The Human Limbic System:
Gross Anatomy & Microscopic Anatomy
Evolution of the Limbic System
Central Pathways and Neurochemistry
Functions of Limbic System
Behavioural and Clinical Correlates on the Human Limbic System

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The **limbic system** is a term for a set of brain structures including the hippocampus and amygdala and anterior thalamic nuclei and a limbic cortex that support a variety of functions including emotion, behavior and long term memory.

The structures of the brain described by the limbic system are closely associated with the olfactory structures.

The term "limbic" comes from **Latin** limbus, meaning "border" or "belt".

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The **"Nose Brain"** (Rhinencephalon)

- 1937 Papez ‘s Limbic System
- “Emotional Brain”
- “Psychosexual Brain”
- 1952 Paul McLean’s The Triune Brain

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**History**

The French physician Paul Broca first called this part of the brain "le grand lobe limbique" in 1878, but most of its putative role in emotion was developed only in 1937 when the American physician James Papez described his anatomical model of emotion, the Papez circuit.

Paul D. MacLean expanded these ideas to include additional structures in a more dispersed "limbic system," more on the lines of the system described above. The term was formerly introduced by MacLean in 1952. The concept of the limbic system has since been further expanded and developed by Nauta, Heimer and others.


Dr. James Papez (1883-1958) was an American neuroanatomist. Dr. Papez received his MD from the University of Minnesota College of Medicine and Surgery. He is most famous for his 1937 description of the Papez circuit which is a neural pathway in the brain thought to be involved in the cortical control of emotion. He was a neurologist at Cornell University when he published a journal article in which he outlined a "new" circuit to account for emotion. He hypothesized that the hippocampus, the cingulate gyrus (Broca's callosal lobe), the hypothalamus, the anterior thalamic nuclei, and the interconnections among these structures constituted a harmonious mechanism which elaborate the functions of emotions. Papez never mentioned Broca's limbic lobe but others noted that his circuit was very similar to Broca's great limbic lobe.


Lima, D.R.. 2004. History of Medicine, Medsi, RJ.

Reflecting on the earlier work of Cannon, Bard, and others, American neurologist James Papez proposed that there is an 'emotion system,' lying on the medial wall of the brain, that links the cortex with the hypothalamus...Papez believed that the experience of emotion was determined by activity in the cingulate cortex and, less directly, other cortical areas. Emotional expression was thought to be governed by the hypothalamus. The cingulate cortex projects to the hippocampus, and the hippocampus projects to the hypothalamus by way of the bundle of axons called the fornix. Hypothalamic effects reach the cortex via a relay in the anterior thalamic nuclei.

Figure 7.3
Much of what is now known to be the limbic system is called out in the Papez circuit.
Components of the Limbic System:
- Olfactory inputs (Rhinencephalon)
- Amygdala Nuclear Complex
- Hippocampus
- Septal Nuclei
- Hypothalamus
- Mammillary Body
- Thalamus (Anterior and Medial thalamic nuclei)
- Habenular nucleus
- Limbic Cortical structures: Cingulate gyrus, Parahippocampal gyrus, Entorhinal cortex, Insula cortex, Orbital gyrus.

Paul D. MacLean (May 1, 1913 – December 26, 2007) was an American physician and neuroscientist who made significant contributions in the fields of physiology, psychiatry, and brain research through his work at Yale Medical School and the National Institute of Mental Health.

MacLean’s evolutionary triune brain theory proposed that the human brain was in reality three brains in one: the reptilian complex, the limbic system, and the neocortex.
The Reptilian Brain: Core brainstem, predominant genetic determined programmes of prenatal development for the control of reflexes and primitive behaviours, relate to homeostasis and survival.

The Paleomammalian Brain: the limbic system, partially genetic and partially modified by early experience and environmental stimulation during early infancy and childhood, spatial and temporal memory circuits, face recognition, emotional and affectional experience of “Self”. “The Emotional Brain” “The Psycho-sexual Brain” relate to the preservation of “Self” and “Species”. Social and emotional attachment and motivated behaviours.

The Neomammalian Brain: neocortex and neocerebellum, predominant postnatally developed by environmental stimulation, tremendously plastic, for skilled movements, logic thinking, languages and higher brain functions.
The "Nose Brain"
(Rhinencephalon)

1937 Papez's Limbic System
"Emotional Brain"
"Psychosexual Brain"

1952 Paul McLean's
The Triune Brain
Hippocampus is important for storage of declarative memory and there is evidence that neurons in the hippocampus show plastic capability of the sort that required for associative learning.
Excitatory pathways used to study long-term potentiation in hippocampal slices.
The limbic system is also tightly connected to the prefrontal cortex. Some scientists contend that this connection is related to the pleasure obtained from solving problems. To cure severe emotional disorders, this connection was sometimes surgically severed, a procedure of psychosurgery called a prefrontal lobotomy. Patients who underwent this procedure often became passive and lacked all motivation.

There is circumstantial evidence that the limbic system also provides a custodial function for the maintenance of a healthy conscious state of mind.
Table 7.1 Agreement on judgments of emotion in five human cultures

<table>
<thead>
<tr>
<th>Emotion</th>
<th>Hindu</th>
<th>Javan</th>
<th>Korean</th>
<th>Malay</th>
<th>Turkish</th>
<th>Urdu</th>
<th>Vietnamese</th>
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</thead>
<tbody>
<tr>
<td>Happiness</td>
<td>97%</td>
<td>92%</td>
<td>93%</td>
<td>88%</td>
<td>87%</td>
<td>91%</td>
<td>94%</td>
</tr>
<tr>
<td>Sadness</td>
<td>87%</td>
<td>86%</td>
<td>93%</td>
<td>90%</td>
<td>88%</td>
<td>86%</td>
<td>92%</td>
</tr>
<tr>
<td>Surprise</td>
<td>92%</td>
<td>92%</td>
<td>96%</td>
<td>94%</td>
<td>89%</td>
<td>92%</td>
<td>92%</td>
</tr>
<tr>
<td>Anger</td>
<td>82%</td>
<td>86%</td>
<td>93%</td>
<td>98%</td>
<td>94%</td>
<td>93%</td>
<td>93%</td>
</tr>
<tr>
<td>Fear</td>
<td>80%</td>
<td>90%</td>
<td>100%</td>
<td>92%</td>
<td>91%</td>
<td>90%</td>
<td>95%</td>
</tr>
</tbody>
</table>

Figure 7.9 Classical fear conditioning can be designed where the animal is placed in a small box with a grid floor and a light above it. After several pairings of the circuitry are plotted, the animal becomes a conditioned stimulus, and the conditioned response is triggered by the presence of the conditioned stimulus.

Figure 7.10 The direct interconnections between the central nucleus of the amygdala and various hypothalamic and brainstem areas that may be involved in different emotional responses.

Figure 8.10 Some of the pathways involved in fear conditioning include the amygdala, which is involved in the expression of fear. The amygdala is connected to the hypothalamus, which is involved in the autonomic nervous system.

Figure 8.11 Brain imaging studies demonstrate the role of the amygdala in emotional processing. For example:

A. In a series of studies, a cat received a painful stimulus while its amygdala was activated using fMRI. The painful stimulus was presented before the activation and the amygdala was found to be more active during the presentation of the painful stimulus.

B. In another study, a dog received a painful stimulus and its amygdala was activated using fMRI. The painful stimulus was presented before the activation and the amygdala was found to be more active during the presentation of the painful stimulus.

C. In another study, a rat received a painful stimulus and its amygdala was activated using fMRI. The painful stimulus was presented before the activation and the amygdala was found to be more active during the presentation of the painful stimulus.

D. In another study, a monkey received a painful stimulus and its amygdala was activated using fMRI. The painful stimulus was presented before the activation and the amygdala was found to be more active during the presentation of the painful stimulus.

E. In another study, a human received a painful stimulus and its amygdala was activated using fMRI. The painful stimulus was presented before the activation and the amygdala was found to be more active during the presentation of the painful stimulus.

Figure 8.12 The effects of amygdala stimulation on fear and anxiety.

- Fear: Increased amygdala activation leads to increased fear responses.
- Anxiety: Increased amygdala activation leads to increased anxiety responses.

ACTH = adrenocorticotropic hormone; CER = conditioned emotional response; EEG = electroencephalographic; N = nucleus.
The limbic system operates by influencing the **endocrine system** and the **autonomic nervous system**. It is highly interconnected with the **nucleus accumbens**, the brain's **pleasure center**, which plays a role in **sexual arousal** and the "high" derived from certain **recreational drugs**. These responses are heavily modulated by **dopaminergic** projections from the limbic system.

In 1954, **James Olds and Brenda Milner** found that rats with metal **electrodes** implanted into their nucleus accumbens repeatedly pressed a lever activating this region, and did so in preference to eating and drinking, eventually dying of exhaustion.

Behavioural Correlates of Limbic System:

Program of stereotyped behaviours according to instructions based on 'Ancestral' learning experience and memories e.g.
- Establishing territory or Nesting, Defending
- Finding shelter
- Hunting Preys by Predators, eating
- Homing
- Courtships and Mating ... Reproductive Behaviours
- Breeding & Parenting Behaviours
- Social Bonding, Attachments, Imprinting
- Forming Social Organization & Hierarchy, Leadings
- Social Communication
- Fighting, Hostility, Aggression, Violence
- Affection, Love, Altruistic Behaviour etc..

Clinical Correlates of Limbic System:

Amygdala ..., Fear, Anxiety, Aggressive, Violence, Rage
Hippocampus ... Episodic Memories
Cingulate Gyrus ... Instinctive Behaviours, Parenting, Social bonding, Moral reasoning, Delayed alternating tasks
Septal Nucleus ... Docility,
Hypothalamus ......ANS, Endocrine, Drive, Motivation
Mammillary Body ..... Memory retrieval, recall
**Clinical Correlates of Limbic System:**

**Kluver-Bucy Syndrome:**
- Fearlessness, Hyperphagia, Hypersexuality, Psychic Blindness

**Korsakoff’s Psychosis:** Confabulation

**Amnesia:** (Retrograde & Anterograde Amnesia)

**Temporal Lobe Epilepsy:**
- Stress, Post-traumatic Stress Disorders
- Anxiety, Fear & Phobia
- Panic Attacks, Emotional Depression
- Obsessive-Compulsive Disorders
- Abnormal Aggressive & Violence Behaviours
- Paranoid, Delusion, Schizophrenia

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**What is Klüver-Bucy Syndrome?**

Klüver-Bucy syndrome is a rare behavioral impairment that is associated with damage to both of the anterior temporal lobes of the brain. It causes individuals to put objects in their mouths and engage in inappropriate sexual behavior. Other symptoms may include visual agnosia (inability to visually recognize objects), loss of normal fear and anger responses, memory loss, distractibility, seizures, and dementia. The disorder may be associated with herpes encephalitis and trauma, which can result in brain damage in humans.

**Klüver-Bucy syndrome** is a behavioral disorder that occurs when both the right and left medial temporal lobes of the brain malfunction. The amygdala has been a particularly implicated brain region in the pathogenesis of this syndrome. The syndrome is named for Heinrich Klüver and Paul Bucy, who removed the temporal lobe bilaterally in rhesus monkeys in an attempt to determine its function. This caused the monkeys to develop visual agnosia, emotional changes, altered sexual behavior, and oral tendencies. Though the monkeys could see, they were unable to recognize even previously familiar objects, or their use. They would examine their world with their mouths instead of their eyes ("oral tendencies") and developed a desire to explore everything ("hypermetamorphosis"). Their overt sexual behavior increased dramatically ("hypersexualism"), and the monkeys indulged in indiscriminate sexual behavior including masturbation, heterosexual acts and homosexual acts.

Emotionally, the monkeys became dull, and their facial expressions and vocalizations became far less expressive. They were also less fearful of things that would have instinctively panicked them in their natural state, such as humans or snakes. Even after being attacked by a snake, they would willingly approach it again. This aspect of change was termed "Placidity".

**In humans:** (Klüver-Bucy syndrome)

People with lesions in their temporal lobes (a bilateral lesion) show similar behaviors. They may display oral or tactile exploratory behavior, such as inappropriate licking or touching; hypersexuality, bulimia, memory disorders, flattened emotions; and an inability to recognize objects or inability to recognize faces. The full syndrome rarely, if ever, develops in humans. However, parts of it are often noted in patients with extensive bilateral temporal damage caused by herpes or other encephalitis, dementias of degenerative (Alzheimer's disease, Pick's Disease) or post-traumatic etiologies or cerebrovascular disease.
<table>
<thead>
<tr>
<th>Case</th>
<th>Ethelogy</th>
<th>Initial</th>
<th>Duration</th>
<th>Psychiatric</th>
<th>Cognitive</th>
<th>Neurological</th>
<th>Intervention</th>
<th>Clinical outcomes</th>
<th>Follow-up</th>
<th>Comments</th>
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<tbody>
<tr>
<td>1</td>
<td>MCI</td>
<td>PIAF</td>
<td>12 mo</td>
<td>Dysthymia</td>
<td>Depression</td>
<td>Dementia</td>
<td>Drug therapy</td>
<td>Poor Outcome</td>
<td>6 mo</td>
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<tr>
<td>2</td>
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<td>CVD</td>
<td>9 mo</td>
<td>Depression</td>
<td>Dementia</td>
<td>Dementia</td>
<td>Drug therapy</td>
<td>Fair Outcome</td>
<td>9 mo</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>MCI</td>
<td>MCI</td>
<td>6 mo</td>
<td>Depression</td>
<td>Dementia</td>
<td>Dementia</td>
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<td>6 mo</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>AD</td>
<td>AD</td>
<td>18 mo</td>
<td>Depression</td>
<td>Dementia</td>
<td>Dementia</td>
<td>Drug therapy</td>
<td>Fair Outcome</td>
<td>18 mo</td>
<td></td>
</tr>
</tbody>
</table>

Notes: MCI = Mild Cognitive Impairment, CVD = Cardiovascular Disease, AD = Alzheimer's Disease, Dysthymia = Dysthymic Disorder, Drug therapy = Drug treatment, Intervention = Various interventions, Clinical outcomes = Various clinical outcomes.