Limbic System & Insula

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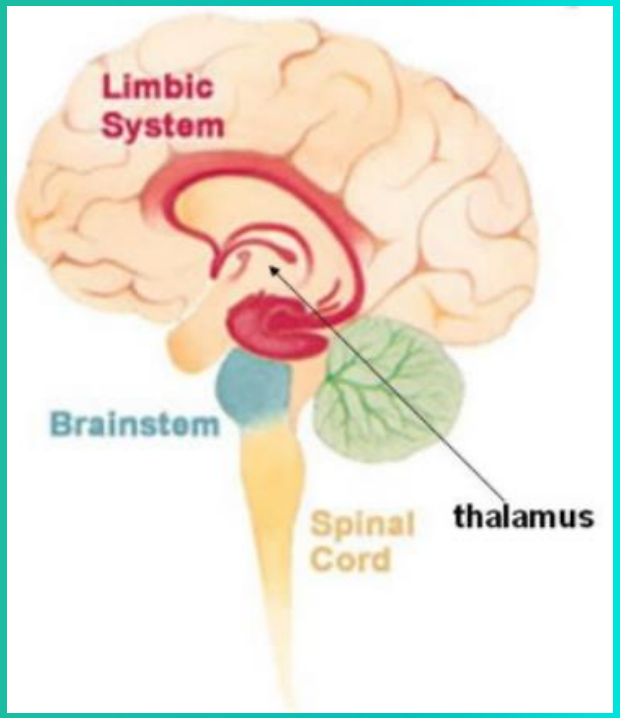
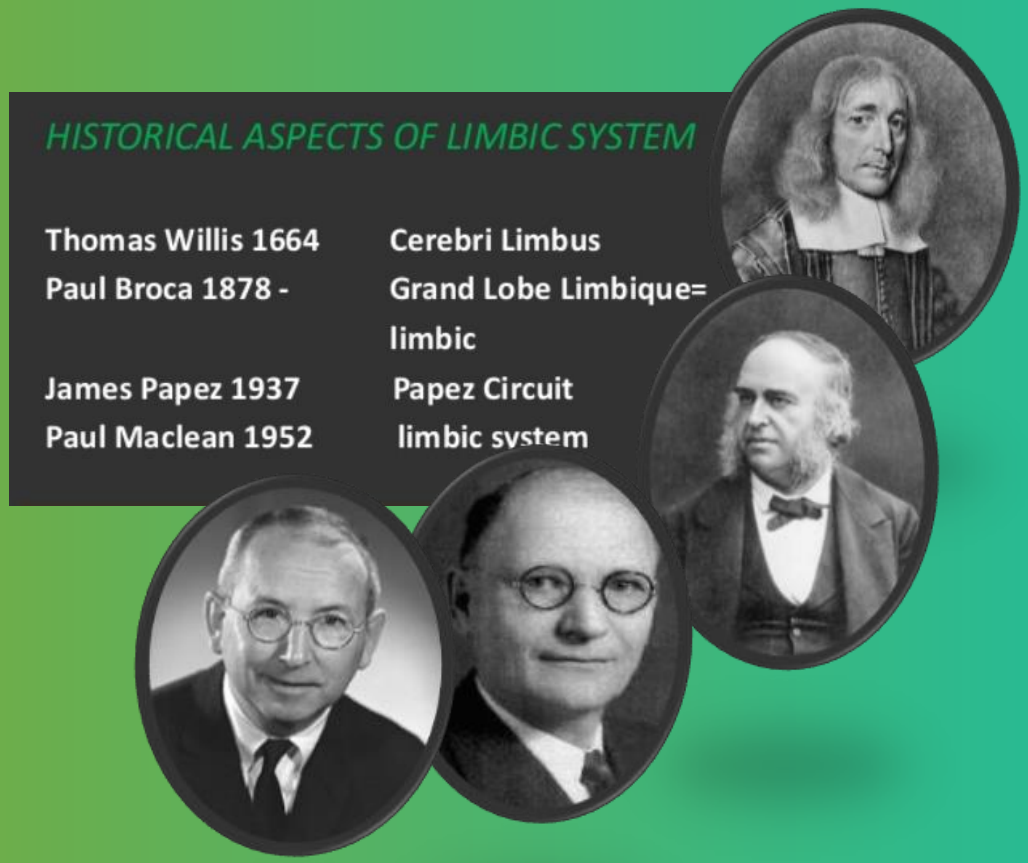
- Limbus (Latin) means “border” or “edge”

→ Includes the structures that lie in the border zone between the cerebral cortex and diencephalon

- Links different areas so integration can occur

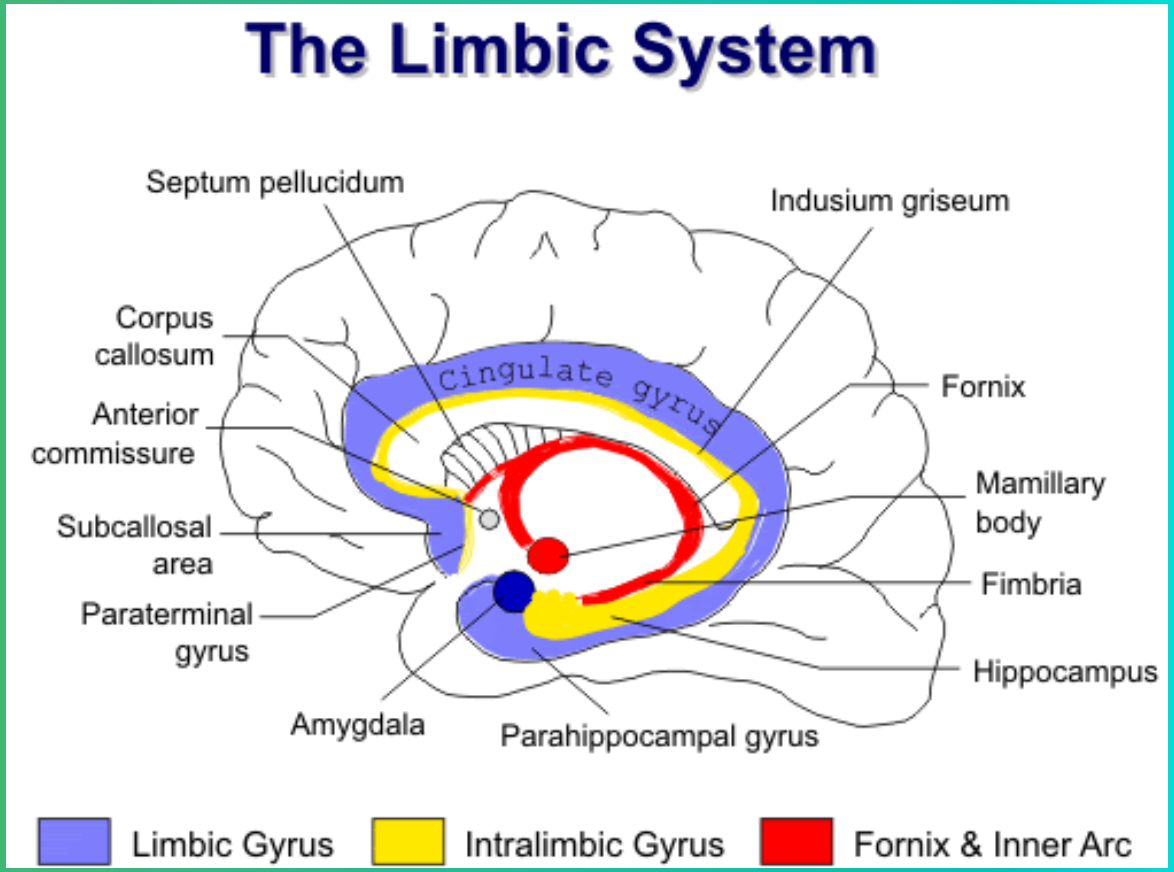
  Integration: separate things are brought together as a whole





Important Functions:

- Emotion
- long-term memory

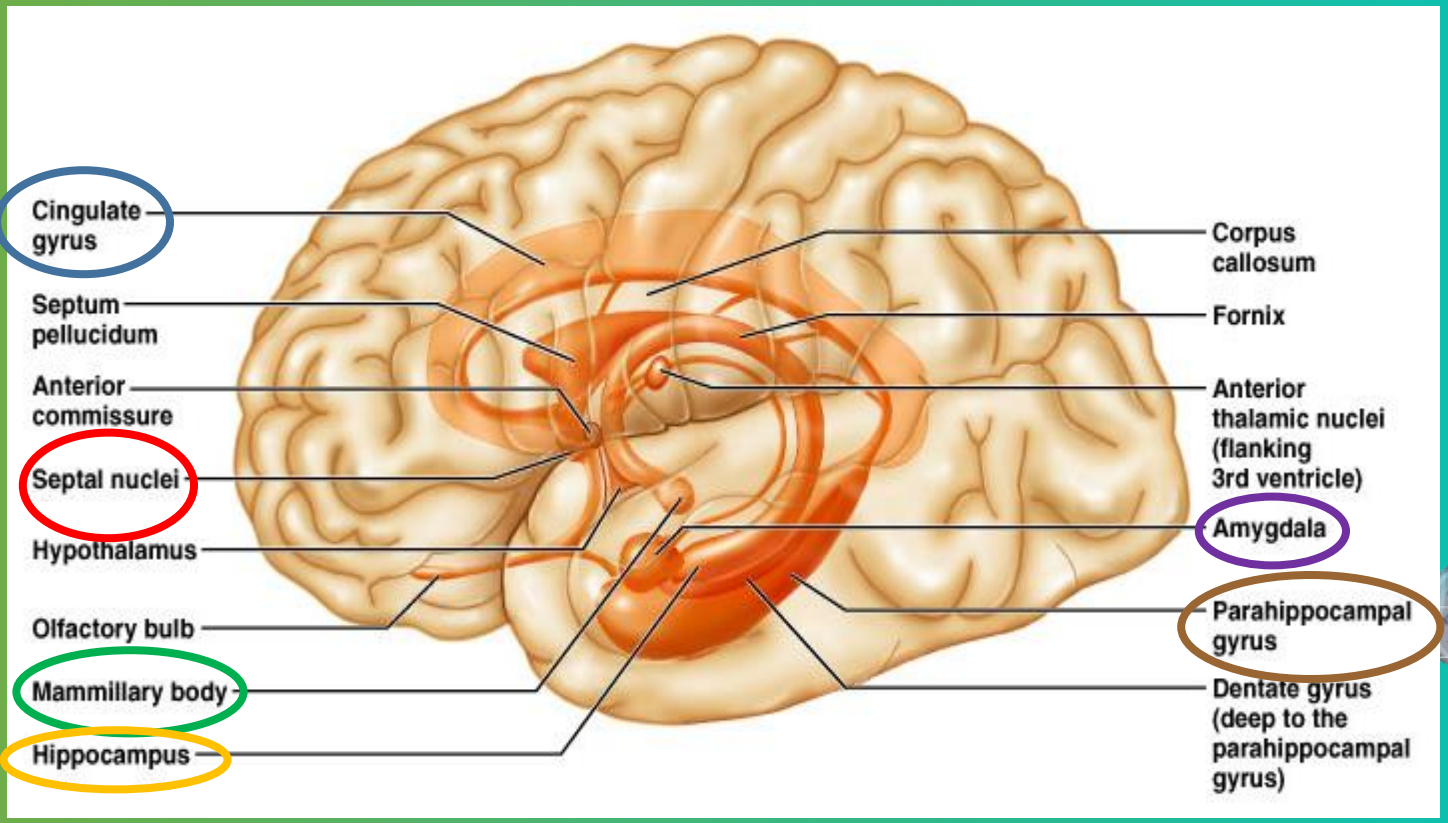


Other Functions:

- Olfaction
- Sexual behavior
- Addiction and motivation
- Social cognition
- …

- Most important parts:
  - Hippocampus
  - Amygdala

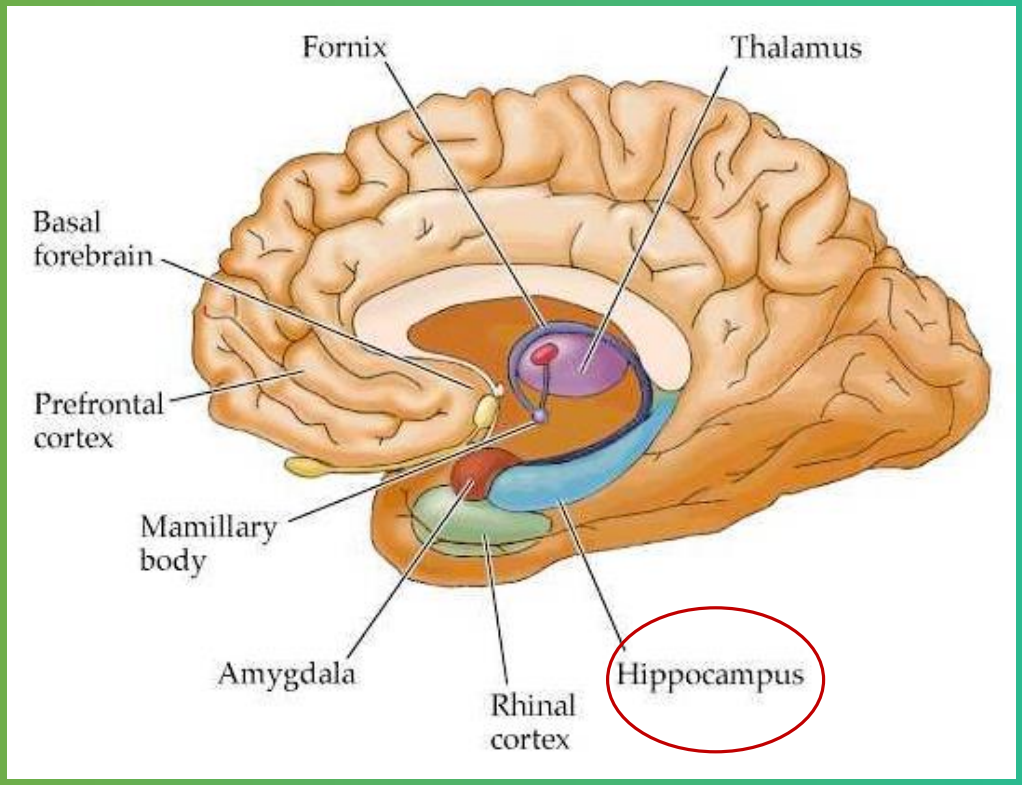
- Other parts:
  - Cingulate gyrus
  - Parahippocampal gyrus
  - Mammillary bodies
  - Septal area
  - Insula
  - Nucleus accumbens
  - Medial prefrontal cortex
  - Uncus

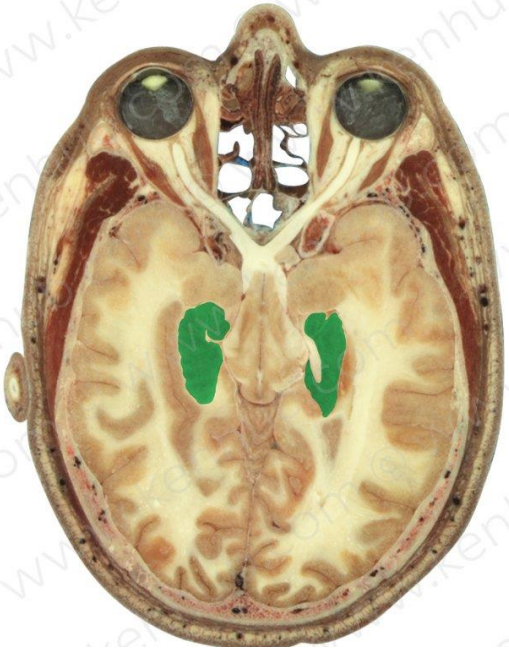


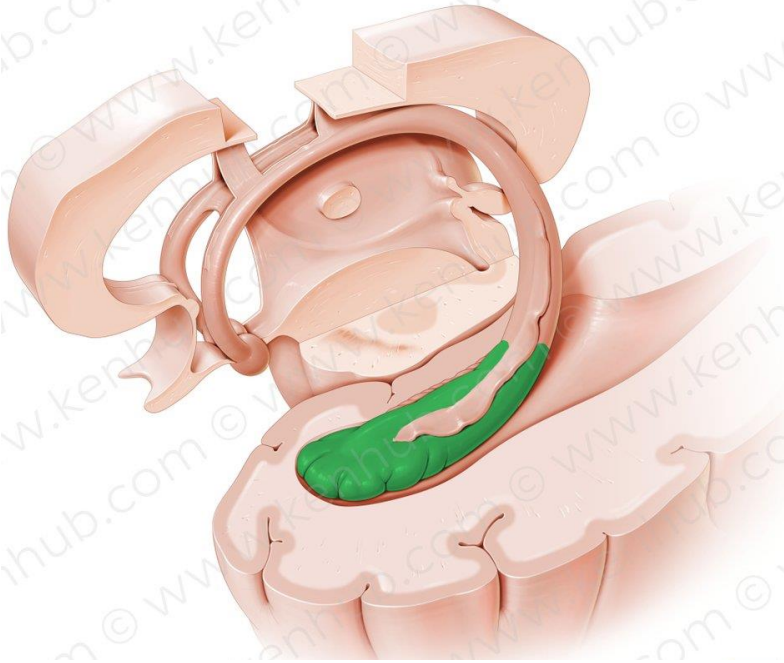
Hippocampus

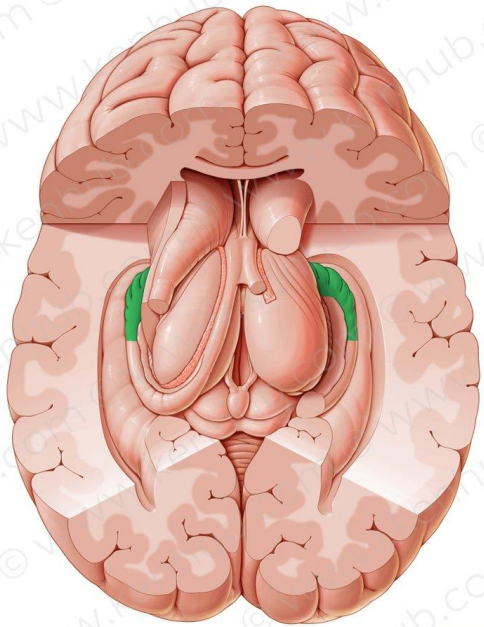
Julius Caesar Aranzi (1587):
who likened it first to a silkworm and then to a seahorse

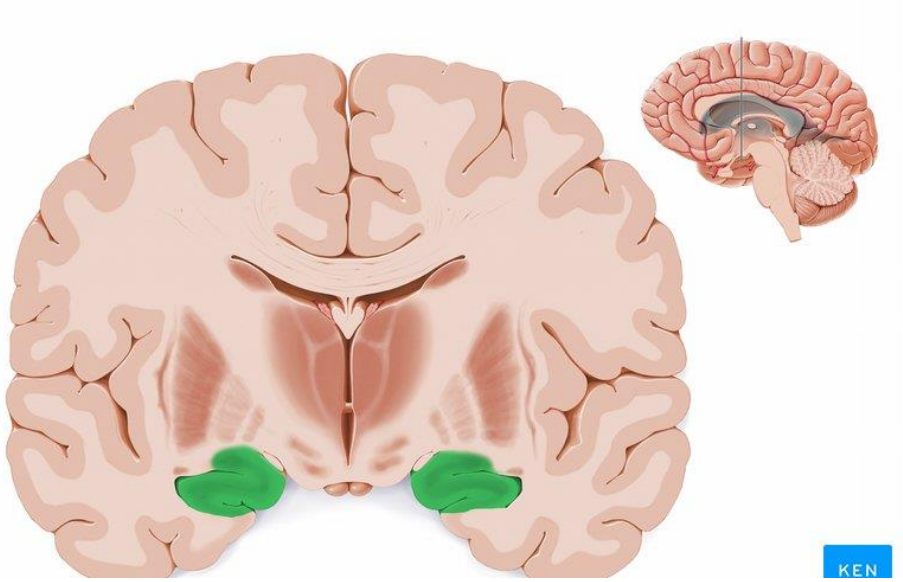
Involved in various processes of cognition (Learning & memory)



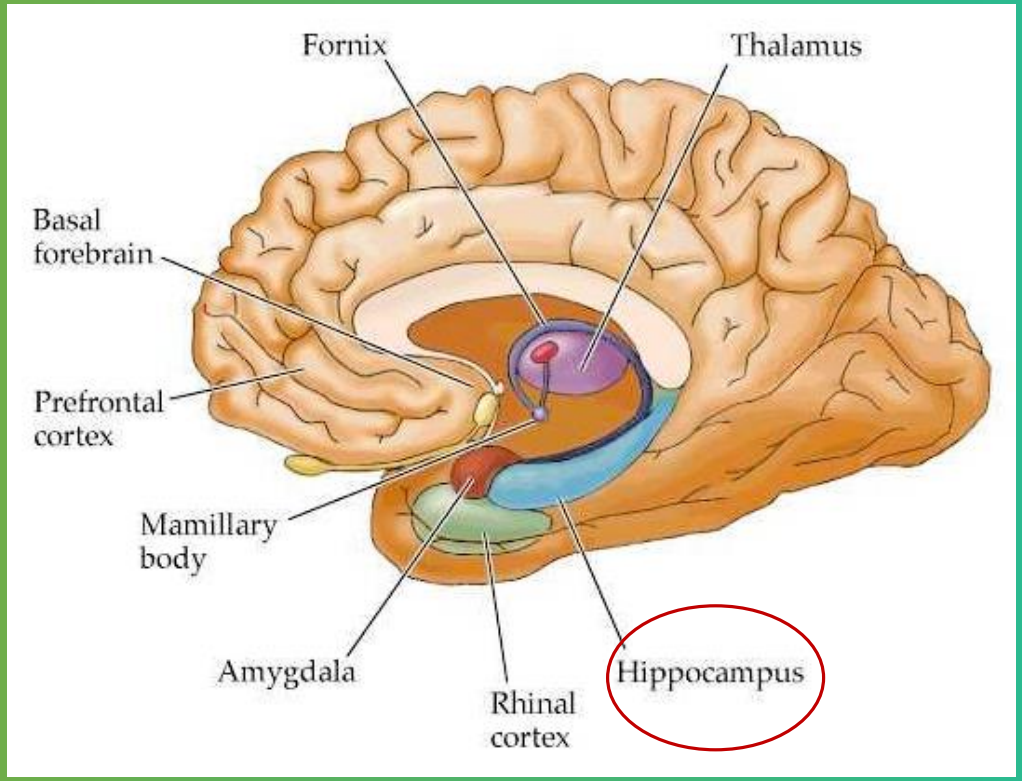








- Formation of new synapse/ Strength exiting synapse ➡ learning
- Formation of long-term memories from short term memory (consolidation)
- General concentrated region for binding together bits and pieces of memory to be recalled at a later time
- Generation of new neurons, in adolescence and adulthood.



Anterograde amnesia:

Severe damage to the hippocampus results in profound difficulties in forming new memories

Retrograde amnesia:

Affects memories formed before the damage occurred

In some cases older memories remain.

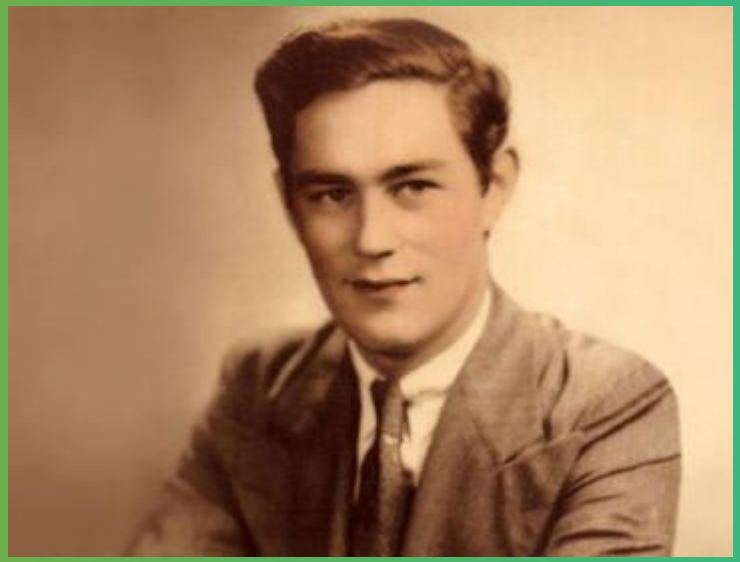
Consolidation over time involves the transfer of memories out of the hippocampus to other parts of the brain

Not affect some types of memory, such as the ability to learn new skills (playing a musical instrument).

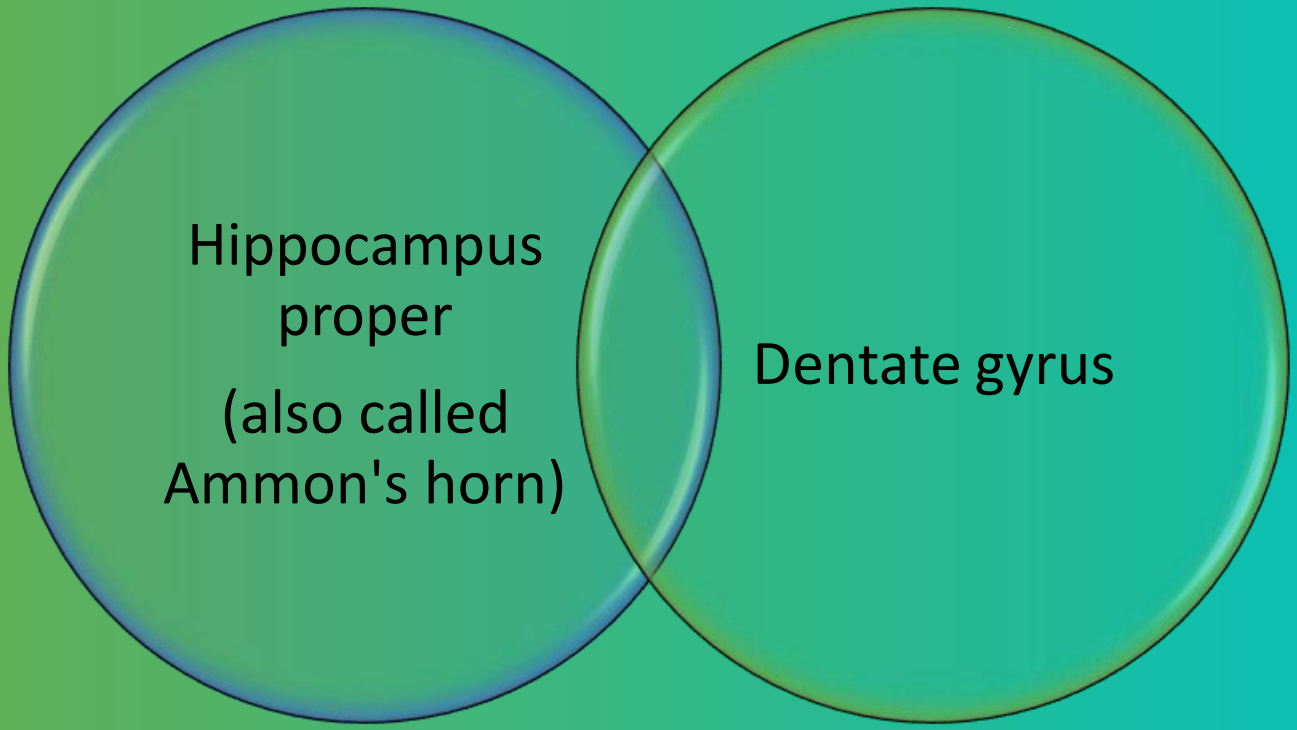
Such abilities depend on different types of memory and different brain regions

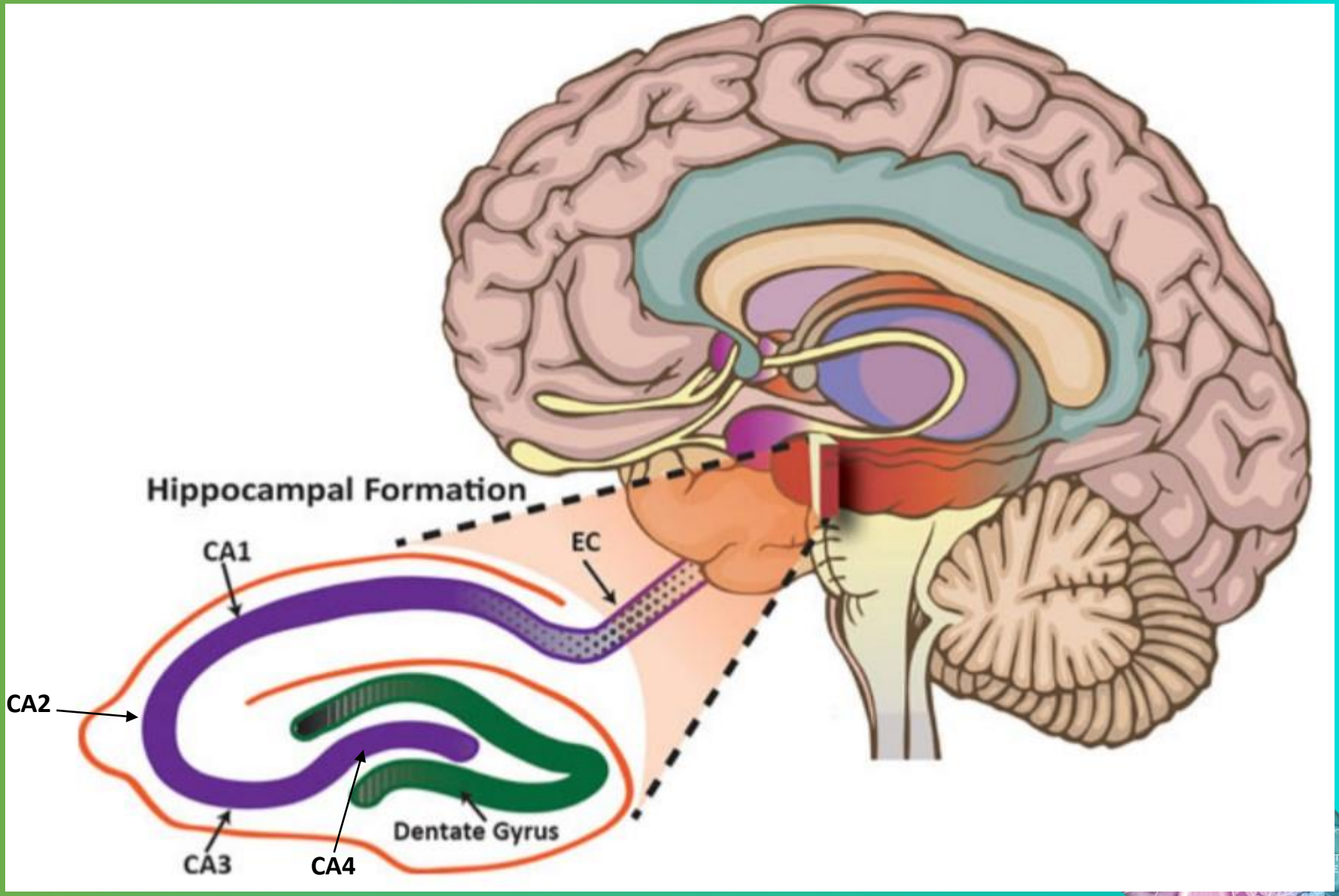
A famous report by William Beecher Scoville and Brenda Milner:

The results of surgical destruction of the hippocampi when trying to relieve epileptic seizures in an American man Henry Molaison, known until his death in 2008 as "Patient H.M."
The unexpected outcome of the surgery was severe anterograde amnesia

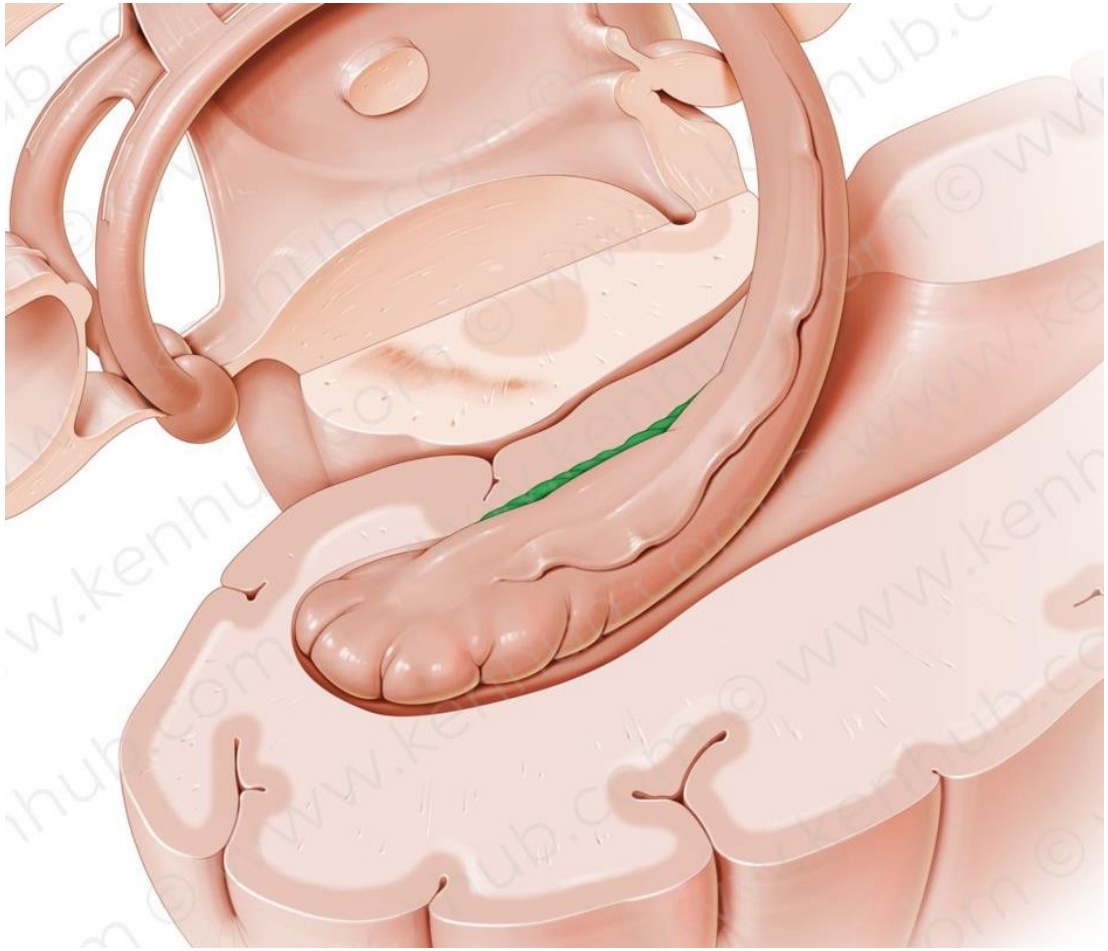


It contains two main interlocking parts:



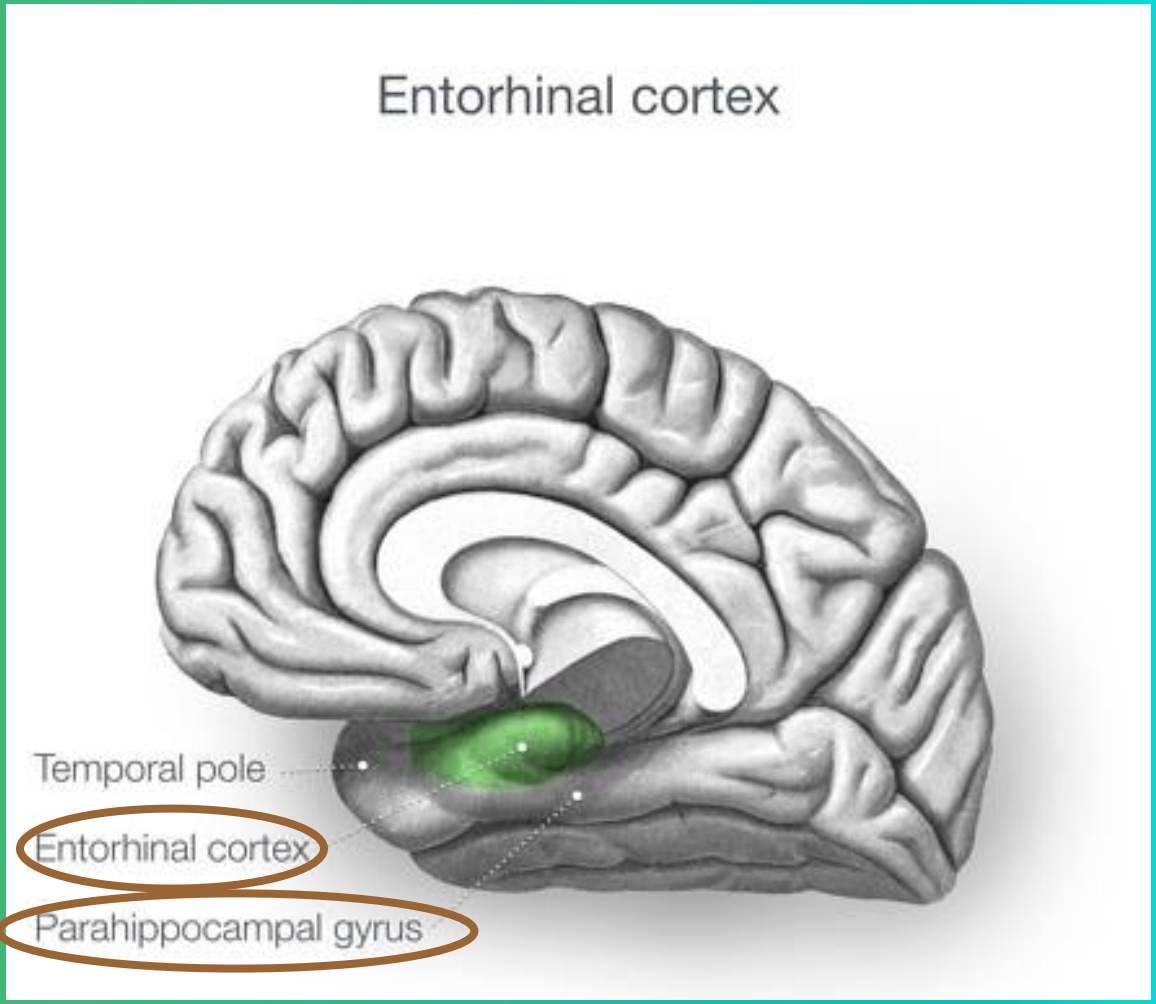

Hippocampal Formation
CA1
EC
CA2
Dentate Gyrus
CA3
CA4

Dentate gyrus



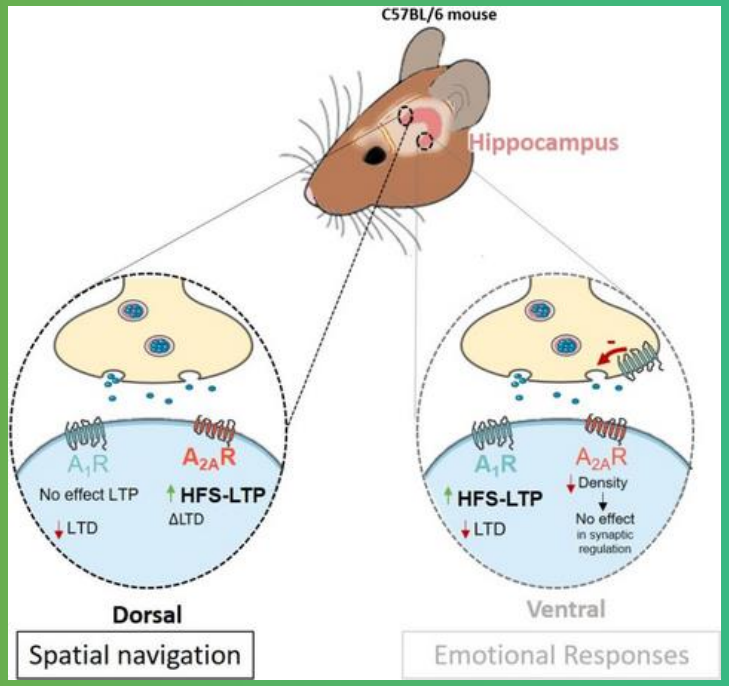
The major input:
Entorhinal cortex (EC)

The major output:
CA1



The EC is located in the parahippocampal gyrus a cortical region adjacent to the hippocampus. This gyrus conceals the hippocampus.

Dorsal hippocampus	Ventral hippocampus	Intermediate hippocampus
• Spatial memory • Verbal memory	• Fear conditioning • Affective processes. With amygdala	• Overlapping characteristics



The dorsal hippocampus also has more place cells than both the ventral and intermediate hippocampal regions.

Role in memory

Hippocampus plays an important role in the formation of new explicit memories:

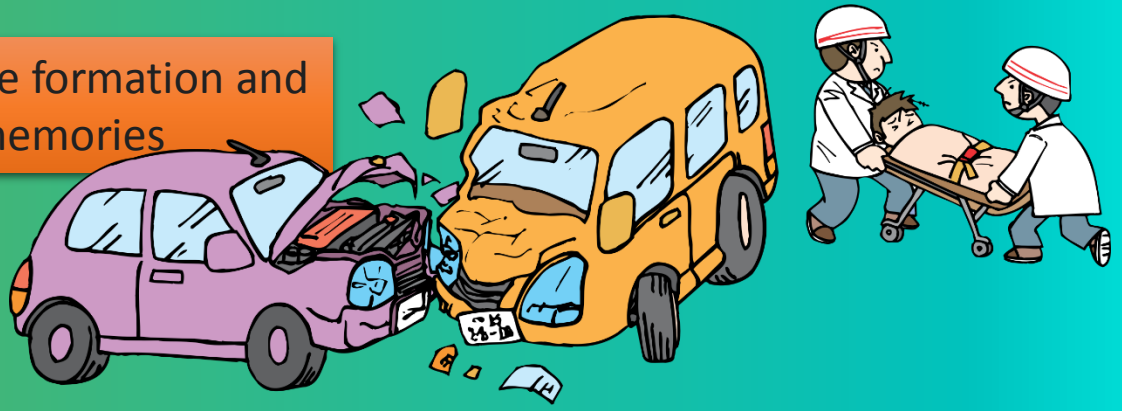
- Episodic or autobiographical memory
- Memory for facts
- Emotional memory (with amygdala)

Why returning to a location where an emotional event occurred may evoke that emotion?

If damage to the hippocampus occurs in only one hemisphere → near-normal memory functioning.

Severe damage to the hippocampi in both hemispheres → profound difficulties in anterograde amnesia.

Hippocampus is required for the formation and recall, but not the storage, of memories



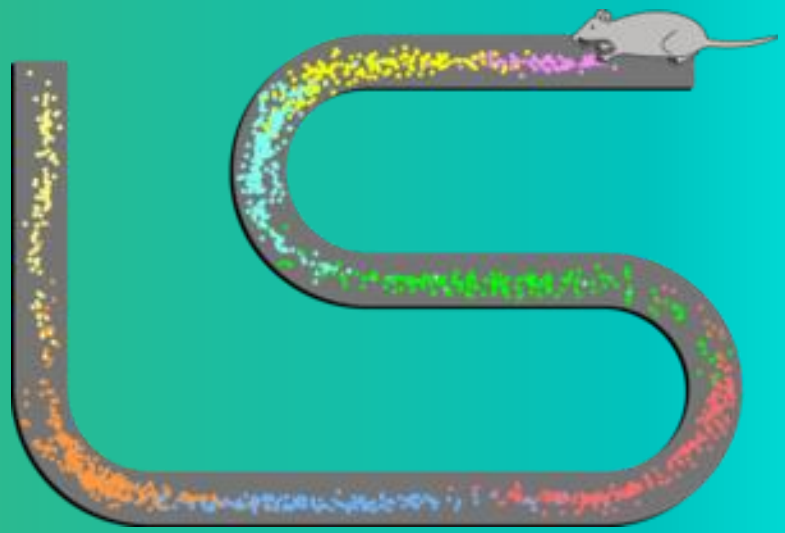
Role in spatial memory and navigation

Many hippocampal neurons act as place cells that cluster in place fields, and these fire bursts of action potentials when the animal passes through a particular location.

Neural activity sampled from 30–40 randomly chosen place cells carries enough information to allow an animal location to be reconstructed with high confidence.

The firing rate of hippocampal cells depends on:

- Place
- Direction of move
- Destination



An interesting study:

London's black cab drivers need to learn the locations of a large number of places and the fastest routes between them in order to pass a strict test.

The posterior part of the hippocampus is larger in these drivers than in the general public, and that a positive correlation exists between the length of time served as a driver and the increase in the volume of this part.
It was also found the total volume of the hippocampus was unchanged, as the increase seen in the posterior part was made at the expense of the anterior part, which showed a relative decrease in size.
There have been no reported adverse effects from this disparity in hippocampal proportions.

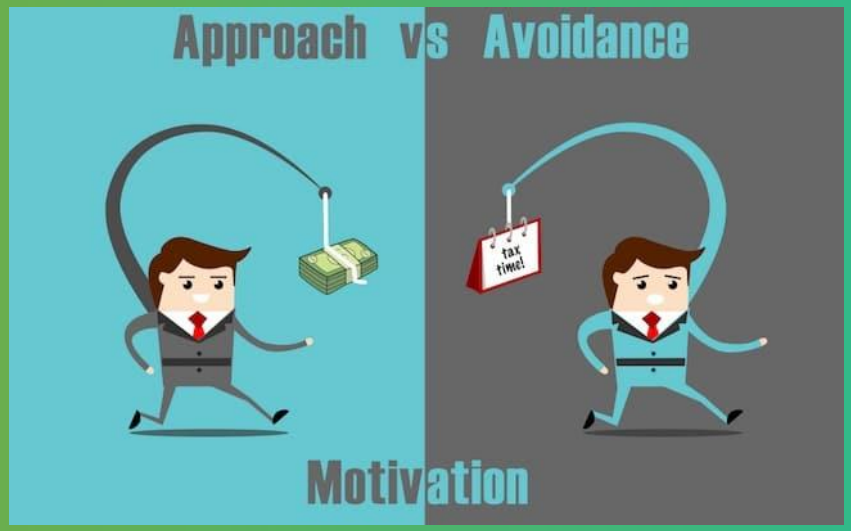
When the hippocampus is dysfunctional, orientation is affected; people may have difficulty in remembering how they arrived at a location and how to proceed further. Getting lost is a common symptom of amnesia.

Role in approach-avoidance conflict processing

Approach-avoidance conflict happens when a situation is presented that can either be rewarding or punishing.

The ensuing decision-making has been associated with anxiety.

The anterior hippocampus is sensitive to conflict (with cingulate & frontal cortex)



Role in Long-term potentiation

Brain stores memory by altering the strength of connections between neurons that are simultaneously active. This idea was formalized by Donald Hebb in 1949, but for many years remained unexplained.

A change in synaptic responsiveness induced by brief strong activation and lasting for hours or days or longer. This phenomenon is referred to as long-term potentiation (LTP).

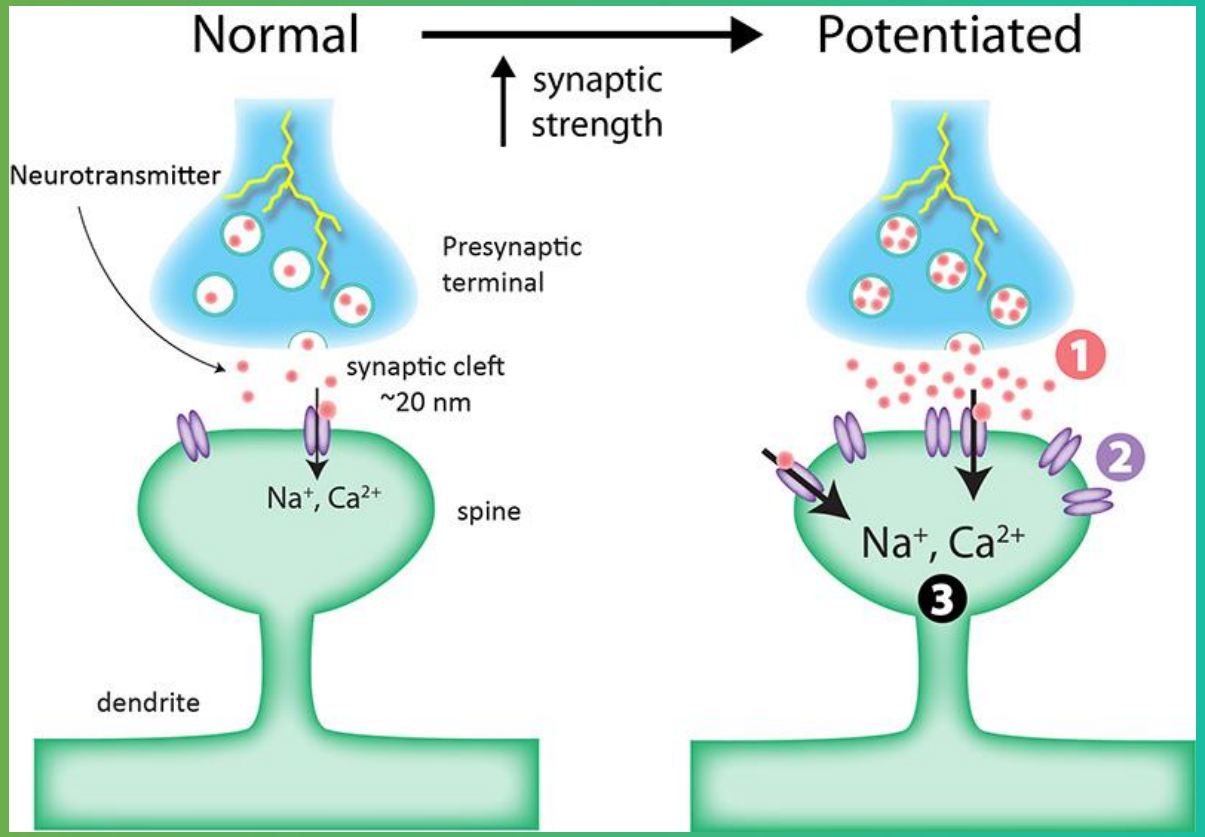
As a candidate mechanism for long-term memory

Use the neurotransmitter glutamate

The synaptic changes depend on a special type of glutamate receptor (NMDA)

Allowing calcium to enter the postsynaptic spine only when presynaptic activation and postsynaptic depolarization occur at the same time.

Drugs that interfere with NMDA receptors block LTP and have major effects on some types of memory, especially spatial memory.



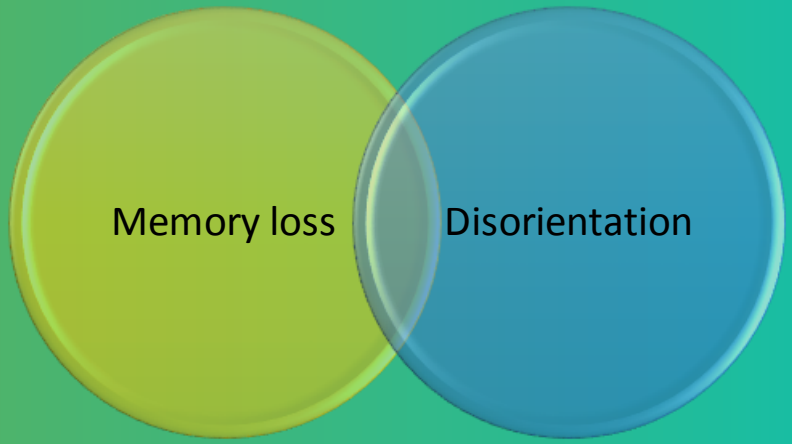
Disorders

Aging

- Normal aging is associated with a gradual decline in some types of memory
- Age-related declines could be caused by hippocampal deterioration.
- Loss of neurons in the hippocampus of elderly people
- Similarly, some MRI studies have reported shrinkage of the hippocampus in elderly people
- A reliable relationship between the size of the hippocampus and memory performance; so that where there is age-related shrinkage, memory performance will be impaired

Age-related conditions such as Alzheimer's disease and other forms of dementia

hippocampal disruption is one of the earliest signs



Damage to the hippocampus can also result from:

Hypoxia

Encephalitis

Medial temporal lobe epilepsy

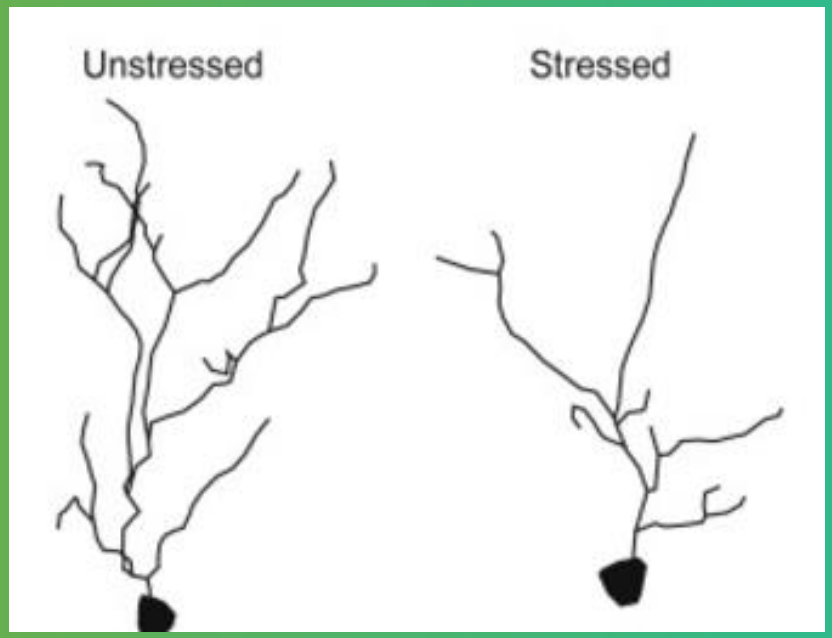
Stress

- The hippocampus contains high levels of glucocorticoid receptors, which make it more vulnerable to long-term stress than most other brain areas.

- There is evidence that humans having experienced severe, long-lasting traumatic stress show atrophy of the hippocampus more than of other parts of the brain.

- A recent study has also revealed atrophy as a result of depression, but this can be stopped with anti-depressants even if they are not effective in relieving other symptoms.

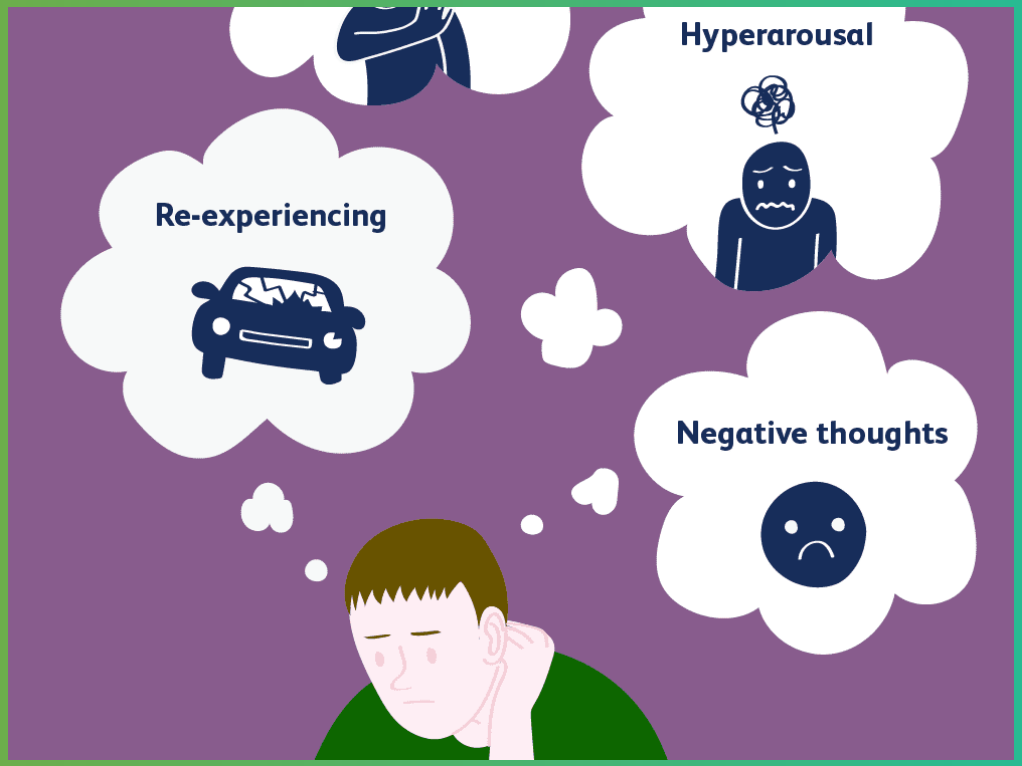
- Another factor that contributes to a smaller hippocampal volume is that of dendritic retraction where dendrites are shortened in length and reduced in number, in response to increased glucocorticoids. This dendritic retraction is reversible.
- **Sex-specific responses to stress** have also been demonstrated in the rat to have an effect on the hippocampus. Chronic stress in the male rat showed dendritic retraction but this was not shown in the female. This was thought to be due to neuroprotective ovarian hormones.



PTSD

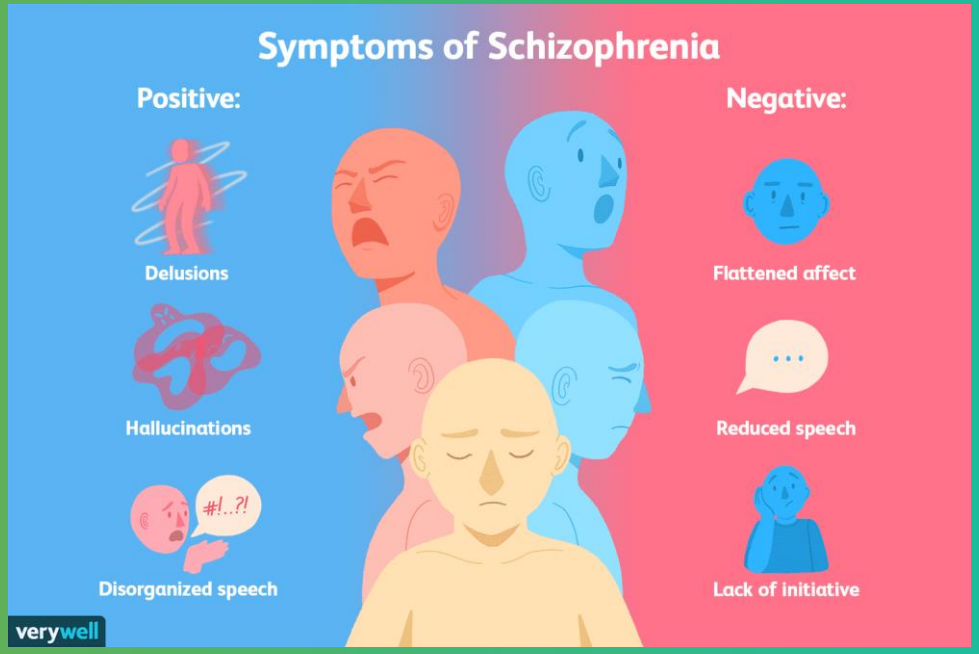
Some studies shows correlation of reduced hippocampus volume and posttraumatic stress disorder (PTSD).

A study of Vietnam War combat veterans with PTSD showed a 20% reduction in the volume of their hippocampus compared with veterans having suffered no such symptoms.



Schizophrenia

- The causes of schizophrenia are not well understood, but numerous abnormalities of brain structure have been reported.
- The most thoroughly investigated alterations involve the cerebral cortex, but effects on the hippocampus have also been described.
- Many reports have found reductions in the size of the hippocampus in people with schizophrenia.
- The left hippocampus seems to be affected more than the right.

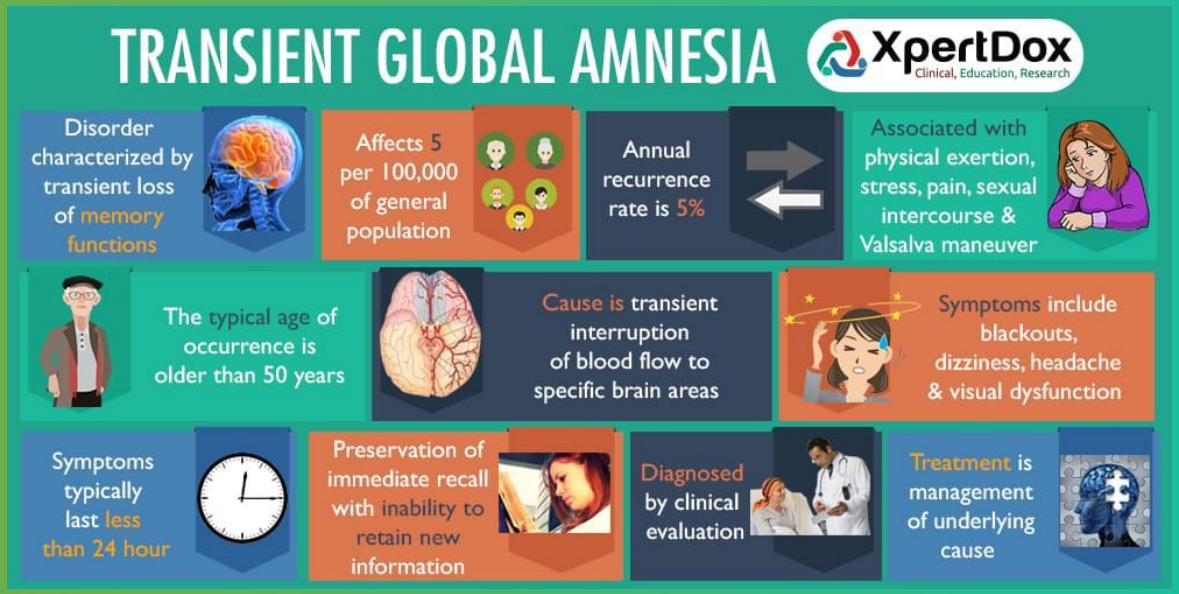


Transient global amnesia

Transient global amnesia is a dramatic, sudden, temporary, near-total loss of short-term memory.

Various causes have been hypothesized including:

- Ischemia
- Epilepsy
- Migraine
- Disturbance of cerebral venous blood flow

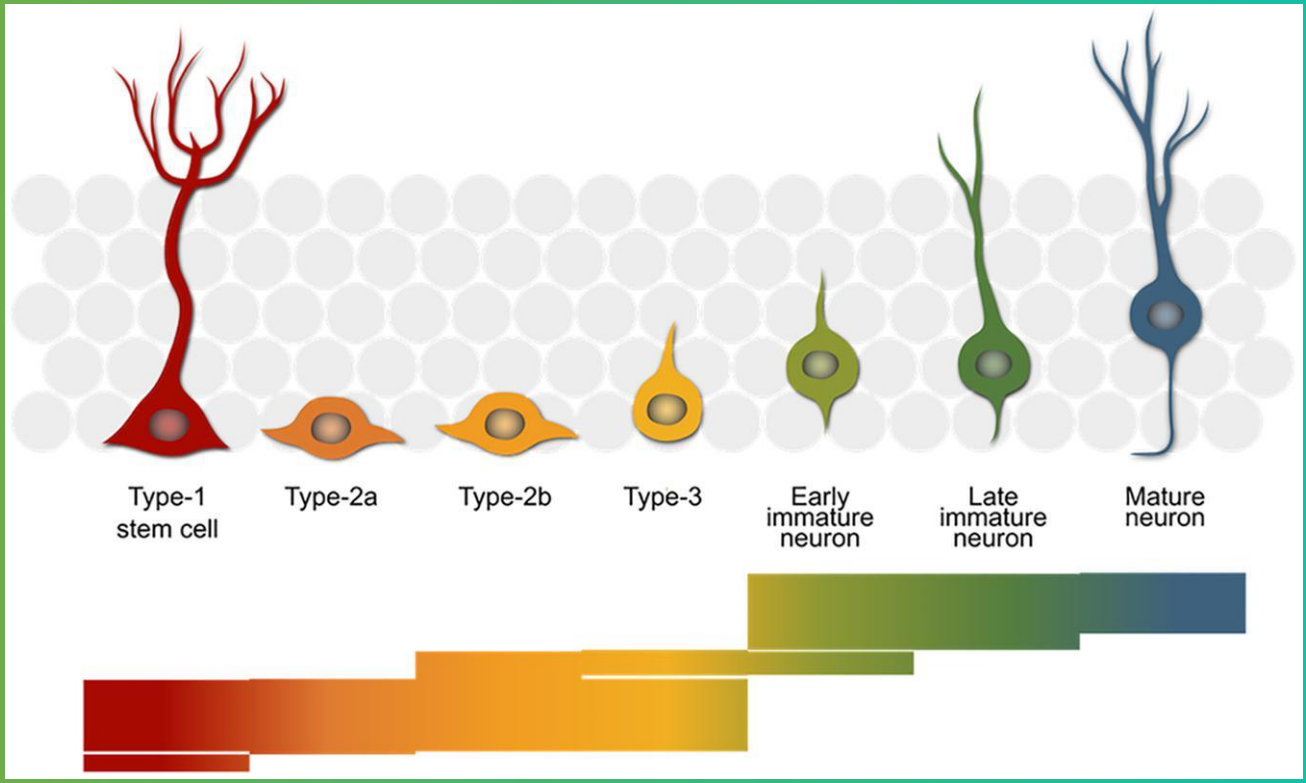


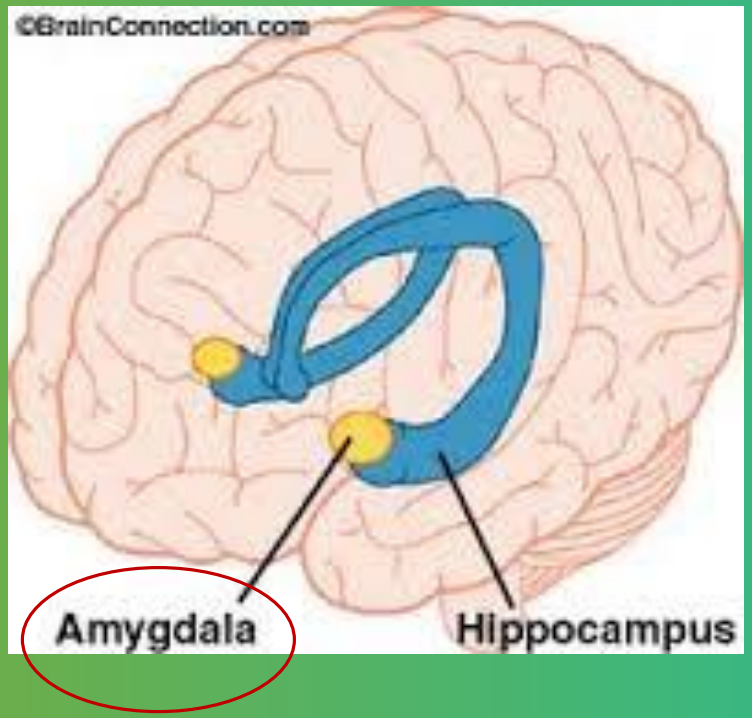
Neurogenesis

The hippocampus is one of the few brain regions where new neurons are generated.

This process of neurogenesis is confined to the dentate gyrus.

The production of new neurons can be positively affected by exercise or negatively affected by epileptic seizures





Amygdala

Almond in shape

- Involved in many cognitive processes (Emotional Learning & memory).
- Related to reward, learning and fear, emotion and mating
- The amygdala stimulate the hippocampus to remember many details surrounding the situation, as well.
- Lays a role in overall social processing such as trustworthiness
- Damage → anxiety disorders & memory impairment

Aggression

Stimulating the amygdala appears to increase both sexual and aggressive behavior.

Decision-Making

The amygdala is accountable for our value-guided behavior and initial emotional response to decisions.

Anxiety

There may also be a link between the amygdala and anxiety.

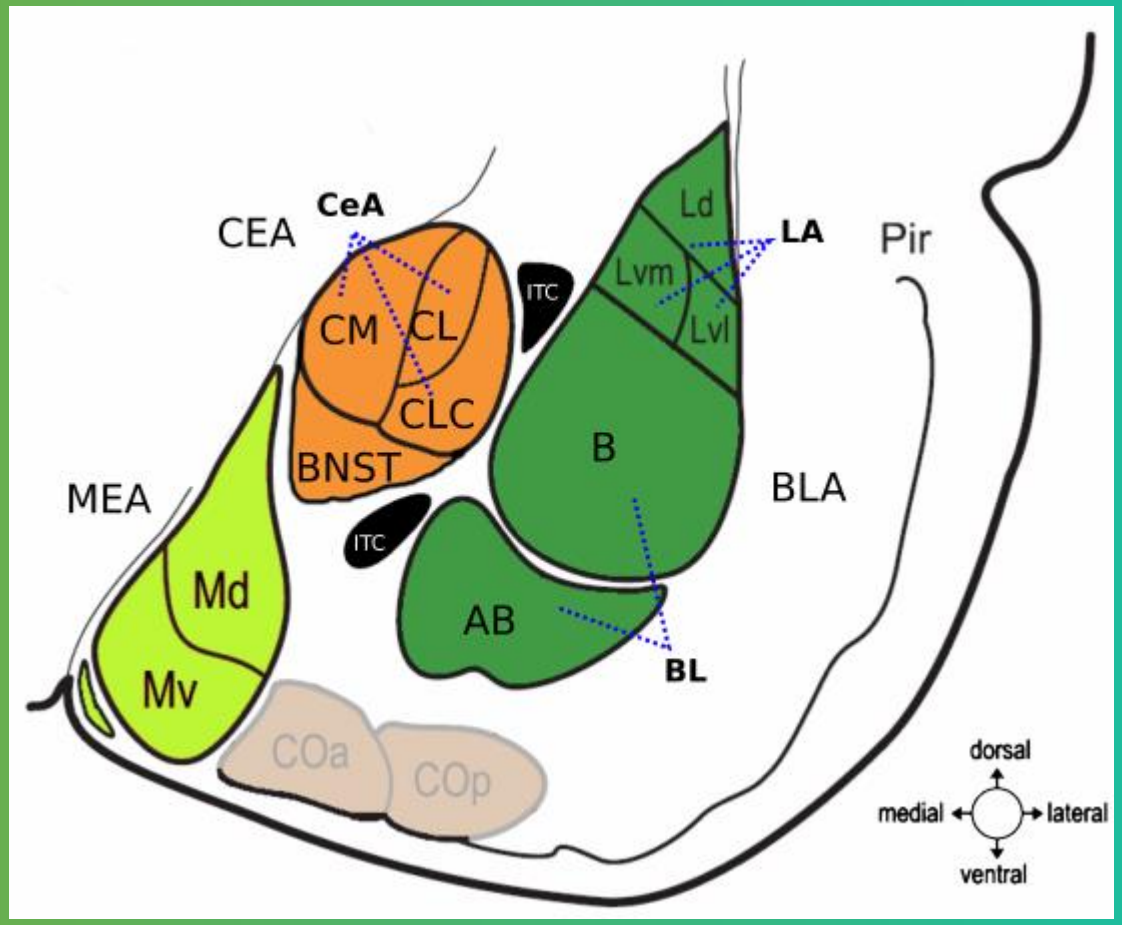
Social behavior

Amygdala volume correlates positively with both the size (the number of contacts a person has) and the complexity (the number of different groups to which a person belongs) of social networks.
Individuals with larger amygdalae had larger and more complex social networks.

Large basolateral region: provides direct input to basal ganglia and motor system

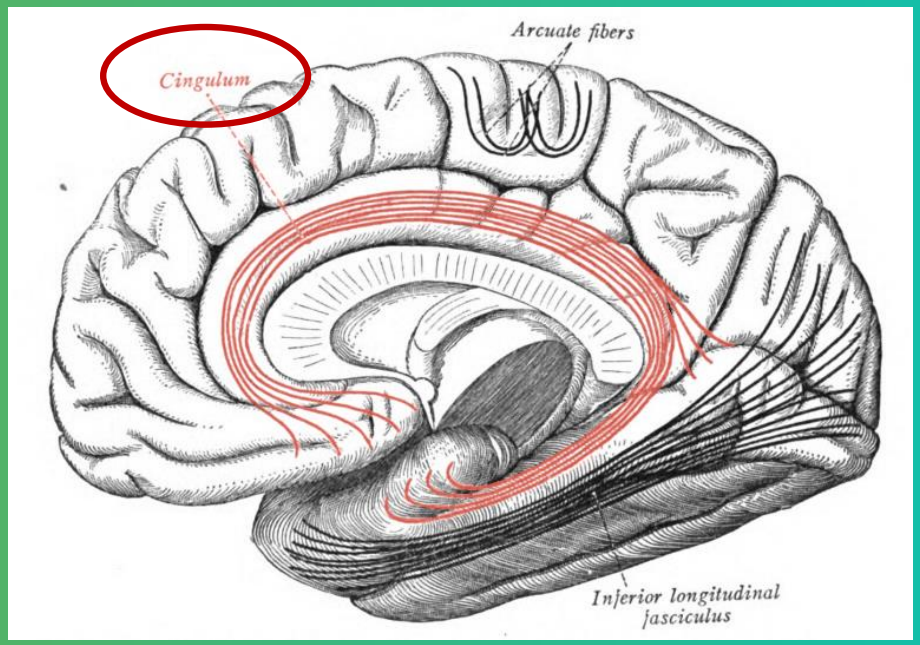
Small corticomedial group of nuclei: Related to olfactory cortex

Medial and central nuclei: Connected to hypothalamus



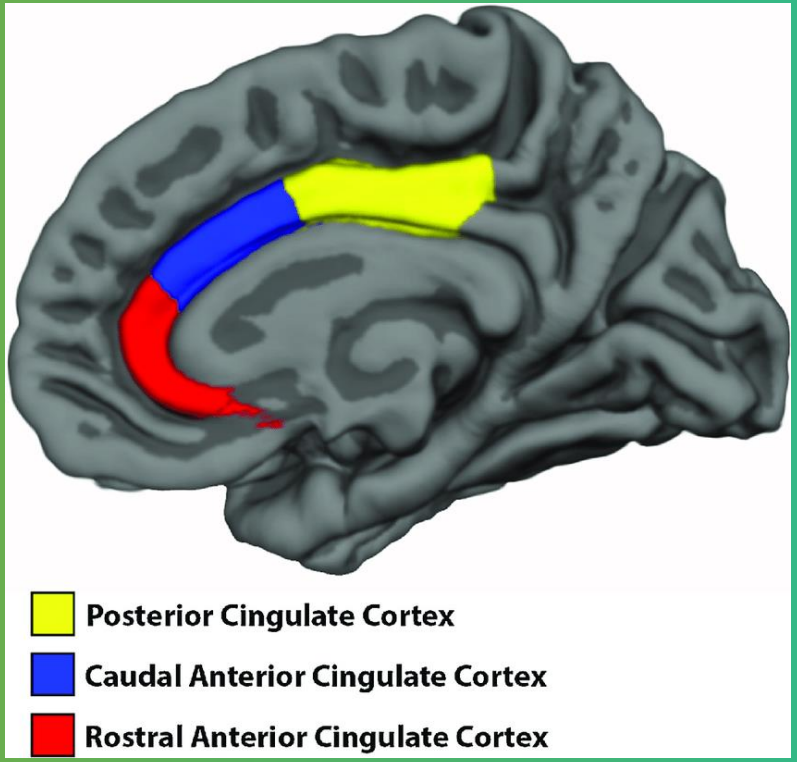
Cingulate

Cingulum: fiber bundle that runs from the cingulate to parahippocampal gyrus



This part of limbic system may be involved in:

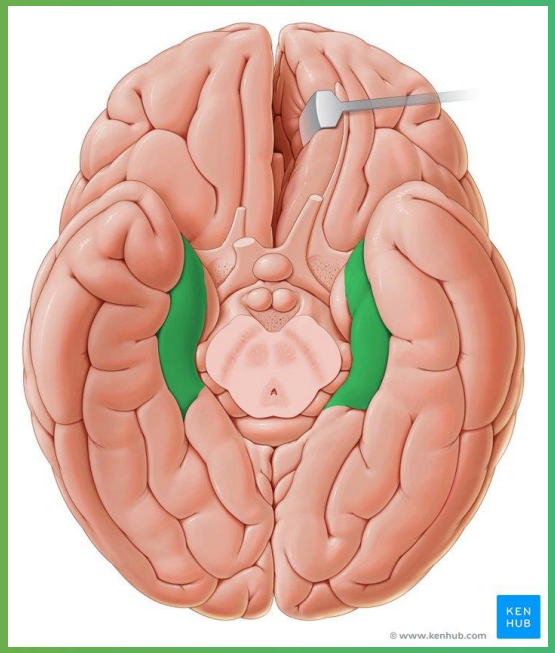
- **Motor responses to drives**
- **Emotions formation**
- **Learning and memory**
- **Attention**
- **Feeling of safety and security**

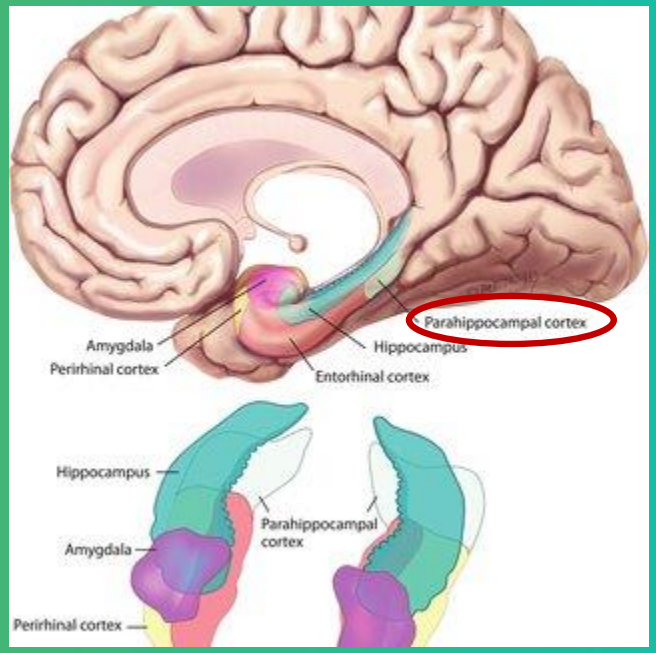


Parahippocampal gyrus

This part of limbic system may be involved in:

- **Memory encoding and retrieval**

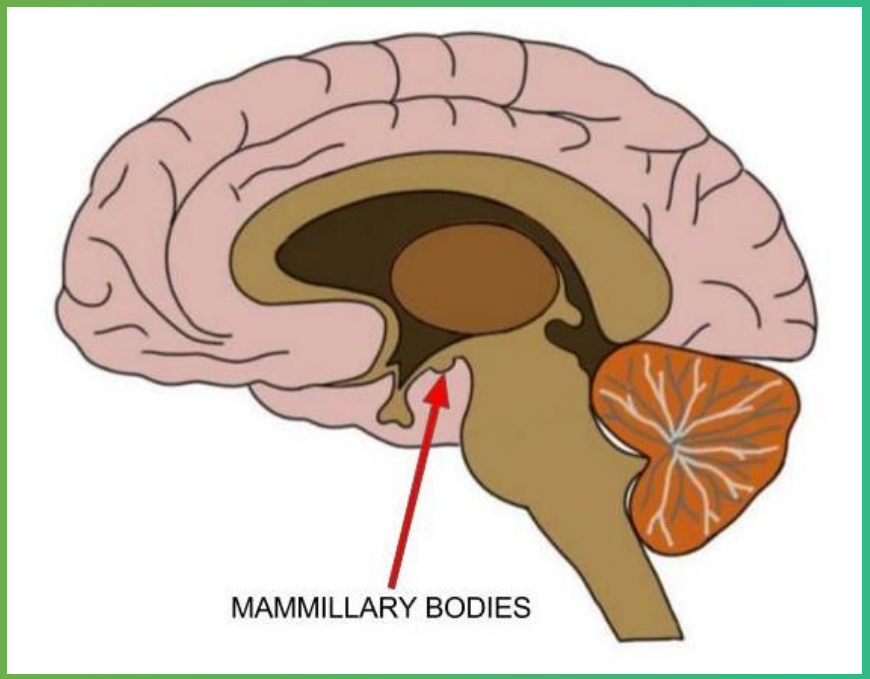




Mammillary bodies

They consist of two groups of nuclei, the medial mammillary nuclei and the lateral mammillary nuclei.

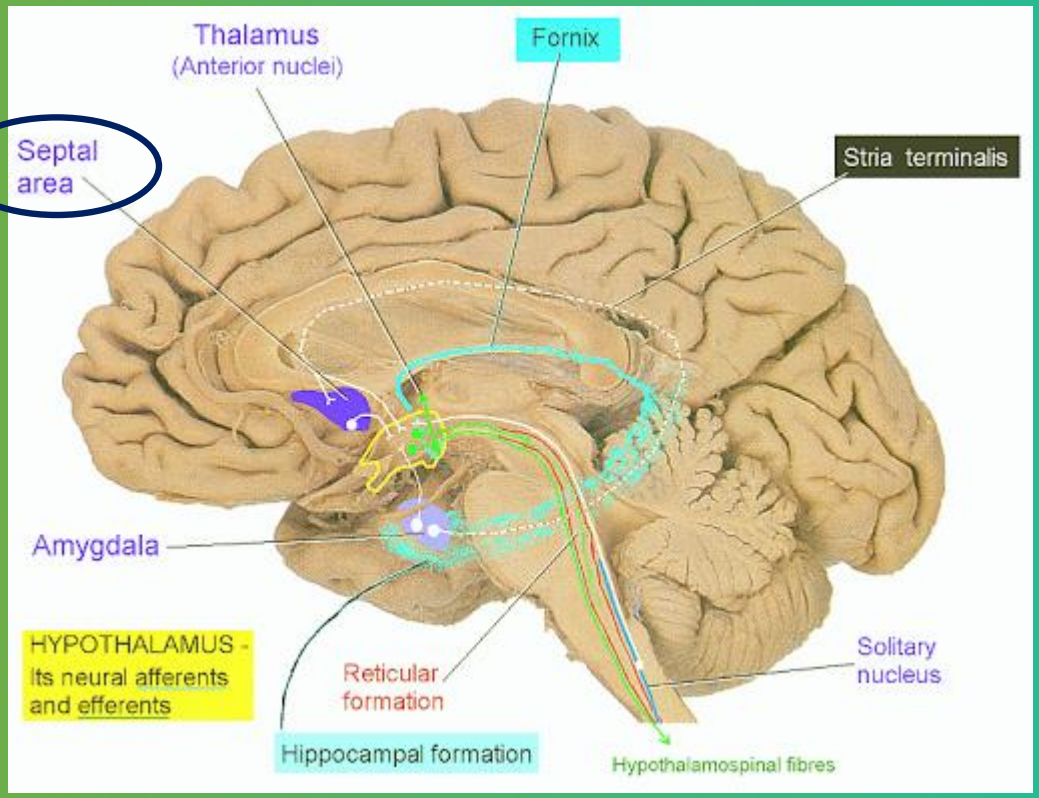
- Recollective memory
- The damage of medial mammillary nucleus leads to spatial memory deficit



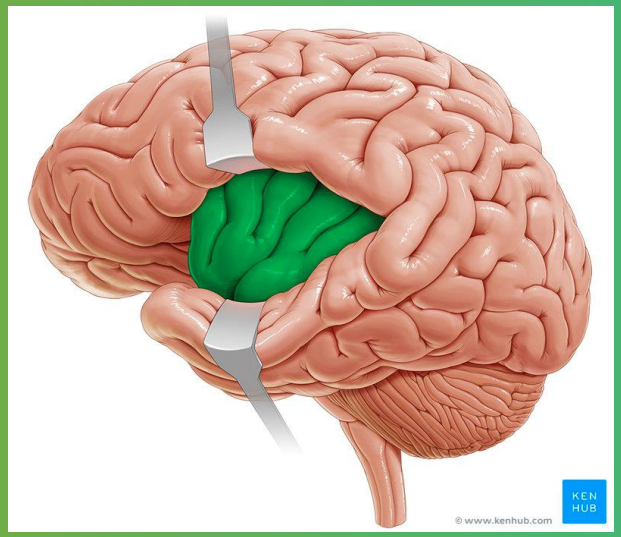
Septal area

The septal nuclei are essential in generating the theta rhythm of the hippocampus. Hippocampal theta rhythm has been observed and linked to *memory formation* and *navigation.*

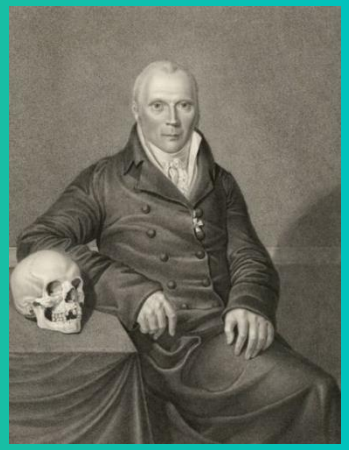
A pleasure zone in animals. The septal nuclei play a role in reward and reinforcement along with the nucleus accumbens

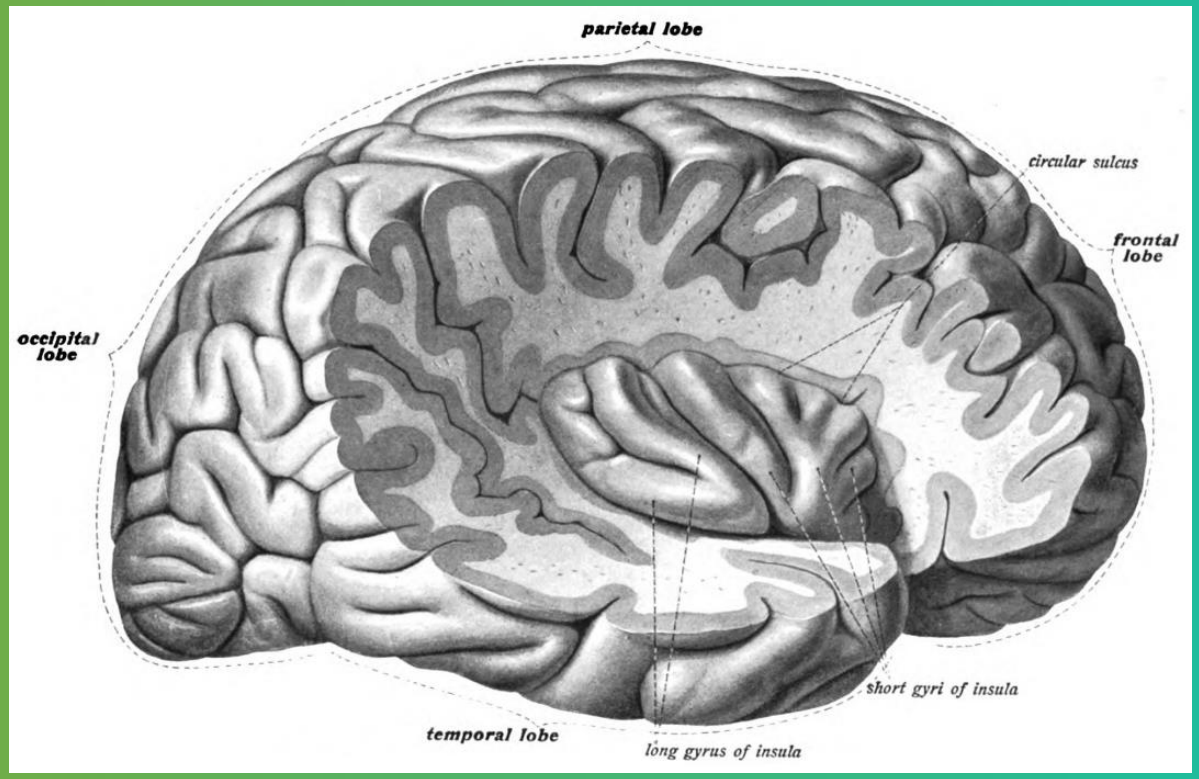


Insula



The insula was first described by Johann Christian Reil

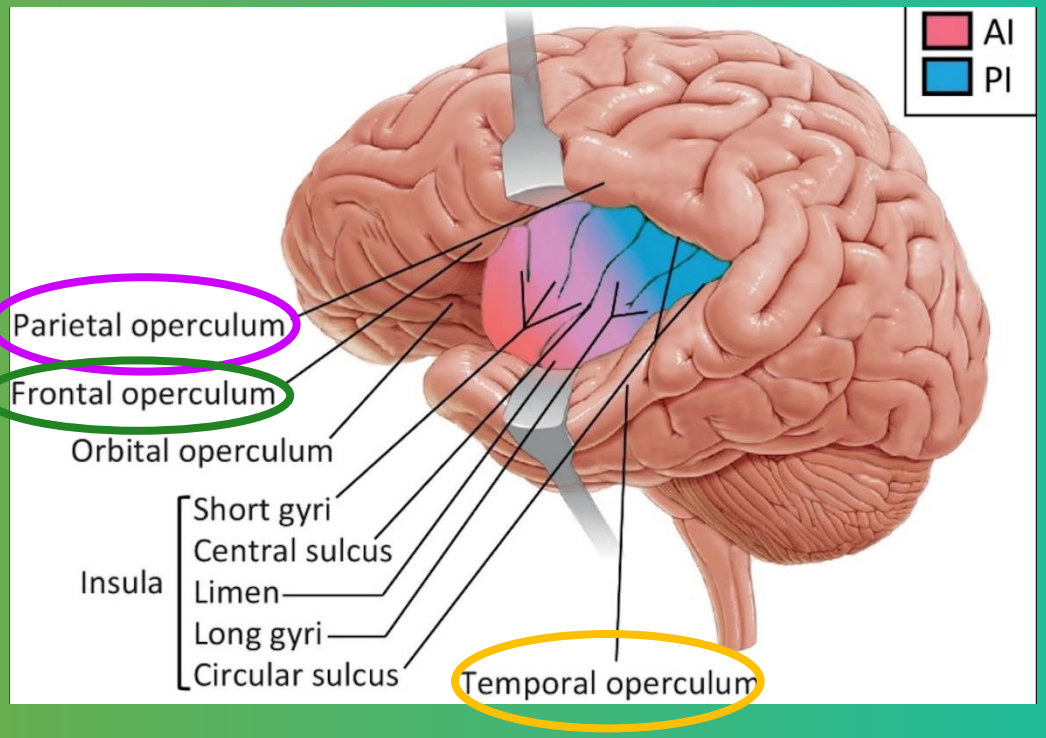




The insular cortex is divided into two parts:

- **The larger anterior insula**
- **The smaller posterior insula**

The cortical area overlying the insula toward the lateral surface of the brain is the operculum (meaning *lid*). The opercula are formed from parts of the enclosing frontal, temporal, and parietal lobes.



The insula are believed to be involved in:

Consciousness
Emotion
Body's homeostasis
Empathy
Taste
Perception
Motor control
Self-awareness
Cognitive functioning
Psychopathology

Multimodal sensory processing, sensory binding

Functional imaging studies show activation of the insula during audio-visual integration tasks.

Taste

The anterior insula is part of the primary gustatory cortex.

Interoceptive awareness

Interoceptive awareness of body states, such as the ability to time one's own heartbeat, Pain

Motor control

It contributes to hand-and-eye motor movement, speech articulation (long and complex spoken sentences).

It has been identified as a "central command" center that ensures that heart rate and blood pressure increase at the onset of exercise.

Homeostasis

It plays a role in a variety of homeostatic functions related to basic survival needs, such as taste, visceral sensation, and autonomic control.

The insula controls autonomic functions through the regulation of the sympathetic and parasympathetic systems.

It has a role in regulating the immune system.

Self

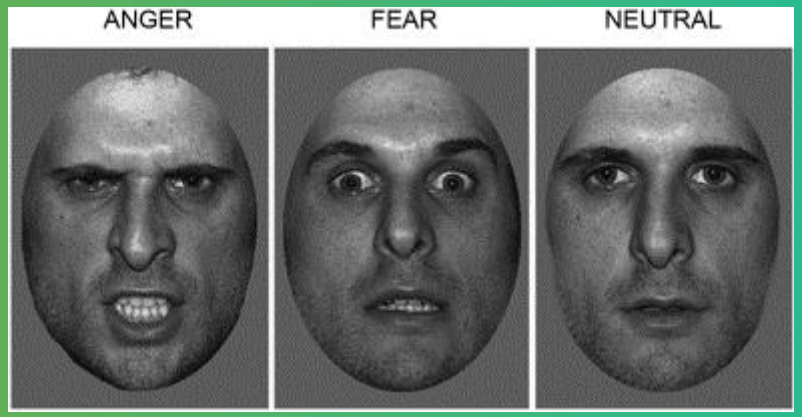
It has been identified as playing a role in the experience of bodily self-awareness, sense of agency, and sense of body ownership.

Social emotions
It is involved in the processing of norm violations, empathy and orgasms.
The insula is active during social decision making.

Individuals with high emotional intelligence scores had left insular activation when processing fearful faces.

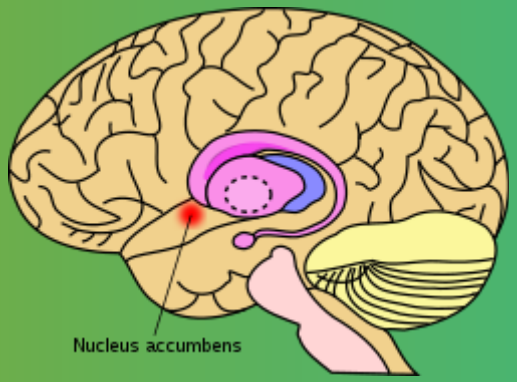
Individuals with low EI scores had left insular activation when processing angry faces.

Auditory perception
Recent research indicates that the insular cortex is involved in auditory perception.



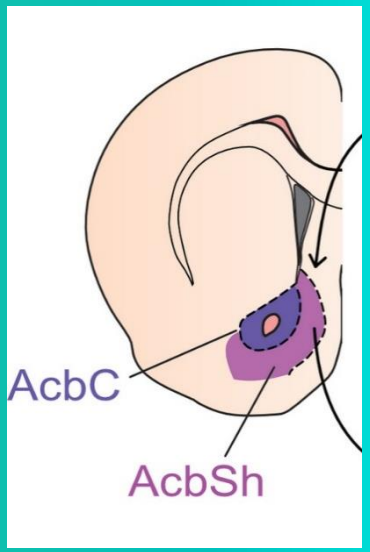
Emotions

- ✓ The insula has an important role in pain experience
- ✓ Also anger, fear, disgust, happiness, and sadness.
- ✓ The anterior insular cortex (AIC) is believed to be responsible for emotional feelings, including maternal and romantic love, sexual arousal, unfairness, inequity, uncertainty, disbelief, social exclusion, trust, empathy, sculptural beauty, a 'state of union with God', and hallucinogenic states.
- ✓ The insula in conscious desires, such as food craving and drug craving.
- ✓ The right anterior insula is significantly thicker in people that meditate.



Nucleus accumbens

Two structures:
The nucleus accumbens core
The nucleus accumbens shell



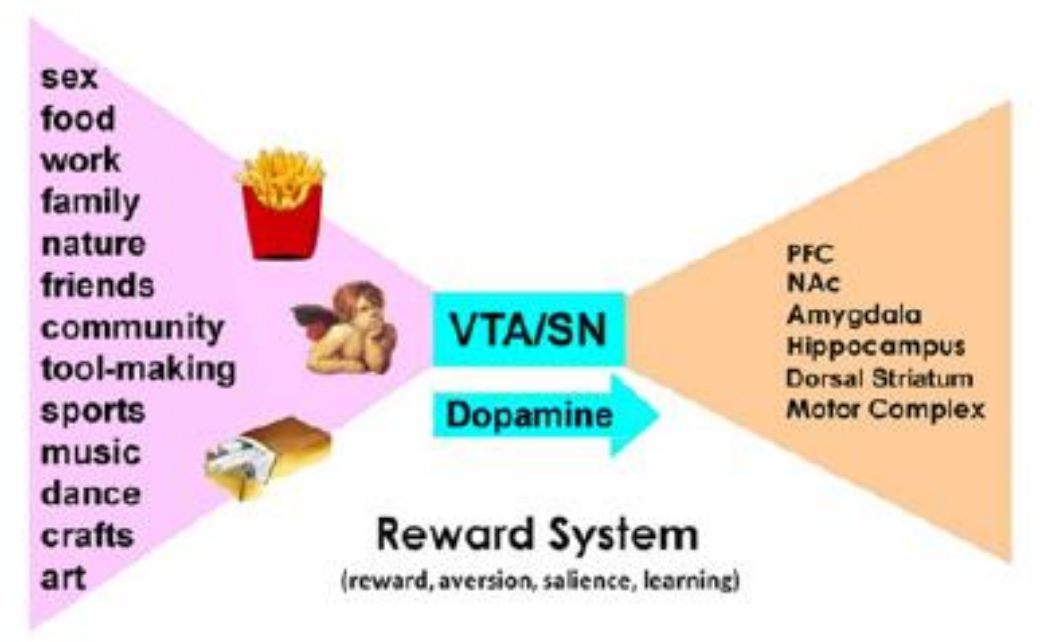
Core is involved in the cognitive processing of motor function related to reward and reinforcement

Shell is involved in the cognitive processing of reward, including subjective "liking" reactions to certain pleasurable stimuli, motivational salience, and positive reinforcement.

Addictive drugs have a larger effect on dopamine release in the shell than in the core

Reward system

- A reward is an appetitive stimulus given to a human to alter its behavior.
- Primary rewards include those that are necessary for the survival of species, such as food, sexual contact, or successful aggression.
- Secondary rewards derive their value from primary rewards such as beautiful music.

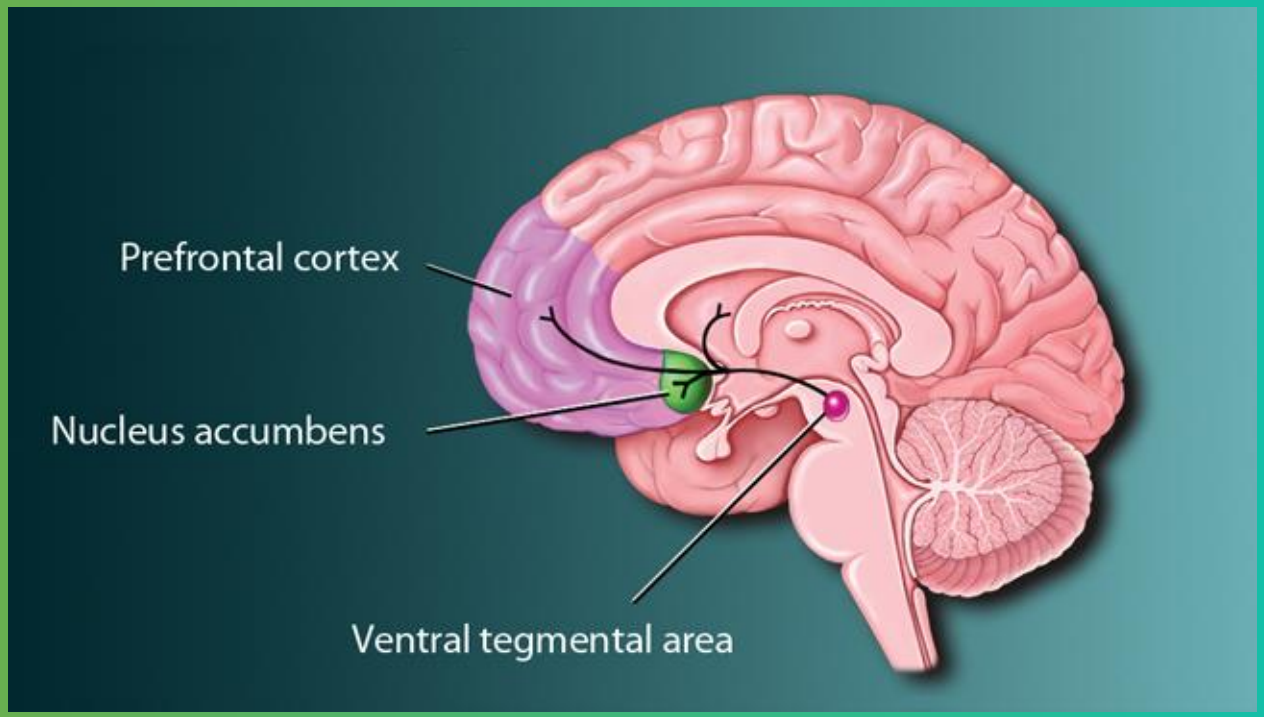


Most important:

- Nucleus accumbens,
- Ventral tegmental area (VTA)
- Prefrontal cortex

Particularly a pathway from the VTA to the nucleus accumbens then to prefrontal cortex that uses the neurotransmitter dopamine.

Over activity of the VTA dopaminergic projection in schizophrenia



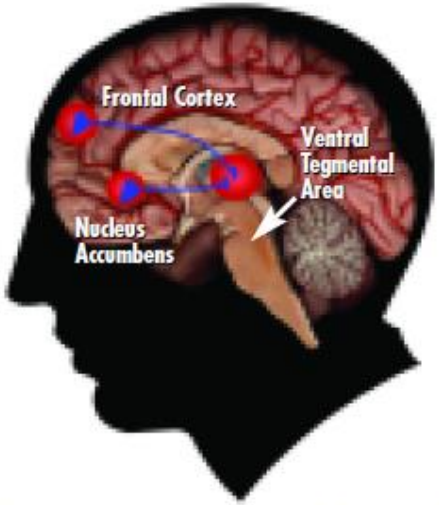
Drugs

Opioids
Nicotine
Amphetamine
Ethanol
Cocaine
Cannabis

Increase the dopamine release in the reward pathway so provide reward that often leads to addiction.
Drugs have many different effects on the brain; however, they all follow the same path.

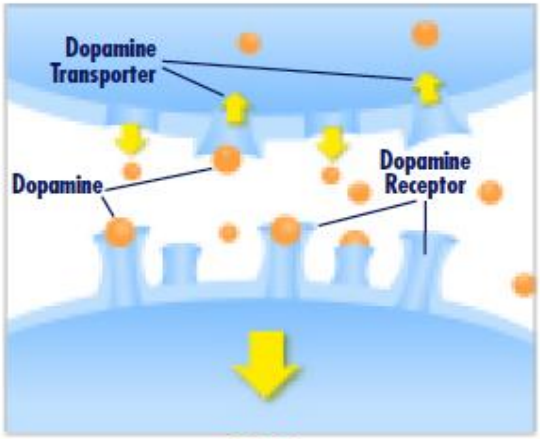
DRUGS OF ABUSE TARGET THE BRAIN'S PLEASURE CENTER

Brain reward (dopamine) pathways

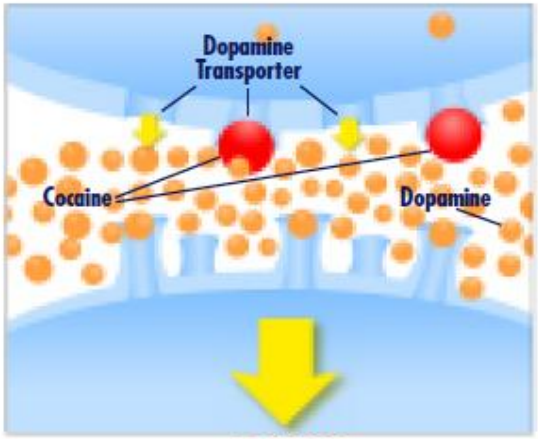


These brain circuits are important for natural rewards such as food, music, and sex.

Drugs of abuse increase dopamine



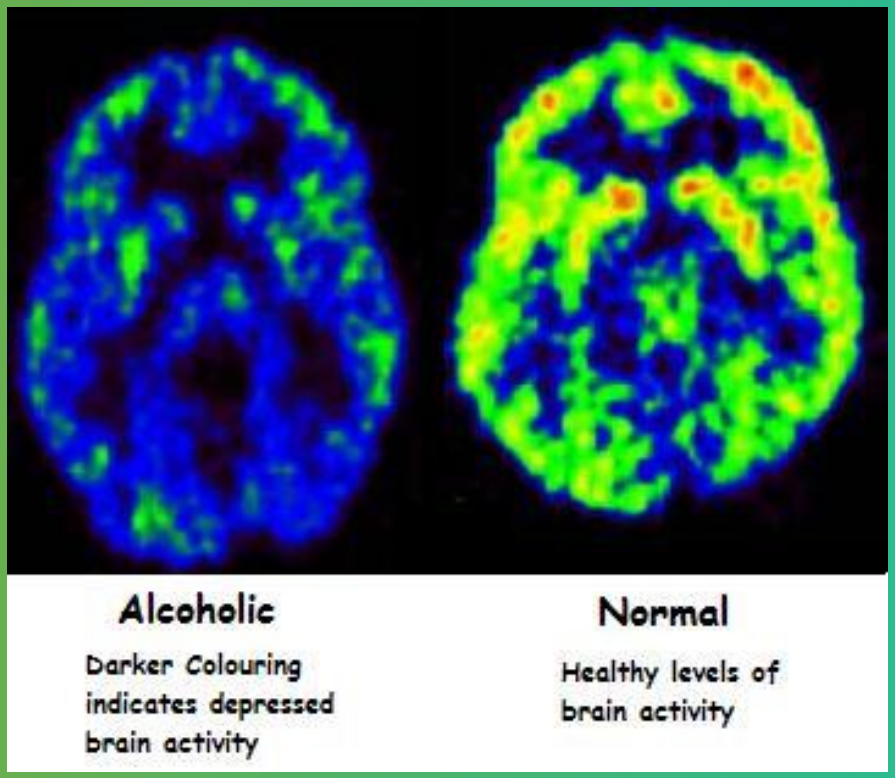
FOOD

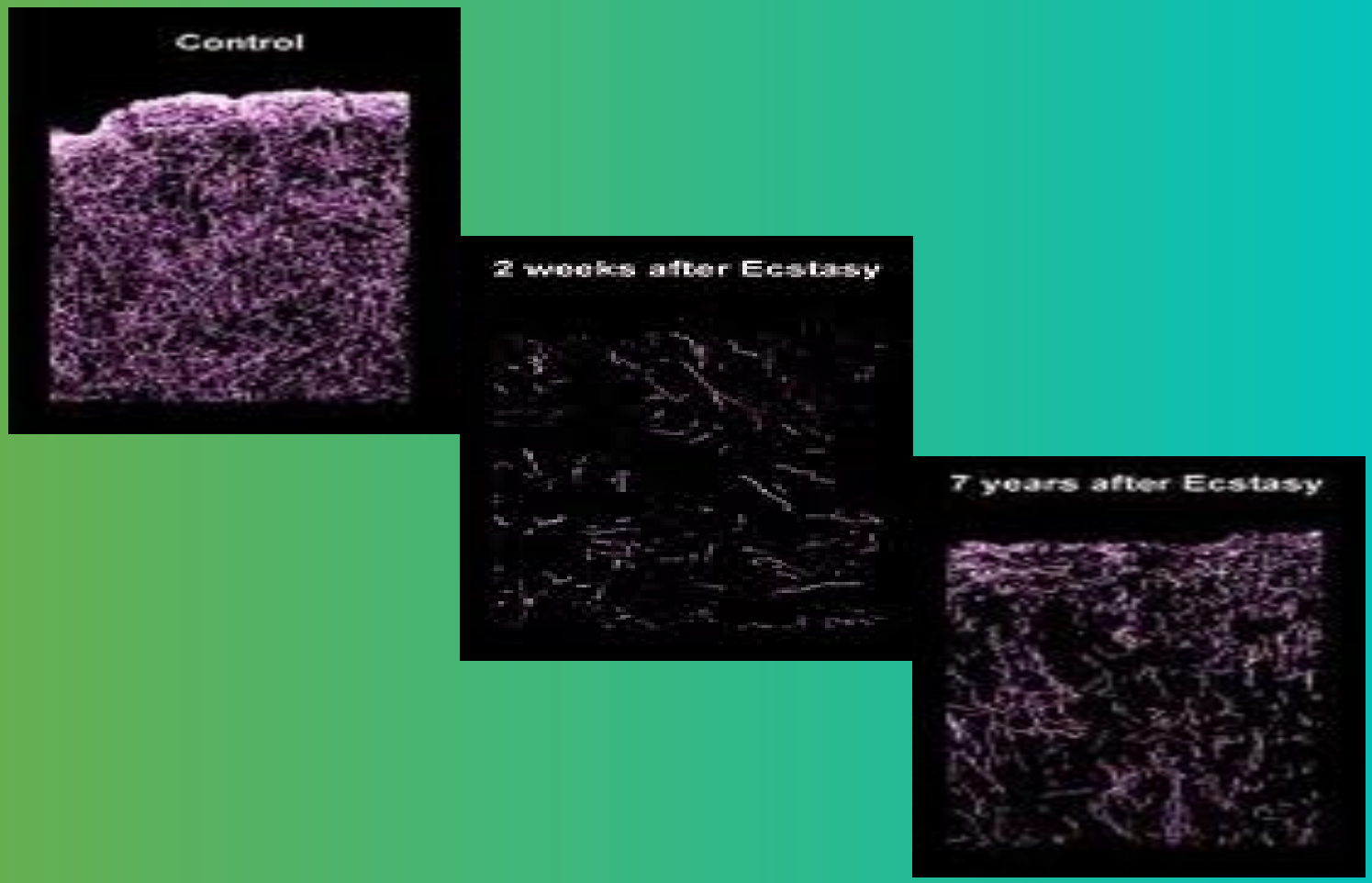


COCAINE

Typically, dopamine increases in response to natural rewards such as food.
When cocaine is taken, dopamine increases are exaggerated, and communication is altered.

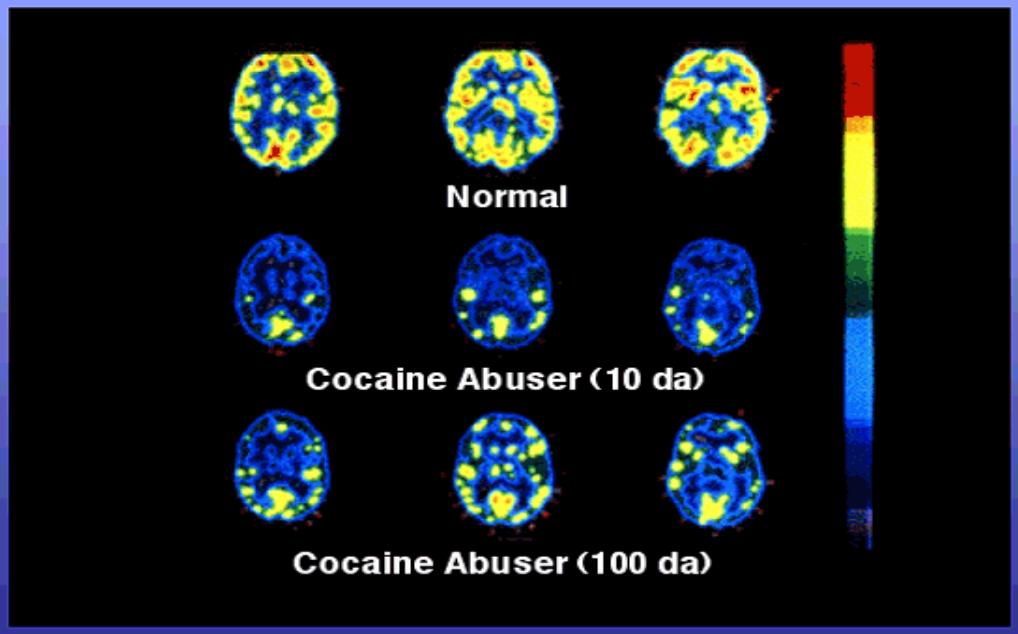
After prolonged use, psychological drug tolerance arises.

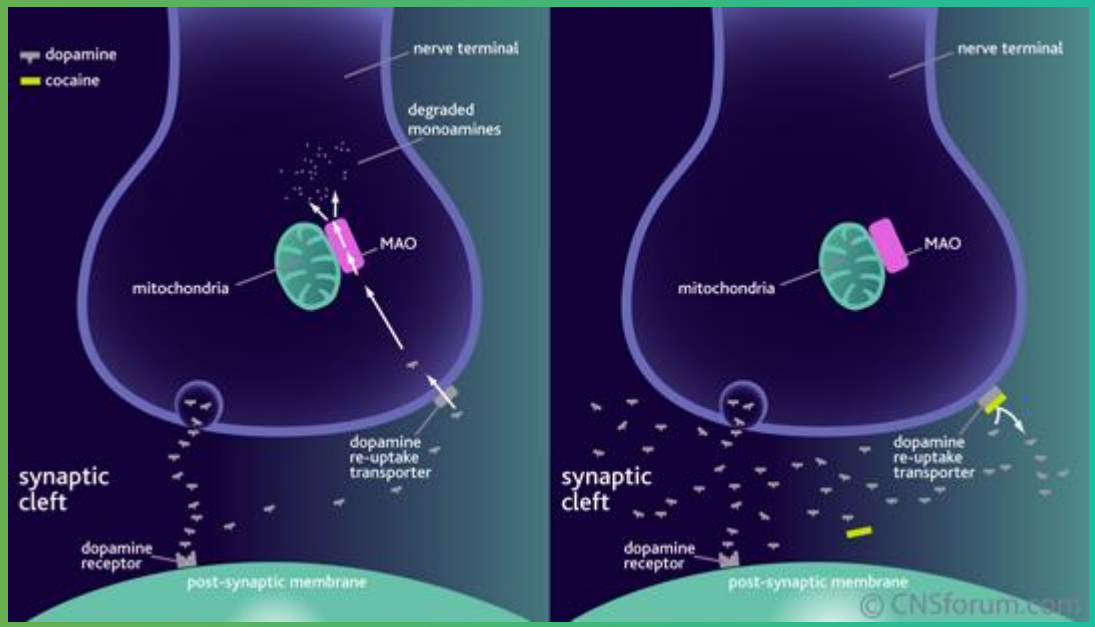



Control
2 weeks after Ecstasy
7 years after Ecstasy

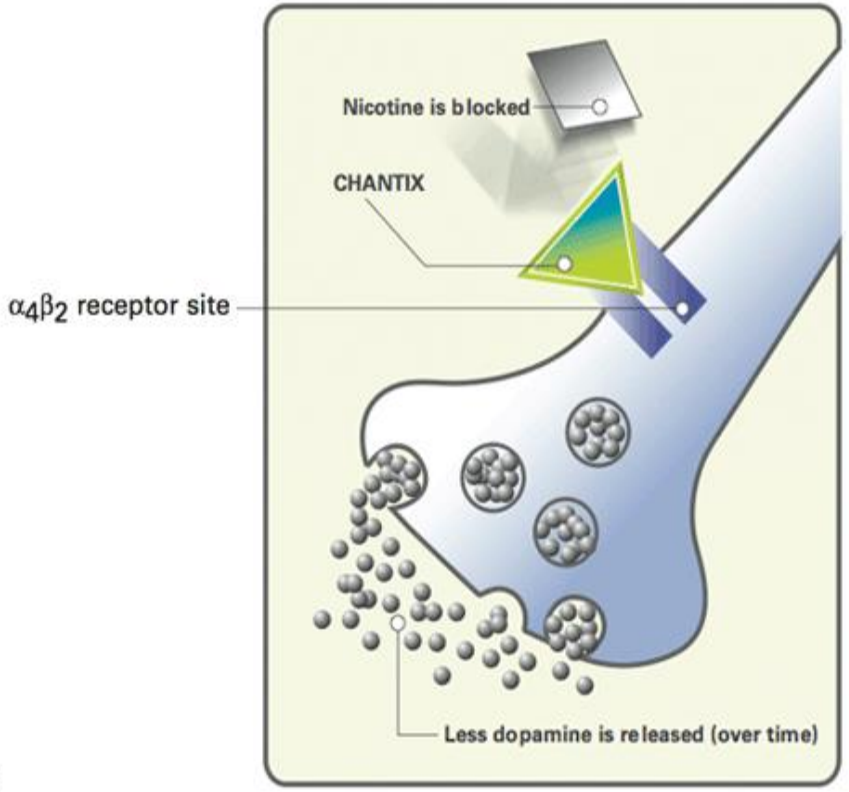

FRONTAL LOBE
LIMBIC LOBE
PARIETAL LOBE
OCCIPITAL LOBE

Your Brain After Drugs

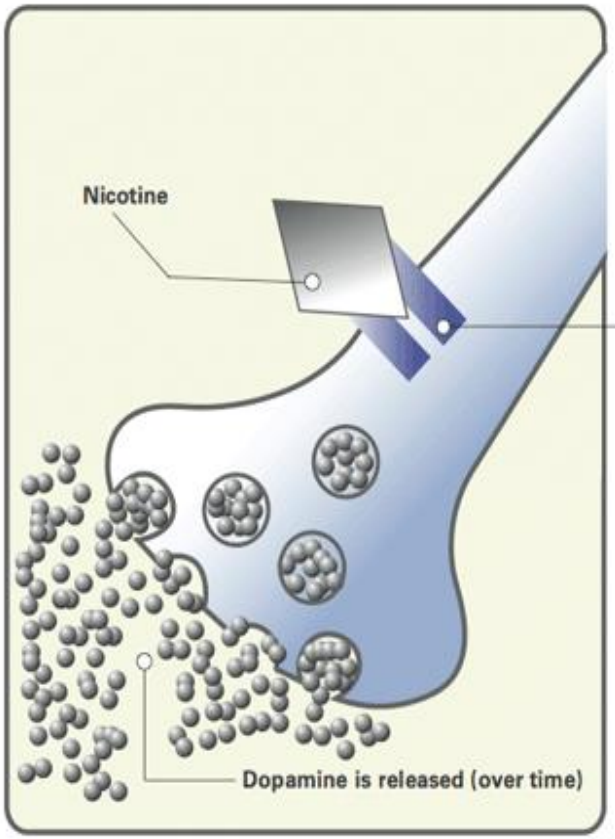




CHANTIX—partial agonist action

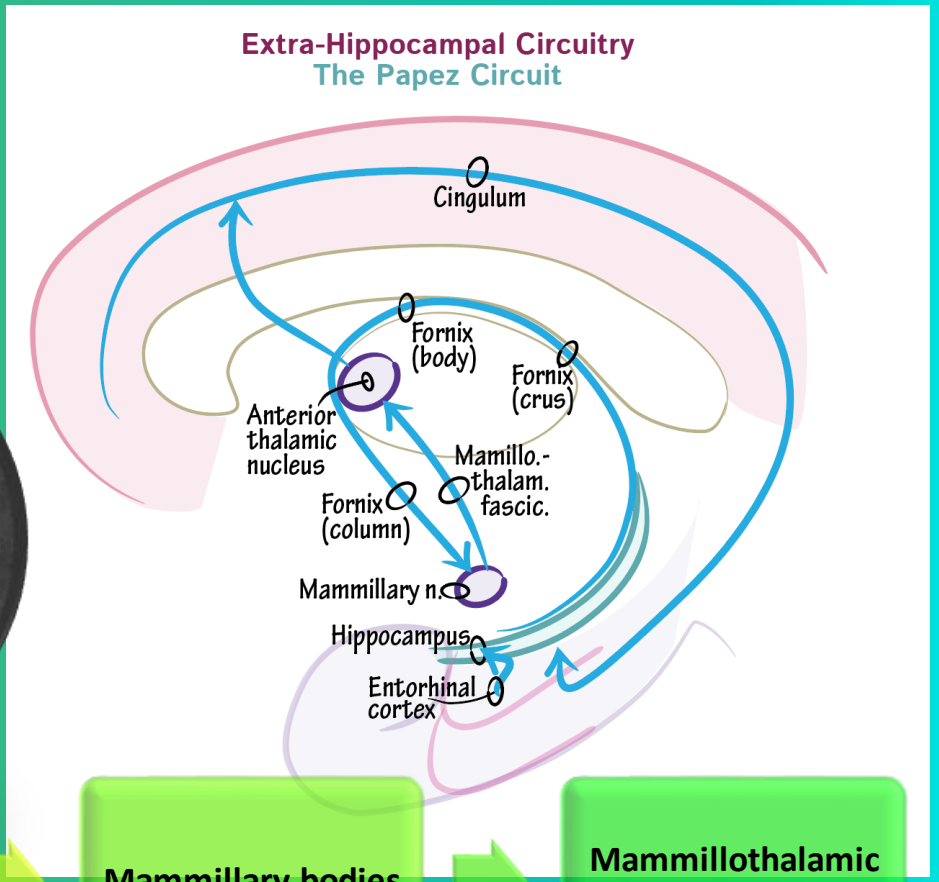


Nicotine—full agonist action

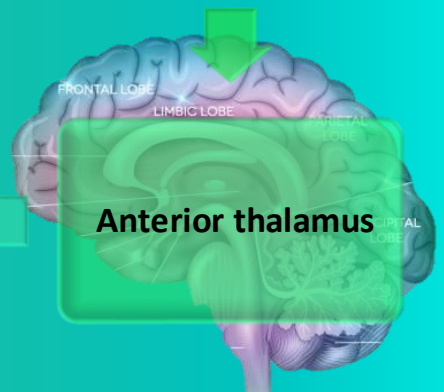


PAPEZ CIRCUIT (NEURAL CIRCUIT FOR EMOTIONS)

- James Papez, 1937
- Cortical control of emotions & emotional expression
- Role in storing memory
- Papez discovered the circuit after injecting rabies virus into a cat's hippocampus and monitoring its progression through the brain



Hippocampus → **Fornix** → **Mammillary bodies** → **Mammillothalamic tract** → **Anterior thalamus** → **Cingulate** → **Parahippocampal gyrus** → **Hippocampus**



Limbic Clinical Syndromes

Hypolimbic

Depression
Apathy
Utilization Behaviour
Amnesia (Hippocampus)
Social disdecorum
Kluver-Bucy Syndrome (Amygdala)
Anxiety/Panic
Psychosis

Hyperlimbic
Mania
OCD