16th NNAC Luncheon seminar
"Functional anatomy of the limbic system"

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What is the limbic system?

The limbic system is a group of structures in the brain that are involved in emotions, motivation, and memory. It is located in the center of the brain and is made up of several interconnected regions, including the amygdala, hippocampus, hypothalamus, thalamus, cingulate gyrus and nucleus accumbens(1–5).

The limbic system described for the first time by Thomas Willis (1664) to indicate cortical regions located around the brainstem. (Fig.1)

The amygdala is responsible for processing emotions, particularly fear and aggression. The hippocampus is involved in the formation and retrieval of memories, especially in the consolidation of short-term memory to long-term memory. The hypothalamus plays a key role in regulating basic survival functions, such as hunger, thirst, and sleep, as well as controlling the release of hormones from the pituitary gland. The thalamus acts as a relay station for sensory information, while the cingulate gyrus is involved in processing emotions and cognitive functions.

Together, these structures work to regulate our emotional responses to external stimuli, form and retrieve memories, and regulate basic physiological functions. Dysfunction in the limbic system can lead to a range of psychiatric and neurological disorders, including anxiety, depression, post-traumatic stress disorder (PTSD), and Alzheimer's disease.

History of anatomical study of limbic system.

The limbic system is a group of interconnected cortical and subcortical structures dedicated to linking visceral states and emotion to cognition and behaviour (Mesulam, 2000). The use of the term 'limbic' has changed over time. Initially introduced by Thomas Willis (1664) to designate a cortical border encircling the brainstem (limbus, Latin for 'border') (Fig. 1)

The term has been used in more recent times to indicate a progressively increasing number of regions dedicated to a wide range of functions (Marshall and Magoun, 1998; Mega et al., 1997). Paul Broca (1878) held the view that 'le grand lobe limbique' was mainly an olfactory structure common to all mammalian brains, although he argued that its functions were not limited to olfaction (Fig. 2). After Broca's publication the accumulation of experimental evidence from ablation studies in animals broadened the role of the limbic structures to include other aspects of behaviour such as controlling social interactions and behaviour (Brown and Schäfer, 1888)(6), consolidating memories (Bechterew, 1900)(7), and forming emotions (Cannon, 1927)(8). Anatomical and physiological advancements in the field led Christfield Jakob (1906) (Fig. 3) and James Papez (1937) (Fig. 4) to formulate the first unified network model for linking action and perception to emotion.(5)

What is the amygdala?

The amygdala is a small but important structure in the brain that is responsible for processing and regulating emotions. It is involved in the formation and consolidation of emotional memories, as well as the detection and response to potential threats in the environment.(9)
The amygdala is composed of several subnuclei, each with distinct functions. The basolateral complex, which includes the lateral, basal, and accessory basal nuclei, is involved in the processing and storage of emotional memories. The central nucleus is responsible for the expression of emotional responses, such as fear or aggression.
The amygdala is connected to other parts of the brain involved in emotional and cognitive processing, including the prefrontal cortex, hippocampus, and thalamus. These connections allow the amygdala to receive input from and modulate the activity of other brain regions involved in emotion regulation and decision making.
Dysfunction or damage to the amygdala can lead to a variety of emotional and cognitive disorders. For example, an overactive amygdala has been implicated in anxiety disorders such as generalized anxiety disorder (GAD) and post-traumatic stress disorder (PTSD). In contrast, a damaged or dysfunctional amygdala can lead to difficulties in processing emotional information and recognizing social cues, which are characteristics of certain psychiatric disorders such as autism spectrum disorder (ASD).
Overall, the amygdala plays a critical role in emotional processing and regulation, and understanding its functions is important for understanding a range of psychological and psychiatric disorders.

What is the hippocampus?

The hippocampus is a key structure in the brain that is essential for learning and memory processes. It is located in the medial temporal lobe of the brain, adjacent to the amygdala and the entorhinal cortex.(10–12) (Fig.6,7,8)
The hippocampus is made up of several subregions, including the dentate gyrus, the CA1, CA2, and CA3 regions, and the subiculum. Each of these subregions plays a unique role in the

hippocampal network.
The hippocampus is primarily known for its role in the formation and retrieval of new declarative memories, which are memories of facts and events that can be consciously recalled. The hippocampus is also involved in spatial memory, which is the ability to remember one's environment and navigate through it.
The hippocampus is also thought to play a role in emotional processing and regulation, as it is connected to the amygdala, which is involved in the processing of emotions such as fear and anxiety.
Finally, the hippocampus is vulnerable to damage and dysfunction in a number of neurological and psychiatric disorders, including Alzheimer's disease, epilepsy, depression, and schizophrenia.

What is the hypothalamus?

The hypothalamus is a small, but very important part of the brain that is located at the base of the brain, just above the brainstem. It plays a crucial role in regulating many of the body's essential functions, including:

1. Temperature control: The hypothalamus helps regulate body temperature by controlling blood flow to the skin and by regulating the activity of sweat glands.

2. Hunger and thirst: The hypothalamus regulates feelings of hunger and thirst, and helps to control the body's intake of food and water.

3. Sleep and wakefulness: The hypothalamus helps to regulate the sleep-wake cycle, by controlling the release of hormones like melatonin.

4. Hormone regulation: The hypothalamus plays a key role in regulating the release of many hormones from the pituitary gland, which helps to control various bodily functions like growth, metabolism, and reproduction.

5. Emotional response: The hypothalamus is also involved in regulating emotional responses, such as fear and aggression.

As a neurosurgeon, you may encounter patients with tumors or other conditions that affect the hypothalamus. Surgical interventions in this area can be very delicate due to the hypothalamus's close proximity to other vital brain structures. Therefore, it is important to have a thorough understanding of the hypothalamus's anatomy and functions in order to safely and effectively treat these conditions.(13,14)

What is the cingulate gyrus?

The cingulate gyrus is a structure in the brain that is part of the limbic system. It is located in the cerebral cortex, above the corpus callosum, and extends from the frontal lobe to the parietal lobe. The cingulate gyrus is divided into four distinct regions: the anterior cingulate cortex, the posterior cingulate cortex, the retrosplenial cortex, and the subgenual cortex.
The anterior cingulate cortex (ACC) is involved in a wide range of functions, including emotional regulation, decision making, and attentional control. It is also involved in pain perception and the modulation of autonomic responses, such as heart rate and blood pressure. Dysfunction in the ACC has been implicated in a number of psychiatric and neurological disorders, including depression, anxiety, and obsessive-compulsive disorder.
The posterior cingulate cortex (PCC) is involved in several cognitive processes, including memory retrieval, spatial orientation, and self-referential processing. It is also involved in the default mode network, which is a network of brain regions that are active during rest and mind-wandering. Dysfunction in the PCC has been linked to Alzheimer's disease and other forms of dementia. The retrosplenial cortex is involved in the integration of spatial information and the formation of spatial memory. It is also involved in the processing of visual and auditory stimuli, and dysfunction in this region has been linked to schizophrenia and other psychotic disorders. The subgenual cortex is involved in emotional processing and regulation and has been implicated in depression and other mood disorders.
Overall, the cingulate gyrus plays a critical role in a wide range of cognitive, emotional, and autonomic functions. Dysfunction in any of its subregions can have significant implications for both physical and mental health.(1,15)

What is the nucleus accumbens?

The nucleus accumbens is a small region located deep within the brain, specifically in the basal ganglia, that plays an important role in the brain's reward system. (Fig.7)
It is involved in the processing of rewarding and pleasurable experiences, such as food, sex, and drugs of abuse, as well as in the regulation of motivation, reinforcement, and addiction.(16–18)
The nucleus accumbens receives inputs from several brain regions, including the prefrontal cortex, hippocampus, and amygdala, and sends outputs to other brain areas, such as the ventral pallidum and the prefrontal cortex. It is also rich in dopamine and other neurotransmitters that modulate its activity.
Abnormalities in the nucleus accumbens have been implicated in a variety of neuropsychiatric disorders, such as addiction, depression, schizophrenia, and Parkinson's disease. Therefore, understanding the functions and dysfunctions of the nucleus accumbens is crucial for the development of effective treatments for these conditions.

Summary:
Understanding the function of the limbic system is important because it is involved in many important physiological and psychological processes that can impact patient health and wellbeing. The limbic system is responsible for regulating emotions and behaviors, and is involved in the formation and retrieval of memories. It also plays a role in the autonomic nervous system, which controls bodily functions such as heart rate, blood pressure, and breathing.
Disruptions in the limbic system can lead to various psychiatric and neurological disorders, such as anxiety disorders, depression, post-traumatic stress disorder, epilepsy, and addiction. For example, abnormalities in the amygdala can result in anxiety disorders, while damage to the hippocampus can lead to memory impairments.
In clinical practice, medical doctors may use various techniques to assess the function of the limbic system, such as neuroimaging, neuropsychological tests, and clinical interviews. Treatment for limbic system disorders may involve medication, psychotherapy, or other interventions depending on the specific condition.
Overall, a solid understanding of the limbic system's function is essential for medical doctors to diagnose and manage various neurological and psychiatric disorders that affect patients.

Disclosure of Conflict of Interest:
The author has disclosed no potential conflict of interest.

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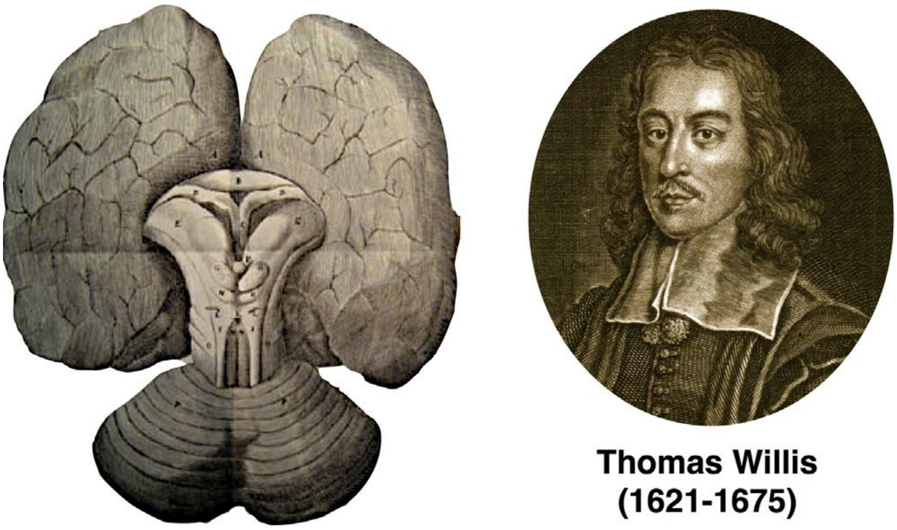


Figure 1. The limbic system described for the first time by Thomas Willis (1664) to indicate cortical regions located around the brainstem.

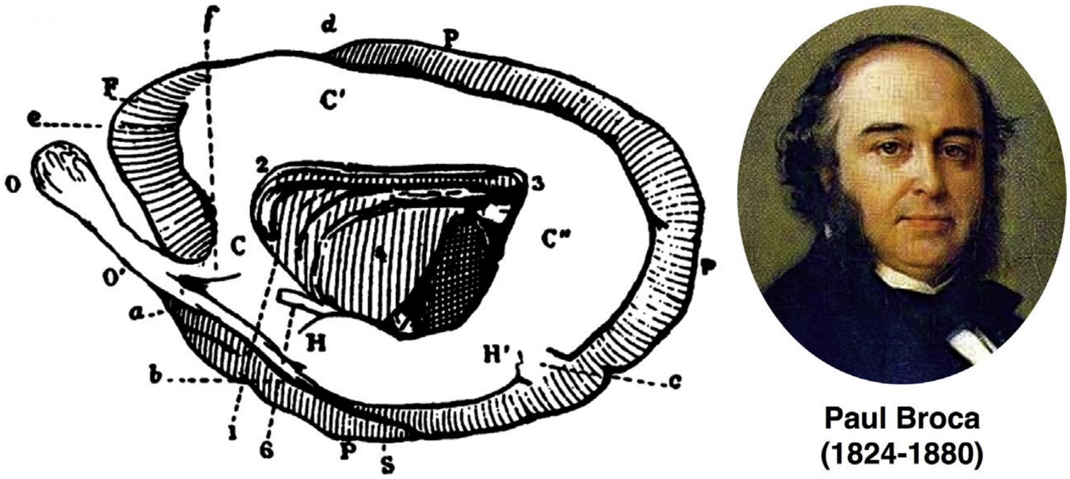
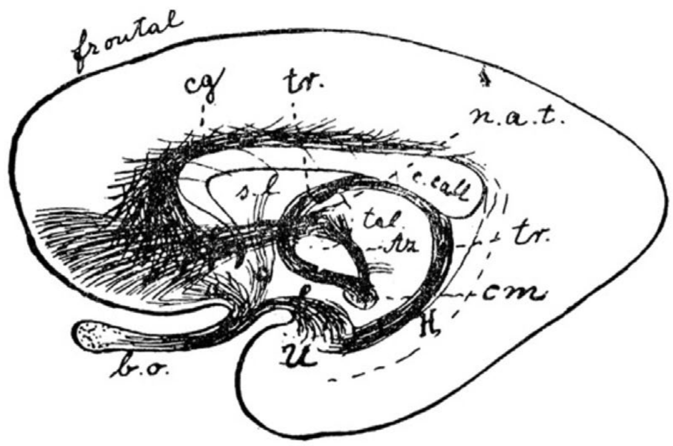
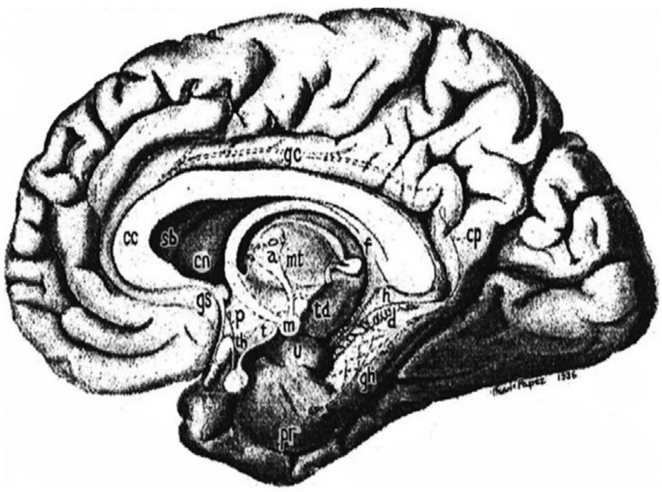


Figure 2. Paul Broca (1878) identified the limbic system as mainly an olfactory structure of the mammalian brain.



Christfried Jakob
(1866-1956)

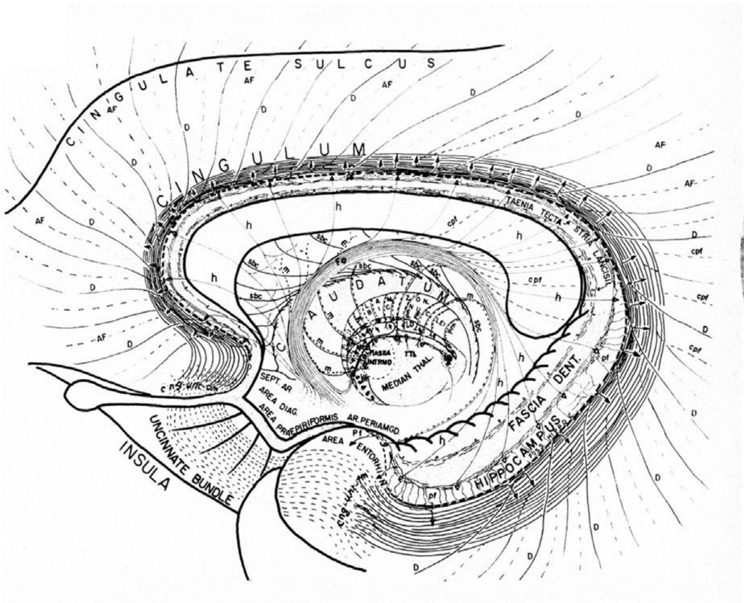
Figure 3: The limbic system as an integrated system of cortical and subcortical structures linked by projection and association tracts wasd escribed for the first time by Christfried Jakob in 1906. Cg, cingulum; Tr, trigonum; C. Call, corpus callosum; N.A.T., anterior thalamic nuclei; Tal., thalamus; Az, bundle of Vicq d’Azyr; CM, mammillary bodies; H, hippocampus; U, uncus; Bo, olfactory bulb; SL, Septum pellucidum.

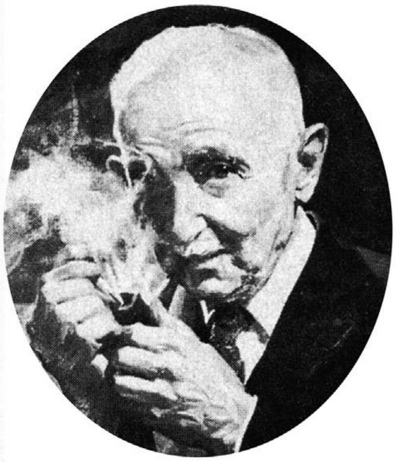


James Papez
(1883-1958)

Figure 4: The limbic system according to James Papez (Papez, 1937) is an exact duplicate of Jakob’s original drawing. Papez never quoted the work of Jakob and it is possible that he didn’t know about his work, which was published in an Argentinean journal with scarce international diffusion (La Semana Médica). Nevertheless the similarities between the two

models are striking. To give credit to the work of Jakob we suggest the use of the eponym Jakob-Papez circuit. a, anterior nucleus; cc, corpus callosum; cn, caudate nucleus; cp, cingulum posterior; d, gyrus dentatus; f, fornix; gc, gyrus cinguli; gh, gyrus hippocampi; gs, gyrus subcallosus; h, hippocampus; m, mammillary body; mt, mammillo-thalamic tract; p, pars optica hypothalami; pr, piriform area; sb, subcallosal bundle; t, tuber cinereum; td, tractus mammillo-tegmentalis; th, tractus hypophyseus; u, uncus.





Paul Ivan Yakovlev
(1894-1983)

Figure 5: Yakovlev’s amygdala-orbitofrontal network (Yakovlev and Locke, 1961; Yakovlev, 1948). AF, supralimbic corticocortical afferents to the limbic cortex; AM, anterior medial nucleus of the limbic thalamus; Area diag., area diagonalis (Filimonov); Area periamgd., area periamygdalaris (Filimonov); Area entorhin., area entorhinalis; AV, anterior ventral nucleus of the limbic thalamus; cng-unc-om, orbitomesial interdigitation of the cingulum and uncinate bundle; cng-unc-tm, temporomesial interdigitation of the cingulum and uncinate bundle; cpf, callosoperforant fibres from the supralimbic cortex; Fascia Dent., fascia dentate of the Ammon’s horn; Fis. Hippoc., parahippocampal fissure; h, hippocampal efferents via fornix brevis; Hb, habenular nuclei; Lam. Zon., lamina zonalis; LD, lateral dorsal nucleus of the limbic thalamus; m, afferent and efferent fibres of the median thalamus (midline nuclei); Massa intrmd., massa intermedia; Pf, corticoperforant temporoammonic fibres (direct and crossed); pf, corticoperforant (direct and crossed) fibres of the cingulum to the hippocampus; pm, afferent and efferent fibres of the paramedianthalamus (limbic nuclei); sbc, subcallosal radiations (lateral, ventral and medial) of the cingulum to the septum and ipsi- and contra-lateral striatum and limbic thalamus; Sept. Ar., septal area; T.TH., taenia thalami; VA, ventral anterior nucleus of the limbic thalamus.

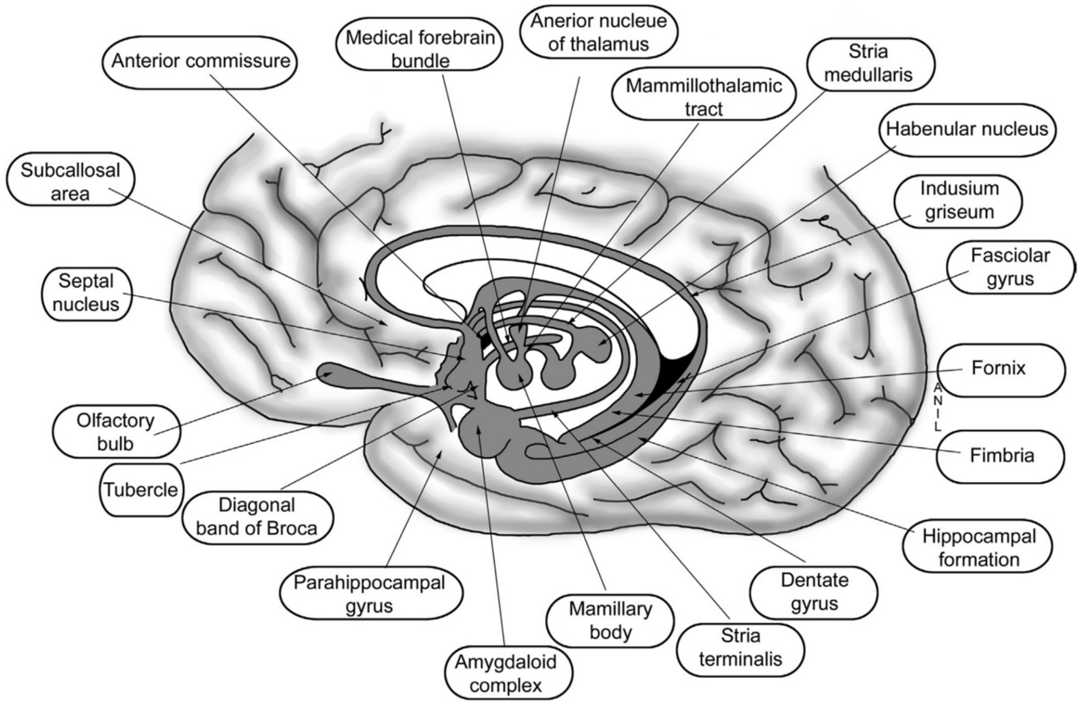


Figure 6.

The limbic system includes the olfactory bulbs, hippocampus, amygdala, anterior thalamic nuclei, fornix, and column of fornix, mammillary body, septum pellucidum, habenular commissure, cingulate gyrus, parahippocampal gyrus, limbic cortex, limbic midbrain areas, and pons.

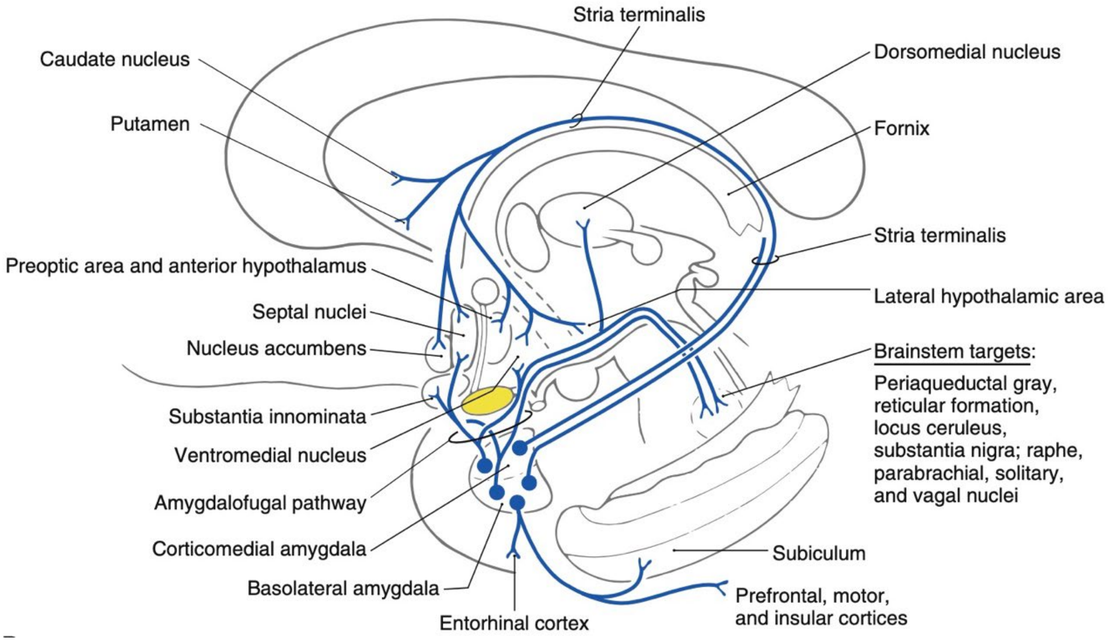


Figure 7: Semidiagrammatic representation of the afferent (A) and efferent (B) connections of the amygdaloid complex. (Willis MA, et al. The Limbic System. In: Haines DE, Mihailoff GA, editors. Fundamental Neuroscience for Basic and Clinical Applications (Fifth Edition). Elsevier; 2018. page 457–67.e1.)

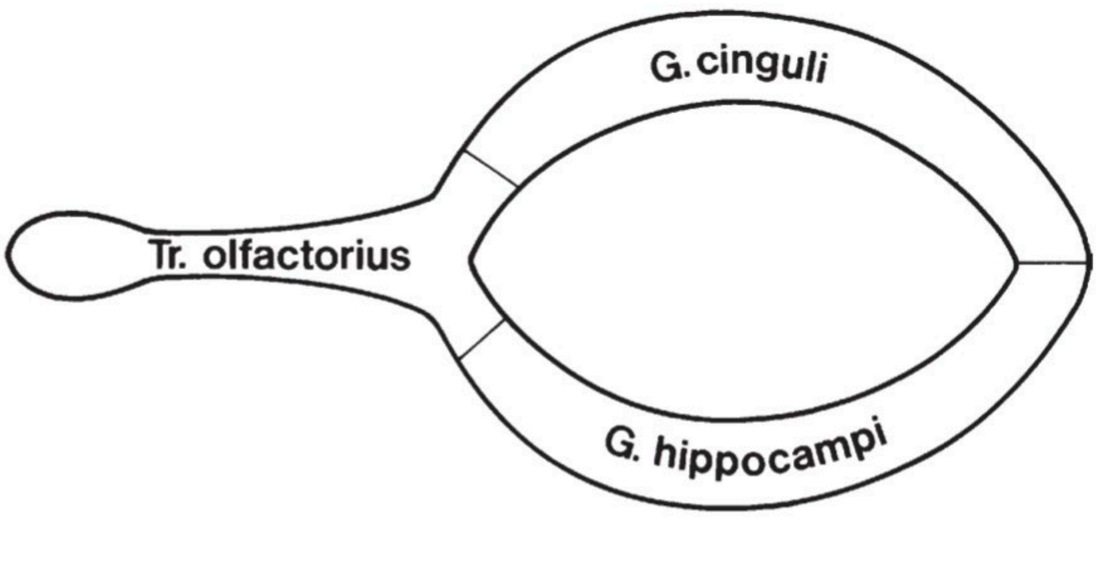


Figure 8. The C-shaped topography of the cingulate gyrus and hippocampal region (gyrus fornicatus) is completed by Broca with olfactory tract and bulb, together forming the racket-shaped limbic lobe