Structure of the Neuromuscular Junction
Introduction to physiology
Motor endplates are distributed across striations

rectus femoris  vastus intermedius  semimembranosus  ext. dig. long.

Pospisilova and Parizek (1976)
Light microscopy of NMJ

Axon(s)

Motor End Plates

Muscle Spindle

Myofibers

Dr. Thomas Caceci, Virginia Tech
Light microscopy of NMJ

Dr. Blanka Pospislova, Charles University
Electron micrographs of NMJ

Scale bar = 0.3 microns
Electron micrographs of NMJ

Dr. John Heuser of Wash. U.
Active Zone Material in presynaptic terminal

Presynaptic SNARE complex

NMJ Structure

NMJ Transmission Sequence

- Nerve action potential propagation to the pre-synaptic terminus opening voltage-gated calcium channels
- Calcium entry triggers acetylcholine vesicle release
- Acetylcholine binding to AChR opens cation channel for about 1 ms
- Post-synaptic membrane depolarization (Endplate potential) builds
- If sufficient to open voltage-gated sodium channels (depolarization threshold) muscle fiber action potential ensues.
End Plate Potential

Byrne and Schultz (1988) An Introduction To Membrane Transport and Bioelectricity
End Plate Potential

Byrne and Schultz (1988) An Introduction To Membrane Transport and Bioelectricity
Synaptic Potential in Muscle

A

Motor axon

Muscle fiber

0 1 2 3 4 mm

B

Motor neuron terminal

Synaptic current

Interior of muscle fiber

Miles, 1969 *Excitable Cells*
Miniature Endplate Potential

Byrne and Schultz (1988) An Introduction To Membrane Transport and Bioelectricity
Quantal Release of Neurotransmitter

Boyd and Martin (1956) J. Physiol.
How many acetylcholine molecules to produce a MEPP?

- Each Vesicle releases about 5000 molecules of ACh
- Each Quantum causes approx. 1 mV depolarization (miniature endplate potential, MEPP)
- About 17,000 ions move through receptor in 1 ms
- Each nerve impulse releases about 50 quanta
- Summated quanta leads to an endplate potential (non-linear)
- Muscle resting potential = -75mV
- VGNC threshold potential = -50mV
- Need around 15 vesicles to fire muscle
- 50 – 15 = 35 vesicles = SAFETY FACTOR
Muscle Action Potential
CMAP setup

Dr. W. David Arnold, OSU
Compound Muscle Action Potential

- Amplitude
- Latency
- Duration

2 mV
2 msec

Dr. Mark Rich, Wright State University
Patterns of motor unit electrical signals
In nerve and muscle diseases

Normal

Neuropathic

Myopathic

Dr. Mark Rich, Wright State University
Recruitment of motor units
Problem with CMAP
Myasthenia Gravis

RNS setup
Myasthenia Gravis
Myasthenia Gravis
What’s going on here?

Dr. W. David Arnold, OSU
Many Opportunities for Disease

Lambert-Eaton Syndrome
Many opportunities for disease

Myasthenia Gravis
Many Opportunities for Disease

[Diagram of the Neuromuscular Junction with a red circle highlighting the Botulism Toxin]
Botulism Toxin Prevents Vesicle Docking

Botulism Toxin Prevents Vesicle Docking

Kornberg (2001) JAMA
Summary of NMJ Disorders

Pre-synaptic: Nerve
- Lambert Eaton
- Botulism
- Congenital MG

Synaptic
- Congenital MG
  (Endplate acetylcholinesterase deficiency)
- Excess anti-acetylcholinesterase medications

Post-synaptic: Muscle
- Myasthenia gravis
- Congenital MG

Dr. John Heuser of Wash. U.
Presynaptic Schwann Cell Interactions

Presynaptic Schwann Cell Interactions
Structure of the Neuromuscular Junction

Introduction to physiology

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