Neuropathy

Biomedical Engineering - URJC

Rafa Carretero, MD, PhD

Internal Medicine Department

29 February 2024

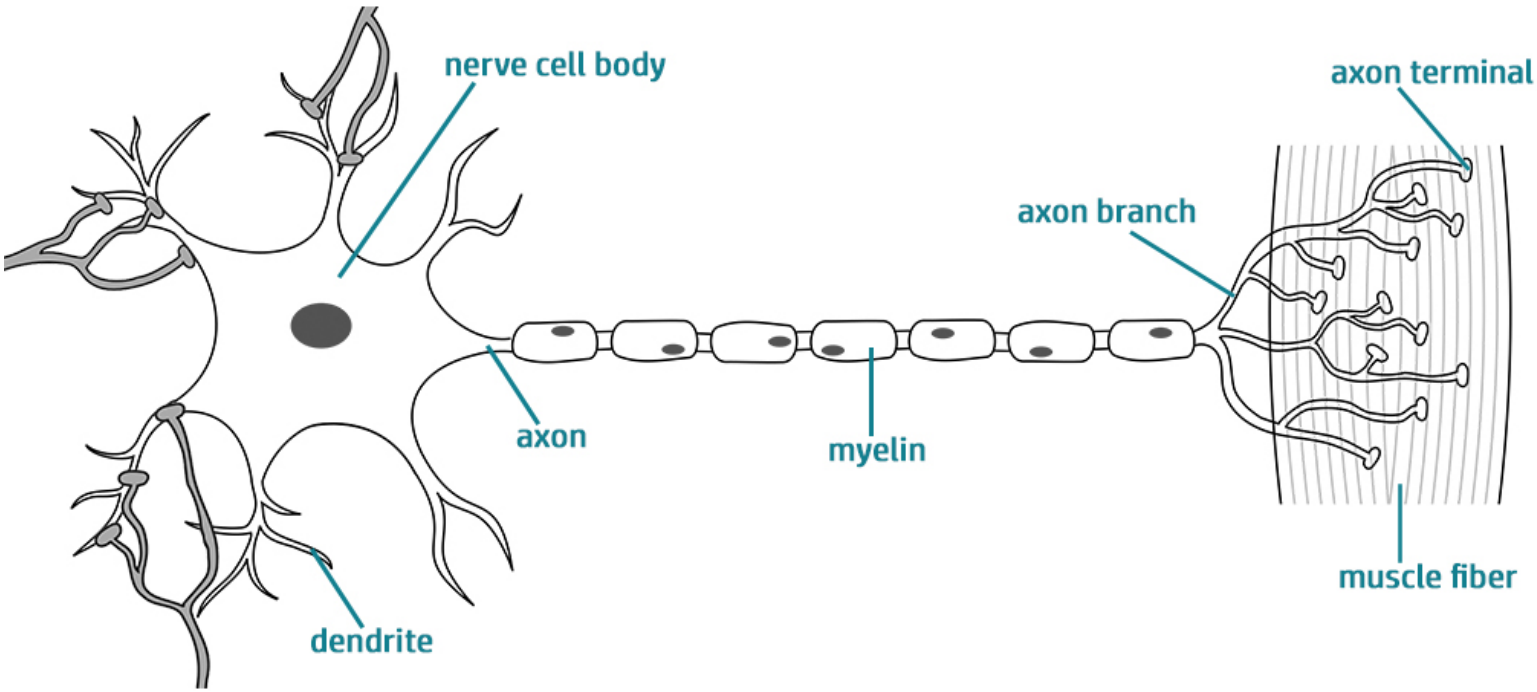
Universidad
Rey Juan Carlos

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



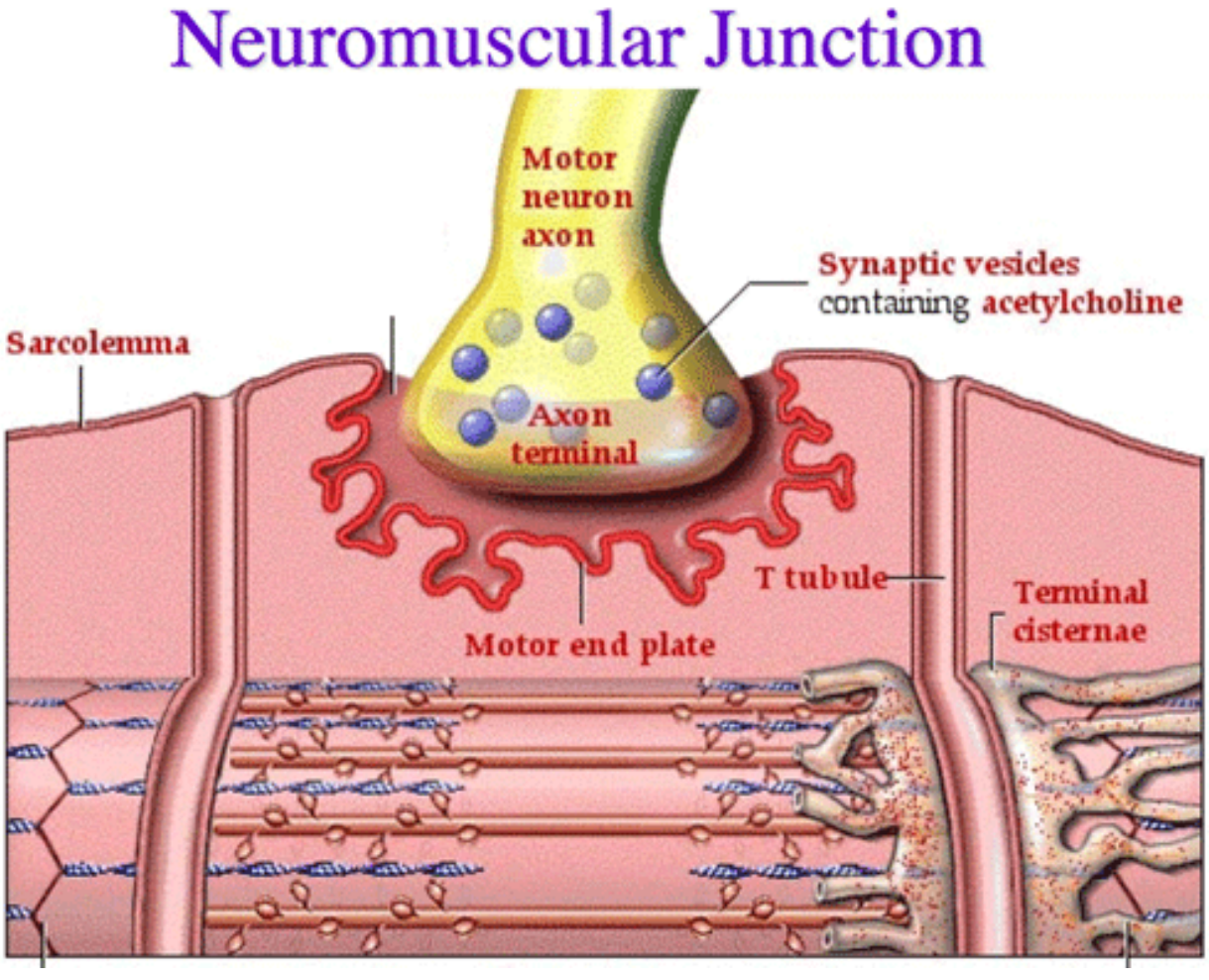
Definition of Neuromuscular Junction

- 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 on muscle fiber with high sensitivity to ACh

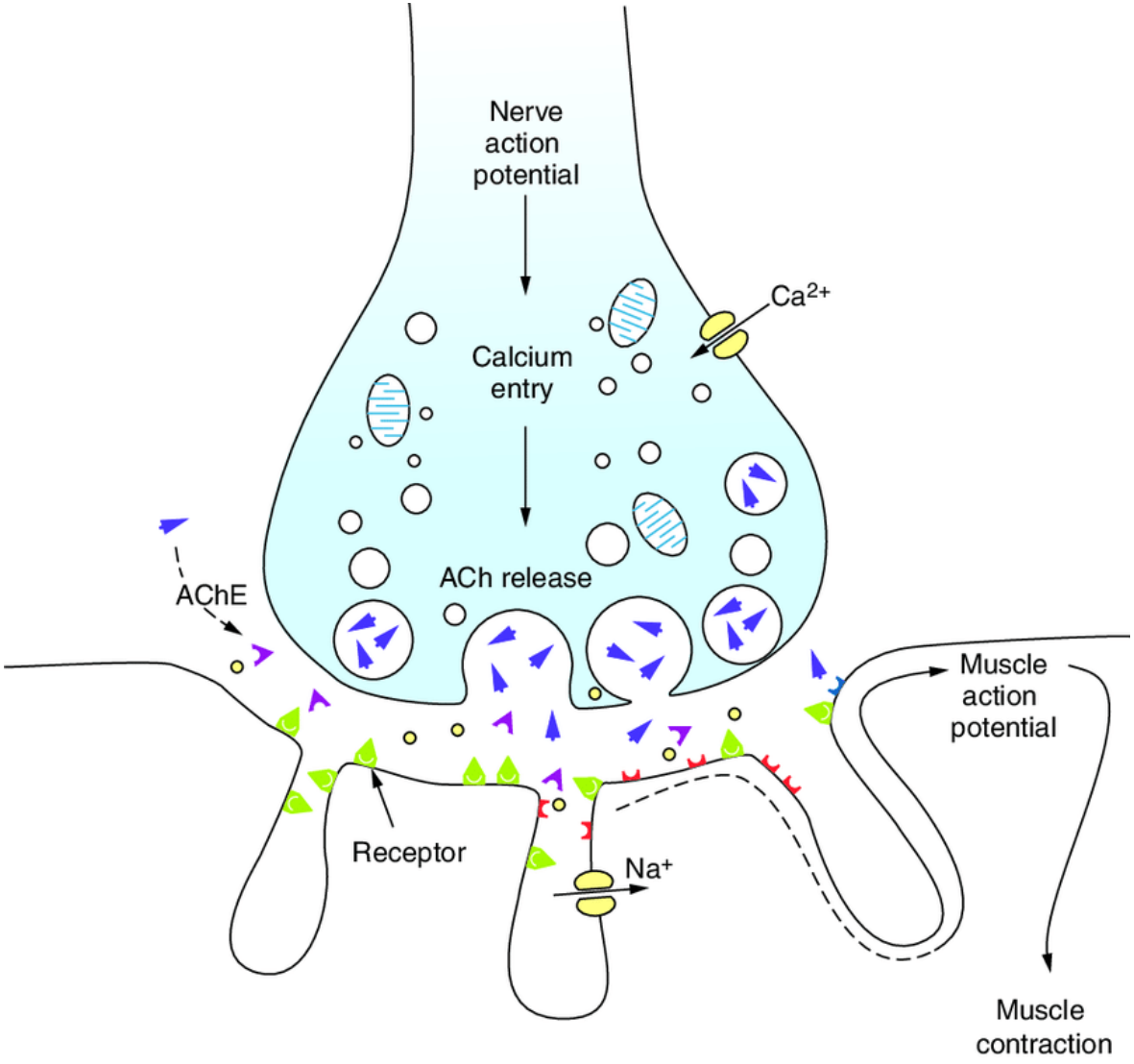
Diseases of the Neuromuscular Junction



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



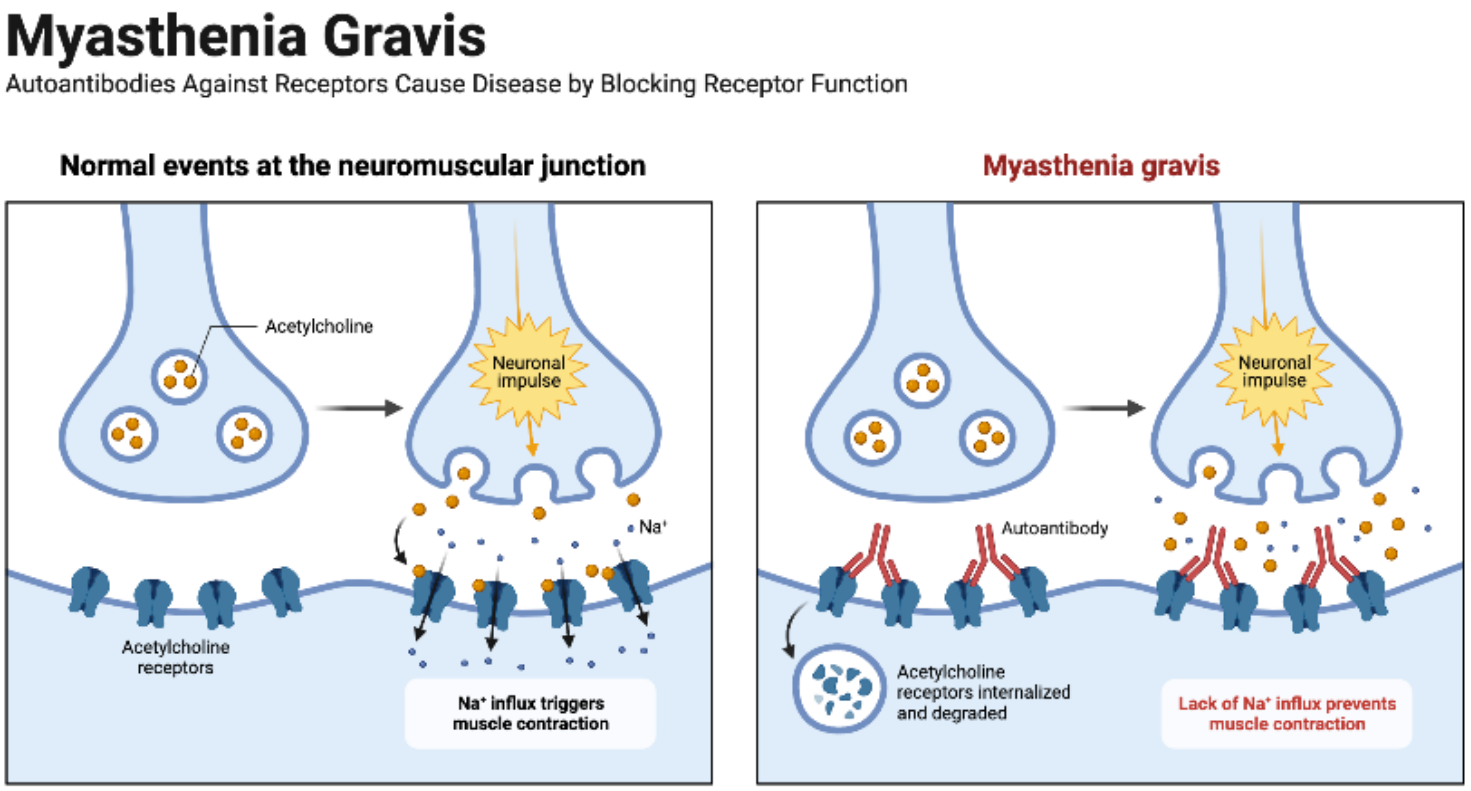
Myasthenia Gravis (MG)

- 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

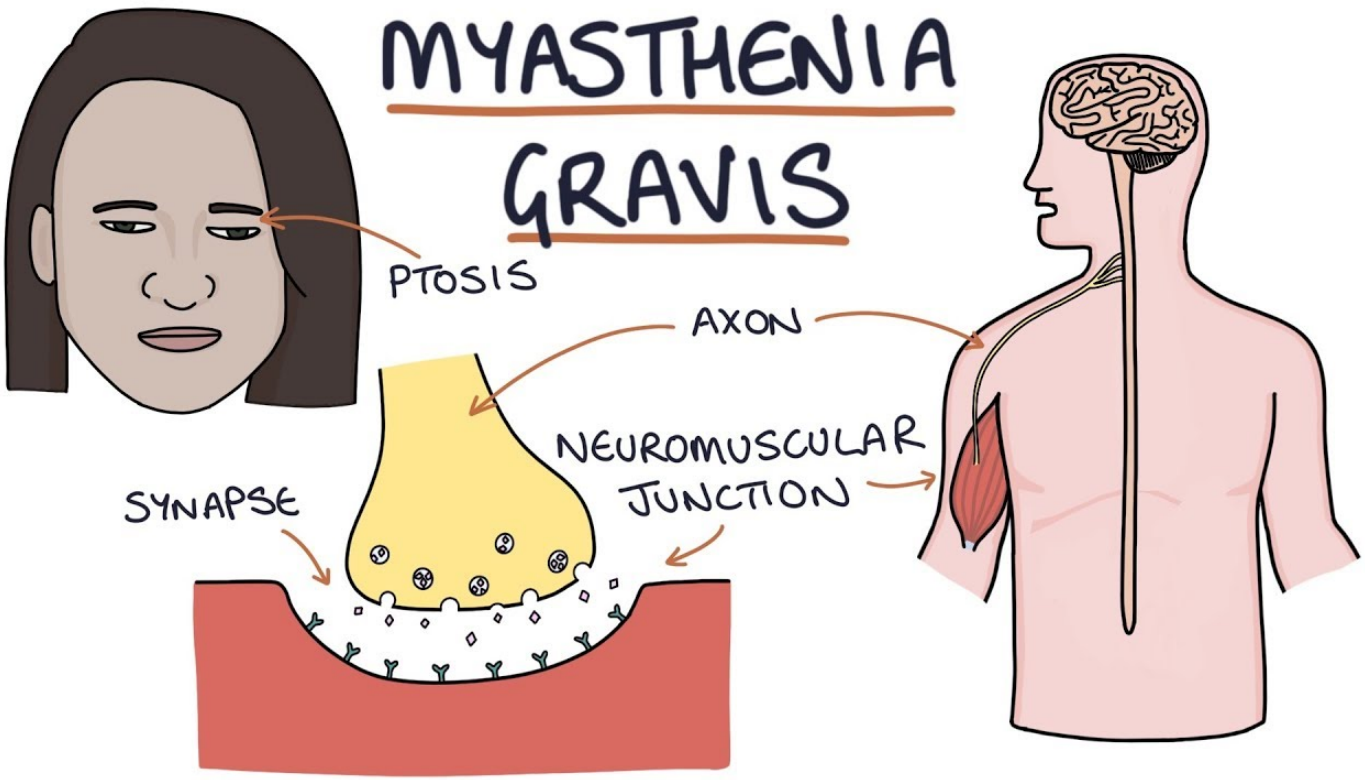
Etiology and Pathophysiology of MG

- 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

Diseases of the Neuromuscular Junction



Diseases of the Neuromuscular Junction



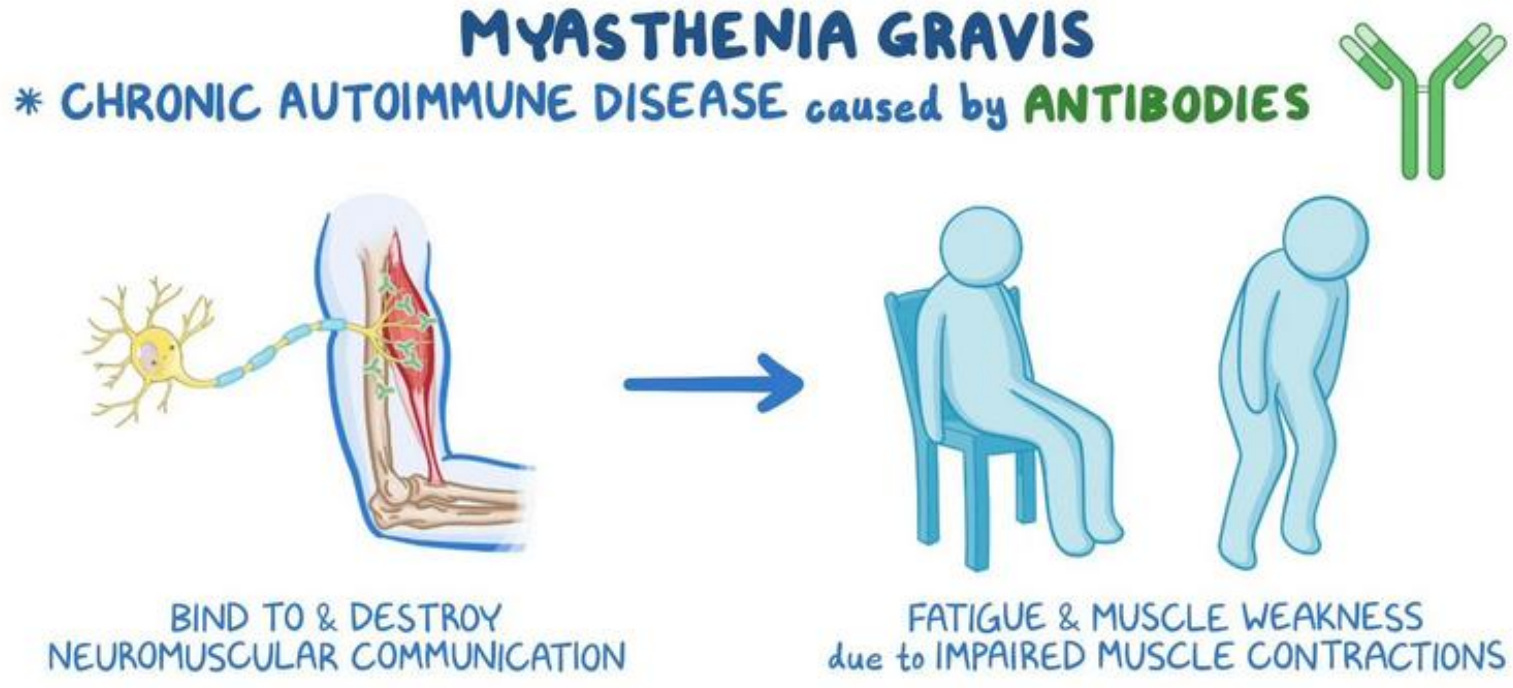
History and Physical Examination in MG

- 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

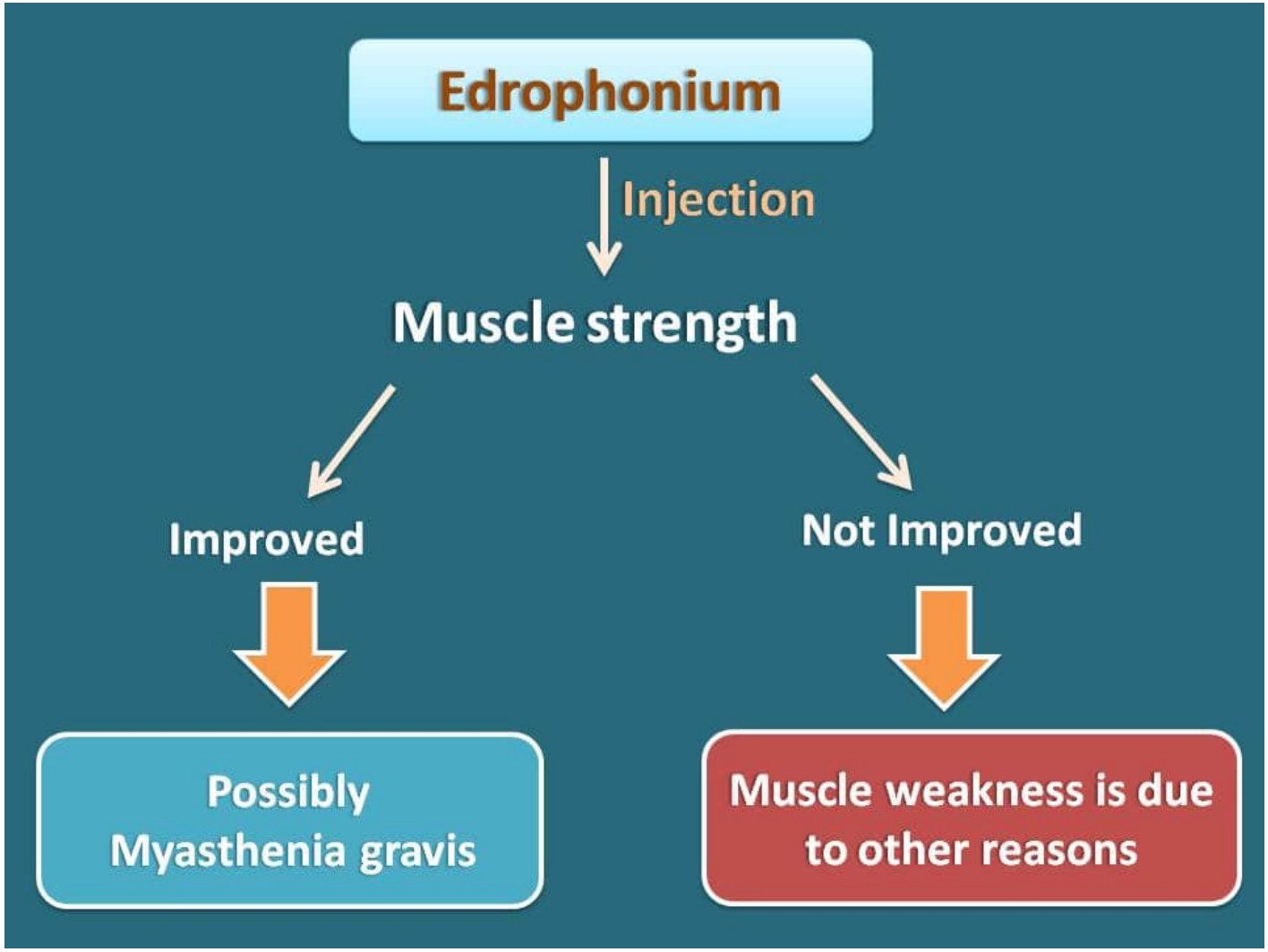


Diseases of the Neuromuscular Junction

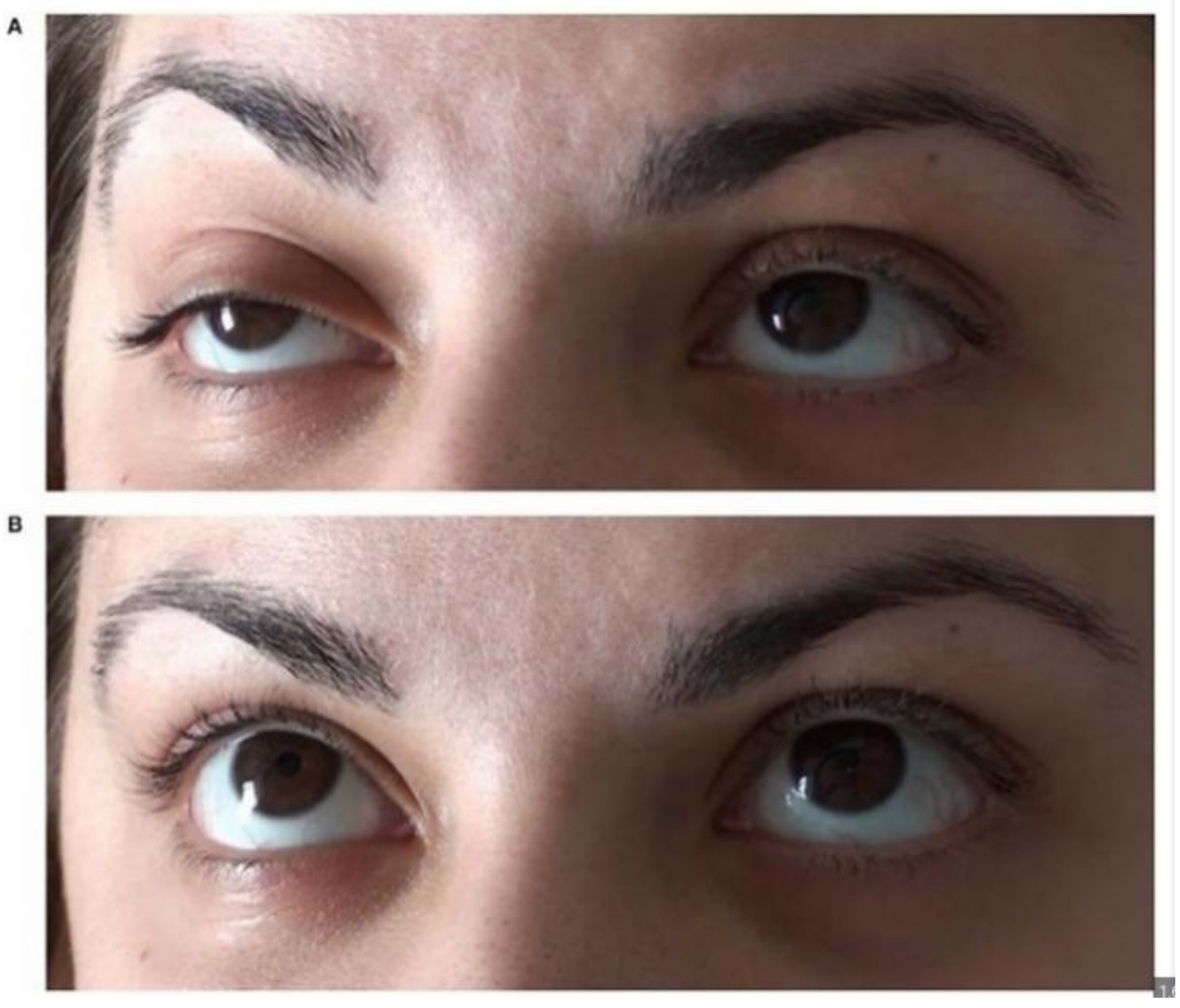
Diagnosis of MG

- 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