Ch 9: Muscle Physiology

Objectives:
1. Review 3 muscle types and how they are regulated.
2. Review muscle anatomy.
5. Energetics of muscle contraction.
7. Voluntary movement VS reflex muscle movements.

1. Differences in function of the 3 muscle types:

<table>
<thead>
<tr>
<th>a) Skeletal Muscle</th>
<th>b) Cardiac Muscle</th>
<th>c) Smooth Muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voluntary (somatic motor)</td>
<td>Involuntary (autonomic motor)</td>
<td>Involuntary (autonomic motor)</td>
</tr>
<tr>
<td>Neurotransmitter =</td>
<td>Parasymp. Neurotrans. =</td>
<td>ACh with muscarinic cholinergic receptors,</td>
</tr>
<tr>
<td>Receptor =</td>
<td>Receptor =</td>
<td>epinephrine with B2 &amp; α-adrenergic receptors</td>
</tr>
<tr>
<td>(for EPSPs) &amp; also</td>
<td>Sympath. Neurotrans. =</td>
<td></td>
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<tr>
<td>Glycine &amp; GABA with</td>
<td>receptor =</td>
<td></td>
</tr>
<tr>
<td>muscarinic receptors (Ch 4)</td>
<td>Effect =</td>
<td></td>
</tr>
<tr>
<td>(for IPSPs – muscle relax)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Requires somatic motor</td>
<td>Is “autorhythmic”, but HR influenced</td>
<td>Is “autorhythmic” – influenced by</td>
</tr>
<tr>
<td>neuron stimulus to contract</td>
<td>by ACh (↓HR) &amp; epinephrine (↑HR)</td>
<td>ACh or epinephrine</td>
</tr>
<tr>
<td>(not “autorhythmic”)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fastest contraction speed</td>
<td>Intermediate contraction speed</td>
<td>Slowest contraction speed</td>
</tr>
<tr>
<td>Prone to fatigue</td>
<td>Fatigue resistant</td>
<td>Fatigue resistant</td>
</tr>
</tbody>
</table>

QUES:
Epineph. binding to β2-adrenergic receptors causes ___________________________________________
___________________________________________________________________________________
Epineph. binding to α-adrenergic receptors causes ___________________________________________
Cardiac muscle versus smooth muscle:

BOTH are: - autorhythmic (stimulus for contraction initiated from within)
- regulated by autonomic motor N.S.
- involve Ca\(^{2+}\) release BUT:

**REVIEW!!!**

1. Cardiac Muscle:
   - AP starts in SA node (pacemaker cells)
   - Rate of contraction influenced sympathetic vs parasympathetic stim.
     - ↑ heart rate by epinephrine & \(\beta_1\)-adrenergic receptors
     - ↓ heart rate by ACh & muscarinic cholinergic receptors

2. Smooth Muscle: Stimulated by a variety of hormones (ACh, epinephrine)
   - ↑ GI activity through ACh and muscarinic cholinergic receptors
   - ↓ GI activity through epineph & \(\alpha\)-adrenergic receptors.
   - bronchodilation through epineph & \(\beta_2\)-adrenergic receptors.
   - bronchoconstriction through ACh & muscarinic cholinergic receptors.

   > Muscle arteriole smooth muscle vasodilation to skeletal muscle through epineph & \(\beta_2\)-adrenergic receptors.
   > GI arteriole smooth muscle vasoconstriction through epineph & \(\alpha\)-adrenergic receptors.

2. Review Anatomy of Skeletal Muscle:

   **muscle organ** = whole muscle group, made of muscle fascicles
   (e.g. biceps brachii, triceps brachii)

   **fascicle** = bundle of muscle fibers.

   **fiber** = single muscle cell that a somatic motor neuron stimulates. Contains muscle myofibrils.

   **myofibril** = contains thousands of sarcomeres.

   **sarcomere** = functional unit of muscle contraction. Has “myofilaments” actin and myosin.
**Sarcomere contains myofilaments Actin & Myosin:**

A) **Actin** = thin filament with active sites, and proteins troponin & tropomyosin.

> **active sites** = where myosin heads want to bind to create a “crossbridge”

> **troponin** = protein that Ca+ binds to.

> **tropomyosin** = protein that normally blocks active sites. It moves out of the way when troponin binds to Ca+2.

B) **Myosin** = thick filament with “heads” that bind to active sites on actin

**Review of Neuromuscular Junction (from Ch 4)**

**Neuromuscular junction** = between a single motor neuron and the muscle fiber it innervates.

**If it’s a somatic motor neuron stimulating a skeletal muscle cell the following happens:**

- **__________** released by presynaptic motor neuron crossed the synapse

- binds to ___________________________ receptors on skeletal muscle fibers.

- Binding of receptor opens _____________ ion channels

- _____ enters muscle cell & causes AP (or EPSP), which causes Ca+ release from sarcoplasmic reticulum.
3. Sliding Filament Theory of Muscle Contraction

1. Somatic motor neuron releases ______ into synapse at neuromuscular junction with skeletal muscles.

2. ACh binds to ___________________ receptors.

3. Opens ______ channels, ______ enters cell, an AP (or EPSP) forms.

4. AP moves to T-tubules of cell.

5. AP causes ______ release from sarcoplasmic reticulum of muscle cell.

6. Ca\(^{+2}\) binds to ______________ (protein on actin).

7. This causes ________________ to move off active sites on actin.

8. ________________ heads “grip” active sites (forms crossbridges)

Role of ATP and ADP in muscle contraction:

Myosin heads “pulling” on actin involves: “Grip & Re-grip” Action

1 & 2) Myosin has ADP – forms crossbridge

3 & 4) ADP released = Power Stroke (myosin pulls on actin)

5) ATP binds
   - myosin breaks crossbridge
   - ATP pumps Ca^{2+} into sarcoplasmic retic.

6) ATP converted to ADP
   - Ready to bind again.
Role of ATP and ADP in muscle contraction:

“Grip & Re-grip” Action of Myosin with Actin requires ADP & ATP

• **ADP** is needed for myosin head to grip active site and to pull on actin.

• **ATP** is needed for myosin head to release active site (break crossbridge) and to pump Ca\(^{+2}\) back into sarcoplasmic reticulum.
**Rigor Mortis**

= sustained whole body muscle tetany 12-18 hrs post-mortem due to lack of ATP in muscle cells at death (No ATP – no breaking of crossbridges between actin & myosin).

At 24 – 36 hrs post-mortem body relaxes because actin & myosin degradation (necrosis).

**Review**

- Contrast how 3 muscle types function
- Muscle anatomy
  - organ, fascicles, fibers, myofibrils, and sarcomere arrangement of myofilaments (actin and myosin)
- Neuromuscular junction
- Sliding filament theory of muscle contraction
- Energetics (ATP & ADP) of muscle contraction
4. Factors Influencing Muscle Contractile Force:

Types of muscle contractions

A) Isotonic contraction =

B) Isometric contraction =

4. Factors Influencing Muscle Contractile Force:

Motor unit =

- There can be as many as 150 muscle fibers innervated by 1 motor neuron. It depends on the “Power versus Precision” principle (see later).
4. Factors Influencing Muscle Contractile Force:

**Tradeoff:**

**Muscle Precision** vs **Muscle Power?**

- one motor neuron innervates few muscle fibers.
- one motor neuron innervates many muscle fibers

Muscle Contractile Force Depends On:

1. **The number of fibers responding:**
   - If more fibers respond = ______________
   - If fewer fibers respond = _______________

2. **Strength of stimulus:** (for 1 motor neuron)
   - If stimulus strong = ______________
   - If stimulus weak = ______________
   - If stimulus VERY strong – get “Recruitment”
     - more than one motor neuron involved & all its muscle fibers.
     - produced greater force than with 1 motor neuron.
**Muscle Contractile Force Depends On:**

3. **Frequency of stimulus:**

A) **Muscle Twitch** = Single stimulus produces single muscle fiber contraction

B) **Treppe** = muscle “warm up”. After repeated low frequency stimuli each muscle contractile force increases until reaches max. force.

   [see tension go back to baseline between stimuli!]

C) **Summation** = repeated high frequency stimuli

Result is each contraction has cumulative increase in force, BUT so rapid muscle cannot relax (don’t go to baseline).

D) **Muscle Tetanus** = repeated highest frequency stimuli produces greatest possible contractile force **BUT** comes at cost. Sustained muscle contraction leads to muscle fatigue and failure.

*Fig. 9.6*
Review

Factor influencing muscle contractile force:

- Types of muscle contraction
  - Isotonic (concentric, eccentric), isometric
- Motor unit
- Muscle precision Vs power
- Contractile force depends on
  - # muscle fibers responding
  - Strength of the stimulus
  - Frequency of stimulus
    (muscle twitch, treppe, summation, & tetanus)

5. Energetics of Muscle Contraction

Muscle Fatigue

Depletion of:
- O2
- ATP
- Glycogen
- Myoglobin

Accumulation of:
- CO2
- ADP
- Lactic acid
- Phosphate (from using creatine phosphate)

Cori Cycle =
Phosphocreatine = natural molecule stored in large supply in resting muscle, is needed to convert ADP back into ATP. (donates a phosphate to ADP to make ATP)

Creatine phosphokinase (CK or CPK) = enzyme (in skeletal muscle, brain, and heart), which is needed to convert creatine into phosphocreatine.

Phosphocreatine is needed to make ATP in tissues requiring high ATP.

Different isoforms of CPK for different organs can be elevated due to death of tissues:

1. CPK isoform MM = elevated form associated with diseased skeletal muscle, like in muscular dystrophy. Clinical App Pg 239 and ONLINE

2. CPK isoform BB = elevated form associated with damaged brain.

3. CPK isoform MB = elevated form associated with damaged heart.
Muscle growth & repair: *Physiology in Health & Disease*

**Satellite Cells**
- muscle stem cells that are activated with muscle injury. Makes new muscle fibers

**Myostatin**
- inhibits muscle growth & repair by inhibiting satellite cells.

Elderly people with muscle atrophy have high myostatin levels.

When myostatin is inhibited – get excessive muscle growth!

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**Review**

**Energetics of muscle contraction**
- Muscle fatigue
- Phosphocreatine & ATP production
- Muscle growth & repair
6. Muscle Disorders

A) Muscular Dystrophy (Duchenne’s)
Clinical App Pg 229
- Most common form of MD.
- Sex-linked recessive genetic disorder (found more in males)
- Early onset in children = walking & balance problems. Muscle atrophy leads to loss of muscle function.
- Loss of dystrophin thought to influence.

“dystrophin” = protein needed for muscle function.

B) ALS (Amyotrophic Lateral Sclerosis)
a.k.a. Lou Gherig’s disease
= loss of motor neurons, leads to muscle atrophy, eventual paralysis.

> Tends to start in motor neurons to hands and feet
> Eventually affects respiratory muscles.
> Life expectancy after diagnosis < 5 yrs.
> Reason?
- Loss of superoxide dismutase (an antioxidant that prevents cell death)
- Glutamate toxicity = excess brain stimulation
  > glutamate supposed to be taken up by astrocytes. (astrocyte problem?)
  > excess glutamate also thought to play role in Parkinson’s & Alzheimer’s disease) Clinical App
C) **Myasthenia gravis** = autoimmune attack on nicotinic ACh receptors of skeletal muscles. Loss of motor control & tone = hypotonia and muscle atrophy.

**Tetanus** = buildup of tetanus toxin from Clostridium tetani bacteria. Toxin acts as an ACh agonist, promoting ACh stimulation of skeletal muscle contraction. Causes spastic paralysis or hypertonia.

**Botulism** = buildup of botulism toxin from Clostridium botulinum bacteria. Prevents ACh release from motor neurons. Muscles not get stimulus to contract. Causes flaccid paralysis or hypotonia.
Review

• Contrast between Cardiac and Smooth Muscle
• Muscle Disorders:
  – Duchenne’s MD
  – ALS
  – Myasthenia gravis
  – Toxins (tetanus & botulism)

Muscle Sensory Organs Provide Sensory Feedback to Brain for Regulating Muscle Tone & Contraction.

2 types of Muscle Sensory Organs:

1. **Golgi tendon organs**:
   - Sense Tension (pull) a muscle puts on a tendon.

2. **Muscle spindle apparatus**:
   - Sense amount of muscle Stretch
Muscle Sensory Organs Provide Sensory Feedback to Brain for Regulating Muscle Tone & Contraction.

2 Muscle Sensory Receptors:

1. Golgi Tendon organs:
   - Senses muscle pull (Tension) on a tendon.

2. Muscle Spindle apparatus:
   - Senses muscle Stretch
     > Sudden rapid stretch = more contractile force
     > slow stretch = less contractile force

Spindle Contains:

A) Extrafusal fibers – thick contracting fibers, faster, thicker, stronger, more numerous.
   - Involved in isometric contraction (muscle shortening)
B) Intrafusal fibers – thin stretch fibers, slower, thinner, weaker, less numerous.
   - Involved in isotonic contraction (muscle tone, no shortening)

Neural control of skeletal muscle

2 types of muscle motor neurons:

1) Upper motor neurons (“interneurons”)
   - In primary motor cortex
   - Communicate w/lower motor neurons

2) Lower motor neurons = “somatic motor neurons”
   - In brainstem & ventral spinal cord.
   - Extend into major nerves of body
     2 types of lower motor neurons:
     1. alpha
     2. gamma

Activity of lower motor neurons of brainstem & spinal cord regulated by feedback from:

A. upper motor neurons in primary motor cortex.
B. feedback from muscle “sensory organs”
   (golgi tendon & muscle spindle apparatus)
2 types of Lower Motor Neurons (in brainstem & spinal cord):

1) Alpha motor neurons:
- Innervate extrafusal (contracting) muscle fibers of muscle spindle
- Result in muscle isotonic contraction (muscle shortens)

2) Gamma motor neurons:
- Innervate intrafusal (stretch) muscle fibers of muscle spindle
- Result in muscle isometric contraction (doesn’t shorten)
- Provides muscle “tone”, more sensitive to stretch.

***Stimulation of both alpha & gamma lower motor neurons, by upper motor neurons in primary cortex at the same time, called co-activation

4. Voluntary reflexes versus spinal reflexes

Somatic Motor Neurons and Skeletal Muscle

- Somatic neurons synapse with skeletal muscle fibers at neuromuscular junctions for VOLUNTARY movement.

If someone tells you to contract your quadriceps muscles after they are touched:

- First, touch receptors on leg stimulated, send ascending info to sensory cortex.
- Sensory info shared with motor cortex. Motor command from motor neurons descends spinal cord.
- Somatic motor neurons (of spinal nerves) release ACh
  - Binds to nicotinic ACh receptors on skeletal muscles
  - Evokes EPSPs by opening Na+ channels
  - Causes contraction
4 “Stretch” or Involuntary Spinal reflexes:

I. Knee-jerk reflex

1) Tapping patellar ligament stretches tendon & quadriceps muscle - stimulates **spindle fiber**
   (stretch receptor) in muscle

2) Stimulating spindle fiber **evokes action potentials in sensory neuron**

3) Sensory neuron synapses **directly** with alpha somatic motor neuron in spinal cord.

4) **Alpha motor neuron stimulates contractile muscle fibers**

   - This is ex. of **monosynaptic reflex**
   - > Only one synapse is crossed (in spinal cord)

   ![Fig 6.3](image)

II. Inhibitory Stretch Reflex

1) Muscle is stretched, muscle tendon is stretched, which stimulates AP in **Golgi tendon organ** (a sensory organ)

2) Sensory neuron goes into spinal cord & **stimulates (+) an interneuron**
   (spans distance between dorsal horn to ventral horn)

3) Interneuron stim **inhibitory (-) neurotransmitter to alpha motor neuron**

4) Effect = Reduces tension in tendon to prevent damage from excessive stretching

   - This is ex. of **disynaptic stretch reflex** = Two synapses are crossed in spinal cord

   ![Fig 6.4](image)
III. Reciprocal Innervation

1) Stretch of primary muscle & tendon **stim. sensory neuron**. Sensory info enters dorsal spinal cord, crosses over to ventral horn & does two things:

2) **Positive (+)** stim. of primary muscle to contract.

3) **Inhibition (-)** of antagonist muscle (stays relaxed).

IV. Crossed Extensor Reflex or double reciprocal innervation

Ex. Painful stimulus on right foot **stim sensory neuron**, goes into dorsal horn spinal cord. Crosses to ventral horn on left and right sides of cord and **does two things**:

1) **Right leg** Flexors contract (+) and extensors relax (-) to withdraw injured foot on R.

2) **Left leg**, Extensors contract (+) and flexors relax (-) to put leg down & support body weight.
IV. Crossed Extensor Reflex or double reciprocal innervation

- Voluntary reflex
  - Involves sensory neurons, spinal cord, brain, and motor neurons
    (longer, slower pathway)

- Spinal reflex
  - involves sensory neurons, spinal cord, and motor neurons
  - shorter, faster pathway under autonomic control

Ex.  Knee jerk reflex (monosynaptic)
      Inhibitory stretch reflex (disynaptic)
      Reciprocal innervation (contract one muscle & inhibit its antagonist)
      Crossed extensor reflex (usually in limbs supporting body)