

Lecture 14
Anatomical Substrates for Somatic Sensation
Dr. Martin
James Houston

For the most part this is the same lecture given last year. I went through last years notes and have edited them where appropriate. Please email me with any questions at jch2029.

We will review anatomy of 2 principle pathways of somatosensory system: DCML and ALS

1. General organization of dorsal column-medial lemniscal (DCML) and anterolateral systems (ALS).

DCML: A single anatomical path that mediates mechanical sensations, including touch, limb position sense, and vibration sense. Role of DCML is very well established both clinically and experimentally. (Historically, syphilis patients often presented with somatic sensory signs including loss of position sense and an inability to stand up with eyes closed, accompanied by degeneration in dorsal column nerves.)

Anterolateral system (ALS): A collection of pathways including the spinothalamic tract, the spinoreticular tract, and the spinomesencephalic tract (tectal tract). Collectively, the ALS mediates protective sensations, including pain, temperature (cold and warmth), and itch. **The role of ALS is not as definitively established as the DCML system for touch because issues involving pain make our understanding of the linkage less complete.** Why? Complications include: experiencing pain without tissue trauma, trauma without pain, and cultural and pathological variability involving pain recognition. For example Mediterranean cultures more likely to express pain and Northern European are less likely.

Each of the peripheral somatic sensory receptors is sensitive to different stimulus qualities. These different receptor classes provide input into the two different systems (ALS vs. DCML) and these two systems feed into distinct thalamocortical systems to mediate our perceptions.

Crude Touch – if the DCML is damaged. You still have a some touch sensation. Not clear exactly how.

Overview of pathways for touch and pain:

(Look at slide for general overview) The **DCML** is a **three neuron chain** that links the periphery with the cerebral cortex. The first neuron in the chain is a sensory receptor neuron, and in the DCML system this input comes from a special class of receptors called mechanoreceptors whose cell body resides in a dorsal root ganglion. This axon projects into the CNS where a small branch terminates in the spinal cord, but the principal branch extends up through the spinal cord in a pathway called the dorsal

column and synapses on neurons in the medulla called dorsal column nuclei. The secondary neuron's axon then crosses the midline and ascends in a brainstem pathway called the medial lemniscus. The third neuron is in the ventral posterior nucleus of the thalamus and its axon projects to the primary sensory cortex in the postcentral gyrus in the parietal lobe.

The anterolateral system is also a **three neuron system**, but several subtle differences turn out to be important clinically. The primary neuron (sensitive to pain, touch, thermal sensations, and itch) is a nociceptor (first difference relative to DCML). The cell body is also in the dorsal root ganglion but the axon terminates in the spinal cord (second difference). This axon synapses on neurons in the spinal cord in the dorsal horn. The secondary neuron crosses over and ascends to the brain in one of several tracts. The spinoreticular (attention) and mesencephalic tracts project to the reticular formation and midbrain and the spinothalamic (perception) tract projects to several locations in the thalamus. One of these projections is to the ventral posterior nucleus, part of which contains neurons that project to the primary somatic sensory cortex just like the touch pathway and is believed to be involved in the localization of pain. Another part of the ventral posterior nucleus sends axons to the insular cortex for the pain representation in the brain. There is also an additional termination site in the thalamus that projects to the medial dorsal nucleus which is the largest thalamic nucleus in humans. This nucleus projects widely throughout the cortex but the pain aspect of this nucleus projects selectively to the cingulate cortex, which is part of the limbic system, and leads us to believe that that part of the projection is involved in the *emotional content of pain*. **All three of these tracts make up the anterolateral system and current thinking incorporates all of the tracts as a unit despite the fact that each of the systems has subtly different roles to play in our behavioral responses to pain.**

2. Peripheral somatic sensory receptors

Dorsal root ganglion neuron: mechanoreceptors vs. nociceptors. Mechanoreceptors have a complex connective tissue capsule surrounding them. Examples: **Meissner's corpuscle, Pacinian corpuscle, or Merkel's receptors**. Details are not important but need to know that there are different kinds. Nociceptors (as well as thermoreceptors and itch receptors) are bare nerve endings. The Dorsal root ganglion neuron in both cases is a huge neuron (it can be up to a meter long and rival pyramidal neurons in the cortex) with receptive, integrative, conductive (myelinated), and output segments. One neuron that does the job of many.

Two key characteristics of the DRG are highlighted because characteristics of these receptors set the stage for all processing of the central nervous system.

(1) **Receptive field organization:** The most important feature of DRG neurons is the **peripheral receptive field**, which is the spatial area within which stimulation activates the sensory neuron. It acts as the interface between the brain and what is going on in the periphery. The terminations of the receptor and their locations determine how large the receptive field of a given DRG will be. These neurons converge on neurons in the CNS which confers a receptive field to these secondary neurons as well. As a result

of this convergence, the receptive field of the neuron in the CNS may be larger, and can even be as large as the sum of the receptive fields of the primary (relay) neurons which synapse onto the CNS (secondary, or “projection”) neuron.

(2) Response to a constant stimulation: **adaptation**. The example given involved touching a probe to the skin and using a recording electrode to record the resulting action potentials. The timing of the action potentials is of more interest experimentally than waveforms or overall shape of the curve, therefore the action potential is now registered as a vertical line rather than a waveform. Experimental results show that slowly adapting receptors (which can recognize the continuity of a signaling event) are a minority in humans and **rapidly adapting receptors that sense salient changes are far more common**.

Note: Most neurons in the PNS have a constant “background” activity even when they are not being stimulated.

Mechanoreceptors and their receptive fields:

Rapidly adapting mechanoreceptors include Meissner’s (tiny receptive field at junction of dermis and epidermis) and Pacinian receptors (very large receptive field with a “hot spot” in the center. Most sensitive mechanoreceptor in body and responds to 500 angstrom displacement of skin, but has a larger receptive field as a consequence), while Merkel (small field) and Ruffini (large receptive field = more sensitive) receptors are slowly adapting receptors. The primary objective of mechanoreceptors is to identify objects that we touch and the smallness of the receptive field is an important feature for resolving objects. The smaller the receptive field, the greater is the resolving capability of the system.

Nociceptors: Bare nerve endings have a special receptive field but their response to noxious stimuli is more important. A blunt probe triggers no action potential in a nociceptive nerve when placed in the receptive field (even at very high pressures) because the stimulus is not noxious. However, a noxious stimulus such as a pinprick or serrated forceps will trigger a large response even when very little force is applied. (Note: noxious means that the stimulus causes tissue trauma or damage.) In other words, nociceptors respond selectively and vigorously to stimuli that are damaging to the skin.

Peripheral nerves: axonal diameters and action potential conduction velocities

To get into the CNS an impulse signal must travel through a peripheral nerve which may be a large myelinated, small myelinated, or unmyelinated nerve. The distribution of diameters of neurons and myelin sheathing in the PNS is not random, but rather falls into discrete categories. For instance, if we examine a sensory nerve and sum the number of axons that have a particular diameter in a histogram, there are three distinct categories. The largest, medium, and smallest (unmyelinated) fibers each have a separate “bump” on the histogram. However, when examining a nerve that innervates a muscle, but still has sensory fibers and provides information about stretch of the muscle and noxious input, one finds an additional bump. The two biggest bumps are generated by

mechanoreceptors which have the largest fibers. Muscle spindle receptors have the largest diameter in muscle, are involved in the knee jerk reflex, and are referred to as Group I or A-alpha fibers. Group II (A-beta) fibers are smaller-diameter myelinated fibers and are also mechanoreceptors such as Meissner's and Pacinian corpuscles. The smaller (Group III and IV or "delta") fibers link up with bare nerve endings and are involved in protective functions.

To review: There are two functional classes of receptors: mechano vs. nociceptors, two morphological classes: encapsulated vs. bare, and also large vs. small diameter neurons. Each of the two clear-cut categories feeds into one of the two different neural systems to mediate somatic sensation.

4. Dermatomes and dermatomal overlap:

Nerves enter the spinal cord with sensory nerves traveling dorsally and motor nerves exiting ventrally. Dorsal roots have a very systematic organization which results in dermatomes: areas of skin innervated by all of the neurons within a given dorsal root. This allows clinicians to link problems peripherally with a specific dorsal root. An important characteristic of dermatomes is that they overlap one another by quite a lot, but pain dermatomes overlap less than touch. For example, mechanoreceptor overlap is probably complete and results in no sensory impairment due to loss of a single dorsal root.

5. Central projections of primary afferent fibers (DRG neurons)

A given axon can do one of two things, it can either send an axon into the grey matter as a termination or send an axon to a part of the white matter where the axon will travel up the spinal cord toward the brain. A given DRG neuron will have many axon branches once it enters the spinal cord. The relationship is more complex than most schematic drawings show because mechanoreceptors will terminate within the grey matter as well as projecting within the dorsal columns and nociceptors have dense terminations within the dorsal horn and also have branches that ascend or descend within another part of the white matter.

The dorsal horn of the spinal cord is the primary recipient of sensory information but the ventral horn also gets some direct input through reflexes such as the knee-jerk reflex. The white matter is divided into several quadrants: the dorsal column (ascending mechanoreceptor pathway), the lateral column (ALS system), and the ventral column.

Large diameter fibers: (Group I or II, A-alpha or A-beta) have terminations within deeper portions of the dorsal horn, but the principal portion ascends up to the brain within the dorsal column of the white matter in a very typical way. This method of organization is called somatotopic organization, which defines a set of rules by which connections are made within the somatic sensory system. This setup is referred to as topographic mapping. Demyelination studies from patients with spinal injuries show that ascending axons degenerate as well as their myelin sheaths and progressively rostral

sections through the spinal cord show the demyelinated region compressed medially as **new neurons add on to the spinal cord laterally.**

Small diameter fibers: (pain, itch, and temperature) have their principal termination site in the superficial lamina of the dorsal horn in layers I and II. A portion just outside of the dorsal horn called Lissauer's tract collects branches of the nociceptors and these axon branches travel up and down within the spinal cord. The secondary neurons then cross the midline and ascend up to the brain as mentioned above.

To summarize: there is information coming directly into the dorsal columns and into the ALS system as well. Comparison: different inputs into the system, different first places where synapse occurs, second neuron crosses in both systems, projection is to the thalamus both systems, (the ALS also has projections to the reticular system as well as to the mesencephalon for mediating arousal and orientation to pain.)

Look at slide of ALS vs DCMLS

Ventral posterior nucleus

VP Lateral: input from spinal and medial lemniscal pathway: back of head, limbs and trunk

VP Medial: Input from **trigeminal system:** face, oral cavity The nucleus contains a gradient where information about pain is projected more caudally, while information about touch is projected to the more rostral part of the nucleus. In addition, the pain pathway terminates within two other nuclei: the medial dorsal nucleus (very large) and the ventral medial posterior nucleus (very selective recipient for pain). Info from ventral posterior nucleus for touch travels up to the postcentral gyrus of the somatic sensory cortex and travels through the internal capsule while preserving the somatotopic organization.

8. Primary somatic sensory cortex: (Post Central Gyrus)

Most cortical areas have at least 6 layers. The layers are divided by neuroanatomists based on the density of neurons. Different areas of the cortex have a different layering pattern, which is the basis for numbered areas of the cortex being associated with different functions.

There are four different somatic sensory areas: 1, 2, 3a, and 3b in the post-central gyrus. Receptors from the skin send their information primarily to areas 3b and 1, while information from deeply located receptors such as muscle spindle receptors or Pacinian corpuscles terminate in areas 3a and 1. Information from the thalamus is projected primarily to the middle layers of the cortex (layer 4) and then interneurons in layer 4 feed that information to pyramidal neurons that are located in different layers. Pyramidal neurons whose cell bodies are located in the deep layers can still get direct input because input is transferred to their dendrites which travel closer to the surface of the brain. There is a very specific routing of information, whereby neurons from layer 5 send axons

to sub-cortical areas and those in layer 6 send axons back to the thalamus, and neurons in layers 2 and 3 send their output to other cortical areas.

From the cortex, information is spread widely throughout the brain to create a diversity of function. Information to the secondary somatic sensory cortex is fed into the insular cortex and this pathway is involved in recognizing the shape of objects without looking at them. Input into the posterior parietal cortex is involved in special sense and mixes sensory information with visual sensation to give us a sense of our body's orientation within the world around us. Finally, information from the primary cortex to motor areas of the frontal lobe is involved in movement control dependent on fine sense of touch.

Summary of pain pathways:

Ventral medial posterior nucleus (VMPo): Projects to the insular cortex and may be the key relay for pain in humans. Insular pain representation is more consistently activated in brain imaging studies when subjects receive painful stimuli. Amygdala may be involved in emotional aspects.

Medial dorsal nucleus: Projects to the cingulate gyrus and is involved in the emotional aspects of pain.

Ventral posterior (VPL/VPM): Projects broadly to parietal and frontal lobes of the primary sensory cortex and is involved in arousal.