Muscle Physiology

Neuromuscular Junction

Ian V. J. Murray, Ph.D.,
Dept. Neuroscience & Physiology

Muscle

St. George’s University
School of Medicine
Fall 2014

Created by: Ian V. J. Murray, Ph.D., Department of Neuroscience & Physiology. St George's University, Grenada West Indies
NEUROMUSCULAR JUNCTION
Why is there a neuromuscular junction?

Electrical signal of nerve must be converted to signal in muscle. Similar to synapses in nerves, this involves a chemical transmitter.

Allows for control and regulation of muscle – one nerve can control few or several muscles to control strength or precision of movement.
Neuromuscular Junction

The following animation displays the various steps of the neuromuscular junction (NMJ):

- Depolarization of the nerve axon terminal results in opening of L-type calcium channels.
- Calcium enters the axon terminal resulting in synaptic vesicles fusing with the membrane surface.
- Acetylcholine (Ach) is released from the vesicles.
- Ach diffuses across the gap in the neuromuscular junction (NMJ) to bind to the nicotinic receptors.
- Opening of the nicotinic receptors allow for sodium to enter the cell resulting in depolarization of the muscle membrane.

Created by: Ian V. J. Murray, Ph.D., Department of Neuroscience & Physiology. St George's University, Grenada West Indies
Depolarization opens L-type calcium channels. Ca²⁺ enters cells. Ach released from synaptic vesicles diffuses across the membrane, binds to the nicotinic receptors. Nicotinic receptors open, Na⁺ enters cell to cause muscle depolarization.
Dysfunction of neuromuscular junction

Under normal conditions, excesses of acetylcholine (Ach) is released to cause a large enough end plate depolarization to generate the subsequent action potential and produce muscle contraction (termed safety factor).

However, NMJ dysfunction occurs in several cases:

- Atrophy - with disuse of muscle or severed nerve.
- Inhibition of Ach release - botulism.
- Inhibition of Ach degradation - specific drugs physostigmine, edrophonium.
- Inhibition of Ach binding to receptors - curare, bungarotoxin.
- Inhibition of Ach receptors - Myasthenia gravis.
Dysfunction of neuromuscular junction

The following figure demonstrates different steps where NMJ dysfunction can occur.
Nifedipine, verapamil, lead, cobalt, manganese, magnesium
Block Ca²⁺ uptake by nerve terminal, thus impairing release of ACh from vesicles, which is normally promoted by Ca²⁺

Nattarin, 
Presynaptic membrane

Mitochondrion

Acetyl CoA

Choline acetyltransferase

ACh

Synaptic vesicle

Hemicholinium
Blocks reuptake of choline, thus impairing formation of ACh

Boctin
Blocks ACh release from vesicles

Acetylcholine (ACh)
Normally binds to receptors on postsynaptic membrane to open cation channels, causing depolarization and initiation of action potential that leads to muscle contraction

Physostigmine (P) and edrophonium chloride (E)
Block AChE from degrading ACh to choline and acetate, thus prolonging action of ACh

Curare (C) and α-hungarotoxin (B)
Bind to ACh receptors and block ACh from binding to open cation channels, thus preventing depolarization

Succinylcholine (S) and decamethonium (D)
Cause cation channels to stay open. Persistent depolarization paradoxically results in relaxation of muscle.
End of
Neuromuscular Junction (NMJ)