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

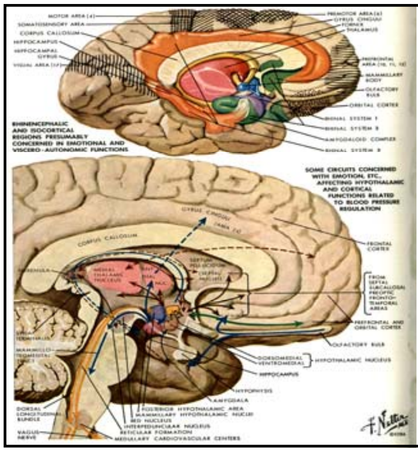
Naiphinich Kotchabhakdi Ph.D.

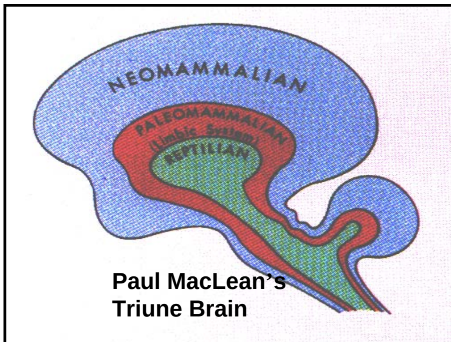
Neuro-Behavioural Biology Center,
Institute of Science and Technology for Research and Development,
Mahidol University, Salaya, Nakornpathom 73170 Thailand
Email: scnkc@mahidol.ac.th
Website: http://neuroscience.mahidol.ac.th

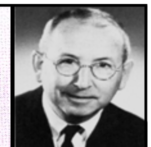
The **limbic system** is a term for a set of brain structures including the hippocampus and amygdala and anterior thalamic nuclei and a limbic cortex that support a variety of functions including emotion, behavior and long term memory.

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

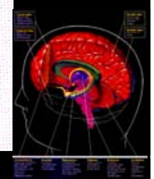
The term **"limbic"** comes from Latin ***limbus***, meaning "border" or "belt".



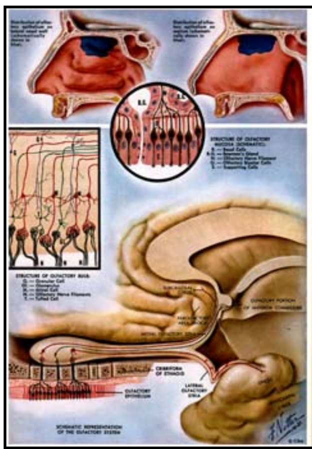




Paul MacLean M.D.



The Reptilian Brain : Core brainstem
The Paleomammalian Brain : the limbic system
The Neomammalian Brain : neocortex and neocerebellum



The "Nose Brain"

(Rhinencephalon)

1937 Papez 's Limbic System

"Emotional Brain"

"Psychosexual Brain"

1952 Paul McLean's The Triune Brain

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.

Broca, P. Anatomie comparée des circonvolutions cérébrales: le grand lobe limbique. *Rev. Anthropol.* 1878;1:385–498.
Papez JW. A proposed mechanism of emotion. 1937. *J Neuropsychiatry Clin Neurosci.* 1995;7(1):103-12.
P. D. Maclean (1952). "Some psychiatric implications of physiological studies on frontotemporal portion of limbic system (visceral brain)". 4 (4): 407–418.

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.

Papez JW. 1937. A proposed mechanism of emotion. 1937. J Neuropsychiatry Clin Neurosci. 1995 Winter;7(1):103-12.
Lima, D.R.,2004. History of Medicine, Medsi, RJ.

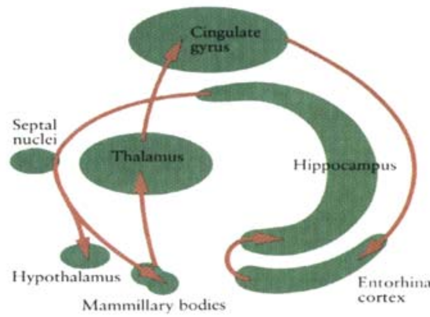
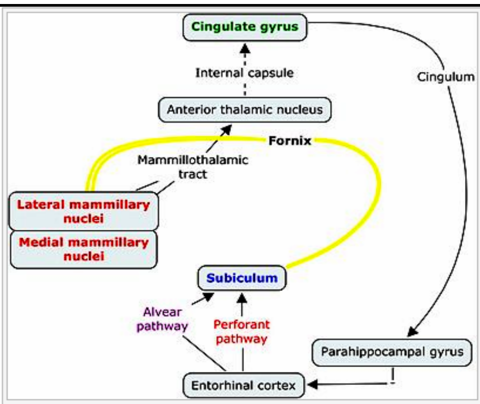


Figure 7.3
Much of what is now known to be the limbic system is called out in the Papez circuit.



Papez Circuit

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

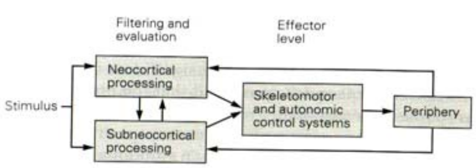


Figure 50-1 Model of the basic neural systems that control emotions. Emotions are typically elicited by a specific stimulus. The stimulus affects both neocortical and subcortical structures, such the amygdala. In turn, cortical structures and the amygdala and other subcortical structures regulate the systems that mediate the peripheral manifestations of emotional behaviors. The particular emotion experienced is a function of cross-talk between neocortical and subcortical structures, as well as feedback from peripheral receptors.

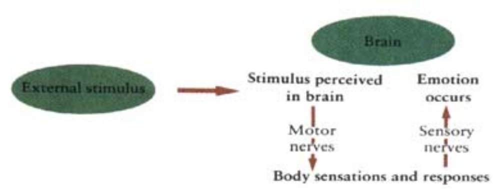


Figure 7.1
The James-Lange theory of emotion holds that the psychological experience of emotion follows the perception of one's own physiological reactions.

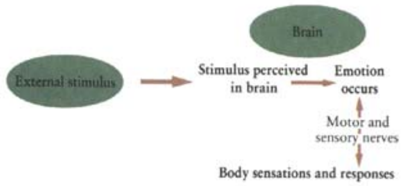


Figure 7.2
The Cannon-Bard theory, in contrast to the James-Lange theory, says that the psychological experience of emotion and the physiological reactions are simultaneous.

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 cortx, Insular cortex, orbital gyrus.

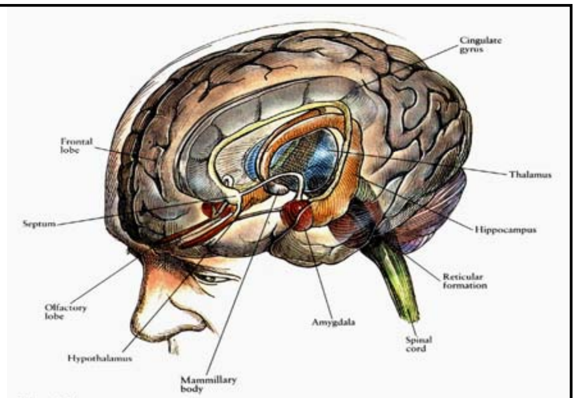
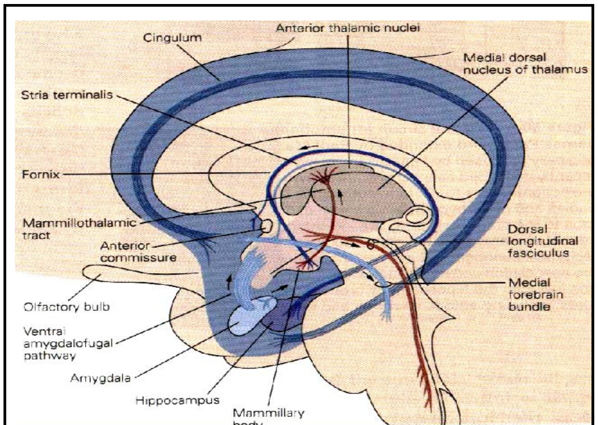
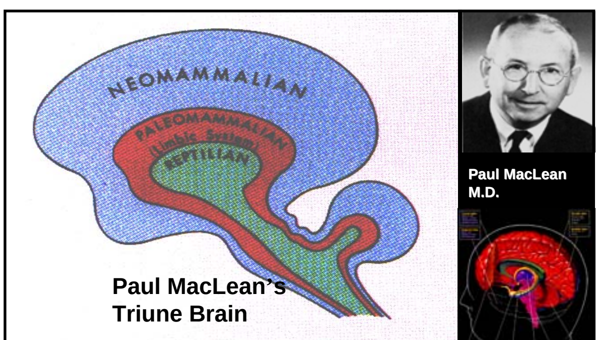


Figure 7.4
The major brain structures forming the limbic system. From this view, their locations around the border, or limbus, of the brain can be appreciated.





The Reptilian Brain : Core brainstem
The Paleomammalian Brain : the limbic system
The Neomammalian Brain : neocortex and neocerebellum

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.

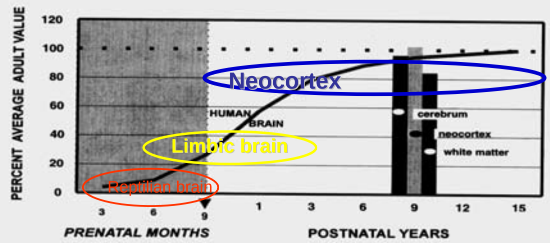
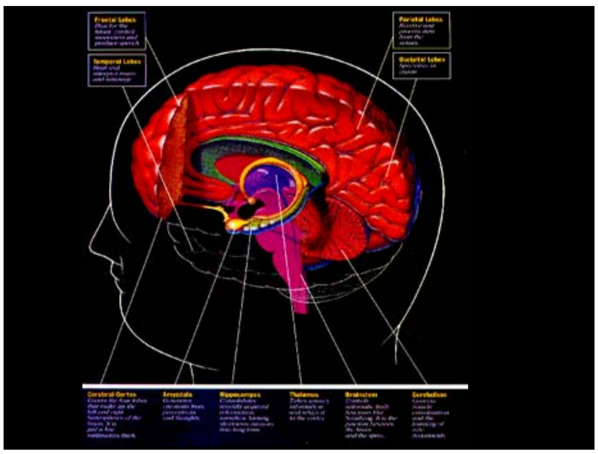


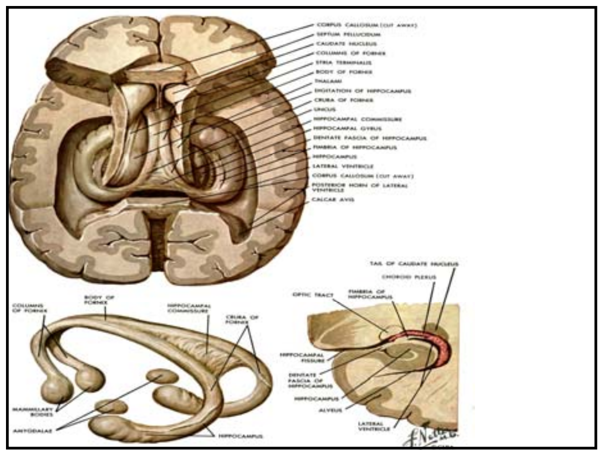
Figure 1 Brain growth. The growth of the human brain is presented from two perspectives. For both perspectives brain weight or volume is expressed as a percentage of the mean adult volume or weight (ordinate: 1 g = 1 centimeter^3), where 100 corresponds to the mean adult value. Age (abscissa) is expressed in months for fetal life and in years for postnatal life. (1) Curve: The first perspective is that of the full profile of brain growth, based upon brain weights obtained postmortem. This is expressed as a continuous change with growth continuing through the fetal months and the first 15 years of postnatal life (adapted from Lamire *et al.*, 1975). (2) Histograms: The second perspective is based upon volumetric analyses of magnetic resonance images. This perspective is the size of the cerebrum, the neocortex, and the cerebral central white matter taken from a cross-sectional analysis in the school age child. We have taken the mean volume for the full series where values for males and females were averaged (n = 30, including 15 male and 15 female brains) over an age range of 6–11 years, mean age 9 years, and have placed the histograms for the mean volumes at the mean age. At school age the overall cycle of growth is approximately completed (histogram in relation to curve; histograms adapted from Caviness *et al.*, 1996). Cerebral volume of the school age child, mean age 9 years, is scaled to overall brain size. That is, cerebral volume at school age,

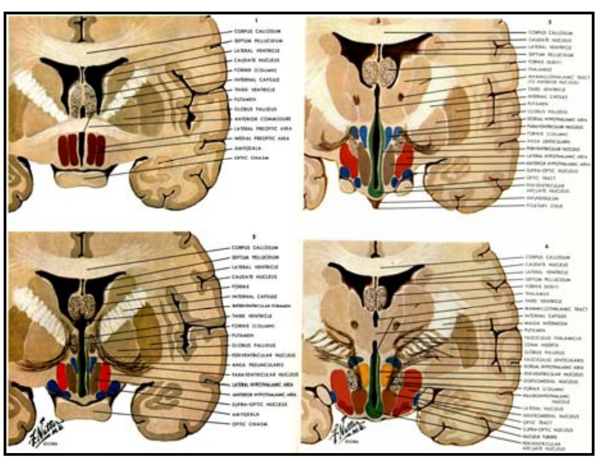
The Reptilian Brain : Core brainstem, predominant genetic determined programmes of prenatal development, for the control of reflexes and primitive behaviours, relate to homeostasis and survival.

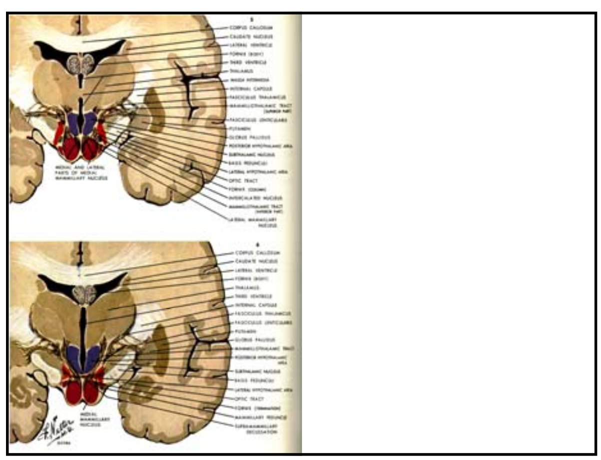
The Paleomammalian Brain : the limbic system, partially genetic and partially modified by early experience and environmental stimulation during early infancy and childhood, spatial and temporal memory circuits, face-recognition, emotional and affectional experience of "Self" . "The Emotional Brain."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

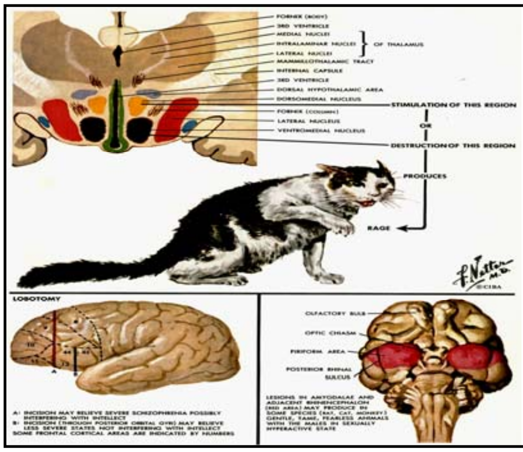
The Neomammalian Brain : neocortex and neocerebellum. predominant postnatally developed by environmental stimulation, tremendously plastic, for skilled movements, logic thinking, languages and higher brain functions.











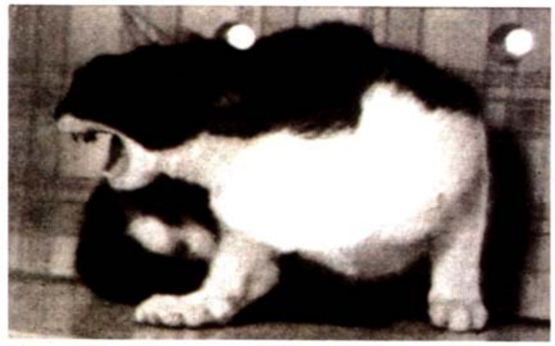
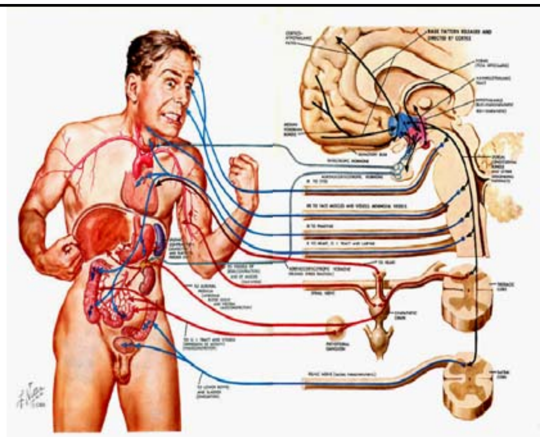
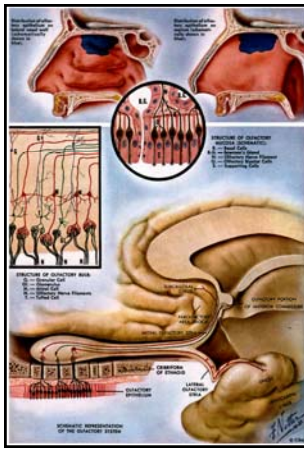


Figure 7.6
With an electrode implanted in one area of its hypothalamus, this cat postures aggressively when electrical stimulation is applied (Hess, 1957).





The "Nose Brain"

(Rhinencephalon)

1937 Papez 's Limbic System

"Emotional Brain"

"Psychosexual Brain"

1952 Paul McLean's The Triune Brain

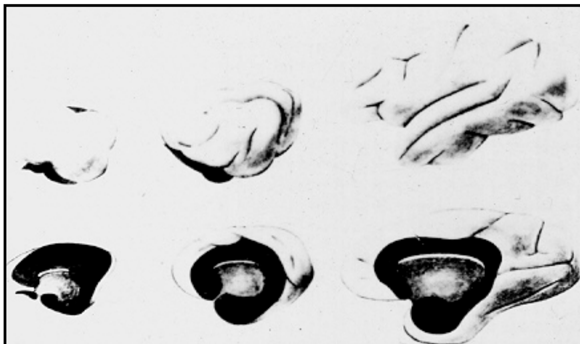


FIGURE 3 Lateral and medial views of brains of rabbit, cat, and monkey drawn roughly to scale. This Figure illustrates that the limbic lobe (dark shading in medial view) is found as a common denominator of the cerebrum throughout the mammalian series. Surrounding the brainstem, the limbic lobe contains most of the cortex corresponding to that of the paleomammalian brain. The greater part of the neocortex, which mushrooms late in evolution, occupies the lateral surface. (After MacLean, 1954b.)

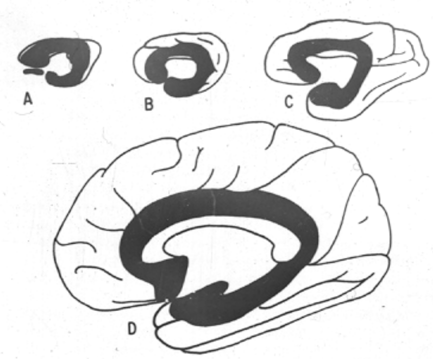
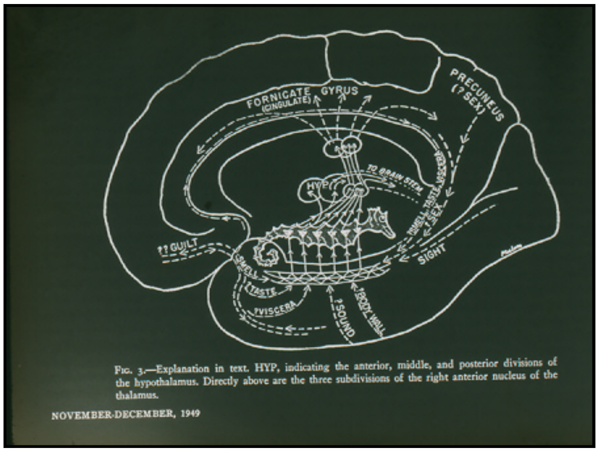
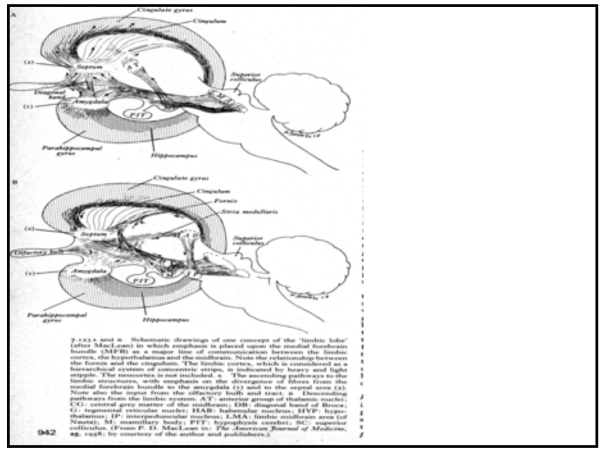
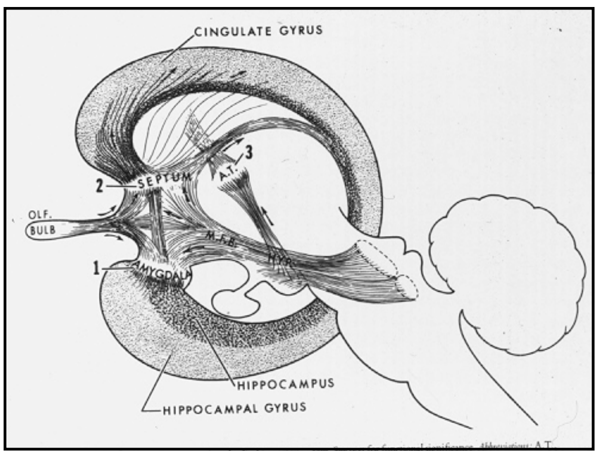
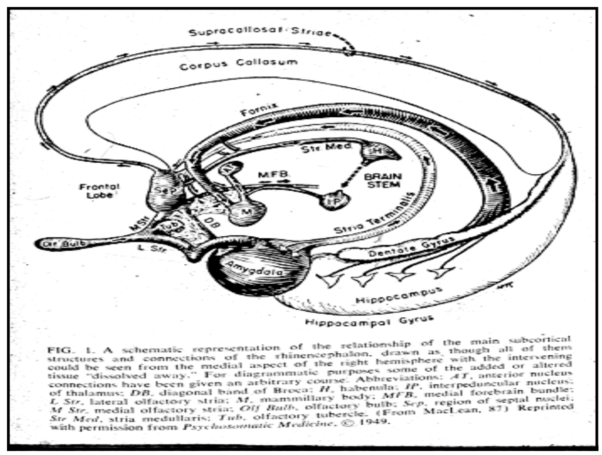


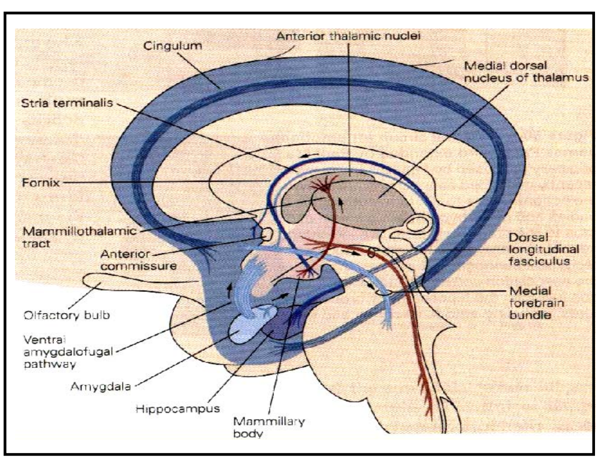
Figure 16.2. The limbic lobe of the brain of the rabbit A; cat B; monkey C; and man D, shown in black. The lobe is seen as a "common denominator" of the medial cortex of the cerebrum. Approximately to scale. (From Russell, 1961, modified from MacLean, 1954)

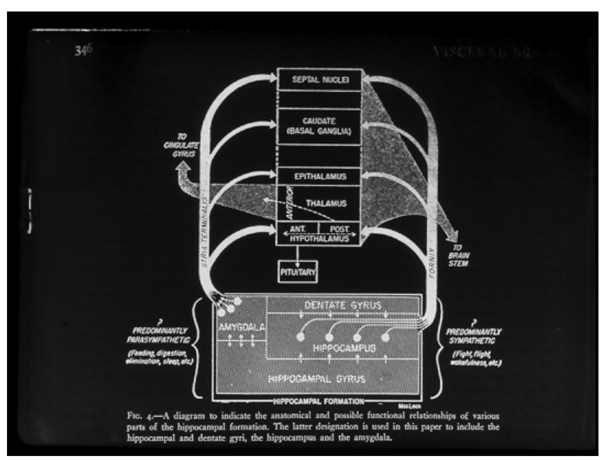

FORNICATE GYRUS
(CINGULATE)
PRECUNEUS
(?SEX)
HYP
TO BRAIN STEM
??GUILT
SMELL
?TASTE
?VISCERA
?SOUND
?BODY WALL
SIGHT
FIG. 3.—Explanation in text. HYP, indicating the anterior, middle, and posterior divisions of the hypothalamus. Directly above are the three subdivisions of the right anterior nucleus of the thalamus.
NOVEMBER-DECEMBER, 1949


Cingulate gyrus
Cingulum
Septum
Amygdala
PIT
Parahippocampal gyrus
Hippocampus
Fornix
Stria medullaris
Superior colliculus
Olfactory bulb
7.12) A and B Schematic drawings of one concept of the 'limbic lobe' (after MacLean) in which emphasis is placed upon the medial forebrain bundle (MFB) as a major line of communication between the limbic cortex, the hypothalamus and the midbrain. Note the relationship between the fornix and the cingulum. The limbic cortex, which is considered as a hierarchical system of concentric strips, is indicated by heavy and light stipple. The neocortex is not included. A The ascending pathways to the limbic structures, with emphasis on the divergence of fibres from the medial forebrain bundle to the amygdala (1) and to the septal area (2). Note also the input from the olfactory bulb and tract. B Descending pathways from the limbic system. AT: anterior group of thalamic nuclei; CG: central grey matter of the midbrain; DB: diagonal band of Broca; G: tegmental reticular nuclei; HAB: habenular nucleus; HYP: hypothalamus; IP: interpeduncular nucleus; LMA: limbic midbrain area (of Nauta); M: mamillary body; PIT: hypophysis cerebri; SC: superior colliculus. (From P. D. MacLean in: The American Journal of Medicine, 25, 1958; by courtesy of the author and publishers.)
942


CINGULATE GYRUS
2
SEPTUM
A.T.
3
OLF.
BULB
1
AMYGDALA
M.F.B.
HYP.
HIPPOCAMPUS
HIPPOCAMPAL GYRUS


Supracallosal Striae
Corpus Callosum
Fornix
Str Med
H
MFB
BRAIN STEM
Frontal Lobe
Sep
IP
M
DB
Tub
M Str
L Str
Olf Bulb
Stria Terminalis
Dentate Gyrus
Amygdala
Hippocampus
Hippocampal Gyrus
FIG. 1. A schematic representation of the relationship of the main subcortical structures and connections of the rhinencephalon, drawn as though all of them could be seen from the medial aspect of the right hemisphere with the intervening tissue "dissolved away." For diagrammatic purposes some of the added or altered connections have been given an arbitrary course. Abbreviations: AT, anterior nucleus of thalamus; DB, diagonal band of Broca; H, habenula; IP, interpeduncular nucleus; L Str, lateral olfactory stria; M, mammillary body; MFB, medial forebrain bundle; M Str, medial olfactory stria; Olf Bulb, olfactory bulb; Sep, region of septal nuclei; Str Med, stria medullaris; Tub, olfactory tubercle. (From MacLean, 87) Reprinted with permission from Psychosomatic Medicine. © 1949.


Anterior thalamic nuclei
Cingulum
Medial dorsal nucleus of thalamus
Stria terminalis
Fornix
Mammillothalamic tract
Anterior commissure
Dorsal longitudinal fasciculus
Medial forebrain bundle
Olfactory bulb
Ventral amygdalofugal pathway
Amygdala
Hippocampus
Mammillary body


346
SEPTAL NUCLEI
CAUDATE (BASAL GANGLIA)
TO CINGULATE GYRUS
EPITHALAMUS
THALAMUS
ANTERIOR
ANT.
POST.
HYPOTHALAMUS
PITUITARY
STRIA TERMINALIS
FORNIX
TO BRAIN STEM
DENTATE GYRUS
AMYGDALA
HIPPOCAMPUS
HIPPOCAMPAL GYRUS
HIPPOCAMPAL FORMATION
? PREDOMINANTLY PARASYMPATHETIC
(Feeding, digestion, elimination, sleep, etc.)
? PREDOMINANTLY SYMPATHETIC
(Fight, flight, wakefulness, etc.)
FIG. 4.—A diagram to indicate the anatomical and possible functional relationships of various parts of the hippocampal formation. The latter designation is used in this paper to include the hippocampal and dentate gyri, the hippocampus and the amygdala.

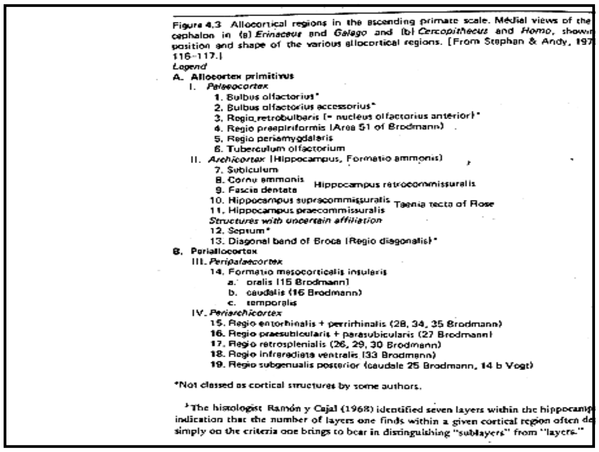


Figure 4.3 Allocortical regions in the ascending primate scale. Medial views of the cephalon in (a) *Erinaceus* and *Galago* and (b) *Cercopithecus* and *Homo*, showin position and shape of the various allocortical regions. [From Stephan & Andy, 197 116–117.]

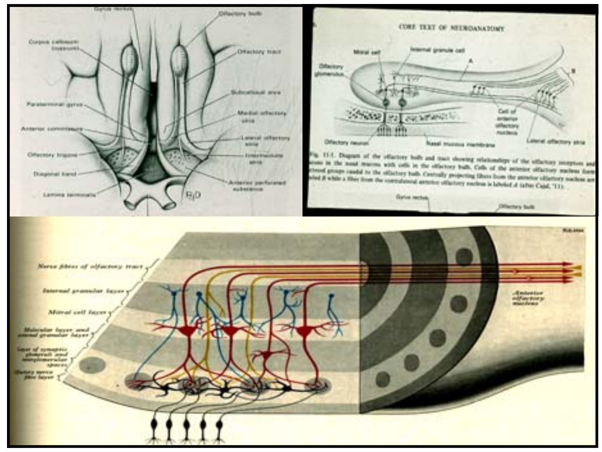
Legend

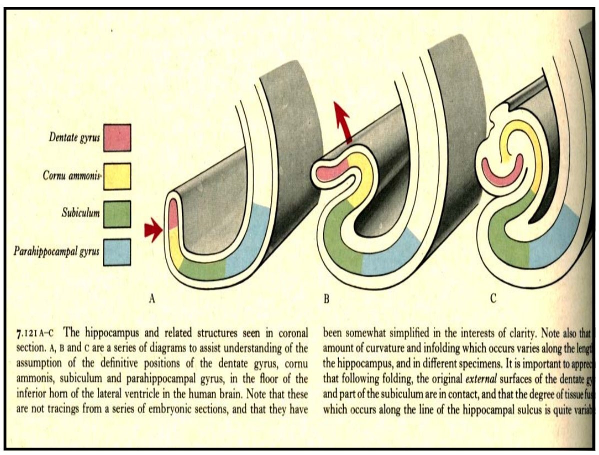
A. Allocortex primitivus
  I. *Palaeocortex*
    1. Bulbus olfactorius*
    2. Bulbus olfactorius accessorius*
    3. Regio retrobulbaris (= nucleus olfactorius anterior)*
    4. Regio praepiriformis (Area 51 of Brodmann)
    5. Regio periamygdalaris
    6. Tuberculum olfactorium
  II. *Archicortex* (Hippocampus, Formatio ammonis)
    7. Subiculum
    8. Cornu ammonis
    9. Fascia dentata
    (8–9: Hippocampus retrocommissuralis)
    10. Hippocampus supracommissuralis
    11. Hippocampus praecommissuralis
    (10–11: Taenia tecta of Rose)
    Structures with uncertain affiliation
    12. Septum*
    13. Diagonal band of Broca (Regio diagonalis)*

B. Periallocortex
  III. *Peripalaeocortex*
    14. Formatio mesocorticalis insularis
      a. oralis (15 Brodmann)
      b. caudalis (16 Brodmann)
      c. temporalis
  IV. *Periarchicortex*
    15. Regio entorhinalis + perrirhinalis (28, 34, 35 Brodmann)
    16. Regio praesubicularis + parasubicularis (27 Brodmann)
    17. Regio retrosplenialis (26, 29, 30 Brodmann)
    18. Regio infraradiata ventralis (33 Brodmann)
    19. Regio subgenualis posterior (caudale 25 Brodmann, 14 b Vogt)

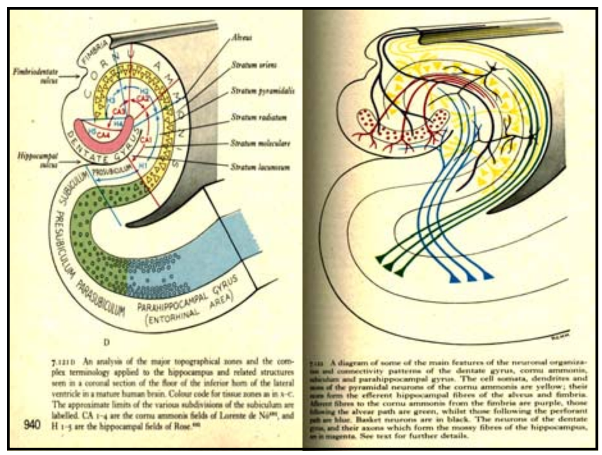
*Not classed as cortical structures by some authors.

[3] The histologist Ramón y Cajal (1968) identified seven layers within the hippocamp indication that the number of layers one finds within a given cortical region often de simply on the criteria one brings to bear in distinguishing "sublayers" from "layers."





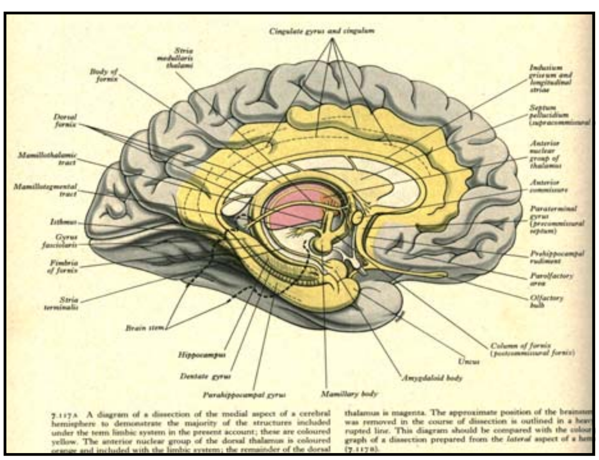
7.121 A–C The hippocampus and related structures seen in coronal section. A, B and C are a series of diagrams to assist understanding of the assumption of the definitive positions of the dentate gyrus, cornu ammonis, subiculum and parahippocampal gyrus, in the floor of the inferior horn of the lateral ventricle in the human brain. Note that these are not tracings from a series of embryonic sections, and that they have been somewhat simplified in the interests of clarity. Note also that amount of curvature and infolding which occurs varies along the lengt the hippocampus, and in different specimens. It is important to apprec that following folding, the original *external* surfaces of the dentate gy and part of the subiculum are in contact, and that the degree of tissue fus which occurs along the line of the hippocampal sulcus is quite variab



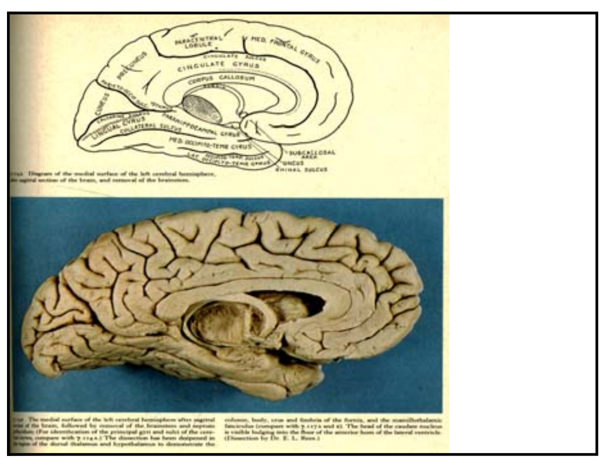
7.121 D An analysis of the major topographical zones and the complex terminology applied to the hippocampus and related structures seen in a coronal section of the floor of the inferior horn of the lateral ventricle in a mature human brain. Colour code for tissue zones as in A–C. The approximate limits of the various subdivisions of the subiculum are labelled. CA 1–4 are the cornu ammonis fields of Lorente de Nó, and H 1–5 are the hippocampal fields of Rose.

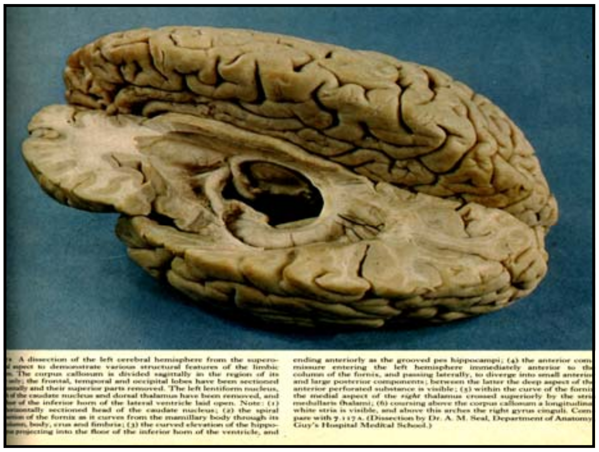
940

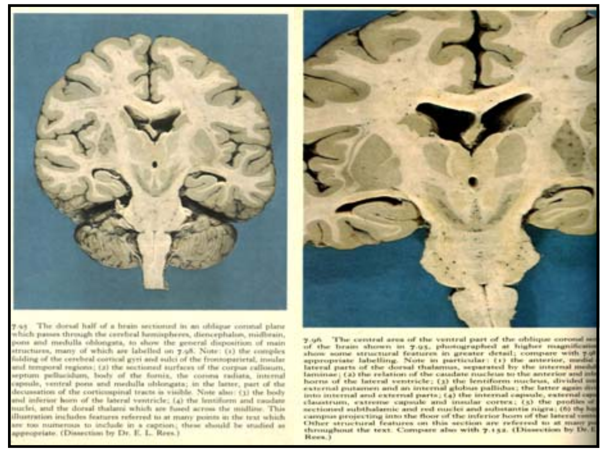
A diagram of some of the main features of the neuronal organization and connectivity patterns of the dentate gyrus, cornu ammonis, subiculum and parahippocampal gyrus. The cell somata, dendrites and axons of the pyramidal neurons of the cornu ammonis are yellow; their axons form the efferent hippocampal fibres of the alveus and fimbria. Afferent fibres to the cornu ammonis from the fimbria are purple, those following the alvear path are green, whilst those following the perforant path are blue. Basket neurons are in black. The neurons of the dentate gyrus, and their axons which form the mossy fibres of the hippocampus, are in magenta. See text for further details.

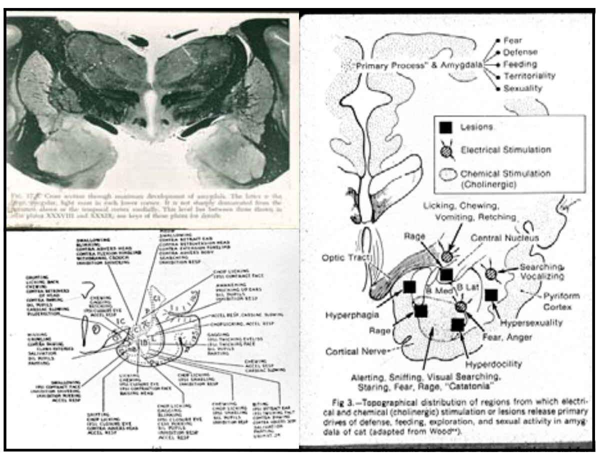


7.117 A A diagram of a dissection of the medial aspect of a cerebral hemisphere to demonstrate the majority of the structures included under the term limbic system in the present account; these are coloured yellow. The anterior nuclear group of the dorsal thalamus is coloured orange and included with the limbic system; the remainder of the dorsal thalamus is magenta. The approximate position of the brainstem was removed in the course of dissection is outlined in a heav rupted line. This diagram should be compared with the colour graph of a dissection prepared from the *lateral* aspect of a hem (7.117 B).

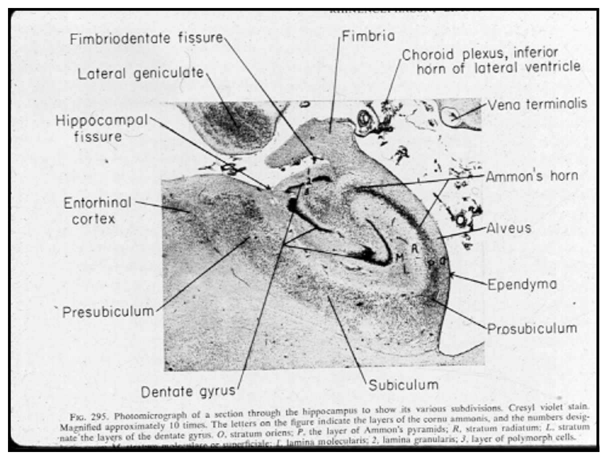




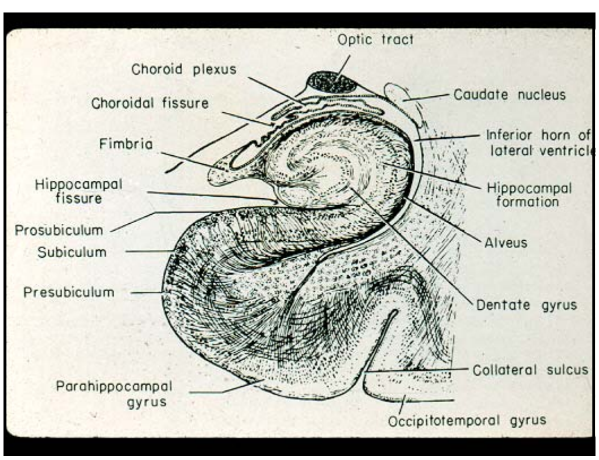




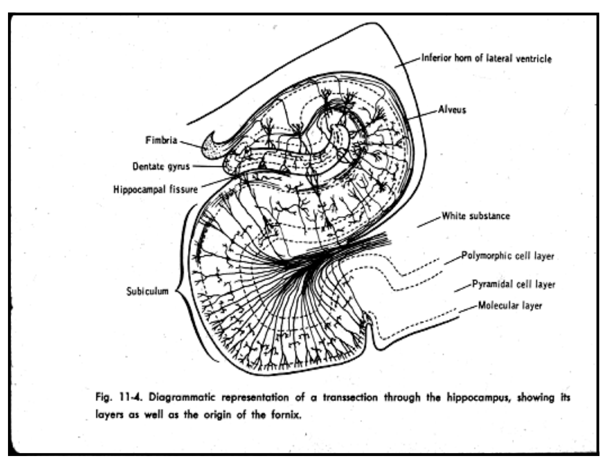
"Primary Process" & Amygdala
Fear
Defense
Feeding
Territoriality
Sexuality
Lesions
Electrical Stimulation
Chemical Stimulation (Cholinergic)
Licking, Chewing, Vomiting, Retching
Optic Tract
Rage
Central Nucleus
Searching Vocalizing
Pyriform Cortex
Hyperphagia
Hypersexuality
Fear, Anger
Cortical Nerve
Hyperdocility
Alerting, Sniffing, Visual Searching, Staring, Fear, Rage, "Catatonia"
Fig 3.—Topographical distribution of regions from which electrical and chemical (cholinergic) stimulation or lesions release primary drives of defense, feeding, exploration, and sexual activity in amygdala of cat (adapted from Wood).



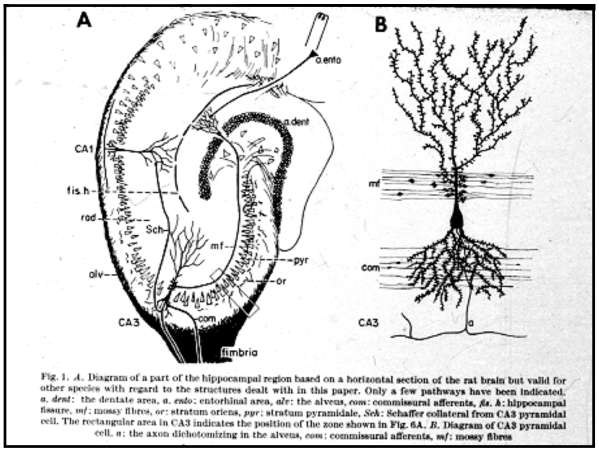
Fimbriodentate fissure
Fimbria
Choroid plexus, inferior horn of lateral ventricle
Lateral geniculate
Vena terminalis
Hippocampal fissure
Ammon's horn
Entorhinal cortex
Alveus
Ependyma
Presubiculum
Prosubiculum
Dentate gyrus
Subiculum
FIG. 295. Photomicrograph of a section through the hippocampus to show its various subdivisions. Cresyl violet stain. Magnified approximately 10 times. The letters on the figure indicate the layers of the cornu ammonis, and the numbers designate the layers of the dentate gyrus. O, stratum oriens; P, the layer of Ammon's pyramids; R, stratum radiatum; L, stratum lamina molecularis; 2, lamina granularis; 3, layer of polymorph cells.

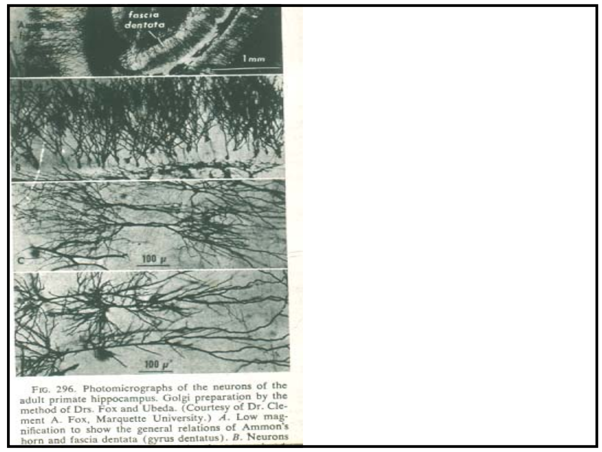


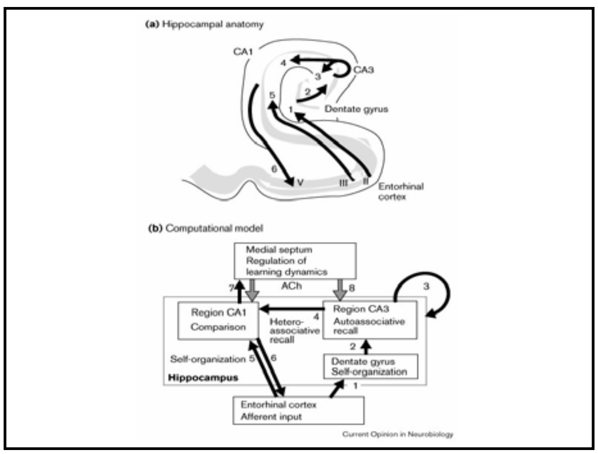
Optic tract
Choroid plexus
Caudate nucleus
Choroidal fissure
Inferior horn of lateral ventricle
Fimbria
Hippocampal fissure
Hippocampal formation
Prosubiculum
Subiculum
Alveus
Presubiculum
Dentate gyrus
Collateral sulcus
Parahippocampal gyrus
Occipitotemporal gyrus

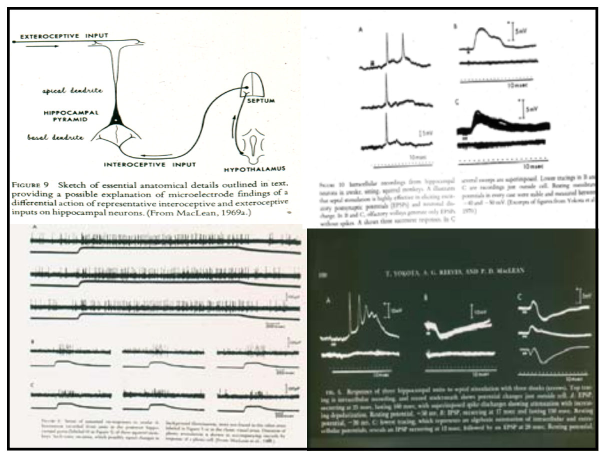


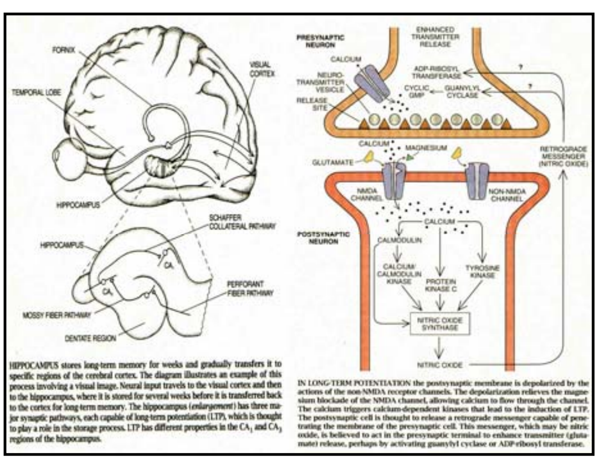
Inferior horn of lateral ventricle
Alveus
Fimbria
Dentate gyrus
Hippocampal fissure
White substance
Polymorphic cell layer
Subiculum
Pyramidal cell layer
Molecular layer
Fig. 11-4. Diagrammatic representation of a transsection through the hippocampus, showing its layers as well as the origin of the fornix.

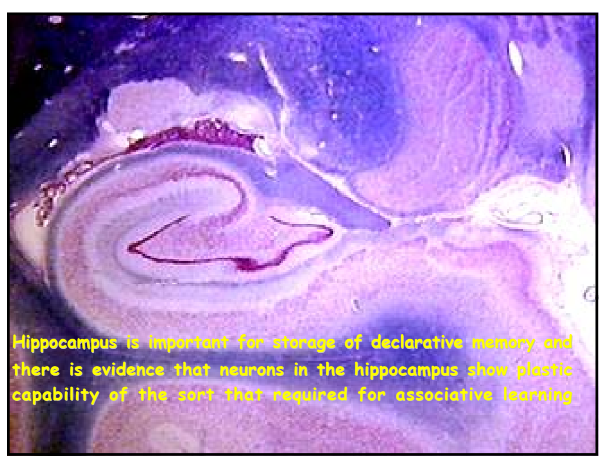

A
B
a. ento
a. dent
CA1
fis. h
rad
Sch
mf
pyr
alv
or
CA3
com
fimbria
mf
com
CA3
a
Fig. 1. A. Diagram of a part of the hippocampal region based on a horizontal section of the rat brain but valid for other species with regard to the structures dealt with in this paper. Only a few pathways have been indicated. a. dent: the dentate area, a. ento: entorhinal area, alv: the alveus, com: commissural afferents, fis. h: hippocampal fissure, mf: mossy fibres, or: stratum oriens, pyr: stratum pyramidale, Sch: Schaffer collateral from CA3 pyramidal cell. The rectangular area in CA3 indicates the position of the zone shown in Fig. 6A. B. Diagram of CA3 pyramidal cell, a: the axon dichotomizing in the alveus, com: commissural afferents, mf: mossy fibres

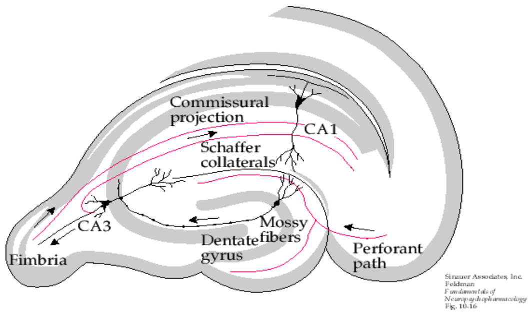

fascia dentata
1 mm
100 μ
100 μ
FIG. 296. Photomicrographs of the neurons of the adult primate hippocampus. Golgi preparation by the method of Drs. Fox and Ubeda. (Courtesy of Dr. Clement A. Fox, Marquette University.) A. Low magnification to show the general relations of Ammon's horn and fascia dentata (gyrus dentatus). B. Neurons


(a) Hippocampal anatomy
CA1
CA3
Dentate gyrus
Entorhinal cortex
(b) Computational model
Medial septum
Regulation of learning dynamics
ACh
Region CA1
Comparison
Hetero-associative recall
Region CA3
Autoassociative recall
Self-organization
Dentate gyrus
Self-organization
Hippocampus
Entorhinal cortex
Afferent input
Current Opinion in Neurobiology

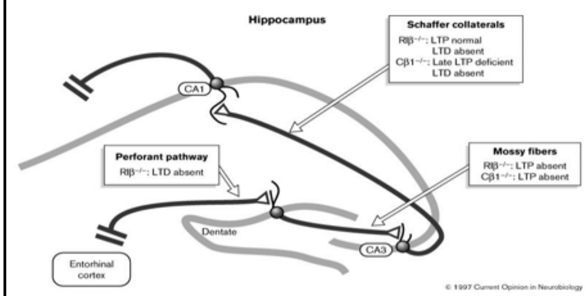

EXTEROCEPTIVE INPUT
apical dendrite
HIPPOCAMPAL PYRAMID
basal dendrite
SEPTUM
INTEROCEPTIVE INPUT
HYPOTHALAMUS
FIGURE 9 Sketch of essential anatomical details outlined in text, providing a possible explanation of microelectrode findings of a differential action of representative interoceptive and exteroceptive inputs on hippocampal neurons. (From MacLean, 1969a.)
T. YOKOTA, A. G. REEVES, AND P. D. MacLEAN

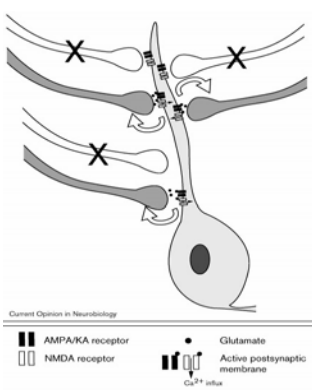

FORNIX
VISUAL CORTEX
TEMPORAL LOBE
HIPPOCAMPUS
SCHAFFER COLLATERAL PATHWAY
HIPPOCAMPUS
PERFORANT FIBER PATHWAY
MOSSY FIBER PATHWAY
DENTATE REGION
HIPPOCAMPUS stores long-term memory for weeks and gradually transfers it to specific regions of the cerebral cortex. The diagram illustrates an example of this process involving a visual image. Neural input travels to the visual cortex and then to the hippocampus, where it is stored for several weeks before it is transferred back to the cortex for long-term memory. The hippocampus (enlargement) has three major synaptic pathways, each capable of long-term potentiation (LTP), which is thought to play a role in the storage process. LTP has different properties in the CA_1 and CA_3 regions of the hippocampus.
PRESYNAPTIC NEURON
ENHANCED TRANSMITTER RELEASE
CALCIUM
NEURO-TRANSMITTER VESICLE
RELEASE SITE
ADP-RIBOSYL TRANSFERASE
CYCLIC GMP
GUANYLYL CYCLASE
GLUTAMATE
MAGNESIUM
NMDA CHANNEL
NON-NMDA CHANNEL
RETROGRADE MESSENGER (NITRIC OXIDE)
POSTSYNAPTIC NEURON
CALMODULIN
CALCIUM/CALMODULIN KINASE
PROTEIN KINASE C
TYROSINE KINASE
NITRIC OXIDE SYNTHASE
NITRIC OXIDE
IN LONG-TERM POTENTIATION the postsynaptic membrane is depolarized by the actions of the non-NMDA receptor channels. The depolarization relieves the magnesium blockade of the NMDA channel, allowing calcium to flow through the channel. The calcium triggers calcium-dependent kinases that lead to the induction of LTP. The postsynaptic cell is thought to release a retrograde messenger capable of penetrating the membrane of the presynaptic cell. This messenger, which may be nitric oxide, is believed to act in the presynaptic terminal to enhance transmitter (glutamate) release, perhaps by activating guanylyl cyclase or ADP-ribosyl transferase.

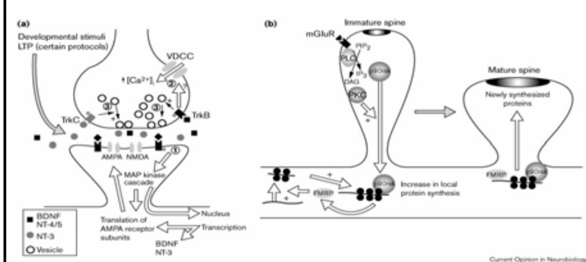

Hippocampus is important for storage of declarative memory and there is evidence that neurons in the hippocampus show plastic capability of the sort that required for associative learning



Excitatory pathways used to study long-term potentiation in hippocampal slices.







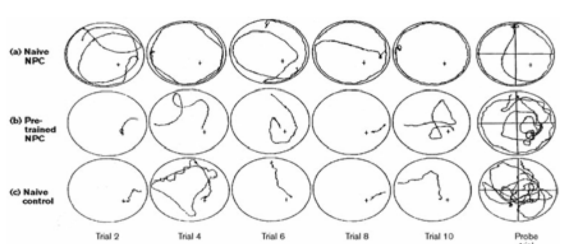
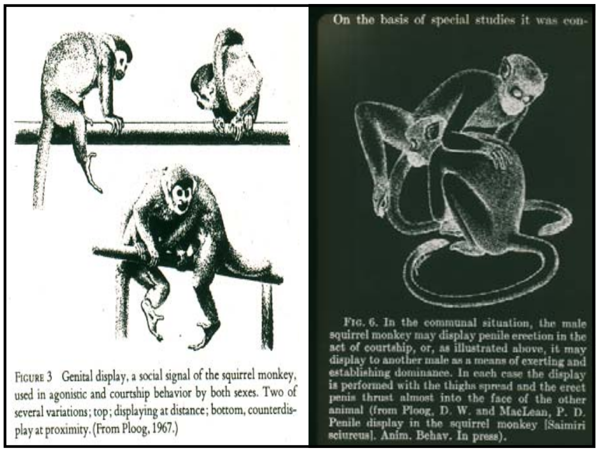
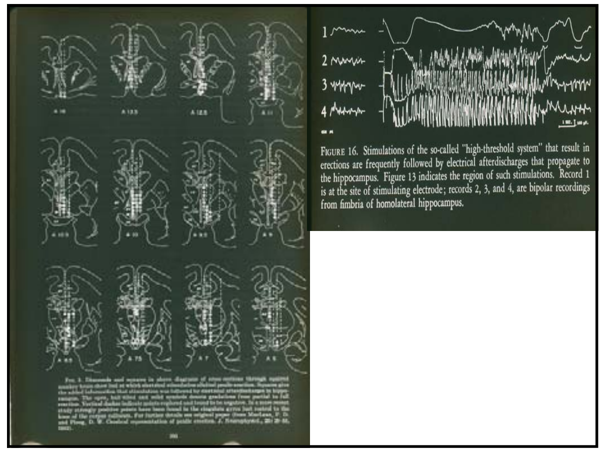
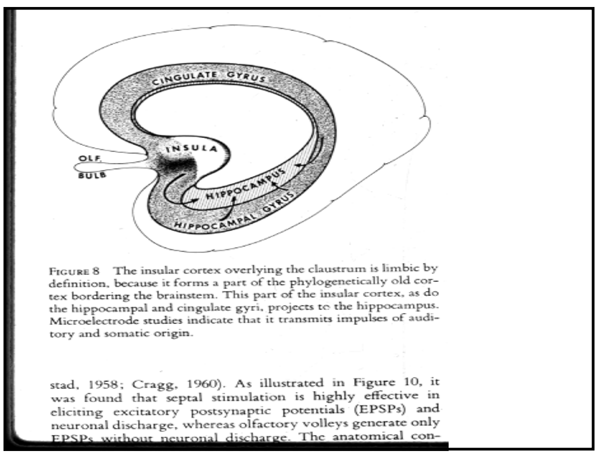
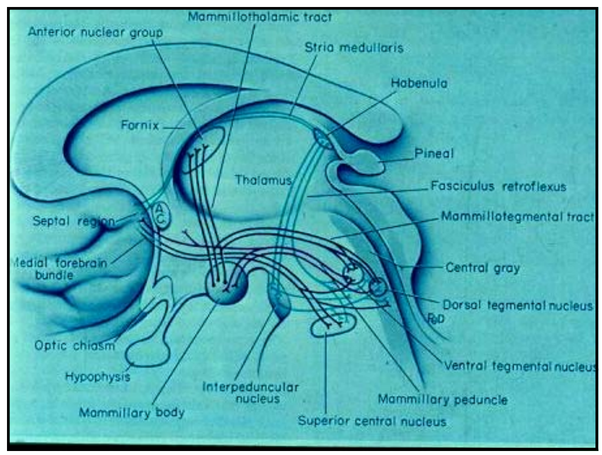


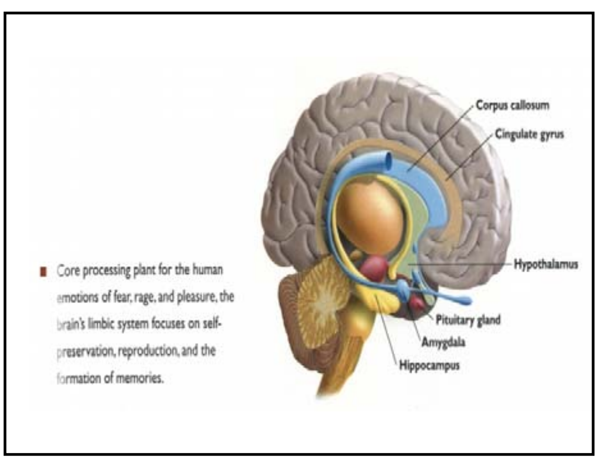
Fig. 2.2 Copulation in rats. The female's posture with raised pelvis and deflected tail is very stereotyped in form. The pressure of the male's fore-limbs on her flanks is one of the stimuli necessary for the female to respond. (From Barnett,[14] 1963, *A Study in Behaviour*. Methuen, London.)

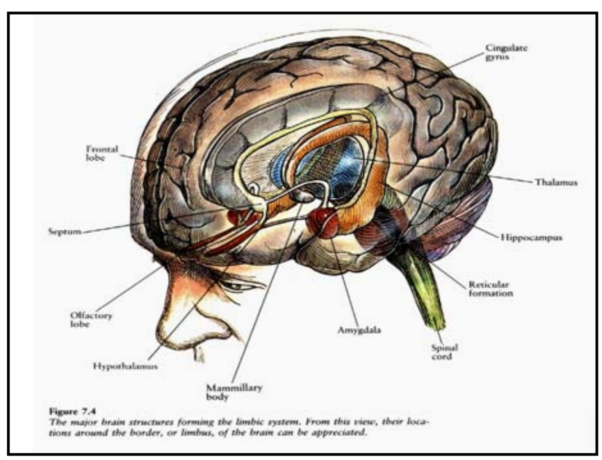

On the basis of special studies it was con-
FIGURE 3 Genital display, a social signal of the squirrel monkey, used in agonistic and courtship behavior by both sexes. Two of several variations; top; displaying at distance; bottom, counterdisplay at proximity. (From Ploog, 1967.)
FIG. 6. In the communal situation, the male squirrel monkey may display penile erection in the act of courtship, or, as illustrated above, it may display to another male as a means of exerting and establishing dominance. In each case the display is performed with the thighs spread and the erect penis thrust almost into the face of the other animal (from Ploog, D. W. and MacLean, P. D. Penile display in the squirrel monkey [Saimiri sciureus]. Anim. Behav. In press).


1
2
3
4
FIGURE 16. Stimulations of the so-called "high-threshold system" that result in erections are frequently followed by electrical afterdischarges that propagate to the hippocampus. Figure 13 indicates the region of such stimulations. Record 1 is at the site of stimulating electrode; records 2, 3, and 4, are bipolar recordings from fimbria of homolateral hippocampus.


CINGULATE GYRUS
INSULA
OLF. BULB
HIPPOCAMPUS
HIPPOCAMPAL GYRUS
FIGURE 8 The insular cortex overlying the claustrum is limbic by definition, because it forms a part of the phylogenetically old cortex bordering the brainstem. This part of the insular cortex, as do the hippocampal and cingulate gyri, projects to the hippocampus. Microelectrode studies indicate that it transmits impulses of auditory and somatic origin.
stad, 1958; Cragg, 1960). As illustrated in Figure 10, it was found that septal stimulation is highly effective in eliciting excitatory postsynaptic potentials (EPSPs) and neuronal discharge, whereas olfactory volleys generate only EPSPs without neuronal discharge. The anatomical con-


Mammillothalamic tract
Anterior nuclear group
Stria medullaris
Habenula
Fornix
Pineal
Thalamus
Fasciculus retroflexus
Septal region
Mammillotegmental tract
Medial forebrain bundle
Central gray
Dorsal tegmental nucleus
Optic chiasm
Ventral tegmental nucleus
Hypophysis
Interpeduncular nucleus
Mammillary peduncle
Mammillary body
Superior central nucleus

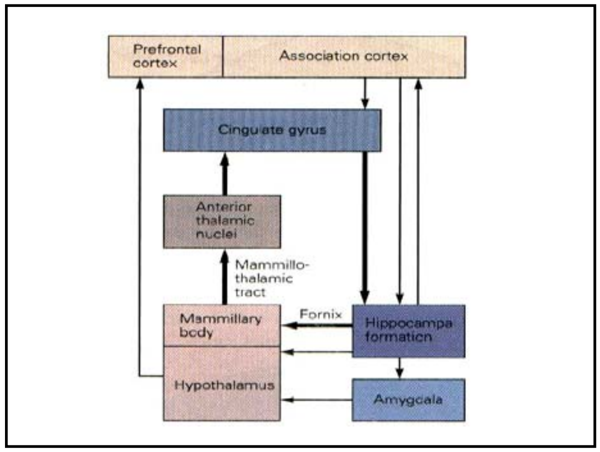

Core processing plant for the human emotions of fear, rage, and pleasure, the brain's limbic system focuses on self-preservation, reproduction, and the formation of memories.
Corpus callosum
Cingulate gyrus
Hypothalamus
Pituitary gland
Amygdala
Hippocampus

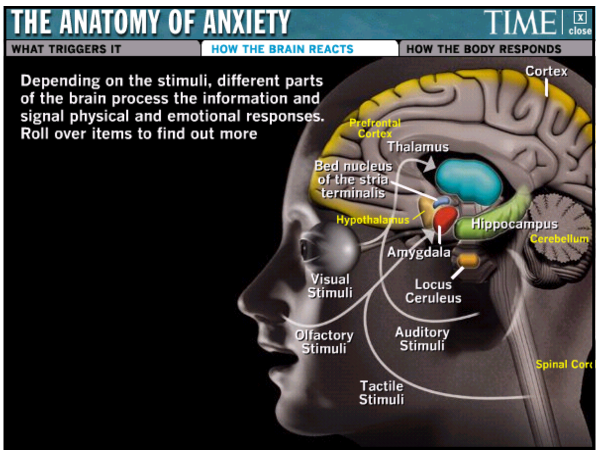

Cingulate gyrus
Frontal lobe
Thalamus
Septum
Hippocampus
Reticular formation
Olfactory lobe
Amygdala
Spinal cord
Hypothalamus
Mammillary body
Figure 7.4
The major brain structures forming the limbic system. From this view, their locations around the border, or limbus, of the brain can be appreciated.

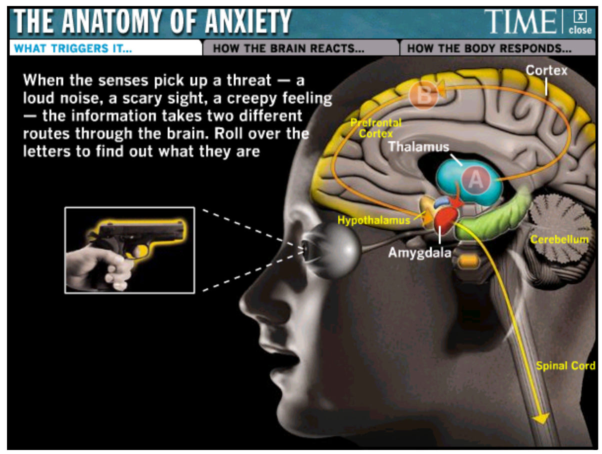
The limbic system is also tightly connected to the prefrontal cortex.

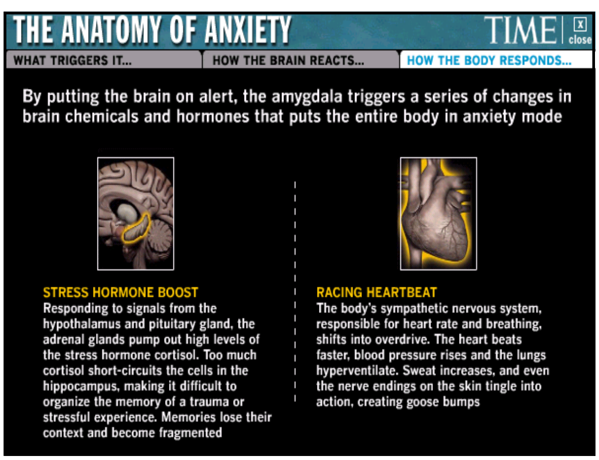
Some scientists contend that this connection is related to the pleasure obtained from solving problems. To cure severe emotional disorders, this connection was sometimes surgically severed, a procedure of psychosurgery, called a prefrontal lobotomy. Patients who underwent this procedure often became passive and lacked all motivation.

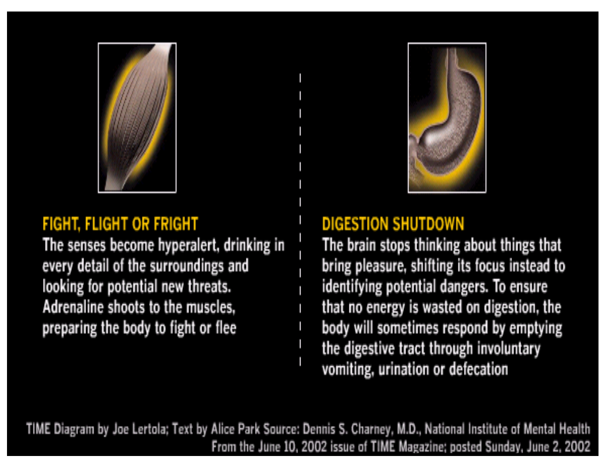
There is circumstantial evidence that the limbic system also provides a custodial function for the maintenance of a healthy conscious state of mind.

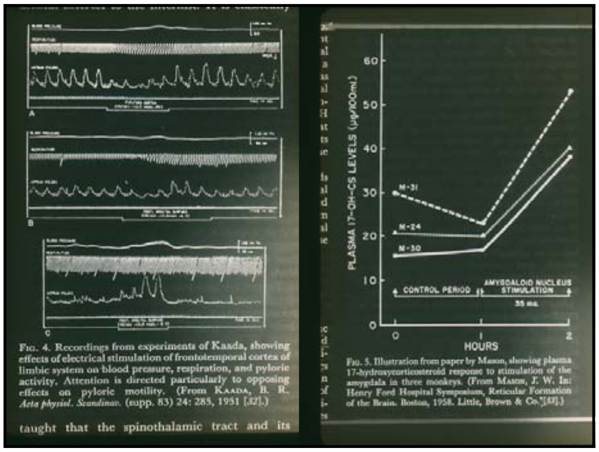


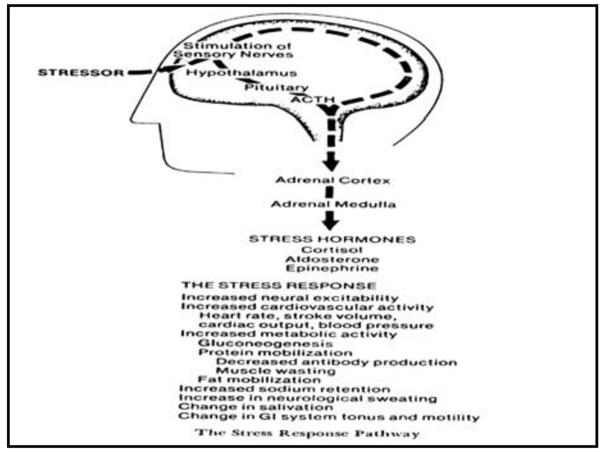


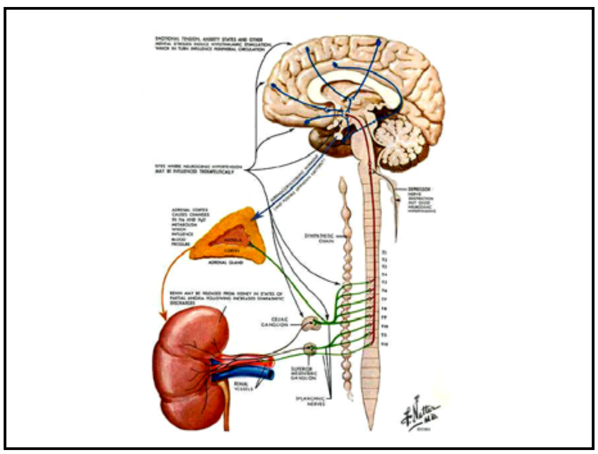


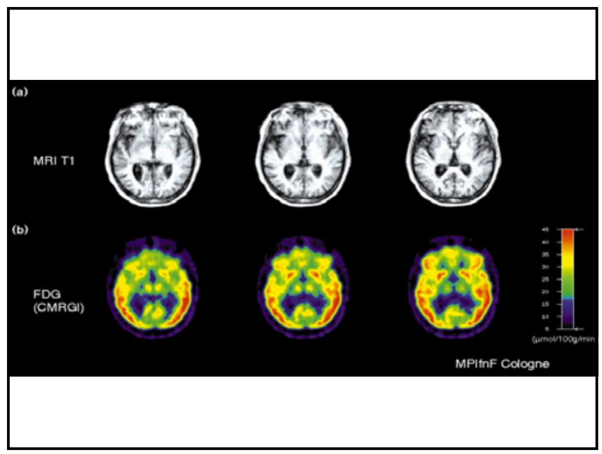


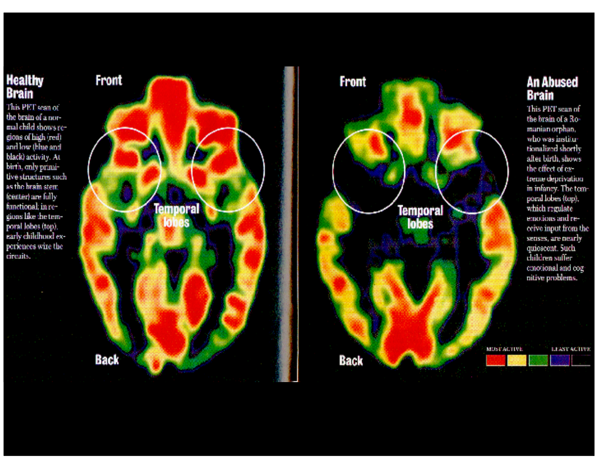



PLASMA 17-OH-CS LEVELS (µg/100ml)
M-31
M-24
M-30
CONTROL PERIOD
AMYGDALOID NUCLEUS STIMULATION
35 ma.
HOURS
FIG. 4. Recordings from experiments of Kaada, showing effects of electrical stimulation of frontotemporal cortex of limbic system on blood pressure, respiration, and pyloric activity. Attention is directed particularly to opposing effects on pyloric motility. (From KAADA, B. R. Acta physiol. Scandinav. (supp. 83) 24: 285, 1951 [32].)
taught that the spinothalamic tract and its
FIG. 5. Illustration from paper by Mason, showing plasma 17-hydroxycorticosteroid response to stimulation of the amygdala in three monkeys. (From MASON, J. W. In: Henry Ford Hospital Symposium, Reticular Formation of the Brain. Boston, 1958. Little, Brown & Co.)


STRESSOR
Stimulation of Sensory Nerves
Hypothalamus
Pituitary
ACTH
Adrenal Cortex
Adrenal Medulla
STRESS HORMONES
Cortisol
Aldosterone
Epinephrine
THE STRESS RESPONSE
Increased neural excitability
Increased cardiovascular activity
Heart rate, stroke volume, cardiac output, blood pressure
Increased metabolic activity
Gluconeogenesis
Protein mobilization
Decreased antibody production
Muscle wasting
Fat mobilization
Increased sodium retention
Increase in neurological sweating
Change in salivation
Change in GI system tonus and motility
The Stress Response Pathway




(a)
MRI T1
(b)
FDG
(CMRGl)
MPIfnF Cologne


Healthy Brain
This PET scan of the brain of a normal child shows regions of high (red) and low (blue and black) activity. At birth, only primitive structures such as the brain stem (center) are fully functional; in regions like the temporal lobes (top), early childhood experiences wire the circuits.
Front
Temporal lobes
Back
Front
Temporal lobes
Back
An Abused Brain
This PET scan of the brain of a Romanian orphan, who was institutionalized shortly after birth, shows the effect of extreme deprivation in infancy. The temporal lobes (top), which regulate emotions and receive input from the senses, are nearly quiescent. Such children suffer emotional and cognitive problems.
MOST ACTIVE
LEAST ACTIVE


Sensitivity Training Separates the Sexes
Men and women were asked whether the expressions on actors' faces were sad or happy and were monitored by PET scans as they decided.
MEN
Men did as well as women—90 percent right—in identifying happy male and female faces. But they were worse at sensing sad women.
WOMEN
Overall, women were better able to judge facial expressions of both sexes. The PET scan showed their brains required less energy than the men's to decide.

Table 7.1 *Agreement on judgments of emotion in five literate cultures*

	Happiness	Disgust	Surprise	Sadness	Anger	Fear
United States	97%	92%	95%	84%	67%	85%
Brazil	95%	97%	87%	59%	90%	67%
Chile	95%	92%	93%	88%	94%	68%
Argentina	98%	92%	95%	78%	90%	54%
Japan	100%	90%	100%	62%	90%	66%

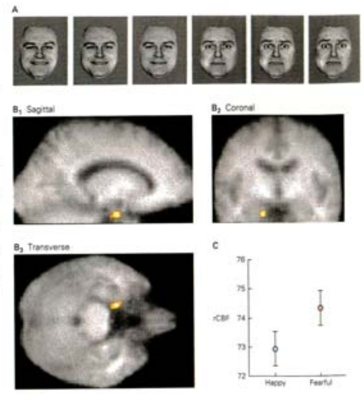


Figure 50-6 Brain imaging studies demonstrate the role of the amygdala in emotional responses. (From Morris et al. 1996.)

A. A series of faces shows a continuum of expression between happiness and fear. Activity in the brain of normal subjects was recorded as they viewed these faces.

B. With the presentation of each of the faces only the left amygdala was found to vary in a systematic fashion. The region with activity that was correlated with the type of face that was shown is indicated in yellow and **red.**

C. The mean regional cerebral blood flow (rCBF) for the predominantly happy and predominantly fearful expressions. These results are consistent with recording and ablation experiments on animals that suggest the amygdala has a critical role in emotions, particularly in fear.

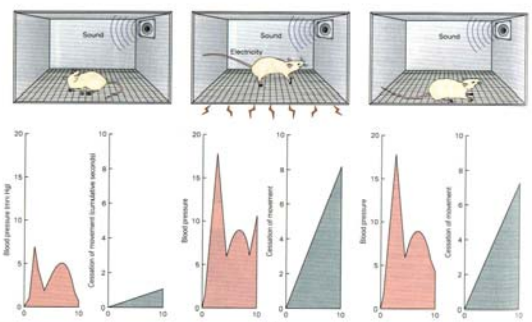


Figure 50-7 Classical fear conditioning can be demonstrated by pairing a sound with a mild electric shock to the foot of a rat. In one set of trials the rat hears a sound (**left panel**), which has relatively little effect on the animal's blood pressure or patterns of movement. Next, the same sound is coupled with a foot shock (**center**). After several pairings the rat's blood pressure rises and the animal freezes; it does not move for an extended period when it hears the sound. The rat has been fear-conditioned. Now, when the sound alone is given, it evokes physiological changes in blood pressure and freezing similar to those evoked by the sound and shock together (**right**). (From LeDoux 1994.)

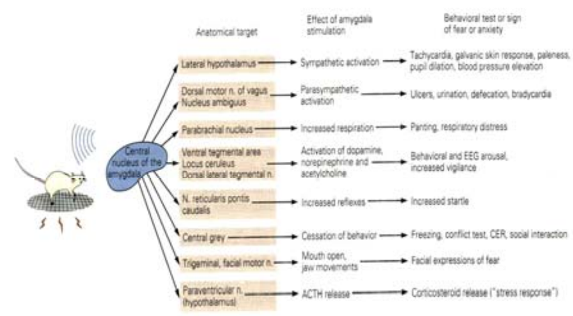
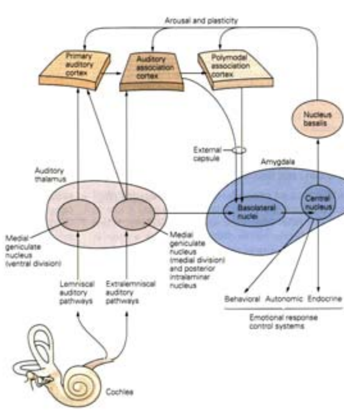
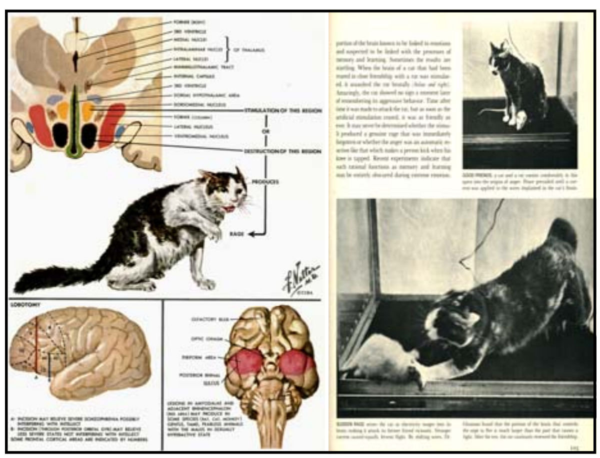
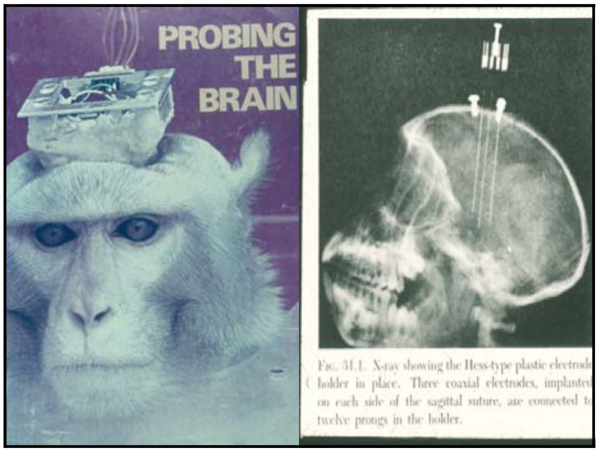


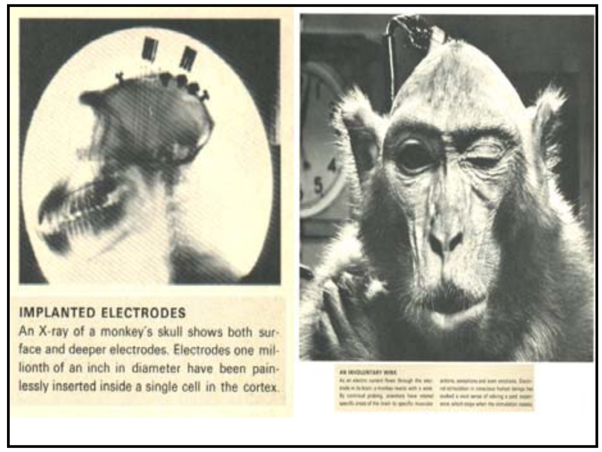
Figure 50-9 The direct connections between the central nucleus of the amygdala and a variety of hypothalamic and brain stem areas that may be involved in different animal tests of fear and anxiety. ACTH = adrenocorticotropin; **CER** = conditioned emotional response; **EEG** = electroencephalographic; **N** = nucleus. (From Davis 1992.)

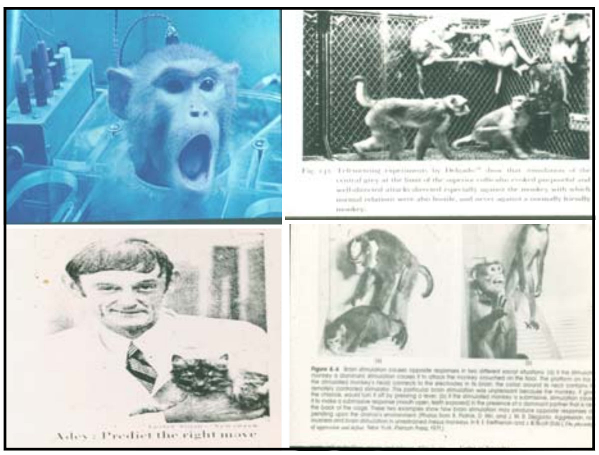
Figure 50-8 Some of the pathways involved in the processing of emotional information. Sensory information is transmitted to the thalamus via lemniscal pathways. The auditory input, for example, arrives in the ventral division of the medial geniculate nucleus. Other extralemniscal pathways deliver auditory information to other parts of the thalamus: the medial division of the medial geniculate nucleus and the posterior intralaminar nucleus. The lemniscal pathway of the ventral division of the medial geniculate nucleus projects only to the primary auditory cortex, but the extralemniscal auditory pathways of the medial geniculate nucleus and posterior intralaminar nucleus project to both the primary auditory cortex and auditory association cortex as well as to the basolateral nuclei of the amygdala. These pathways from the thalamus to the amygdala have been implicated in emotional learning. The anterior nucleus (not shown) projects widely to cortical areas and the central nucleus of the amygdala. The output nucleus of the amygdala, the central nucleus, makes extensive connections with brain stem areas involved in the control of emotional responses. It also projects to the nucleus basalis, which projects widely to cortical areas. The cholinergic projections from the nucleus basalis to the cortex have been implicated in cortical arousal. (Adapted from LeDoux 1992.)

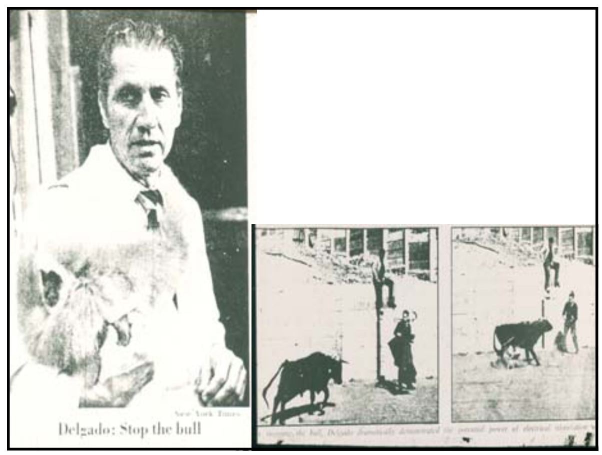


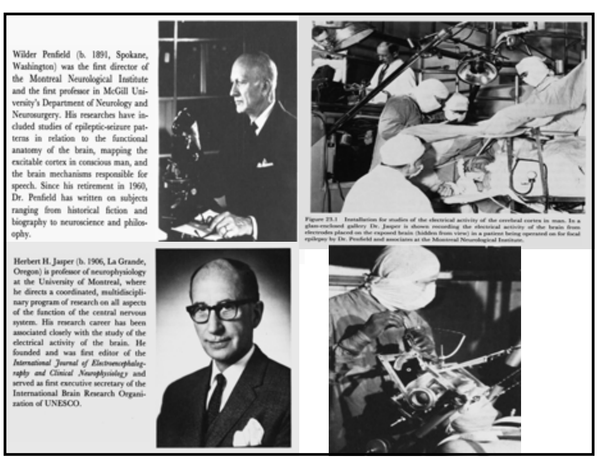



PROBING THE BRAIN
FIG. 31.1. X-ray showing the Hess-type plastic electrode holder in place. Three coaxial electrodes, implanted on each side of the sagittal suture, are connected to twelve prongs in the holder.


IMPLANTED ELECTRODES
An X-ray of a monkey's skull shows both surface and deeper electrodes. Electrodes one millionth of an inch in diameter have been painlessly inserted inside a single cell in the cortex.


Adey: Predict the right move


New York Times
Delgado: Stop the bull


Wilder Penfield (b. 1891, Spokane, Washington) was the first director of the Montreal Neurological Institute and the first professor in McGill University's Department of Neurology and Neurosurgery. His researches have included studies of epileptic-seizure patterns in relation to the functional anatomy of the brain, mapping the excitable cortex in conscious man, and the brain mechanisms responsible for speech. Since his retirement in 1960, Dr. Penfield has written on subjects ranging from historical fiction and biography to neuroscience and philosophy.
Herbert H. Jasper (b. 1906, La Grande, Oregon) is professor of neurophysiology at the University of Montreal, where he directs a coordinated, multidisciplinary program of research on all aspects of the function of the central nervous system. His research career has been associated closely with the study of the electrical activity of the brain. He founded and was first editor of the International Journal of Electroencephalography and Clinical Neurophysiology and served as first executive secretary of the International Brain Research Organization of UNESCO.


TAKING ACCURATE SOUNDINGS
A metal "halo," clamped to an epileptic patient's head at Massachusetts General Hospital, Boston, holds an electrode implanted in his brain. A simple ground wire is taped to his chin. By detecting changes in electrical impulses in the brain, electrodes locate abnormal cells, such as those that cause epilepsy and Parkinson's disease. They can then be surgically removed or treated with drugs.

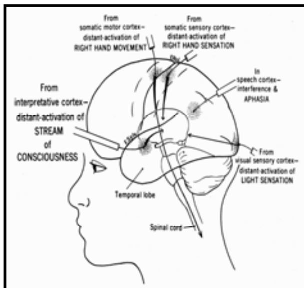


Figure 25.1 Activation of the brain's record of consciousness and some other results of stimulation. The left hemisphere of the brain is outlined, with the brainstem and spinal cord shown beneath, to illustrate the results of electrode stimulation of the cortex in motor, sensory, and what may be called psychical areas for the recall of past experience. The dotted zone about each stimulating electrode tip (unipolar) suggests the area of interference in which local cortical elaborative action is arrested by electrical interference. In addition to this interference, a positive response is described from each of these electrodes, except the one on the area where speech is localized. Stimulation of the speech cortex produces only interference aphasia. The positive responses, on the other hand, are caused by normal axonal conduction from cells near the electrode to a distant but functionally related area of gray matter. Thus the active response is a physiological activation of that distant gray matter. In the case of stimulation of the interpretive cortex, it is the sequential record of successive conscious states from the past that is activated. In the case of motor cortex the target of activation is gray matter in lower brainstem or spinal cord. In the case of sensory areas the target is in the higher brainstem. Drawing by Eleanor Sweeney.

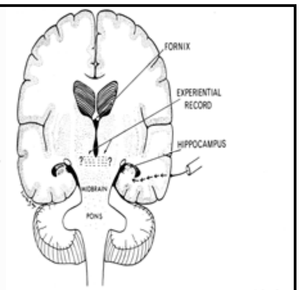


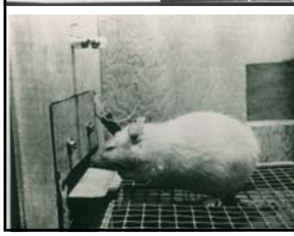
Figure 25.7 The experiential record of consciousness and its reactivation. A stimulating electrode is shown here applied to a convolution in the interpretive cortex. It recalls the past by activating a functional circuit (experiential response). The circuit has yet to be completely defined but may well include the hippocampus and fornix. The beginning of the pathway of neuronal activation is shown by the line of arrows from beneath the electrode. It may be that it passes directly through white matter into the higher brainstem. Or it may enter the hippocampus and pass along the fornix, which conducts from hippocampus to brainstem. The hippocampus evidently plays an essential role, together with the interpretive cortex, in the function of scanning the experiential record and recalling memories. Removal of one hippocampus affects memory little. Removal of both abolishes the ability to recall past experience, either voluntarily or for the purposes of automatic interpretation. In the case of a simple bilateral loss of the hippocampi, other forms of memory are retained, e.g., memory of language and of skills and of nonverbal concepts. (See Penfield and Mathieson, 1974.) Drawing by Eleanor Sweeney.

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.

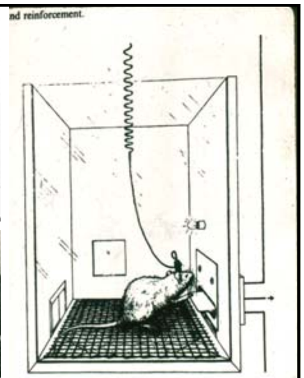
In 1954, **James Olds and Brenda Milner** found that rats with metal electrodes implanted into their nucleus accumbens repeatedly pressed a lever activating this region, and did so in preference to eating and drinking, eventually dying of exhaustion.

Olds, J., Milner, B. 1954. Positive reinforcement produced by electrical stimulation of septal area and other regions of rat brain. *J.Comp. Physiolo. Psycholo.* 47, 419–427

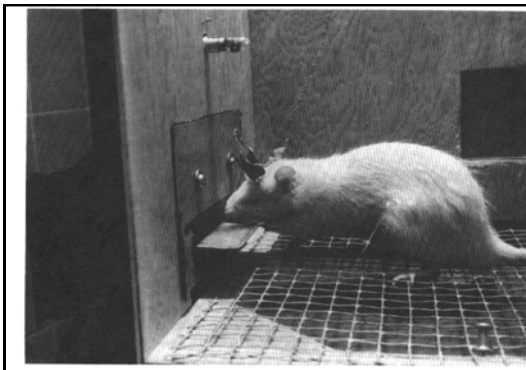
James Olds (b. 1922, Chicago, Illinois) is Bing Professor of Behavioral Biology at the California Institute of Technology. His research has dealt with reward, punishment, drive, and learning, especially as investigated by the electrical self-stimulation experimental method he helped pioneer.



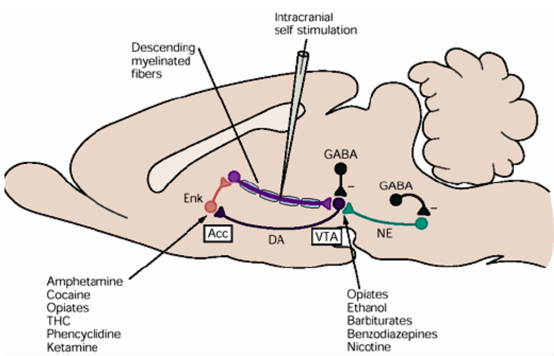
nd reinforcement.



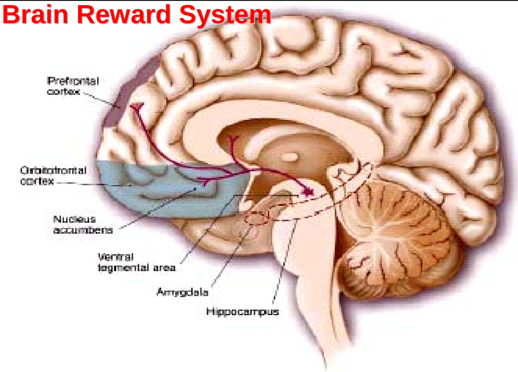
20. Experimental arrangement for intracranial self-stimulation. When the rat p
t triggers an electrical stimulus to its brain and simultaneously records action v
From Olds, J. Pleasure centers in the brain. Copyright © 1956 by Sci
, *Inc.* All rights reserved.)



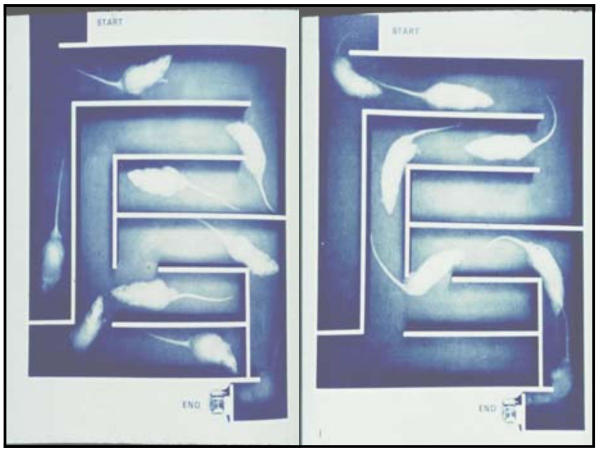
With an electrode implanted in an area of the hypothalamus that has come to be known as a "pleasure center," this rat pushes a lever to apply electrical stimulation to its own brain (Olds, 1953).

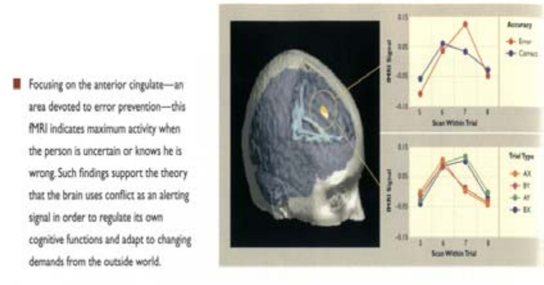


Brain Reward System



Wired. Dopamine projections link the ventral tegmental area, nucleus accumbens, and parts of the frontal lobe in a reward circuit that even nondrug compulsions may alter.

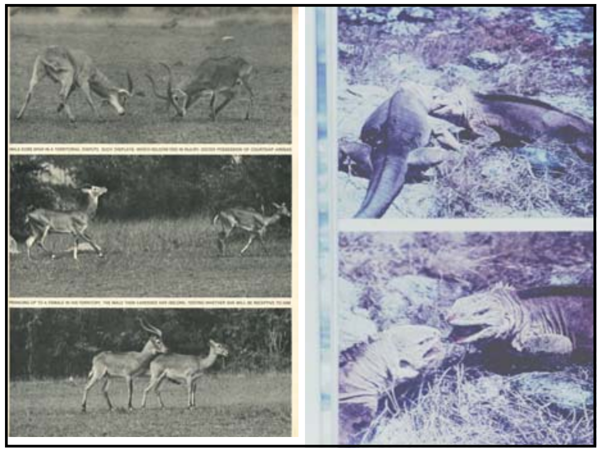




Behavioural Correlates of Limbic System:

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, Leaderships
- Social Communication
- Fighting, Hostility, Aggression, Violence
- Affection, Love, Altruistic Behaviour etc..



Limbic System → Corpus Striatum

Limbic System → Hypothalamus → Pituitary Gland → Endocrine Glands → **Hormonal Responses**

Hypothalamus → ANS → Autonomic → **Visceral Responses**

Corpus Striatum → Basal Ganglion → Reticular Formation → Stereotyped Behaviours → **Somatic Motor Responses**

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

- Amygdala:[3][4][5] Involved in signaling the cortex of motivationally significant stimuli such as those related to reward and fear in addition to social functions such as mating.
- Hippocampus:[3][4][5] Required for the formation of long-term memories
  - Parahippocampal gyrus:[4] Plays a role in the formation of spatial memory and is part of the hippocampus
- Cingulate gyrus:[3][4][5] Autonomic functions regulating heart rate, blood pressure and cognitive and attentional processing
- Fornix:[5][3] carries signals from the hippocampus to the mammillary bodies and septal nuclei.
- Hypothalamus:[3][5] Regulates the autonomic nervous system via hormone production and release. Affects and regulates blood pressure, heart rate, hunger, thirst, sexual arousal, and the sleep/wake cycle
- Thalamus:[3][5] The "relay station" to the cerebral cortex

In addition, these structures are sometimes also considered to be part of the limbic system:

- Mammillary body:[3] Important for the formation of memory
- Pituitary gland:[3] secretes hormones regulating homeostasis
- Dentate gyrus:[4] thought to contribute to new memories and to regulate happiness.
- Entorhinal cortex and piriform cortex:[5] Receive smell input in the olfactory system.
- Fornicate gyrus: Region encompassing the cingulate, hippocampus, and parahippocampal gyrus
- Olfactory Bulb: Olfactory sensory input
- Nucleus accumbens: Involved in reward, pleasure, and addiction
- Orbitofrontal cortex: Required for decision making

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

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

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 dulled, 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 (socially 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.

Drug-Responsive Mania in a Man With a Brain Tumor

SIR: We report a case in which a large temporal lobe tumor induced a classic presentation of manic psychosis that was rapidly responsive to neuroleptic treatment.

Case Report

A 61-year-old man was admitted for his first psychiatric hospitalization after a several-week history of severe, progressive changes in mood and behavior. At the time of admission, the patient exhibited decreased need for sleep, increased energy, racing thoughts, mood lability, hypersexuality, bizarre behavior, and grandiose delusions. His neurologic examination was nonfocal. His mental status examination was remarkable for mania and psychosis. There was no history of seizures.

The patient's past medical history was significant only for aqueductal stenosis. This was diagnosed incidentally by MRI following an episode of loss of consciousness 1 year prior to admission. This initial MRI demonstrated no mass lesions or midline shift. A 24-hour EEG and neurological examination were both normal at that time. A follow-up MRI 5 months prior to the current admission was again remarkable only for aqueductal stenosis, with no episodes of seizure or loss of consciousness reported by the patient. The patient had no prior psychiatric contact, but he reported mild mood swings for the past 10 years, consisting of periods during which he had more energy, needed less sleep, and worked 70 hours per week, followed by periods of lethargy, increased sleep, and blue mood.

During the current admission, the

FIGURE 1. Gadolinium-enhanced MRI showing a 5×3×4-cm mass in the right temporal lobe with surrounding necrosis and hemorrhage.

NEUROLOGY INDIA
Publication of the Neurological Society of India

Clos

Table 1: Outline of clinical features of the 6 patients of Kluver Bucy Syndrome

	Age/ sex	Etiology	Visual agnosia	Orality	Hypermeta-morphosis	Behavior	Sexual hyperactivity	Dietary habits	Seizures	Cranial imaging
1	7/M	CA	-	HO	Present	Placid	Pelvic thrusting	-	GTCS	Diffuse cerebral atrophy
2	14/M	HSE	Present	HO	-	Violent,Irritable	Rubbing of genitals	-	GTCS	B/I T P involvement
3*	12/F	NCC	-	HO	Present	Violent	Hypersexuality	Bulemia	CPS	Multiple NCC
4	11/M	Head injury	-	HO	Present	Offensive	Hypersexuality	Bulemia	CPS	Temporal atrophy
5*	3/M	TBM	-	HO	Present	Hostile	Hypersexuality	-	-	Mild hydrocephalus
6	9/ M	CA	-	HO	-	Apathetic	Pelvic thrusting	-	GTCS	Cerebral atrophy (FT)

TBM – Tuberculous meningitis, CA – Cerebral anoxia, HSE – Herpes simplex encephalitis, NCC – Neurocysticercosis, T P-Temporoparietal, GTCS- Generalized tonic clonic seizures, CPS- complex partial seizures, FT –frontotemporal, HO- Hyperorality

* - detailed in text