SKELETAL MOTOR CONTROL

MOTOR CONTROL HIERARCHY

Each level of the hierarchy performs a certain task in the control of skeletal muscles.

1) The highest level of the hierarchy comprises many regions of the brain, including those associated with memory, emotions and motivation. The intent to move is formed in the highest level of the hierarchy, in the command neurons.

2) This information is relayed to the middle level, which is located in the sensorimotor cortex of cerebral cortex, the basal ganglia of the subcortical nuclei, the cerebellum, and the brainstem. Here, postures and movements required to perform the task are determined. The structures in the middle level have extensive interconnections. Neurons in the middle level also receive input from receptors in the muscles, the joints, the skin, the vestibular apparatus, and the eyes, about current posture and surroundings. All this complex information creates a motor program, that defines the information required to perform the desired task.
3) Information is sent via *descending pathways* to the *motorneurons* and *interneurons*, the lowest level in the hierarchy. These pathways originate in the sensorimotor cortex and brainstem. The lower levels specify the tension of muscles and the angle of joints.

**Note that:**
- Movements are constantly being monitored and updated to provide for unexpected occurrences.
- If a movement is repeated, then learning can occur, where the middle levels provide more accurate information and fewer corrections are required.
- Crude, rapid movements are performed according to the initial motor program and no modification occurs during execution of those movements.

**Voluntary and involuntary actions**

**Voluntary:**
- i) movement is accompanied by conscious awareness.
- ii) attention is directed toward the action.

**Involuntary:** reflex actions

All voluntary actions require some involuntary control, and vice-versa.
LOCAL CONTROL OF MOTOR NEURONS

These systems relay information from middle centers to the motor neurons and adjust motor unit activity as required. Local control systems obtain information from sensory receptors and transmit it to: i) the higher centers and, ii) within the local level.

Interneurons

Most input from descending pathways goes to interneurons that then synapse with motor neurons. There are 2 general types of interneurons:

i) local interneurons, that are confined to the general region of the motor neuron they regulate,

ii) intersegmental interneurons, that extend along the spinal cord and into the brainstem and regulate the coordinated interactions of different muscles.

Interneurons integrate inputs from higher centers, peripheral receptors, and from other interneurons. Crucial for determining which muscles are activated, and when. Can switch the signal to a muscle on, or off, under the control of the higher center.

Axons onto a local interneuron

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**Local afferent input**

Afferent fibers from many sources synapse on interneurons:

i) the same muscles controlled by the motor neuron,

ii) other nearby muscles,

iii) tendons, joints and skin surrounding the muscles.

Thus, afferent input from these sources provide negative-feedback and awareness of limb and body position.

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**Skeletal muscle length monitoring systems**

**Definitions:**

Skeletal muscle cells = *muscle fiber*

Muscle = *a number of muscle fibres*

The bulk of a muscle is made up of muscle fibers called *extrafusal* fibers. Muscle length and changes in length are monitored by *stretch receptors* in the muscle. These receptors are called *intrafusal fibers*, and are afferent nerve fiber endings that are wrapped around modified muscle fibers. A number of *intrafusal fibers* are called a *muscle spindle*.

There are 2 different types of intrafusal fibers:

i) those that respond to the amount of stretch,

ii) those that respond to the rate of stretch.

These different types of intrafusal fibers are collectively known as *muscle-spindle stretch receptors*. 
A muscle spindle and Golgi tendon organ

Stretch of the muscle pulls on the intrafusal fibers and activates the receptor endings. Firing from the receptors increases with increased stretch or rate of stretch, whereas contraction of the muscle fiber decreases firing rate.

Passive stretch/contraction of the muscle
The Stretch reflex

The most familiar stretch reflex is the knee jerk reflex.

Mechanism of knee jerk reflex: tapping the patellar tendon stretches the attached extensor muscles and the stretch receptors within them. Action potentials are generated in the afferent nerve fibers and transmitted to the motor neurons that innervate the same muscles, eliciting a contraction that extends the leg, i.e. activation. The stretch reflex is monosynaptic because afferent nerve fibers synapse directly on motor neurons (path A). All other reflexes are polysynaptic because >1 interneuron is involved.

In addition:
The antagonistic muscles, i.e. the flexor muscles, are inhibited so as not to interfere with extension of the leg (path B). This is termed reciprocal innervation.
Synergistic extensor muscles are activated to aid the intended motion (path C). Activated muscles are on the same side of the body, i.e. ipsilateral.
Feedback to the higher centers provides conscious perception of the motion that occurred (path D).

The knee jerk reflex is used in the clinic as a test for functional afferent fibers, synaptic input, motor neurons and neuromuscular junctions.
**Alpha-Gamma Coactivation**

*Function:* maintains constant level of stretch in intrafusal fibers during contraction and relaxation to provide optimal feedback.

Contraction of a muscle leads to slackening of the stretch receptors. Thus, firing stops and feedback from the receptors becomes absent. To prevent this, intrafusal fibres are also stimulated to contract to maintain tension on the stretch receptors. Note that intrafusal fibers are not large, and thus, contraction is not strong enough to shorten a muscle.

Intrafusal and extrafusal fibers are innervated by different classes of motoneurons that can be activated by both interneurons and neurons of the descending pathways.

Extrafusal => innervated by alpha motor neurons.
Intrafusal => innervated by gamma motor neurons.
**Tension-monitoring systems**

This pathway monitors muscle tension.

Performed by *Golgi-tendon organs* that are located in the tendons near the junction with the muscle. Afferent fibers are wrapped around the collagen fibers of the tendon. Contraction of the muscle straightens the tendon and distorts the receptors, leading to an increase in the firing of action potentials. Activation of golgi tendon organs leads to:

i) **inhibition** of the contracting muscle and synergistic muscles via interneurons in the spinal cord,

ii) **activation** of antagonistic muscles.

**SUMMARY:**

Muscle spindle afferents monitor muscle length.

Golgi tendon organs monitor muscle tension.

$\alpha$-motorneurons innervate extrafusal fibers.

$\gamma$-motorneurons innervate intrafusal fibers.
**The withdrawal reflex**

*Function:* This mechanism provides further input from sensory receptors.  
e.g. a response to pain may involve the withdrawal reflex

Pain stimulus:

1) activates ipsilateral flexor motor neurons and inhibits the ipsilateral extensor motor neurons.  
2) activates contralateral extensor motor neuron and inhibits contralateral flexor motor neurons.  
Result: leg retracts from painful stimulus and body is supported by extending the other leg.
CONDUCTION PATHWAYS FOR PAIN

<table>
<thead>
<tr>
<th></th>
<th>FAST</th>
<th>SLOW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulated by:</td>
<td>Mechanical</td>
<td>Chemical</td>
</tr>
<tr>
<td></td>
<td>Thermal</td>
<td>(K⁺, bradykinin)</td>
</tr>
<tr>
<td>Pain Sensation</td>
<td>Sharp</td>
<td>Aching, nauseous</td>
</tr>
<tr>
<td></td>
<td>Acute</td>
<td>Chronic</td>
</tr>
<tr>
<td>Fiber Type to Spinal Cord</td>
<td>Aδ (small 1–5 µm, myelinated)</td>
<td>C (small 0.5–2 µm, unmyelinated)</td>
</tr>
<tr>
<td>Transmission Velocity</td>
<td>6 - 30 m/sec</td>
<td>0.5 - 2 m/sec</td>
</tr>
<tr>
<td>Purpose of Sensation</td>
<td>Remove pain rapidly</td>
<td>Seek medical attention</td>
</tr>
</tbody>
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Ascending neuronal tracts that carry pain information

Both the Fast and Slow pain pathways ascend in a different sub-division of the Anterolateral tract.
Each pathway terminates in a different CNS area

Fast Pain Pathway: Most all fibers pass to thalamus and terminate in the “ventrobasal complex”. Signals then further ascend to somatosensory cortex – i.e. localization of pain source is good.

Slow Pain Pathway: Terminates widely in brainstem with 1/4 of fibers continuing on to the thalamus. i.e. terminates in lower brain regions when compared with fast pathway and localization of pain source is poor.

The principal neurotransmitter for each pathway is different

Fast Pain Pathway: Glutamate, a common short acting CNS excitatory neurotransmitter.

Slow Pain Pathway: Mainly substance P, slow release taking seconds or minutes to reach maximal concentration.
ANALGESIA

The reaction to a pain stimulus can vary dramatically between patients. One reason for this is the level to which the brain suppresses pain signals. The pain control system is called the “analgesia system”.
The analgesia system initiates in areas of the mesencephalon and upper pons => raphe magnus nucleus => inhibitory complex located in the dorsal horn of the spinal cord.
Release of peptides called “enkephalins” leads to pre- and postsynaptic inhibition of incoming type C and Aδ pain fibers where they synapse in the dorsal horns.

Two other mechanisms used to reduce pain sensation by activating the analgesic system are:
Tactile inhibition: rubbing the skin near painful areas is leads to local lateral inhibition in the spinal cord.
Electrical Stimulation: TENS (Transcutaneous Electrical Nerve Stimulation). Stimulating electrodes placed over skin or spinal cord stimulate the dorsal columns.

PRE- AND POST SYNAPTIC INHIBITION OF INCOMING PAIN SIGNALS
CLINICAL ABNORMALITIES OF PAIN SENSATION
Hyperalgesia is defined as a hypersensitivity to pain.

There are two types:
1) primary, due to an increase in the sensitivity of nociceptors;
2) secondary, due to an increase in the facilitation of transmission.
Sunburn is a common example. Tissue damage leads to release of prostaglandins etc., which sensitizes nociceptors to mechanical and thermal stimulation.

Thalamic syndrome
Artery supplying posterior thalamus blocks, leading to degeneration, but not destruction of the nuclei in this area.

Medial and anterior portion of the thalamus remain intact. It is thought that the medial nuclei become facilitated giving enhanced sensitivity.

Symptoms are loss of sensation from opposite of body; ataxia (loss of control of body movement); after a few weeks/months some sensation returns but produces pain regardless of stimulus.

Tic Douloureux (also called trigeminal neuralgia or glossopharyngeal neuralgia)

Lancinating pain in one side of the face served by the fifth or ninth cranial nerves. May occur for a few seconds or be continuous. Usually induced by mechanical trigger, e.g. swallowing.

Treated by surgically cutting the peripheral nerve from the sensitive area. This leaves the area permanently anesthetized. This treatment may be unsuccessful, indicating that the cause is a lesion in the brainstem.
PHARMACOLOGICAL PAIN ALLEVIATION
Drugs that control pain are some of the most widely used. These agents are divided into 3 major categories: 1) GENERAL ANESTHETICS and 2) ANALGESICS, which act systemically, and 3) LOCAL ANESTHETICS, which act locally.

General Anesthetics
The molecular shape of inhalation anesthetics does not appear to be important, suggesting that there is no specific receptor protein for these agents.

Three hypotheses for cellular action:
1) alter the physical state of the lipid membrane;
2) cause the ordering of water molecules on the lipid membrane;
3) direct interaction with proteins.
All these mechanisms lead to changes in receptor and ion channel function which leads to inhibition of synaptic transmission.

Intravenous general anesthetics act more quickly than inhalation anesthetics (seconds versus minutes). These agents fall into 2 major categories: induction agents, such as thiopentone, and basal anesthetics, such as ketamine.

Thiopentone: a highly lipid soluble barbiturate. Induces unconsciousness in ~20s and lasts for ~5-10min. Has no analgesic effect, and can induce respiratory depression. Therefore, no good for surgical anesthesia – but good for induction prior to inhaled anesthetic.

Ketamine: similar structure to phencyclidine (PCP), but induces less euphoria. Induced “dissociative anesthesia” – analgesia and paralysis, without loss of consciousness. Main side-effect – hallucinations can occur during recovery.
Analgesics
Analgesic drugs can be subdivided into 2 main categories: i) morphine-like drugs, which act on the CNS; and ii) non-steroidal anti-inflammatory drugs (NSAIDs).

1) Morphine like drugs are a diverse group of compounds that include morphine, heroine, and codeine.

Bind to opioid receptors (of which there are several subtypes; µ, δ, γ) on neurons. Opioid receptor activation leads to an increase in K\(^+\) conductance, membrane hyperpolarization, inhibition of action potential firing, and pre-synaptic inhibition of transmitter release.
Analgesia of both acute and chronic pain by reducing both sensation and perception; euphoria; respiratory depression; nausea (due to large increase in tone of the GI tract).

2) NSAIDs (e.g. indomethacin, aspirin, ibuprofen) are among the most commonly used pharmacological compounds. NSAIDS act by inhibiting cyclo-oxygenase, and this mechanism provides their 3 major actions: anti-inflammatory, analgesic, and antipyretic (∞ body temperature).
Prostaglandins sensitize nociceptor nerve terminals to pain mediators such as bradykinin, serotonin, and histamine. Therefore, in the presence of subthreshold mediators, prostaglandins will induce a pain sensation. NSAIDS reduce prostaglandin production, and are particularly useful for inflammatory pain.
Local Anesthetics
1) As their name suggests, local anesthetics are useful for alleviating pain at the site of nociception. All compounds (e.g. procaine, lidocaine) in this category have the same basic mechanism of action. All are essentially Na+ channel blockers, blocking the initiation and propagation of action potentials.

Local anesthetic blocks here