CHAPTER 7

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

(1) 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 cortical association areas.*

FUNCTIONS OF THE THALAMUS

(1) The thalamus conveys all sensations to the cerebral cortex *except olfaction (smell)* 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).

** *Recently, it was reported that part of the olfactory sensation also relays in the thalamus.*

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

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

(4) The nonspecific projection nuclei are relay station in the ***ascending reticular activating system*** (= **ARAS**, page 133).

(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 ***behaviour and personality*** (through its connections with the prefrontal cortical areas).

THE THALAMIC SYNDROME

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

(1) Early in the disease, there is complete loss of all sensations. The ***facial sensations are usually less affected*** because the damage occurs mainly in the VPLN (while the VPMN is little affected).

(2) The loss of kinesthetic sensations results in ***sensory ataxia*** (page 113) as occurs in tabes dorsalis (page 32).

(3) Within the next few weeks or months, protopathic (= crude) sensations recover (page 21). This is accompanied by ***emotional disturbances***, and although the threshold of pain is elevated, yet it is accompanied by an exaggerated central effect called ***thalamic hyperpathia***. The latter is a ***release phenomenon*** that occurs due to facilitation of the intralaminar and middle nuclei (probably as a result of interruption of the signals that activate the analgesic brain areas, page 35).

(4) The epicritic (= fine) sensations are permanently lost resulting in loss of both tactile localization and discrimination as well as ***astereognosis***.

(5) Damage of 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*** (page 112).

(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*** (page 101).

** In the thalamic syndrome, the **ataxia is mixed** i.e. it is both sensory and motor (page 113) due to loss of the kinesthetic sensations as well as the cerebellar control on the cortical motor areas

CHAPTER 8

THE HYPOTHALAMUS AND LIMBIC SYSTEM

The hypothalamus is a part of the ***diencephalon*** located below and anterior to the thalamus. *It is a main component, and the major output pathway of the limbic system, so their functions are closely interrelated* (see below). It contains the **following groups of nuclei** (figure 51) **:**

(1) Anterior group (supraoptic, suprachiasmatic, preoptic and paraventricular nuclei).
(2) Lateral group (mainly a large lateral nucleus).
(3) Medial group (dorsomedial and ventromedial nuclei as well as the arcuate nucleus).
(4) Posterior group (posterior nucleus and the mamilllary bodies).
(5) Periventricular nuclei (refer to the analgesia system, page 35).

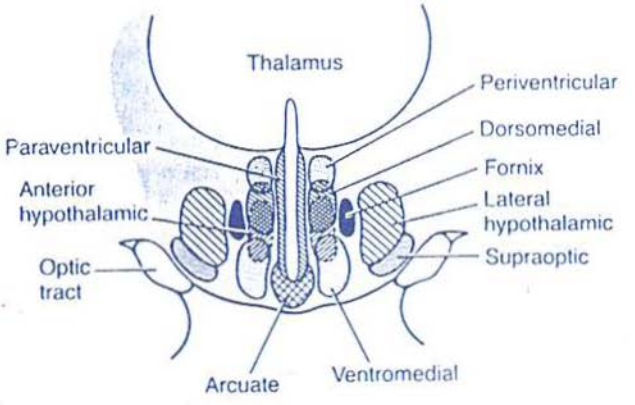


Figure 51 : Coronal view of the hypothalamus showing some of its nuclei.

NERVOUS CONNECTIONS OF THE HYPOTHALAMUS

(1) Afferent (input) fibres : The hypothalamus receives afferent fibres from **(a)** Limbic system i.e. the limbic lobe, hippocampus and amygdaloid nucleus (figure 53) **(b)** Thalamus **(c)** Reticular formation (through which it receives collaterals from the sensory tracts) **(d)** Optic chiasma.
(2) Efferent (output) fibres : The hypothalamus sends efferent fibres to **(a)** Limbic system **(b)** Thalamus **(c)** Reticular formation (through which it controls centres in the brain stem and spinal cord) **(d)** Posterior pituitary gland.

FUNCTIONS OF THE HYPOTHALAMUS

The hypothalamus is essential for **homeostasis** through the following :

(1) Control of autonomic functions : The anterior nuclei control parasymp. functions while the posterior and lateral nuclei control symp. functions.

(2) Control of the endocrine system : This occurs by 2 ways :

A- Nervous control : The hypothalamus controls 2 endocrine glands by sending nerve signals **(a)** ***The adrenal medulla*** (through affecting the vasomotor centre) **(b)** ***The posterior pituitary gland*** (through the ***hypothalamo-hypophysial tract***). The hormones of this gland (ADH and oxytocin) are also synthesized in the hypothalamus.

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

(3) Regulation of body temperature : The hypothalamus contains *sensitive thermoreceptors* as well as the *thermoregulatory centre*. The latter consists of a ***heat loss centre*** in the anterior nuclei and a ***heat gain centre*** in the posterior nuclei (see in energy metabolism).

(4) Control of water balance : This occurs by the hypothalamic ***osmoreceptors***, which regulate both water intake and water loss as follows :

(a) Water intake : This occurs through affecting activity of the ***thirst centre***, which leads to drinking when stimulated e.g. in cases of dehydration.

(b) Water loss : This occurs through adjusting release of ***ADH*** from the posterior pituitary gland, which controls the urinary water loss.

(5) Control of food intake : This occurs by activity of the ***hypothalamic appestat centre***, which is subdivided into 2 parts :

(a) A feeding centre in the lateral nuclei : This centre is continuously active. Its stimulation increases the appetite and its damage causes ***anorexia***.

(b) A satiety centre in the ventromedial nucleus : Stimulation of this centre decreases the appetite by inhibiting the activity of the feeding centre, while its damage increases the appetite and leads to ***hyperphagia***.

The appestat also has a ***glucostatic function*** e.g. in hypoglycemia, the satiety centre is inhibited, and this increases the activity of the feeding centre.

(6) Control of circadian (=diurnal or 24 hours) rhythms : This occurs by the ***suprachiasmatic nuclei***, which are the pacemakers for the circadian rhythms in the body (e.g. the rhythms in the secretion of *ACTH and melatonin*, the *sleep-wake cycles and the body temperature rhythm*). These nuclei receive signals from the eyes (via the *retino-hypothalamic fibres*) and their function is to synchronize the various body rhythms to the 24-hour light-dark cycle (but the mechanism remains unknown).

(7) Regulation of sexual functions : The hypothalamus regulates release of ***GTHs***, which control spermatogenesis and ovulation as well as the secretion of sex hormones from the gonads. This is shown by the ***ovulation reflex*** (= *a*

neuroendocrinal reflex ovulation at the time of copulation). The anterior hypothalamic neurons are also excited by the circulating estrogens & androgens resulting in an increase of both libido (sexual desire) and sexual ability.

(8) Relation to sleep : *The hypothalamus has* ***no direct role*** *in the regulation of sleep.* It *was* believed that it contains sleep and wakefulness centres since lesions or stimulation of certain hypothalamic areas induced sleep changes. However, this was found to be due to *effects on ascending pathways that control sleep* (page 137).

(9) Control of motivation by the ***reward & punishment systems*** (page 96). In addition, the hypothalamus shares in the control of **memory & learning** .

(10) Emotional expression (reactions) : Emotions may be associated with either ***excitation*** e.g. rage (anger) or ***worry*** e.g. depression, anxiety and fear (see below). The expression of emotions involves activity of **(a)** The prefrontal lobe **(b)** The hypothalamus **(c)** The limbic system (page 95).

FEAR and RAGE

These are the commonest forms of expression of emotions. They are closely-related since both result in ***protective reactions*** i.e. if an animal is threatened, it attempts to escape (***fear, fleeing or avoidance reaction***) while if it is cornered, it shows rage and fights (***rage, fighting or attack reaction***).

(a) The fear reaction : This consists of ***autonomic responses*** (e.g. sweating and pupil dilatation) as well as ***somatic responses*** (turning the head from side to side seeking escape). Such reaction can be produced in animals by stimulating the ***amygdaloid nucleus or a fear centre in the periventricular nucleus of the hypothalamus.***

(b) The rage reaction : This also consists of ***autonomic responses*** (e.g. piloerection and pupil dilatation) and ***somatic responses*** (biting and clawing). Such reaction can be produced by ***also*** stimulating the ***amygdaloid nucleus or a rage centre in the lateral nuclei of the hypothalamus.***

RAGE (=ANGER) & PLACIDITY (=ABNORMAL CALMNESS)

In addition to the rage centre, the hypothalamus also contains a ***placidity centre in the ventromedial nucleus***, and the ***emotional state of the subject is determined by the balance between the activity of both centres***. The rage centre is normally stimulated by signals from the amygdaloid nucleus and inhibited by signals from the placidity centre and the neocortex (see next).

SHAM RAGE REACTION

This is a severe rage reaction ***in response to minor stimuli***. It is a true rage reaction, so the term *" sham (= false) rage " should be dropped.* It can

be produced by **(a)** Removal of the neocortex or lesions of the placidity centre in the ventromedial hypothalamic nucleus (***release phenomena***) **(b)** Stimulation of the amygdaloid nucleus. The reaction includes the following :

(1) ***Sympathetic effects*** (tachycardia, rise of the arterial blood pressure, piloerection and pupil dilatation).

(2) ***Somatic effects*** (e.g. biting and clawing), as well as hissing, spitting and growling (specially in cats).

EFFECTS OF HYPOTHALAMIC LESIONS

One or more of the following effects may occur due to hypothalamic lesions

(1) Endocrinal disorders e.g. ***diabetes insipidus*** (due to deficient ADH secretion), ***Frohlich 's syndrome or precocious puberty***.

(2) Hyperthermia or hypothermia.

(3) Sleep disturbances e.g. insomnia and narcolepsy (= hypersomnia).

(4) Hyperphagia or anorexia.

(5) Disturbances in motivation, memory or learning.

(6) Autonomic disturbances e.g. spontaneous V.C. or V.D. or sweating.

(7) Abnormal emotions (e.g. fear, rage or placidity).

(8) Sexual disturbances.

THE LIMBIC SYSTEM

This system consists of 2 components :

(1) The limbic lobe of the cerebral cortex : This 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*** in addition to the *uncus, the piriform and entorhinail cortex* (figure 52).

(2) Certain subcortical structures : These include the ***amygdaloid nuclei, hippocampus, hypothalamus, fornix, anterior thalamic nucleus, septal nuclei and upper part of the midbrain*** (***= limbic midbrain area***).

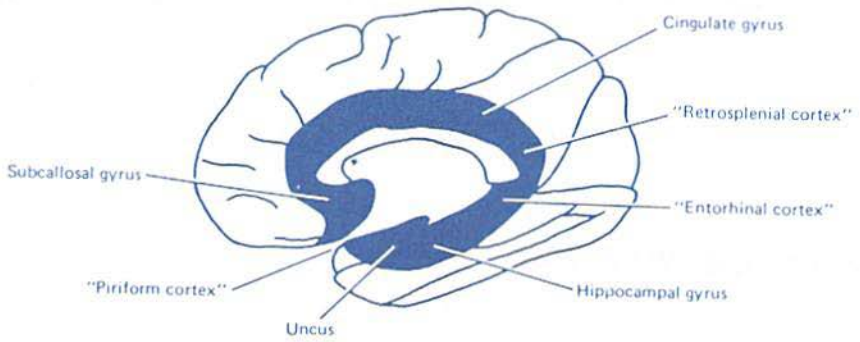


Figure 52 : The limbic lobe (the dark area).

Connections of the limbic system

(1) Between its different parts, specially between the hypothalamus and the amygdaloid nucleus via the ***stria terminalis*** (figure 53).

(2) A few connections with the neocortex.

(3) The **Papez circuit** (figure 53) **:** The hippocampus is connected via the fornix to the mamillary bodies, and these are connected via the mamillo-thalamic tract to the anterior thalamic nucleus, which projects to the cingulate gyrus, and this finally discharges to the hippocampus again.

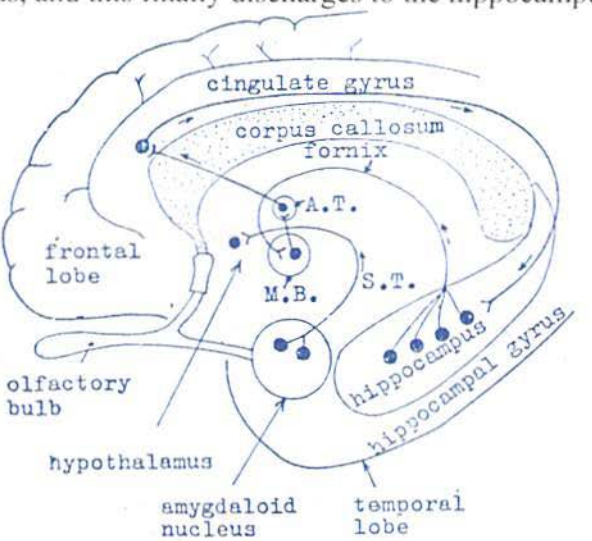


Figure 53 : The Papez circuit. A.T .= anterior thalamic nucleus. M.B. = mamillary bodies. S.T .= stria terminalis.

FUNCTIONS OF THE LIMBIC SYSTEM

(1) Perception of **olfactory (smell) sensation**.

(2) Control of the feeding behaviour : This is one of the functions of the ***amygdaloid nuclei*** Its stimulation causes chewing and licking movements while its damage causes severe hyperphagia (to food and other objects).

(3) Control of autonomic functions : Many limbic structures control autonomic effects (specially changes in the blood pressure and respiration).

(4) Control of sexual behaviour : The behaviour 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 behaviour together with hypersexuality.

(5) Memory and learning (pages 127 and 128)

(6) Control of emotions : Together with the hypothalamus, the limbic system controls the emotional reactions. Stimulation of the ***amygdaloid nuclei*** can produce fear or rage (page 93) while their damage produces placidity &

disappearance of the fear response (so monkeys, which are normally terrified by snakes, can approach, pick and even eat them) in addition to oral exploration of objects , hypersexuality and depression of memory (see above).

(7) Control of motivation : Motivation is controlled by ***reward and punishment systems***. The former is located along the medial forebrain bundle (specially the ***reward centre in the lateral and ventromedial hypothalamic nuclei***) while the latter includes mainly a ***hypothalamic punishment centre in the periventricular nucleus***. The transmitter in the reward system is ***dopamine*** and the stimuli that excite it produce a sense of pleasure and ecstasy (happiness) which increases motivation and leads to repetition of these stimuli (see below). On the other hand, stimuli that excite the punishment system produce a sense of displeasure, fear or terror, which inhibits motivation and leads to avoidance of these stimuli (see next).

Experimental localization of the reward and punishment areas

An animal (e.g. a monkey) is placed in a cage containing a bar that can be pressed by the animal. This bar is connected to an electric stimulator in such a way that each press delivers a stimulus to an electrode implanted in the animal's brain (figure 54). Electrodes are placed successively at different areas in the brain. If stimulation gives a sense of reward, the animal will press the bar repetitively again and again. On the other hand, if stimulation gives a sense of punishment, the animal will avoid pressing the bar.

Figure 54 : Method of localizing the reward and punishment areas.

(6) High sensitivity to the following :

1- Blood pH : Alkalosis increases while acidosis decreases synaptic transmission. Thus, a rise of blood pH from 7.4 to 7.8 leads to convulsions while its fall is associated with drowsiness (or coma in severe acidosis).

2- Blood O_2 level : Hypoxia decreases synaptic transmission, so unconsciousness occurs if the cerebral circulation stops for only 3-5 seconds.

3- Drugs and chemicals :

A- ***Drugs that increase synaptic transmission*** **:**

- Theophylline, caffeine and theobromine.
- Strychnine and tetanus toxin (by blocking the action of glycine).
- Picrotoxin (by blocking the action of GABA).

B- ***Drugs that decrease synaptic transmission :***

- Anesthetic drugs.
- Anti-anxiety and tranquilizer drugs (e.g. diazepam), hypnotic drugs (e.g. barbiturates) and alcohol. All these act by facilitating the action of GABA.

(7) Plasticity and learning :

This means changes in the strength of synaptic transmission (which represent forms of ***learning & memory***, page 129). Such changes are ***presynaptic and postsynaptic***, and they include **potentiation, depression & sensitization**

Synaptic potentiation (or facilitation)

This is 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 accumulation of excess Ca^{2+} in the presynaptic knobs as a result of the repeated stimulation (which increases the release of the neurotransmitter, and in turn increases the EPSP).

2- Long-term potentiation (LTP)

This specially 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 which increases Ca^{2+} influx in the postsynaptic neuron, thus increasing the EPSP. The postsynaptic neuron in turn 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 reduction of the intracellular* Ca^{2+} (which occurs as a result of closure of the Ca^{2+} channels by an unknown mechanism).

2- Long-term depression (LTD) : This is the opposite of LTP, and is produced by slower stimulation of the presynaptic neurons (which is associated with a smaller rise of the Ca^{2+} content in the postsynaptic neuron).

Synaptic sensitization

This is 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 :

1. The noxious stimulus arrives in a *facilitatory neuron which terminates on the presynaptic ending* (figure 24).

2. The released transmitter from the facilitatory neuron (commonly **serotonin**) causes 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 prolongation of the action potential in the presynaptic ending. This prolongs the period of opening of the Ca^{2+} channels in the presynaptic ending, which leads to more Ca^{2+} influx and consequently, more release of the neurotransmitter (resulting in an augmented PSP).

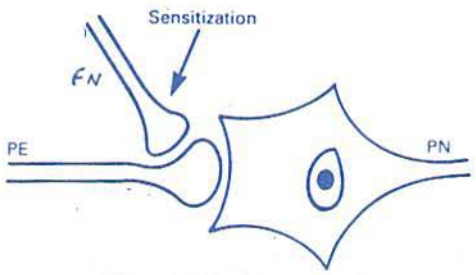


Figure 24 : Synaptic sensitization by the presynaptic facilitation mechanism FN= facilitatory neuron. PE= presynaptic ending. PN = postsynaptic neuron.

THE SYNAPTIC TRANSMITTERS

There are classified as follows :

1. ***Acetylcholine***.

2. ***Amines*** (epinephrine,norepinephrine,dopamine, serotonin and histamine).

3. ***Amino acids*** : These are either *excitatory* (e.g. glutamic and aspartic acids), or *inhibitory* e.g. glycine and gamma amino-butyric acid (GABA).

LEARNING

(A) Non-associative learning

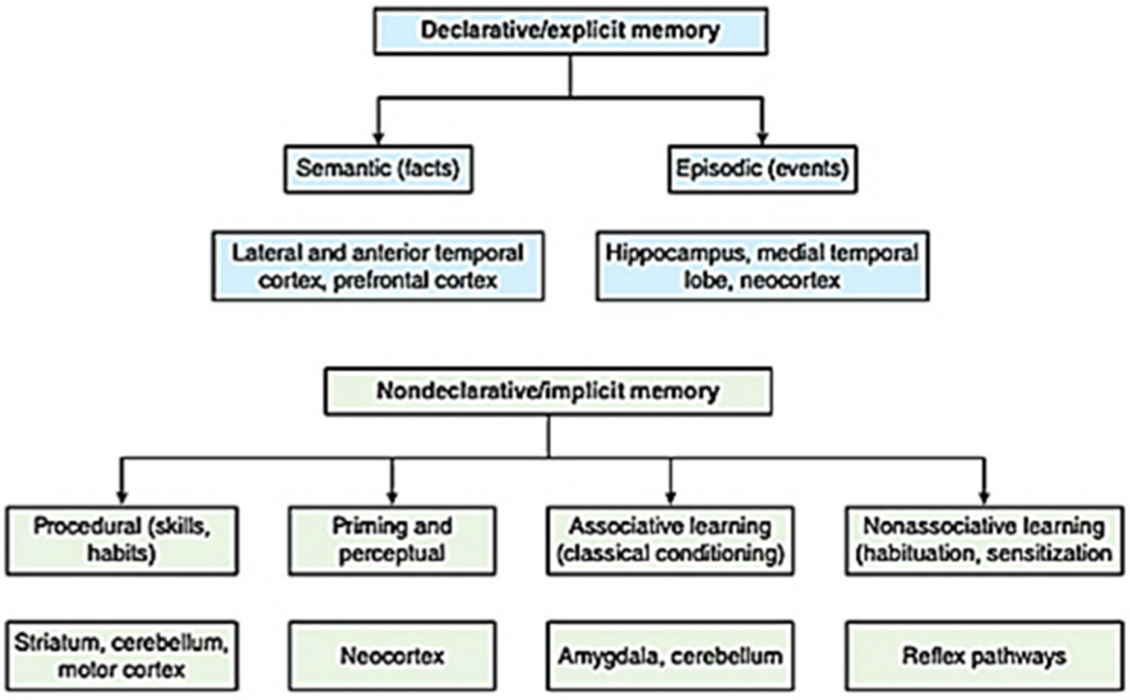
This is learning about ***a single stimulus that is repeated many times.*** There is 2 forms of this type :

(1) Habituation : This is a gradual decrease in the response to a particular stimulus when repeated. This learns the individual to ignore a large number of nonsignificant stimuli (so it is considered a ***negative memory***). It is due to a decrease in Ca^{2+} in the nerve endings that mediate the response (page.42)

(2) Sensitization : This is potentiation of the response to a particular stimulus when repeated (so it is considered a ***positive memory***). It occurs if the stimulus is coupled once with an unpleasant (or a pleasant) stimulus. It is due to prolongation of the action potential in nerve endings.(page 43)

(B) Associative learning

This is learning by ***pairing of stimuli***, and the best example in this case is learning through **conditioned reflexes.** In such reflexes, the subject is learned to respond to stimuli that normally do not produce responses. These stimuli are called ***conditioned stimuli*** **(CS),** while the stimuli that normally produce the response are called the ***unconditioned stimuli*** **(US).**



There are 2 main types of memories :

(A) **Implicit (reflexive) memory** (= memory of which the person is *unconscious or unaware*). It includes (1) *Associative and nonassociative learning* (see above) (2) *Learned skills* (= *skill memory*) (3) *Habits* (e.g. *driving cars becomes a habit by training and occurs automatically without need for conscious recall of information*) (4) *Priming* (= *facilitation of recognition of words or objects by previous exposure to them*).

(B) **Explicit or declarative memory** (= *conscious recall of information*) which includes the following types :

(1) **Short-term (primary or recent) memory :** This is memory that lasts a few seconds to a few minutes (or at most a few hours) then fades away unless it is converted to long-term memories..

(2) **Long-term (secondary or remote) memory :** This is memory that lasts for long times (*years and may be for the whole life*).

CONSOLIDATION OF MEMORY

This is the conversion *of short-term memory into long-term memory*. It requires 5-10 minutes for minimal consolidation and 1- 4 hours for more strong consolidation. Therefore, *short-term memory is vulnerable during the first 5 minutes* (i.e. it is liable to be erased) if disrupted by external stimuli such as anesthesia, electroshock or hypothermia.

Mechanism of consolidation

This is produced (and also accelerated and potentiated) by *rehearsal of the short-term memory* i.e. repitition of the information in mind again and again (so consolidation is reduced in mentally-fatigued persons). It involves *protein synthesis in neurons* (so drugs and antibiotics that inhibit protein synthesis do not affect short-term memory but prevent its consolidation).

THE MEMORY TRACES

Memories are stored in the brain through *facilitation of synaptic transmission*. The facilitated (or new) pathways are called **memory traces**, and once they are established, they can be activated by the mind to reproduce the memories. They can occur at all levels of the nervous system but *particularly in the cerebral cortex*.

New informations are first *processed in the hippocampus*, and what proves to be significant is *codified into specific classes* that will be *consolidated then stored in association with other memories of the same type*. This is *necessary to search for various memories when required*.