptic membrane

- **on effector cells:** **Muscarinic receptors**.

Clarifying picture for the previous slides

Receptors & Channels



The effector cells now also of the second neuron of parasympathetic is releasing acetylcholine, and the acetylcholine is acting over receptor that is found in effector cells and these receptors are called **muscarinic receptor**

NOTE: They can be stimulated by Muscarine

Muscarine: is a type of natural molecules that can be found in toxic mushroom so when the muscarine is ingested it can activate the muscarinic receptors

Receptors and Signal transduction mechanisms

Muscarinic Receptors (M1-M5)

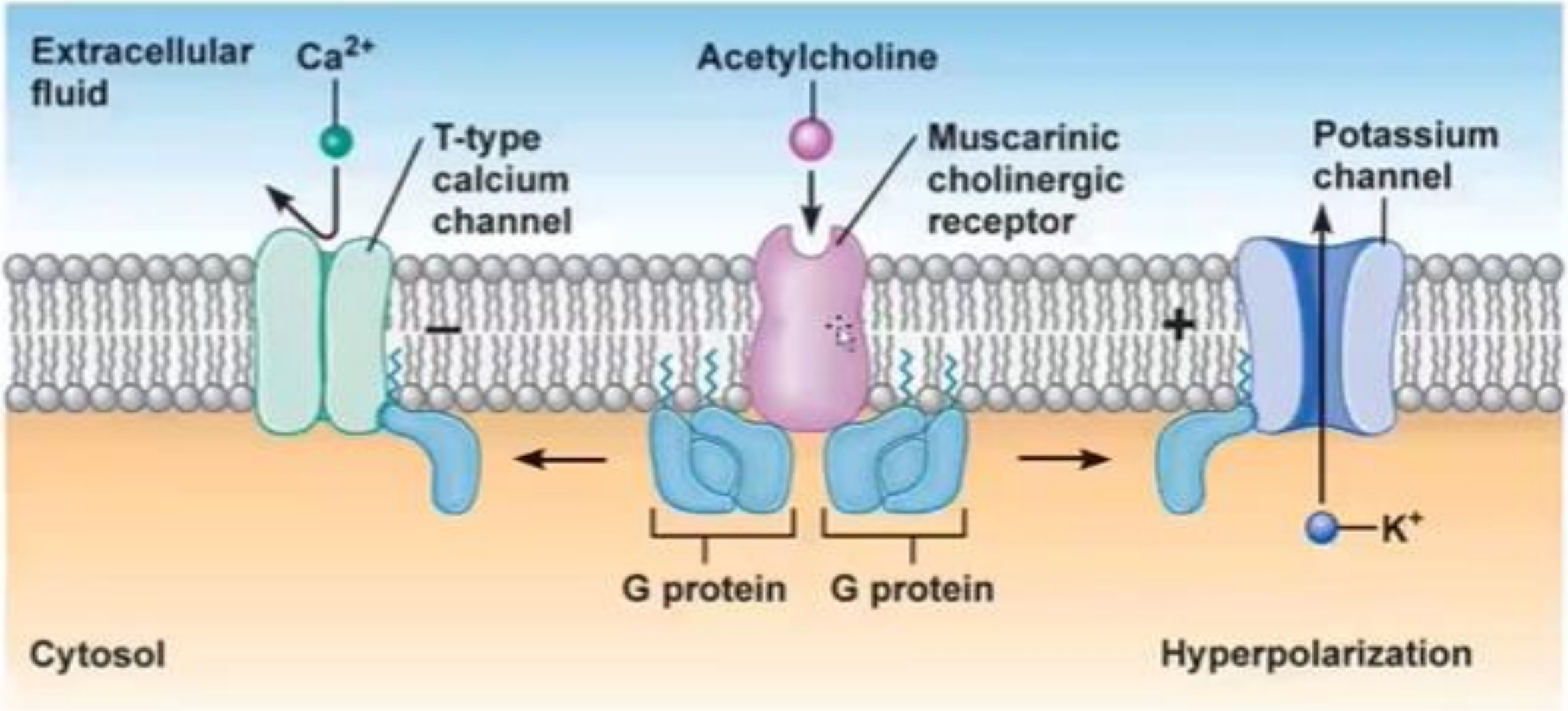
Inhibitory:

-**M2 in the heart**: G protein→K+ channel → slow the rate of depolarization.

- Other inhibitory receptors:

Gi→adenylyl Cyclase→ reduce cAMP

In the heart, we have M2 type of these receptors this M2 type is linked to G inhibitory protein to reduce the activity of adenylyl cyclase so it reduces the cyclic AMP inside the conductive tissue of the heart (slowing the heart rate)



(b) Parasympathetic

the increase of the concentration of calcium in this type of self-descriptor cells or smooth muscle cells hey will be activated(**smooth muscle will contract and secretory cells will release secretion**) so we call these types of receptors (M1 M3 M5) excitatory receptors

NOTICE: We can have both types of inhibitory and excitatory receptors of muscarine

Receptors and Signal transduction mechanisms

Muscarinic Receptors (M1-M5)

Excitatory Rceptors: (M1, M3, M5)

Found on **smooth muscle** **and** **glands** are coupled

Gq protein →phospholipase C.

This enzyme increases production of inositol-1,4,5-trisphosphate (**IP3**)

Activation of Muscarinic Receptors

-Stimulation of secretory activity: salivation, tearing, sweating, nasal and bronchial secretion.

-Increase gastrointestinal tract motility→ vomiting and diarrhea.

- Contraction of urinary bladder →urination.

- Slowing of the heart →Bradycardia.

Blocking of Muscarinic Receptors by ATROPIN

Atropin can block the muscarinic receptors

-Inhibition of glandular secretions→ dry mouth, dry eyes, and dry nasal passages.

- Tachycardia. (increase heart rate).

- Loss of pupillary light reflex → Mydriasis

- Loss of ability to focus the lens for near vision.

By giving atropin to pupil it will cause dilation

People who have been at the ophthalmologist have received some drops of eye drops for atropin to dilate the pupil and to enable the doctor to see the fundus of the eye

Receptors and Signal transduction mechanisms

Both of them are acting on the same receptors but with different abilities they don't have the same ligands but they're very similar and they're called catecholamines both of them are acting on adrenergic receptors with different abilities for different types and subtypes of receptors

Adrenergic receptors:

These receptors respond to **catecholamines**: (epinephrine (EP) and norepinephrine (NE)).

Neurotransmitter released by the nerve endings

Receptors and Signal transduction mechanisms

Alpha receptors:

- The **alpha 1 (α_1)**: Excitatory: PLC→ IP3

- **Alpha2** receptors: Nerve Adrenergic terminals→ reduce NE release

Alpha 2 Heteroreceptors: Nonadrenergic -

Gi→ Adenylyl cyclase→ decrease cAMP

The A1 receptor is found over smooth muscle cells of vessels that are innervating skin.and small vessels

The effect of A2 is Inhibitory and its working by the division of adenylyl cyclase

The A2 receptors are found at the ending of adrenergic terminals so the terminals at the central nervous system they are bearing the A2 receptors once we have released norepinephrine by these terminals that norepinephrine is binding to the A2 receptors and reducing the release of more norepinephrine from this terminal

Receptors and Signal transduction mechanisms

Beta receptors:

- **Beta 1 (β_1) receptors**: found on heart

- **Beta 2 (β_2) receptors**: found on tracheal and bronchial smooth muscle, in the gastrointestinal tract, and on smooth muscles of blood vessels supplying skeletal muscles

Gs→Adenylyl cyclase→ increase cAMP

B1 adrenergic receptors that are found in the heart they can increase the heart rate activation of these receptors and also can increase thee force of contraction because the cardiac muscle cells are having B1 receptors

B1 receptors is as considered excitatory: activating sodium channels and the three types of calcium channels

B2 receptors are considered as inhibitory receptors they are found over smooth muscle cells in addition some smooth muscle cells or vessels

Both of them are working with the same mechanisms activating the adenylyl cyclase but different issues were getting different effects at the hearts