The Limbic System

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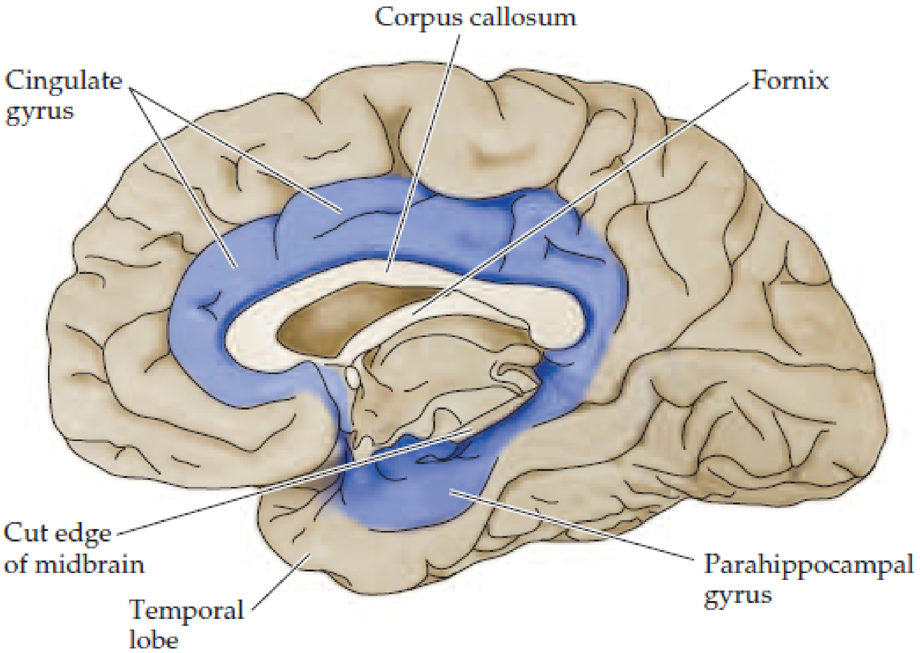
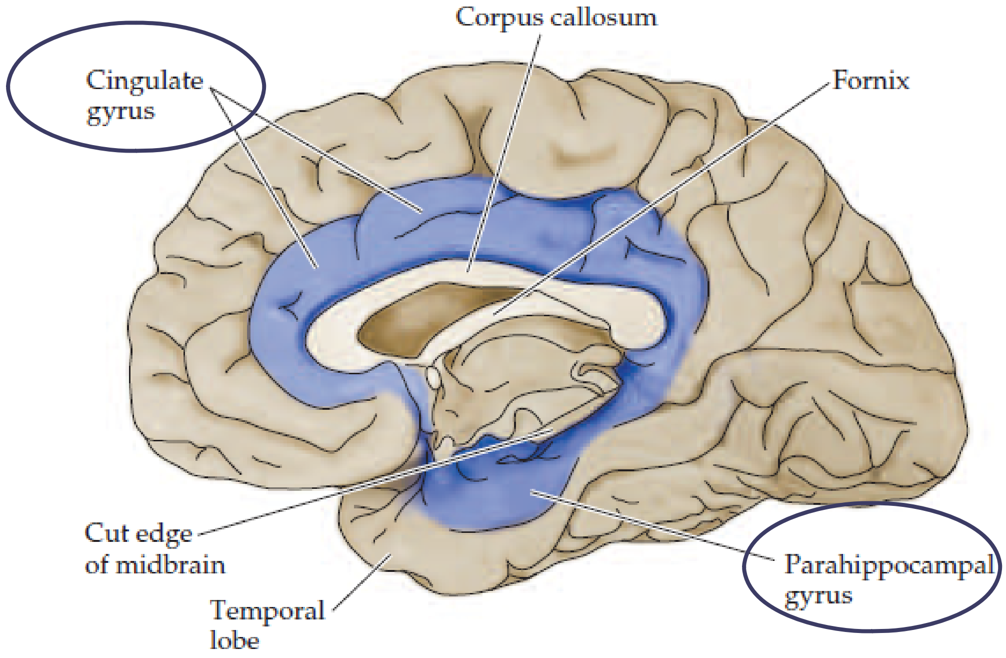
Effector systems that control emotional behavior

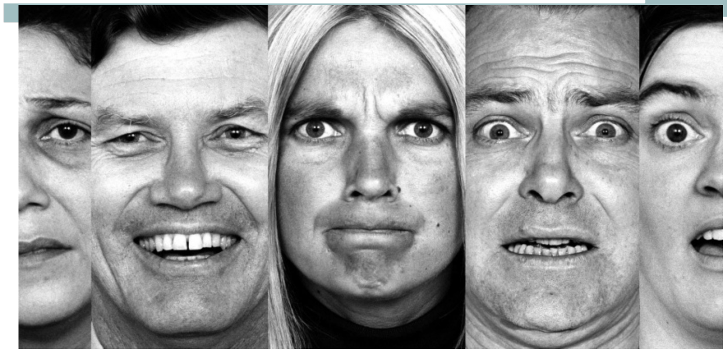
- Attempts to understand the effector systems that control emotional behavior, have a long history.
- In 1937, James Papez first proposed that specific brain circuits are devoted to emotional experience and expression (much as the occipital cortex is devoted to vision, for instance).
- In seeking to understand what parts of the brain serve this function, he began to explore the medial aspects of the cerebral hemisphere.



- In the 1850s, Paul Broca used the term "**limbic lobe**" to refer to the part of the cerebral cortex that forms a rim (*limbus is Latin for rim) around the corpus callosum and diencephalon on* the medial face of the hemispheres.



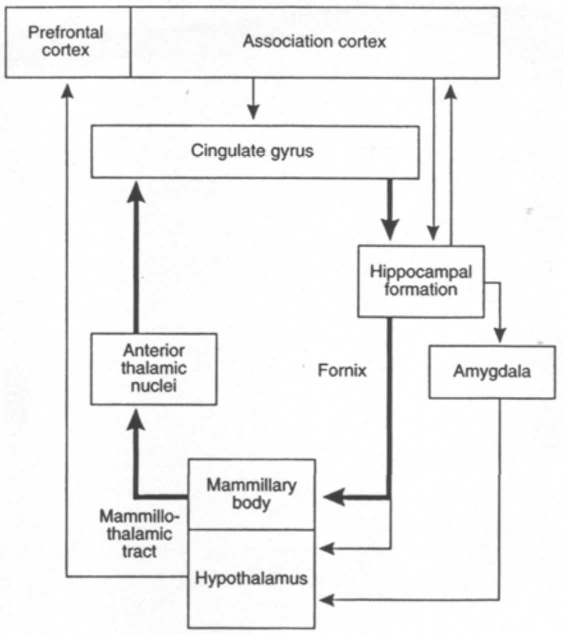
- Two prominent components of this region are the **cingulate gyrus**, which lies above the corpus callosum.
- and the **parahippocampal gyrus**, which lies in the medial temporal lobe.

- **limbic system links a group of** functionally related structures that are interposed between the cerebral cortex and the underlying diencephalon.
- For many years, these structures, along with the **olfactory bulbs**, were thought to be concerned primarily with the **sense of smell**.
- Papez, however, speculated that the function of the limbic lobe might be more related to **emotions**.

- Papez knew that emotions reach consciousness, and that higher cognitive functions affect emotional behavior.

- He showed that the cingulate cortex and hypothalamus are interconnected via projections from the **mammillary bodies** (part of the posterior hypothalamus) to the anterior nucleus of the dorsal **thalamus**, which projects in turn to the **cingulate gyrus**.
- The cingulate gyrus projects to the **hippocampus**.
- Finally, he showed that the hippocampus projects via the **fornix** (a large fiber bundle) back to the **hypothalamus**.



- Papez suggested that these pathways provided the connections necessary for cortical control of emotional expression, and they became known as the "Papez circuit."

The limbic system

- Over time, the concept of a forebrain circuit for the control of emotional expression, has been revised to include parts of the:
  - **hippocampal formation**
  - **septal area**
  - **amygdala**

  - **prefrontal cortex**
  - **cingulate gyrus**
- These structures differ with respect to physiological, pharmacological, and behavioral properties

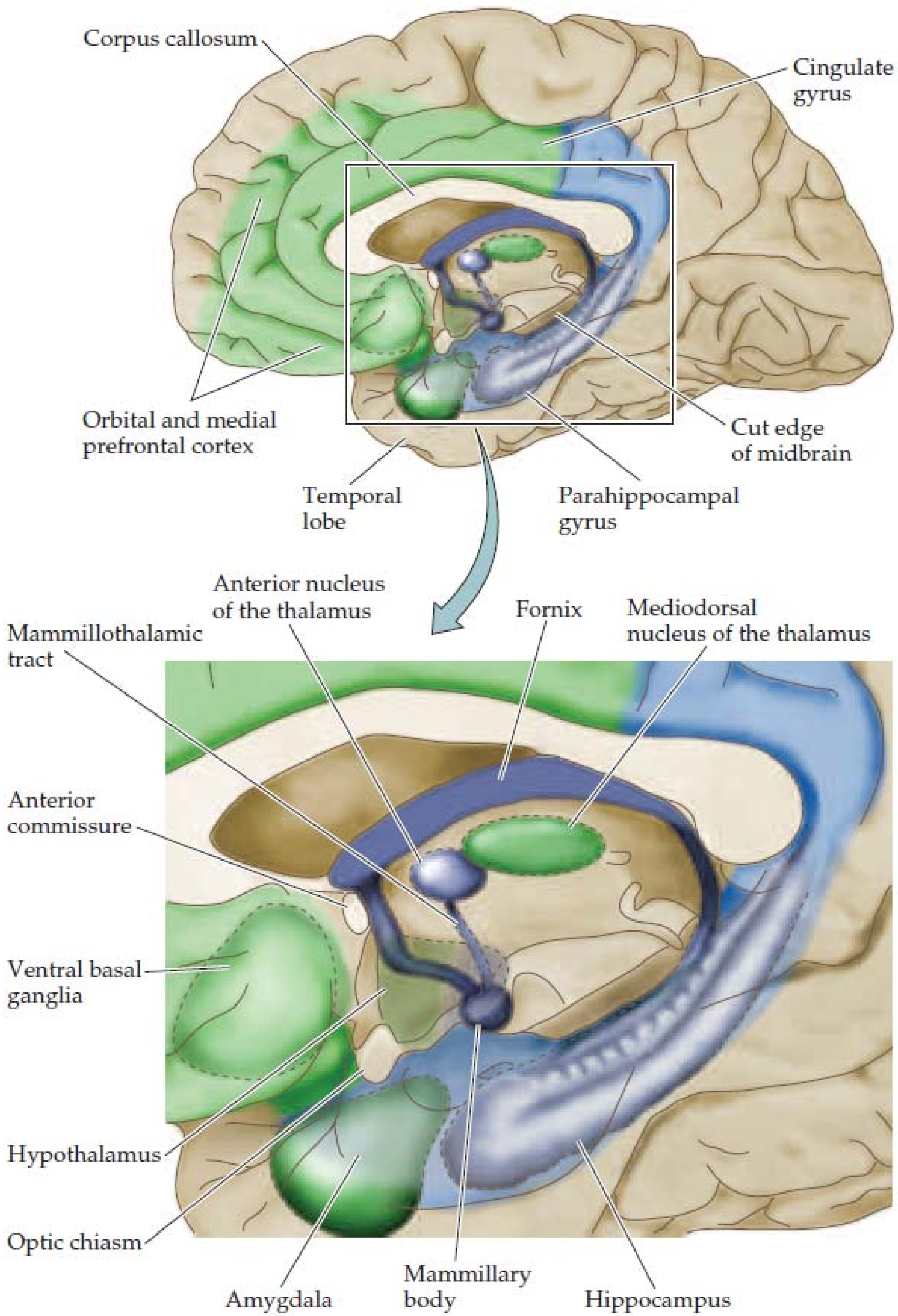
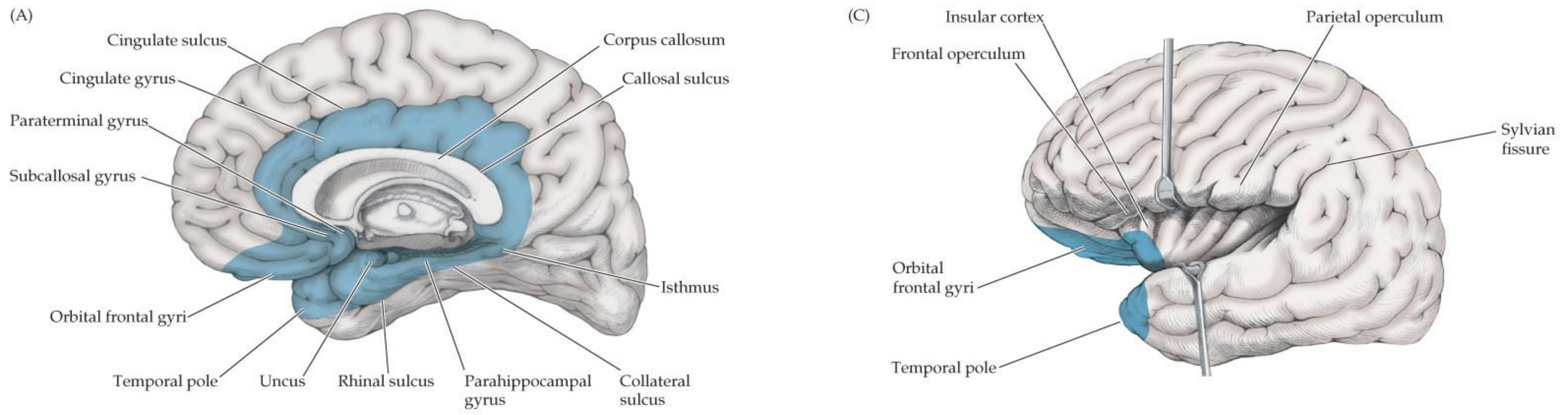


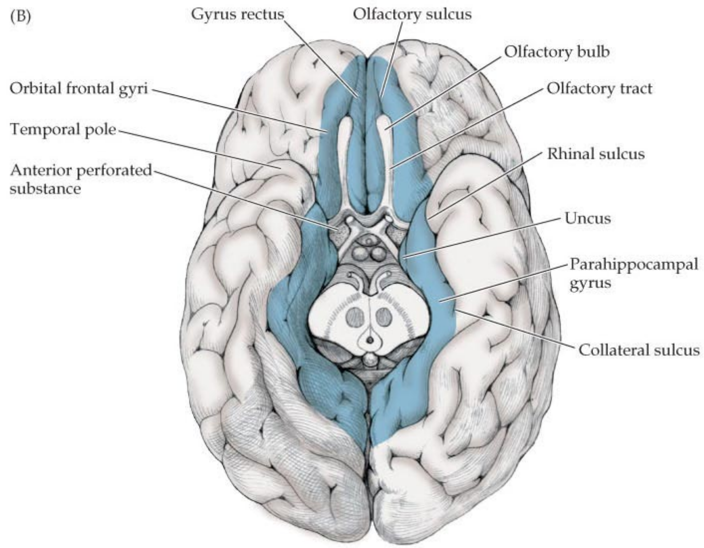
Figure 28.4 Modern conception of the limbic system. Two especially important components of the limbic system not emphasized in early anatomical accounts are the orbital and medial prefrontal cortex and the amygdala. These two telencephalic regions, together with related structures in the thalamus, hypothalamus and ventral striatum, are especially important in the experience and expression of emotion (colored green). Other parts of the limbic system, including the hippocampus and the mammilary bodies of the hypothalamus, are no longer considered important neural centers for processing emotion (colored blue).

The limbic system

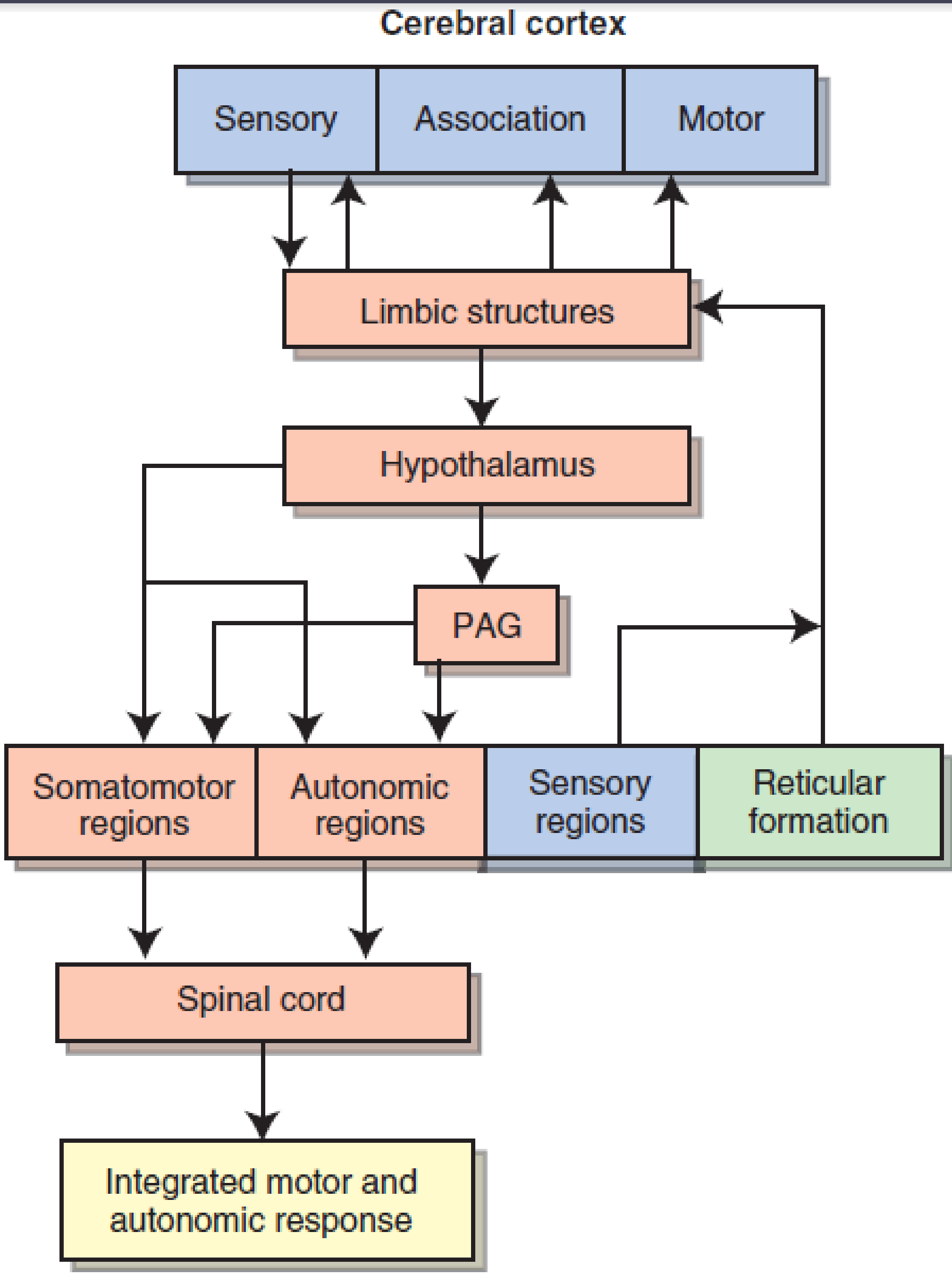
- **consists of** the
  - **hippocampal formation,**
  - **septal area**
  - **and amygdala**
- **limbic structures** communicate with the hypothalamus or midbrain periaqueductal gray (PAG).
- short-term memory
- epileptogenic activity

The main components of limbic cortex visible on a medial view are the **cingulate gyrus** (*cingulum* means “girdle” or “belt” in Latin) and the parahippocampal gyrus





The **parahippocampal gyrus** is separated from the remainder of the temporal lobe by the **collateral sulcus**, which continues anteriorly as the **rhinal sulcus**



Inputs from the:

1. Sensory systems,
2. Cortex,
3. Reticular formation of the brainstem (monoamine neuronal groups)

Outputs to the:

1. Hypothalamus, PAG (provides the integrating mechanism for different forms of emotional behaviors and visceral and autonomic responses)
2. Cortex

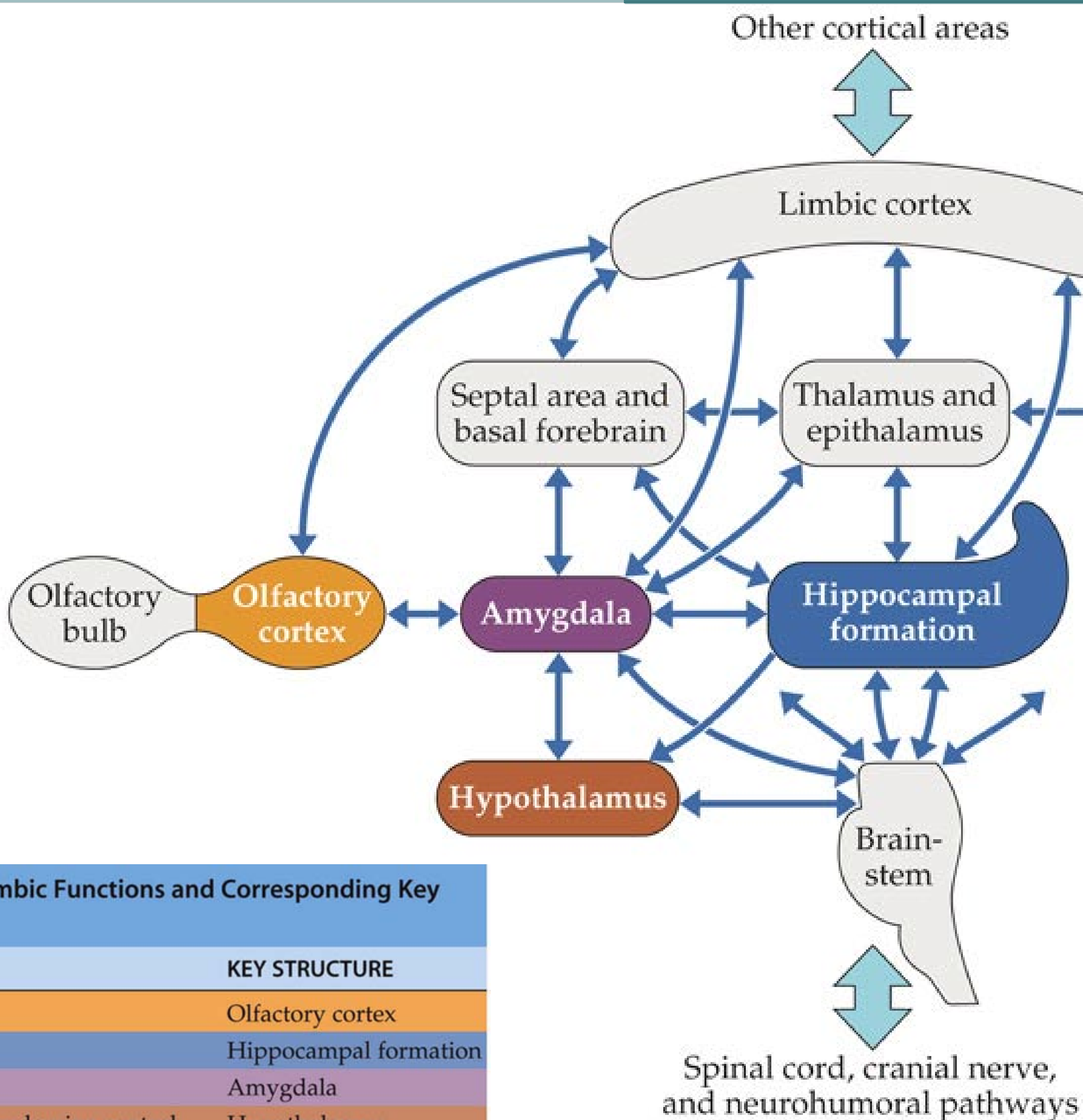


TABLE 18.2 Simplification of Limbic Functions and Corresponding Key Structures

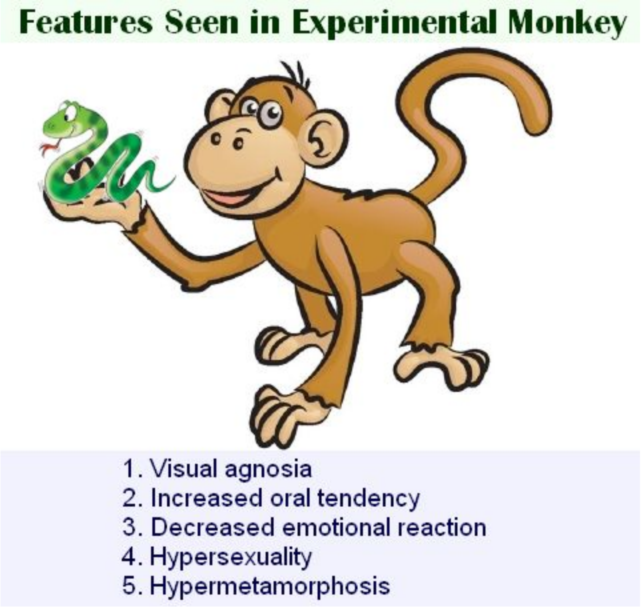
LIMBIC FUNCTION	KEY STRUCTURE
Olfaction	Olfactory cortex
Memory	Hippocampal formation
Emotions and drives	Amygdala
Homeostasis; autonomic and neuroendocrine control	Hypothalamus

Limbic system function

- **Olfaction**
- **Memory**
- **Emotions and drives**
- **Homeostatic functions, including autonomic and neuroendocrine control**
- An aid to remembering these functions is **HOME** (**H**omeostasis, **O**lfaction, **M**emory, and **E**motion).

Klüver-Bucy syndrome

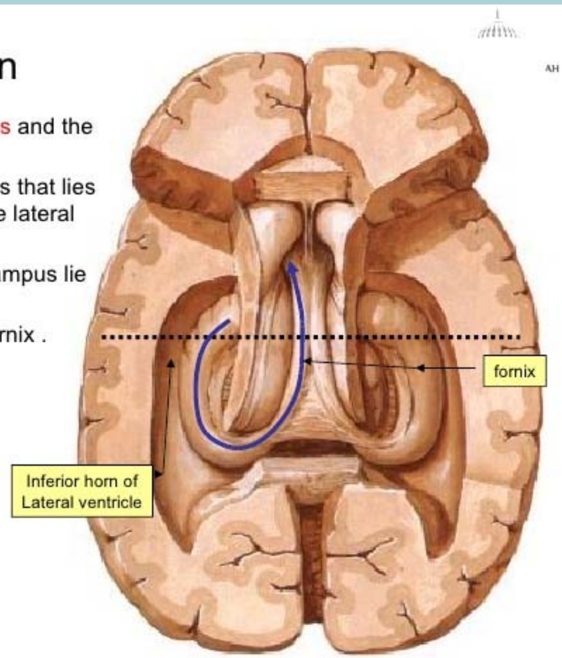
- Heinrich Klüver and Paul Bucy removed a large part of both medial temporal lobes, thus destroying much of the limbic system.
- Set of abnormal behaviors in these animals is now known as the Klüver-Bucy syndrome
- **Visual agnosia**: the animals appeared to be unable to recognize objects, although they were not blind, a deficit similar to that sometimes seen in human patients following lesions of the temporal cortex
- **Bizarre oral behaviors**: these animals would put objects into their mouths that normal monkeys would not.
- **Hyperactivity** and **hypersexuality**,
- Marked changes in **emotional behavior**

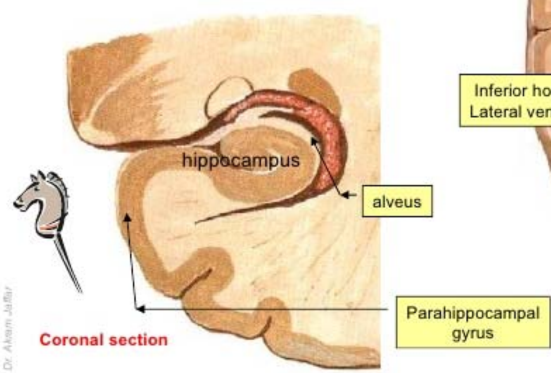


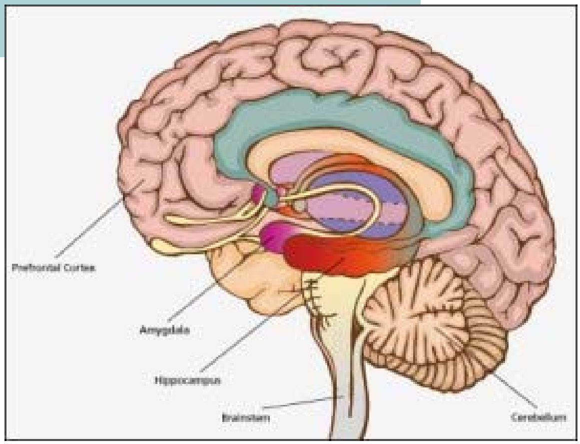
1.HIPPOCAMPAL FORMATION

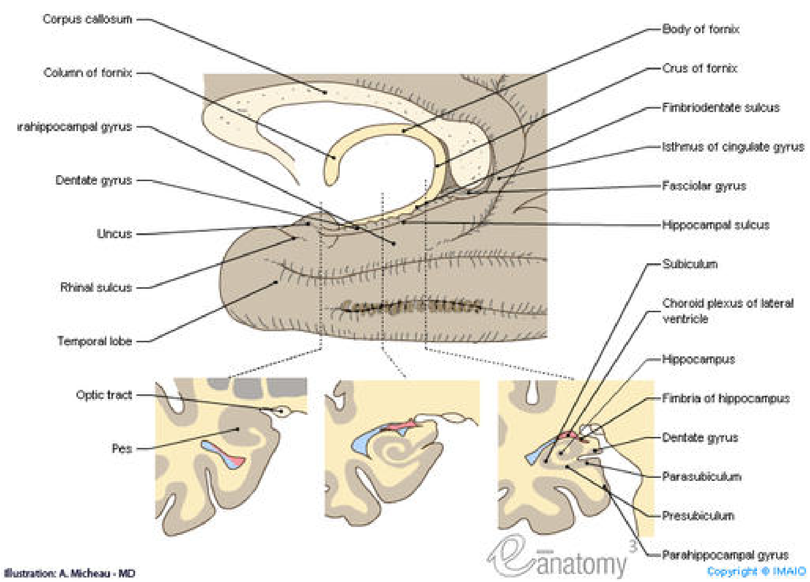
Hippocampal formation

- Consists mainly of the hippocampus and the parahippocampal gyrus.
- The hippocampus is a nuclear mass that lies in the floor of the inferior horn of the lateral ventricle.
- The axons arising from the hippocampus lie on its surface and form the alveus.
- The fibers of the alveus form the fornix .





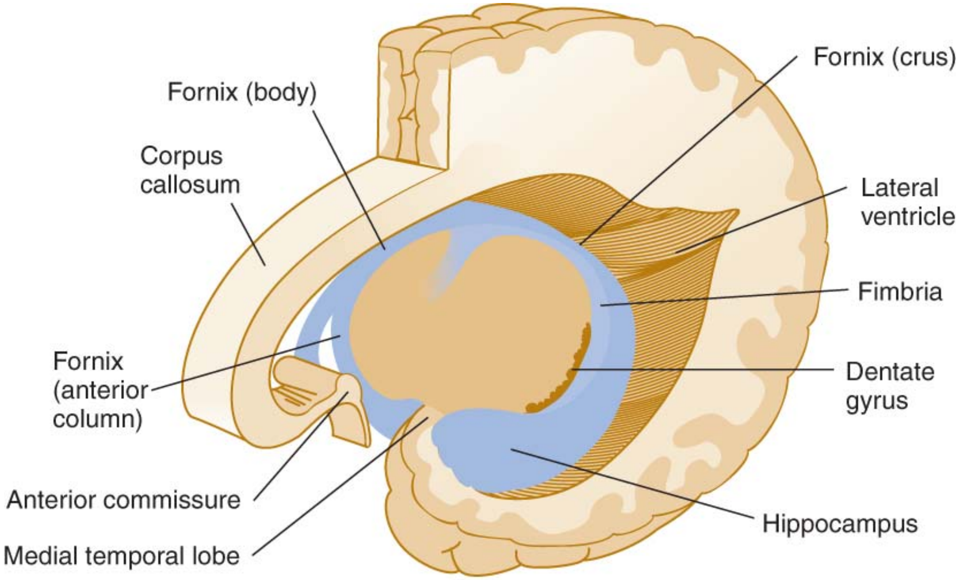




HIPPOCAMPAL FORMATION
Histology and Local Anatomical Connections

- consists of the:
  - **hippocampus,**
  - **dentate gyrus,**
  - **and subicular cortex**

Connections to the:
a) cortex (3-synaptic path)
b) hypothalamus and subcortical structures (Papez circuit)

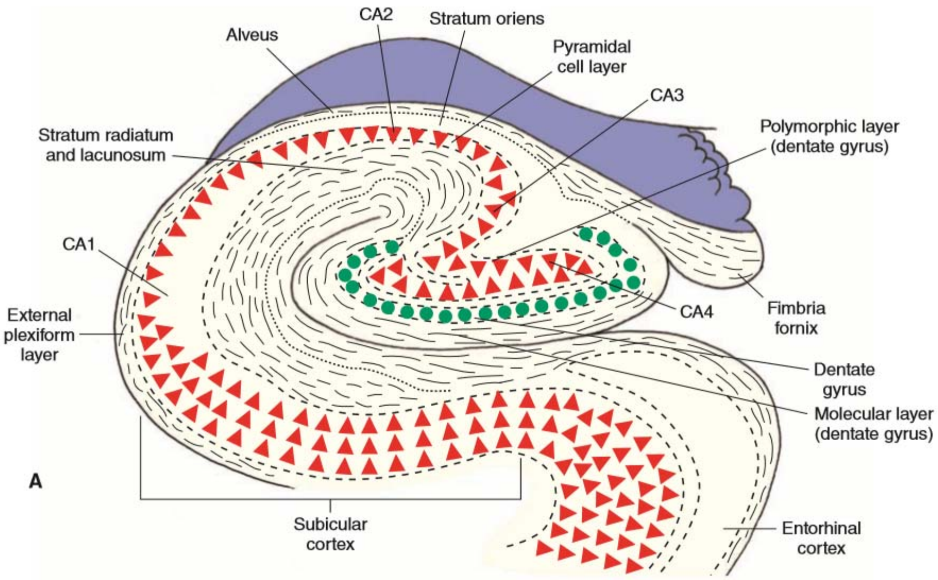


Source: Waxman SG: *Clinical Neuroanatomy: Twenty-Seventh Edition:* www.accessmedicine.com

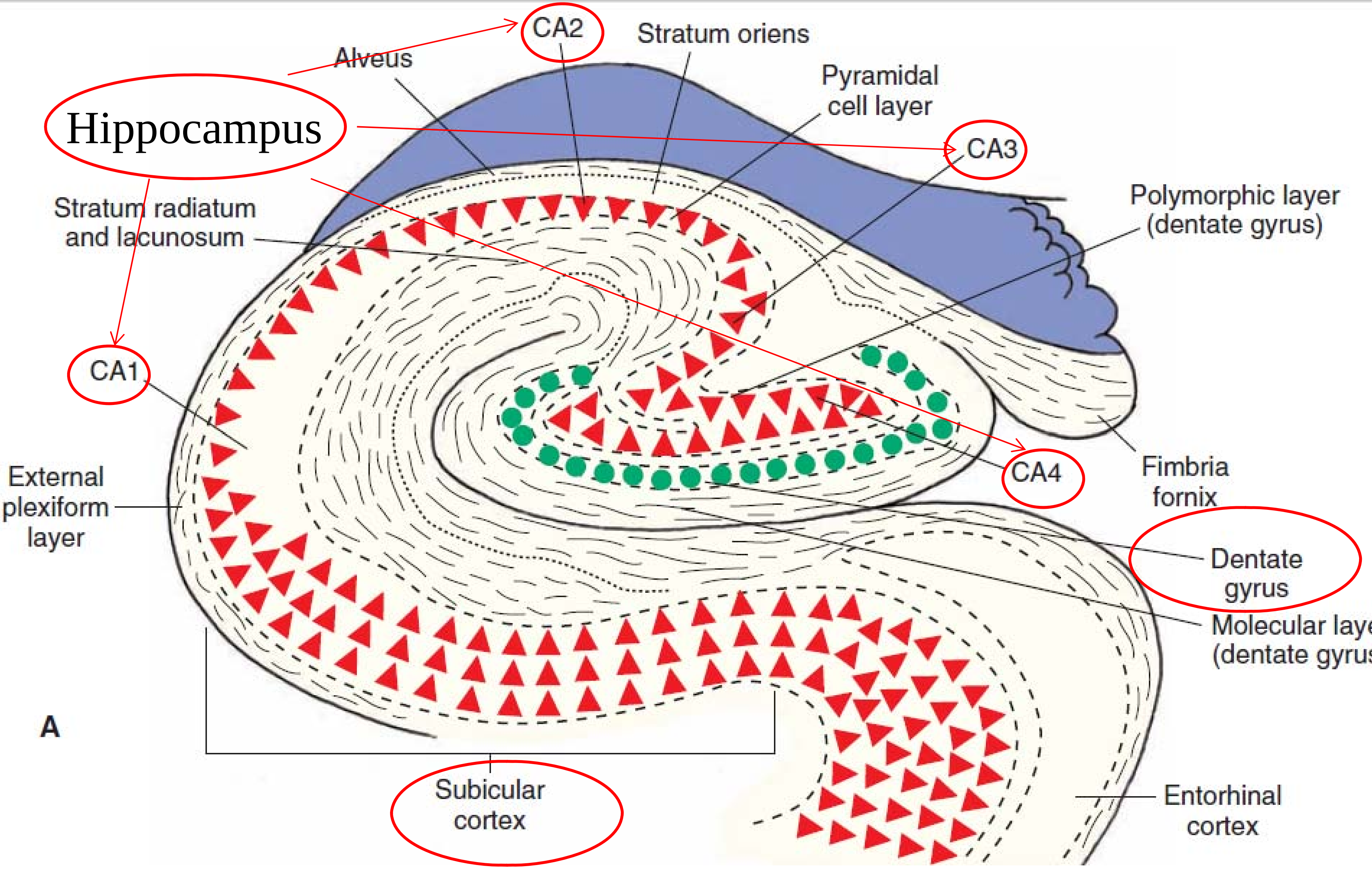
HIPPOCAMPAL FORMATION

Hippocampus

- The hippocampus can be viewed as a primitive form of three-layered cortical tissue
- 1. external plexiform layer
- 2. stratum oriens
- 3a. pyramidal cell layer
- 4 (3b). stratum radiatum and stratum lacunosum-moleculare,



- The hippocampus is divided into a number of distinct fields.
- sectors: CA1, CA2, CA3, and CA4
- The pyramidal cells situated closest to the subiculum are referred to as the *CA1 field*
- the *CA4 field is located within the hilus of the dentate gyrus.*
- Collaterals of axons arising from CA3 pyramidal cells (called **recurrent or Schaffer collaterals**) project back to the CA1 field.



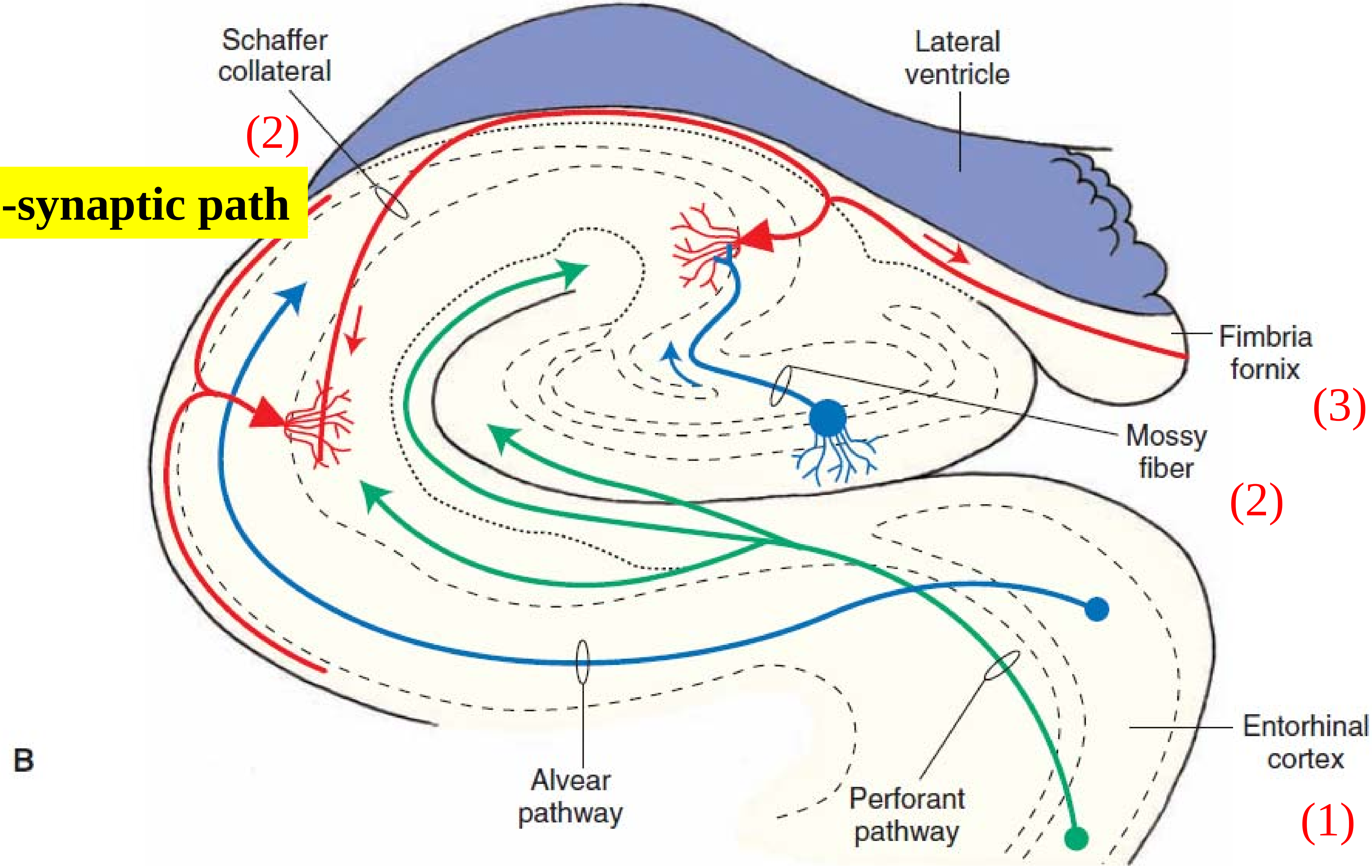
Hippocampus
CA2
Alveus
Stratum oriens
Pyramidal cell layer
CA3
Stratum radiatum and lacunosum
Polymorphic layer (dentate gyrus)
CA1
External plexiform layer
CA4
Fimbria fornix
Dentate gyrus
Molecular laye (dentate gyrus
A
Subicular cortex
Entorhinal cortex

- The CA1 pyramidal cells are highly susceptible to anoxia, especially during periods of temporal lobe epilepsy. This region is referred to as **Sommer's sector.**

HIPPOCAMPAL FORMATION
The Dentate Gyrus

- The **dentate gyrus can also be thought of as a primitive** three-layered cortical structure.
- principal cell type is the **granule cell**
- The **axon of the granule cell**, called a **mossy fiber, makes synaptic contact** with pyramidal cells in the CA3 region.

3-synaptic path



(1) inputs from the entorhinal region, which include the perforant and alveolar pathways;
(2) internal circuitry, which includes the connections of the mossy fibers and Schaffer collaterals;
(3) efferent projections of the hippocampal formation through the fimbria-fornix system of fibers.
CA1–CA4 denote the four sectors of the hippocampus.

3-synaptic path

- Connection from the hippocampus to the cerebral cortex
- *fasciculus perforans – mossy fibers– Schaffer collaterals*
- 1st order neuron aksons of the piramidal neurons II. and III. Layer of the entorhinal cortex
- They form *tractus perforans*
- Make synaptic connection to the dendrites of the grannular cells of FD

3-synaptic path

- 2nd order neuron are aksons of the grannular cells of the FD – *mosy fibers*
- Pass through the *hilus* FD
- Synaptically connect to the piramidal neurons of the field CA3
- 3rd order neuron are aksons of the piramidal neurons of the field CA3 – *Schaffers collaterals*
- Synaptically connect to the piramidal neurons of the field CA1 – (*Schaffers = recurrent collat.)*
- Their axons go to the *subiculum*

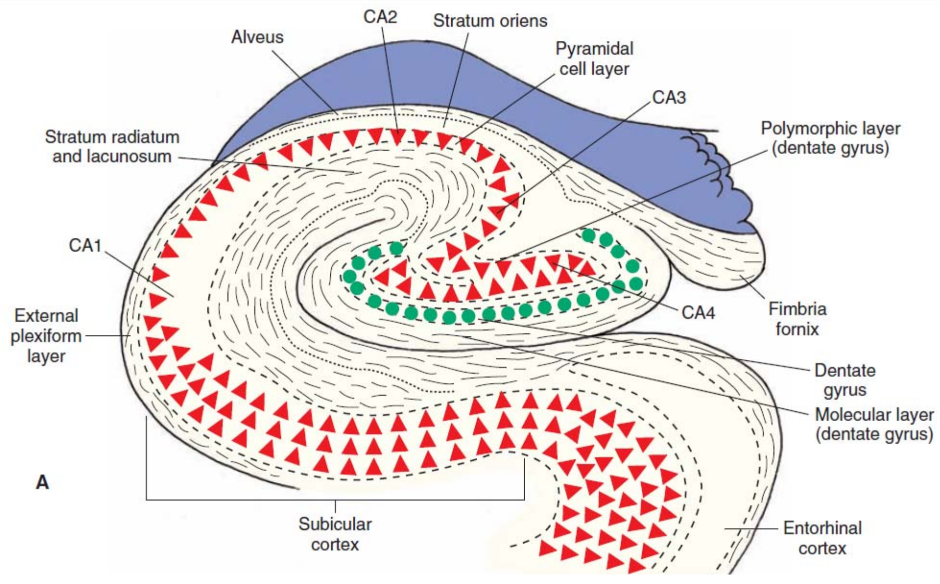
HIPPOCAMPAL FORMATION

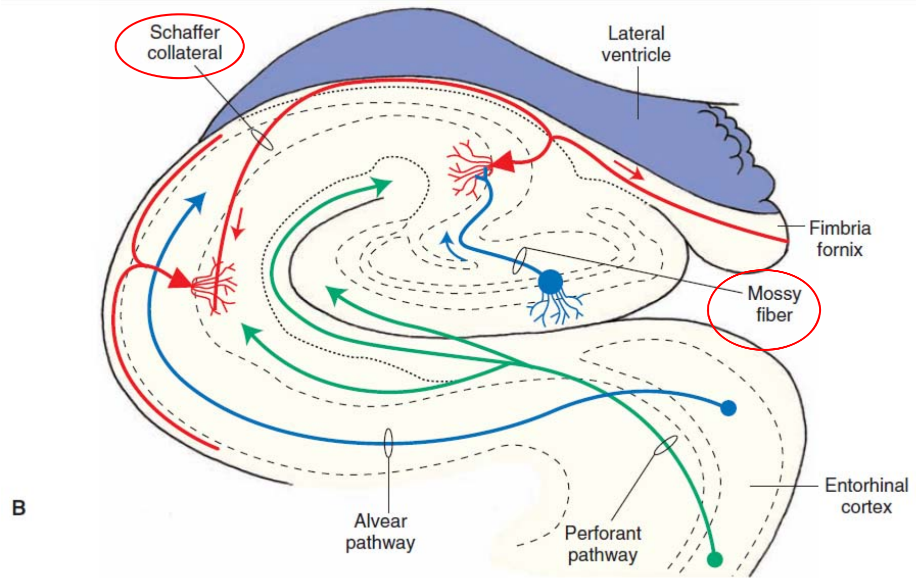
The Subiculum

- The last component of the hippocampal formation is the **subicular cortex**

Schaffer collaterals-
-Axons from CA3 pyramidal cells

mossy fiber - axon of the granule cell.





Afferent Connections

- **ORIGINATE FROM**:
- entorhinal cortex,
- the diagonal band of Broca (of the septal area),
- prefrontal cortex,
- anterior cingulate gyrus,
- premammillary region
- monoamine neuronal projections from the brainstem reticular formation (i.e., locus ceruleus, ventral tegmental area, and pontine and midbrain raphe neurons)

Afferent Connections

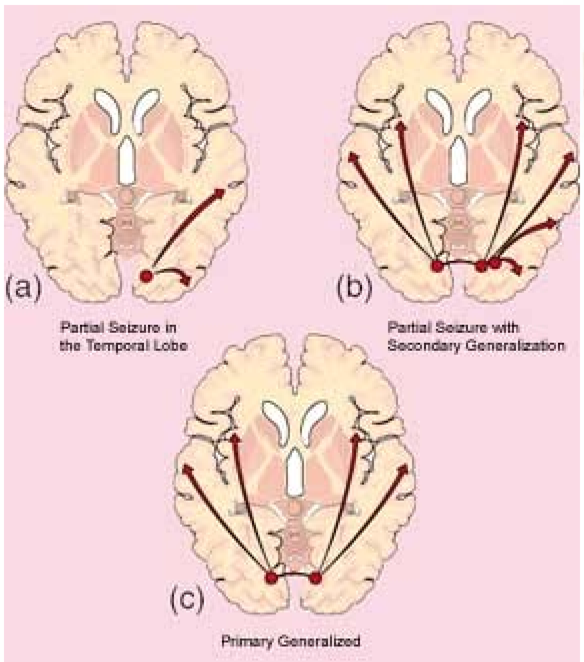
- major source of inputs is the **entorhinal cortex**
- **lateral perforant pathway:** from the lateral entorhinal cortex into the molecular layer of the hippocampus
- **medial perforant pathway:** enters the alveus of the hippocampus
- **Represent:**
  - tertiary **olfactory**, **visual**, and **auditory** fibers

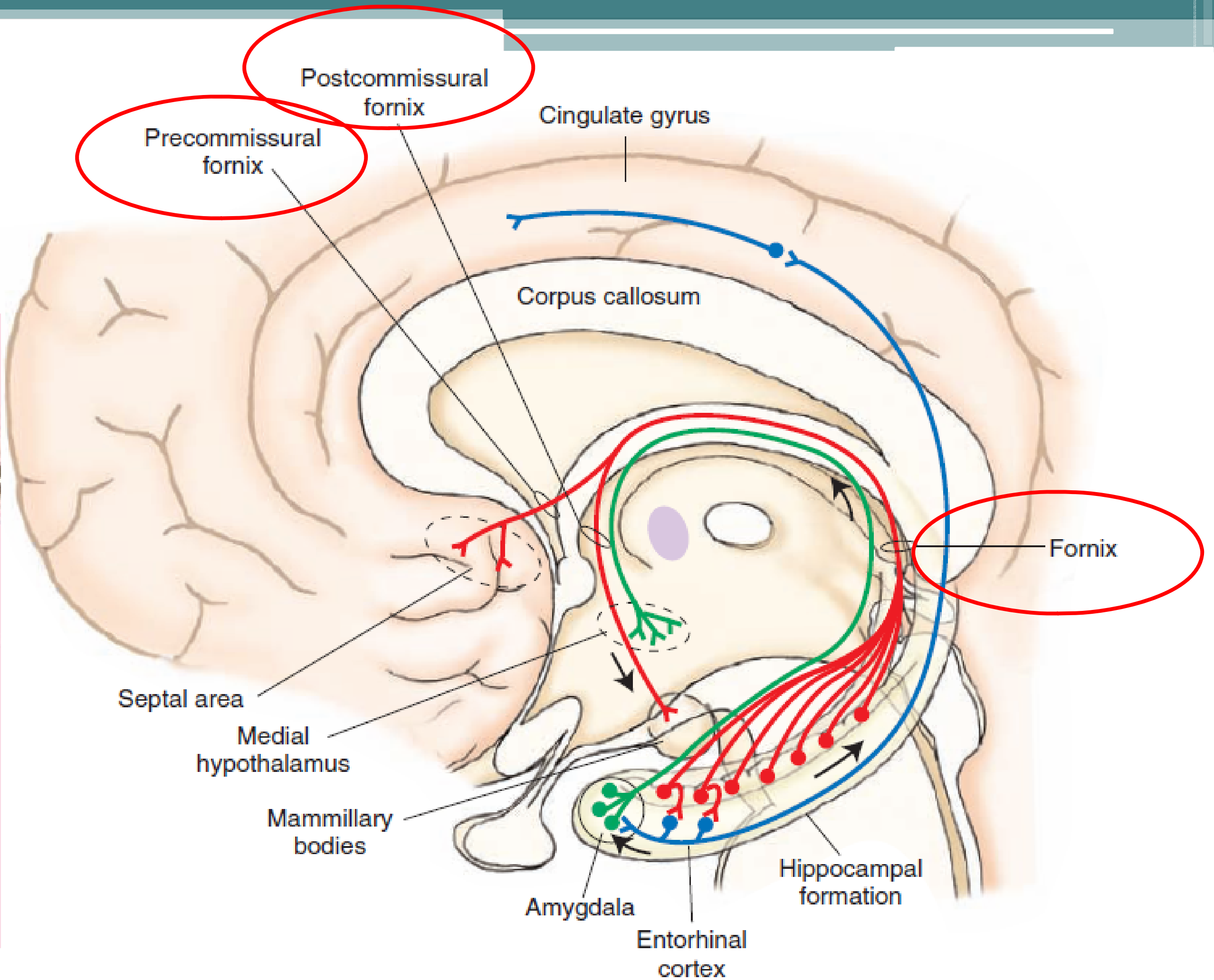
Afferent Connections

- monoamine neuronal projections from the brainstem reticular formation (mood regulation)
- by receiving inputs from these varied sources, the **hippocampal formation** can respond to sudden changes in brainstem and cortical events and relay such changes to the **hypothalamus**, which then provides a visceral (and/or emotional) quality to these events.

Efferent Connections

- arise from pyramidal cells located in both the hippocampus and subicular cortex
- Their axons contribute to the fornix system:
- **1. precommissural component -** passes rostral to the anterior commissure and supplies the septal area
- **2. postcommissural component -**innervates the diencephalon.
- **3. commissural component –** connects hippocampus on each side of the brain





Commissural component - Clinical significance: It may provide the structural basis by which seizures spread from the hippocampus on one side of the brain to the hippocampus on the other side

- The significance of the projections of the subicular and entorhinal cortex is that they enable the hippocampal formation to communicate with widespread regions of neocortex, including areas that receive different modalities of sensory information.

- Such projections may constitute the substrate by which signals from limbic regions of the brain serve to provide affective properties to various modalities of sensory signals.

Functions and Dysfunctions of the Hippocampal Formation

- modulation of aggressive behavior
- autonomic and endocrine functions
- certain forms of learning and memory

Aggression and Rage

- Lesions, tumors, and epileptogenic activity of the hippocampal formation can be linked with aggressive reactions.
- hostility and explosive acts of physical violence
- The hippocampal formation contributes to the regulation of **aggressive** forms of behavior.
- It is likely that such effects are mediated on the hypothalamus via interneurons in the septal area.

Endocrine Functions

- The hippocampal formation (like other regions of the limbic system) has significant inputs to different parts of the hypothalamus.
- (1) estradiol-concentrating neurons in the ventral regions of the hippocampal formation,
- (2) corticosterone
- (3) stimulation of the hippocampal formation inhibits ovulation
- (4) lesions of the hippocampus disrupt the diurnal rhythm for ACTH release.

Learning and Memory Functions of the Hippocampal Formation

- Theta rhythm (4-7 Hz) when approaching the goal, in conditioning
- *Spatial learning*
- *Cognitive maps*

Learning and Memory Functions of the Hippocampal Formation

- **Korsakoff's syndrome is a** memory disorder in which the patient displays memory loss of anterograde and retrograde memory due to hippocampal damage.
- Associated with the toxic effects of alcohol or from a vitamin B deficiency.
- Neurons in the hippocampal formation and other parts of the Papez circuit are affected.

Learning and Memory Functions of the Hippocampal Formation

- Patients sustaining hippocampal lobectomies display a **short-term memory disorder .**
- the patient displays anterograde amnesia, but retrograde amnesia is less severe, with little diminution of intellectual abilities.
- hippocampal mechanism that has been proposed as a model for memory consolidation is called **long-term potentiation (LTP) .**
- It represents a change in synaptic strength as a manifestation of synaptic plasticity

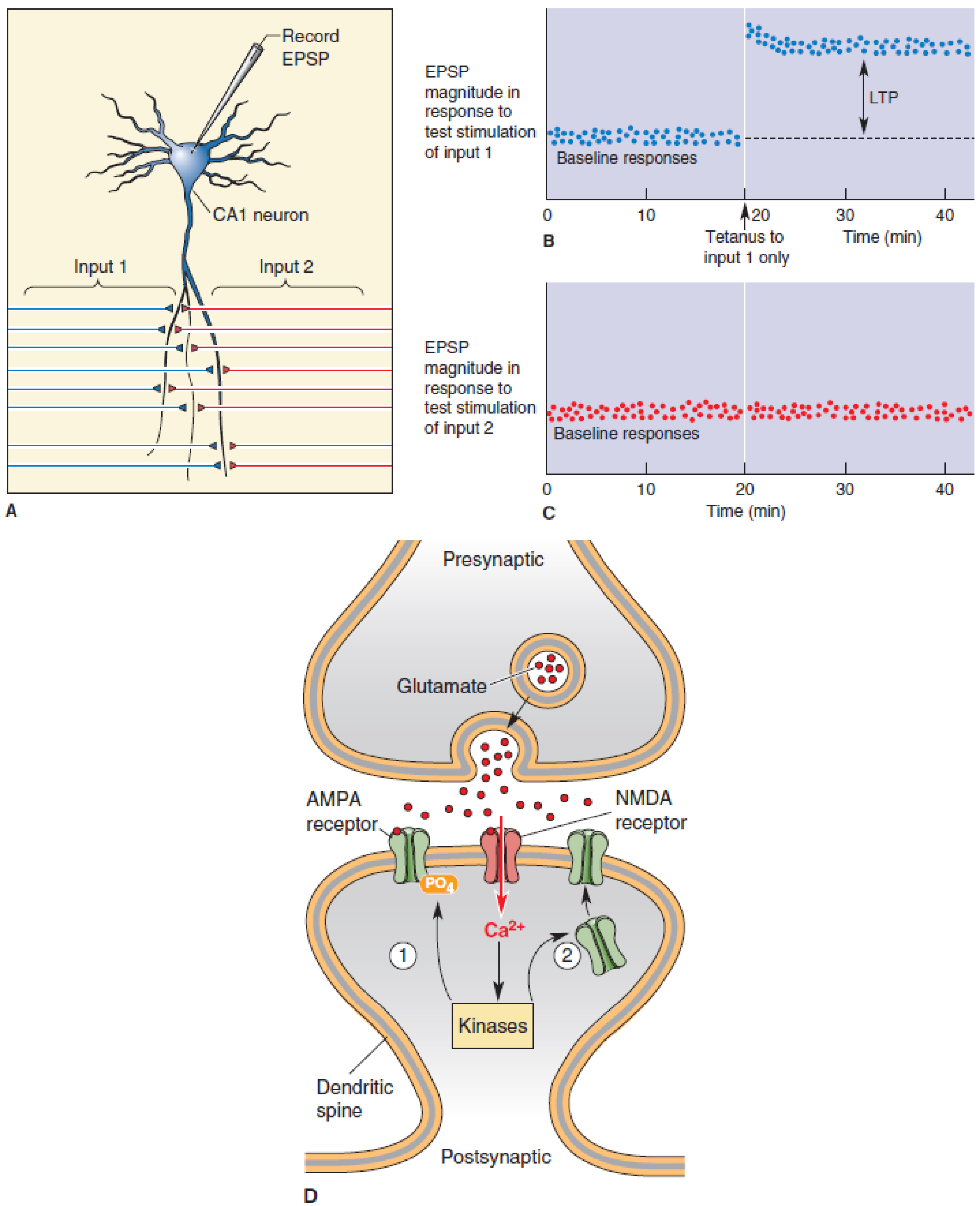


FIGURE 25–5 Long-term potentiation (LTP).

(A) Activity within the CA1 field of hippocampus is recorded with a microelectrode following alternate stimulation of inputs 1 and 2.

(B) In this experiment, high-frequency (tetanus) stimulation applied in input 1 at the time indicated by the arrow potentiated the response as shown in the time period to the right of the arrow.

(C) This graph shows the specificity of the response because there was no change in response following stimulation of input 2. EPSP = excitatory postsynaptic potentials.

(D) Calcium (Ca^{2+}), which enters through NMDA receptors and activates protein kinases, can induce LTP by either altering the efficiency of AMPA receptors or inducing new AMPA receptors.

(From Bear MF, et al.: Neuroscience: Exploring the Brain, 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2007, p. 778.)

2. SEPTAL AREA

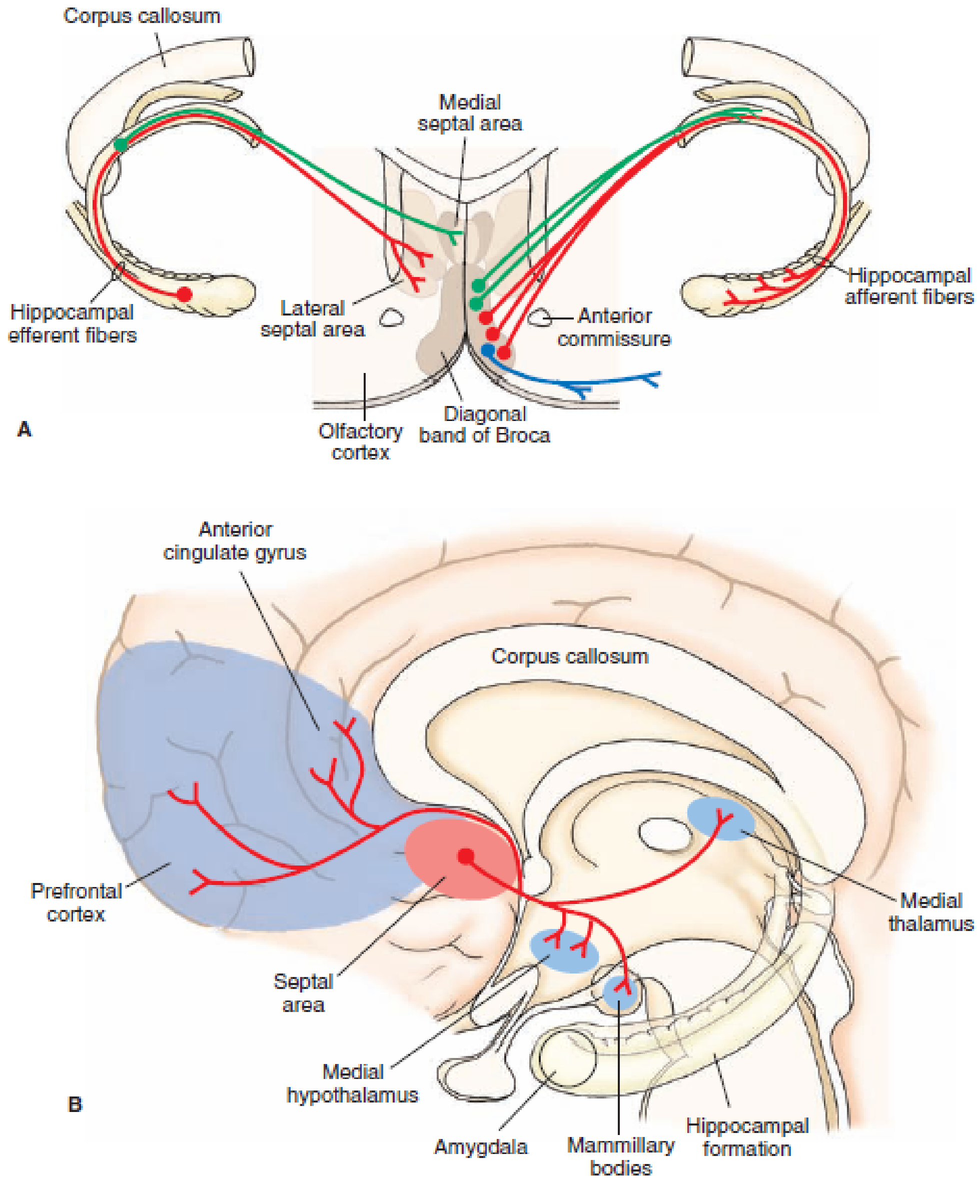


FIGURE 25–6 Connections of the septal area. **(A)** Topographically organized projections from the hippocampal formation to the septal area (*left side*) and topographically arranged efferent projections from the diagonal band of Broca to the hippocampal formation (*right side*) **(B)** Diagram illustrates other projections from the septal area to the medial hypothalamus, mammillary bodies, medial thalamus, prefrontal cortex, and anterior cingulate gyrus.

Functions of the Septal Area

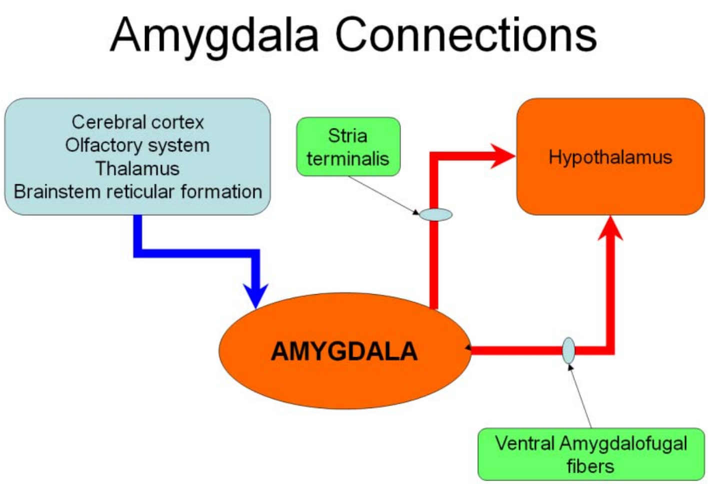
- relay for the transmission of hippocampal impulses to the hypothalamus, but also as a feedback system
- aggression, rage, autonomic functions, self-stimulation, and drinking behavior

3.RELATED BASAL FOREBRAIN NUCLEI

- bed nucleus of the stria terminalis,
- nucleus accumbens,
- substantia innominata (**basal nucleus of Meynert, Ach-Alzheimer's disease)**

4. AMIGDALA

Located deep to the uncus, comprises various nuclei



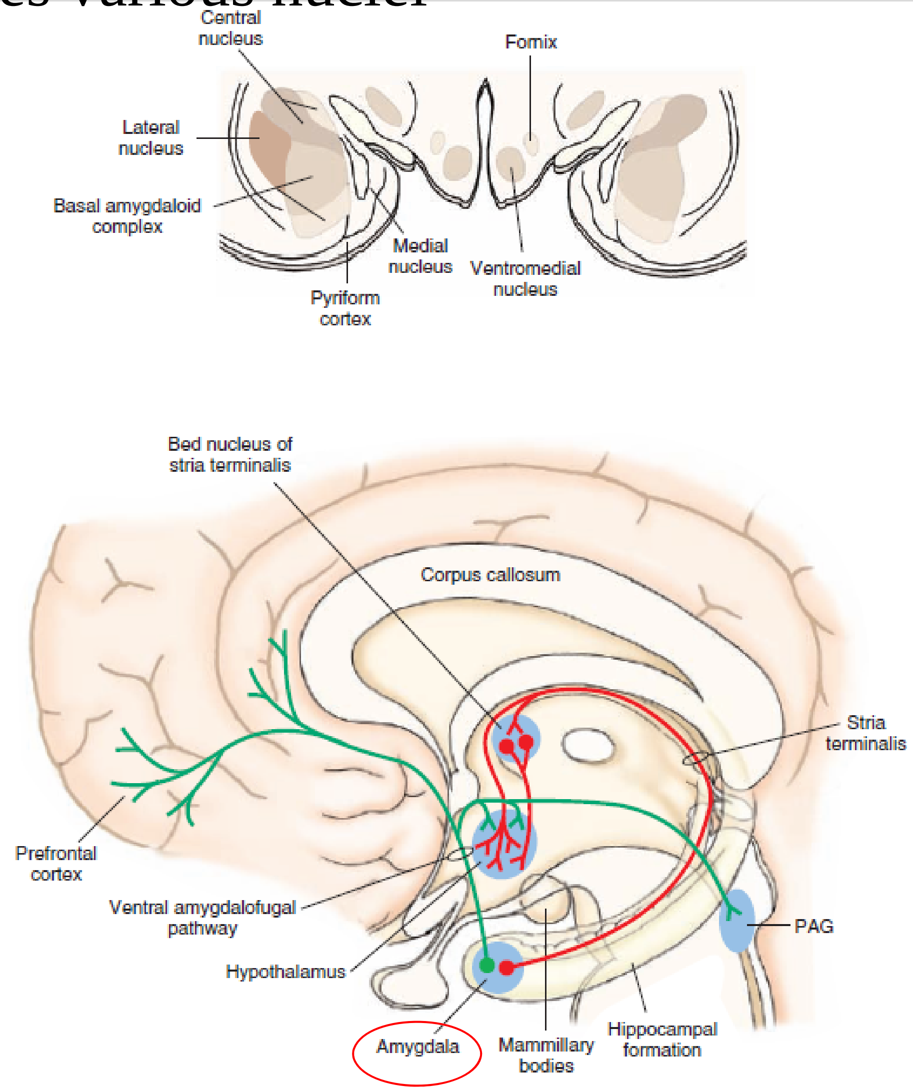


FIGURE 25–7 Efferent projections of the amygdala. The diagram in the upper panel indicates the organization of the nuclei of the amygdala. Schematic diagram in the lower panel identifies the major efferent projections of the amygdala. One principal output includes the stria terminalis, which projects to the bed nucleus of the stria terminalis and to the rostrocaudal extent of the medial hypothalamus. Fibers from the bed nucleus also supply similar regions of the hypothalamus. Another important output to the hypothalamus and midbrain periaqueductal gray matter (PAG) uses the ventral amygdalofugal pathway. Other fibers pass rostrally from the amygdala to the prefrontal cortex.

AMYGDALA

- **Functions and Dysfunctions of the Amygdala**
- **Klüver-Bucy syndrome.**
- Different regions of amygdala exert differential effects on different forms of aggressive behavior.
- Stimulation of the amygdala has affects on the **cardiovascular system**: increases in blood pressure, heart rate, and pupillary dilation
- It affects **endocrine function** (ovulation, growth hormone, ACTH)

AMYGDALA

- important role in the organization and regulation of fear responses.
- Patients with **Urbach-Wiethe disease** **(**calcification of parts of the anterior aspect of the temporal lobe including the amygdala**) may have difficulties in recognizing** stimuli that one would normally characterize as fearful.

LIMBIC COMPONENTS OF THE CEREBRAL CORTEX

- **Functions of the Cerebral Cortex**
- *Prefrontal Cortex*
- The prefrontal cortex is associated with both emotional and intellectual processes
- The importance of the human prefrontal cortex in the control of human aggression has also been recognized for many years

Papez cycle – emotional processes

- In year 1937, James Papez indicated that emotions are not function of a single center in the brain, but rather relay on a neuronal circuit which includes several structures.

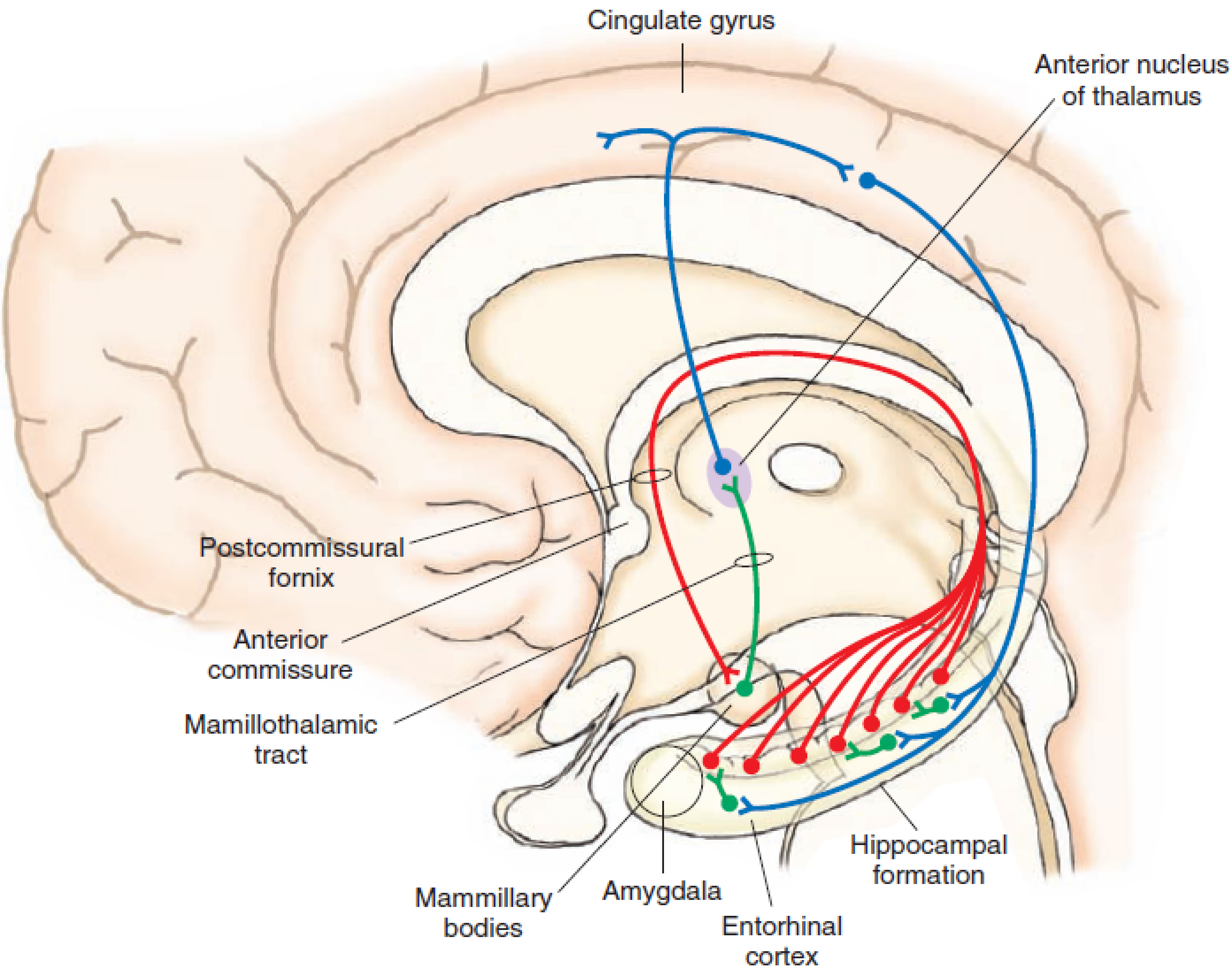


FIGURE 25–4 Papez circuit. In the Papez circuit, hippocampal fibers project to the mammillary bodies, which, in turn, project through the mammillothalamic tract to the anterior nucleus. The anterior thalamic nucleus then projects to the cingulate gyrus, and the axons of the cingulate gyrus then project back to the hippocampal formation.

Components of the Papez cycle:

- HYPOTHALAMUS with CORPORA MAMILLARIA
- THALAMUS (anterior nucleus)
- GYRUS CINGULI
- HIPPOCAMPUS

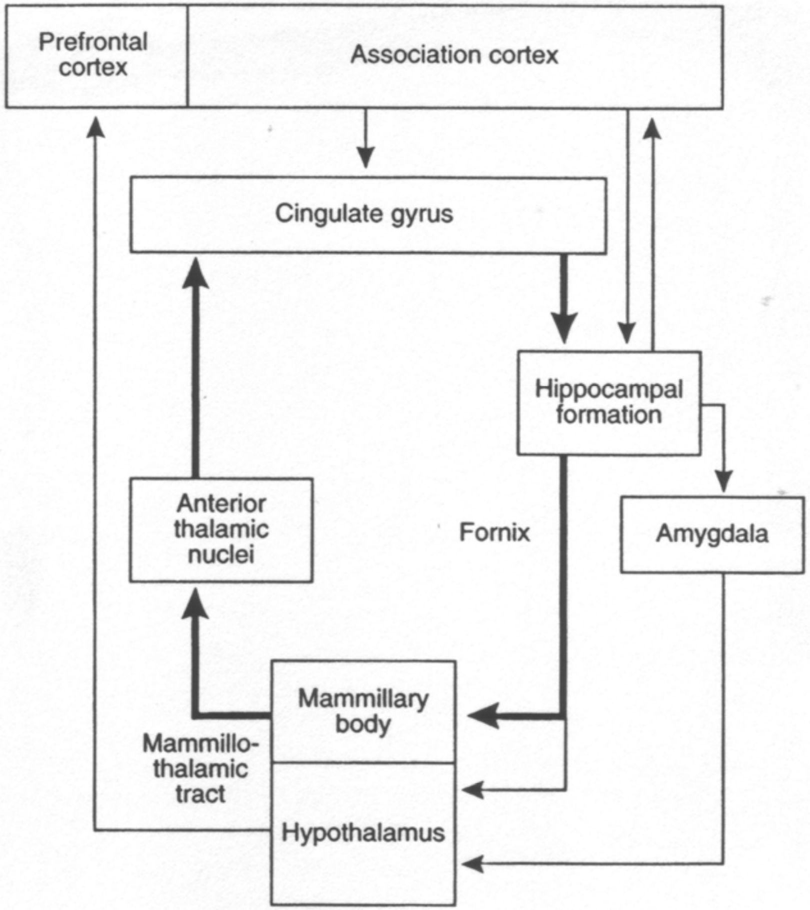
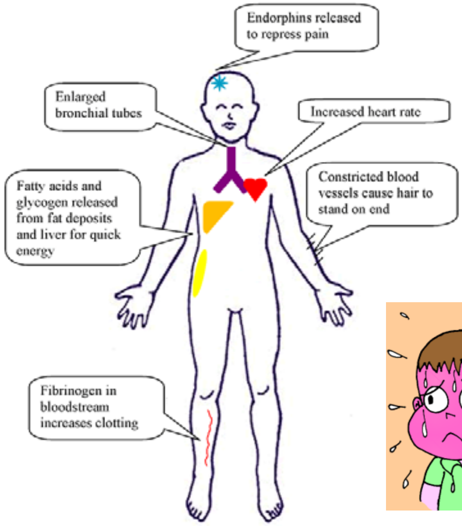
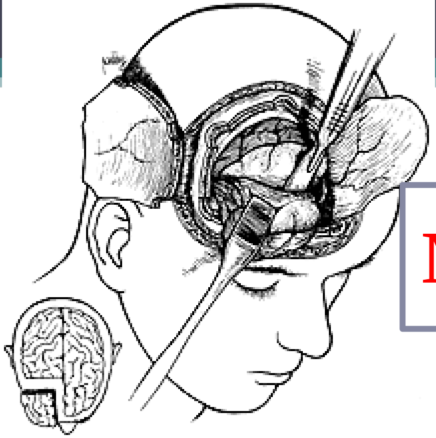


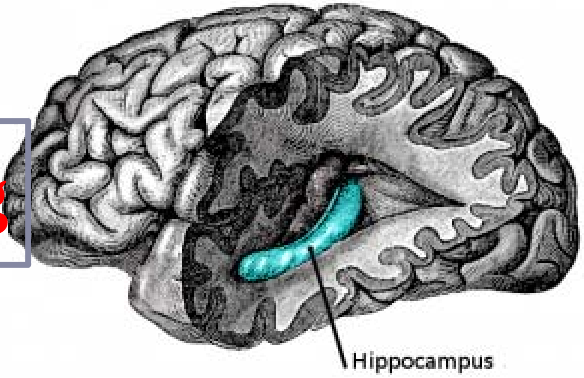
FIGURE 47–2
A proposed neural circuit for emotion. The circuit originally proposed by James Papez is indicated by **thick lines;** more recently described connections are shown by **fine lines**. Known projections of the fornix to hypothalamic regions (mammillary bodies and other hypothalamic areas) and of the hypothalamus to the prefrontal cortex are indicated. A pathway interconnecting the amygdala to limbic structures is shown. Finally, reciprocal connections between the hippocampal formation and the association cortex are indicated. The hippocampal formation includes the hippocampus proper and surrounding structures, including entorhinal cortex and the subicular complex.

- Papez cyrcuit:: *central regulation of emotions* (fear, rage, love, hate, agression)
- and their *expression* (autonomic reactions, heart rate, breathing)





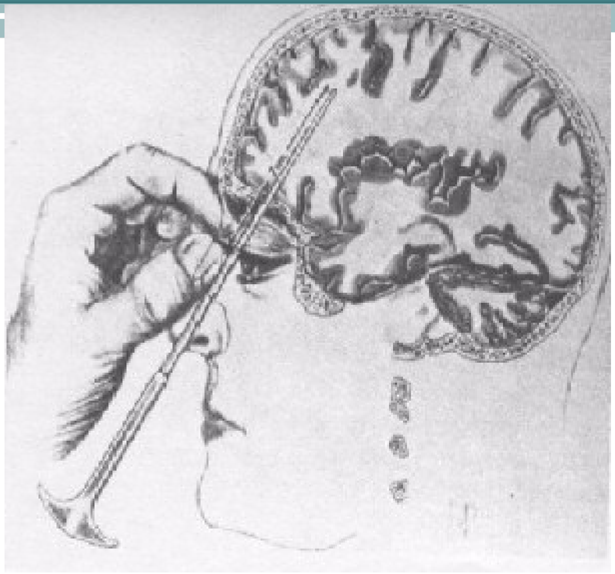
Memory and learning



- memory loss due to hippocampal ablation (lobectomy)
- patients could not remember of people or events that happened after the surgery
- hippocampus contribute to the consolidation of memory functions by transferring short-term memories to long-term memories.

- One hippocampal mechanism that has been proposed as a model for memory consolidation is called **long-term potentiation (LTP).**
- **It represents a change in synaptic** strength as a manifestation of synaptic plasticity.

- **prefrontal lobotomy** was developed in 1936 by Egaz Moniz for controlling human violence
- The use of prefrontal lobotomies has been replaced by other (noninvasive) therapeutic measures such as antipsychotic drugs.



PATHOLOGICAL ACTIVITY WITHIN LIMBIC CIRCUITS

- **epilepsy** is a major disorder associated with the limbic system
- If **alpha rhythm** is slow or absent, there may be a neurologic problem.

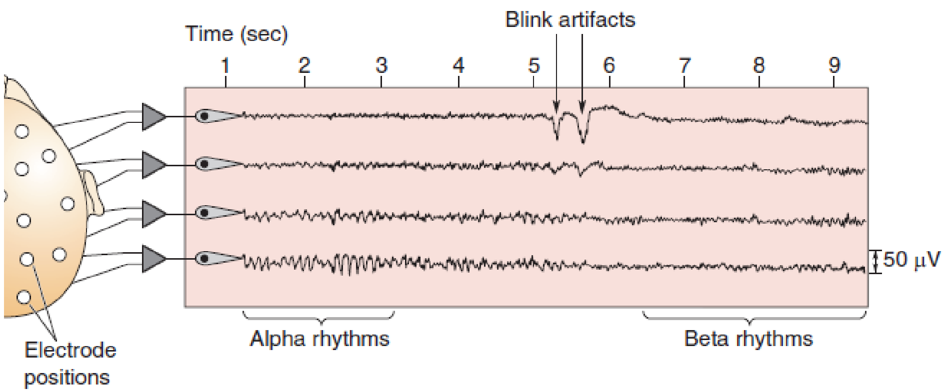


FIGURE 23–10 Tracings of a normal electroencephalogram. The locations of the recording electrodes, shown on the left side of the figu
an individual who is quiet but awake. Initially, the subject displays an alpha rhythm during the quiet period, but when he opens his
blink artifacts), the alpha rhythm is replaced by a beta rhythm. (Used with permission from Bear MF, et al.: Neuroscience: Exploring
Philadelphia: Lippincott Williams & Wilkins, 2007, p. 590.)

Epilepsy

- condition in which seizures are recurrent
- The time of the occurrence of the seizure is called the **ictal period**
- the time following the seizure is called the **postictal period**
- and the time between seizures is called the **interictal period**

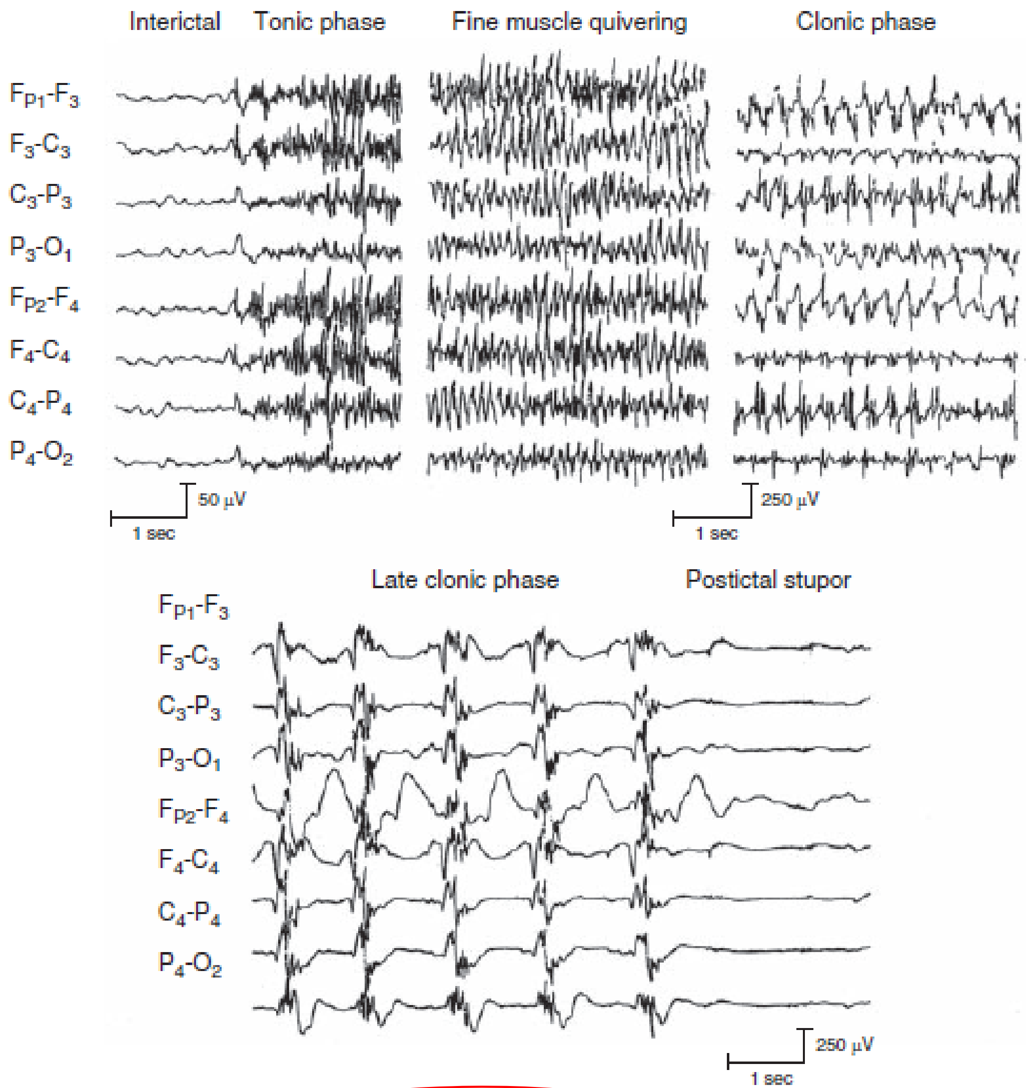


FIGURE 25–8 Electroencephalogram records showing a generalized tonic-clonic seizure. The various segments illustrate the interictal phase (prior to the seizure); the tonic phase (where the body is stiff) with repetitive spiking; a clonic phase (where body is jerking), which shows spike and waves; and a postictal phase (where no seizure activity is present). (From Westmoreland BF, et al.: Medical Neurosciences, 3rd ed. Boston: Little, Brown & Co., 1994, p. 484.)

Jacksonian March epilepsy

- **Seizure activity** begins locally over the cortex, causing either sensory or motor activity directly corresponding to the **homunculus.**
- The patient experiences a “march” of sensory or motor activity from muscle to muscle in the same order as the homunculus.

Absence seizures

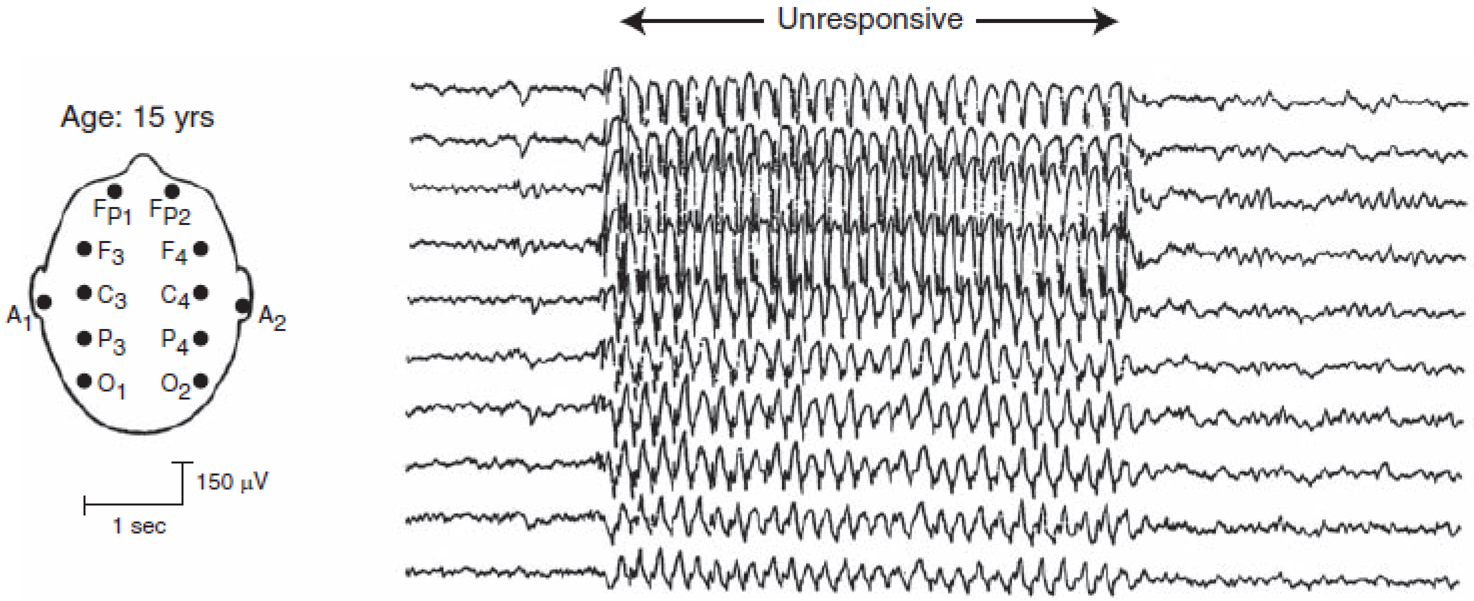
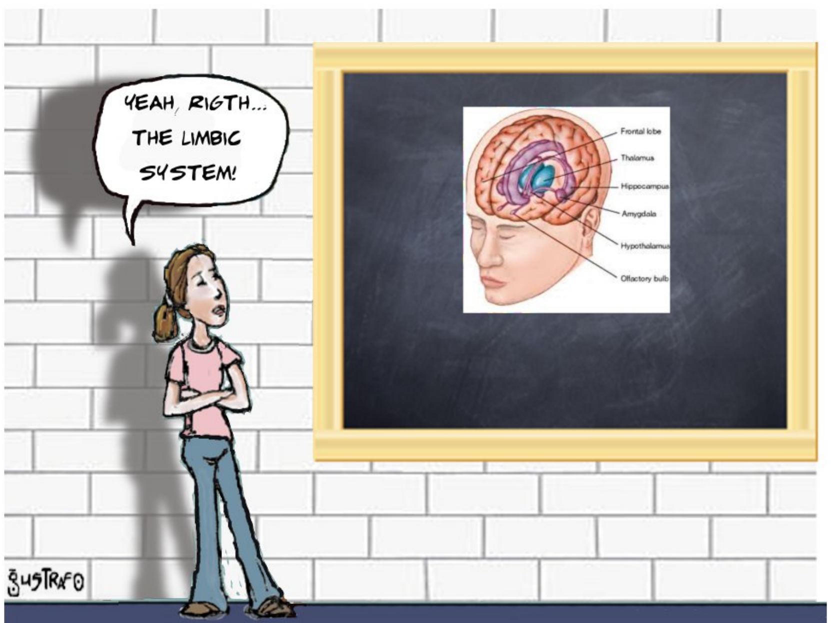
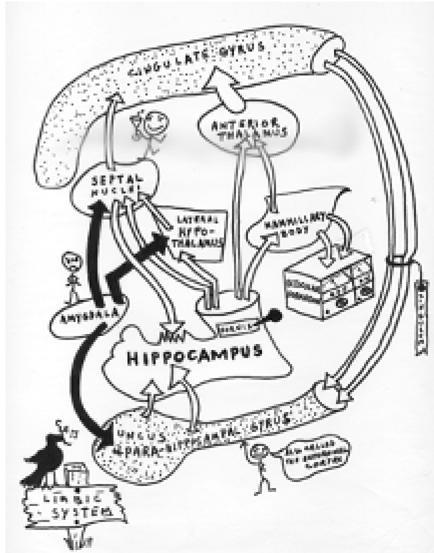
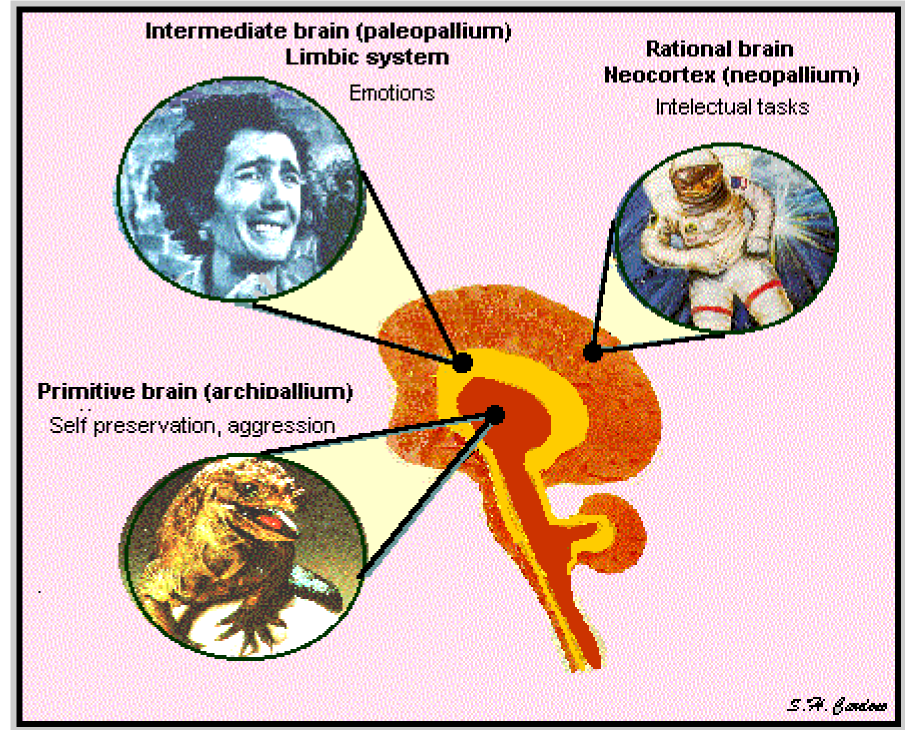


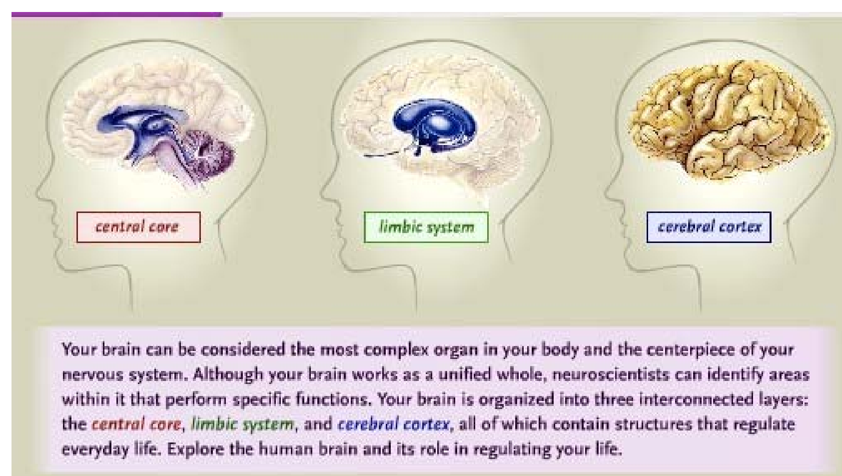
FIGURE 25–9 Absence seizure. Electroencephalogram records illustrating an absence seizure consisting of a 3-Hz spike and wave pattern, at which time the patient was unresponsive. (From Westmoreland BF, et al.: Medical Neurosciences, 3rd ed. Boston: Little, Brown & Co., 1994, p. 485.)

- very brief (approximately 3–10 seconds long)
- the patient is unresponsive
- commonly described as “daydreaming”


YEAH, RIGTH...
THE LIMBIC
SYSTEM!
Frontal lobe
Thalamus
Hippocampus
Amygdala
Hypothalamus
Olfactory bulb
GUSTRAFO


CINGULATE GYRUS
ANTERIOR THALAMUS
SEPTAL NUCLEI
LATERAL HYPO-THALAMUS
MAMMILLARY BODY
AMYGDALA
HIPPOCAMPUS
UNCUS
PARA-HIPPOCAMPAL GYRUS
LIMBIC SYSTEM


Intermediate brain (paleopallium)
Limbic system
Emotions
Rational brain
Neocortex (neopallium)
Intelectual tasks
Primitive brain (archipallium)
Self preservation, aggression


central core
limbic system
cerebral cortex
Your brain can be considered the most complex organ in your body and the centerpiece of your nervous system. Although your brain works as a unified whole, neuroscientists can identify areas within it that perform specific functions. Your brain is organized into three interconnected layers: the central core, limbic system, and cerebral cortex, all of which contain structures that regulate everyday life. Explore the human brain and its role in regulating your life.

https://www.youtube.com/watch?v=ErpxEwlWww4