The limbic system. A maze on the essentials: memory, learning and emotion.

Poster No.: C-0257
Congress: ECR 2011
Type: Educational Exhibit
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Keywords: Neuroradiology brain, MR, MR-Functional imaging, Education, Dementia
DOI: 10.1594/ecr2011/C-0257

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Learning objectives

The limbic system is a complex circuit, whose study and compression are difficult to address. Our intention with this work is...

To explain the structural and functional anatomy of the limbic system. We will use drawings, layouts and images simple and understandable.

To acquire the basic knowledge for a proper radiologic evaluation of the limbic system as well as for planning of functional Magnetic Resonance Imaging (MRI) studies.

To review some pathologies which pathological substrate is the alteration of the limbic system.
Background

The limbic system is a set of nuclear structures located in medial regions both cerebral hemispheres and with numerous connections between them and other areas of the central nervous system and the rest of the body.

In 1878, Paul Broca described, for the first time, a ring-shaped area that connected the midbrain with each cerebral hemisphere. He named it "Limbic Lobe" (from the Latin "limbus", "limit", "border") and related it with the olfactory functions. (Figure 1)

In 1937, James Papez proposed that the limbic lobe is responsible for emotions and behavior. He described the "Papez Circuit", which connects the hippocampus with the thalamus, through the cingulate gyrus. (Figure 2)

Today, the limbic system is considered a set of structures interconnected among themselves and with other areas, in the brain and in the body. It is located in the medial faces of both cerebral hemispheres and their functions are multiple and complex (learning, memory, behavior and emotions). It is crucial to define our personality...what we are, what we feel, our reactions to the environment that surrounds us and our development and survival depend of this intricate region. The alteration of its components are related to complex and devastating disorders, which still are not well known, such as dementia, schizophrenia and other psychiatric disorders. We will try to clarify this puzzle that is essential in humans.

The components of the limbic system are:

- Cerebral Hemisphere: Hippocampal formation, amygdala, limbic association cortex and ventral striatum.
- Diencephalon: Thalamus, hypothalamus and the habenula.
- Midbrain: Periaqueductal gray matter and reticular formation.

The two main components are the Hippocampal Formation and the Amygdala

- HIPPOCAMPAL FORMATION:

  It proceeds from the Greek "hippocampus": "Seahorse". It has morphology of inverted "S" in coronal sections.

  It’s also known as Ammon's horn, that comes from the Latin "Cornu Ammonis" (horn of the ancient and Egyptian Amun God, who had a ram's head)

  It is located medial to the parahippocampal gyrus, in the medial temporal lobe. It forms the floor of the temporal horn of lateral ventricle.
The hippocampal formation is composed by the dentate gyrus, hippocampus and subiculum.

During embryological development, the medial temporal lobe folds back on itself. Thus:
- The dentate gyrus relies on the subiculum and they both form the hippocampal sulcus.
- The subiculum is above the hippocampal formation.
- The medial groove of temporal lobe, located above the hippocampus, is called choroid fissure.

AMYGDALA (AMYGDALOID COMPLEX)

It comes from the Greek or Latin: "amygdalon" or "amygdalum" that means almond.

It is formed by multiple nuclear structures. (Figure 5)

It is located at the anterior end of the hippocampus and temporal horn of the lateral ventricle. It merges with periamygdaloid cortex and it forms part of the uncus and the parahippocampal gyrus. The UNCUS constitutes the rostral and medial portion of the amygdala and hippocampus, producing a highlight in this region. (Figure 5)

The amygdala consists of several nuclear structures that are organized into three major groups, with different functions:

- MEDIAL GROUP: It is adjacent to the periamygdaloid cortex.
- CENTRAL GROUP.
- BASOLATERAL GROUP: The larger size. It is similar to the cortex but without layers. It is formed by pyramidal neurons.

LIMBIC ASSOCIATION CORTEX

There are three fundamental association cortical areas:
- Parieto-occipito-temporal association cortex
- Prefrontal association cortex
- Limbic association cortex: it is formed by the circumvolutions located in the medial surface of the cerebral hemispheres, and it receives information from higher cortical areas which are transmitted to the hippocampus and amygdala. The cingulated gyrus and
the parahippocampal gyrus surround the corpus callosum, diencephalon and midbrain. (Figure 7)

The cingulum is a tract of axons in the depth of both and it contains cortical association fibers that reach to the parahippocampal gyrus. (Figure 8)

The Parahippocampal Gyrus consists of several cortical areas (Periamygdaloid and Piriform cortex; Entorhinal Cortex; Perirhinal Cortex; Parahippocampal Cortex). (Figure 9)

- VENTRAL STRIATUM

The basal ganglia are composed of different nuclear complex, one of them is the STRIATUM which is formed by the caudate nucleus, putamen and n. accumbens. The striatum that relates to the rest of the limbic system are called Ventral Striatum.

- HYPOTHALAMUS

The hypothalamus is a small region of the diencephalon, prior to the thalamus. It is divided into two halves by the third ventricle, where it is delimited for the thalamus by a small groove: Hypothalamic Sulcus. (Figure 10)

The Tuber Cinereum is the lower region of the hypothalamus, which is exposed to the subarachnoid space. It is delimited ahead by the optic chiasm and it extends by the infundibular stalk towards the pituitary gland. (Figure 10)

We can divide the hypothalamus in different areas, from earlier to later ...

- ANTERIOR REGION: Above the optic chiasm. It includes preóptic area (preóptic nucleus)
- MEDIAL/TUBERAL REGION: Between the optic chiasm and mamillary bodies. Includes the infundibular stalk (Paraventricular n., Supraoptic n., Arcuate n., suprachiasmatic n. …)
- POSTERIOR REGION: Includes mammillary bodies and tuberomammillary nucleus

(Figure 11)

Longitudinally it is divided in...

- PERIVENTRICULAR ZONE: Traversed by the Dorsal Longitudinal fasciculus (hypothalamic fiber tract). With the Suprachiasmatic N. and Arcuate N.
- MEDIAL ZONE
- LATERAL ZONE: Lateral to the fornix. With the Medial Forebrain Bundle.

The fornix passes between the lateral and the medial zones.
In the figure 13 we can see the case of a male patient, 19 years, with neurofibromatosis type I and hypothalamic pilocytic astrocytoma.

Figure 13. A) T1 axial and sagittal images, where we observe a heterogeneous lesion with component similar to cerebrospinal fluid and a solid pole, located in the hypothalamus.
Figure 13. B) T2 axial section, where you can see that there is indeed a cystic component and a solid component.
Figure 13. C) FLAIR axial. In this sequence the entire lesion has a signal gain, more or less homogeneous.
Figure 13. D) T1 Gad, axial and sagittal images. We can observe an intense and homogeneous enhancement of the solid part of the lesion.
This lesion corresponds to a hypothalamic pilocytic astrocytoma.

- THALAMUS

It comes from the Greek "Thalamus" (bedroom) and it is a nuclear structure which constitutes a fundamental processing station in the center of the brain. It is the "Gateway" with the cerebral cortex. Makes up a large part of the diencephalon. It has an oval shape, with a small and rear appendix.

It’s anterior to the foramen ventricular, forming the floor of the lateral ventricles. Both thalamus are communicated by the Interthalamic Adhesion in their central zone. (Figure 14)

It’s divided into three groups, delimited by a white substance called Internal Medullary Lamina.

The thalamus has several nuclear divisions. We can see them in figure 15 and 16.

- HABENULA

It a nuclear structure located in the epithalamus, next to the pineal gland. The pineal gland is joined with the diencephalon through two stems that show a prominence called Habénula (habenular n.). It has connections with the thalamus and the midbrain. (Figure 17)

- PERIAQUEDUCTAL GRAYAND RETICULAR FORMATION

Periaqueductal Gray: It is a nuclear region surrounding the aqueduct of Silvio. These neurons seem to be in relation to the abolition of the sensation of pain in certain circumstances (intense emotional situations). Eg, pain during childbirth or pain during combat. (Figure 18)
Reticular Formation: It’s located in the centre of the midbrain. It is a long structure that extends cranially with some nuclei of the diencephalon (Rostral Reticular Formation) and, caudally, with the intermediate zone of spinal cord (Caudal Reticular Formation). They are related with two fundamental functions: the RRF with the alert status, and the CRF with motor and autonomic functions and reflexes. (Figure 19)

**CONNECTIONS OF THE LIMBIC SYSTEM**

- **CONNECTIONS OF THE HIPPOCAMPAL FORMATION**

  - **Fornix:** Fornix means "arch" in Latin. It is a structure of white substance that surrounds the lateral ventricle, from hippocampal formation to the diencephalon. The parts of the fornix are: 1. Alveus. 2. Fimbria. 3. Crura. 4. Body. 5. Columns. 6. Postcommissural fornix. (Figure 20)
    - Alveus: it originates from the neurons in the hippocampus and the subiculum. It forms a layer of white substance in the ventricular face of the hippocampus. (Figure 21)
    - Fimbria: It is the grouping of the alveus. (Figure 21)
    - Cruras: they are the continuation of the fimbria, leaving the hippocampus and they curve below of the callosum corpus. Both crura are connected by *Hippocampal Commissure*. (Figure 21)
    - Body: it is the set of the cruras below of the callosum corpus. (Figure 21)
    - Columns of the fornix. (Figure 22)
    - Postcomissural fornix ends in the mammillary bodies. (Figure 23)

  The fibres of the fornix have 3 main stops:

  - **Mammillary bodies**
  - **Lateral Septal Nucleus.**
  - **Anterior thalamic nucleus.**

  The fibres of the medial septal nuclei travel to the hippocampus through the fornix. Both septal nucleus are communicated and they have relationship between hippocampus and the medial septal n. They have involvement in memory. (Figure 24)

  The hippocampal formation has an intrinsic circuitry and it emits connections to the association cortical areas. (Figures 25 and 26)
• CONNECTIONS OF THE AMYDALA

Each nuclear group presents specific connections: The Basolateral Group gives emotional meaning to a stimulus and the central nucleus is involved in emotional responses. It modulates the autonomic nervous system. (Figures 27 and 28)

• CONNECTIONS OF THE VENTRAL STRIATUM

The ventral striatum gets informations of amygdala, hippocampus and the limbic association area.

It carries information to the thalamus, which is connected with the amygdala, hippocampus and the limbic association area, too.

• CONNECTIONS OF THE HYPOTHALAMUS:

We can see them in the figure number 29. The hypothalamus is related to endocrine, autonomous, emotional and somatic feature. Its main function is to maintain a balance in our organism. A stimulus will provoke to us an emotion, as well as a neuroendocrina response mediated by the hypothalamus.

• CONNECTIONS OF THE THALAMUS

The most of the information that reaches the brain hemispheres "passes" by thalamus. Not only processes sensory information, also…

1. cerebellar motor inputs and from the basal ganglia.
2. information from the rest of the limbic system
3. relatioship with behavior inputs and circadian cycle.

Each part of the thalamus processes, connecting and controls different areas.

It presents numerous and complex connections. We will make a summary of the most important in the figure 30.

In the figure 31 we can observe the case of a male patient, 30 years, with neurological symptoms. He presents a diffuse involvement in the left temporal and parietal lobes. A) T2 axial, we see increased signal in the temporal pole and hippocampal formation. B) FLAIR axial, also with increased signal in the same locations. C) DWI, without alterations in the restriction. D) T1 GAD without pathological enhancements. Suspicion of gliomatosis cerebri, diffuse infiltrating glioma, demyelinating disease, ... still under study.
Images for this section:

**Fig. 0:** Picture of Paul Broca and image of the limbic lobe

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**Fig. 0:** Picture of J. Papez and scheme of "Papez Circuit"

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**Fig. 0:** Hippocampal Formation

**Fig. 0:** Hippocampus.

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Fig. 0: Amygdala and uncus.

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Fig. 0: Nuclear groups of the amygdala.

Fig. 0: Limbic association cortex

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Fig. 0: Images using tractography: Cingulum

Fig. 0: Cortical areas of the parahippocampal gyrus.

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Fig. 0: Hypothalamus.

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**Fig. 0:** Parts of the hypothalamus.

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**Fig. 0:** Different zones of the hypothalamus.

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**Fig. 0:** Patient with neurofibromatosis type I and hypothalamic pilocytic astrocytoma.

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**Fig. 0:** Thalamus.

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Fig. 0: Nuclear divisions of the thalamus.

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Fig. 0: Nuclear group of the thalamus.

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Fig. 0: Habenula.

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Fig. 0: Periaqueductal Gray

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Fig. 0: Reticular Formation

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Fig. 0: Parts of the fornix

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PARTS OF THE FORNIX:
1. Alveus.
2. Fimbria.
3. Crura.
5. Columns.
6. Postcommissural fornix
Fig. 0: Alveus, fimbria, cruras and body of the fornix.

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**Fig. 0:** Columns of the fornix.

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**Images using tractography:**
**Fornix**

**Fig. 0:** Images using tractography: Fornix.

**Fig. 0:** Connections of the fornix.

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**Fig. 0:** Intrinsic circuitry of the hippocampal formation.

In turn, hippocampal formation receive projections similar to the emitted pathways.
Note that most of the fibers connecting the subiculum to the entorhinal cortex → ESSENTIAL FOR STORING, CONSOLIDATE AND RECOVER MEMORY

**Fig. 0**: Connections of the parahippocampal formation with association cortical areas.

**Fig. 0:** Connections of the amygdala. I.


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**Fig. 0:** Connections of the amygdala. II.

Fig. 0: Connections of the hypothalamus.

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Fig. 0: Connections of the thalamus.
**Fig. 0:** Patient who presents a diffuse involvement in the left temporal and parietal lobes, including the hippocampal formation.

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Imaging findings OR Procedure details

With our work, we have reviewed the complex anatomy and the function of this cerebral area, with comprehensible schemes and images from conventional MR and advanced techniques, as tractography, clarifying the connections and the integration of this region with the rest of the central nervous system.
Conclusion

Radiology plays a key role in the knowledge of the limbic system, not only for its structural features but also for the study of its functionality. This functionality has been specially explored with functional MRI which has allowed us to know something more about this complex region as well as to understand and progress in the knowledge of the essentials of the human being.
References


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- Images by tractography provided by Dr. Juan Alvarez Linera (Ruben Internacional Clinic).

- Conventional MRI images acquired from patients from our health area.