

Diseases of the Neuromuscular junction

Biomedical Engineering - URJC

Rafa Carretero, MD, PhD

Internal Medicine Department

20 de marzo de 2025



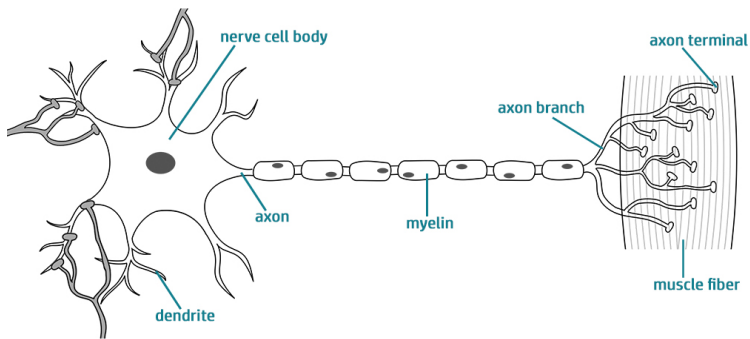
Universidad
Rey Juan Carlos

Diseases of the Neuromuscular Junction

Introduction

- Neuromuscular junction (NMJ) crucial for communication between nervous and muscular systems
- Interface for translating nerve signals into muscular contractions
- Key for precise control and coordination of voluntary movements

Diseases of the Neuromuscular Junction



Definition of Neuromuscular Junction

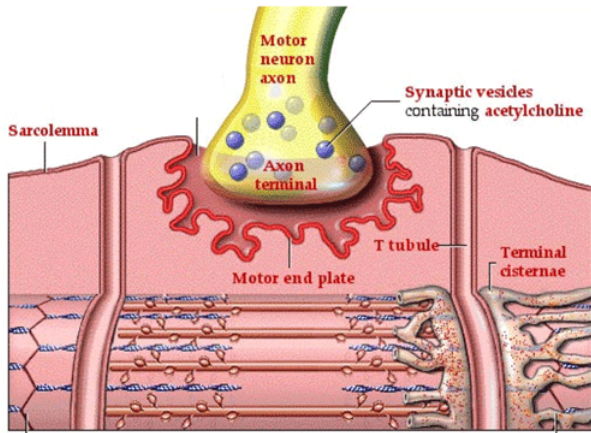
- Synapse/connection between motor neuron and skeletal muscle fiber
- Facilitates transmission of nerve impulses to muscle fiber, leading to contraction
- Critical for proper muscular system functioning

Structural Components

- Nerve terminal with synaptic end bulbs releasing **acetylcholine** (ACh)
- Synaptic cleft between nerve terminal and muscle fiber
- **Motor end plates** (the same as neuromuscular junction) on muscle fiber with high sensitivity to ACh

Structural Components

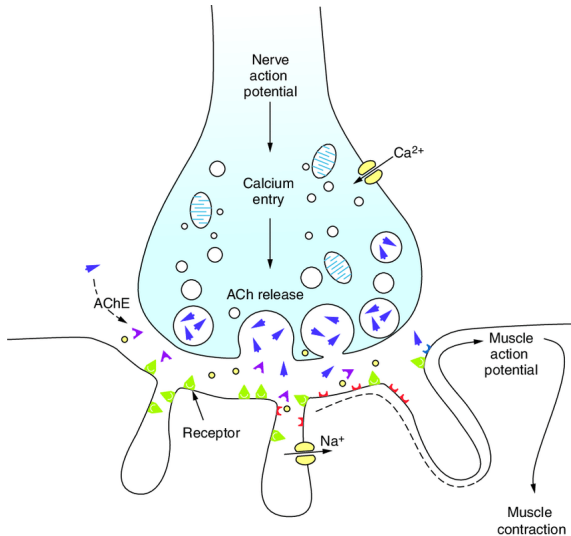
Neuromuscular Junction



Mechanism of Action

- Action potential along motor neuron axon
- Opening of voltage-gated calcium channels in nerve terminal
- Release of ACh into synaptic cleft
- ACh binding to motor end plate receptors, inducing muscle fiber action potential
- Muscle contraction through calcium release and actin-myosin interaction

Diseases of the Neuromuscular Junction



Myasthenia Gravis

- Most common disorder affecting neuromuscular junction
- Fluctuating weakness, prominent in the afternoon
- Involves muscles of eyes, throat, and extremities
- Autoantibodies against postsynaptic membrane proteins cause reduced impulse transmission
- Complications include myasthenic crisis with acute respiratory paralysis

Etiology and Pathophysiology of myasthenia gravis

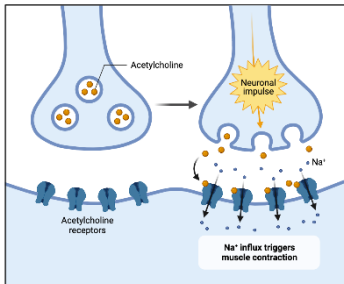
- **Autoimmune** disorder with **antibodies** against **acetylcholine receptor** (AChR)
- **Autoantibodies** lead to complement system activation and ACh receptor degradation
- Approximately 10 % of MG patients have thymoma

Myasthenia Gravis

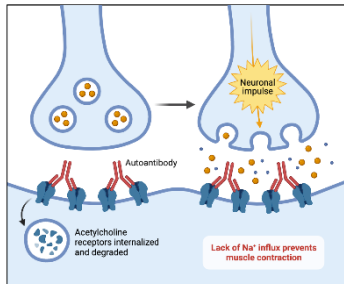
Myasthenia Gravis

Autoantibodies Against Receptors Cause Disease by Blocking Receptor Function

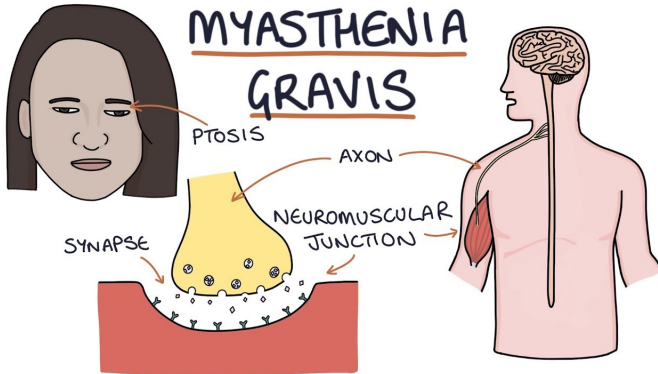
Normal events at the neuromuscular junction



Myasthenia gravis



Myasthenia Gravis



History and Physical Examination in MG

- Fluctuating muscle weakness, worsens with activity and improves with rest
- Precipitating factors: infections, surgery, immunization, heat, stress, pregnancy, drugs
- Symptoms: diplopia, ptosis, difficulty chewing/swallowing, hoarseness, limb weakness

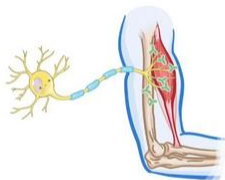
Clinical Features and Severity Classes in MG

- Extraocular Muscle Weakness (85 %)
- Bulbar Muscle Weakness (15 %)
- Limb Weakness (proximal, upper limbs more affected)
- Myasthenic Crisis (emergency due to respiratory muscle involvement)
- No autonomic symptoms
- Classes I-V based on clinical features and severity

Diseases of the Neuromuscular Junction

MYASTHENIA GRAVIS

* CHRONIC AUTOIMMUNE DISEASE caused by **ANTIBODIES**



BIND TO & DESTROY
NEUROMUSCULAR COMMUNICATION



FATIGUE & MUSCLE WEAKNESS
due to IMPAIRED MUSCLE CONTRACTIONS

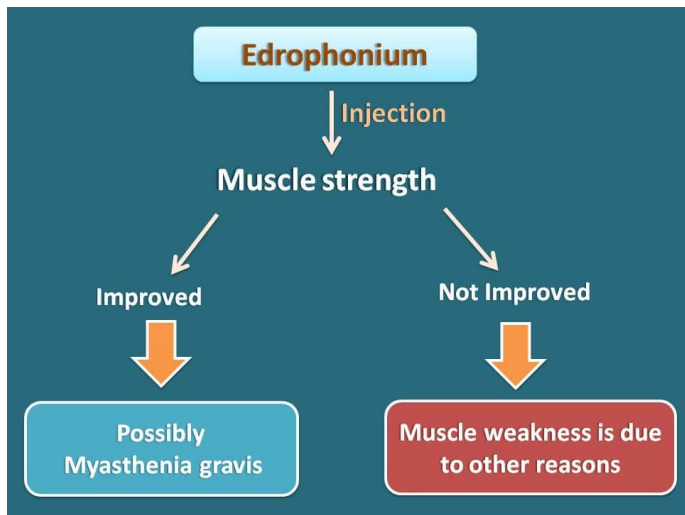
Diseases of the Neuromuscular Junction



Diagnosis of MG

- Clinical diagnosis, confirmed by serologic and electrophysiologic tests
- Serologic tests: Anti-AChR antibodies test
- Electrophysiologic tests: Repetitive nerve stimulation (RNS)
- Edrophonium (Tensilon) Test for ocular MG

Diseases of the Neuromuscular Junction



Diseases of the Neuromuscular Junction



Treatment and Management of MG

- Cholinesterase enzyme inhibitors (Pyridostigmine) for symptomatic treatment
- Immunosuppressive agents (Glucocorticoids, Azathioprine) for resistant cases
- Plasmapheresis or Intravenous Immunoglobulins for myasthenic crisis

Lambert-Eaton Myasthenic Syndrome (LEMS)

- NMJ disorder, often **paraneoplastic**
- Majority associated with **small-cell lung cancer** (SCLC)
- Antibodies target voltage-gated calcium channels, reducing ACh release
- Diagnosis often precedes SCLC diagnosis by 5 to 6 years
- Electromyography testing, CT/MRI chest scan for diagnosis

Botulism

- Neuroparalytic syndrome caused by botulinum **neurotoxin** (BoNT)
- Potentially fatal, results in diffuse, flaccid paralysis
- Inhibition of ACh release at **presynaptic** nerve terminals
- Acquired through exposure to improperly-stored food
- Immediate **antitoxin** administration, hospital admission, respiratory support

Conclusion

- Neuromuscular junction crucial for nervous-muscular communication
- Disorders like MG, LEMS, and botulism affect NMJ function
- Diagnosis involves clinical, serologic, and electrophysiologic tests
- Treatment includes cholinesterase inhibitors, immunosuppressive agents, and supportive measures