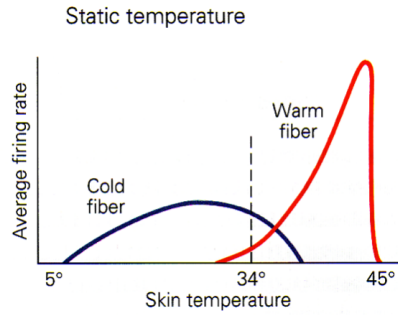
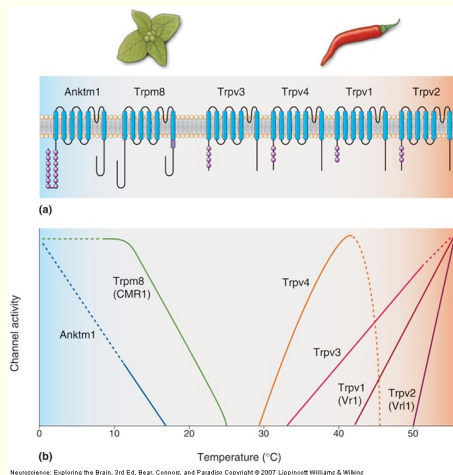


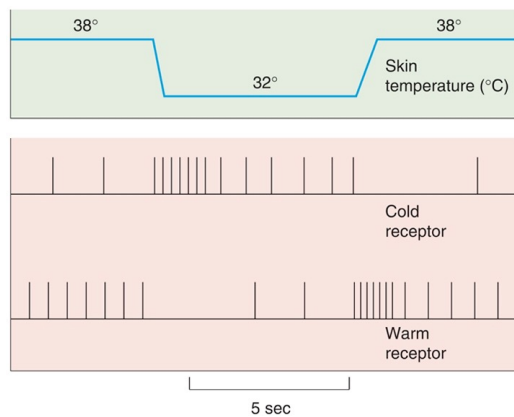
Thermoreceptors (hot & cold fibers)



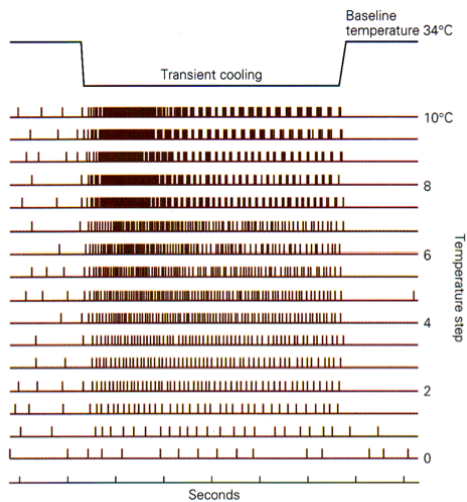
Temperature gated Na⁺ channels



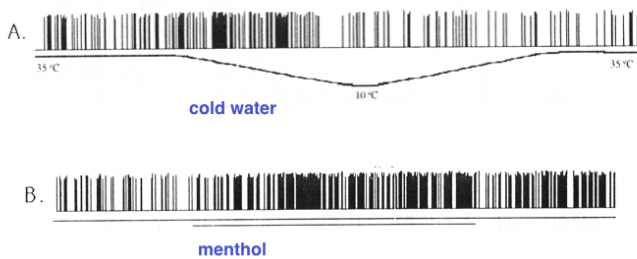
Adaptation in thermoreceptors



Response of a cold receptor



Drugs can mimic sensory stimuli



Response of taste nerve to cold water or menthol

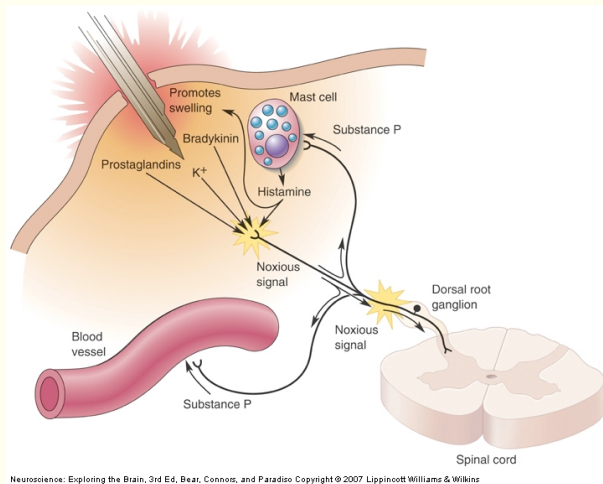
Pain

•Pain and nociception

- Pain - feeling of sore, aching, throbbing
- Nociception - sensory process, provides signals that trigger pain

•Nociceptors: Transduction of Pain

- Bradykinin
- Mast cell activation: Release of histamine

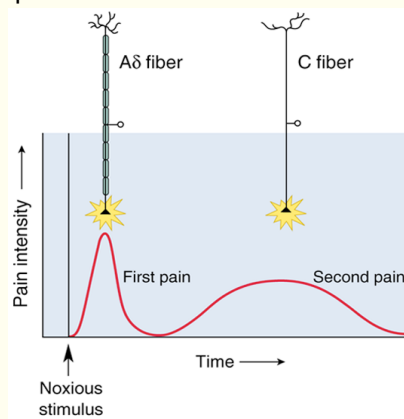


• Nociception and the Transduction of Painful Stimuli

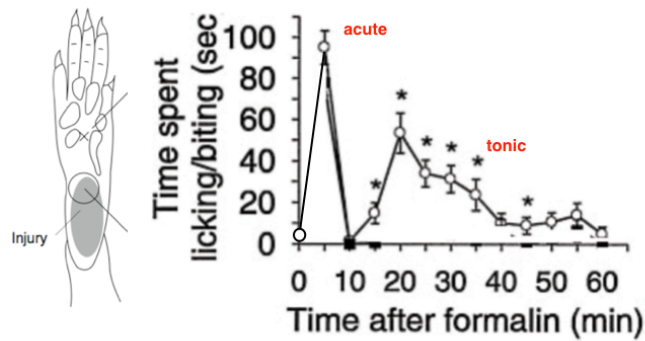
- Types of Nociceptors
 - Polymodal nociceptors, Mechanical nociceptors, Thermal nociceptors
- Hyperalgeia
 - Primary and secondary hyperalgesia
 - Bradykinin, prostaglandins, and substance P

• Primary Afferents and Spinal mechanisms

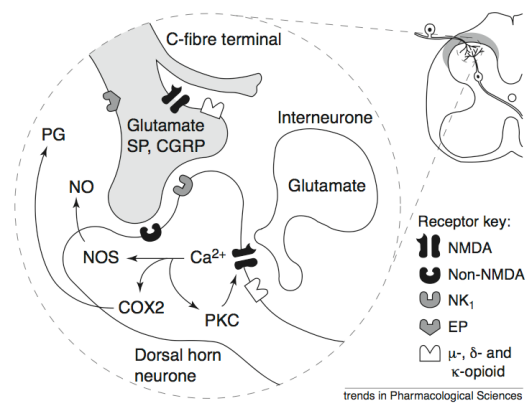
- First pain and second pain



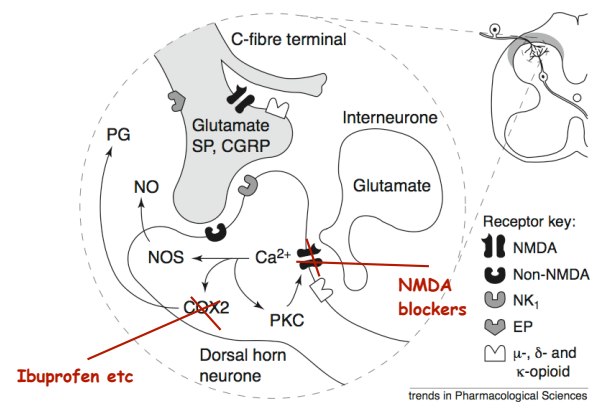
Formalin paw-licking test
Acute and tonic phases



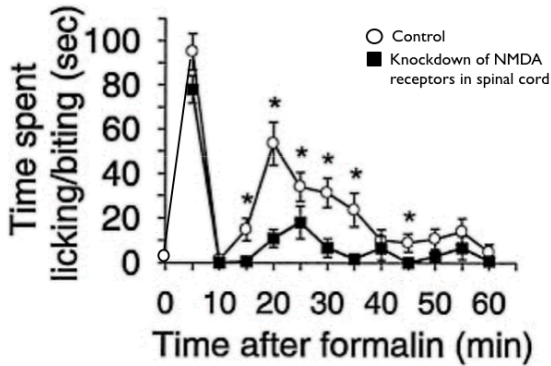
Central Sensitization
at first dorsal horn synapse



Central Sensitization
at first dorsal horn synapse

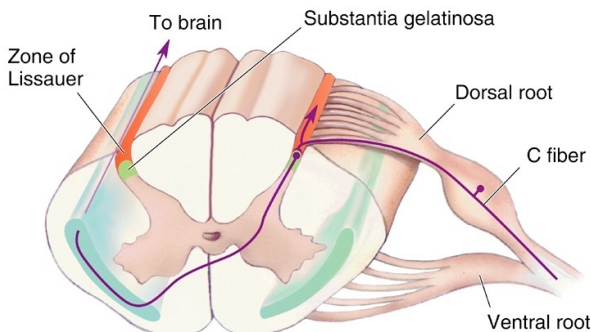


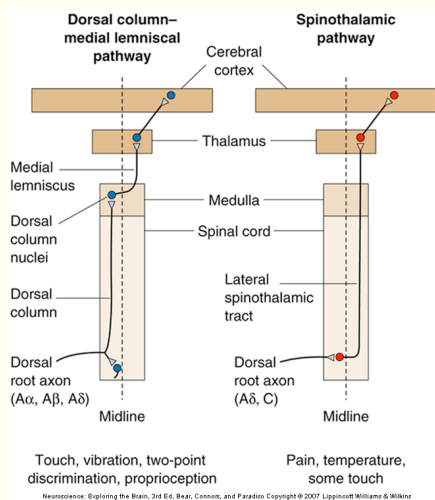
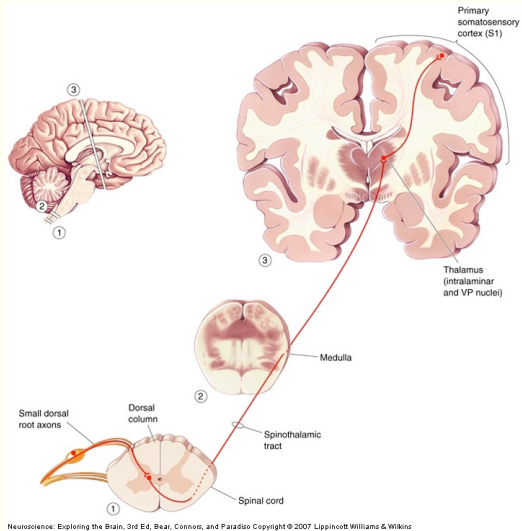
Tonic Phase of formalin paw-licking requires spinal NMDA glutamate receptors



•Ascending Pain Pathways

- Differences between touch and pain pathway
 - Nerve endings in the skin
 - Diameter of axons
- Connections in spinal cord
 - Touch – Ascends Ipsilaterally (crosses over in brainstem)
 - Pain – Ascends Contralaterally (crosses over right after entering spinal cord)





• Ascending Pain Pathways (Cont'd)

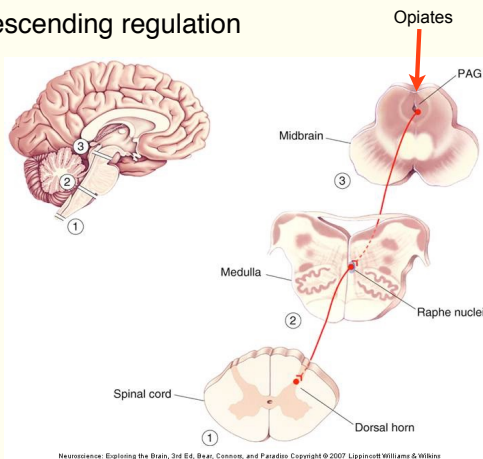
- Spinothalamic Pain Pathway
- The Trigeminal Pain Pathway
- The Thalamus and the Cortex
 - Touch and pain systems remain segregated
 - Pain and temperature information sent to various cortical areas

- The Regulation of Pain

- Afferent Regulation
- Descending Regulation
- The endogenous opiates
 - Opioids and endomorphins

- The Regulation of Pain (Cont'd)

- Descending regulation



Analgesia is the relief of pain.

Pain is normally defined as an unpleasant sensory and emotional experience associated with potential or actual tissue damage. Pain is difficult to assess in animals because of the inability to communicate directly about what the animal is experiencing. Instead, indirect [signs of pain](#) are often used.

Because of the difficulty of determining when an animal is in pain, animal welfare regulations require that analgesia be provided whenever a procedure is being performed or a condition is present that is likely to cause pain. In the absence of evidence to the contrary, it is assumed that something that is painful in a human will also be painful in an animal.

Assessment of pain or distress may be based on many different criteria including:

- Decreased activity
- Abnormal postures, hunched back, muscle flaccidity or rigidity
- Poor grooming
- Decreased food or water consumption
- Decreased fecal or urine output
- Weight loss (generally 20-25% of baseline), failure to grow, or loss of body condition (cachexia)
- Dehydration
- Decrease or increase in body temperature
- Decrease or increase in pulse or respiratory rate
- Physical response to touch (withdrawal, lameness, abnormal aggression, vocalizing, abdominal splinting, increase in pulse or respiration)
- Teeth grinding (seen in rabbits and farm animals)
- Self-aggression
- Inflammation
- Photophobia
- Vomiting or diarrhea
- Objective criteria of organ failure demonstrated by hematological or blood chemistry values, imaging, biopsy, or gross dysfunction

Anesthesia is a state of unconsciousness induced in an animal. The three components of anesthesia are **analgesia** (pain relief), **amnesia** (loss of memory) and **immobilization**.

Curariform skeletal muscle relaxants or neuromuscular blockers (e.g. *succinylcholine*, *decamethonium*, *curare*, *gallamine*, *pancuronium*) are not anesthetics and have no analgesic effects. They may only be used in conjunction with general anesthetics. Normally, artificial respiration must be provided. Physiologic monitoring methods must also be used to assess anesthetic depth, as normal reflex methods will not be reliable.

Local Anesthetics: Block nerve impulses at the site of application, eg. lidocaine which blocks voltage-sensitive sodium channels

Inhalation Anesthetics: Depress cortical activity by interactions with membranes of neurons

Sedative Anesthetics: Provide sedation or anticonvulsant action by enhancing GABAergic chloride channels which inhibit cortical function, e.g. barbituates and benzodiazepines

Dissociative Anesthetics: The dissociative anesthetics include **ketamine** (Vetalar, Ketaset) and **tiletamine** (Telazol). These drugs are easy to use and have a wide margin of safety for most laboratory species. They are cyclohexamine compounds, chemically related to piperazine and phencyclidine (PCP).

The dissociative anesthetics uncouple sensory, motor, integrative, memory and emotional activities in the brain, providing there is a functional cerebral cortex. The state induced by high doses of ketamine is best described as catalepsy and is not accompanied by central nervous system depression. There is depression of respiratory function, but cardiovascular function is maintained. Muscle relaxation is very poor.

Muscle Afferents & Spinal Reflexes

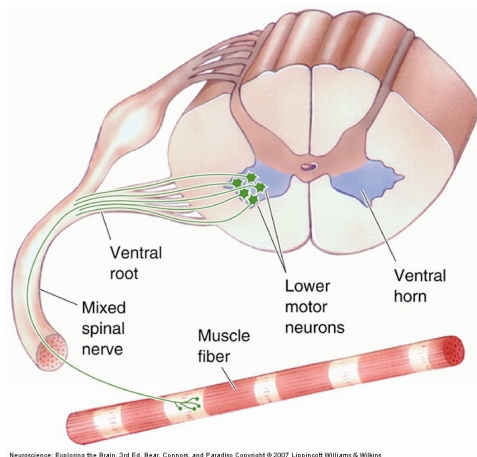
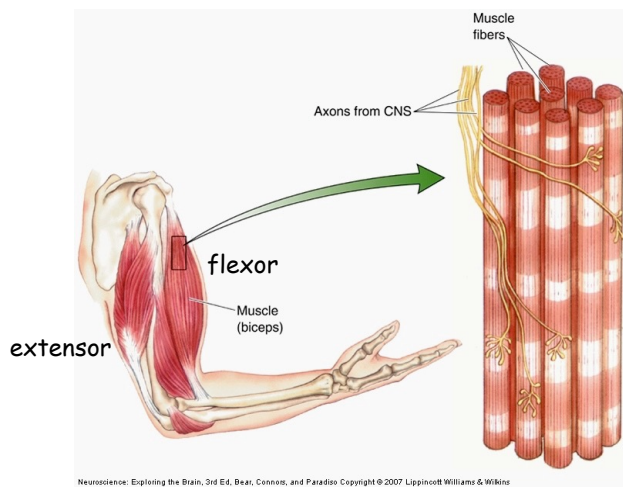
input -> processing -> output

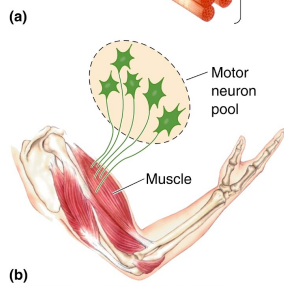
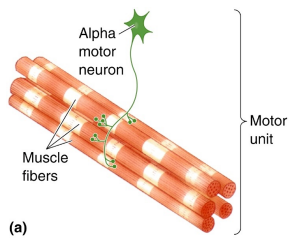
receptors -> afferents -> spinal cord -> efferents -> muscles

afferents -> dorsal horn -> ventral horn -> efferents

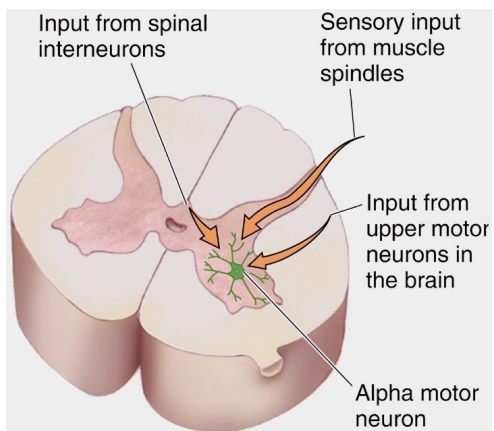
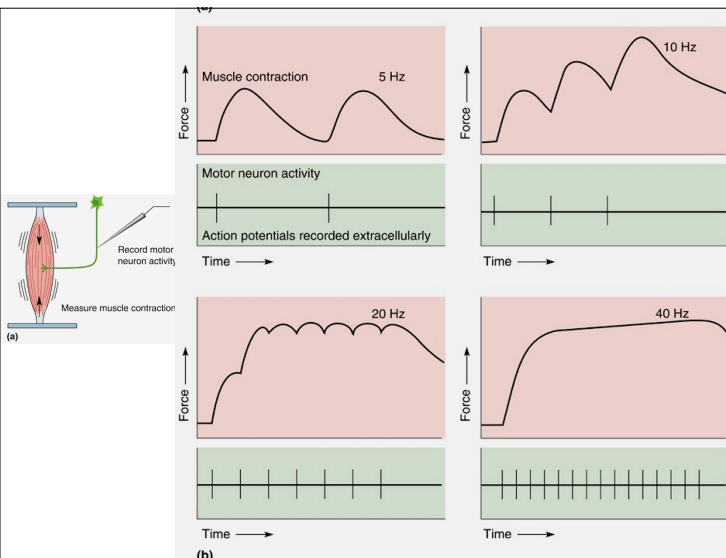
afferents = towards the spinal cord/brain

efferents = away from the spinal cord/brain



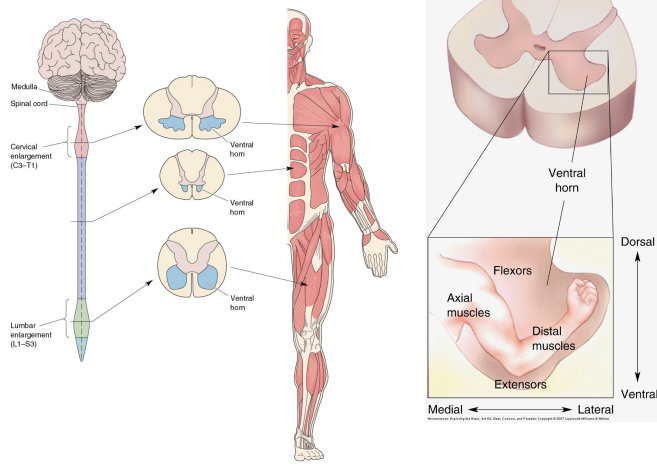


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Distribution of Motor Neurons



Muscle Afferents

help control the action of muscles

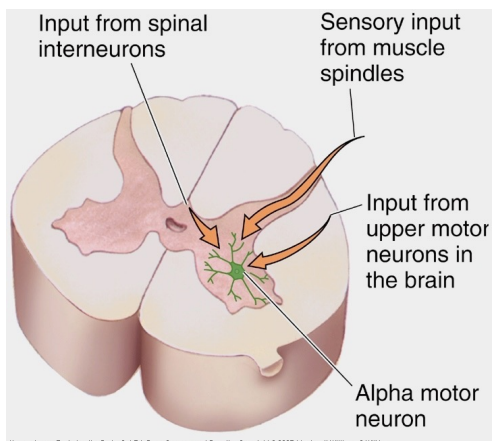
relay position of limbs (proprioception)

convey sense of movement (kinesthesia)

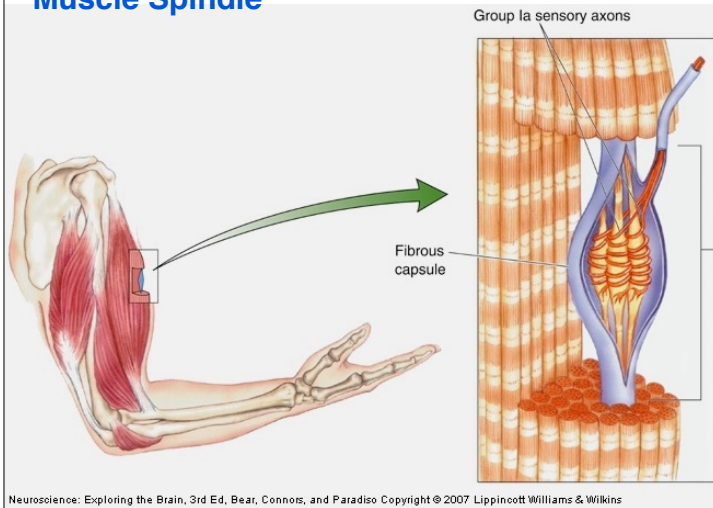
Two receptor organs:

Spindles: stretch info via Ia and II afferents

Golgi Tendon Organs: force info via Ib afferents



Muscle Spindle



Muscle Spindle

sensory organ in parallel with muscle fibers to provide info on muscle stretch (= length changes).

Very dense in fine muscles (e.g. thumb).

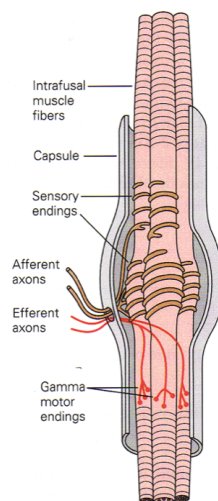
Highest density in neck, because head position important.

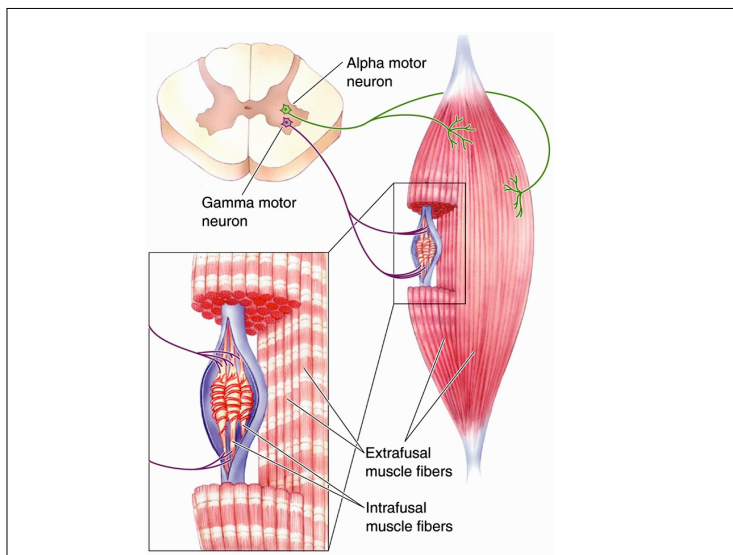
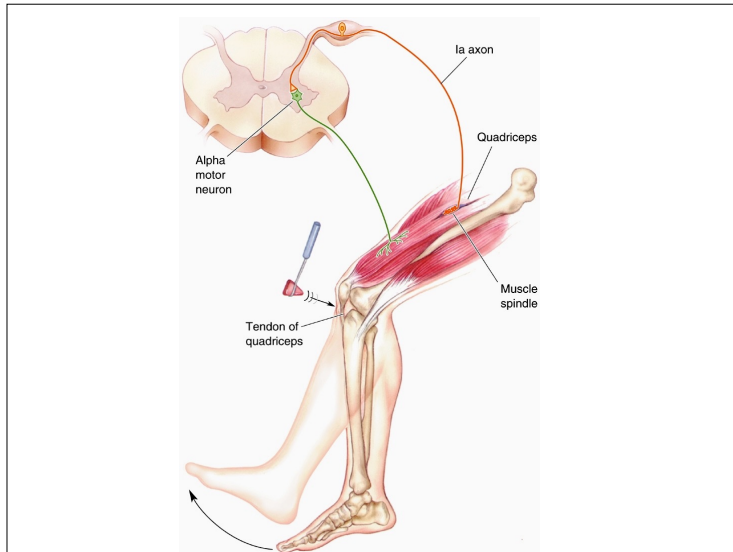
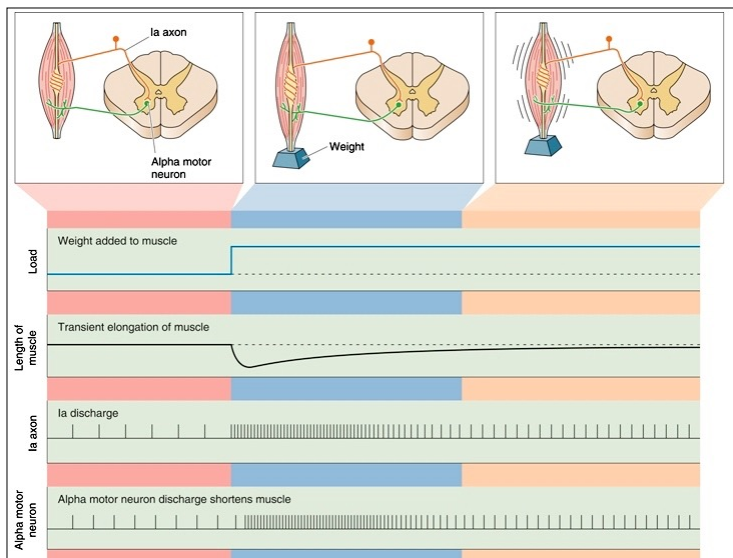
Fusiform bundle of 5-10 intrafusal muscle fibers
(extrafusal = rest of muscle; *fusus* = spindle).

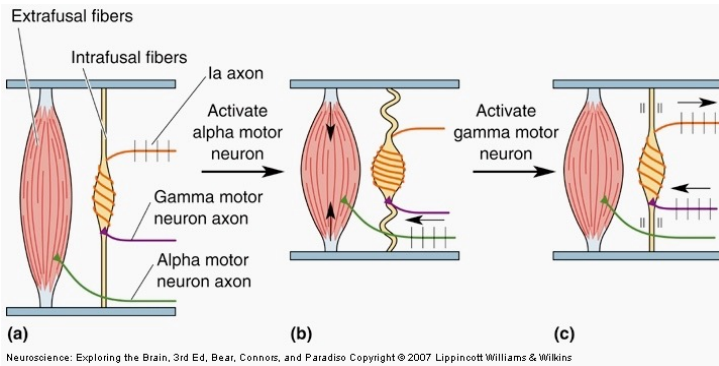
Afferents = 1a sensory axons

Efferents = alpha motor neurons to muscle
= gamma motor neurons to spindle

Muscle Spindle







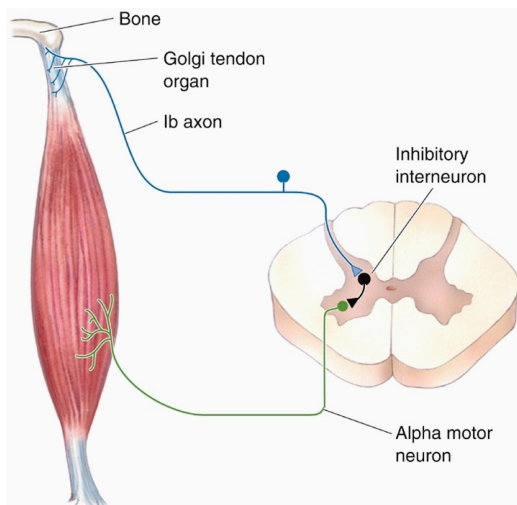
Golgi Tendon Organ

sensory organ in series with muscle fibers to provide info on muscle force (= load on the muscle).

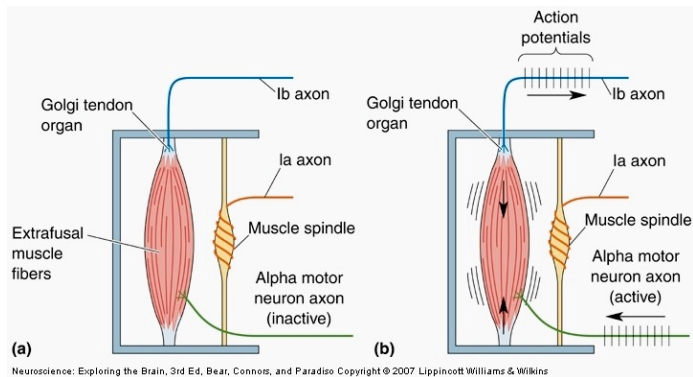
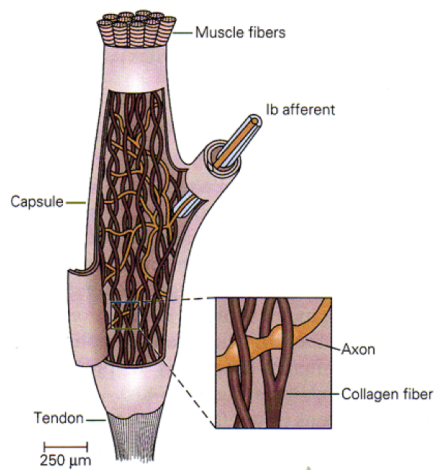
Located in tendons where muscle inserts on bone.

Sensitive to changes in muscle force, but only to tension of a small number of motor units attached near to the tendon.

Afferents = 1b sensory axons



Golgi Organ



44

Afferent Nerves

cell bodies in dorsal root ganglion, enter dorsal horn of spinal cord.

Ia afferent (primary afferent of spindle)

large diameter, so high speed (12-20 μm, 72-120 m/sec).

dynamic - responds to changes in length, peak firing rate proportional to **velocity of stretch**.

Ib afferent

large diameter that wraps around Golgi tendon organ. Responds to **force**.

II afferent (secondary afferent of spindle)

smaller diameters (4-12 μm, 24-72 m/sec).

static -firing rate increases with **increased stretch**.

Alpha & Gamma Fibers

alpha motor neurons:

cause motor units to contract for skeletal muscle movements

gamma motor neurons:

cause intrafusal fibers to contract to maintain tension as fiber is stretched

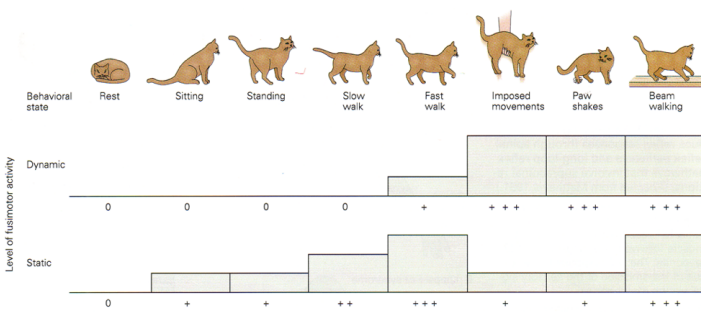
Afferent Firing Patterns

Stretch -> increased firing of Ia & II afferents

Contraction

- > unloading of spindle
- > decreased Ia & II firing
- > increased tension on tendon, Golgi tendon organ
- > increased Ib firing

Afferent firing in real life



Spinal Reflexes

Reflexes – stereotyped motor behaviors evoked by specific sensory stimuli

- threshold of stimulus
- applied to specific regions, motor response is stereotyped (not very variable)
- only a few synapses, so not much processing and very fast
- often under descending inhibition so revealed or exaggerated after spinal or brain injury (in dogs by Sherrington, after WWI by Head).
- mediated by spinal cord or brainstem

Stretch Reflex (myotactic)

skeletal muscle contracts, if stretched

phasic component

brief and quick response – e.g. knee jerk

tonic component

sustained over many seconds – hard to elicit in normal person

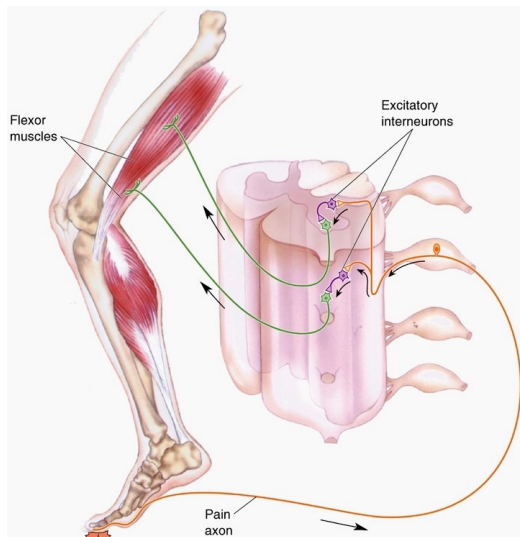
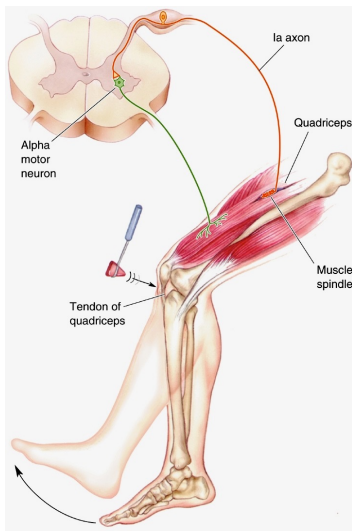
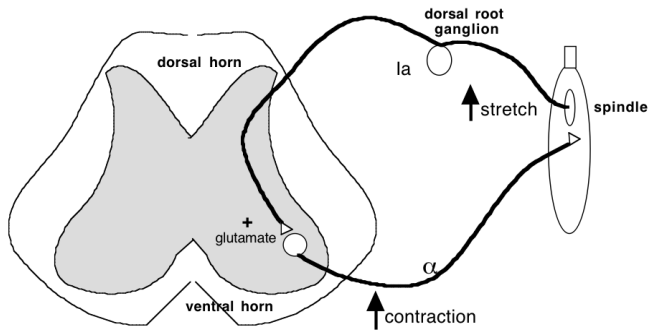
Knee jerk (Phasic Stretch Reflex):

patellar tendon ->
spindle stretch in quadriceps ->
firing of dynamic Ia afferents ->

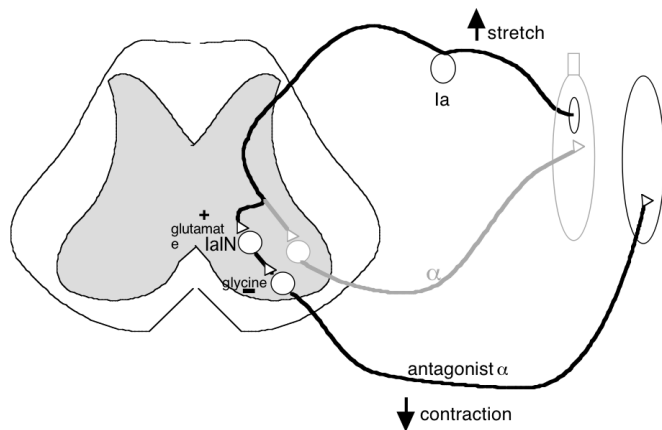
monosynaptic connection on a motor neurons (via glutamate)

- > quadriceps contraction
- > decreased stretch of spindle
- > silent Ia afferents.

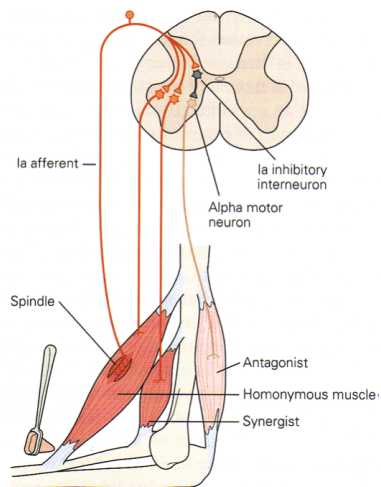
Stretch Reflex: monosynaptic



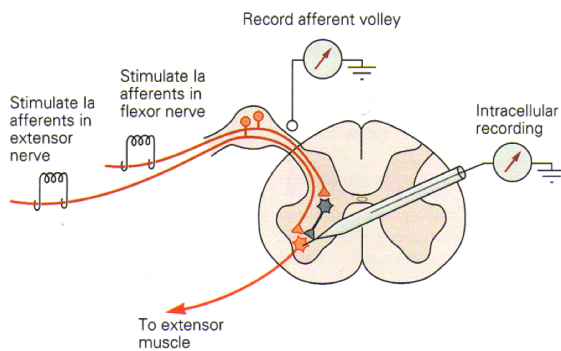
Reciprocal Inhibition



Stretch Reflex



Number of Synapses in a Reflex Pathway

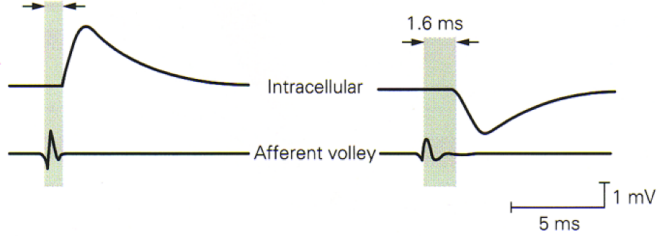


Number of Synapses in a Reflex Pathway

B Inferring the number of synapses in a pathway

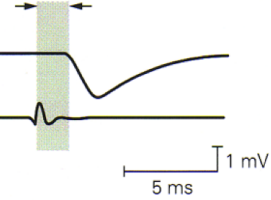
1 Monosynaptic

0.7 ms



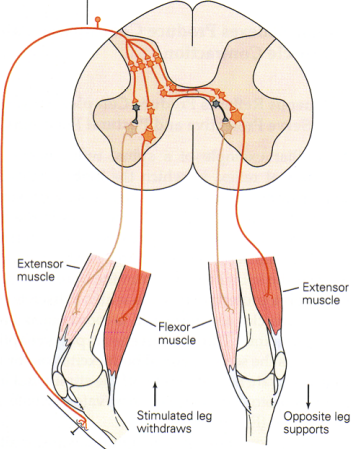
2 Disynaptic

1.6 ms

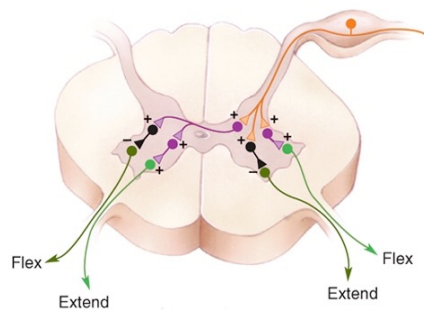
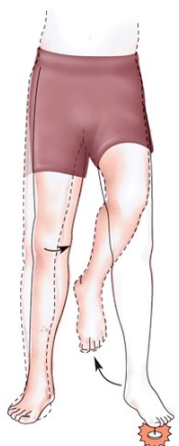


Flexion and Cross Extension Reflex

Cutaneous afferent fiber from nociceptor (Aδ)



specific to spinal se

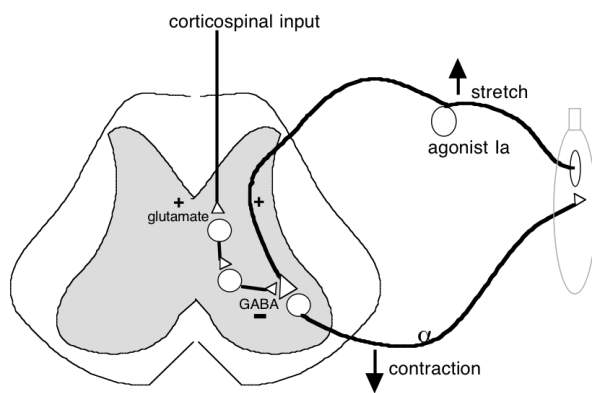


Tonic Stretch Reflex:

stretch muscle and hold at extended length

- > extended spindle stretch
- > activation of static II afferents
- > gamma motor neurons
- > continued stretch of spindle
- > continued stretch reflex via Ia & alpha motor neurons
- > maintenance of tension

Descending Corticospinal Inhibition



Lesions of spinal cortical tract

spasticity

increase in muscle tone and hyperexcitability of stretch reflex

exaggerated phasic stretch reflex:

tap -> large contraction, and even clonus (oscillatory contractions & relaxations) (babinski reflex)

exaggerated tonic response:

resist stretch all the time, rapid straightening of limb -> long lasting contraction. Slow straightening -> jackknife response.

A plastic reflex: Micturition Reflex

driven by internal sensory stimuli
mechanoreceptors on bladder wall
-> relaxation of sphincter -> micturition.
Comes under supraspinal voluntary control during development,
but after spinal injury spinal reflex takes time to re-emerge.

In rats:

micturition reflex present in utero
-> replaced by cutaneous reflex (pups voided by licking of mother)
-> re-emerges after weaning
-> never much voluntary control.
Thus reflexes can be plastic.

Modifiable Reflexes: pain

