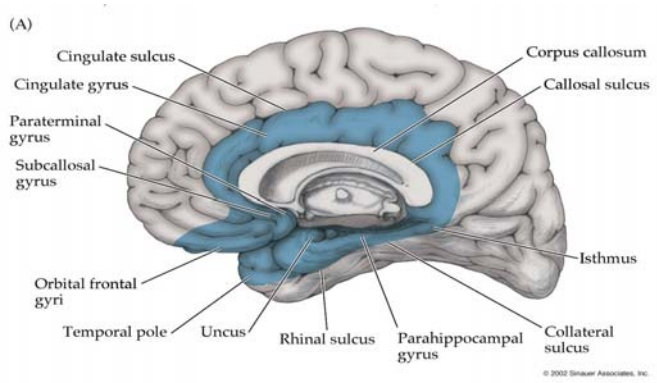
MODULE 7: LIMBIC SYSTEM

This module will summarize the important neuroanatomical and key clinical concepts from Chapter 18 of the course textbook. The anatomical section of this module will cover an overview of the limbic system structures, hippocampal formation and other memory related structures, the amygdala, and the limbic pathways. This module also will discuss memory disorders and some emotional functions.

OVERVIEW OF LIMBIC STRUCTURES. The limbic system is a network of brain structures lying on the medial and inferior aspects of the brain that are vital in mediating memory and emotional functions. Other related limbic structures and networks are involved in olfaction and homeostasis. The most important structure for each of these functions is listed below, although in reality these functions are mediated by a widely distributed network.

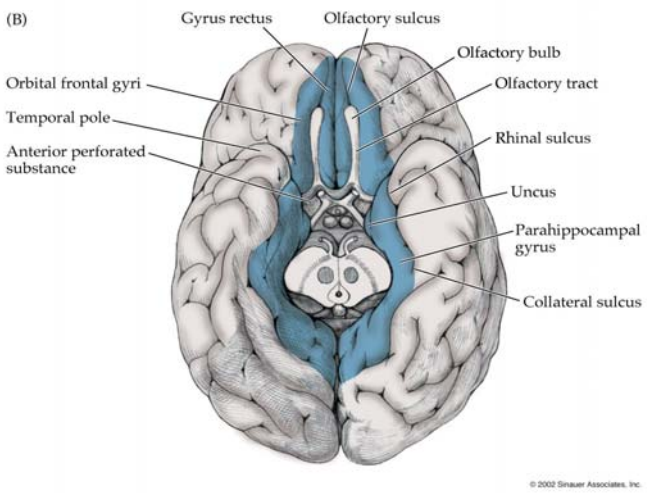
	FUNCTION	STRUCTURE
1.	Memory	= Hippocampus
2.	Emotion & drives	= Amygdala
3.	Olfaction	= Olfactory cortex (perirhinal & orbitofrontal)
4.	Homeostasis	= Hypothalamus

Limbic cortex is also called paralimbic cortex or limbic association cortex. The limbic cortex forms a ring on the medial aspect of the brain consisting mainly of the ***cingulate gyrus*** and the ***parahippocampal gyrus*** (see figure below).

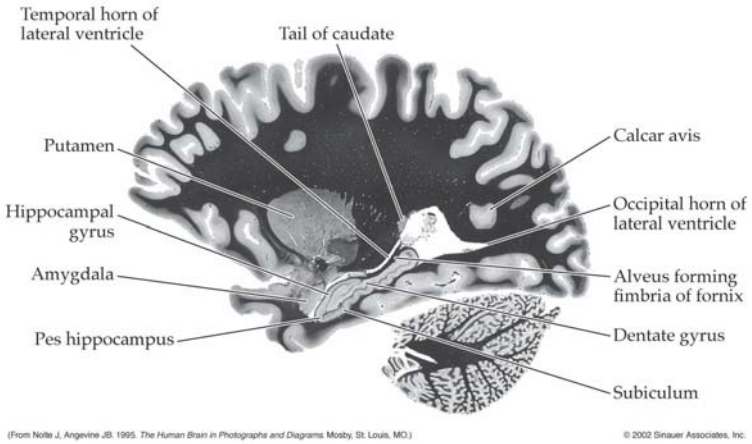


Other components of the limbic system include ***medial*** and ***orbital-frontal cortex***, ***temporal pole***, ***anterior insula***, ***hippocampal formation***, ***amygdala***, ***olfactory cortex***, ***portions of the thalamus and hypothalamus***, ***portions of the basal ganglia***, ***basal forebrain***, ***septal nuclei***, and some brainstem nuclei.

Some of these structures are better visualized by looking at the ventral undersurface of the brain as shown below.

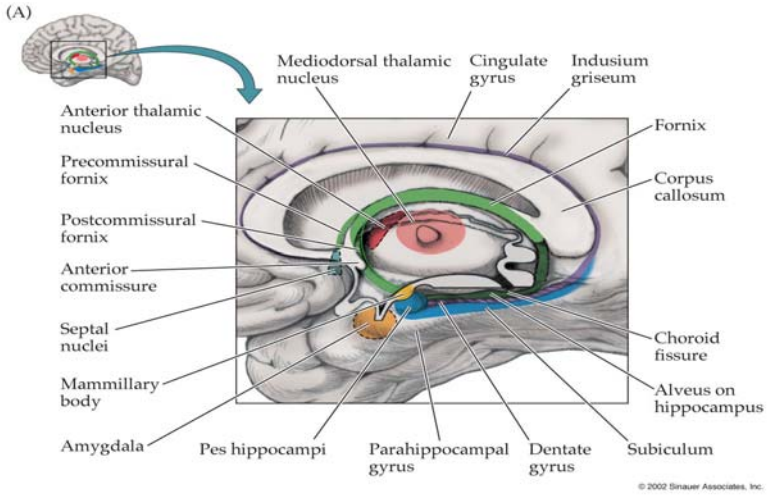


HIPPOCAMPUS. Within this ring and in the temporal lobe lies the simple three-layered ***archicortex*** of the ***hippocampal formation***. The hippocampal formation consists of three gyri, named from medial to lateral, the ***dentate gyrus***, ***hippocampal gyrus***, and ***subiculum***. Unlike the six-layered neocortex making up most of the brain surface, the gyri of the hippocampal formation each consist of only three layers. A saggital section through the hippocampus shows each of the hippocampal gyri (see below).

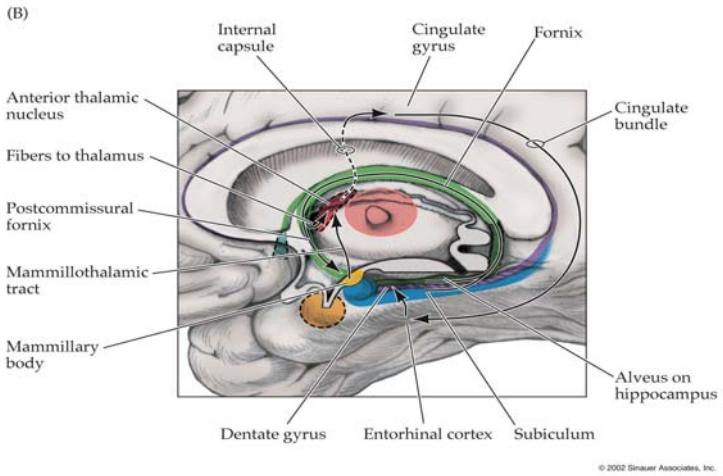


The hippocampal formation is crucial to memory function. The hippocampus has rich reciprocal connections with all association cortices with most inputs coming from the entorhinal cortex and most cortical outputs leaving via the subiculum. The hippocampal formation also has connections with subcortical structures, especially the ***mammillary bodies***, ***dorsomedial nucleus of thalamus***, other ***medial diencephalic*** nuclei, and ***the septal nuclei*** via the ***fornix*** among others.

The most well-known of these subcortical limbic circuits is the circuit of Papez which is shown below.



This is figure 18.9 (A) taken from the text on page 774 which shows the important structures within the circuit of Papez. The circuit itself is given below in (B).



Although the structures in the circuit of Papez have many other important connections beyond those in this circuit, it nonetheless remains useful since it reviews many of the major limbic pathways.

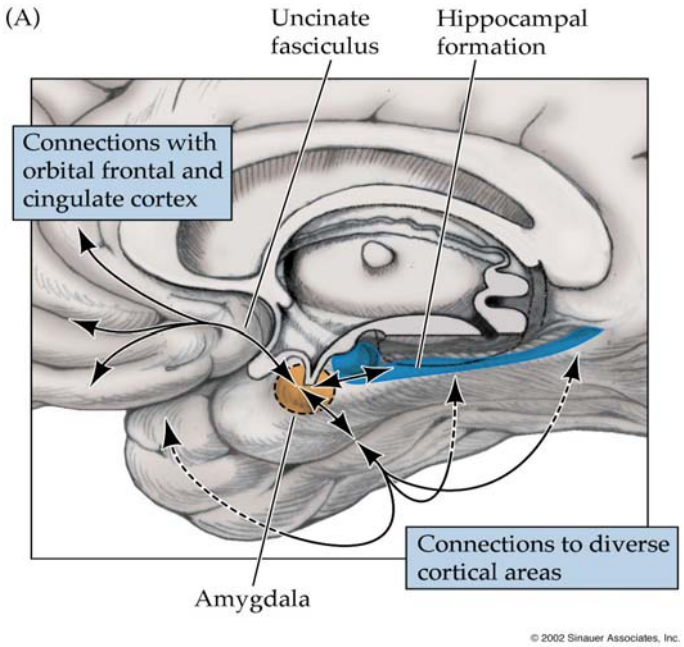
The ***Papez circuit*** (see figure above) begins with fibers leaving the ***hippocampus*** (via the subiculum) which enter the ***fornix*** and travel forward to the ***mammillary nuclei***. The mammillary body then projects to the ***anterior nucleus of the thalamus***. The anterior thalamic nucleus next projects through the internal capsule to the ***cingulate gyrus***. Finally, a prominent white matter pathway underlying the cingulate gyrus, called the ***cingulum bundle*** or cingulum, passes from the cingulated cortex to the ***parahippocampal gyrus***, from which projections continue to the ***entorhinal cortex*** and hippocampal formation, completing the circuit.

MEMORY DISORDERS. Lesions of the ***medial temporal lobe memory system*** (hippocampal formation and parahippocampal gyrus) or of the ***medial***

diencephalic memory system (thalamic dorsomedial nucleus, anterior nucleus, internal medullary lamina, and other periventricular diencephalic nuclei) can cause ***amnesia*** (inability to learn new declarative information; recent memory dysfunction).

When the amnesia has been caused by some trauma, there is an ***anterograde amnesia*** (a deficit in forming new memories from the time of the brain injury onward) usually in conjunction ***retrograde amnesia***, in which material from a period of time prior to the lesion cannot be recalled.

THE AMYGDALA meaning “almond” in Greek is also called the amygdaloid nuclear complex. The amygdala is a group of nuclei located in the anteromedial temporal lobes, just anterior to the anterior tip of the hippocampus and temporal horn of the lateral ventricle (see figure below). The amygdala is important in mediating emotions, drives, among other functions.



Most connections of the amygdala are ***bidirectional***. The amygdala receives and transmits information from ***heteromodal association cortex*** and limbic cortex as well as subcortical structures including ***thalamus*** (dorsomedial nucleus), ***hypothalamus***, ***septal nuclei***, ***basal forebrain nuclei***, and ventral ***striatum***.

Emotions and drives appear to be mediated by complex interactions among these cortical and subcortical connections. The amygdala is important for attaching emotional significance to various stimuli perceived by the association cortex. When both amygdalae have been ablated, behavior tends to be placid.

Tame, nonaggressive behavior, together with hypersexuality and hyperorality, constitutes the ***Kluver-Bucy syndrome***. Electrical stimulation of the amygdala or seizures involving the amygdala can cause fear and panic. While the amygdala has been found to be important in fear, anxiety, and aggression ("fight or flight" emotions), the septal nuclei are important in mediating pleasurable states.

CLINICAL CASE – LIMBIC SYSTEM DYSFUNCTION

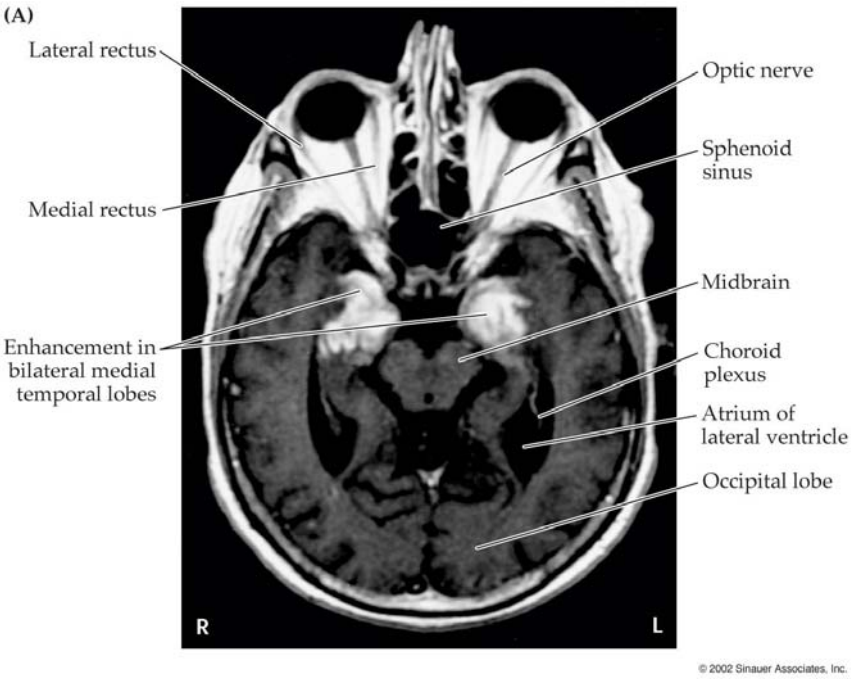
Case presentation. A 75 year-old man was brought to the emergency room because of severe, progressive memory problems that developed over the course of several weeks. The patient had missed appointments and forgotten the names of people he know well. His conversational speech was normal except that he was completely unaware of all recent events. There is no history of alcohol abuse or psychiatric illness.

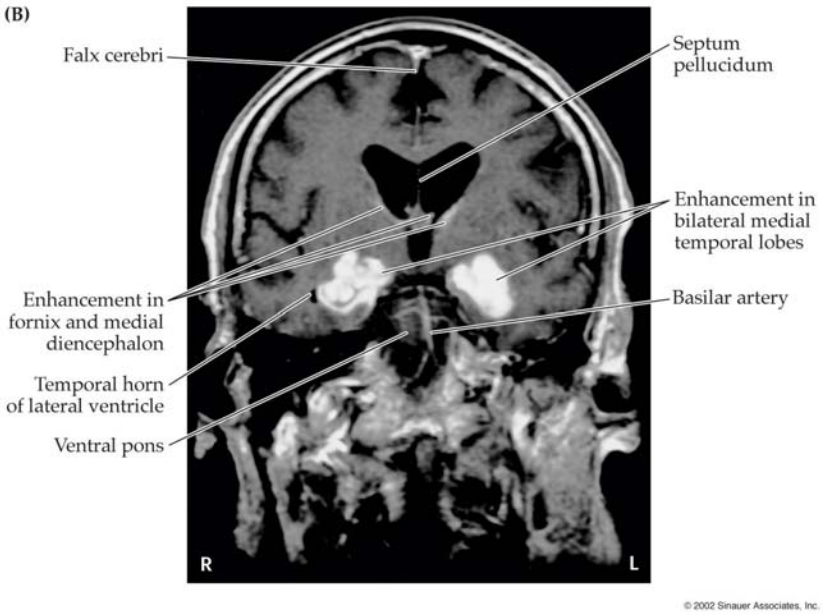
Neurological examination was normal except for the mental status examination which found profound problems with recent memories and milder problems with remote memories. The patient was disoriented to time and place (could not provide the name of the hospital) and could remember 0 of 3 words after 3 minutes. When the examiner left the room and came back a few minutes later, the patient had no recollection of having met him before. Immediate memory was normal with a digit span of 7 forwards and 5 backward.

Case formulation. Severe progressive problems with recent memory suggest dysfunction of the bilateral medial temporal lobes or bilateral diencephalic structures. The time-course of onset of the memory decline (~3 weeks) was too rapid to be caused by a neurodegenerative disorder such as Alzheimer's disease, which progresses over months to years rather than weeks as in this case. Wernicke-Korsakoff syndrome resulting from thiamine deficiency should be considered. However, there was no known alcoholism or nutritional deficiency in this case, and onset of Korsakoff's syndrome is often more abrupt.

Given the insidious onset, other important possibilities to consider include tumor, multiple transient ischemic attacks or small infarcts, paraneoplastic limbic encephalopathy, or other inflammatory or infiltrative disorder affecting the bilateral medial temporal lobes or bilateral diencephalic structures.

Neuroimaging. The patient underwent a brain MRI with contrast (gadolinium) which revealed markedly abnormal enhancement in the bilateral medial temporal lobes, including the amygdala and anterior hippocampal formation bilaterally (see MRI below).





Several lumbar punctures and blood tests were done but did not yield a diagnosis. Over the course of several days, he became more disoriented and lost his sense of smell, which suggested further spread of the disease. Therefore, a brain biopsy was undertaken and revealed an atypical lymphoma.

The patient was treated with steroids and multiple cycles of intravenous chemotherapy with methotrexate, and he had a dramatic improvement in his memory. Repeat MRI 3 months after diagnosis showed complete disappearance of the enhancing lesions, and he had resumed most of his previous activities.