



PresenterMedia

NEUROMUSCULAR TRANSMISSION

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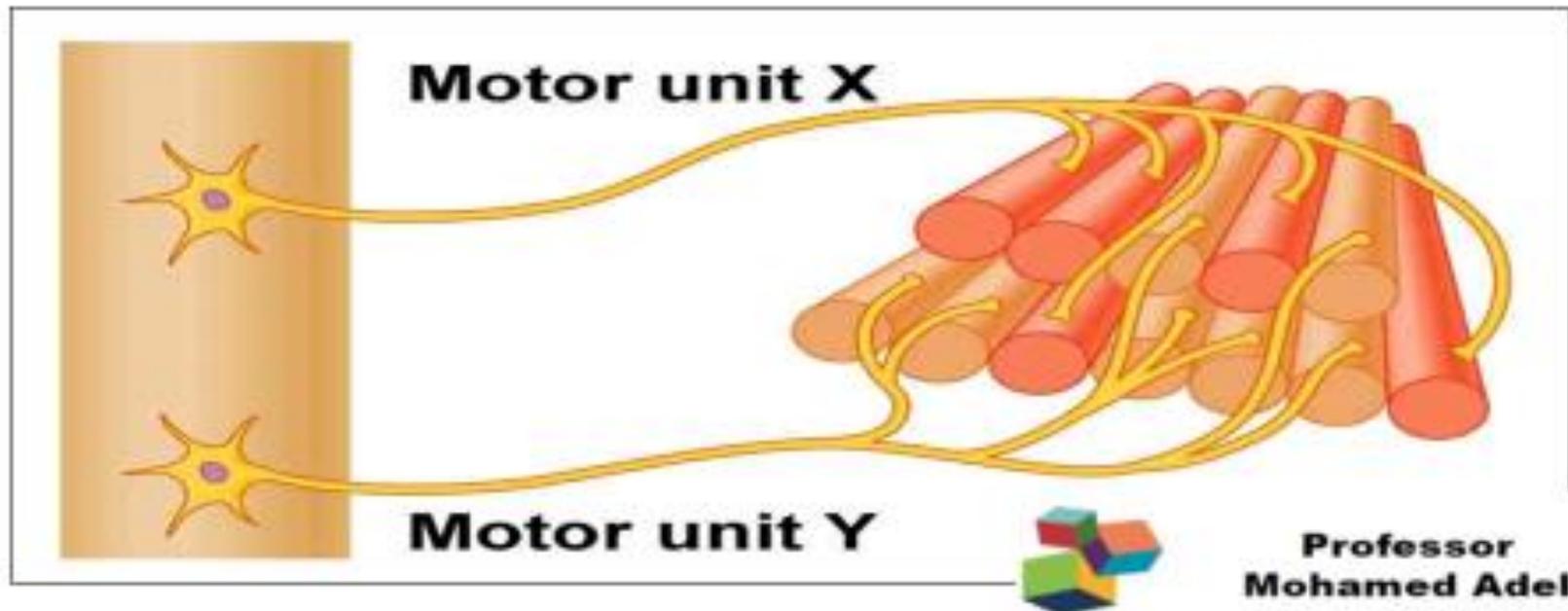


Neuro-Muscular Junction

□ Is the area of contact between motor nerve fiber and a muscle fiber.

Motor Unit

- Is a motor neuron, plus the muscle fibers supplied by it.





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The number of muscle fibers in the "motor unit" varies:

Muscles which perform fine and delicate movements e.g eye ms.

-only a few (less than 10) muscle fibers are supplied by one motor neuron.

Muscles which perform coarse movements e.g thigh ms.

-huge number of muscle fibers (1000-2000) are supplied by a single neuron.



Neuro-Muscular Junction

• Parts:

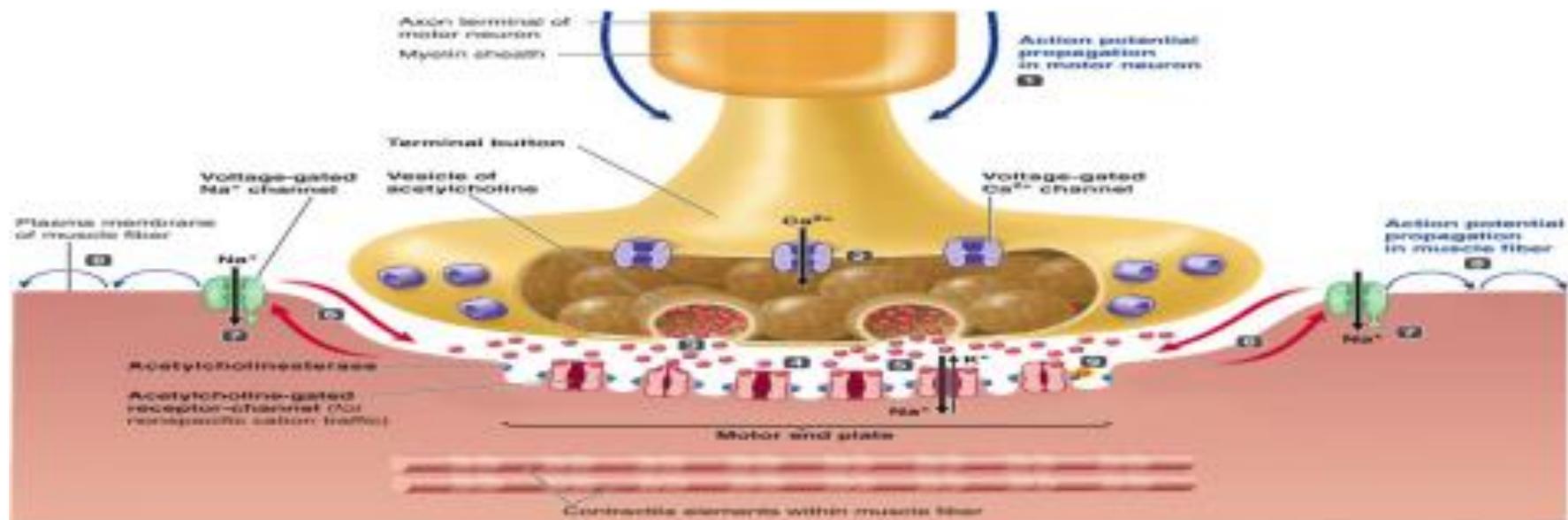
1. **Pre-synaptic membrane = Synaptic knob**
2. **Synaptic cleft**
3. **Post-synaptic membrane = Motor end plate**

Functional anatomy of the neuromuscular junction

- When the nerve fiber approaches muscle fiber, it loses its myelin sheath and divides into many terminal branches which end in synaptic knobs.
- Each branch forms a junction with a single muscle fiber near its middle.



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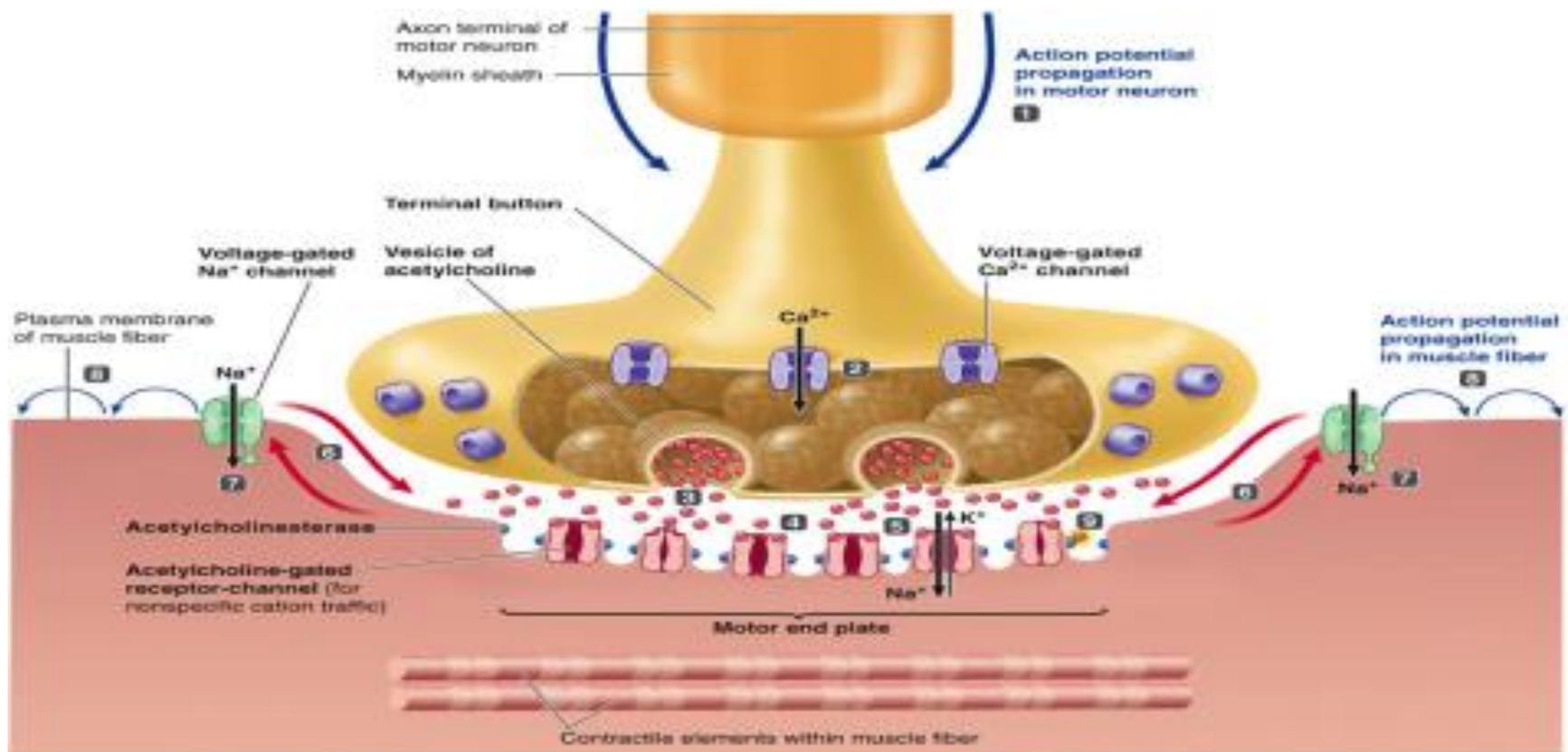


1) Pre-synaptic membrane (Synaptic knob) contains:

- Acetylcholine vesicles.
- Multiple mitochondria (to supply energy required for A.ch. synthesis).
- Multiple voltage gated Ca^{++} channels.



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2) Synaptic cleft:

It is the space between the nerve and muscle membrane.



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3) Post-synaptic membrane = Motor end plate



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- ❑ It is the invaginated muscle fiber plasma membrane under the synaptic knob.
- ❑ It is **thrown into folds** to increase the surface area for A.ch. action.

3) Post-synaptic membrane = Motor end plate, contains:

i) Acetylcholine receptors (Cholinergic, nicotinic receptors) which are ligand gated ion channels.

ii) Cholinesterase enzyme (True cholinesterase):
which breaks down acetylcholine to an inactive form
once it has done its action.



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Mechanism of neuromuscular transmission

1) When a nerve impulse reaches the axon terminal, it opens voltage gated Ca^{++} channels thus allowing calcium influx. this leads to movement and fusion of A.ch vesicles with the presynaptic membrane and lastly rupture of these vesicles and release of A.ch. by exocytosis into synaptic cleft.



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Mechanism of neuromuscular transmission

2) A.ch diffuses across the cleft to the motor end plate where it binds with **the receptors** (ligand-gated ion channel) leading to increase in Na⁺ and K⁺ permeability at the same time. Because of the electrochemical gradient differences Na⁺ influx is greater than K⁺ efflux → action potential is produced and propagated along the muscle fiber.



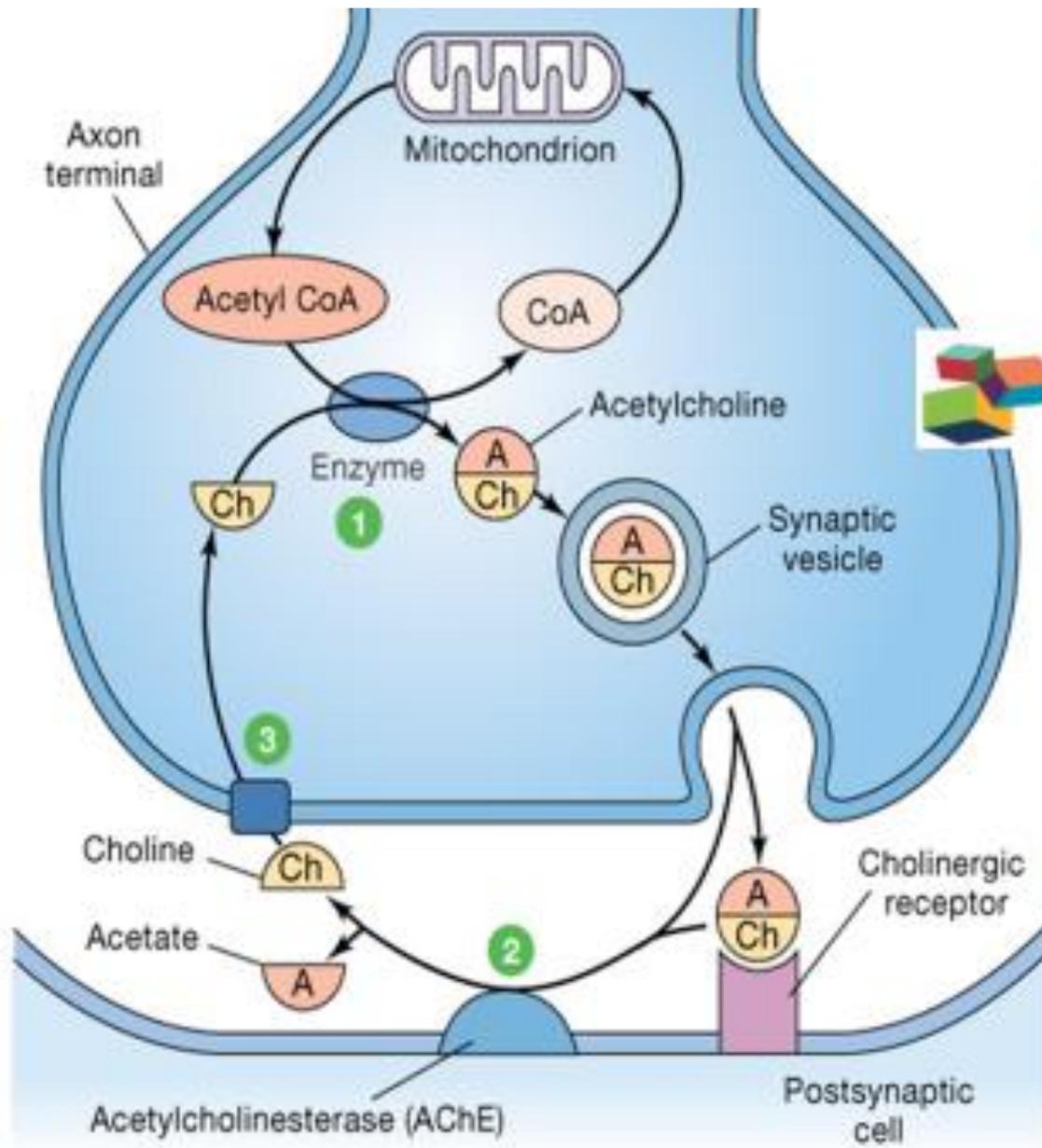
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Mechanism of neuromuscular transmission

3) Once A.ch. produces its action, it is rapidly removed mostly by hydrolysis with choline-esterase enzyme, to prevent occurrence of multiple contractions.



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1 Acetylcholine (ACh) is made from choline and acetyl CoA.

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2 In the synaptic cleft ACh is rapidly broken down by the enzyme acetylcholinesterase.

3 Choline is transported back into the axon terminal and is used to make more ACh.

Properties of neuromuscular transmission (NMT)

- ❑ **One way conduction (Unidirectional):**
- ❑ From the nerve to the muscle **only**.
- ❑ Because A.ch vesicles are **present only in the nerve terminal not in the muscle fiber**.

Properties of neuromuscular transmission

□ Delay:

- About 0.5 m. sec. between arrival of the nerve impulse at neuromuscular junction and the generation of muscle action potential.
- It is the time needed for A.ch. release, diffusion through the synaptic cleft and the generation of action potential.

Properties of neuromuscular transmission (NMT)

□ Fatigue:

□ Caused by rapid repetitive stimulation which leads to depletion of A.ch.

□ O₂ lack facilitates the onset of fatigue because it decreases the metabolic reactions needed to reform A.ch.

□ Effect of ions:

A) Ca⁺⁺ ions: helps neuromuscular transmission.

B) Mg⁺⁺ ions: stabilizes A.ch. vesicles.

C) K⁺ ions: have anti-curare effects on MEP.

Myasthenia gravis

□ **Def.:** an auto-immune disease that affects the neuro-muscular junction & it is characterized by muscle weakness and rapid onset of fatigue.



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□ **Incidence:** 1/ 20,000 usually female.

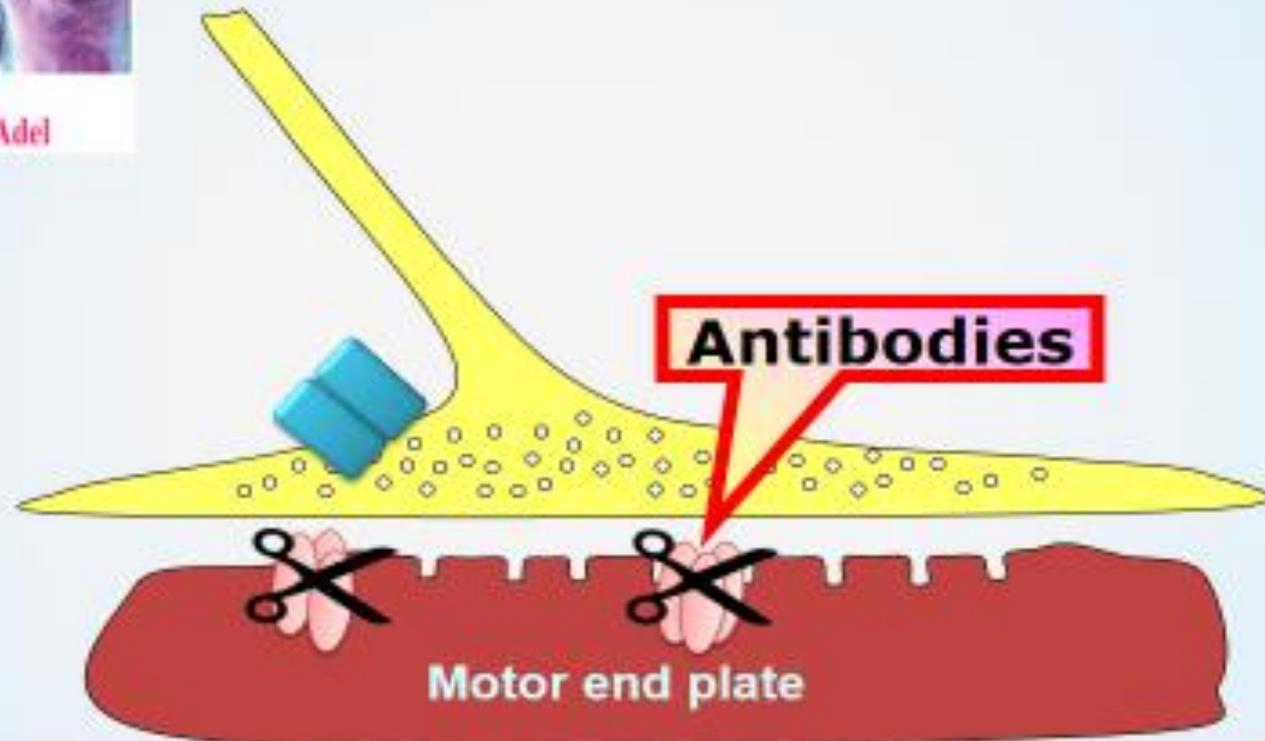
Myasthenia gravis

Causes:



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- 1- ↓ Number of acetyl choline vesicles in the axon terminal.
- 2- ↓ A. Ch content in the vesicles.
- 3- Widening of the synaptic cleft.
- 4- ↓ Number of junctional folds thus decreasing the surface area.
- 5 - ↓ Number of A.ch. receptors on postsynaptic membrane due to production of auto-antibodies against them.



Myasthenia gravis

Myasthenia gravis



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Clinical picture:

- The motor end plate potential is very weak and the muscle fails to contract.
- The first muscles to be affected are those supplied by cranial nerves e.g eye muscles.
- In severe cases there is:
 - i- General muscle weakness.
 - ii- Death may occur due to respiratory muscle paralysis.

Myasthenia gravis

Diagnosis:

1- Electromyogram.

2-Therapeutic test: the patient is given a dose of prostigmine, if improved this confirms the diagnosis.



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THANKS