CNS
PHYSIOLOGY

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In the previous lectures we talked about the brainstem, basal ganglia and cerebellum. It's time to switch gears and talk about the cerebral cortex and its functional areas. Try to enjoy it as it has many interesting topics 😊

Cortical control of motor function

The motor cortex is divided into three subareas:

1) **Primary motor cortex,** which is located in the precentral gyrus in front of the central sulcus.
   - It has topographical representation of our body which is proportional to the number of motor units in each area. The higher the number of motor units in any area, the more precise the movement is, and the larger the area it occupies on the motor cortex. For example, the hands have large number of motor units relative to the trunk, because they are involved in skilled and delicate movements, and thus they are represented by a large area on the primary motor cortex.
   - Stimulation results in movement of **single muscles**, so it's responsible for **discrete movements**.

2) **Premotor area**, which lies in front of the primary motor area.
   - It has topographical organization similar to the primary motor cortex.
   - Stimulation results in movement of **muscle groups** on the **contralateral side** of the body to perform a specific task. So it's involved in **more complex patterns of movement (programmed movement)** rather than the discrete patterns generated in the primary motor cortex.
   - It works in concert with other motor area.

   ➲ How does this area produce complex patterns of movement?
   In the premotor area there are different areas that represent groups of muscles, when these areas are stimulated, the stimulus is sent to the primary motor area to execute it in a sequential manner to produce a **purposeful movement**. (premotor area develops a motor image of the total muscle movement, then this image excites each successive pattern of muscle activity required to achieve this image).

3) **Supplementary motor area,** which is located in front of primary motor area.
   - It is topographically organized, but it has more **coarse organization** that is different from primary and premotor areas.
   - Stimulation often elicits **bilateral movements**.
   - functions in concert with the premotor area to provide **wide attitudinal movements, fixation movements** of different segments of the body, or **positional movements** as background for the finer motor control of the arms and hands produced by premotor and primary motor cortex.

- it receives input from both the primary and premotor areas.

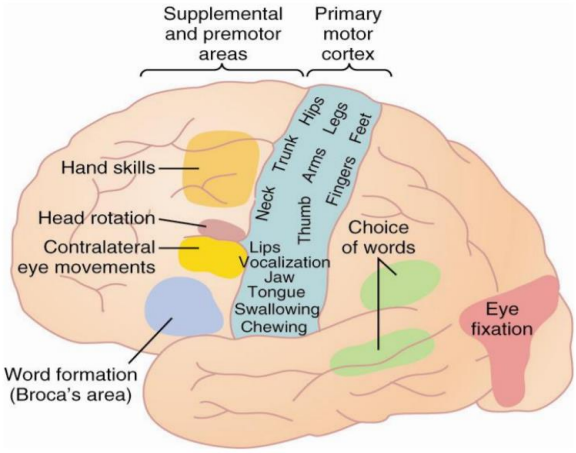
Specialized areas in the motor cortex

- **Broca's area**
  This area is located in the inferior part of premotor area. it represents the motor area of the speech. When it's stimulated, it sends the stimulus to the primary motor cortex to have **sequential** contractions and relaxations of the muscles of mouth and tongue to produce speech.
  ⇒ Damage to this area results in decreased speech capability.

  - A closely associated area controls appropriate respiratory function for speech.

- **Eye fixation and head rotation area**
  → for coordinated head and voluntary eye movements.

- **Hand skills area**
  Damage causes **motor apraxia** (inability to perform fine hand movements such as writing).



Transmission of cortical motor signals

Motor signals are transmitted from the cerebral cortex to the muscles through two pathways:

1) **Direct pathway**: corticospinal tract (pyramidal) → for discrete detailed movement of distal muscles.
2) **Indirect pathway**: extrapyramidal tract, which signals to basal ganglia, cerebellum and brainstem nuclei.

In physiology, the preferred classification is the functional one which classifies the motor pathways into **lateral system pathway** → controls extremities, and **medial system pathway** → controls axial muscles.

- Corticospinal fibers originate from motor areas, and they may also arise from the sensory areas. They consist of two types of fibers:

1) 34,000 **Betz cells fibers**, which are giant cells and make up only 3% of the total number of fibers. They synapse **directly** with the lower motor neuron in the anterior horn.

2) 1 million small diameter fibers which make 97% of the fibers. They synapse **indirectly** with LMN through interneurons.
They also conduct background tonic signals and feedback signals from the cortex to control the intensity of various sensory signals to the brain. These are the **corticofugal fibers** that we talked about previously.

- Pathway of corticospinal fibers:
They pass from the cerebral cortex through the posterior limb of internal capsule → descend to reach the medulla oblongata (pyramid) → more than 90% of fibers cross to the opposite side → descend in the lateral column (lateral corticospinal tract) and synapse with LMN that control **distal flexors.**
  - Corticobulbar fibers pass through the genu of internal capsule.
  - Lateral corticospinal tract with rubrospinal tract form the lateral system pathway.

The remaining fibers which don't cross at the medulla descend in the anterior column (anterior corticospinal tract) → cross at the level of spinal cord and synapse with LMN that control **axial muscles.**

Other motor pathways of motor cortex

- Betz cells collaterals back to cerebral cortex sharpen the boundaries of the excitatory signals.
- Fibers to caudate nucleus and putamen of the basal ganglia.

> Remember that **caudate nucleus** receives from motor area as well as association areas, thus it's involved in **cognitive functions and motor activity**.
>
> Whereas **putamen nucleus** receives from the motor area only, so it's involved only in **motor activity.**

- Fibers to the red nucleus, which then sends axons to the spinal cord in the **rubrospinal tract.**
- Fibers to reticular formation (especially medullary) to the spinal cord in the **reticulospinal tract.**

> Remember that the cortex sends excitatory signals mainly to the **medullary reticulospinal** tract which inhibits the **pontine reticulospinal** tract, so the tone is continuously checked.

- Fibers to reticular formation, vestibular nuclei and pons → to the cerebellum (mainly lateral hemisphere).

➲ So the basal ganglia$_1$, brainstem$_2$ and cerebellum$_3$ receive a large number of signals from the cortex.

Incoming sensory pathways to the motor cortex

- Subcortical fibers from adjacent areas of the cortex especially from **somatic sensory areas** of parietal cortex, **visual** and **auditory** cortex.
- Subcortical fibers from opposite hemisphere which pass through corpus callosum, anterior and posterior commissures.
- Somatic sensory fibers from ventrobasal complex (VPL, VPM) of thalamus (i.e., **cutaneous and proprioceptive fibers**).
- Ventrolateral and ventroanterior (VL, VA) nuclei of thalamus for coordination of function between **motor cortex, basal ganglia, and cerebellum**.
- Fibers from the intralaminar nuclei of thalamus (control level of excitability of the motor cortex), some of these may be **pain fibers**.

Sensory feedback for the motor control

- Feedback from muscle spindle, tactile receptors, and proprioceptors to tune the muscle movement. (to cerebellum → VA, VL of thalamus → cortex). Length mismatch in spindle causes auto-correction.
- Compression of skin provides sensory feedback to motor cortex on degree of effectiveness of intended action. Such feedback comes from large tactile receptors around the joints.

Spinal motor neurons

- Motor neurons in cortex reside in layer 5. Excitation of 50-100 giant cells is needed to cause muscle contraction.
- **Most** corticospinal fibers synapse with **interneurons**. Some corticospinal and rubrospinal neurons synapse **directly** with alpha motor neurons especially in cervical enlargement, these motor neurons innervate muscles of fingers and hands (for precise movements).

Final common pathway

Alpha motor neuron receives a lot of synapses from the corticospinal, rubrospinal, reticulospinal, reflex sensory fibers, etc. Some of them are excitatory and others are inhibitory. Summation of these synapses occurs at the level of alpha motor neurons forming what is called **grand potential.** Then the ventral spinocerebellar tract transmits a copy of this grand potential to the cerebellum to keep it informed with the updates.

➲ So the cerebellum knows about the **intension**$_1$ (cerebro-ponto-cerebellar), **feedback**$_2$ (dorsal spinocerebellar), **efference copy of the anterior horn motor signals**$_3$ (ventral spinocerebellar).

Lesions of the motor cortex

- Primary motor cortex - loss of voluntary control of discrete movement of the distal segments of the limbs on the opposite side of the body (contralateral hemiplegia).
- Basal ganglia - muscle spasticity from loss of inhibitory input from accessory areas of the cortex that inhibit excitatory brainstem motor nuclei.

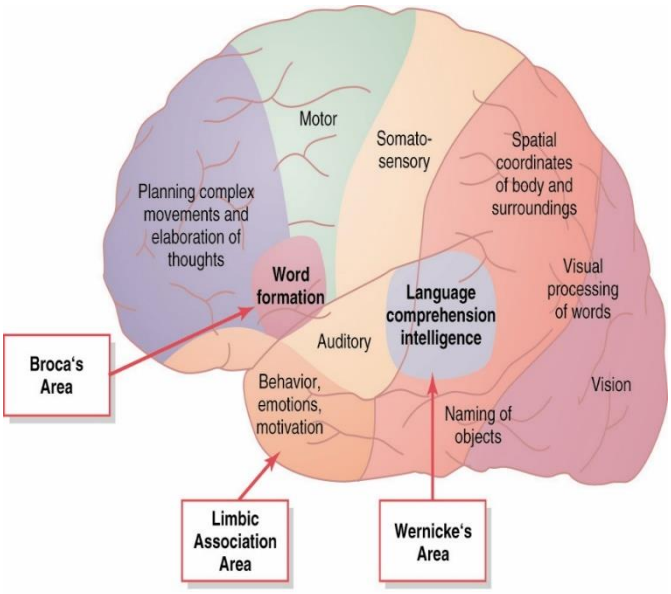
We are finished talking about the motor cortex, now we will discuss the intellectual functions of cerebral cortex, learning and memory.

Cerebral Cortex; Intellectual Functions of the Brain

Physiologic anatomy of the cerebral cortex

* Each area of the cortex is connected to a specific part of the thalamus:
  - VPL, VPM → postcentral gyrus (primary somatosensory area)
  - VA, VL → precentral gyrus (primary motor cortex)
  - LGN → occipital lobe (visual cortex)
  - MGN → temporal lobe (auditory cortex)
* When the thalamic connection is lost, function stops.
* All sensory pathways pass through the thalamus with the exception of some olfactory signals.

let's talk about the different functional areas of the cerebral cortex which are represented in the figure aside:



- Limbic association area
  - This area is found on the most anterior part of temporal lobe.
  - It's concerned with **behavior**, **emotions** and **motivation**.

- Somatosensory association area
  - It's located posterior to the somatosensory area in the parietal lobe.
  - It interprets the sensory information and is concerned with spatial coordinates of the body and surroundings. By the function of this area you can

feel the 3D shape of objects and localize different sensations and know their relations to other parts of the body.
    - If damaged → **Amorphosynthesis:** the person loses the ability to recognize the shape of the objects. Also he loses most of the sense of form of his own body on the opposite side (neglect it, forget that it's there).

- Visual association area
    - Located in the occipital lobe.
    - If damaged → word blindness.

- Auditory association area
    - Located in the temporal lobe.
    - If damaged → word deafness.

- Wernicke's area
    - Located anterior to visual cortex, inferior and posterior to somatosensory association area, and posterior to auditory association area.
    - It's the **sensory area of speech** (responsible for understanding of speech).
    - It's where the ideas about what you feel (sensations), what you see, and what you hear are formed.
    - These ideas are then transmitted in the form of signals to **Broca's area**, and from there to the **primary motor area** to produce speech. (more on this is coming)

- Prefrontal association area
    - The most anterior part of frontal lobe
    - This area is essential **for planning complex movements** and **elaboration of thoughts**, in fact this area is what forms your **personality**.
    - In the past it was believed that this area has no function, but how did they discover its function?
      This area was accidentally damaged in a railway worker named Phineas Gage, after which he became distracted, socially disinhibited, he lost the ability to prognosticate (foretell, predict). He lost the ability to do mathematical equations and make complex movements. His personality changed significantly and he acquired bizarre behavior.

- Area for recognition of faces and naming of objects
    - located in the inferomedial aspect of temporal lobe.
    - damage to this area → Prosopagnosia (inability to recognize faces).

Dominant and nondominant hemisphere

* When we say dominant and nondominant we refer to the **language areas only**.
* Almost 95% of the right-handed people have a left dominant hemisphere.
* More than two thirds of left-handed people also have a left dominant hemisphere. The remaining third: half of them have right dominant hemisphere, and the other half have no dominant hemisphere.
* But what do we mean by a dominant hemisphere?
  It means that the language areas are **larger** in the dominant hemisphere than the areas in the other nondominant hemisphere, this is called **lateralization of the cerebral cortex.**
  Wernicke's area can be as much as 50% larger in the dominant hemisphere.
* This doesn't mean that areas in the non-dominant side have no function. They are related to other forms of sensory intelligence (art, music, sensory, feelings).
* Damage to dominant Wernicke's area leads to **dementia** because it's also related to memory.
* Damage to language areas in the dominant hemisphere results in aphasia, whereas damage to the right hemisphere doesn't cause aphasia.
* Hemiplegia on the right side of the body is more likely to be associated with aphasia (damage to the left cerebral cortex that involves multiple areas), hemiplegia on the left side is less likely to be associated with aphasia.

- The dominance has no relation to handedness. **Handedness** means that right-handed individuals are born with the area that controls the movement of the right hand in the left cerebral hemisphere being larger than the opposite area, and as they grow up they tend to use the right hand, so this area grows and becomes dominant, and vice versa for the left-handed people.
- Left-handed individuals can convert to right-handed if they start to use their right hand instead, and the younger the individual the easier it will be because his/her brain is plastic. This applies to any learning skill (the younger the easier).
- Same applies for using the legs
- Close to 90% of people are right-handed and close to 10% are left-handed and a small number are ambidextrous (use both hands).

TABLE 14.3

Functional Differences Between the Two Cerebral Hemispheres

LEFT HEMISPHERE FUNCTIONS	RIGHT HEMISPHERE FUNCTIONS
Receives somatic sensory signals from and controls muscles on right side of body.	Receives somatic sensory signals from and controls muscles on left side of body.
Reasoning.	Musical and artistic awareness.
Numerical and scientific skills.	Space and pattern perception.
Ability to use and understand sign language.	Recognition of faces and emotional content of facial expressions.
Spoken and written language. (verbal)	Generating emotional content of language.
	Generating mental images to compare spatial relationships.
	Identifying and discriminating among odors.

Table 14.03 Tortora - PAP 12/e

Language areas

* Located in large area surrounding the left (or language dominant) lateral sulcus.
* Major parts and functions:

  - Wernicke's area
    Damage → **sensory aphasia** (receptive aphasia), in which individuals have difficulty understanding written and spoken language. They demonstrate **fluent** speech, but their speech lacks content or meaning.

  - Broca's area
    Damage → **motor aphasia** (expressive aphasia), in which individuals can understand written and spoken language and form ideas, but they have difficulty expressing their ideas by speech and their speech is **non-fluent**.

  ⇒ If both Wernicke's and Broca's areas are damaged → **global aphasia** (both expressive and receptive language skills are reduced).

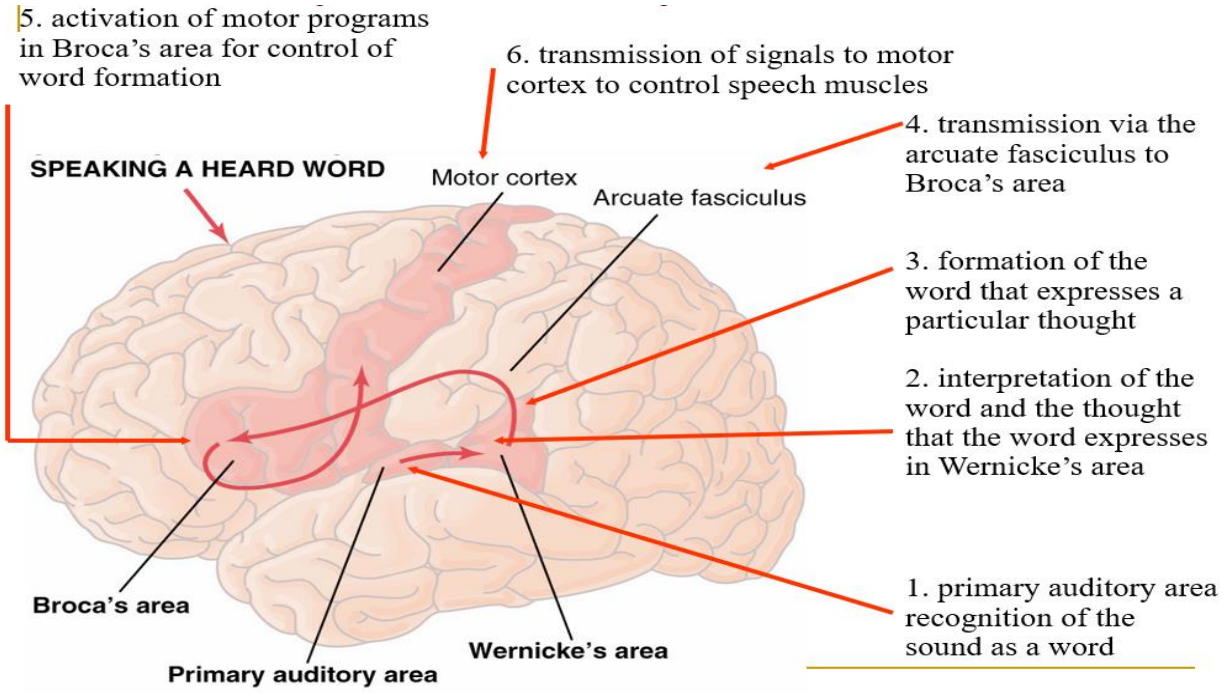
  - Lateral prefrontal cortex: for language comprehension and word analysis.

  - Lateral and ventral temporal lobe: coordinate auditory and visual aspects of language.

Intellectual functions of the prefrontal association area

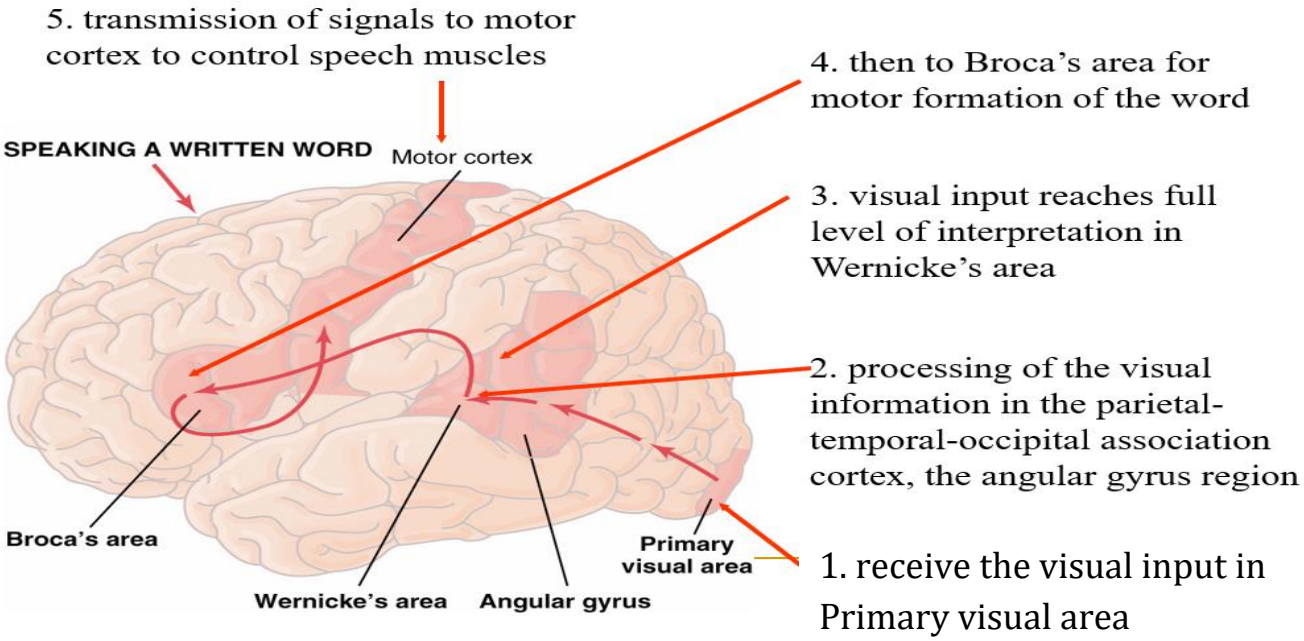
- responsible for calling forth stored information and using it to obtain a goal.
- responsible for concerted thinking in a logical sequence.
- elaboration of thought.
- prognosticate, plan, consider consequences of motor actions before they are performed.
- correlate widely divergent information, control one's activities.
- Personality trait and behavior that confines to values and manners of the culture.
- damage causes an inability to keep tract of simultaneous bits of information, easily distracted.

Pathways for auditory communication



⇒ Note: after the primary auditory area it's transmitted to the auditory association area and then to Wernicke's area.

Pathways for visual communication



- Speech involves two things:
  - ✓ formation in the mind of thoughts to be expressed and the choice of words.
  - ✓ motor control of vocalization and the act of vocalization.

⇒ Formation of word, thought and choice of words is function of **Wernicke's area**.
⇒ **Broca's area** controls the motor coordination required for speech.

➲ Destruction of the visual and auditory association areas results in an inability to understand the written words (word blindness) or spoken words (word deafness).

What is the difference between sensory aphasia and word deafness?
Word deafness results from damage to the auditory association area, and it leads to total loss of the ability to understand spoken words. **Sensory aphasia** results from damage to the Wernicke's area, some people might be capable of understanding spoken words (auditory association area is intact) but are unable to put together the appropriate sequences of words to express the thought, but in more severe damage they might be unable to formulate the thoughts.

■ Corpus callosum

- Connects the two hemispheres and allows transfer of information.
- Interruption of these fibers can lead to bizarre types of anomalies.
  People whose corpus callosum is completely sectioned have two entirely separate conscious portions of the brain.
  In a person with a sectioned corpus callosum, only the dominant hemisphere could understand the spoken word, whereas the non-dominant hemisphere could understand only the written word but not the spoken word*. The non-dominant hemisphere can elicit motor response to the written word without the dominant hemisphere ever knowing why the response was performed!

*non-dominant hemisphere has the angular gyrus, which is partly responsible for the interpretation of written words, but it doesn't have the Wernicke's area because it's only present in the dominant hemisphere.

■ Thoughts, learning and memory

- Neural mechanism 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.
- **Learning** is acquiring new sensory information or motor skills.
  - Learning results from the change in the capability of synaptic transmission from neuron to neuron as a result of prior stimulation.
- **Memory** is the ability to recall specific information.
  - Memory trace is a specific pattern or pathway of signal transmission.
  - the more important the information is, the more easily you remember it.

There are three types of memory:

1) **Immediate memory**: lasts for seconds or minutes (remembering 10 digit phone number).
   Mechanism: may result from **synaptic potentiation** through the accumulation of calcium in the presynaptic membrane, which promotes neurotransmitter release.

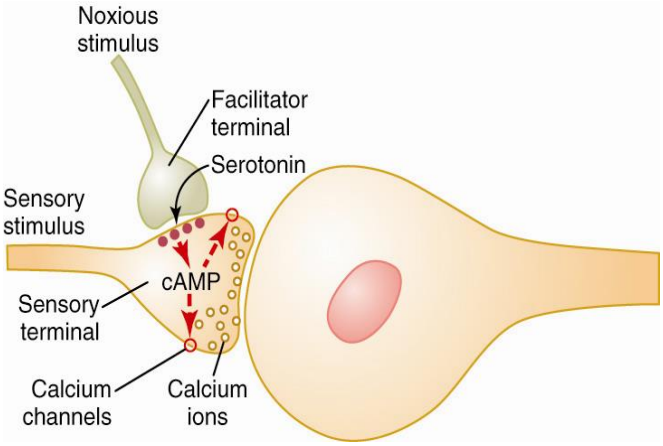
2) **Short term memory**: lasts for days to weeks (remembering exam material 🙃).
   Mechanism: result from a **temporary physical or chemical change** in the pre- or postsynaptic membrane.

3) **Long term memory**: lasts for years or for a lifetime (your name, date of birth..).
   Results from **permanent changes** (to be discussed after a while).

- **Molecular basis for intermediate memory**

now let's talk about the molecular mechanism in which our memory is formed and even how we forget things!

- There are two synaptic terminals, one is sensory terminal from a sensory input neuron, and the other is facilitator terminal which is activated by noxious stimulus (when you **try** to remember something).
- The facilitator terminal is connected presynaptically with the sensory terminal and stimulates it by releasing a transmitter (serotonin).
- The transmitter activates G protein in the sensory terminal which in turn activates adenylate cyclase resulting in an increase in cAMP.
- cAMP activates a protein kinase that phosphorylates a component of the K+ channel blocking its activity.
- This causes prolonged depolarization and prolonged action potential which results in prolonged activation of calcium channels allowing high amounts of calcium to enter the sensory synaptic terminal.
- These calcium ions cause greatly increase transmitter release by the sensory terminal, thereby markedly facilitating synaptic transmission to the subsequent neuron.



➲ Important notes:

Even when the facilitator neuron is not stimulated (that is, you don't try to remember something again, like when you don't revise the material before the exam), there is continuous stimulation for the sensory terminal. However, without the stimulation of the facilitator terminal, signal transmission at first is great, but it becomes less and less intense with repeated stimulation until transmission almost ceases. This phenomenon is called **habituation**. It's a form of **negative memory** that causes the neuronal circuits to lose its response to repeated events that are insignificant, or a bad experience that you don't like to remember.

So habituation is a progressive decline in sensitivity. But how does this occur? This results from progressive decline in the number of active calcium channels → less calcium entry → less transmitter released.

On the other hand, the associative effect of stimulating the facilitator terminal at the same time that the sensory terminal is stimulated causes **prolonged** increase in the excitatory sensitivity of the sensory terminal, which establishes the **memory trace**, and this prevents habituation. (isn't that crazy? 😯)

- **Mechanism of Long-term memory**

Long term memory is believed to result from actual **structural and functional changes (permanent),** instead of only chemical changes.

- An increase in the **area for vesicular release**, therefore, more transmitter is released. (the number of neurons can't increase, rather, the number of synapses and spikes is increased) → permanent anatomical (structural) change.
- This enlargement of the release site area results from synthesis of **release site proteins.** (long term memory involves genetic changes. some genes are dormant, when you activate these genes you activate the formation of new proteins) → permanent physiological (functional) change.

✓ during periods of inactivity the area decreases in size.

- **Consolidation of memory**

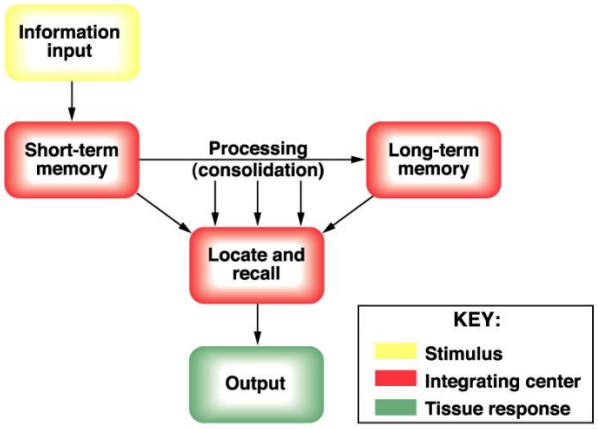
* It means converting immediate into short and long-term memory.
* There are two ways to speed up consolidation:
  1. Rehearsal (repetition of the information).
  2. Filing of information.

✓ It results from chemical, physical and anatomical changes in the synapse (as we discussed).

✓ It requires time.

✓ interruption of the process by electrical shock or by anesthesia will prevent memory development.

⇒ The first stage of memory is called **registration,** when you receive the information into the short-term memory. **Retrieval** is recalling back the stored information in response to some cues. You can convert short-term memory to long-term memory through consolidation.
-Immediate memory doesn't need registration.



■ Brain centers and memory

- One of the areas in the brain that is important for recalling memory is **thalamus**. Thalamus scans the cortex for the area and the circuit for the stored memory (search).

  Damage to thalamus causes **retrograde amnesia** or the inability to recall stored experiences from the **recent past events**. When the damage is more severe, more distant past memories will be lost.

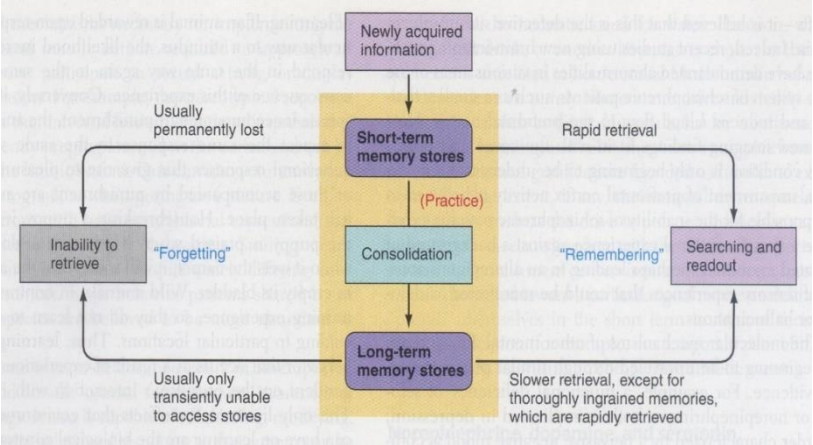
- **Hippocampus** also has a very important role in memory.

● Comparison between 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 to days and weeks	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

- The **capacity** of short-term memory is limited, that's why we forget (delete :p) much of the information after an exam to leave a space for the next exam material, but if these information were consolidated into the long-term memory, it has a very large capacity which is enough to huge amounts of information.

- On the other hand, the **retrieval time** (remembering) of the information from the short-term memory is rapid, whereas remembering information from the long-term memory takes longer time, that's why sometimes you try hard to remember something and you give up, but after a while the information pops into your head.



Good Luck