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Faculty of Medicine

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Physiology Lecture notes

(L1-L12)

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Physiology Lectures Plan

Lectures	Topic	Content	Pages
1	Spinal Cord	Sensory Receptors & Coding of Sensory	2-4
2	Spinal Cord	Somatic sensations/Mechanoreceptive sensations	5-8
3	Spinal Cord	Thermoreceptive sensations/Pain (types, perception, control)	9-12
4	Spinal Cord	Spinal reflexes, Strech reflex (circuit, types, skeletal muscle tone), functions of the stretch reflex.gamma-spindle loop, Functions of stretch reflex.	13-15
5	Spinal Cord	Supraspinal control of stretch reflex, Inverse stretch reflex, alpha versus gamma rigidity, and Polysynaptic reflexes.	16-18
6	Brain stem	-Brain stem (Reticular formation, ARAS functions, factors affecting the activity of ARAS) -UMNL versus LMNL	19-22
7	Cerebellum	Functional division of the cerebellum, connections, cerebellar neuronal circuits.	23-24
8	Cerebellum	Functions of the cerebellum, Neocerebellar syndrome	25-26
9	The limbic system, Basal Ganglia, and diencephalon	Basal ganglia (connections, circuits, function, Parkinsonism) Thalmus (Functions, thalamic syndrome), forms of ataxia, and pattern of motor tremors.	27-30
10	The limbic system, Basal Ganglia, and diencephalon	Hypothalamus, limbic system, types of memory and synaptic plasticity	31-33
11	Cerebral Cortex and Electrical activity of the brain	Electrical activity of the brain, sleep-wakefulness cycle, types of sleep	34-36
12	Cerebral Cortex and Electrical activity of the brain	Mechanism of sleep, sleep abnormalities	37-39

Spinal Cord & Somatic Sensations

Lecture 1

THE SENSORY RECEPTORS

The sensory receptors are specialized structures located at the peripheral ends of sensory afferents) neurons may be a part of the neuron or a separate organ. They are excitable structures since they respond to various forms of energy (i.e., various stimuli) by generating action potentials.

FUNCTIONS OF THE SENSORY RECEPTORS

(I) They act as detectors and transducers: They detect energy changes in both the external and internal environments and transform such changes into action potentials (i.e., nerve impulses).

(2) They inform the CNS about changes occurring inside and outside the body: The nerve impulses generated at the receptors are transmitted to the CNS via afferent neurons. They give rise to various sensations and initiate appropriate reflex actions that maintain homeostasis. Accordingly, the CNS becomes almost useless without receptors.

TYPES & CLASSIFICATION OF SENSORY RECEPTORS ACCORDING TO THE SPECIFICITY OF THE RECEPTORS

(I) Mechanoreceptors: These are stimulated by mechanical forms of energy. Moreover, they include the following:

(a)Touch (or tactile) receptors: These are present in the skin and include free nerve endings, Merkel's disks, Meissner's corpuscles, Pacinian corpuscles, and hair end organs basket endings around hair follicles).

(b)The baroreceptors elsewhere (refer to the cardiovascular system).

(c)The proprioceptors in the muscles, tendons, ligaments, and joints (e.g., the muscle spindles and Golgi tendon organs).

(II) Thermoreceptors: These are stimulated by thermal forms of energy, and those present in the skin are specialized free nerve endings.

(III) Chemoreceptors: These are stimulated by chemical forms of energy, and they include the taste receptors, the smell receptors (in the olfactory mucous membrane), and nociceptors (These are free naked nerve endings that perceive pain sensation).

PROPERTIES OF THE SENSORY RECEPTORS

(1) SPECIFICITY (differential sensitivity): Each type of receptor responds to a specific form of energy called its adequate stimulus and produces a particular sensation. Some receptors can respond to other stimuli called inadequate stimuli, e.g., the retinal receptors' adequate stimulus is light, but they can also be stimulated by mechanical pressure. However, to produce a response. The threshold of such inadequate stimuli must be high, and they produce the same sensation for which the receptor is specialized (i.e., light in the case of retinal receptors).

(2) EXCITABILITY (THE RECEPTOR POTENTIAL): This is the property of responding to stimuli by generating action potentials. It has been studied in certain mechanoreceptors called Pacinian corpuscles. Each corpuscle consists of a sensory nerve ending surrounded by multiple concentric lamellae of connective tissue, and the terminal part of the nerve ending is unmyelinated. In contrast, its remaining part is myelinated, and the first node of Ranvier is present inside the corpuscle. When the corpuscle is not stimulated, the sensory nerve ending is in the polarized state (with a resting membrane potential of about -70 mV). However, if it is stimulated (by applying pressure), the unmyelinated part is partially depolarized due to increased Na influx secondary to Na channel activation. This state of partial depolarization of the sensory nerve ending is called the receptor or generator potential, and its magnitude is proportionate to the intensity of the stimulus.

The receptor potential is passively conducted to the first node of Ranvier (by local circuits of current flow), causing its depolarization. If this reaches the firing level, it initiates an action potential that is propagated along the afferent nerve to the nervous system, and if its magnitude rises above that level (depending on the intensity of the stimulus). the frequency of discharge increases proportionately.

Properties (characteristics) of the receptor potential

a-It does not obey all or none law so that it can be graded.

b- It leads to a propagated action potential reaching the threshold level.

(3) DISCHARGE OF IMPULSES The frequency of discharge of impulses from receptors depends on the intensity of stimulation, which determines the magnitude of the perceived sensation. According to the Weber-Fechner law, it states that " the frequency of discharge from receptors is directly proportional to the logarithm of the intensity of the applied stimuli. However, this law was found to apply only to high intensities of stimulation, and the following power function (known as the power law) expresses the mathematical relation between the intensity of stimulation and the frequency of discharge more accurately: **R = log S x K**

Where R is the sensation felt, S is the intensity of the stimulus, K and A are constants (which vary with each type of sensation).

(4) ADAPTATION

This is a decline in the frequency of discharge of action potentials from receptors on maintained stimulation by stimuli with a constant strength.

According To Adaptation, Receptors Can Be Classified Into:

(1) Rapidly adapting receptors: These are called the phasic (or rate) receptors because their discharge of impulses declines rapidly despite maintained stimulation. They include mainly the touch receptors (especially the Meissner's and Pacinian corpuscles), the rapid adaptation of which is important to avoid unnecessary or excessive sensations that might be irritating (e.g., there is no need for continuous information about the presence of clothes).

(2) Slowly adapting receptors: These are called the tonic receptors because they continue discharging as long as they are stimulated. They include the pain receptors, muscle spindles, and baroreceptors, and slow adaptation is important because the continuous discharge of the pain receptors elicits protective reflexes that prevent tissue damage by noxious agents. In contrast, the muscle spindles continuously inform the CNS about the body posture and position of the limbs, and the baroreceptors are essential to maintaining a normal level of arterial blood pressure.

(3) Moderately adapting receptors: These include the smell and taste receptors and the thermoreceptors (the warmth receptors adapt more rapidly than the cold receptors).

CODING OF SENSORY INFORMATION

This is the ability of the nervous system to identify the modality (= type), locality, and intensity of various sensations. However, all sensations are transmitted from the receptors to the higher centers as action potentials.

(1) MODALITY DISCRIMINATION: The various sensory pathways are discrete (i.e., separate from each other), and the modality of a certain sensation is discriminated at the specific brain area where its pathway terminates. This agrees with **Muller's law of specific nerve energies**. This law states that stimulation of a certain sensory pathway, no matter how or where produces the sensation to which its receptors are specialized. Such effect is also called the **labeled line principle,** i.e., each sensory pathway (from the receptors till the termination at the higher centres) is labeled for a specific sensation (so stimulation of the retinal receptors, whether by light or mechanically by pressure, always produces a light sensation).

(2) LOCALITY DISCRIMINATION: The discrimination of the locality of a certain sensation also depends on the specific pathway of that sensation. When this pathway is stimulated anywhere along its course, the evoked sensation is projected to (i.e., referred to) the location of its receptors. This effect is called **the law of projection,** and it is evident in patients whose limbs are amputated, who may feel severe pain in the phantom limb (i.e., the non-existing limb) due to irritation of the sensory nerves at the site of amputation.

Types classification or

(3) INTENSITY DISCRIMINATION: The discrimination of the intensity of a certain sensation depends on the number of activated receptors and their frequency of discharge as well as on the state of nerve centers (if they are depressed, e.g., due to O2 lack or hypoglycemia, the sensations become dull and their intensity is decreased).

Weber-Fechner principle:

This is a logarithmic function which states that: the perceived sensation is proportional to log intensity of the stimulus.

$$R = \log S \times K$$

R: perceived sensation.

S: stimulus intensity.

K: constant.

This means that 100-fold increase in stimulus intensity, will increase the perceived sensation by 2 times, 1000 fold increase will increase the sensation by 3 times and so forth.

LAWS IN SENSORY PHYSIOLOGY

1. **Muller's Doctrine of specific nerve energies:** No matter where along the nerve pathway one stimulates, the type of sensation will depend on which part of the brain is finally going to be stimulated.
2. **Law of Projection:** No matter where along the nerve pathway one stimulates, the sensation will be felt at the site of the receptor Phantom limb sensation is best described by this law.
3. **Bell-Megendie Law:** This law states that the dorsal root is sensory and ventral root is motor.
4. **Labelled-line theory:** All the sensations from the different parts of the body travel along specified paths. For example, in the posterior column, fibers from the lower parts of the body are placed medially.
5. **Weber-Fechner's law:** In 1834, Weber demonstrated that the *sensitivity of a sensory system* to differences in intensity depends on the absolute *strength of the stimuli*. We easily perceive that 1 kg is different from 2 kg, but it is difficult to distinguish 50 kg from 51 kg. Yet both sets differ by 1 kg. This relationship is expressed in the equation now known as:
   - **Weber's law: $\Delta S = K. S$** 舰舰…[where ΔS is the minimal difference in strength between a reference stimulus S and a second stimulus that can be discriminated, and K is a constant.]
   - **Fechner** extended Weber's law to describe the relationship between the stimulus strength (S) and the intensity of the sensation (I) experienced by a subject: **$I = K \log (S/S_0)$**..... [where S_0 is the threshold amplitude of the stimulus and K is a constant.]
   - **Stevens' law** states that: **$I = K (S - S_0)^n$**

Lecture 2

THE SOMATIC SENSATIONS

The various sensations in the body include (1) Somatic sensations (from the skin and deep tissues, e.g., muscles, joints, and bones), (2) Visceral sensations, (3) Special sensations (vision. hearing, smell, taste and equilibrium) (4) Organic sensations (e.g., hunger, thirst, and sexual sensations).

The sensory pathway or axis: The perception of a certain sensation requires that its pathway (or axis) should be intact. A sensory axis includes (I) A receptor, (2) An afferent (or sensory) nerve that transmits the signals to the nervous system (3) A transmitting tract to the higher centres and cortical sensory areas.

The sensory unit and the receptive field:

The sensory unit consists of a single afferent nerve and all its peripheral branches, while ***the receptive field*** is the area supplied by a certain unit. There is a considerable overlap of the receptive fields of neighbouring sensory units. This is evident in the skin in which each spinal nerve innervates a definite area called a dermatome, and that shows marked overlapping.

Recruitment of receptors and sensory units

Threshold (or minimal) stimuli activate only the highly sensitive receptors, leading to a little discharge of impulses. However, as the intensity of stimulation increases, more receptors become activated (= recruitment of receptors), and the higher centers interpret more sensory unit discharge (recruitment of sensory units), which increases the intensity of the sensation.

CLASSIFICATION OF THE SOMATIC SENSATIONS The somatic sensations can be classified in 2 ways:

(A) ACCORDING TO THE SITE OF THE SENSATION

(1) Superficial (or exteroceptive) sensations: These are the skin sensations (pain, touch, and temperature).

(2) Deep sensations These are the sensations from skeletal muscles, tendons, joints, bones, and ligaments, and they include the following types : (a) Proprioceptive sensations: These include the sense of position and the sense of the rate of movement kinaesthetic sensation) (b) Pressure sense (c) Muscle tension sense (d) Muscle sense (= pain elicited by a firm squeeze of skeletal muscles). Sometimes the vibration sense is included in this group.

(3) Combined or synthetic senses: These include stereognosis and the vibration sense (and sometimes tactile discrimination).

(B) ACCORDING TO THE MODALITY OF THE SENSATION

(1) Mechanoreceptive sensations: These include the touch, pressure, vibration, itch, and tickle sensations, as well as muscle tension and proprioceptive sensations.

(2) Thermoreceptive sensations (heat and cold sensations).

(3) Pain sensation.

THE SENSORY PATHWAYS (ASCENDING TRACTS)

Each sensory pathway consists of (1) The afferent nerves, which have their cell bodies in the dorsal root ganglia and terminate at the various laminae of the dorsal horn of the grey matter (2) Second-order neurons that start at the dorsal horns and form bundles called the ascending tracts which terminate at subcortical centers.

Some sensations require third-order neurons that transmit signals to centers in the cerebral cortex. Depending on the position in the spinal cord, there are 2 systems of the ascending tracts called the anterolateral and the dorsal column systems.

THE DORSAL COLUMN SYSTEM

This system includes the gracile and cuneate tracts and the spinocervical tract, consisting mainly of types A-alpha and A-beta nerve fibers. It transmits mainly fine sensations from the same side.

The gracile and cuneate tracts

These tracts transport (1) Fine tactile sensations (tactile Localization and tactile discrimination), (2) Stereognosis and texture of material sensation, (3) Fine pressure and muscle tension sensations, (4) vibration sense, (5) proprioceptive and kinaesthetic sensations. The pathways of these tracts consist of 3 neurons:

First-order neurons: These are mostly type A-beta afferent nerve fibers. They enter the spinal cord and divide into medial and lateral branches. The medial branch turns upwards in the ipsilateral dorsal column and ascends without relay as the gracile and cuneate tracts till relaying at the gracile and cuneate nuclei medulla oblongata.
** The gracile tract carries sensations from the lower part of the body and lies medially in the dorsal column. In contrast, the cuneate tract carries sensations from the upper part of the body lies laterally.
** The neurons that form the lateral branch synapse with neurons in laminae Ill, IV, V, and VI of the dorsal horn from which some fibers reenter the dorsal column and some form the spinocervical and spinocerebellar tracts, while other fibers elicit certain spinal reflexes.
Second-order neurons: These start at the gracile and cuneate nuclei in the medulla, cross in the sensory decussation to the opposite side (in which the fibers are called the internal arcuate fibers), then ascend as the medial lemniscus, and finally, they terminate at the thalamus in the VPLN.
Third-order neurons start at the thalamic VPLN and terminate at the cortical sensory areas in the postcentral gyrus.

(A) THE ANTEROLATERAL SYSTEM:

This system consists of the lateral and ventral spinothalamic tracts, mainly consisting of types A-delta and C nerve fibers. These tracts conduct signals from the opposite side, and their fibers are arranged in the spinal cord, with the fibres from the sacral region being the most superficial while those from the cervical region are the deepest.

The ventral (anterior) spinothalamic tract

This tract transports crude touch pressure as well as the itch-tickle sensations. Its pathway consists of the following 3 neurons:
First-order neurons: These are A-delta and C afferent nerve fibers. They enter the spinal cord via the dorsal roots and terminate in the dorsal horn's upper 4 laminae, especially at the main sensory nucleus.
Second-order neurons: These constitute the tract. They start in the dorsal horn, cross to the opposite side, ascend in the anterior column of the spinal cord, and terminate in the ventrobasal thalamic complex, especially at the ventral posterolateral nucleus.
Third-order neurons start in the thalamus, pass in the sensory (thalamic) radiation in the posterior limb of the internal capsule, and terminate at the cortical sensory areas in the postcentral gyrus.

***THE LATERAL SPINOTHALAMIC TRACT**

This tract transmits pain, thermal and sexual sensations. It consists of 2 tracts which are the following:
(1) The paleo-spinothalamic tract: This tract transports slow pain and crude thermoreceptive sensations. Its pathway consists of the following 2 neurons:
First-order neurons: These mainly type C afferent nerve fibers. They enter the spinal cord via the dorsal roots, ascend or descend a few segments in the Lissauer's tract, and then terminate in the upper 3 laminae of the dorsal horn, especially at the substantia gelatinosa of Rolandi (= SGR), which occupies lamina II and part of lamina III.
Second-order neurons: They start at the SGR, cross to the opposite side close to the central canal, ascend in the lateral column of the spinal cord, and terminate at the following sites (where the transported sensations are perceived): The reticular formation, the periaqueductal grey area in the midbrain and the nonspecific thalamic nuclei (especially the intralaminar nuclei) in addition to other subcortical centers.
(2) The neo-spinothalamic tract: This tract transports fast pain and fine thermoreceptive sensations. Its pathway consists of the following 3 neurons:
First-order neurons: These are mainly A-delta afferent nerve fibers. They ascend or descend in the Lissauer's tract and terminate mainly at laminae I and V of the dorsal horn.
Second-order neurons: These constitute the tract. They start at the dorsal horns, cross to the opposite side and ascend in the lateral column of the spinal cord. In the brain stem, they combine with the palaeospinothalamic and ventral spinothalamic tracts forming the spinal lemniscus. These fibers finally terminate at the thalamus.
Third-order neurons are similar to those of the ventral spinothalamic tract (see above).

THE MECHANORECEPTIVE SENSATIONS

(1) TOUCH (TACTILE) SENSATION: There are 2 types of touch (tactile) sensation:
Crude touch: This is a poorly localized gross tactile sensation.

Receptors: Free nerve endings and hair end organs. Afferent nerves: A-delta nerve fibers- Central pathway: Ventral spinothalamic tract.

Testing: By stroking the skin lightly with a piece Of cotton.

Fine touch: This includes tactile Localization and discrimination, stereognosis, and the sense of the texture of the material. Receptors: Meissner's corpuscles and Merkel's disks.

Afferent nerves: A-beta nerve fibers. Central pathway: The gracile and cuneate tracts.

Tactile Localization (topognosis): The ability to localize a touched skin point while the eyes are closed. It is tested by touching the skin lightly with a marker pencil (e.g., a charcoal pencil), and the subject is asked to touch the stimulated point with another pencil. The closer the 2touch points are to each other, the more accurate the Localization is.

Tactile Discrimination (T.D. or 2-point discrimination): T.D. is the ability to distinguish 2 touch stimuli applied simultaneously to the skin as 2 separate points of touch. It is tested by repeated touching the skin with the 2 blunt points of a Weber compass, starting with a closed compass, then increasing the distance between its limbs gradually till finding the 2-point threshold (i.e., the minimal distance at which the 2 points are separately perceived). It is a highly educated cortical sensation that requires the excitation of 2 separate receptors and 2 separate areas in the sensory cortex. Accordingly, it is more accurate (i.e., the 2-point threshold is small) in areas that are rich in receptors and their representation in the sensory cortex is wide such as the lips and fingers (e.g., it is only about 2 mm in the fingers) while it is less acute (i.e., the 2-point threshold is large) in areas lacking these characteristics such as the shoulders, thighs, and back (e.g., it is 65 mm or more in the back).

Important

Two-point Discrimination:

- 1 mm on the fingertips of young adults; by the sixth or seventh decade of life it declines on average to ~ 2 mm.
  - **Receptor: *Merkel cell*>>*Meissner's*** corpuscle (as Merkel cell has the smallest receptive field).
- Braille Reading: For blind person, **Braille** dots (spaced ~ 3 mm apart) are perceived as separate dot because of **Merkel cell**. Meissner's corpuscle also contributes to detection of Braille patterns because they sense motion.

Stereognosis: This is the ability to recognize the nature of objects by handling them without using vision (from their shapes, sizes, weights, etc.). It is tested by giving the subject a familiar object (e.g., a key, pen, or coin), and with closed eyes, he is asked to recognize its nature. It is a highly educated cortical sensation that depends mainly on the tactile and pressure sensations and the integrity of the high cortical sensory centers.

The sense of the texture of the material is a type of stereognosis. It is the sensation evoked by touching materials and is concerned with identifying their natures. It is tested by asking the subject to differentiate between various materials, e.g., pieces made of silk, wool, or cotton.

(**2) THE PRESSURE SENSATION**: This sensation is perceived mainly by the Pacinian corpuscles and Ruffini's endings in the skin (for light pressure) and subcutaneous tissues. It is tested by asking the subject to differentiate between various weights without lifting them (by placing them in his hand while it is supported on a table). There are 2 types of pressure sensation like touch: fine (which is transmitted by the gracile and cuneate tracts) and crude (which is also transmitted by the ventral spinothalamic tract).

The muscle tension sensation is evoked by traction on the tendons and is concerned with discrimination or weights while lifting them. Its receptors are the Golgi tendon organs transmitted by the gracile and cuneate tracts. It is tested by asking the subject to differentiate between various weights placed in his unsupported hand.

(3) THE VIBRATION SENSE: This is the sense of buzzing (or thrill) felt when the base of a vibrating tuning fork is placed on the skin. During testing, it is better to place the tuning fork on a bony prominence, e.g., the lower end of the radius bone or one of the malleoli, because bone magnifies the sense of vibration. It is produced as a result of rhythmic pressure stimuli (which is interpreted as vibration) that stimulate 2 types of rapidly adapting mechanoreceptors (a) Meissner's corpuscles, which respond to vibrations up to 80 Hertz: (b) Pacinian corpuscles, which respond to vibrations up to 800 Hertz

Vibration is closely related to proprioception. The gracile and cuneate tracts transmit both, and both are impaired if these tracts degenerate.

(4) THE TICKLE AND ITCH SENSATIONS: A tickle is a pleasurable sensation (often causing laughing) that results from mild tactile stimulation of the skin, while an itch is an annoying sensation that results from skin irritation by moving tactile stimuli (e.g., a crawling flea).

Receptors: Rapidly adapting free nerve endings. Afferent nerves: Unmyelinated type C nerve fibers.

Central pathway: Ventral spinothalamic tract.

Itch often initiates the scratch reflex, which helps remove the stimulus and initiates pain signals that help suppress this sensation.

(**5) THE PROPRIOCEPTIVE SENSATIONS:** These sensations arise mainly from receptors in the deep structures, especially the muscles & joints) including the muscle spindles and Golgi tendon organ-like receptors. They are transmitted to the high centers by the gracile and cuneate tracts and include 2 types:

(a) Sense of position (static proprioception) This is the conscious perception of the position of different body parts with respect to each other. It is tested by placing one of the patient's limbs, toes, or fingers in an unusual position (with his eyes closed) and asking him to place the corresponding part on the other side in a similar position.

(b) Sense of movement (dynamic proprioception): This is the sensation of movement of joints. It is tested by moving one of the patient's fingers or toes passively (i.e., by the examiner) while his eyes are closed and asking him to determine the start and end of the movement and its rate and direction.

** Both types of proprioception are frequently called kinaesthetic sensations (although only the dynamic type is kinetic).

Lecture 3

THE THERMORECEPTIVE SENSATIONS

THE THERMORECEPTORS: There are 2 types of thermoreceptors *(1) Internal thermoreceptors* located in the anterior hypothalamus for detection of the head temperature *(2) External thermoreceptors*: These include cold and warmth receptors and also certain pain receptors that are stimulated only by extreme degrees of heat and cold (leading to the freezing cold and burning hot sensations). These receptors are located under the epithelial layer of the skin, and there are discrete cold and warmth sensitive spots (with thermally insensitive areas in between), and the cold spots are 4-10 times more in number.

THE WARMTH RECEPTORS are special free nerve endings that transmit warmth sensation along with type C afferent nerve fibers.

THE COLD RECEPTORS: They are free nerve endings transmitting cold sensation along type C and type A-delta nerve fibers.

The thermosensitive pain receptors are brought into action below 10^{o} C and above 45^{o}C.

Stimulation of the thermoreceptors is stimulated chemically by changes in their metabolic rates produced by the thermal stimuli.

Adaptation of the cutaneous thermoreceptors: These receptors are moderately adapting, and the warmth receptors adapt more rapidly than the cold receptors.

Central pathway of thermal sensations: the lateral spinothalamic tract.

Testing thermal sensations: This is carried out by touching the skin with the end of a metal tube that is electrically heated in a controlled manner, and the subject with closed eyes is asked to differentiate between various temperatures. Test tubes containing hot and cold water at different temperatures can also be used

PAIN SENSATION: Pain is a specific unpleasant sensation, but its adequate stimulus is not specific (produced by any noxious stimulus, whether mechanical, thermal or chemical. It has a protective function and is almost non-adapting.

Pain receptors (the nociceptors) are specific naked free nerve endings. They are more abundant in the skin than in the deep tissues and viscera, and they are stimulated mainly chemically by substances released from damaged tissue, especially bradykinin and certain proteolytic enzymes.

Actually, nociceptors are ion channel, which are called Transient Receptor Potential channel (TRP).

All TRP channels are gated by temperature and various chemical ligands, but different types respond to different temperature ranges and have different activation thresholds. At least six types of TRP receptors have been identified in sensory neurons.

Fast and slow pain: According to its site, pain may be classified into cutaneous, deep, and visceral pain. However, it is more frequently divided into fast and slow types.

	FAST PAIN	**SLOW PAIN**
Site (origin)	Almost only in the skin	Skin. deep tissues and viscera
Stimulus	Mainly the mechanical and thermal noxious stimuli	Mechanical, thermal, and chemical. noxious stimuli
Quality	Pricking (sharp or acute)	Burning (aching or chronic)
Perception	0.1 second after stimulation	second or more after stimulation
Duration	Less than one second	Many seconds to a few minutes
Localization	Well-localized	Diffuse (poorly-localized)
Afferent nerve	Type A-delta nerve fibers which release glutamate	Type C nerve fibers which release substance P
Carrying tract	Neospinothalamic tract	Paleospinothalamic tract
Centre in CNS	Cerebral cortex	Reticular formation & thalamus

Central perception of pain sensation

Pain sensation is transmitted to the higher centers by the lateral spinothalamic tract, which consists of 2 parts

(l) Palaeospinothalamic tract transmits slow pain and terminates subcortically, especially at the reticular formation and the intralaminar thalamic nuclei.

*(2) Neospinothalamic tract:*transmits fast pain, and its fibers relay first in the ventrobasal complex of the thalamus, then finally terminate at the cortical somatic sensory areas.

Removal of the cortical somatic sensory areas does not abolish the perception of both types of pain. This indicates that pain is generally perceived mainly at a subcortical level (in the thalamus, reticular formation, and other lower centers). However, the cortical centers are essential for interpreting the quality and locality of pain.

CUTANEOUS PAIN: This may be fast, well-localized, pricking, or slow, diffuse burning pain. It is not referred to and is tested by either pricking the skin with a pin or heating the subject's skin and recording the temperature at which pain occurs.

CUTANEOUS HYPERALGESIA: This is pathological hypersensitivity to pain. It is of 2 types:

(I) Primary hyperalgesia: This occurs in the injured skin area and the surrounding area of flare V.D.), in which the pain threshold is lowered so that non-noxious stimuli become painful). It is due to sensitization of the pain receptors by some substances released from the damaged tissues (histamine, kinins, K, certain enzymes, or prostaglandins). It has also been suggested to be due to the release of substance P from nerve endings due to a local axon reflex through antidromic impulses, which sensitizes the pain nerve endings and produces V.D. (i.e. flare), the triple response.

(2) Secondary hyperalgesia: This occurs in the healthy skin area beyond primary hyperalgesia. The pain threshold is not lowered in this area but is normal or even elevated. However, the pain aroused from such an area is prolonged and exaggerated. This is explained by the convergence facilitation mechanism, which occurs as follows: The central neurons are facilitated by impulses discharged from the area of injury, and afferent fibers from the area of secondary hyperalgesia converge on the facilitated neurons. Thus the pain aroused in this area becomes exaggerated.

** Secondary hyperalgesia can occur in the absence of primary hyperalgesia if there is central facilitation of sensory transmission. This occurs in certain thalamic and spinal cord lesions.

DEEP PAIN: This originates from muscles, joints, periosteum. It initiates reflex contraction of near muscles

Deep pain may result from trauma to the deep structures, bone fractures, and inflammation, arthritis inflammation of joints) and muscle ischemia.

ISCHEMIC PAIN: This occurs due to either a severe muscle spasm cramp) or occlusive vascular disease. A certain metabolite known as the Lewis P factor causes pain if it accumulates in the muscle. At rest, muscle ischemia causes the liberation of a small amount of this factor (due to damage of some muscle fibers) that can often be washed off, so pain is absent during rest. However, on performing an exercise, the P factor is formed in larger amounts that accumulate in the muscle (due to the impaired blood flow), leading to pain. Thus, ischemic pain appears only after a latent period from the start of exercise. Examples of this pain are (a) Angina pectoris and (b) Intermittent claudication (severe pain in the muscles of the lower limbs during walking that commonly occurs as a result of vascular occlusive disease).

VISCERAL PAIN: Pain is almost the only sensation produced from the viscera (since there are only a few thermal and touch receptors and no proprioceptors in the viscera). Most viscera contain only a few pain receptors, so localized damage does not cause significant pain. However, generalized damage causes significant pain. Also, if a viscus is inflamed, minor stimuli may cause severe pain, a type of primary hyperalgesia. Some viscera are pain insensitive, e.g., the liver tissue, lung alveoli, the visceral layers of the peritoneum, pleura, and pericardium (but the parietal layers of these membranes are very painful).

Characters of visceral pain: It is frequently referred to specific areas in the skin. It is often associated with sweating, nausea, parasympathetic effects (e.g., bradycardia and hypotension), and some somatic effects, e.g., contraction of the near abdominal muscles (known as guarding rigidity).

REFERRED (RADIATING) PAIN: This pain is felt away from its original site. It is most common with visceral pain (deep pain may be referred, but cutaneous pain is not referred). The structure in which pain originates and the structure to which pain is referred develop from the same embryonic segment, and frequently they are far away from each other due to the migration of the various organs during development.

EXAMPLES OF REFERRED PAIN

(I) Pain of an inflamed gall bladder is transmitted by afferent phrenic nerve fibers, so it is usually referred to the tip of the right shoulder.

(2) Cardiac pain is usually referred to the left shoulder and inner side of the left arm (less frequently to the right shoulder or the epigastrium).

(3) Pain from the kidneys and ureters is referred to the testicular region.

(4) Pain of appendicitis is referred to the umbilical region.

MECHANISM OF REFERRED PAIN: The main cause of referred pain is the convergence of peripheral and visceral pain fibers on the same spinothalamic neurons that project to the high centers in the brain (in addition to plasticity in the CNS). It is explained by ***the convergence projection*** mechanism as follows: Pain stimuli from a diseased viscus excite the spinothalamic neurons at a certain segment of the spinal cord, which then discharges to the brain. However, pain is projected to the somatic area from which the sensory nerves enter the same spinal segment. Normally, the brain does not receive signals from the viscera, and it is even unaware of their existence.

HEADACHE

This is a painful sensation at the head that is referred from other structures, and its causes are either intracranial or extracranial in origin.

(A) Intracranial causes of headache

The intracranial pain-sensitive structures include (a) The venous sinuses (b) The blood vessels of the meninges, especially the middle meningeal artery (c) The dura at the base of the brain (d) The tentorium cerebelli.

Irritation of the supra-tentorial pain-sensitive structures initiates signals transmitted by the trigeminal nerve (leading to frontal headache). In contrast, irritation of the infra-tentorial structures initiates signals transmitted by the second cervical nerve (leading to occipital headache).

The brain tissue itself is insensitive, and the commonest causes of intracranial headache include the following :

(l) Meningeal irritation by inflammation (= meningitis), tumours, alcohol, and constipation by toxic products absorbed from the colon (although some authors believe that constipation headache is due to rectal distention).

(2) Lowering of CSF pressure: Removal of only about 20 ml of the CSF by a lumbar puncture needle causes severe headaches, especially in the upright position due to stretching and distortion of the various dural surfaces.

(3) Distention of the intracranial arteries, e.g., fevers, hypertension (which causes throbbing headache), and **migraine.** The latter has a genetic tendency, and it occurs more in females commonly following prolonged tension or emotions. These conditions lead to reflex V.C. of the cerebral arteries, which results in ischemia, followed by intense V.D. that causes the headache.

(B) Extracranial causes of headache

(I) Eye diseases e.g., glaucoma (due to rise of the intraocular pressure) and hypermetropia (due to persistent contraction of the ciliary muscle), which cause retro-orbital or peri-orbital headache.

(2)Teeth diseases associated with toothache.

(3)Sinusitis The headache may be retro-orbital or in the forehead (in case or the frontal sinus) or in the face (in case of the maxillary sinus).

(4) Otitis media and otitis externa.

(5)Prolonged emotions and tension (psychogenic headache) partly due to spasm of the muscles attached to the scalp and occiput.

THE PAIN CONTROL ANALGESIA SYSTEM

This is a specific system that blocks pain transmission in the CNS (Its major constituents include the following:

1. The periventricular nuclei in the hypothalamus.
2. The periaqueductal gray area (PAG) in the midbrain and upper pons.
3. The raphe Magnus nucleus (RMN) in the lower pons and upper medulla.
4. pain inhibitory complex (PIC) in the spinal cord's dorsal horns.

Certain cortical areas are also involved in the pain analgesia system (especially the limbic association areas), and the principal mediators in this system are the opioid peptides (see next).

THE OPIOID PEPTIDES

These are morphine-like neurotransmitters naturally formed in the body (so they are called the own body's morphine). Morphine (the active substance in opium) is a potent analgesic substance that produces its effect by

binding to specific opiate receptors in the nervous system. Similarly, opioid peptides are analgesic substances that act by binding to opiate receptors. The most important opioid peptides include the following:
(1) Enkephalins : These are 2 types, met- enkephalins and leuenkephalin.
(2) Endorphins: There are several types, the commonest of which is beta-endorphin.
(3) Dynorphins are normally present in minute amounts in the CNS.

The opiate receptors

These are 5 types, and they are especially present in the analgesia system and on the central endings of the pain-conducting nerve fibers at the dorsal horns. They can be stimulated both exogenously (by morphine) and endogenously (by the opioid peptides).

Mechanism of pain control by the analgesia system

The Gating Theory: Ronald Melzak and Patrick Wall proposed this theory in 1960.The hypothesis focused on the interaction of neurons in the dorsal horn of the spinal cord (Lamina I to IV).
The analgesia system produces its effect by stimulating the Pain Inhibitory complex (PIC). The PIC consists of short enkephalinergic neurons that terminate on the central endings of the pain-conducting afferent nerves. The released enkephalin is believed to cause both presynaptic and postsynaptic inhibition of incoming type C and type Aδ pain fibers where they synapse inthe dorsal horns.. Pain inhibition by this mechanism occurs through the following 2 pathways:
(A)Peripheral pathway of pain inhibition (spinal inhibition): Collaterals from the thick A-beta nerve fibers that transmit mechanoreceptive sensations directly stimulate the PIC. This explains how pain is relieved by counterirritants, mechanical stimuli (e.g. skin rubbing), and acupuncture (see below). Depending on such a mechanism, severe pain can be relieved by electrical stimulation of the thick sensory nerve fibers.
(B)Central pathway of pain inhibition (supraspinal inhibition): Excitation of the hypothalamic periventricular nuclei or certain cortical areas depresses pain as follows:
(I) The nerve fibers from the hypothalamic or the cortical areas release beta-endorphins, which stimulate the PAG.
(2) The PAG projects enkephalinergic neurons (i.e. neurons that release enkephalin) that stimulate the raphe Magnus nucleus (RMN).
(3) The RMN projects serotonergic neurons (i.e., neurons that release serotonin) that block pain signals by activating the PIC.
It is also probable that the analgesia system can inhibit pain transmission at other points than the PIC, especially at the thalamic intralaminar nuclei and the reticular nuclei in the brain stem.
Stress analgesia: Certain stress conditions are associated with analgesia e.g. during the stress of a battle, severely-wounded soldiers frequently feel no pain till the battle is over. Such analgesia is produced by impulses discharged from the cerebral cortex and hypothalamus, which excite the central pathway of pain inhibition (see above).
Acupuncture: Acupuncture relieves pain by activating the peripheral pathway of pain inhibition and psychogenic excitation of the central pathway. Both mechanisms lead to stimulation of the PIC in the dorsal horns of the spinal cord, which blocks pain transmission by releasing enkephalins (see above).
Transcutaneous electrical nerve stimulation (TENS) activates a complex neuronal network to result in a reduction in pain. At frequencies and intensities used clinically, TENS activates large-diameter afferent fibers.

PROTOPATHIC AND EPICRITIC SENSATIONS

(1) Protopathic (primitive) sensations: These are crude sensations that are perceived at a subcortical level (mainly at the thalamus). They include gross movements ("joints, crude pain and tactile sensations and extremes of temperature.
(2) Epicritic (cortical) sensations: These are fine sensations perceived in the cortical sensory areas, e.g. tactile Localization and discrimination, stereognosis, and fine grades of temperature. These sensations are well localized.

Lecture 4

THE REFLEXES & THEIR PROPERTIES

A reflex can be defined as an involuntary response to a stimulus, and various reflexes are essential for homeostasis. Reflex actions are performed through pathways called reflex arcs. A reflex arc consists of (a) An afferent (or input) neuron which starts at a receptor, (b) One or more (and sometimes no) interneurons, (c) A nerve center, (d) An efferent (or output) neuron, which terminates at an effector organ.

The nerve cell bodies of afferent neurons are located in the dorsal root ganglia. Inter-neurons are present in all reflexes, so they are polysynaptic except the stretch reflex, which is thus monosynaptic, and it is probably the only monosynaptic reflex in the body.

The nerve centers of somatic reflexes are the anterior horn cells (= spinal motor neurons), while the nerve centers of visceral reflexes are the lateral horn cells. Some cranial nerve nuclei are also centers in certain reflexes.

TYPES OF REFLEXES: Reflexes are generally classified into peripheral and central reflexes.

(A) PERIPHERAL REFLEXES

(1) Local axon reflexes (e.g., producing flare of the triple response).

(2) Local enteric reflexes, e.g., those involved in gastrin secretion and intestinal peristaltic movements.

(B) CENTRAL REFLEXES

(l) Conditioned reflexes: These are acquired (i.e., develop by learning) and are integrated in the cerebral cortex.

(2) Unconditioned reflexes: These are inherent (or inborn) i.e. occur without learning, and include (a) Hypothalamic reflexes (regulate many functions e.g. body temperature and water balance) (b) Midbrain reflexes (mediate postural reflexes and most visual reflexes) (c) Medullary reflexes (mediate cardiovascular. respiratory and digestive reflexes) (d) Spinal reflexes which include superficial, deep and visceral reflexes or monosynaptic and polysynaptic.

THE STRETCH REFLEX AND SKELETAL MUSCLE TONE

The stretch reflex is the contraction of a skeletal muscle in response to passive stretch. It is also called the myotatic or muscle spindle reflex (MSR)

Structure of the muscle spindle

Muscle spindles are fusiform stretch receptors present in the fleshy parts of skeletal muscles parallel to the muscle fibers called extrafusal fibers. Each spindle consists of several small muscle fibers called intrafusal fibers enclosed in a connective tissue capsule attached to the sides of the extrafusal fibers. The central parts of these fibers are noncontractile and constitute the receptor areas ol' the spindles. On the other hand, their peripheral parts are contractile, and when they contract, they stretch the central receptor areas. There are 2 types of intrafusal muscle fibers (based on morphology), which are the following:

(I) Nuclear bag fibers: These have a dilated central area filled with nuclei, and there are typically 2 of these fibers per spindle. Functionally there are 2 types of nuclear bag fibers: dynamic that respond to dynamic pattern of stretch and rapidly adapting and static nuclear bag fibers that respond to sustained stretch and are slowly adapting.

(2) Nuclear chain fibers: These also have multiple nuclei, but they are arranged as a chain in the receptor area. They are attached to the sides of the other type, and there are 4-8 of these fibers per spindle.

Innervation (nerve supply) of the muscle spindles

(A) Afferent nerves arising from the spindles:

(1) Type la nerve fibers: These type A alpha fibers are thick (average diameter 17 microns) and rapidly conducting (velocity of conduction meters/second). They arise from the receptor areas of both the nuclear bag and nuclear chain muscle fibers, where their endings wrap around the fibers forming primary endings.

(2) Type Il nerve fibers: These type A-beta fibers are thinner and slower in conduction than the la fibers (average diameter of 8 microns). They arise from secondary endings at the sides of the nuclear chain fibers' primary endings and static nuclear bag fibers.

(B) Efferent nerves supplying the spindles (gamma efferent):

The intrafusal fibbers' peripheral (contractile) parts are supplied by thin myelinated motor nerve fibers called gamma-efferent nerves. These are the axons of small anterior horn cells called the gamma motor neurons, and are 2 types:

(1) Gamma-d (dynamic) fibers supply the dynamic nuclear bag fibers.

(2) Gamma-s (static) fibers supply the nuclear chain fibers and static nuclear bag fibers.

-Nervous pathway of the stretch reflex

Its fast-conducting afferent nerve fibers transmit impulses from the muscle spindles to the CNS. These proceed directly without intervening interneurons to the ventral horns, where they excite the alpha motor neurons that supply the stretched muscle (by releasing glutamate). The alpha motor neurons then transmit impulses to the stretched muscle leading to contraction of its extrafusal fibers.

Therefore, the stretch reflex arc contains only one synapse, and it is probably the only monosynaptic reflex in the body.

Mechanism of stimulation of the muscle spindles: The adequate stimulus for excitation of the muscle spindles is stretch, and this can be produced by either passive stretch of the whole muscle or stimulation of the gamma efferent fibers. The latter causes contraction of the peripheral parts of the intrafusal fibers, which stretches their central parts, and the resulting muscle contraction is said to occur via **a gamma-spindle loop**.

-Function of the muscle spindles

The muscle spindles constitute a feedback mechanism that maintains the muscle length constant. Elongation (stretch) of the muscle excites the muscle spindles, which leads to contraction and shortening of the muscle.

-Responses of the muscle spindles to stretch

(I) Dynamic response: This occurs while the muscle length increases, and it informs the CNS about the rate of muscle length change. It is produced mainly due to a stretch of the dynamic nuclear bag fibers. The response is an increase in the discharge rate from the primary endings in these fibers, followed by a marked decrease when the new length is maintained (because these receptors are rapidly adapting).

(2) Static response: This occurs while muscle stretch is maintained, and it informs the CNS about muscle length changes. It is produced mainly as a result of a stretch of the nuclear chain fibers and static nuclear chain fibers, and the response is an increase in the rate of discharge from the primary and secondary endings in these fibers, which continues as long as the new muscle length is maintained (because these receptors are almost non-adapting).

TYPES OF THE STRETCH REFLEX

(***1) Dynamic stretch reflex:*** This is initiated by a sudden stretch of the muscle, and the response is a brief strong contraction that ends rapidly because it occurs as a result of the dynamic response of the muscle spindles. It is the basis of the tendon jerks.

(2) Static stretch reflex: This is initiated by a steady stretch of the muscle, and the response is a continuous contraction as long as the stretch is maintained because it occurs as a result of the static response of the muscle spindles. It is the basis of skeletal muscle tone.

THE SKELETAL MUSCLE TONE

DEFINITION: The skeletal muscle tone is a state of continuous mild or partial (or subtetanic) contraction of skeletal muscles during rest.

MECHANISM: It is a static type of stretch reflex produced due to a continuous mild stretch of skeletal muscles during rest by the series of elastic elements present in the tendons.

DISTRIBUTION: It is present in all skeletal muscles but especially in the antigravity muscles (because they are subjected to more stretch by the force of gravity). These muscles include (1) Extensors of the lower limbs (2) Flexors of the upper limbs (3) The muscles of the back and back of the neck (4) The elevators of the lower jaw.

FUNCTIONS OF THE SKELETAL MUSCLE TONE

(I) It is essential for the maintenance of an erect posture.

(2) It helps both the venous and lymph return.

(3) The abdominal muscles' tone prevents visceral ptosis.

(4) It is an important source of heat production, so it is markedly increased on exposure to cold.

FUNCTIONS OF THE GAMMA EFFERENT NERVES

Stimulation of these nerves leads to the stretch of the central parts of the muscle spindles, which increases the sensitivity of the muscles to stretch and may result in reflex muscle contraction.

CONTROL OF GAMMA EFFERENT DISCHARGE

The gamma motor neurons are controlled by signals discharged from

(1) Certain supraspinal areas

(2) The skin: Noxious stimulation of the skin increases the gamma efferent discharge to the flexor muscles, which potentiates the withdrawal reflex.

(3) The skeletal muscles: Signals from skeletal muscles also increase the gamma efferent discharge, as shown in the Jendrassik maneuver.

Alpha gamma linkage (or coactivation): Whenever the alpha motor neurons are activated (whether by supraspinal signals or by impulses discharged from skeletal muscles), the gamma motor neurons are activated simultaneously. The role of gamma efferent coactivation is to prevent relaxation of the muscle spindles during extrafusal muscle contraction and maintain them capable of adjusting the alpha motor neuron discharge throughout the movement.

FUNCTIONS OF THE STRETCH REFLEX

(1) Maintenance of the erect posture against the force of gravity: This occurs through producing a strong muscle tone in the antigravity muscles.

(2)Damping (smoothing) function: The signals discharged to a muscle usually have varying intensities, resulting in uncoordinated movements. However, the signals are adjusted through the alpha-gamma linkage to produce smooth movements (= signal averaging).

(3)Increasing muscle contraction power: Due to the alpha-gamma linkage, both the extrafusal and intrafusal fibers contract when a muscle is stimulated. The intrafusal fibers elicit a stretch reflex by the gamma-spindle loop mechanism, which results in a more powerful contraction of the extrafusal fibers (= ***servo-assistant function***).

Lecture 5

HIGHER CONTROL OF THE STRETCH REFLEX

(A) SUPRASPINAL FACILITATORY AREAS

(1) The facilitatorv reticular formation: This is a wide active area that discharges spontaneously by intrinsic activity. It is present mainly in the pons, and its signals reach the spinal cord through the ventral reticulospinal tract. It facilitates the stretch reflex mainly by activating the gamma motor neurons, and almost all other facilitatorv areas stimulate it.

(2)The primary cortical motor area (area 4): This discharges facilitatory signals to the alpha motor neurons through the corticospinal tract.

(3)The vestibular and inferior olivary nuclei: stimulate the facilitatory reticular formation and discharge direct facilitatory signals to the alpha motor neurons through the vestibulospinal and olivospinal tracts.

(4)The caudate nucleus and neocerebellum stimulate the Facilitatory reticular formation and the vestibular and inferior olivary nuclei.

(B)SUPRASPWAL INHIBITORY AREAS

(l)The inhibitory reticular formation: A small inactive area (i.e., no intrinsic activity) is present mainly in the medulla oblongata. Signals from the other inhibitorv areas activate it, and its signals reach the spinal cord through the lateral reticulospinal tract, where they inhibit mainly the gamma motor neurons.

(2)Certain cortical areas: These include mainly the premotor area (= area 6) and area 4 S (= main cortical suppressor area). These areas activate the inhibitory reticular lòrmation both directly and by stimulating the lenticular nucleus of the basal ganglia (see below).

(3)The red nucleus (in the midbrain): This nucleus discharges inhibitory signals to the alpha motor neurons through the rubrospinal tract.

(4)The lenticular (or lentiform) nucleus and paleocerebellum: These activate the inhibitory reticular formation and inhibit the vestibular nucleus.

The main facilitatory tracts are the ventral reticulospinal, the vestibulospinal, and the corticospinal tracts, while the main inhibitory tracts are the lateral reticulospinal and the rubrospinal tracts. The reticulospinal tracts terminate at the gamma motor neurons, while the other tracts terminate at the alpha motor neurons.

GAMMA RIGIDITY AND ALPHA RIGIDITY

	Gamma rigidity (Spasticity)	**Alpha rigidity**
Cause	Increased gamma discharge	Increased alpha discharge
Muscles affected	Antigravity muscles	All muscles
Resistance to movement	Uni-directional	Bi-directional
Type of rigidity	Clasp -knife	Lead- Pipe or cogwheel
Effect of velocity	Increases with velocity	Not velocity-dependent
Tendon jerks	Exaggerated and clonus may also be present	Not necessarily exaggerated
Common diseases	Upper motor neuron lesion	Parkinsonism

THE GOLGI TENDON ORGANS (GTOs)

These are the receptors present in the tendons of skeletal muscles. Each GTO consists of a netlike collection of knobby nerve endings that give rise to thick myelinated type 1b afferent nerve fibers (A type of A alpha fibers).

The GTOs are tension receptors (i.e., they detect muscle tension), and they are stimulated by both passive stretch and active contraction of skeletal muscles. They are slowly adapting and are not under nervous control because they do not receive efferent nerve supply.

Effect of stimulation of the GTOs:

Signals from the GTOs excite inhibitory interneurons called Golgi bottle neurons which produce IPSPs at both the alpha and gamma motor neurons. Therefore, such Golgi tendon reflex is disynaptic and leads to relaxation of the muscle from which it originates.

The main function of the GTOs is the maintenance of constant muscle **tension** by a negative feedback mechanism (i.e., if the muscle tension increases. the GTOs are stimulated, resulting in muscle relaxation and reduction of its tension, and vice versa).

The inverse stretch reflex (autogenic inhibition): This is the reflex relaxation of a muscle in response to excessive stretch. It is an inhibitory reflex that occurs if the muscle tension markedly increases. It is initiated by the excitation of the GTOs and is a protective reaction against the tearing of the muscle or avulsion.

The lengthening reaction (= clasp knife effect)

This reaction is obtained in spastic (or hypertonic) muscles, e.g., in upper motor neuron lesions. It is demonstrated by flexion of a patient's limb at its main joint by means of the examiner e.g., the lower limb at the knee joint. The reaction consists of muscle contraction upon moderate stretch of the quadriceps muscle followed by sudden muscle relaxation upon overstretch, and it occurs as follows: As the limb is flexed, the quadriceps femoris muscle is lengthened (so it is called the lengthening reaction), and resistance is encountered due to contraction of this muscle as a result of the stretch reflex. However, with sustained flexion, the inverse stretch reflex is initiated, so the initial resistance suddenly disappears, and the limb gives up and flexes easily, as occurs during closing a pocket knife (so it is also called the clasp knife effect).

** When the examiner tries to extend the limb after its flexion, he will also initially find resistance, then the limb suddenly gives up and extends easily. This is due to a sequence of stretch and inverse stretch reflexes in the hamstring (flexor) muscles. This effect is sometimes called the shortening reaction (referring to the shortening of the extensor muscles).

THE TENDON JERKS (TENDON REFLEXES)

A tendon jerk is the response of a skeletal muscle to a sudden stretch produced by tapping its tendon sharply and strongly with a medical hammer. It is a dynamic type of stretch reflex, and it consists of rapid muscle contraction followed by rapid relaxation.

	STRETCH REFLEX	INVERSE STRETCH REFLEX
synapses	Monosynaptic	Disynaptic
Receptor	spindles	Golgi tendon organs
Stimulus	Muscle stretch (increased muscle length)	Excessive muscle stretch (increased muscle tension)
Effect	Muscle contraction	Muscle relaxation
Function	Maintenance of erect posture and smoothing movements	It prevents the tearing of tendons during strong muscle contraction

CLONUS

This is alternating rhythmic contractions and relaxations of a muscle in response to sudden maintained stretch. It occurs when the spinal motor neurons are facilitated (particularly in upper motor neuron lesions), which can be demonstrated at both the knee and ankle.

The Polysynaptic Reflexes: They include the following reflexes:

(1)The plantar reflex: Scratching the outer (lateral) edge of the sole by a blunt object (e.g. a key) causes plantar flexion of all toes in normal awake adults and infants more than one year of age. Such response is changed in many conditions into the Babinski's sign, and its centre lies in L5, Sl, and S2 segments of the spinal cord.

(2)The abdominal reflexes Striking the abdominal skin lightly (e.g. by a pin) leads to contraction of the underlying muscles, as indicated by the movement of the umbilicus. They are a type of withdrawal reflex (see below), and their centres lie in the 7th to the 12th thoracic segments of the spinal cord (depending on the stimulation site).

(**3)The cremasteric reflex:** Striking the skin at the medial side of the upper part of the thigh in males causes contraction of the cremasteric muscle and upward retraction of the testis on the same side. It is a type of withdrawal reflex, and its centre lies in the spinal cord's first and second lumbar segments.

(4)The withdrawal (flexor) reflex: This is a protective, powerful reflex (because it inhibits other reflexes occurring at the same time). Noxious stimulation of the skin (e.g. at a limb) leads to contraction of the flexor muscles of that limb and its withdrawal away from the stimulus.

(5)The crossed extensor reflex This is the reflex extension of' a limb during flexion of the other limb due to a withdrawal reflex. It occurs with strong noxious stimuli and is supportive in function.

(6)The positive supporting reflex (reaction): Applying pressure to the sole (e.g. the pressure exerted by the body weight during standing) leads to contraction of both the flexor and extensor muscles of the lower limbs. It is the only reflex that does not obey the principle of reciprocal innervation. Its center extends from the first lumbar segment to the first sacral segment of the spinal cord, and during standing, it renders the lower limbs to act as 2 solid pillars that support the body against gravity.

(7)The scratch reflex: This is initiated by the sensation of itching, particularly caused by multiple tactile stimuli (e.g. the reflex initiated by a crawling insect). It can also be produced experimentally by stimulating the skin with a weak faradic current, and it results in rhythmic scratching movements to remove the irritant stimulus (and sometimes the production of pain, which also relieves the effect of the irritant stimulus).

Lecture 6

Brain Stem

THE RETICULAR FORMATION

This is a network of neurons located in the brain stem, extending upwards to the diencephalon (thalamus. hypothalamus, and subthalamus) and downwards to the upper part of the spinal cord.

Many nuclei and centers are present within its meshes (e.g., the respiratory and cardiac centers. the substantia nigra. and the red, vestibular, and raphe nuclei). It is divided into sensory and motor parts.

(A)THE SENSORY PART OF THE RETICULAR FORMATION

This consists of small neurons with multiple interconnections (which allows for convergence. divergence, and after discharge). It receives a rich sensory input (afferent fibers) from (1) All ascending lemnisci, (2) The visual, auditory, and olfactory nervous pathways, (3) The basal ganglia, (4) The cerebellum, (5) The cerebral cortex (Via corticofugal fibers) (6) The hypothalamus (7) The vestibular apparatus.

(B)THE MOTOR PART OF THE RETICULAR FORMATION

This consists of large neurons that receive signals from the sensory part, and their axons constitute the output (efferent) fibers from the reticular formation. It contains facilitatory and inhibitory parts:

(l) Facilitatory (excitatory) reticular formation:

This is located mainly in the pons. It has an inherent activity, and the axons of its neurons divide into 2 branches:

(a)An ascending branch that excites the cerebral cortex is called the Ascending Reticular Activating System or ARAS.

(b)A descending branch (= Ventral reticulospinal tract) exerts a facilitatory effect on the spinal gamma motor neurons.

(2) Inhibitory reticular formation: This is located mainly in the medulla oblongata. It has no inherent activity, and it descends as the lateral reticulospinal tract, which inhibits the spinal gamma motor neurons.

FUNCTIONS OF THE RETICULAR FORMATION

(1)Control the level of consciousness through the ascending reticular activating system.

(2)Regulation of the stretch reflex and muscle tone through the reticulospinal tracts.

(3)Pain inhibition by the raphe Magnus nucleus.

(4)Control of sleep by 2 specific centers in its meshes (see below)

(5) Control visceral functions (e.g., cardiac activity) by controlling the spinal lateral horn cells.

ASCENDING RETICULAR ACTIVATING SYSTEM ARAS or RAS)

This multineuronal polysynaptic system of nerve fibers originates at the facilitatory reticular formation. Its fibers extend upwards, then some project directly to the cerebral cortex, while the majority relay first at the nonspecific thalamic nuclei, from which other fibers arise and project diffusely to almost all parts of the cerebral cortex. The latter pathway is called the reticulo-thalamo-cortical pathway.

FUNCTIONS OF THE ARAS

The ARAS controls the electric activity of the cerebral cortex and is concerned with consciousness and production of the alert response, so reduction of its activity leads to sleep.

FACTORS THAT AFFECT THE ACTIVITY OF THE ARAS

(A) Factors that increase the ARAS activity

(l) Sensory signals (especially pain).

(2) Signals from the cerebral cortex (via the corticofugal fires) that increase alertness and resist the desire to sleep (e.g., during emotions and voluntary movements).

(3) Certain drugs are called analeptic, e.g., catecholamines, amphetamine, and caffeine.

(**B) Factors that decrease the ARAS activity**

(l) Reduction of signals from the sensory pathways or the cerebral cortex.

(2) Stimulation of the sleep centres.

(3) Extensive damage of the ARAS (e.g., by tumors).

(4) General anesthetic drugs: These drugs lead to unconsciousness by depressing the ARAS activity (inhibiting the synaptic transmission between its neurons).

UPPER and LOWER MOTOR NEURON LESIONS

UMNL results from damage of the cortical motor areas or anywhere along the course of their descending tracts, commonly in the internal capsule due to cerebral hemorrhage or thrombosis. On the other hand, a LMNL results from either damage of the spinal (or cranial) motor neurons by disease (commonly poliomyelitis) or injury of the motor nerves by trauma or disease (e.g. polyneuropathy).

DIFFERENCES BETWEEN UMNL and LMNL

Although both lesions result in paralysis of skeletal muscles, yet each has characteristic manifestations.

(I) Extent of paralysis (widespread in UMNL and localized in LMNL).

(2) Site of paralysis: This is always at the same side in LMNL, but it may be on either side in the case of UMNL e.g. a hemisection or the spinal cord at the cervical region leads to ipsilateral hemiplegia, while a lesion in the internal capsule leads to contralateral hemiplegia.

(3) Recovery: UMNL does not recover because the upper motor neurons cannot regenerate due to the absence of neurolemma. Conversely, LMNL can recover if it is due to injury of' the motor nerves (because these nerves can regenerate due to the presence of neurolemma), but they cannot recover if the motor nerve cells themselves are damaged (e.g. in poliomyelitis).

(4) Muscle tone: In LMNL, there is hypotonia or atonia (i.e. muscle flaccidity) due to interruption of the efferent limb of the stretch reflex.

On the other hand, in UMNL there is hypertonia i.e. muscle spasticity mainly in the antigravity muscles. It is a type of gamma rigidity that shows the lengthening (clasp-knife) reaction. It occurs as a release phenomenon with reversed supraspinal balance on the gamma motor neurons from inhibition to excitation.

(5) Tendon jerks: These are lost in LMNL- and exaggerated in UMNL due to the same causes of hypertonia. Also, clonus often appears in UMNL and is the most diagnostic feature of this lesion.

(6) Superficial reflexes:

(a) The abdominal and cremasteric reflexes are lost in both lesions due to loss ot- pyramidal facilitation in UMNL and interruption of their efferent limbs in LMNL.

(b) The plantar reflex is lost in LMNL, but is modified in UMNI.s and the response becomes dorsiflexion of the big toe and fanning of the other toes (probably due to interruption of the pyramidal and extrapyramidal fibers respectively). Such response is known as the positive Babinski's sign or the plantar extensor reflex. However, this sign may be present in some normal individuals (see below).

(7) Muscle status: Muscle wasting atrophy) occurs rapidly and markedly in LMNL due to degeneration of the motor nerves that supply the muscles. On the other hand, the paralyzed muscles in UMNL are atrophied only after relatively long periods due to disuse atrophy).

(8) Response to electric stimulation: Normally, stimulation of skeletal muscles by Faradic (alternating) currents produces tetanus while their stimulation by Galvanic (direct) currents produces contraction only at the make closing) and break (= opening) of the circuit. whether the cathodal or the anodal electrode was used for stimulation. Therefore. in the latter condition, there are 4 contraction states (1) CCC (= cathodal closing contraction) (2) COC (= cathodal opening contraction) (3) ACC anodal closing contraction) (4) AOC anodal opening contraction). and the strength of contraction was found to be as follows:

CCC > ACC > AOC > COC

In UMNL, the paralyzed muscles respond normally to both currents and their chronaxies are also normal. On the other hand, the response in the case of LMNL is altered and is called the reaction of degeneration.

REACTION OF DEGENERATION (RD)

This is an abnormal response of skeletal muscles to electric stimuli that occurs in LMNL only. It is characterized by:

(l) The chronaxie of the paralyzed muscles is prolonged.

(2) There is no response to Faradic currents.

(3) There is a sluggish (= weak) response to Galvanic currents.

(4) The ACC becomes stronger than the CCC (due to unknown causes).

The RD is one of the manifestations of muscle denervation. The reaction of denervation is the diagnostic feature of LMNL.

*The Babinski's response is a part of the flexor withdrawal reflex and is normally inhibited by the pyramidal tracts (so it becomes positive in UMNL). However, these tracts are non-functioning in some normal subjects, leading to a +ve Babinski's sign in the absence of UMNL. This occurs in:
(l) Infants below one year of age (because the pyramidal tracts are unmyelinated and not completely developed).
(2) Adults during sleep, coma, and anesthesia (because the high cortical centers are depressed in these conditions).

	U M NL	**L M NL**
Extent of paralysis	Widespread	Localized
Site of paralysis	Commonly contralateral	Only ipsilateral
Recovery	No recovery	Occurs if AHC are intact
Muscle tone	Hypertonia	Hypotonia or atonia
Tendon jerks	Exaggerated with clonus	Lost
Superficial reflexes	Lost, + ve Babinski's	Lost
Muscle status	Normal (disuse atrophy in Long-standing cases	Rapid atrophy
Electric stimulation	Normal response	Reaction of degeneration

COMPLETE TRANSACTION OF THE SPINAL CORD
This is fatal if it was above the origin of the phrenic nerve (i.e. above the 3 rd cervical segment) e.g. in hanging due to paralysis of the respiratory muscles. However, at lower levels, patients pass in 3 stages (a) Spinal shock (b) Recovery of spinal reflex activity (c) Failure of spinal reflex activity.

(A) STAGE OF SPINAL SHOCK
The manifestations of this stage include the following:
(l) Loss of all sensations below the level of the lesion.
(2) Quadriplegia or paraplegia (depending on the level of the lesion).
(3)VD below the level lesion due to interruption of the descending fibers from the vasomotor center (may lead to hypotension in severe cases).
(4) Loss of spinal reflex activity below the level of the lesion because the spinal centers at this part become functionless. This causes loss of a- The withdrawal reflex and other superficial reflexes.
(5) Micturition (retention with overflow)
CAUSE (MECHANISM) OF SPINAL SHOCK
Spinal shock is due to the sudden withdrawal of supraspinal facilitation on the spinal alpha motor neurons.
DURATION OF THE SPINAL SHOCK: this varies directly with the degree of encephalization (= degree Of the development of the cerebral cortex). Accordingly. the lower the degree of encephalization, the shorter the duration of the spinal shock will be (e.g. it lasts only a few minutes in frogs and rats, 1-2 hours in dogs and cats, and several days in monkeys). On the other hand, in man (who is maximally encephalized), it lasts 2-6 weeks.

(B) STAGE OF RECOVERY OF SPINAL REFLEX ACTIVITY
After the spinal shock, the spinal centers recover gradually as follows:
(1) The flexor (withdrawal) reflex and Babinski's sign are usually the first responses to reappear, followed by the extensor reflexes e.g. the knee jerk.
(2) The static stretch reflex (muscle tone) recovers resulting in spastic paralysis. It appears first in the flexor muscles (resulting in paraplegia in flexion) then in the extensor muscles a few months later (resulting in paraplegia in extension) accompanied by the positive supporting reaction.
(3) The activity of the spinal vasomotor centers (the lateral horn cells) is restored, leading to V.C., so the arterial blood pressure rises.

(4) Urination: automatic bladder (like in infants)
(5) Appearance of the **MASS REFLEX**: This hyper-reactive spinal reflex response appears after a few months. Mild noxious stimuli applied to the skin below the level of the lesion, resulting in widespread effects including (a) Exaggerated withdrawal of the stimulated part, (b) Urination and defecation, (c) pallor with sweating, and (d) Rise of the arterial blood pressure. It is due to hyperexcitability of the spinal centers accompanied by irradiation of signals in the spinal cord.
** Patients are trained to induce urination or defecation by producing intentional mass reflexes (by striking or pinching the skin of the thigh).
** Spinal recovery and the mass reflex may be attributed to denervation hypersensitivity of the spinal neurons as well as to the growth of new collaterals that constitute additional excitatory endings on the spinal neurons.

(C) STAGE OF FAILURE OF SPINAL REFLEX ACTIVITY

This is a terminal stage that usually results from bad management during the recovery stage. It is often associated with general toxemia due to infection of the bed sores or the urinary tract (and the latter frequently terminates by uremia).

Lecture 7

Cerebellum

Anatomically, the cerebellum (CB) consists of 3 lobes (a) A small anterior lobe (b) A large posterior lobe (c) a floccullonodullar lobe. The anterior and posterior lobes on either side constitute 2 large hemispheres, which are separated by a narrow band called the vermis.
3 pairs of peduncles connect the cerebellum to the brain stem (the superior peduncle to the midbrain. the middle peduncle to the pons, and the inferior peduncle to the medulla oblongata)

FUNCTIONAL DIVISIONS OF THE CB

From the functional point of view, the anterior and posterior lobes are organized along their longitudinal axes, and the CB is divided into 3 parts:
(1) Vestibulocerebellum (= archicerebellum): This is the oldest part of the CB. and it consists mainly of the floccullonodullar lobe.
(2) Spinocerebellum (paleo-cerebellum): This consists of the intermediate zones of the 2 hemispheres and most of the vermis.
(3) Cerebrocerebellum (neo-cerebellum): It consists of the large lateral zones of the 2 hemispheres. The various parts of the body are topographically represented in the CB. The axial parts of the body lie in the vermal part, while the limbs and facial regions lie in the intermediate zones. Also, the body is represented upright in the posterior lobe and upside down in the anterior lobe.

CONNECTIONS OF THE CEREBELLUM

The CB has an external layer of gray matter cerebellar cortex), and an inner layer of white matter. In the latter, there are 3 deep nuclei (a) Dentate nucleus laterally (b) Fastigial nucleus medially (c) Interpositus nucleus (formed of the globose and emboliform nuclei) between the other 2 nuclei.
Both the afferent and efferent connections of the CB pass through the 3 cerebellar peduncles (= CPS). The afferent nerve fibres relay first at the cerebellar cortex then the latter discharges to the deep nuclei from which the efferent nerve fibres originate and leave the CB.

AFFERENT (INPUT) NERVE FIBRES TO THE CB

The CB receives both sensory and motor information as follows:
(A) Through the superior CP, the CB receives fibers from :
I. The tectum of the midbrain (= the superior and inferior colliculi) transmits visual and auditory signals to the CB.
2. The ventral spinocerebellar tract, terminates in the spinocerebellum and informs about the signals that reach the spinal motor neurons from the cortical motor areas (efference copy).
(**B) Through the middle CP, the CB receives few fibres from:** the reticular formation, but mainly fibres from the contralateral motor areas of the cerebral cortex via the cortico-ponto-cerebellar pathway.
(C) Through the inferior CP, the CB receives fibres from:
1. The inferior olivary nucleus.
2. The vestibular apparatus
3. The reticular formation
4. The dorsal spinocerebellar tract, transmits signals from proprioceptors that inform the CB about the performance of movements.

EFFERENT (OUTPUT) NERVE FIBRES FROM THE CB

There are 3 efferent pathways from the 3 parts of the CB:
(A) From the Vestibulocerebellum: Fibres from this part relay at the fastigial nucleus, from which efferent fibres arise and pass through the inferior CP to the vestibular nuclei and reticular formation (then to the spinal motor neurons via the vestibulospinal and reticulospinal tracts).
(B) From the spinocerebellum: Fibres from this part relay at the nucleus Interpositus, from which efferent fibers arise and pass through the superior CP to (1) The opposite ventrolateral thalamic nucleus, then to the

opposite cortical motor areas (2) The red nucleus. then to the spinal cord via the rubrospinal tract (3) The reticular formation in the upper part of the brain stem, then to the spinal cord via the reticulospinal tract.

(C) From the Cerebrocerebellum: Fibres from this part relay at the dentate nucleus, from which efferent fibres arise and pass through the superior CP to the opposite ventrolateral thalamic nucleus, then to the opposite cortical motor areas cerebello-dentato-thalamo-cortical pathway).

Structure of the cerebellar cortex

** Each cerebellar hemisphere is connected to the contralateral cerebral cortex by both afferent and efferent fibers, which constitute a neuronal circuit that starts and ends in the cerebral cortex. This circuit is called the cortico-ponto-cerebello-dentato-thalamo-cortical circuit.

** Since each cerebellar hemisphere controls the contralateral cortical motor areas, then it is clear that the cerebellum exerts its effects mostly on the same side of the body (because almost all fibres of the pyramidal tract cross to the opposite side).

The cerebellar cortex is formed of 3 layers (I) the Molecular layer that contains parallel interconnecting fibers as well as 2 types of cells called basket and stellate cells (2) the Purkinje cell layer (PCs), the axons of which are the only fibres that leave the cerebellar cortex (3) Granule cell layer that contains granular cells.

The afferent fibers entering the CB are divided into 2 groups:

(A) Climbing fibers: These are afferent fibres from the inferior olivary nucleus.

(B) Mossy fibers: These include all other afferent fibres that enter the CB + some fibres from the inferior Olivary nucleus.

The basket and stellate cells cause lateral inhibition of the adjacent PCs which sharpens the output signals from the CB.

FEATURES OF THE CEREBELLAR NEURONAL CIRCUITS

(1) The inhibitory neurons in the CB release GABA while the excitatory neurons release glutamate.

(2) The PCs continuously fire inhibitory signals to the DNCs. However, the excitatory effect of the climbing and mossy fibers on the DNCs normally predominates, so during rest, they continuously fire excitatory signals.

Functions of the mossy fiber circuit

This circuit helps the precise execution of voluntary movements as follows: A copy of the signals discharged from the cortex to perform a certain movement is conducted to the CB via the pontine mossy fibers (the cortico-pontocerebellar pathway). These signals stimulate the DNC's, which discharge excitatory "turn on signals that help initiation of the movement. At the end of the planned movement, the PCs would have been excited by the granule cells. so they send inhibitory "turn off " signals to the DNCs, which thus stop discharging. This mechanism has been called negative feedforward inhibition. and it leads to the relaxation of the muscles (which helps the termination of the movement without overshooting or oscillation).

Functions of the climbing fibre circuit

This circuit is important for learning the CB to perform new patterns of movement. The inferior olivary nucleus receives information about (I) the intended movement (from the motor cortex) and (2) the performed movement (from the contracting muscles). It compares both pieces of information, and if there is a mismatch (which usually occurs when a new pattern of movement is performed for the first time) its firing rate is modified leading to a change in the sensitivity of the PCs. If the new movement is repeated over a period of time. such change in the sensitivity of the PCs (plus other possible cerebellar processes) will learn the CB to perform such movement co-ordinately.

Lecture 8

FUNCTIONS OF THE CEREBELLUM

The cerebellum is concerned with the subconscious control of motor activity. Its functions as well as the involved parts include the following:

(A) CONTROL OF EQUILIBRIUM AND POSTURAL MOVEMENTS

This is the function of the Vestibulocerebellum.

(B) CONTROL OF THE STRETCH REFLEX

The neocerebellum stimulates the stretch reflex and increases the muscle tone, while the spinocerebellum exerts an inhibitory effect. However, normally the facilitatory effect predominates so cerebellar disease often results in hypotonia.

(C) CONTROL OF VOLUNTARY MOVEMENTS

(1) ROLE OF THE SPINOCEREBELLUM

(I) Comparing function: When a movement is performed, the spinocerebellum receives 2 information (a) Signals from the motor cortex via the cortico-ponto-cerebellar pathway) that inform about the intended plan of movement afference copy) (b) Feedback signals from the periphery (via the spinocerebellar tracts). The ventral tract informs about the cortical signals that reach the spinal motor neurons (= efference copy) while the dorsal tract informs about the performance of the movement. The CB compares all this information, and if there is an error in performance, it sends signals to the motor cortex, red nucleus, and reticular formation resulting in an adjustment of the performance to match the intention, which leads to coordinated movements.

(2) Damping function: Almost all movements are pendular (due to momentum) so they have a tendency to overshoot. However, the spinocerebellum prevents this by subconscious signals that stop the movement at the intended point.

If the CB was damaged. the cerebral cortex can consciously recognize the overshoot and it then initiates a movement in the reverse direction by contraction of the antagonistic muscles. However, this movement also overshoots and is corrected again by overshooting cortical signals. This process is repeated, so the arm oscillates back and forth for several cycles before it finally settles at the intended point(kinetic, intention or action tremor).

(3) Coordination of ballistic movements: Ballistic movements are those which occur very rapidly (e.g. the fingers during typing. and the eyes during reading).

(2) ROLE OF THE CEREBROCEREBELLUM

(I) Planning of movements: The Cerebrocerebellum is informed about the desired movement before it starts (via the cortico-ponto-cerebellar pathway). The basal ganglia receive similar information, and both provide the plan of execution of the movement.

(2) Prediction of movements: The Cerebrocerebellum predicts the next movement at the same time a present movement is occurring. This function is necessary for a smooth transition from one movement to the next (thus joining the sequential movements and preventing decomposition).

(3) Timing of movements: The Cerebrocerebellum also provides appropriate timing for each succeeding movement. This function determines when the next movement should begin, so its absence causes the succeeding movement to begin too early or too late, resulting in incoordination of the movement (especially rapid movements e.g. writing, running, and talking).

THE NEOCEREBELLAR SYNDROME: The manifestations are ipsilateral, and include:

(A)Hypotonia: This is due to the loss of the facilitatory effect on the stretch effect. and is associated with a pendular knee jerk.

(B)Asthenia (= muscle weakness): This is due to difficulty in initiation of muscle contraction caused by loss of the function of the mossy fibre circuit.

(C)Motor ataxia: This is incoordination of voluntary movements, especially the rapid movements. Its manifestations include the following:

(l) Dysmetria: This is inability to control the distance of a motor act, which may either overshoot the intended point (=hypermetria or past pointing) or stops short before it hypometria).

(2) Kinetic (intention or terminal) tremor: This is an oscillatory movement that appears on performing movements (specially at their end) but is absent at rest. It is due to cortical correction of the overshoot.
(3) Rebound phenomenon: This is overshooting of a limb when a resistance to its movement is suddenly removed. It is well demonstrated by the arm pulling test, in which the patient may hit his face by his forearm after the release of the resistance that is exerted by the examiner.
(4) Failure of progression of movements: This is manifested by (a) Adiadochokinesia i.e. Inability to perform rapidly alternating opposite movements e.g. repeated pronation and supination of the hands (b) Decomposition fragmentation) of movements i.e. performing the movement in steps and not as a continuous act.
(6) Dysarthria: This is difficulty in producing clear speech. The syllables may be too long or too short (resulting in jumbled vocalization), and speech may also become staccato or scanning (i.e. cut off into separate syllables).
(7) Nystagmus: This is a tremor of the eyeballs that occurs on fixing the eye at an object placed at one side of the head.
(8) Staggering (or drunken) gait: The patient walks unsteadily and on a wide base zigzag-like gait) in a drunken (swaying) manner and tends to fall on the diseased side.

Lecture 9

Basal Ganglia &Diencephalon

THE BASAL GANGLIA: The basal ganglia (B.G.) are subcortical masses of gray matter that include the following nuclei: (1)The caudate nucleus. (2)The lentiform (or lenticular) nucleus This consists of 2 parts (a) An outer part called the putamen (b) An inner part called the globus pallidus, which is further divided into external and internal segments. Both the caudate nucleus and putamen are called the corpus striatum.
(3) The subthalamic nucleus (= subthalamus or body (4)The substantia nigra (in the midbrain).

CONNECTIONS OF THE BASAL GANGLIA

The B.G. constitutes a basic part of the extrapyramidal system. Their afferent (input) fibers are derived mainly from the cerebral cortex to the corpus striatum, while their efferent (output) fibers originate mainly from the globus pallidus. Their connections can generally be divided into 3 parts:

(A) Cortical connections of the basal ganglia

(1) Putamen circuit: Fibres start from the cortical motor areas and end at the putamen, from which new fibers arise and end at the internal globus pallidus. From the latter, fibers arise and relay at the thalamic ventrolateral nucleus, from which fibers arise and finally end at the cortical motor areas, especially the primary motor area (area 4).

(2) Caudate circuit: Fibres start from both the cortical motor and sensory association areas and end at the caudate nucleus, from which new fibers arise and end at the internal globus pallidus. Fibers arise from the latter and relay at the thalamic ventrolateral nucleus, from which fibers arise and finally end at the cortical motor association areas.

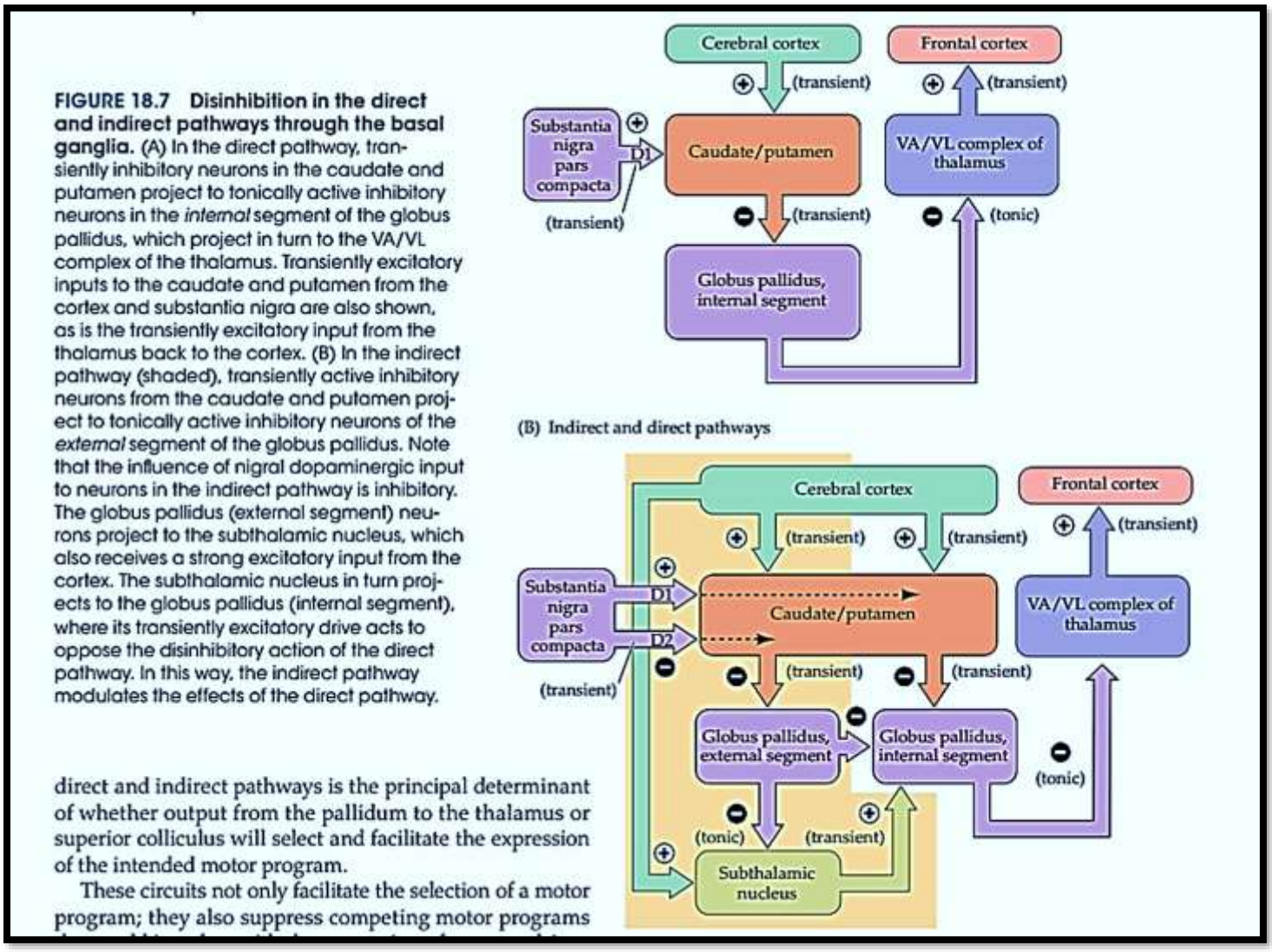


FIGURE 18.7 Disinhibition in the direct and indirect pathways through the basal ganglia. (A) In the direct pathway, transiently inhibitory neurons in the caudate and putamen project to tonically active inhibitory neurons in the *internal* segment of the globus pallidus, which project in turn to the VA/VL complex of the thalamus. Transiently excitatory inputs to the caudate and putamen from the cortex and substantia nigra are also shown, as is the transiently excitatory input from the thalamus back to the cortex. (B) In the indirect pathway (shaded), transiently active inhibitory neurons from the caudate and putamen project to tonically active inhibitory neurons of the *external* segment of the globus pallidus. Note that the influence of nigral dopaminergic input to neurons in the indirect pathway is inhibitory. The globus pallidus (external segment) neurons project to the subthalamic nucleus, which also receives a strong excitatory input from the cortex. The subthalamic nucleus in turn projects to the globus pallidus (internal segment), where its transiently excitatory drive acts to oppose the disinhibitory action of the direct pathway. In this way, the indirect pathway modulates the effects of the direct pathway.

direct and indirect pathways is the principal determinant of whether output from the pallidum to the thalamus or superior colliculus will select and facilitate the expression of the intended motor program.

These circuits not only facilitate the selection of a motor program; they also suppress competing motor programs

(B) Interconnections of the basal ganglia

(1)A negative feedback interconnection between the external of the globus pallidus and the subthalamus.
(2) Dopaminergic nigrostriatal connection.
(3) GABA-ergic striato-nigral striato-pallidal projections.

(C) Brain stem connections of the basal ganglia

Fibers from the globus pallidus project to (a) reticular formation, (b) The red nucleus, (c) The vestibular nucleus (d) The inferior olivary nucleus. Signals from the B.G. are transmitted through such connections to the spinal centres via the extrapyramidal tracts.

NEUROTRANSMITTERS IN THE BASAL GANGLIA These are multiple and include the following:

1. Acetylcholine (mainly from intra-striatal neurons).
2. Dopamine (from the nigrostriatal neurons).
3.GABA (from the striato-nigral and striaio-pallida/ neurons).
4. Norepinephrine, serotonin, and enkephalin (from the neurons that project from various centres in the brain stem to the basal ganglia).
5. Glutamate (from the cortico-striatal and subthalamic neurons).

Acetylcholine, glutamate, and norepinephrine are excitatory transmitters, while all the remaining transmitters are inhibitory, and the balance between inhibition and excitation in the B.G. maintains normal motor function. Normally, the inhibitory effect predominates (which decreases the excitatory discharge of the B.G. Also, the discharge of the B.G. to the thalamus is mainly inhibitory via GABA-ergic nerve fibers. These factors decrease the excitatory discharge from the thalamus to the cortical motor areas.

** The predominance of inhibitory neurons in the B.G. makes the circuits described above (especially the putamen circuit and its associated circuits) act as negative feedback loops that stabilize the motor control system and prevent excessive and undesirable movements.

Excessive deposition of copper in the liver and B.G. occurs in Wilson's disease resulting in their damage (= hepatolenticular degeneration). Also, if the bile pigments' blood level increases markedly, they cross the blood-brain barrier and deposit in the B.G. leading to their damage).

FUNCTIONS OF THE BASAL GANGLIA

The functions of the B.G. are purely motor and include the following :

(A) Control of the muscle tone: The lentiform nucleus decreases the muscle tone by inhibiting the vestibular nucleus and activating the inhibitory reticular formation. On the Other hand, the caudate nucleus increases muscle tone by stimulating the facilitatory reticular formation and the vestibular and inferior olivary nuclei. However, generalized stimulation of the B.G. decreases the muscle tone (indicating a predominance of the inhibitory effect of the lentiform nucleus).

(B) Control of voluntary movements:

(1) The B.G. discharges before the movements start and is concerned with planning and programming of movements:(a) The putamen circuit is concerned with the execution of learned patterns of movement (b) The caudate circuit is concerned with converting thoughts into motor actions. This involves the determination of (i) The pattern of movements to be used and their sequence, (ii) The timing and rapidity of performing the movements (iii) The scale (intensity) of movements. An example of such a function is what happens to a person who sees a lion (he automatically and rapidly turns away, begins to run, and even attempts to climb a tree).
(2)As a part of the extrapyramidal system, the B.G. initiates subconscious automatic movements (e.g., swinging the arms during walking).

PARKINSON'S DISEASE:

This is due to lesions of the substantia nigra, which leads to degeneration of the dopaminergic nigrostriatal fibers(resulting in a marked reduction of the dopamine content in the B.G.).It occurs more in old age (because there is normally a steady loss of the dopaminergic neurons and receptors in the B.G. with the progress of age) and is hastened by atherosclerosis and prolonged use of phenothiazine tranquilizers (which block the D)? receptors).

Manifestations of Parkinson's disease (Parkinsonism) Parkinsonism is characterized by both hyperkinetic features (rigidity and static tremors) and hypokinetic features (akinesia and bradykinesia).

(1) MUSCLE RIGIDITY

This occurs in all muscles (but the tendon jerks are usually not exaggerated). When the limbs are passively moved, it is either continuous lead-pipe rigidity) or interrupted cogwheel rigidity). It is primarily an alpha rigidity that occurs due to a release phenomenon. Destruction of the dopaminergic neurons releases the corpus striatum from dopamine's inhibitory effect, which leads to increased output of excitatory signals to the cortical motor areas, which consequently discharge excess excitatory signals to the spinal alpha motor neurons via the corticospinal tract resulting in rigidity.

(2) AKINESIA OR HYPOKINESIA (LACK OF MOVEMENTS)

This is associated with bradykinesia (= slow movements) and is manifested by (a) Marked difficulty in initiating voluntary movements (b) Mask face clue to lack of facial expression (c) Slow, monotonous and low-volume speech (d) Shuffling gait, i.e., walking rapidly in short steps without lifting the legs from the ground (e) Absence of the associated movements e.g., swinging of the arms during walking.

The real cause of akinesia is unknown. However, it was found that dopamine is also decreased in the limbic system, which might greatly reduce the psychic drive of the motor activity, leading to akinesia.

(3) STATIC TREMOR

This tremor appears during rest and disappears during sleep and on doing voluntary movements. It occurs at a rate of 3-6 or 8 cycles per second due to regular alternating contraction of the antagonistic muscles (probably due to oscillation of activity in the feedback circuits after the loss of their inhibition caused by dopamine deficiency). It is marked in the upper limbs and in the hands; it often appears as pill-rolling movements.

THE THALAMUS

The thalamus is a subcortical mass of gray matter located at the lateral wall of the third ventricle. It contains the following nuclei:

(A) Nonspecific projection nuclei: These include mainly the middle and intralaminar nuclei. They receive signals from the reticular formation and discharge to almost all areas of the cerebral cortex.

(B) Specific projection nuclei

(I) Ventro-posterior nucleus (VPN): Its lateral part (VPLN) receives the spinal and medial lemnisci while its medial part (VPMN) receives the trigeminal lemniscus, and both parts then project to the cortical sensory areas in the postcentral gyrus.

(2)Lateral geniculate body This projects visual impulses to the occipital lobe (refer to the visual pathway in special senses).

(3)Medial geniculate body This projects auditory impulses to the temporal lobe (refer to the auditory pathway in special senses).

(4)Ventrolateral nucleus (= thalamic motor nucleus) This receives signals from both the cerebellum and the basal ganglia and projects to the cortical motor areas (playing a major role in the control of motor functions).

(5)Anterior nucleus: This receives signals from the hypothalamus and discharges to the cortical, limbic lobe.

(6)Dorsomedial and dorsolateral nuclei: These are association nuclei that receive signals from other thalamic nuclei, then the dorsomedial nucleus projects to the prefrontal cortical area, while the dorsolateral nucleus projects to the prefrontal cortex nucleus projects to the cortical association areas.

FUNCTIONS OF THE THALAMUS

(I) The thalamus conveys all sensations to the cerebral cortex because its nuclei are relay stations in the pathways of (a) Epicritic sensations from the opposite side (the VPN), (b) Visual signals (the lateral geniculate body), (c) Auditory signals (the medial geniculate body).

(2) The intralaminar and middle nuclei are the center for the perception of protopathic (crude) sensations and slow pain from the opposite side.

(3)The thalamus is a relay station for signals from the contralateral cerebellum and ipsilateral basal ganglia to the cortical motor areas (through the lateral ventral nucleus).

(4)The nonspecific projection nuclei are relay stations in the ascending reticular activating system.

(5)The thalamus is a part of the systems concerned with (a) Recent memory and emotional reactions (through its connections with the hypothalamus and limbic lobe, page 129) (b) The high intellectual functions (through its connections with the cortical association areas) (c) The behavior and personality (through its connections with the prefrontal cortical areas).

THE THALAMIC SYNDROME

This is a disease that results from thrombosis, or a branch of the posterior cerebral artery called the thalamogeniculllate artery (which supplies a large part of the thalamus, especially its lateral and posteroventral parts). It leads to the following manifestations on the opposite side of the body:

(I) Early in the disease, all sensations are completely lost. The facial sensations are usually less affected because the damage occurs mainly in the VPLIN (while the VPMN is little affected).

(2) The loss of kinaesthetic sensations results in sensory ataxia.

(3)Within the next few weeks or months, protopathic crude) sensations recover. Emotional disturbances accompany this, and although the threshold of pain is elevated, it is accompanied by an exaggerated central effect called thalamic hyperpathia. The latter is **a release phenomenon** that occurs due to the facilitation of the intralaminar and middle nuclei (probably due to interruption of the signals that activate the analgesic brain areas).

(4)The epicritic (= line) sensations are permanently lost, resulting in loss of both tactile Localization and discrimination and astereognosis.

(5)Damage to the ventrolateral nucleus (= thalamic motor nucleus) leads to the following:

(a)Loss of the cerebellar control on the cortical motor areas, which results in asthenia (= muscle weakness or paresis), hypotonia, and manifestations of cerebellar ataxia.

(b)Interruption of the connections between the basal ganglia and the cerebral cortex may result in abnormal movements similar to those occurring in chorea and athetosis.

Motor CAUSES OF TREMORS

1. Static tremor: This occurs in Parkinsonism. It is present during rest and is associated with hypertonia.
2. Kinetic tremor: This occurs in neocerebellar disease. It is especially present at the end of movements and is associated with hypotonia.

ATAXIA

This means incoordination of voluntary movements, and it is either sensory or motor (sometimes mixed in the thalamic syndrome).

(A)Sensory ataxia: This occurs as a result of lesions (or diseases) of the proprioceptive sensory pathways, commonly in the dorsal column of the spinal cord (= the gracile and cuneate tracts).

The manifestations (features) of sensory ataxia include (a) Loss of dorsal column sensations (b) +ve Romberg's sign. There is a stamping gait high steppage gait with a slap when the foot reaches the floor), and the patient walks at a broad base and always looks at his feet.

(B)Motor ataxia: This is due to defects in the coordinating system of voluntary movements.

(C) Mixed ataxia: as ataxia in thalamic syndrome.

ASSESSMENT OF COORDINATION (TESTS FOR ATAXIA)

(A) COORDINATION TESTS IN THE UPPER LIMBS

(I) Finger-to-nose test: Ask the patient to extend his arm. then to place his forefinger on the tip of his nose, first with open then with closed eyes.

(2) Finger-to-finger test: Ask the patient to extend both arms and then touch the tips of his 2 fingers. first with open then with closed eyes.

(3) Tests for Adiadochokinesia: Ask the patient to pronate and supinate his hand repeatedly or tap his leg with his hand rapidly.

(4) Tests for rebound: (a) The arm pulling test (b) The wrist-slapping test: The hand of the patient is suddenly tapped downward. An exaggerated displacement of the arm occurs in motor ataxia.

(B) COORDINATION TESTS IN THE LOWER LIMBS

(I) Heel-knee test: At recumbency, the patient is asked to place his heel on the opposite knee, then run it down the shin of the tibia to the foot.

(2)Test the gait while walking along a straight line.

(3)Test for Romberg's sign by closing the eyes.

Lecture 10

THE HYPOTHALAMUS AND LIMBIC SYSTEM

The hypothalamus is a part of the diencephalon located below and anterior to the thalamus. It is the main component and the major output pathway of the limbic system, so their functions are closely interrelated. It contains the following groups of nuclei :

(I) Anterior group (supraoptic, suprachiasmatic, preoptic and paraventricular nuclei).
(2)Lateral group (mainly a large lateral nucleus).
(3)Medial group (dorsomedial and ventromedial nuclei and the arcuate nucleus).
(4)Posterior group (posterior nucleus and the mamillary bodies).
(5) Periventricular nuclei (refer to the analgesia system).

FUNCTIONS OF THE HYPOTHALAMUS

The hypothalamus is essential for homeostasis through the following:

(1) Control of autonomic functions (sympathetic and parasympathetic).
(2) Control of the endocrine system: This occurs in 2 ways :

A-Nervous control: The hypothalamus controls 2 endocrine glands by sending nerve signals to (a) The adrenal medulla (through affecting the vasomotor centre) (b) The posterior pituitary gland (through the hypothalamohypophysial tract). This gland's hormones (ADH and oxytocin) are also synthesized in the hypothalamus.

B-Hormonal control: The hypothalamus controls the anterior pituitary gland (and consequently most endocrine glands) by releasing the hypophysiotropic hormones from its median eminence (refer to endocrines).

(3) body temperature regulation: The hypothalamus contains sensitive thermoreceptors and the thermoregulatory center.
(4) Control of water balance: Hypothalamic osmoreceptors regulate water intake and loss.
(5) Control of food intake: This occurs by activity of the hypothalamic appestat center, subdivided into 2 parts: a feeding center and a satiety center.
(6) Control of circadian (=diurnal or 24-hour) rhythms: This occurs by the suprachiasmatic nuclei, which are the pacemakers for the circadian rhythms in the body.
(7) Regulation of sexual functions: The hypothalamus regulates the release of gonadotropins which controls spermatogenesis and ovulation and the secretion of sex hormones from the gonads.
(9) Control of motivation by the reward-punishment systems. In addition, the hypothalamus shares in the control of memory & learning.
(10) Emotional expression (reactions).

THE LIMBIC SYSTEM

The word “limbic” means “border.” Originally, the term “limbic” was used to describe the border structures around the basal regions of the cerebrum, but according to the functions of the limbic system, the term limbic system has been expanded to mean the entire neuronal circuitry that controls emotional behavior and motivational drives. This system consists of 2 components:

(l) The limbic lobe of the cerebral cortex is a rim of primitive cortical tissue around the hilum of the cerebral hemispheres. It is also called the rhinencephalon, and it contains mainly the cingulate and hippocampal gyri and the uncus. the piriform and entorhinal cortex.
(2) Certain subcortical structures: These include the amygdaloid nuclei, hippocampus, hypothalamus, fornix, anterior thalamic nucleus, septal nuclei, and upper part of the midbrain area.

Connections of the limbic system

(1)Between its different parts, especially between the hypothalamus and the amygdaloid nucleus via the stria terminalis.
(2)A few connections with the neocortex.

(3)***The Papez circuit***: The hippocampus is connected via the fornix to the mamillary bodies, and these are connected via the mamillothalamic tract to the anterior thalamic nucleus, which projects to the cingulate gyrus, and this finally discharges to the hippocampus again.

FUNCTIONS OF THE LIMBIC SYSTEM (I) Perception of olfactory (smell) sensation.
(2) Control of the feeding behavior (3) Control of autonomic functions.
(4)Control of sexual behavior: The behavior that accompanies the sexual act is regulated in the limbic system, particularly the amygdaloid nuclei, since bilateral damage of these nuclei in males leads to abnormal sexual behavior together with hypersexuality. (5) Memory and learning.
(6)Control of emotions: The limbic system controls emotional reactions with the hypothalamus.
(7) Control of motivation: Motivation is controlled by reward and punishment systems.

Types of Memory

Two major types:

■ ***Implicit or non-declarative memory:***

➢ Does not require conscious or, awareness

➢ Does not usually involve the hippocampus.

➢ Example: remembering how to brush your teeth

■ ***Explicit or Declarative memory***: Memory of words, rules, and language

➢ Associated with consciousness or, at least awareness

➢ Dependent on the hippocampus

➢ Example recalling the first day in college

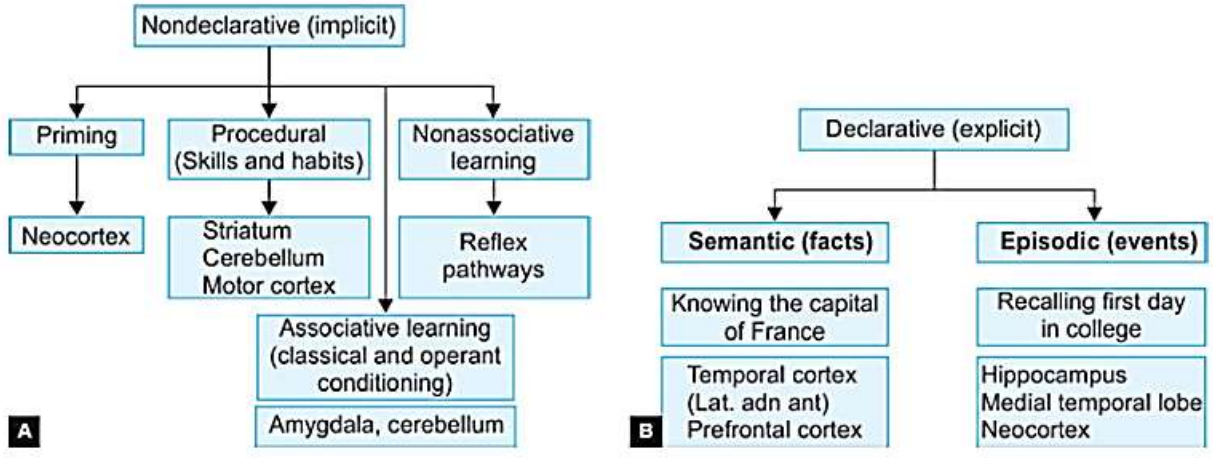
Implicit memory is subdivided into four types:

1. Procedural memory includes skills and habits, which, once acquired, become unconscious and automatic.
2. Priming is the facilitation of recognition of words or objects by prior exposure to them. An example is improved recall of a word when presented with the first few letters of it (Name a fruit with GR….
GRAPE).
3. Associative learning is related to classical and operant conditioning in which the organism learns about the relation of one stimulus to another (check below).
4. Non-associative learning includes habituation and sensitization and is dependent on various reflex pathways. Here the organism learns about a single stimulus.

Explicit memory is subdivided into two types:

1. Episodic memory for events
2. Semantic memory for facts (e.g. words, rules, and language).

The different parts of brain areas involve in processing and formation of implicit and explicit memory memory is given in the Flowchart:



Explicit Memory and Many Forms of Implicit Memory Involve

1. ***Working memory (recent memory):*** It is a form of short-term memory that keeps information available, usually for very short periods, while the individual plans action based on it. Capacity is 7 ± 2 'chunks' of information and duration of storage is 18–20 secs only.

2. Short-term memory: This lasts seconds to hours, during which processing in the hippocampus and elsewhere lays down long-term changes in synaptic strength.

3. Long-term memory: This stores memories for years and sometimes for life. During short-term memory, the memory traces are subject to disruption by trauma and various drugs, whereas long-term memory traces are remarkably resistant to disruption.

The neural mechanisms of memory depend on the following forms of synaptic plasticity:

Synaptic plasticity means changes in the strength of synaptic transmission (which represent forms of learning memory). Such changes are presynaptic and postsynaptic, and they include potentiation, depression & sensitization.

SYNAPTIC POTENTIATION (OR FACILITATION)

This is the production of high-amplitude EPSPs in response to stimulation. It occurs after a brief period of rapidly repeated stimulation of the presynaptic neuron (= tetanizing train of stimuli), and is 2 types :

1-Short-term potentiation (= post-tetanic potentiation): This lasts up to one minute and is due to excess Ca- in the presynaptic knobs due to the repeated stimulation (which increases the release of the neurotransmitter and, in turn, increases the EPSP).

2-Long-term potentiation (LTP): This especially occurs in the hippocampus, where the excitatory transmitter is glutamate. It lasts a few hours or days, and both the pre and postsynaptic neurons participate in its production. The presynaptic neuron releases glutamate, increasing the Ca^{+2} influx in the postsynaptic neuron, thus increasing the EPSP. In turn, the postsynaptic neuron releases a chemical signal (NO) that causes more glutamate secretion from the presynaptic neuron.

SYNAPTIC DEPRESSION

This is a decrease in the response of postsynaptic neurons, and is 2 types:

1 - Habituation: This is a gradual decrease of the postsynaptic response when a stimulus to the presynaptic neuron is repeated over and over. It is due to less release of the neurotransmitters from the presynaptic terminals secondary to the reduction of the intracellular Ca+2 (which occurs due to the closure of the Ca+2 channels by an unknown mechanism).

2- Long-term depression (LTD): This is the opposite of LTP, produced by slower stimulation of the presynaptic neurons (Occurs if presynaptic neuron stimulation→ depolarization of postsynaptic neuron less than 20mv (the threshold for NMDA receptors to open)).

SYNAPTIC SENSITIZATION

This is the augmentation of a PSP in response to a habituated presynaptic stimulus if the latter is paired one or more times with a noxious stimulus. It may be transient or prolonged (becoming in the latter condition a form of memory). It occurs by a presynaptic facilitation mechanism as follows:

The noxious stimulus arrives in a facilitatory neuron that terminates on the presynaptic ending.

2. The released transmitter from the facilitatory neuron (commonly serotonin) causes the closure of the K channels in the presynaptic ending, which decreases K efflux.

3. As a result of the decrease of the K efflux, the repolarization process becomes slow, leading to the prolongation of the action potential in the presynaptic ending. This prolongs the opening of the Ca- channels in the presynaptic ending, which leads to more Ca influx and, consequently, more release of the neurotransmitter (resulting in an augmented PSP).

Cerebral Cortex & Electrical activity of the brain

Lecture 11

The brain has a marked electric activity, and 2 types of potentials can be recorded (1) Evoked potentials that occur in the cerebral cortex after stimulation of receptors (2) Spontaneous potentials (= the electroencephalogram).

Types of Evoked potentials :
1- Somatosensory stimuli → SSEP
2- Auditory stimuli → AEP
3- Visual stimuli → VEP

The EEG is a record of the spontaneous brain electric activity in conscious subjects. Recording of EEG is achieved through applying unipolar or bipolar leads, and 4 main types of waves are usually recorded.

(1) Alpha waves: are the dominant waves recorded in conscious adults during rest while relaxed and their eyes closed. Their voltage is about 50 mV (mV = microvolt) and are most probably produced by the activity of the nonspecific thalamic nuclei. The frequency of the alpha (or Berger's) rhythm is 8-13 Hz (Hz= Hertz = cycles / second) and is most marked in the occipital and parietal regions.

(2) Beta waves: These waves have the lowest voltage and are recorded in infants and during brain activity and increased tension in adults. Its frequency is 18-30 Hz and is most marked in the frontal region.

(3) Theta waves: These waves have a higher voltage than the alpha waves and are recorded in children, during emotional stress in some adults, and during light sleep (see below). Its frequency is 4-7 Hz and is most marked in the temporal and parietal regions.

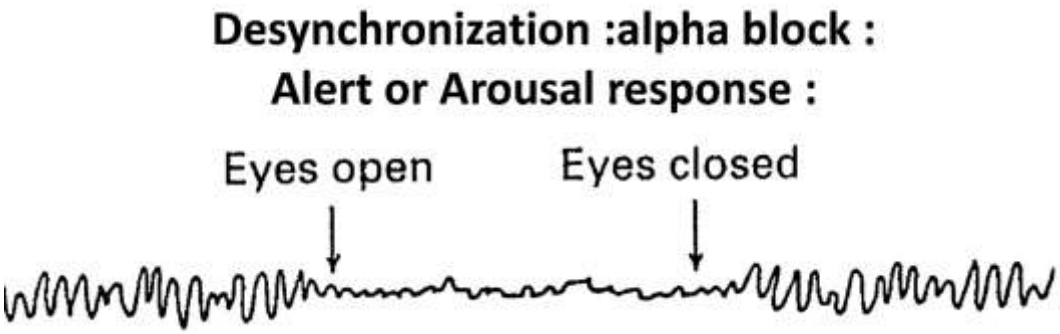
(4) Delta waves: These waves have the highest voltage and lowest frequency (less than 4 Hz) and are recorded in young infants and during deep sleep (see below). Other waves may be recorded in certain conditions, e.g., the lambda waves in the occipital area during visual attention.

The frequency of the alpha rhythm is decreased by:
- Low blood glucose
- Low body temperature
- Low levels of glucocorticoid hormones
- High $PaCO_2$
- Hyponatremia
- Vitamin B12 deficiency
- Acute intoxication with alcohol, amphetamines, barbiturates, phenytoin, and antipsychotics.

THE AROUSAL OR ALERTING RESPONSE

This is an EEG response that occurs when the subject becomes alert (e.g. on opening his eyes or when solving a mathematical problem). The alpha rhythm is replaced by rapid irregular low-voltage beta waves. It represents the breaking up of the synchronized neuronal alpha activity, so it is also called **alpha block or desynchronization**.

Such response is reversible (so if the eyes are closed, the alpha rhythm is resumed). It is due to stimulation of the ascending reticular activating system (= ARAS, see below). Such system can also be stimulated by cortical signals discharged via corticofugal fibers (providing a pathway through which certain cortical events can initiate arousal e.g. during emotions).



CLINICAL SIGNIFICANCE OF THE EEG

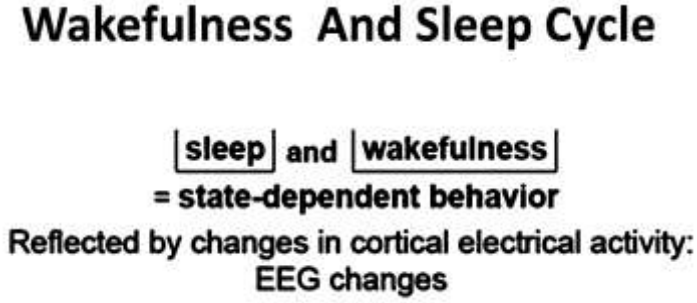
(1) It helps in determining the sites of focal pathological processes in the brain e.g. the sites of tumours (in which the EEG waves are distorted) or the sites of fluid collection e.g. a subdural hematoma (in which the EEG waves are damped).

(2) It helps in the diagnosis of certain brain diseases, particularly grand mal and petit mal epilepsy (each of which causes characteristic EEG changes).

Sleep is a physiological state of temporary unconsciousness. Its duration varies inversely with age (average 18 hours in infants, 8 hours in adults, and 6 hours in old persons). The sleep/wakefulness 24-hour rhythm is determined mainly by synchronization with the 24-hour light/dark cycle (see below). However, it is also affected by various habits and conditioned reflexes, as well as by many psychological and physical factors.

PHYSIOLOGICAL CHANGES DURING SLEEP

(1) Circulatory system: The heart rate, cardiac output, vasomotor tone, and arterial blood pressure are all decreased, and the circulation time is prolonged (2) Respiratory system: The rate and depth of respiration are decreased (so pulmonary ventilation is decreased with a tendency to acidosis) and periodic breathing may also occur (refer to respiration). (3) Nervous system: Most reflexes disappear, the voluntary activity and. sensory perception are abolished, and a positive Babinski's sign is obtained. (4) The skeletal muscle tone, body temperature and metabolic rate are all decreased (the latter by 10-30%). (5) Most endocrine secretions are decreased (but secretion of the growth hormone increases during sleep). On the other hand, the secretions of the GIT tend to increase during sleep.



2 types of sleep normally alternate with each other:

(A) Slow wave sleep (= non-rapid eye movement or non-REM sleep)

This type is the first to occur when the person falls asleep. It is characterized by slow EEG waves and no REM (= Rapid Eye Movements). EEG recordings during this type of sleep pass in 4 stages that occur respectively as follows:

Stage 1 sleep is very light in this stage, and the EEG shows a slow theta wave rhythm.

Stage 2: In this stage, sleep is light, and the EEG shows characteristic sleep spindles (= bouts of large alpha-like waves with a frequency of 12-15 Hz).

Stage 3: Sleep is moderately deep in this stage, and the EEG shows delta waves at a frequency of about 3-4 Hz.

Stage 4: In this stage, sleep is deepest, and the EEG shows delta waves with maximal slowing called delta-max waves (frequency about 1 Hz). ** Sleep talking and walking often occur during this type of sleep. Dreams may also occur, but they are not consolidated in memory (not remembered)

(B) Rapid Eye Movement (REM, desynchronized or paradoxical) sleep

This type is characterized by rapid roving eye movements, and it normally follows 4th stage of slow wave sleep. The EEG shows a desynchronized beta rhythm as encountered in the arousal response. This indicates brain activity, but the person is still asleep (so this type of sleep is also called paradoxical sleep). Dreams that can be remembered, and penile erection frequently occur during REM sleep.

DISTRIBUTION OF SLEEP STA GES (= SLEEP CYCLES)

Sleep normally starts with the slow wave type for about 70-110 minutes. (average 90 minutes), then REM sleep follows for about 20 minutes, which is repeated cyclically with gradual prolongation of the RFM sleep periods. Therefore, there are 4-6 sleep cycles during a single night, and REM sleep constitutes about 20-25 % of the total sleep time.

Most, if not all, living cells in plants and animals have rhythmic fluctuations in their function on a circadian cycle. Normally they become entrained, that is, synchronized to the day–night light cycle in the environment. If they are not entrained, they become progressively more out of phase with the light–dark cycle because they are longer or shorter than 24 h.

The entrainment process in most cases is dependent on the suprachiasmatic nuclei (SCN). These nuclei receive information about the light–dark cycle via a special neural pathway, the retinohypothalamic fibers. Efferent fibers from the SCN initiate neural and humoral signals that entrain a wide variety of well-known circadian rhythms including the sleep–wake cycle and the secretion of the pineal hormone melatonin.

Lecture 12

MECHANISMS (THEORIES) OF SLEEP

Sleep primarily results from depression of the cerebral cortex and secondary inhibition of the ARAS activity. ARAS inhibition can occur by either:

(1) Passive mechanism, i.e., as a result of its fatigue (after a period of wakefulness) or by decreasing its activity through the elimination of its exciting stimuli, e.g., the visual, auditory, painful, and other stimuli.

(2) Active mechanism: This is a more accepted sleep mechanism. There are many sleep centers, the excitation of which inhibits the ARAS activity and induces sleep. These centers are located in the following sites:

(a) The reticular formation in the medulla oblongata, the diencephalon, and the diagonal band of Broca. Stimulation of these parts induces slow wave (non REM) sleep.

The hypothalamic suprachiasmatic nuclei constitute the center that synchronizes the sleep/wakefulness rhythm with the 24-hour light-dark cycle, thus acting as a waking/sleeping regulator center.

(b) The reticular formation in the pons. Stimulation of this part. induces REM sleep.

One theory regarding the basis for transitions from sleep to wakefulness involves alternating reciprocal activity of different groups of RAS neurons.

In this model, wakefulness and REM sleep are at opposite extremes. When the activity of norepinephrine- and serotonin-containing neurons is dominant, there is a reduced level of activity in acetylcholine-containing neurons in the pontine reticular formation.

This pattern of activity contributes to the appearance of the awake state. The reverse of this pattern leads to REM sleep.

When there is a more even balance in the activity of the aminergic and cholinergic neurons, NREM sleep occurs. In addition, an increased release of GABA and reduced release of histamine increase the likelihood of NREM sleep

The orexin released from hypothalamic neurons may regulate the changes in activity in these brainstem neurons.

A METABOLIC THEORY OF SLEEP

The CSF of animals kept awake for several days were found to contain substances that induce sleep if injected into other animals. The nature of the sleep-inducing factors was suggested to be a specific lipid or peptide, but it is now believed to be adenosine because caffeine (a powerful alerting substance) is an adenosine antagonist. According to this theory:

■ Accumulation of metabolites in the cerebral cortex stimulates the GABAergic neurons in the basal forebrain.

■ GABAergic neurons in turn stimulate the ventrolateral preoptic area, sleep-promoting areas of the hypothalamus

Sleep disorders:

1- Insomnia:

It is insufficient sleep that occurs in adults due to :

1- Psychological factors e.g. anxiety

2- Intake of analeptics e.g. coffee.

2- Somnambulism:

"sleep walking"

-More common in male children.

-The person walks with eyes opened, and avoid obstacle and when awakened can not remember what he did.

3- Narcolepsy:

Irresistible sleep during daytime activities which starts with sudden onset of REM sleep.

4- Sleep apnea:

-Caused by obstruction of the airways during sleep

-Effort to overcome the obstruction awakens the person from sleep.

5- REM behavior disorder:

- Hypotonia fails to occur.
- The patients with this condition act out their dreams, they even jump out of bed to do battle with imagined aggressors.

Narcolepsy has a familial incidence strongly associated with a class II antigen of the major histocompatibility complex on chromosome 6 at the HLA-DR2 or HLA-DQW1 locus, implying a genetic susceptibility to narcolepsy.

The HLA complexes are interrelated genes that regulate the immune system Compared to brains from healthy persons, the brains of persons with narcolepsy often contain fewer hypocretin (orexin)-producing neurons in the hypothalamus.

It is thought that the HLA complex may increase susceptibility to an immune attack on these neurons, leading to their degeneration.

Obstructive sleep apnea (OSA) is the most common cause of daytime sleepiness due to fragmented sleep at night and affects about 24% of middle-aged men and 9% of women in the United States. Breathing ceases for more than 10 s during frequent episodes of obstruction of the upper airway(especially the pharynx) due to reduction in muscle tone.

The apnea causes brief arousals from sleep in order to reestablish upper airway tone. An individual with OSA typically begins to snore soon after falling asleep. The snoring gets progressively louder until it is interrupted by an episode of apnea, which is then followed by a loud snort and gasp as the individual tries to breathe.

OSA is not associated with a reduction in total sleep time, but individuals with OSA experience a much greater time in stage 1 NREM sleep (from an average of 10% of total sleep to 30–50%) and a marked reduction in slow-wave sleep (stages 3 and 4 NREM sleep).

The pathophysiology of sleep apnea includes both a reduction in neuromuscular tone at the onset of sleep and a change in the central respiratory drive

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