Neural Activation of Muscle

- Neuromuscular Junction (NMJ)
- Twitches, Tetani and Fatigue
- Motor Units
Drugs/Molecules Affecting the NMJ

- Curare
  - Inhibitor of AChR-binding site
- Botulinum Toxin
  - Blocks release of ACh from NMJ
  - Causes flaccid paralysis
- Tetanus Toxin
  - Blocks inhibition of motorneurons
  - Causes rigid paralysis
- Acetylcholine Agonists
  - Nicotine, Methacholine, Carbachol
- Desensitizing Agents
  - Succinyl choline
**Drugs/Molecules Affecting the NMJ**

- **Acetylcholine-Esterase Inhibitors**
  - *Physostigmine and Neostigmine are derived from plants*
  - *Diisopropyl fluorophosphate is a human-made “nerve gas”*
  - *Used clinically for myasthenia gravis and early stages of Alzheimer’s Disease*

- **Black widow spider venom**
  - *complete depletion of acetylcholine*
  - *initial spasms and then paralysis.*

- **Cobra toxin**
  - *specifically blocks the acetylcholine receptor*
  - *slow breakdown of toxin*

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**Drugs/Molecules Affecting the NMJ**

- **Myasthenia gravis**
  - *Symptoms include poor muscle tone*
  - *Autoimmune disease in which AChRs are attacked*
  - *AChE inhibitors are effective treatments*

- **Eaton-Lambert syndrome:**
  - *Antibodies to the calcium channel in the nerve terminal*
  - *decreased release of quanta of acetylcholine*
  - *Symptoms are proximal weakness, often with autonomic features (blurred vision and dry mouth); reflexes are absent.*
Time-Course of Electrical Signaling and Muscle Contraction
Motor Systems and Motor Control
Motor Movements

Reflex Responses
(Spinal Cord)

Rhythmic Motor Patterns
(Brainstem)

Voluntary Movements
(Cerebral Mechanisms)
Reflex Responses

Muscle Control
Must convey accurately timed commands not only to one muscle group but to many groups.

Agonist and Antagonist muscle groups.

Motor Plant

Sensory Systems

Are vital to the correct functioning of motor systems
Feedback Mechanism

- Slow Processing
- Mainly limited to slow movements & sequential acts.

Feed Forward Mechanism

- Predicting movements
- Quick dynamic movements
B Feed-forward control: command specifies response

1. Feed-forward controller (with memory)
2. Input processing (i.e., filtering, amplification)
3. Sensor detects distant events (e.g., eye)
4. Anticipatory command
5. Controller (i.e., filtering, amplification)
6. Actuator (e.g., muscle)
7. Feedback signal
8. Input processing
9. Sensor

Disturbance (e.g., ball)
Muscle Receptors, Spinal Reflexes, and Local Control of Motor Movements
Muscle Stretch Receptors:

- Muscle Spindles
- Golgi Tendon Organs
**Muscle Spindle Receptors:**

- Specialized muscle fibers
  - Nuclear chain fibers
  - Nuclear bag fibers

Very sensitive to the rate of change of muscle length.

**Velocity Sensitivity**

**Diagram**

- **A**
  - Linear stretch
  - Tap
  - Vibration
  - Release

- **B**
  - Impulse/sec
  - Steady state response
  - Dynamic response
  - 5 mm/sec
  - 15 mm/sec
  - 30 mm/sec
  - 1 sec
Muscle Spindle Receptors:

- Motor neuron innervation is located on ends of intrafusal fibers.
- Regulate muscle length.
- Regulate muscle sensitivity

**Gamma Motor Neurons**
Golgi Tendon Organ:

- Located at the junction of muscle and tendon.
- Loss myelination & braids itself within the collagen fibers of the tendon.

Stretching of capsule compresses nerve endings, causing the neuron to fire.

Very sensitive to changes in tension of muscle.
The Stretch Reflex

Myotatic Reflex
Ipsilateral

Contralateral
Flexion - Withdrawal Reflex

Input from spinal interneurons

Sensory input from muscle spindles

Input from upper motor neurons in the brain

Alpha motor neuron
Neural circuits (microcircuits) within the spinal cord play an essential role in motor coordination.

Interneurons are a vital player in these microcircuits.

Interneurons can be either inhibitory or stimulatory within the circuits they are residing.

Divergence - the distribution of the output of a single neuron (or a group of neurons) to a number of target neurons by branching of the axon.

Convergence - the processing of input from several neurons (or groups of neurons) onto one neuron (or neuronal group).
Gating - intermediate neurons (interneurons) or intermediate connections utilized by higher centers to preselect which of several possible responses will follow a stimulus.

Spatial Organization

Temporal Organization
Renshaw Cell (neuron) - Inhibitory interneuron

The connections of Renshaw cells to presynaptic motor neurons form a negative feedback system, which regulates the firing rate of the motor neurons.

They not only inhibit certain motor neurons, they also disinhibit antagonist motor neurons.

Spinal and Postural Mechanisms
Posture

Reasons for Postural Motor Mechanisms:

• Support the head and body against gravity and other external forces.

• Maintain the center of the body’s mass: aligned and balance.

• Stabilize supporting parts of the body while other muscles are being moved.

Mechanisms:

• Anticipatory or Feedforward

• Compensatory or Feedback
The first muscles to contract are those that are closest to the base of support.” (ks&j, pg 597)

Triggering mechanism:
- Muscle proprioception
- Vestibular sensation
- Visual sensation

“An individual’s postural response to a stimulus is shaped by experience, and the form of the response is adjusted so that balance is maintained.” ks&j pg. 598
Postural muscles contract to maintain equilibrium before destabilizing movements are executed.

Postural adjustments anticipate the occurrence of changes that would cause the loss of balance.

This feedforward control is essential for coordinating posture with voluntary movement.

When changes actually occur, feedback mechanisms produce rapid corrective responses. When we can predict the nature of the change, but not its exact timing, higher motor centers enhance or reduce the strength of short-latency pathways that operate automatically.
Vestibular and Neck Reflexes

Vestibular reflexes are evoked by changes in the position of the head.

Neck reflexes are evoked by tilting/bending of the neck.

Vestibulocollic reflexes - counteract head movements keeping the head stable.

Vestibulospinal reflexes - contract the limb muscles and prepare the subject for landing during falls.
Cervicocollic reflexes contract neck muscles that are stretched. (vestibulocollic reflexes)
Rhythmic Movements
Spinal Circuits for Rhythmic Locomotor Patterns

- Normal locomotion is attributed to spinal circuits.
- Decerebrate and sensory lesioned preparations both demonstrated rhythmic activity for locomotion.
- Central pattern generators for locomotion are innate and specialized for each limb individually.
- Mesencephalic locomotor region controls locomotor activity (Dopamine, Norepinephrine, Glutamate (NMDA))
Control of Voluntary Motor Movement by the Brainstem Nuclei
3 Main Brainstem Motor Pathways

Ventral Pathway -
• Terminate in the ventromedial part of the spinal grey matter.
• Influence motor neurons that innervate axial and proximal muscles.

Lateral Pathway -
• Terminate in the dorsolateral part of the spinal grey matter.
• Influence motor neurons that control distal muscles of the extremities.

Aminergic Pathway -
• Terminate at all levels of the spinal cord.
• Modulate excitability of neurons at all levels of the cord.

Ventral Pathway
Vestibulospinal Tract
• Reflex control and posture

Tectospinal Tract
• Coordination of head and eye movements
Reticulospinal Tract
- Control of posture, suppression of spinal reflexes

Lateral Pathway

Rubrospinal Tract
- Medial & Lateral
- Red nucleus
- Control of fine motor movements
Voluntary Movement & Cortical Control of Motor Movement
• Differs from the postural and spinal reflexes.

• Different strategies to achieve same goal.

• Improves with experience.

• Doesn’t need to use stimuli to elicit activity.
Primary Motor Cortex

Neurons encode for the force of contraction.

Individual neurons will control small groups of muscles.
- usually distal muscles.
- more than one muscle (or group of muscles) may be activated by a single cortical neuron.
- divergence of cortical neurons at the brainstem and spinal cord level.
- Make direct and powerful excitatory connections with alpha motor neurons
- Although the corticospinal tract projects to motor nuclei controlling proximal and distal muscles, the corticospinal tract is the only pathway that controls the distal muscles of the fingers.
Individual neurons will encode for the amount of force to be exerted and not the position of the limb.

This activity typically occurs before the contraction of the muscle.

Individual neurons vary their activity with the direction of movement.

Voluntary behavior (movement) is determined by the activity of a rather large population of neurons and cannot be predicted from the discharge patterns of any one neuron.
Neurons in the primary motor cortex are kept informed about the position of the limb and the speed of movement through sensory input.

Motor cortex functions in parallel with the spinal cord stretch reflex.

Provide assistance, supplementing the stretch reflex, when the moving limb encountered an unexpected obstacle.

Primary Motor Cortex Projections
Corticospinal or Pyramidal Tract
Premotor Areas of Cortex
(Supplementary motor area and Premotor cortex, Area 6)

Programming and preprogramming complex sequences of movement.

Movements are more complex in nature and require larger stimulus currents than those produced by stimulation of the primary motor cortex.
Supplementary Motor Cortex is only important in programming and planning of complex movements, not executing them.

Basal Ganglia Involvement in Motor Control
A collection of overlapping circuits responsible for higher order cognitive planning of motor control and cognitive functioning in general.

Cortical Inputs to Striatum = Glutamate (+)

Thalamic Inputs to Striatum = Glutamate (+) and Opioid?

Most output connections utilize GABA (-) as their neurotransmitter.
What do the Basal Ganglia do?

- Selectively facilitate some movements and suppress others.
- Compare commands for movement from the precentral motor fields with proprioceptive feedback from the evolving movement.
- Involved in the initiation of internally generated movements.
Movement Disorders of the Basal Ganglia

Parkinson’s Disease: clinical make-up

- Alternating tremor (resting tremor): “pill-rolling”, oscillating
- Plastic rigidity, increase tone in all muscles
- Flexed posture
- Difficulty in moving (akinesia, hypokinesia)
- Mask like facial expression, absence of arm movements when walking
- Massive degeneration of Substantia Nigra, Striatum, and frontal cortex
Huntington’s Disease: clinical make-up

- Severe Choreiform motor disability, random and continuous
- Decrease in muscle tone
- Reflexes and sensations are normal
- Athetosis
- Progressive, inherited, onset usually 35 - 40 yrs of age.
- Atrophy of striatum
Huntington's disease results from a gene mutation causing abnormal repetition of the DNA sequence CAG that codes for the amino acid glutamine. The resulting gene product, a large protein called huntingtin, has an expanded stretch of polyglutamine residues, which leads to disease via unknown mechanisms.

Huntington's disease affects both sexes equally. The caudate nucleus atrophies, the inhibitory medium spiny neurons in the corpus striatum degenerate, and levels of the neurotransmitters γ-aminobutyric acid (GABA) and substance P decrease.
The Cerebellum and the Control of Motor Movement
Cerebellar Function:

Regulates movement and posture indirectly by adjusting the output of the major descending motor systems of the brain.
Cellular Circuitry of the Cerebellum
Cells of the Molecular Layer

• **Stellate**
  - receive stimulatory input from parallel fibers
  - deliver inhibitory Input from Purkinje Cells

• **Basket Cells**
  - receive stimulatory input from parallel fibers
  - deliver inhibitory Input to Purkinje Cells

Cells of Granule Layer

• **Granule Cells**
  - receive stimulatory input from mossy fiber pathway
  - deliver powerful stimulatory Input to Purkinje Cells by parallel fibers

• **Golgi Cells**
  - receive stimulatory input from parallel fibers and adjacent granule cells
  - deliver inhibitory Input to granule cells
Purkinje Cells - The most important cell in the cerebellum.

- Inhibitory
- Only output neuron of the cerebellum
- Large dendritic tree receiving both stimulatory and inhibitory information

Cerebellum acts as a comparator that compensates for errors in movement by comparing intention with performance.

- Receiving information about plans for movement from structures concerned with programming and execution (*Corollary Discharge*).
- Receiving information about motor performance from sensory systems during movement (*Reafferance Feedback*).
- Sends information to descending motor systems.
Control of Motor Circuitry
**Vestibulocerebellum**
Governs eye movements and body equilibrium
Control of axial and proximal limb muscles that are used to maintain balance.

**Spinocerebellum (2 parts)**
- Originates from Vermal region of cerebellum
- Inputs from special senses, vestibular apparatus, and spinocerebellar tracts.
- Axial and proximal motor control of ongoing execution of movement.
Spinocerebellum
Two (2) sections

Originates from Intermediate region of cerebellum
Inputs from spinocerebellar tracts (distal body parts).
Distal motor control of ongoing execution

Sensory Input

Intermediate region

Interpositus Nuclei

Red Nucleus (Bilaterally) Thalamic Nuclei (Bilaterally)

Rubrospinal pathway Motor Cortex
Cerebrocerebellum
Two (2) sections

Originate from Lateral posterior lobe of cerebellum

Inputs from Sensory/motor cortex, premotor, and parietal cortex by way of the pontine nuclei.

Achieving precision in control of rapid limb movements and in tasks requiring fine dexterity.