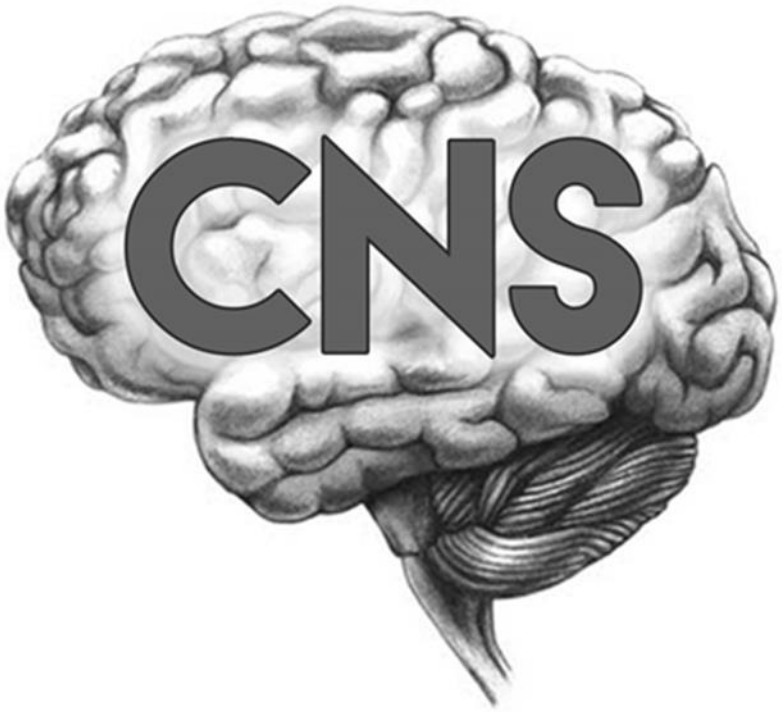

PHYSIOLOGY

☑ Sheet ○ Slide ○ Handout

Number

21

Subject

Intellectual Functions of the Brain 2

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Price:

⟡ Before we start

- This sheet was written according to the recording that belongs to section 3.
- The order of ideas in this sheet is a little bit different from that in the recording.
- Enjoy ☺

..... I. Review .....

⟡Last time we started talking about higher intellectual functions of the cerebral cortex [figure 1]

- We said that each area in the cortex has a corresponding area in the thalamus, and the cortex is nothing without the thalamus! As any ascending (sensory) and descending (motor) fibers must enter the thalamus. That's why قايتون العظيم considers the cortex and thalamus as one entity called *thalamocortical system*.
- Now each part of the cerebral cortex has certain function; so we have the *primary Motor area*, *primary Somatosensory area*, *primary visual area* and *primary auditory area*. These areas are responsible for primitive functions for the cortex, like moving one muscle (primary Motor area) or receiving sensation (primary Somatosensory, visual and auditory areas).
- And each primary area need secondary (or association) area that makes sense out of the signals in the primary areas; the *supplementary and premotor areas* for primary motor area, *visual and auditory association areas* for vision and audition, etc.. . These areas are responsible for perception and integration for information
- And finally, there are "actual" association areas, they integrate more than one modality of information, carry out complex processes to make thoughts and specific higher intellectual functions; for example, the *limbic association area* is responsible for motivation, emotions and memory; *prefrontal association cortex* is important for social behavior.

- Other important association areas are *inferior temporal lobe* that's <u>important for naming the faces</u> and *Wernicke's area* that's the most important region in the entire brain for the higher intellectual functions, as it integrates all types of sensation (that's why it is called "general interpretive area"), we will talk about it in more details later.

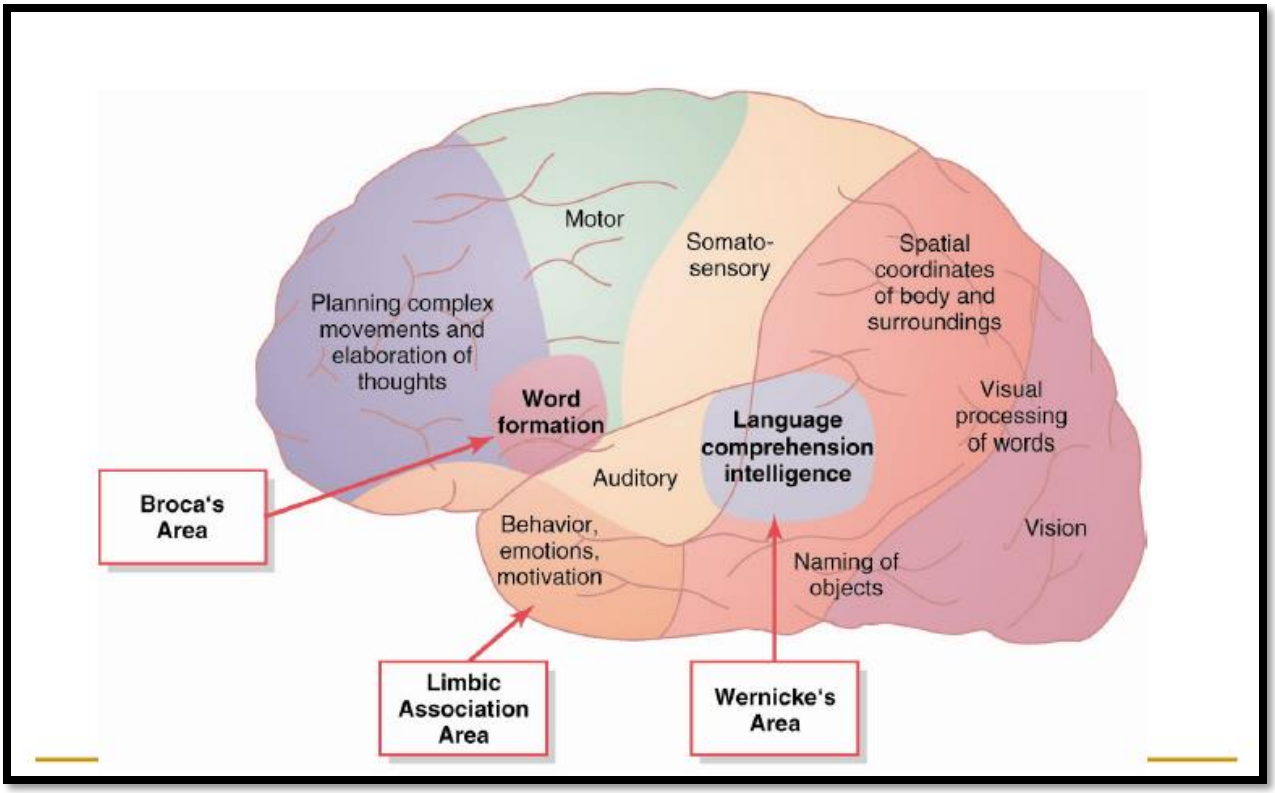

***Figure 1**: physiological anatomy of the cerebral cortex.*

Note: according to Guyton's, Wernicke's area and inferior temporal lobe belongs to parieto-occipitotemporal association area, which is the third "actual" association area.

Clinical Correlate

- lesions in these association areas present with very peculiar but characteristic presentation; a lesion in prefrontal association cortex may lead to social disinhibition, lesion in inferior temporal lobe results in Prosopagnosia (inability to name the faces- عمى الوجوه) and lesions in Wernicke's area results in many syndromes, like amorphosynthesis (the patient is unaware of somatic sensations from one side of the body) and dementia.

⟰ We talked also about the concept of *dominant and nondominant hemisphere*.

- Dominance is related to Language not hand skills, as dominance of the left or right hand is determent by training.
- Dominant side is important for language, reasoning, logic, and scientific skills.
- While the non-dominant side related to other forms of sensory intelligence (music, sensory feelings).

..... II. Language Areas .....

⟰ Wernicke's area and Broca's area (motor area of speech) in the dominant hemisphere are the main areas that are responsible for talking.

⟰Speech and language are complex processes, starting from receiving sensory information from receptors through primary sensory areas, perception (or understanding) of these information through secondary areas, integration of these information with thoughts, and finally sending these information to the motor areas to communicate (by talking or writing).

A) pathways for communication

⟰We have two pathways for communication, Visual Communication pathway and Auditory Communication pathway see [figure 2] &[figure 3]. Each pathway has sensory aspects and motor aspects:

- Sensory aspects:
    1. **Primary sensory areas receive the information**. In Visual pathway, primary visual area receive the visual input, While in auditory pathway, primary auditory area is responsible for recognition of the sound as a word.
    2. **interpretation of the word and the thought that the word expresses in Wernicke's area.** Notice that, in visual pathway, the information must undergo processing in the angular gyrus region to be converted from figures into sounds before reaching Wernicke's area.

    ֍Note: In Wernicke's area, somatosensory, visual and auditory information are associated and correlated, the precise mechanism for this is not will understood, some scientists say that some new synapsis are formed, others claim that it may be due to release of chemicals, etc…

- Motor aspects:

1. **Formation of the word that expresses a particular thought in Wernicke's area.**
2. **Transmission of these words via the arcuate fasciculus to Frontal cortex.** Here the thoughts and ideas are formed, and sent into the premotor area to be expressed, if the expression was through words, it may go to Broca's area, while if it was through writing, it will go to hand skills area.
3. **motor control of vocalization and the act of vocalization or writing.** Broca's area and hand skills area carry the programs of talking and writing, these programs control the actions of the primary motor area, resulting in contraction of muscles of speech (or writing) in a sequential manner, resulting in words.

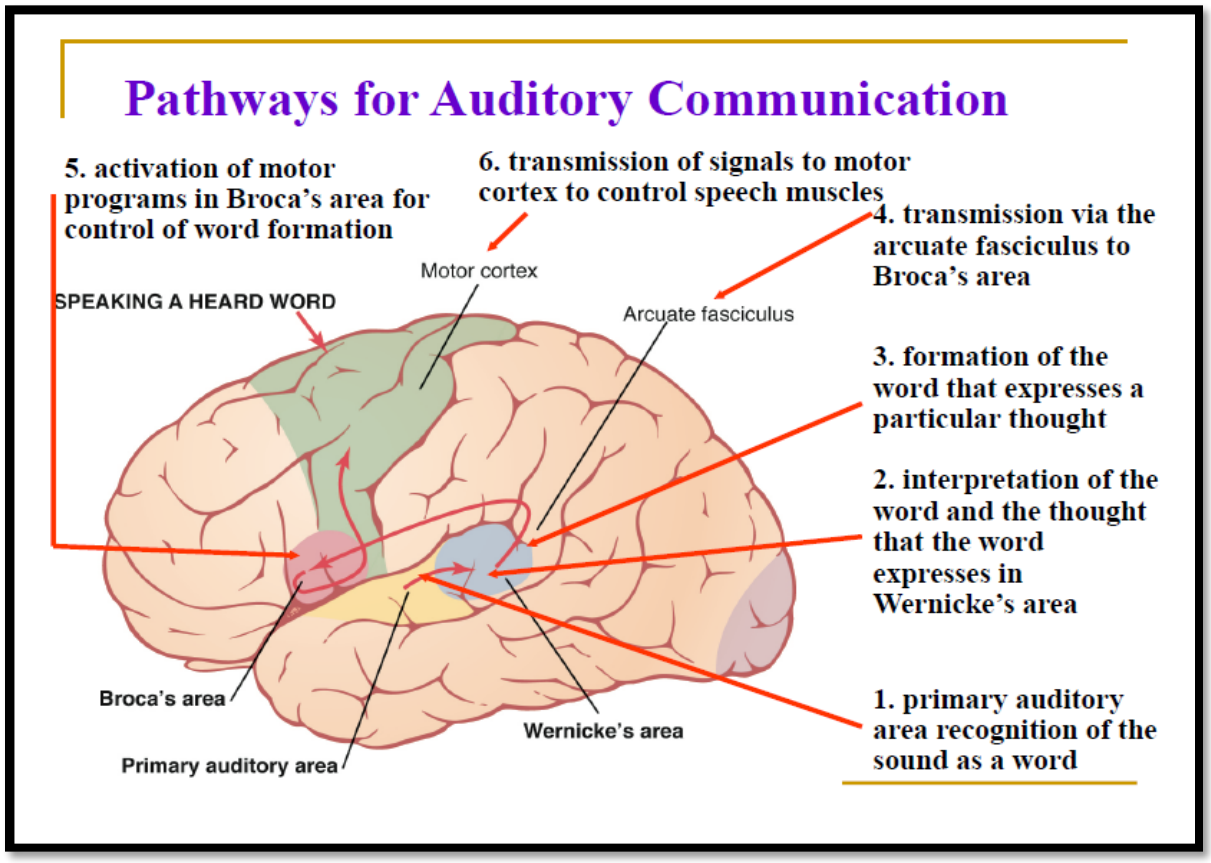

***Figure 2**: Pathways for auditory communication.*

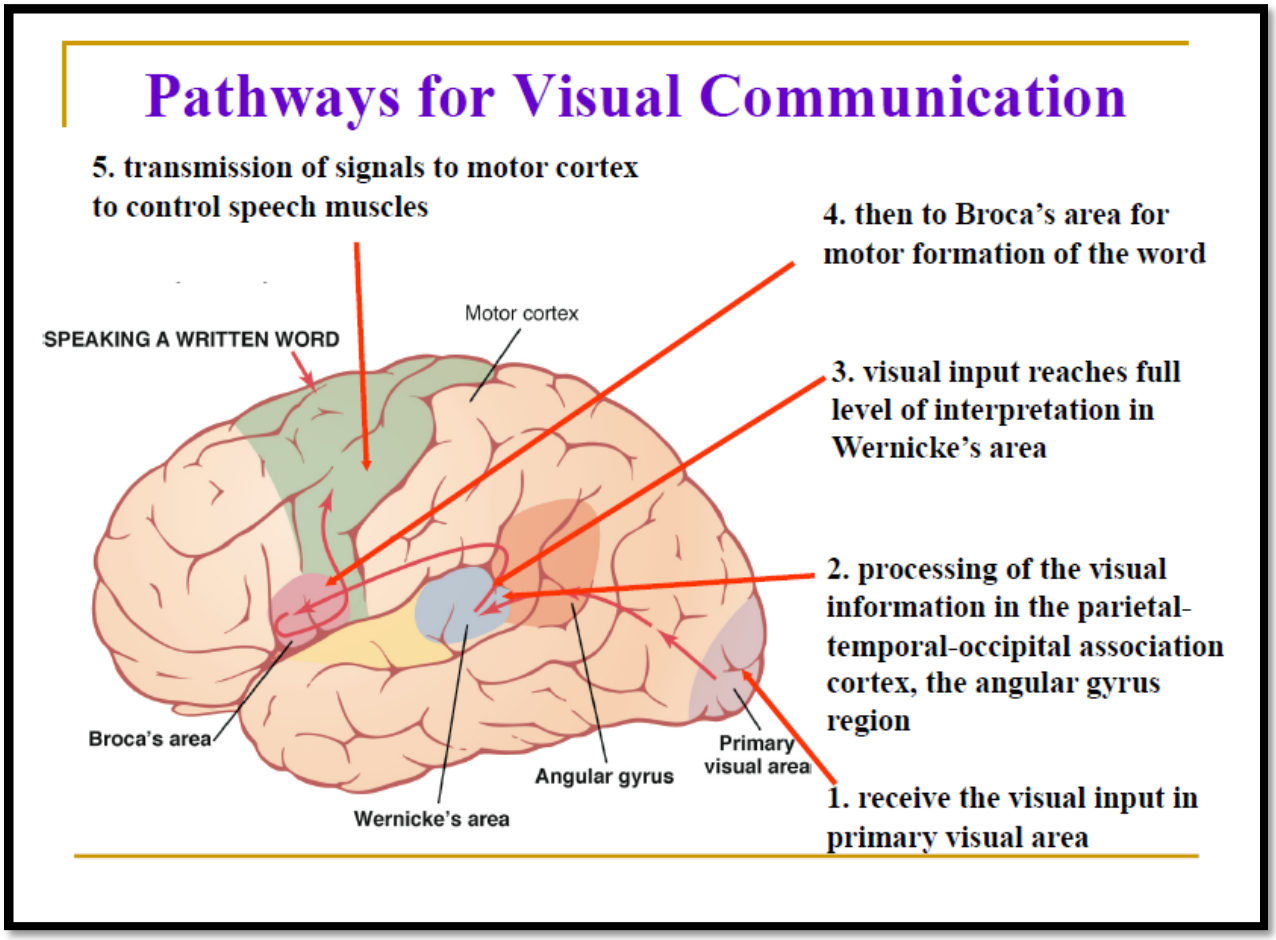

***Figure 3**: Pathways for visual communication.*

Clinical Correlate

lesions in any part of these pathways will result in a disturbance in communication process, or aphasia:

- lesions in Wernicke's area may cause sensory aphasia (Receptive aphasia), the patient here is can speak fluently, but his/her speech will not make any sense, as he/she is unable to understand language in its written or spoken form.
- Lesions is Broca's area may lead to another form of aphasia, known as Expressive aphasia (non-fluent aphasia) which is characterized by the loss of the ability to produce language (spoken or written). A person with expressive aphasia will exhibit effortful speech.
- Global aphasia may result from generalized lesion in dominant hemisphere, the patient here can't talk, and doesn't have thoughts or expressions

B) Corpus Callosum

⏇Now the strong question is, if the both hemispheres can comprehend (think and analyze), and only left hemisphere is able to talk, how does left hemisphere express itself?

- This is done through the *Corpus Callosum*, which is a group of commissural fibers that connects both hemispheres, so the non-dominant hemisphere can't express itself without the presence of Corpus Callosum.
- Remember also, that almost all sensory and motor fibers are crossed before reaching the cortex, that's why we said each hemisphere controls the contralateral side of the body, so without Corpus Callosum, the human actions will be separated.

֍Note: Why do we have the crossing ?? nobody knows exactly why, but the Dr thinks that it might be حكمة كبيرة من الله سبحانه و تعالى to tell us that the human being is one, you can't divide him into two, as each side of the body is represented on the opposite side of the brain.

…… III. Thoughts and memory ……..……..

A) Thoughts

⏇Nobody exactly knows how and why thoughts are formed, some scientists claim that it could be due to anatomical changes others say that it's due to chemical or electrical changes, actually, both theories have some evidences.

- Regarding the first theory, many research groups have found that they can modify brain circuits through experience. One of these experiments was done by suturing one of the eyes of a newborn kitten and reopen it after a certain period. Surprisingly kittens with one eye deprived of vision for the first 3 month remain blind on that eye for their whole life. Moreover, in the healthy eye, normal exposure to light after birth stimulated the formation of new neuronal circuits and synapses (anatomical growth in visual areas), such changes were not noticed in sutured eyes.
- On the other hand, there are other proves for chemical changes inside the neurons, and when we say chemical changes, it means forming new proteins. Scientists have found that there are some dormant genes in the neurons, these genes are reactivated by certain stimuli, thus forming new proteins, these proteins represent our ideas!

Despite these theories, precise anatomical localization for thought is not known.

- Most likely a specific pattern of simultaneous neural activity in many brain areas.
- Destruction of cerebral cortex does not prevent one from thinking.
- However, depth of thought and level of awareness may be less. This is because cerebral cortex is the area for alertness and awakens, so the loss of awakens will affect the depth but not the process of thinking, this proves also that we have other areas other than cerebral cortex responsible for thinking.

B) Memory and learning

Learning is acquiring new sensory information or motor skills.

- Acquiring information means that you have to memorize these information, so you can think about memory as the tool that we use for learning.
- And you can think about this relation in another way; The first step of memory is learning (registration).

So now, let's focus on memory, how can we classify the memory??

- Memory could be classified into *immediate memory*, *short term memory* and *long term memory*.
- Other people may classify it into *short term and long term*, then they subclassify short term memory into *immediate short term memory and intermediate short term memory*.
- But for simplification, we will follow the first classification.

As we said earlier in this sheet, thoughts and memory may result from anatomical changes (new synapses formation) or chemical changes, regardless the precise mechanism, Memories are stored in the brain by changing the basic sensitivity of synaptic transmission between neurons as a result of previous neuronal activity.

- This changing in sensitivity could be positive *"sensitization"* creating memories, or could be negative *"habitation",* resulting in neglecting this thought or sensation.

- Actually, most of our memories are negative, that's why you can't memorize many events in your daily live.
- The Cellular and molecular mechanisms for sensitization and habitation are explained next.

C) Cellular and chemical basis for Memory[figure 4]

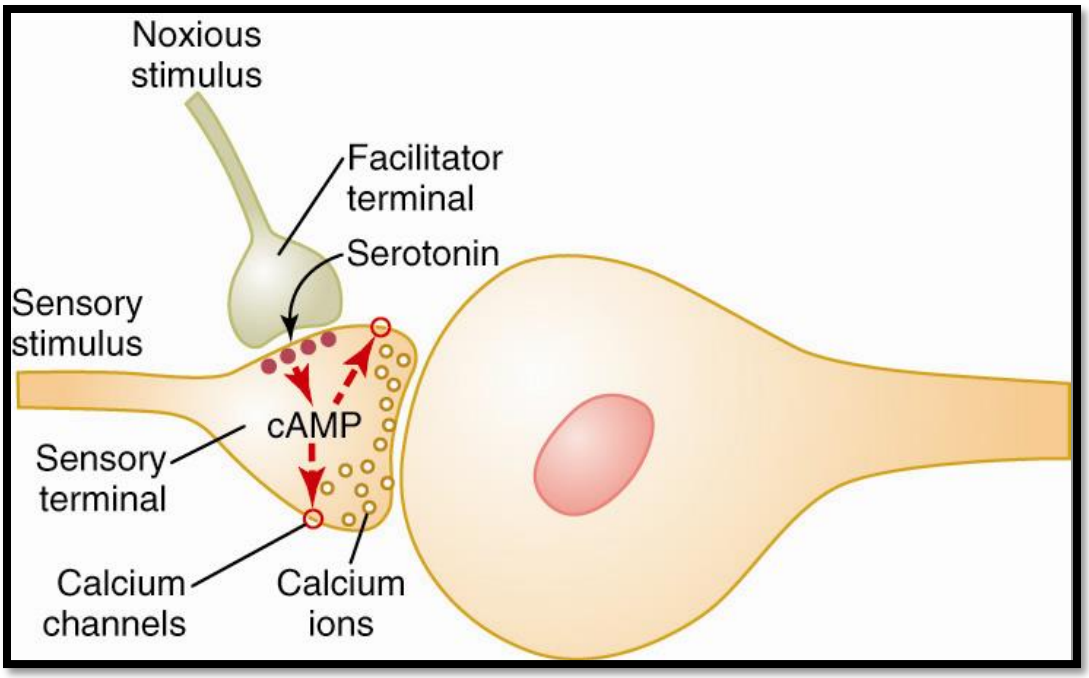

***Figure 4**: Molecular and cellular Basis for Memory*

In this figure, we have two terminals participating in memory formation.

- The first terminal, which is the presynaptic terminal, brings impulses from sensory input neuron, is called *sensory terminal*. when this terminal is stimulated, it will release certain chemicals to the postsynaptic membrane forming memory.
- Another terminal called *"facilitator terminal"* synapses with the presynaptic terminal "sensory terminal" itself, this terminal brings stimuli called "noxious stimuli"

- Now what happens, is that, repetitive stimulation of the sensory terminal alone (without facilitator terminal) will lead to a progressive decline in sensitivity of the sensory terminal, due to the decrease in the sensitivity of the presynaptic calcium channels → less Ca^{+2} entry →less transmitter release upon stimulation → "habitation".

- But when the facilitator terminal is stimulated (by noxious stimuli) along with the sensory terminal, everything will change; (1) the facilitator terminal will release serotonin along with other neuromodulators, (2) that will bind to receptors in the presynaptic terminal, (3) Transmitter activates G protein which in turn activates adenylate cyclase resulting in an increase in cAMP, (4) cAMP activates a protein kinase that phosphorylates a component of the K+ channel blocking its activity, (5) This prolongs the action potential "stabilize the membrane" which increases transmitter release "sensitization".

D) Types of memory

now let's discus each type of memory in more details, we will define each one, give some examples and talk about possible mechanism of forming it:

1- immediate memory

Immediate memory: is the ability to remember a small amount of information over a few seconds.

- For example, if someone that's not important for you told you his name, you will forget his name in seconds, unless this person was important for you.
- Another example is remembering 10 digit phone number.

proposed mechanism for immediate memory:

- Immediate memory may result from synaptic potentiation through the accumulation of calcium in the presynaptic membrane.
- This would promote neurotransmitter release (very short duration of action) or neuropeptides/neuromodulator (longer duration of action).

How can you convert the immediate memory into short or long term memory??

- This depends on the importance of the information, so if it was important, you will force your brain to register it in short term or even in long term memory, while if you face some problems recalling information or events regarding someone or something, it means that it was never important for you ;) .

2- short term memory

Short-term memory: is the capacity for holding, but not manipulating, a small amount of information in mind in an active, readily available state for a short period of time.

- It lasts for days to weeks.
- here you need registration and recall, the most obvious example for this type of memory is when you study one night before an exam, here you'll be able to recall most of the information in the exam, but forget all what you studied a couple of days later.
- Short term memory is easy to recall, but once forgotten you will lose it permanently, this is because The capacity for short term is limited.

proposed mechanism for short term memory:

- Short-term memory may result from a temporary physical or chemical change in the pre- or postsynaptic membrane, through release of neurotransmitters for a longer time (what's explained previously about figure 4).

How can you convert short term memory into long term memory??

- Is needs Consolidation, as we will see in the next section.

3- Long term memory

long-term memory: is the memory that lasts for years or for a lifetime.

- It needs registration, followed by second Consolidation "activation of the memory by repeating for example" and recall.
- Examples are: your name, Names of important people in your live (like me :p) and (سورة الفاتحة).

- We said that the capacity for short term is limited, but for the long term memory it is unlimited, that's why they say العلم في الصغر كالنقش في الحجر, as children's' brains have higher plasticity (flexibility) because they try to store everything in the long term memory.
- And it's obvious that information stored in the long term memory are not easily forgotten, however, the retrieval time for long term memory is longer

proposed mechanism for long term memory:

- Long term memory results from permeant anatomical and chemical changes, like new synapses (new spurts of the axons), or new proteins formation.
- This results in increase in the area for vesicular release therefore, more transmitter is released.

Note: there is a protein called 100s protein which is important in the formation of memory and thoughts, they are trying to use it for memory strengthening.

The concept of Consolidation of Memory

- For immediate and short term memory, the information are registered immediately, But in order to transfer these information into deeper mind areas (long term memory) it needs *Consolidation*, which may take a few minutes to hours depending on the person, information and other circumstances.
- It results from chemical, physical and anatomical changes in the synapse.
- three criteria affect the efficacy of Consolidation

1- **Filing of the information,** so when you study different subjects together, you have higher chance to forget everything, but when you arrange the information in your mind by saying "oki, I'm going to study the 21th lec in physiology of the CNS" you will recall it faster.
2- **Relaxation**, so you will study better after restful sleep, while you won't memorize anything if you stay awake in the night to study (because your brain circuits are fatigued).
3- **The repetition and rehearsal of the information.** the more you repeat it, the best you memorize it.

Note: interruption of this process by electrical shock or by anesthesia will prevent memory development. Why?? (see next page)

- Answer : for memory to be formed, the cortex has to be active, whenever its inactive, you can't remember anything, So for example, you can't remember any dream during sleep unless this dream occurred in the state of cerebral cortex activity (REM stage).

4-Comparison of Long-Term and Short-Term Memory

CHARACTERISTIC	SHORT-TERM MEMORY	LONG-TERM MEMORY
Time of Storage after Acquisition of New Information	Immediate	Later; must be transferred from short-term to long-term memory through consolidation; enhanced by practice or recycling of information through short-term mode
Duration	Lasts for seconds to hours	Retained for days to years
Capacity of Storage	Limited	Very large
Retrieval Time (remembering)	Rapid retrieval	Slower retrieval, except for thoroughly ingrained memories, which are rapidly retrieved
Inability to Retrieve (forgetting)	Permanently forgotten; memory fades quickly unless consolidated into long-term memory	Usually only transiently unable to access; relatively stable memory trace
Mechanism of Storage	Involves transient changes in functions of pre-existing synapses, such as altering amount of neurotransmitter released	Involves relatively permanent functional or structural changes between existing neurons, such as formation of new synapses; synthesis of new proteins plays key role

E) Brain centers for memory

hippocampus and thalamus are critical for memory formation.

- The role of these structures has been identified through observation of the effects of lesions in these areas.
- Damage in hippocampus causes inability to form new verbal or symbolic long-term memory (anterograde amnesia)
- Damage to thalamus causes retrograde amnesia or the inability to recall stored experiences.

This is my last sheet in this semester, and probable in the medical school, hope you have enjoyed it.

"The difficulties you face in life do not come to destroy you, but to show you what you're made of and just how strong you are"

Mohammad Qussay Al-Sabbagh

☺ The end ☺