Unit VIII – Problem 1 – Physiology: Sensory Pathway

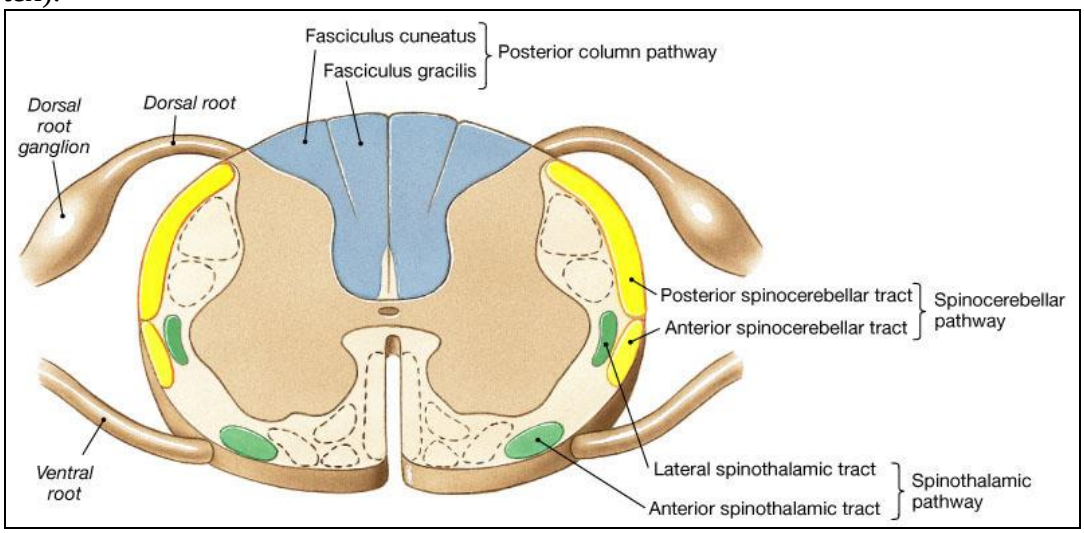
- **Process of sensation:**
  - **Sensory receptors**: they are specialized cells considered as biologic signal transducers which can detect stimuli and convert them to electromagnetic energy known as action potential.
  - **Generator potentials**: sensory fibers are going to detect the stimulus and generate action potential if the stimulus is strong enough. Examples include: free nerve endings and capsulated nerve endings.
  - **Receptor potentials**: sensory fibers cannot detect the stimuli but must be aided by receptors which will detect them and cause the release of neurotransmitters leading to the generation of action potentials.
- **Signal integrity:**
  - **Signal intensity: determined by:**
    - ✓ Spatial summation: stimulation coming from many presynaptic neurons and causing the postsynaptic neuron to reach its threshold and generate action potential.
    - ✓ Temporal summation: repeated stimulations (increased firing frequency) from a single presynaptic neuron causing the postsynaptic neuron to reach its threshold and fire.
- **4 events occurring in sensation:**
  - **Stimulation**: receptors are specific (e.g. Pain receptors will only be stimulated by pain not temperature).
  - **Transduction**: sensory fibers converting different types of energy to electrochemical energy (action potential) which can be understood by the brain. Notice that action potentials can travel for long distances.
  - **Generation**: action potential are going to travel to the brain where there will be:
  - **Integration**: processing of information (determining frequency, intensity… etc).
- **Perception**: it is the conscious awareness and interpretation of sensations (this process occurs in the cerebral cortex). Sensations are going to be connected to previous experiences which happened with the same sensation (if it was experienced before).
- **Receptors: they are divided to:**
  - **Extero-receptors**: which are detecting stimuli from outside of the body. Examples include: hearing, vision, smell, taste, touch, pressure, vibration, temperature and pain.
  - **Intero-receptors**: which are detecting stimuli from inside of the body (not reaching the consciousness level). These receptors are present in blood vessels, visceral organs, muscles and nervous system.
- **Types of receptors:**
  - **Mechanoreceptors.**
  - **Thermoreceptors.**
  - **Nociceptors (pain receptors).**
  - **Photoreceptors (present in rods and cons in retina of the eye).**
  - **Chemoreceptors.**
- **How does the brain know what is the stimulus, where is it coming from and what sensory modality is it (pain, touch, pressure… etc)?**
  - Each receptor has its own special pathway which is going to the brain and this will allow the brain to recognize what modality of sensation is this. Each of these special pathways are going to end in special areas in the cortex indicating to the brain which part of the body is transmitting the stimulus.
- **How does the brain know if the stimulus is moving and in which direction does it move?**

- Specific cells in the cortex of the brain are sensitive for specific movements which are occurring in specific directions.

- **Adaptation**: it is the reduction in the sensitivity to the stimulus when it becomes constant/continuous. Adaptation can be central or peripheral. There are two types of adaptation:
  - **Rapid adaptation**: if the stimulus is pressure, touch or smell.
  - **Slow adaptation**: if the stimulus is pain, body position or chemical levels of different substances in the blood.
- **How does adaptation occur in Pacinian corpuscles?**
  - These corpuscles receive pressure –applied to the skin- in their concentric layers which will transmit the pressure to the nerve fiber –surrounded by these layers- and this will lead to generation of an action potential. If the pressure becomes constant, it is going to be distributed equally to the layers and action potential will diminish (adaptation).
- **Signal transduction**: any stimulus which is causing the entrance of sodium/calcium will lead to depolarization and stimulation of the nerve fiber.
- **Receptive field**: it is the area of skin stimulation of which will be recorded from 1 neuron. There are 2 types of receptive fields:
  - **Small receptive field**: containing small branches of the nerve fiber – precise (example: fingertips).
  - **Large receptive field**: containing extensive branches of the nerve fiber – not precise (eg. If you stimulate 2 points in the same large receptive field this is going to be felt as stimulation of 1 point).
- **Dermatome**: it is the area of skin which is supplied by a spinal segment. It is important for diagnosing certain diseases. The most accurate examination to be done to check for the dermatome is stimulating pain (pain has the less overlap).
  - **Important dermatomes:**
    - ✓ C6: thumb.
    - ✓ C7: middle finger.
    - ✓ C8: little finger.
    - ✓ T4: nipple.
    - ✓ T10: umbilicus.
    - ✓ L3: knee.
    - ✓ L4: medial malleolus.
- **Lumbar puncture**: is done at the level of L3-L4 (in adults) and L4-L5 (in children).
- **Mechanoreceptors:**
  - **All of those which are starting with "M" are superficial:**
    - ✓ Merkel.
    - ✓ Meissner

      Note: the receptive field of these receptors is small.
  - **Deep receptors are**: pacinian and ruffini.
    Note: the receptive field of these receptors is large.
  - **Rapidly adapting receptors are**: corpuscles.
- **RA = rapidly adapting receptors = corpuscle = stimulated by changing pressure.**
  - **RA1 = rapidly adapting superficial = Meissner (fine movements, flutter edge).**
  - **RA2= rapidly adapting deep = pacinian (for vibration).**
- **SA = slowly adapting = stimulated by continuous pressure**
  - **SA1 = slowly adapting superficial = Merkel (for pressure)**
  - **SA2 = slowly adapting deep = ruffini (for stretching)**
- **Stereognozis**: interpretation which occurs in the brain for things touched by the skin while eyes are closed.

- **Reading Braille letters:**
  - A blind person places his finger on the dots → small receptive field will be stimulated → "slowly-adapting receptor (Merkel) will be stimulated"
- **Itch:**
  - There is chemical stimulation of free nerve endings by substances such as: histamine and bradykinin.
  - When something is breaching the skin → chemical irritation is going to be produced → initiating reflex of minor injury → to trigger inflammation.
- **Tickle:**
  - From free nerve endings and pacinian corpuscles.
  - Attempts to tickle oneself (eg. If you try to tickle yourself) is blocked by the cerebellum that's why you don't feel it.
- **1st order neurons**: transmitting information from PNS to CNS.
- **2nd order neurons**: terminating in the thalamus either in:
  - **Ventro-posterior lateral nucleus of the thalamus**: receiving information from the body.
  - **Ventro-posterior medial nucleus of the thalamus**: receiving information from head and neck.
- **3rd order neurons**: from the thalamus to higher centers in the brain (especially the cortex).



- **Medial-lateral rule**: in the dorsal column of the spinal cord, information from lower parts of the body are carried by the medial aspect (f. gracilis) while those coming from upper parts of the body will be carried by the lateral aspect (f. cuneatus).
- **Sensory information are carried through:**
  - **Dorsal column pathway**: for fine touch, vibration, conscious proprioception and 2-point discrimination. These precise sensory input are carried in the dorsal column by large myelinated fibers which do not branch and thus these information will not be lost. In addition, these sensory inputs will be conducted to a large area in the cortex (where a lot of cortical neurons are present which are required for analysis of these precise sensory information).
  - **Spino-thalamic pathway**: which is further subdivided to:
    - ✓ Lateral spino-thalamic tract: conducting pain and temperature.
    - ✓ Anterior spino-thalamic tract: carrying crude touch.

    Notes:
    - ❖ Nerve fibers of the spino-thalamic tract have smaller diameter, less conduction velocity and they are branching to stimulate the reticular formation and thus keeping us aware and conscious about what is going around us.

- ❖ Why are these fibers (of the spino-thalamic tract) not myelinated?
- ❖ Because there is no enough space in the spinal cord + information which are carried by this pathway are not as important as those which are carried by the dorsal column.

- **Spino-cerebellar pathway:**
  - ✓ It is starting at the level of the spinal cord and ending in the cerebellum.
  - ✓ We are not aware of this pathway (it is under the unconscious level) because the fibers are not reaching the cortex.
  - ✓ It is carrying information about the position and state of our body parts (position of muscles, tendons, joints… etc).

- **Dorsal column-medial lemniscus:**
  - **For**: fine touch, vibration, conscious proprioception and 2-point discrimination.
  - The sensory fibers are going to enter the spinal cord through the dorsal root ganglia and dorsal horn.
  - **It has 2 branches:**
    - ✓ Medial branch: ascending up to medulla → crossing → then to thalamus → then to post-central gyrus in the cortex.
    - ✓ Lateral branch: which will ascend to the cerebellum –not under our conscious level- and mediate:
      - ❖ Pain inhibition.
      - ❖ Recognition.
      - ❖ Stretch reflexes.
  - **In the dorsal column of the spinal cord, the medial branch will form:**
    - ✓ Fasciculus gracilis (medially): which is carrying sensory information of fine touch, vibration and conscious proprioception from lower part of the body (T7 and below).
    - ✓ Fasciculus cuneatus (laterally): which is carrying sensory information of fine touch, vibration and conscious proprioception from upper part of the body (T6 and above).

      Note: if lesion occurs in the dorsal column of spinal cord in these fibers before they reach the medulla and cross → loss of sensation will occur in the same side (eg. Lesion in left side of dorsal column, loss of sensation in left side of the body) resulting in:
      - ❖ *Astereognosia*: inability to identify an object by active touch of the hands without other sensory input (eyes are closed).
      - ❖ *Agraphesthesia*: inability to recognize a written number or a letter on the skin (eyes are closed).
      - ❖ *Sensory Ataxia:* tested by Romberg's sign.
  - F. gracilis and F.cuneatus are goint to ascend until they reach medulla oblongata where they will terminate in nucleus gracilis and nucleus cuneatus (termination of 1st order neurons).
  - From n.gracilis and n.cuneatus, 2nd order neurons will be formed, they will cross, and ascend through pons and midbrain until they terminate in the ventro-posterior lateral (VPL) nucleus of the thalamus.
    - ✓ **Note**: if lesion occurs at this level (the level of crossing fibers in the medulla or thalamus) → loss of sensation will occur in the opposite site of the body.
  - From the thalamus, 3rd order neurons will ascend through the posterior limb of internal capsule to terminate in the cerebral cortex (post-central gyrus).

- **Sensations which are transmitted from the face go through the trigeminal system. These sensations include:**
  - Pain and temperature.
  - Conscious proprioception and fine touch.

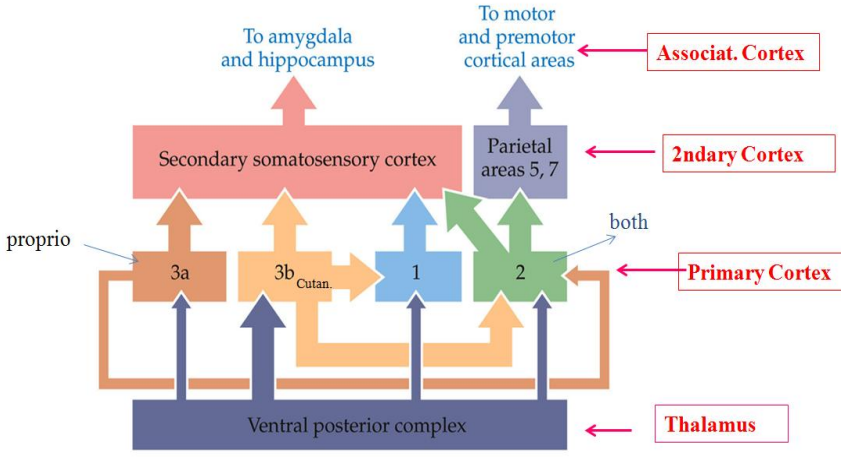
- Unconscious proprioception.

- **In the thalamus there are 2 types of nuclei:**
  - **VPL (ventro-postero-lateral) nucleus**: which is receiving sensory fibers coming from the body.
  - **VPM (ventro-postero-medial) nucleus**: which is receiving sensory fibers coming from head and neck.
- **Those sensations coming from the face will be transmitted to the trigeminal ganglion (in the middle cranial fossa) → and then sensory fibers from trigeminal ganglion will transmit these information to 3 nuclei:**
  - **Principle nucleus**: which will be receiving fibers of fine touch (a lesion in this nucleus will lead to loss of fine touch sensation from the same side of the face).
  - **Spinal nucleus**: which will be receiving fibers of pain and temperature.
  - **Mesencephalic nucleus**: which will be receiving fibers of unconscious proprioception. From there, some fibers will go to the motor nucleus to stimulate stretch reflexes and others will go ipsilaterally to the cerebellum.
- **Unconscious proprioception:**
  - It is occurring in the cerebellum (the cerebellum is coordinating the movement of our body by knowing the position of joints, muscles tendons... etc).
  - Information which are carried to the cerebellum must be transmitted very rapidly. This is why the spinocerebllar tract has only 1 synapse (delay occurs in this synapse).
- **Sensory information from muscle spindles, Golgi tendon organs and joint receptors will enter the spinal cord through the dorsal horn and can have 3 pathways:**
  - **Either going to the dorsal column** → for conscious proprioception.
  - **Going to α-motor neurons** → to stimulate reflexes.
  - **Going to the dorsal spinocerebellar tract by terminating in Clark's nuclei** → for unconscious proprioception.
    - ✓ Clark's nuclei are only present between L2-T1:
      - ❖ *If information are coming from level lower than L2* → fibers are going to ascend with those fibers of conscious proprioception in the dorsal column until they reach the level of L2 where Clark's nuclei are present → and synapse will occur.
      - ❖ *If information are coming from level higher than T1* → fibers are going to ascend with those fibers of conscious proprioception in the dorsal column and then terminate in accessory cuneate nucleus.
    - ✓ Transmission of information in the dorsal spino-cerebellar tract is ipsilateral.
    - ✓ Fibers of dorsal spinocerebellar tract will terminate in the cerebellum through the inferior cerebellar peduncle.
    - ✓ Ventral spinocerebellar tract:
      - ❖ It is crossing the midline of the spinal cord at the level of entry → ascending to reach the cerebellum through the superior cerebellar peduncle → and then re-cross again (the only tract in the CNS which has double-crossing).
    - ✓ Note that ataxia results from:
      - ❖ Any disease which is affecting the spinocerebellar tracts.
      - ❖ Any disease affecting the peduncles or cerebellum.
- **Comparison between conscious and unconscious proprioception:**

	Conscious proprioception	Unconscious propioception
	• Kinesthesia. • Position & vibration sense • Muscle spindles, golgi tendon organs & joint receptors. • Discriminative touch. • Cutaneous mechanoreceptors.	• Golgi tendon organ (Ib nerve fibers) • Muscle spindle (Ia nerve fibers). • Muscle contraction information.

Clinical signs	• Unable to locate limbs in space with eyes closed. • Cannot identify objects by touch alone. • Loss of 2-points discrimination • Inability to perceive vibration. • Unable to stand steadily if eyes are closed and feet close together.	• Uncoordinated movement. • Walk with a wide base. • Stagger. • Fall often.

- **Freidreich's ataxia → it occurs with degeneration of:**
  - Dorsal column.
  - Spino-cerbellar tract.
  - Corticocerebellar tract.
- **The cortex has → a central gyrus**
  - **Pre-central gyrus**: is for motor activity.
  - **Post-central gyrus**: is for sensation.
- **The primary somatosensory cortex is composed of 3 areas:**
  - **Area 2** → for cutaneous stimuli and proprioception.
  - **Areas I & 3b** → for cutaneous stimuli.
  - **Area 3a** → for proprioception.
    Note: most of cutaneous information from the nuclei of the thalamus are terminating in area 3b of the primary somatic sensory cortex (the most serious types of lesion is in this area).
- **The secondary somatosensory cortex is important for recognizing the nature of an object which is felt and fibers from it will go to:**
  - **Amygdala**: for emotional background.
  - **Hippocampus**: for memories.
- **Information from area 2 (in the primary somatosensory cortex) will go to areas 5 & 7 (in the secondary somatosensory cortex) and from there fibers will go to motor and premotor cortical areas. Note that premotor area is the one which is programming the movement. If there is movement incoordination → it means that there might be an injury/lesion in:**
  - Dorsal column.
  - Area 2 in the primary somatosensory cortex.
  - Parietal areas 5 & 7 in the secondary somatosensory cortex.
  - Or in the premotor area.

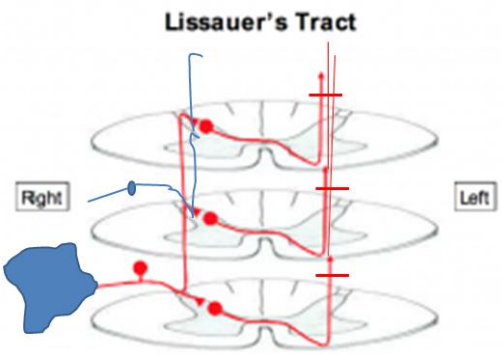


- **Plasticity of adult cortex**: each area in the cortex is specialized to analyze information coming from specific part of the body. Example, if a finger is amputated → area in the cortex which is responsible to receive information from it will be taken by other areas (it will vanish).
- **Spino-thalamic tracts:**
  - **Anterior: which is responsible for transmitting crude touch.**

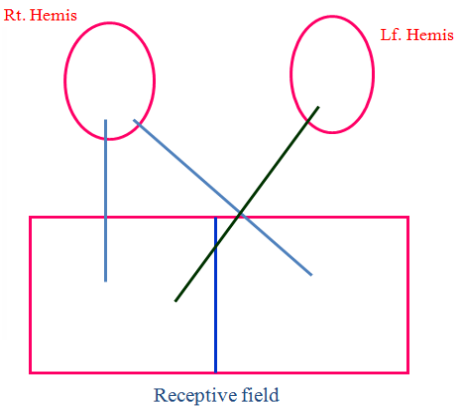
- ✓ 1st order neurons will enter the spinal cord through the dorsal horn and synapse 2-3 segments above the level of entry in the anterior spinal comissure.
- ✓ 2nd order neurons will ascend to reach the VPL nucleus of the thalamus.
- ✓ 3rd order neurons from the thalamus to the post-central gyrus of cerebral cortex.

- **Lateral: which is responsible for transmitting pain and temperature.**
  - ✓ 1st order neurons will enter the spinal cord through the dorsal horn and synapse 1-2 segments above the level of entry to cross the midline of the spinal cord.
  - ✓ 2nd order neurons will ascend to reach the VPL nucleus of the thalamus.
  - ✓ 3rd order neurons from the thalamus to post-central gyrus of cerebral cortex.

Note: lissauer's tract → fibers of lateral spino-thalamic tract which are entering the dorsal horn of the spinal cord will cross the midline and give ascending branch for the upper segment → this ascending branch will enter the upper segment to cross the midline and also gives ascending branch to the upper segment and so on… (this insures that pain sensation will not be lost).



- **Hemispatial neglect:**
  - **The 1st response to any stimulus received by the body is attention → this is mediated by the parietal lobe.**
  - **Lesions of the parietal lobe:**
    - ✓ Right parietal lobe lesion: there will be no attention to the left side of the body and no attention to the left side of surrounding (as this side is not existed at all).
    - ✓ Left parietal lobe lesion: there will still be attention to the right side of the body (because the right side of the body is supplied by both the left and right parietal lobes).



- **Nociceptors:**
  - They are present in: skin, joint capsules, covering of bones and around blood vessels walls.
  - They are tonic receptors (slowly-adapting).
  - There is a central adaptation by which the perception of pain may be decreased through the release of endorphins.
  - Nurotransmitters for pain transmission are: glutamate (fast pain) and substance-P (slow pain).
- **Fibers carrying pain are classified to:**
  - **A-δ fibers**: which are carrying fast pain and cold sensation – they are large and heavily myelinated – their conduction velocity is high (5-30 m/s).
  - **C fibers**: which are carrying slow pain and warmth sensation – they are small and lightly myelinated – their conduction velocity is low (2 m/s). slow pain stays for high duration and is continuous and diffuse (because C-fibers are divergent). Instead, sharp pain is localized, so a withdrawal reflex can happen.
    Note: fibers of pain have high threshold which means that low intensity stimulation will not activate them.

- **A false theory from the past says: that excessive stimulation of mechanical receptors result in pain (eg. Stimulation of thermoreceptors with increased heat will result eventually in pain).**
  - **The truth is**: that when thermoreceptors are stimulated with increased heat they will get activated until they reach a certain point (threshold) where no more activation will occur and instead nociceptors are the ones which will be activated resulting in pain.
- **Receptors of pain are of two types:**
  - Heat receptor.
  - Capsaicin receptor which is present in chilli.
- **Pain is transmitted through the lateral spino-thalamic tract (as it was mentioned previously).**
  - **1st order neurons** will enter the spinal cord through the dorsal horn and synapse to cross the midline of the spinal cord 2-3 segments above.
  - **2nd order neurons will ascend and they can reach:**
    - ✓ The VPL nucleus of thalamus and then to cerebral cortex (for analysis and evaluation).
    - ✓ Reticular formation: for enhancement of alertness.
    - ✓ Cingulated gyrus (limbic system): for connecting physical stimulation to emotional state of pain.
    - ✓ Insular cortex: for autonomic reflexes during pain (tachycardia, sweating, vomiting and breathing).
- **Spino-mesecephalic pathway**: terminated in periaquidactal grey region which is involved in pain control.
- **Pain from the face**: fibers will reach the trigeminal nucleus (spinal nucleus) → they will descend until they reach medulla oblongata → where they will cross → and ascend again to terminate in the VPM nucleus of the thalamus.
  - **A lesion in medulla oblongata will lead to loss of pain sensation from the same side of the face.**
- **Hyperalgesia**: it is increased sensitivity to pain stimuli due to the release of inflammatory substances in the damaged area.
- **Referred pain**: pain in internal organs is referred to a certain area in the skin because they both share the same spinal segment.
- **Visceral pain:**
  - **1st order neurons** will enter the spinal cord through the dorsal horn and reach the intermediate grey matter of the spinal cord where they will synapse.
  - **2nd order neurons** will ascend medially to the fibers of dorsal column until they reach the medulla where they will synapse.
  - **3rd order neurons** will cross in the medulla and ascend to reach VPL nucleus of the thalamus.
  - **4th order neurons** from thalamus to insular cortex.
    Note: midline myelotomy is done to alleviate irresistible cancer visceral pain.
- **Control of pain:**
  - **Gate theory of pain**: pain fibers which are entering the spinal cord through the dorsal horn are going to synapse and stimulate the 2nd order neurons (which will cross the midline of the spinal cord). At the same time, pain fibers will inhibit the inhibitory interneurons and thus pain can be transmitted. If the fibers of the dorsal column are stimulated while someone is having pain → inhibitory interneurons will be activated through collateral branches from the dorsal column fibers → therefore pain will be decreased.
  - **Endogenous opioid system**: enkephalins, endorphins and dynorphins will be released from periaquiduct grey matter.