

The Neuromuscular Junction

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Page 1. Introduction

- Motor neurons stimulate muscle cells to contract at the neuromuscular junction.

Page 2. Goals

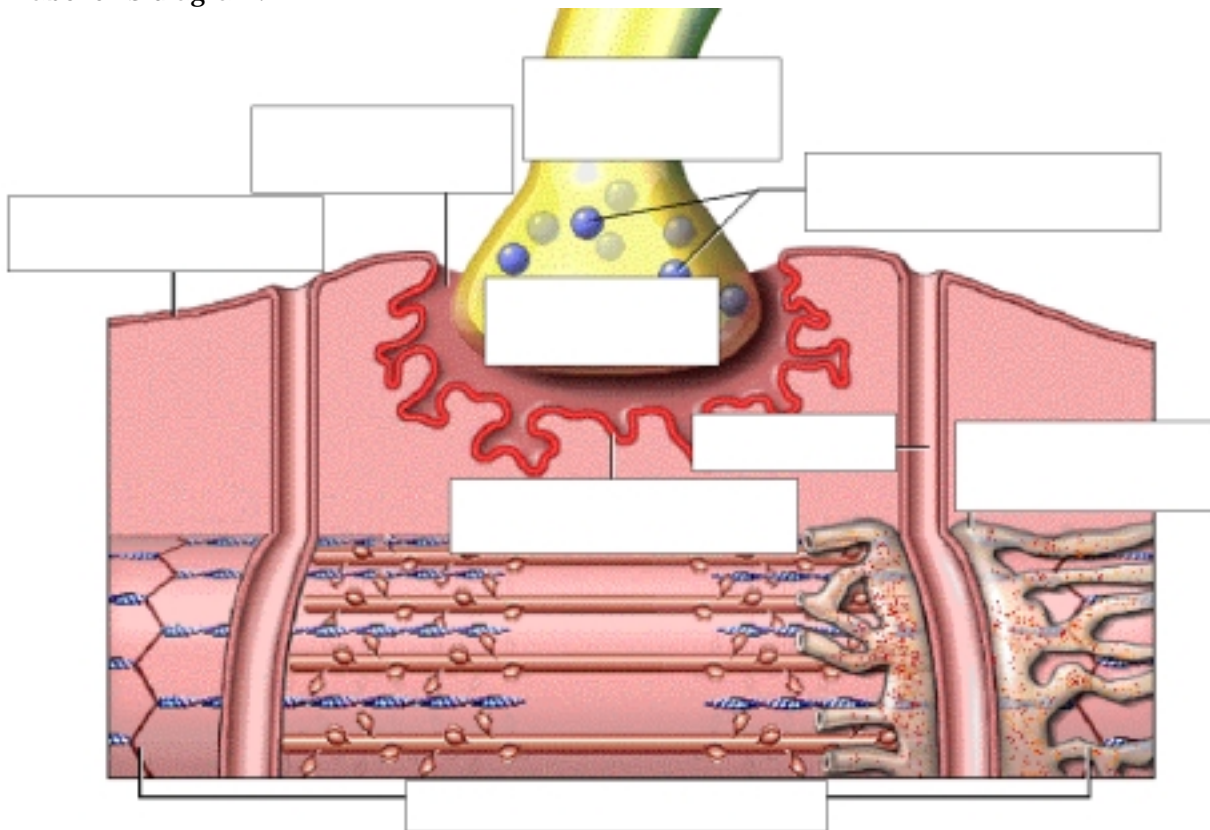
- To examine the structure of a neuromuscular junction.
- To understand the sequence of events occurring at the neuromuscular junction following a stimulus.

Page 3. Role of Motor Neuron

- Axons of motor neurons innervate skeletal muscle cells at the neuromuscular junction.

Page 4. Anatomy of a Neuromuscular Junction

- The following parts of a neuromuscular junction and skeletal muscle cell are described:
Axon terminal Synaptic Vesicles Synaptic Cleft
Motor End Plate T Tubule Sarcolemma
Terminal Cisternae & Sarcoplasmic Reticulum Sarcomere
- Label this diagram:



** Now is a good time to go to quiz question 1:

- Click the Quiz button on the left side of the screen
- After answering question 1, click the Back to Topic button on the left side of the screen.
- To get back to where you left off, click on the scrolling page list at the top of the screen and choose "5. Overview of Neuromuscular Junction Activity"

Page 5. Overview of Neuromuscular Junction Activity

- The muscle cell, including the T Tubules are polarized. Stimulation of the motor end plate on a muscle cell by acetylcholine triggers depolarization resulting in contraction of the sarcomeres.

Page 6. Arrival of Action Potential at Axon Terminal

- When the action potential arrives at the axon terminal voltage-regulated calcium channels open allowing calcium ions to enter the axon terminal.

- ** Note that when the action potential moves down the axon, there is a reversal of charge from positive out, negative in, to positive in, negative out. This process is called depolarization. The charge then reverses in a process called repolarization. The action potential moves down the axon in a wave-like fashion.

Page 7. Fusion of Synaptic Vesicles

- Presence of calcium ions in the axon terminal cause synaptic vesicles to fuse with the membrane.

Page 8. Release of Acetylcholine

- Acetylcholine is released into the synaptic cleft & calcium ions are pumped out of the axon terminal.
- ** During the animation note that in addition to the acetylcholine going into the synaptic cleft (blue), calcium ions also move out of the axon terminal (red).

Page 9. Acetylcholine Binds to Receptor Sites

- Acetylcholine binds to receptor sites on the motor end plate, causing an influx of sodium ions and a small efflux of potassium ions which results in a local depolarization of the motor end plate.
- ** Carefully note the following steps that occur during this animation:
 1. Acetylcholine (light blue ball) binds to the acetyl choline receptor (green).
 2. The chemically regulated ion channel (purple) opens.
 3. Sodium ions, Na^+ (gold balls) ,diffuse from their higher concentration (in the synaptic cleft) to their lower concentration (inside the muscle cell). Potassium ions, K^+ , (bright blue balls) diffuse from their higher concentration (inside the muscle cell) to their lower concentration (in the synaptic cleft).
 4. Depolarization of the membrane within the motor end plate.
- ** What is not shown in this animation is what happens to the positive and negative charge across the membrane during depolarization. Before the membrane is depolarized, there is more positive charge on the synaptic cleft side of the membrane of the motor end plate and more negative charge inside the muscle cell. When the chemically regulated ion channel opens, this charge reverses so now there is more negative charge in the synaptic cleft and more positive charge inside the cell. This occurs because much more sodium (which is positive) enters the cell, than potassium which leaves the cell. In fact, there is so little potassium that leaves the cell through this chemically regulated ion channel that your textbook or your instructor may not even mention it.

Page 10. Breakdown of Acetylcholine

- Acetylcholine diffuses away from its receptor site, the ion channel closes, and acetylcholine is then broken down by acetylcholinesterase.
- ** Carefully note the following steps that occur during this animation:
 1. Acetylcholine (light blue ball) diffuses away from the acetylcholine receptor (green) which is a part of the chemically regulated ion channel (purple). Note that as the acetylcholine falls off the receptor, the ion channel on the receptor closes, preventing further flow of sodium and potassium ions.
 2. The acetylcholine binds to the enzyme acetylcholinesterase (aqua-colored).
 3. The acetylcholinesterase breaks down the acetylcholine into two pieces, inactivating it.
- ** Note that after the acetylcholine has broken down, its parts are taken back up into the axon terminal where they can be reassembled into acetylcholine again. This is not shown on the animation.

Page 11. Action Potential Propagation

- An action potential is generated which propagates along the sarcolemma in all directions and down the T Tubules.

Page 12. Calcium Release from Terminal Cisternae

- The action potential causes the release of calcium ions from the terminal cisternae into the cytosol.

Page 13. Contraction of the Muscle Cell

- Calcium ions trigger a contraction of the muscle cell.

Page 14. Neuromuscular Animation

- The sequence of events in the neuromuscular animation are given.

Page 15. Summary

- Each skeletal muscle cell is individually stimulated by a motor neuron.
- The neuromuscular junction is the place where the terminal portion of a motor neuron axon meets a muscle cell membrane, separated by a synaptic cleft.
- An action potential arriving at the axon terminal brings about the release of acetylcholine, which leads to depolarization of the motor end plate.
- Depolarization of the motor end plate triggers an action potential that propagates along the sarcolemma and down the T Tubules.

- This action potential causes the release of calcium ions from the terminal cisternae into the cytosol, triggering contraction of the muscle cell.
- ** Now is a good time to go to quiz questions 2-8:
 - Click the Quiz button on the left side of the screen..
 - Click on the scrolling page list at the top of the screen and choose "2. Chemically-regulated ion channels".
 - Work through quiz questions 2-8.

Notes on Quiz Questions:

Quiz Question #1: Labeling the Neuromuscular Junction

- This question allows you to label the parts of the neuromuscular junction.

Quiz Question #2: Chemically-Regulated Ion Channels

- This question asks you to locate chemically-regulated ion channels.

Quiz Question #3: Reservoirs of Calcium Ions

- This question asks you to locate stores of calcium ions.

Quiz Question #4: Structures Containing Acetylcholine

- This question asks you to locate structures containing acetylcholine.

Quiz Question #5: Sequence of Events at the Neuromuscular Junction

- This question asks you to list the sequence of events at the neuromuscular junction.

Quiz Question #6: Molecule "X"

- This question asks you to watch an animation of drug action on the neuromuscular junction, then predict the effect of the drug.

** Be patient, this animation plays several times before the question appears.

** This is an important animation because many drugs and poisons work like molecule "X" to disrupt events at the synapse. Think of molecule "X" (bright green ball) as a drug or poison. When it is present in the synaptic cleft, it binds to the receptor site (light green) on the chemically regulated ion channel (purple) and prevents acetylcholine (light blue) from attaching. The acetylcholine (light purple ball) is then broken down in the synaptic cleft by acetylcholinesterase (aqua) without causing a depolarization because the ion channels don't open. Molecule "X" is a drug or poison that prevents muscle contraction.

** Molecule "X" acts like curare and other drugs which compete with acetylcholine. By binding to acetylcholine receptor sites, these drugs block neuromuscular transmission and thus paralyze skeletal muscles. During surgery drugs of this type may be used to immobilize patients.

Quiz Question #7: Molecule "Y"

- This question asks you to watch an animation of drug action on the neuromuscular junction, then predict the effect of the drug.

** Again be patient, this animation takes quite a long time to play before the question appears.

** Again, think of molecule "Y" (bright yellow ball) as a drug or poison. When it is present in the synaptic cleft, it binds to acetylcholinesterase (aqua), preventing the breakdown of acetylcholine (light purple ball). The acetylcholine builds up in the synaptic cleft, binding to the receptor site (light green) on the chemically regulated ion channel (purple). This causes the ion channel to stay open, generating one depolarization after another. The net effect is one muscular contraction after another.

** Molecule "Y" acts like neostigmine and related drugs which increase the availability of acetylcholine by preventing its breakdown by acetylcholinesterase. This type of drug can be used to treat diseases such as myasthenia gravis, characterized by muscle weakness due to inadequate acetylcholine stimulation. In large amounts this drug will cause severe muscle spasms and possibly death.

Quiz Question #8: Molecule "Z"

- This question asks you to watch an animation of drug action on the neuromuscular junction, then predict the effect of the drug.

** Molecule "Z" (pink ball) is a drug or poison which, when it is present in the synaptic cleft, binds to the receptor site (light green) on the chemically regulated ion channel (purple) and prevents acetylcholine (light blue) from attaching. But this drug is not broken down by acetylcholinesterase and holds the ion channel open, generating one depolarization after another. The net effect is one muscular contraction after another.

** Molecule "Z" acts like nicotine, the active ingredient in tobacco. Nicotine binds to acetylcholine receptor sites and opens the ion channels, thus mimicking acetylcholine. However, nicotine is not hydrolyzed immediately by acetylcholinesterase and therefore continues to cause depolarization of the motor end plate. In small amounts (as from cigarette smoke), nicotine acts as a stimulant and may cause visible muscle tremors. In large doses, nicotine can cause convulsions and death.

Study Questions on the Neuromuscular Junction:

1. (Page 1.) What causes skeletal muscle cells to contract?
2. (Page 1.) What is the place called where a motor neuron stimulates a muscle cell?
3. (Page 3.) How are skeletal muscle cells are electrically insulated from each other?
4. (Page 3.) What is a motor neuron?
5. (Page 3.) What part of the motor neuron carries impulses to the muscle? Describe its structure.
6. (Page 4.) Match the following terms to their description:

Axon terminal
Motor End Plate
Terminal Cisternae & Sarcoplasmic Reticulum

Synaptic Vesicles
T Tubule

Synaptic Cleft
Sarcolema
Sarcomere

- a. Invaginations of the sarcolemma penetrating deep into the interior of the muscle cell.
- b. The space between the axon terminal and the motor end plate.
- c. The swollen distal end of the motor neuron axon.
- d. The muscle cell membrane.
- e. Structures within the axon terminal that contain the neurotransmitter acetylcholine.
- f. The contractile unit of the muscle cell that extends from one Z line to the next.
- g. Structures within skeletal muscle cells that serve as reservoirs of calcium ions.
- h. A folded region of the sarcolemma at the neuromuscular junction.

7. (Page 5.) What is a polarized membrane?
8. (Page 5.) Describe the resting membrane potential with respect the neuromuscular junction?
9. (Page 5.) Describe the T Tubules when they are at resting membrane potential.
10. (Page 5.) List the following events in the order they occur:
 - _____ a. The motor end plate is depolarized.
 - _____ b. The sarcomeres contract.
 - _____ c. Acetyl choline is released from the axon terminal into the synaptic cleft.
 - _____ d. The depolarization triggers an action potential which propagates along the sarcolemma and the T tubules.
 - _____ e. An action potential arrives at the axon terminal
11. (Page 6.) What happens at the neuromuscular junction when the action potential arrives at the axon terminal.
12. (Page 7.) What is the effect of the presence of calcium ions inside the axon terminal?
13. (Page 8.) What two events happen after the synaptic vesicles fuse with the membrane of the axon terminal?
14. (Page 9.) What happens to acetylcholine after it is released into the synaptic cleft?
15. (Page 9.) What happens after the acetylcholine binds to the acetylcholine receptor on the motor end plate?
16. (Page 10.) When does the chemically regulated ion channel on the motor end plate close?

17. (Page 10.) What happens to the acetyl choline after it diffuses away from its receptor on the motor end plate?
18. (Page 11.) The movement of the sodium ions through the chemically regulated ion channel initiates a depolarization of the motor end plate. What happens after this depolarization is generated?
19. (Page 12.) What happens as the action potential moves down the T Tubules?
20. (Page 13.) What happens when calcium ion is present in the cytosol of the muscle cell?
21. (Page 14.) Place the following events in their proper sequence:
 - _____ a. Acetyl choline is released into the synaptic cleft.
 - _____ b. Action potential propagates along the sarcolemma and down the T Tubules.
 - _____ c. Synaptic vesicles fuse to membrane of axon terminal.
 - _____ d. Motor end plate becomes depolarized.
 - _____ e. Action potential is initiated on the sarcolemma.
 - _____ f. Action potential arrives at the axon terminal.
 - _____ g. Calcium ions are released from the terminal cisternae.
 - _____ h. Acetylcholine binds to receptor sites on the motor end plate.
 - _____ i. The muscle cell contracts.
 - _____ j. Calcium ions enter the axon terminal.

Answers to Questions on the Neuromuscular Junction:

1. Impulses from motor neurons.
2. A neuromuscular junction.
3. By endomysium.
4. A nerve cell which extends from the brain or spinal cord to the muscle, where it can stimulate several skeletal muscle cells. (Note motor neurons can also stimulate smooth muscle, cardiac muscle and gland cells, but in this module we will only consider those motor neurons which stimulate skeletal muscle cells.)
5. The axon, which is an elongated process that extends from the brain or spinal cord to the muscle.
6. a. T Tubule
 - b. Synaptic Cleft
 - c. Axon Terminal
 - d. Sarcolemma
 - e. Synaptic Vesicles
 - f. Sarcomere
 - g. Terminal Cisternae & Sarcoplasmic Reticulum
 - h. Motor End Plate
7. A membrane that has more positive charge on one side and more negative charge on the other side.
8. The membranes of both the axon of the motor neuron, and the muscle cell have more positive charges outside the membrane and more negative charges inside the cell.
9. There is more positive charge in the interior of the T Tubule and more negative charge inside the cell.
10. e, c, a, d, b
11. The voltage change of the membrane opens the voltage-regulated calcium channels, allowing calcium ions to enter the axon terminal.
12. The calcium ions cause several synaptic vesicles to fuse with the membrane of the axon terminal.
13. The neurotransmitter acetylcholine is released by exocytosis into the synaptic cleft and calcium ions are pumped out of the axon terminal.
14. It binds to receptor sites on chemically-regulated ion channels on the motor end plate.
15. The chemically regulated ion channel opens allowing sodium ions to diffuse from the synaptic cleft to the inside the muscle cell and potassium ions to diffuse from the inside of the muscle cell into the synaptic cleft. This action causes a depolarization of the membrane within the motor end plate.
16. When the acetyl choline diffuses away from its receptor site.
17. It is then broken down by the enzyme acetylcholinesterase.

18. An action potential is generated which propagates along the sarcolemma in all directions and down the T Tubules.
19. There is a release of calcium ions from the terminal cisternae into the cytosol.
20. The muscle cell contracts.
21.
 1. f. Action potential arrives at the axon terminal.
 2. j. Calcium ions enter the axon terminal.
 3. c. Synaptic vesicles fuse to membrane of axon terminal.
 4. a. Acetyl choline is released into the synaptic cleft.
 5. h. Acetylcholine binds to receptor sites on the motor end plate.
 6. d. Motor end plate becomes depolarized.
 7. e. Action potential is initiated on the sarcolemma.
 8. b. Action potential propagates along the sarcolemma and down the T Tubules.
 9. g. Calcium ions are released from the terminal cisternae.
 10. i. The muscle cell contracts.