Somatic Sensory and Pain Structures & Pathways

Laboratory
Wednesday, February 19 - 1:00 pm

"Anatomy without function is uninteresting; function without anatomy is meaningless."
J.E. Rose, ca 1950

Goals:
• Solidify acquaintance with the external features of the spinal cord, brainstem and cerebral hemispheres
• Comprehend the organization of PNS and its relation to CNS with particular reference to somatic sensation
• Clarify the general internal organization of the spinal cord, brainstem, thalmus and cerebral cortex with emphasis on somatic sensation and pain
• Understand the functional organization and topography of the following ascending systems:
•• fine touch and position sense
•• touch, temperature and pain
•• pathways to the cerebellum and brain stem

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USE BRAINS, OVERHEAD PROJECTORS AND COMPOUND MICROSCOPES.
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A. External Structure of Brain

B. Spinal Cord

1. External features, regional variation, blood supply. Review the overall structure of the spinal cord including the **anterior median fissure**, the **dorsolateral sulcus** , the **cervical** and **lumbar enlargements**, and the **filum terminale**. (See Heimer p. XX.) For blood supply review pp. 48-9 in Woolsey. What is the explanation for the enlargements?

2. Segmental organization. Connections to the periphery are "segmented" based on the relation of the spinal nerves to the vertebral column. Review Heimer for appearance; p.8 Woolsey for general scheme.

   a. Spinal nerves. Make sure you understand what a spinal root is.

   b. Peripheral nerves - axon Diameter Distribution **Slides 1 & 2** are osmium tetroxide stained cross-sections of a peripheral motor and sensory nerve respectively. Individual **myelinated fibers** appear as black rings; **unmyelinated fibers** are individually indistinguishable but are located in paler, orange stained areas. How do the two sections differ? Examine the myelinated axons and note the range and density of different size axons. Slide 2 shows examples of peripheral sensory myelinated fibers of all sizes (1 to 20 microns in diameter). Why do myelinated fibers support faster conduction? Why do larger diameter fibers support faster conduction?

c. Spinal roots, dorsal root ganglia and dorsal root entry zone. **Slides 12 and 13** are sections from a cat spinal cord stained for cytoskeleton and cell bodies respectively. These sections show the anatomical relationship between the peripheral **mixed spinal nerve**, **dorsal root ganglion**, **dorsal and ventral roots** and the dorsal root entry zone into the spinal cord.

Figure 1. Microscope slide 13

Study these slides using the 4X lens on your microscope. Use pp. 49, 136-40, 172-3 in Woolsey to guide you.

1) Identify the different levels of the spinal cord from which the sections on these slides were taken. How do you know this?

2) Identify the *gray matter* of the spinal cord (4X). Within the cell zone of the spinal cord find the **dorsal horn, ventral horn and intermediate gray areas**.

3) Identify the *white matter* of the spinal cord (4X). This is divided into three bundles of axons called columns or fasciculi the **dorsal, lateral and anterior columns**. These are made up of myelinated and unmyelinated axons ascending to and descending from other regions of the brain and spinal cord. At the end of this lab review the principal direction of information flow in each of these.

4) Lateral to the spinal cord, identify the dorsal root ganglion, dorsal root and ventral root (4X). Using the 40X lens on your microscope, examine the dorsal root ganglion cells. Neurons have large, round, clear nuclei and a prominent nucleolus. Supporting cells have bean-shaped, dark nuclei that lack a distinct nucleolus. Note the distribution of soma sizes, which roughly correlates with the distribution of different diameter axons in the sensory nerve shown on slide 2. The small, more darkly staining ganglion cells (not to be confused with the much smaller Schwann cell nuclei) support the smallest peripheral fibers (A∂ and C fibers). The largest cells maintain the largest myelinated sensory fibers that innervate muscle spindles and Golgi tendon organs.

5) Using the cytoskeleton stained slide, trace the dorsal root fibers into the spinal

cord. Note that many fibers course medially, directly into the dorsal columns. These are larger diameter fibers that send an ascending branch into the dorsal columns. Collateral branches from these also enter the dorsal horn from its medial aspect. Try to identify these fiber bundles on your section.

6) Identify the dorsolateral sulcus. I Thinner fibers from the dorsal root enter **Lissauer's tract** (a.k.a. dorsolateral tract) at this location. Lissauer's tract appears as a pale, triangular-shaped region that caps the dorsal horn. Some dorsal root A∂ and C fibers ascend or descend several segments within Lissauer's tract before sending collaterals directly into the dorsal horn.

C. Spinal Cord: Internal organization (pp. 136-140 in Woolsey)

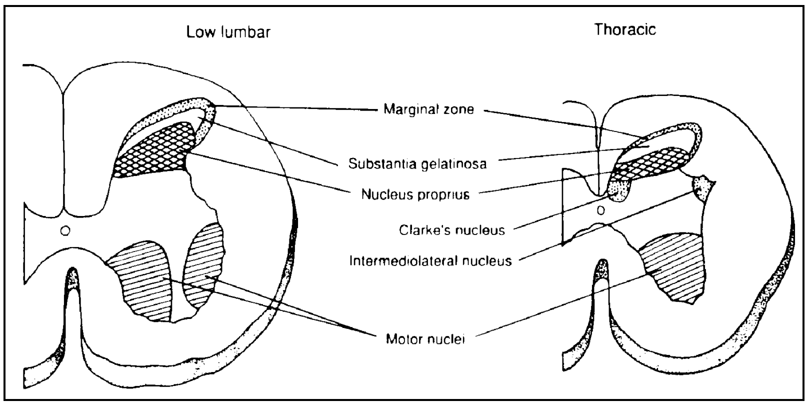

Figure 2. Schematic of divisions of spinal gray matter. (from Kandel, Schwartz & Jessell)

1. Identify the zones of the dorsal horn on **slides 213, 250** with reference to your atlas. The lumbar segments of the cord are often best for this purpose. Note the size and appearance of the cells in different laminae (e.g., the cells of the substantia gelatinosa are small and densely packed, while some of those in the nucleus proprius are large).

2. **Marginal zone**. The thin marginal or posteromarginal layer is composed of large cells whose dendrites are arrayed tangentially within the lamina. The axons from these cells contribute to the spinothalamic tract and other contralateral ascending projections.

3. **Substantia gelatinosa**. Most of the small cells of the substantia gelatinosa (SG) send their axons to other segments of the spinal cord to end within SG of those segments. In addition, axons from SG distribute over the dendrites of the marginal layer neurons. SG is probably the most critical region within the dorsal horn for sensory integration of, especially (but not exclusively), inputs from pain fibers.

4. **Nucleus proprius**. Cells from nucleus proprius contribute to the spinothalamic tract, spinoreticular tract, spinotectal tract, spinocervical tract ascending in the lateral columns.

5. Identify **nucleus dorsalis (a.k.a. Clarke's nucleus)**, which occurs only in thoracic and upper lumbar segments of the cord (L1 - L3). It is an area of large cells found

lateral to the dorsal columns and in the ventral corner of the dorsal horn. The nucleus dorsalis is the origin of the major fiber system that sends information about the status of muscle spindle receptors to the cerebellum: the **dorsal spinocerebellar tract** (pp. 206-7 Woolsey). It is especially large in the upper lumbar segments because this part of the nucleus receives afferent information from all of the lower limb; the nucleus itself is not found below L2 or L3. (Since the nucleus is also not present above T1, another system is required for equivalent input to the cerebellum from the upper limb. The Ia and Ib axons from the arm project through the fasciculus cuneatus of the dorsal columns to the lateral (or external) cuneate nucleus in the lower medulla.) Projections to the cerebellum are ipsilateral (see below).

6. Identify **motor neurons** in the anterior horn of the spinal cord. They are clustered into groups called motor nuclei. What is the significance of this pattern? Are there differences between the groupings and sizes of motor neurons in relation to spinal level? If so, why? The motor neurons are divisible into 2 groups larger α motor neurons and smaller γ motor neurons that supply the work mucles and the muscles of muscle spindles respectively. How does this correlate with axons seen in slide 1?

7. Identify **intermediolateral** cells in the thoracic spinal cord. What is there function and where do their axons travel?

D. Spinal Cord Ascending Somatic Pathways.

1. Identify the segments containing both **dorsal column fasciculi: gracilis and cuneatus**. At what level does the fasciculus cuneatus first appear?

2. Variations by level: The cross-sectional shape of the spinal cord varies at different levels. The size of the dorsal and ventral horns is larger in the cervical and lumbo-sacral regions (approximately C3 to T1 and L1 to S2, respectively) due to the greater number of cells devoted to the innervation of the upper and lower limbs. Both the sensory (dorsal) and motor (ventral) horns enlarge. Some cell groups are found only in restricted parts of the cord. The most notable of these is the intermediolateral cell column (lateral horn), which contains preganglionic sympathetic neurons (restricted to T1 to L2) and preganglionic parasympathetic neurons (S2 to S4), and the nucleus dorsalis (T1 to L3). The ratio of white matter (myelinated axons) to gray matter (cells and cellular processes) is much greater in the upper (e.g., cervical) segments than in the lower (e.g., sacral) segments of the spinal cord.

3. Identify the following ascending sensory pathways in the white matter: **dorsal columns (dorsal funiculi), containing the gracile and cuneate fasciculi lateral funiculi; lateral funiculi, containing dorsal and ventral spinocerebellar tracts; and the spinothalamic tract**. (pp.184-189 Woolsey)

E. Illustrative Neuropathology

Pathological material helps identify fiber systems because lesions or disease cause degeneration and/or demyelination that show the location of specific tracts.

Figure 3.
Cervical spinal cord from a case of tertiary syphilis (tabes dorsalis).

Slide 21 shows demyelination of the gracile fasciculus in the cervical cord in a patient with tabes dorsalis (syphilis). A manifestation of tertiary syphilis is death of infected dorsal root ganglion cells. Accordingly, the central processes of spinal ganglion cells degenerate. Axonal degeneration distal to the cell soma leads to secondary loss of myelin known as Wallerian degeneration. The infection kills dorsal root ganglia in spinal segments from sacral to lumbar ganglia. Thus, this slide illustrates the medial position of degenerating fibers from lower spinal segments. These contrast with the lateral location of normal fibers from higher segments. This slide provides an example of the "topographic" organization within the dorsal columns.

Slides 22 & 23 contain spinal cord tissue from a patient with subacute combined sclerosis. In this disease demyelination occurs in large diameter axons of the long spinal cord pathways, i.e., the dorsal columns, dorsal spinocerebellar tracts and lateral corticospinal tracts. This condition occurs in pernicious anemia because of severe vitamin B12 deficiency. What happens to conduction in a myelinated axon when a patch of myelin is lost? Why does this happen?

E. General Aspects of the Internal Organization of the Brain Stem

1. Look at the brainstem on you brain specimens and review the external features with reference to the atlas (pp. 40-45 Woolsey). What are the functions of the superior colliculus, inferior colliculus?

2. Referenced structures can be found in on four series of slides with sections through the brainstem: three sets have myelin staining (**slides 51-58, 222-227**) and one set has cell and fiber staining (**301-314**). Use the images in the atlas for identification (pp. 141-154 Woolsey). Lay these sets out in caudal to rostral order to provide alternate views through some levels. In finding the nuclei and fiber tracts noted below, we recommend following sequentially the course of each structure or set of related structures on several adjacent sections.

3. For orientation identify the central canal/ventricle/cerebral aqueduct. Review the general layout of sensory and motor cranial nerves and nuclei as summarized in the atlas (pp. 174-183 Woolsey).

F. Dorsal Column/Meidal Lemniscal System - Brainstem

1. **Dorsal Column Nuclei**. The **medial cuneate and gracile nuclei** are paired structures in the closed medulla and caudal part of the open medulla. The gracile nuclei are slender, singular structures that lie close to the midline (pages 184-185, Woolsey). The medial cuneate nuclei are slightly rostral, and are larger and more lobulated (pages 141-141, Woolsey).

2. **Medial Lemniscus**. The secondary fibers from the dorsal column nuclei cross to the contralateral side and ascend to the thalamusas the medial lemniscus. As these fibers cross to form the medial lemniscus, they arc ventrally and medially to pass underneath the central canal as **internal arcuate fibers** (pages 143-145, Woolsey).

Throughout much of the medulla, the **medial lemniscus** occupies a vertical strip close to the midline, medial to the inferior olivary nucleus and, dorsal to the pyramidal tract (page 142, Woolsey). Sacral to cervical parts of the body, respectively, map onto ventral to dorsal portions of the medial lemniscus. In the caudal pons the bundle flattens across the dorsal surface of the pontine grey (pages 146-149, Woolsey); this orientation persists up through the midbrain (pages 150-154 Woolsey). Upon assuming a horizontal alignment, the sacral representations are lateral, while representations from the face, contributed by the trigeminal system (see below), are medial.

G. Anterolateral System – Brain Stem

The anterolateral system consists of the **spinothalamic, spinoreticular and spinomesencephalic tracts.** From the anterolateral funiculus of the spinal cord, fibers continue through the medulla in the same position. In the closed medulla this tract is lateral to part of the reticular formation known as the lateral reticular nucleus (another cerebellar relay center) (pp. 186-187 Woolsey). In the open medulla, the tract occupies a hilus found dorsal to the bump created by the inferior olivary nucleus. Many fibers in the tract at this point are destined for brainstem targets (e.g., raphe nuclei, periaqueductal grey, and portions of the reticular formation). In the pons the tract is difficult to identify because the middle cerebellar peduncle covers it laterally and fibers associated with the auditory relay nuclei cross through it . In the upper pons the tract adjoins the lateral edge of the medial lemniscus with which it associates until reaching termination targets in the thalamus.

H. Trigeminal System

1. **Spinal Trigeminal Nucleus and Tract** (see pp 188-189 Woolsey). This structure is the caudal extension of a longitudinally arranged trigeminal complex that starts in the pons. It exists in three parts (see below). First order, sensory

projections to this nucleus course in the **spinal tract of the trigeminal nerve**. Identify this fiber tract where it surrounds the lateral boundary of the **spinal trigeminal nucleus**. In the closed medulla the nucleus lies ventrolateral to the medial cuneate nucleus and displays a laminar array of cells that resembles the dorsal horn (Figs. 40-41). Here the spinal trigeminal nucleus is called **subnucleus caudalis** Projections from this nucleus cross the midline to join the spinothalamic tract, while information from peri-oral and oral structures projects bilaterally. These connections convey pain and temperature information from the head and face. Identify the substantia gelatinosa, marginal layer and nucleus proprius regions of subnucleus caudalis. Note the resemblance to the dorsal horn of the spinal cord. At the level of the open medulla the spinal trigeminal nucleus loses its dorsal horn-like lamination and its name changes to subnucleus interpolaris. It contributes crossed and uncrossed connections to the spinothalamic tract. Most of this concerns information from low threshold cutaneous receptors.

2. **Main or Principal Sensory Nucleus of the Trigeminal Nerve** This nucleus exists in the rostral pons. It is located at the level where the superior cerebellar peduncle lines the lateral walls of the 4th ventricle. The ventrolateral tip of this peduncle points toward the nucleus; the middle cerebellar pedunclesurrounds it laterally and ventrally. The nucleus is rostral to the entry point of the trigeminal nerve. Crossed projections from this nucleus add to the medial aspect of the medial lemniscus and convey discriminative touch information from the face and head. Cell groups in the nucleus representing peri- and oral structures send a separate, uncrossed projection to the thalamus. This ipsilateral bundle courses through the dorso-lateral corner of the central tegmentum and only joins the medial lemniscus in the rostral midbrain. Consequently, unilateral infarcts that interrupt the medial lemniscus spare somatosensory sensations from the mouth.

3. **Mesencephalic Trigeminal Nucleus and Tract** This small nucleus first appears at the same level as the principal sensory trigeminal nucleus. It lies between the ependymal lining of the IVth ventricle and the fibers of the superior cerebellar peduncle. A thin, underlying fiber tract, the mesencephalic trigeminal tract, marks its position. This nucleus remains in approximately the same location through the midbrain where its large sensory ganglion-like cells pepper the lateral border of the periaqueductal grey. The nucleus contains displaced sensory ganglion cells that innervate muscle spindle receptors in face musculature.

I. Proprioception to the cerebellum

1. **Spinocerebellar Tract and Inferior Cerebellar Peduncle** The dorsal spinocerebellar tract from nucleus dorsalis (Clarkes' nucleus) in the spinal cord relays proprioceptive information from the lower limb to the cerebellum (pp. 206-207). In the open medulla this tract disappears as a separate structure. The fibers join with the outflow from the lateral cuneate nucleus (see below) to form part of the inferior cerebellar peduncle. The inferior cerebellar peduncle contains projections to the cerebellum from a vast array of brainstem nuclei (e.g., inferior olivary nucleus, vestibular nuclei, various nuclei of the reticular formation, etc.). The ventral spinocerebellar tract parallels that of the spinothalamic tract. Its presence as a separate bundle of axons cannot be detected on your slides.

2. **Lateral (External) Cuneate Nucleus** The lateral nuneate nucleus relays

proprioceptive information from the upper limb to the cerebellum . The major projection joins the ipsilateral **inferior cerebellar peduncle** and a minor projection crosses with the internal arcuate fibers to join the medial lemniscus.

J. Brain Stem Nuclei Implicated in Pain Control Mechanisms

1. **Raphe nuclei (raphe magnus)** These nuclei occupy the midline throughout the center of the brainstem. Serotonergic connections to the brainstem nuclei and spinal cord arise from these nuclei.

2. **Nuclei of the Periaqueductal Grey** This collection of nuclei surrounds the cerebral aqueduct of sylvius in the midbrain. Many of these cells interconnect with the raphe nuclei in a circuit concerned with modulation of sensory signals from pain receptors.

K. Thalamus

1. General aspects of the Thalamus. Study slides **307-312, 221-224.** Use a general diagram such as **XX** in Heimer to review the general organization of the thalamus. It is divided in to distinct nuclei named by position. Recall the location and function of the lateral and medial geniculate nuclei (see pp. 40-45, 155-162, 192-193, 196-197 Woolsey).

2. **Ventral Posterior Medial and Lateral Nuclei** (VPM and VPL of the thalamus). These nuclei appear in the ventral and posterior third of the thalamus. They lie close to the junction with the midbrain where the medial lemniscus and spinothalamic (see below) tracts coalesce before entering the thalamus. The ventroposterior nuclei appear more darkly stained than surrounding nuclei in fiber stained sections because of the heavier myelination of incoming axons from the medial lemniscus and spinothalamic tract (pages 160-161 Woolsey). Identify **ventroposterior medial nucleus** for the face (see trigeminal system, below) and **ventroposterior lateral nucleus**for the rest of the body. Fiber bundles separate these nuclei.

L. Cortex

1. Review the principal lobes, gyri and sulci of the cerebral hemisphere (pp. 20-21, 24-25, 36, 37 Woolsey). Locate the central sulcus on your brain's slices (plastic embedded slices). Review the location of the histologically defined areas as described by Brodmann (p.12 Woolsey).

2. Slide 230 has three sections across the central sulcus. What distinguishes precentral (motor) cortex from post central (somatosensory) cortex? Is the cell body pattern in the latter the same all across the postcentral gyrus?

BEFORE LEAVING THIS LABORATORY...

Know the location of the major ascending somatosensory tracts in the brainstem. For each somatosensory tract, know its cells of origin, submodality, topographic organization, and the side of the body represented.

cervical and lumbosacral enlargements
cuneate and gracile nuclei
dorsal and ventral spinocerebellar tracts
dorsal columns (gracile and cuneate fasciculi)
dorsal horn
dorsal root
dorsal root ganglion
dorsal spinocerebellar tract
dorsolateral sulcus
intermediate grey
internal arcuate fibers
lateral (external) cuneate nucleus
lateral funiculi
Lissauer's tract (dorsolateral tract)
main or principal sensory nucleus of the trigeminal nerve
medial lemniscus
mesencephalic trigeminal nucleus and tract
nucleus dorsalis
nucleus proprius
posteromarginal zone
spinal nerve roots
spinal tract of the trigeminal nerve
spinal trigeminal nucleus, subnucleus caudalis
spinothalamic tract
Spinothalamic tract
substantia gelatinosa
ventral horn
ventroposterior lateral nucleus (VPL)
ventroposterior medial nucleus (VPM)