Medical Neuroscience | Tutorial Notes

Overview of the Limbic Forebrain

MAP TO NEUROSCIENCE CORE CONCEPTS[1]

NCC1. The brain is the body's most complex organ.

LEARNING OBJECTIVES

After study of the assigned learning materials, the student will:

1. Discuss the localization of the amygdala and the hippocampus in the medial temporal lobe.
2. Discuss the major functions associated with the limbic forebrain.

NARRATIVE

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Overview

Now that we have nearly completed our brief survey of human brain anatomy, let's make one final pass through the forebrain, focusing on structures that have been considered parts of the "limbic system". A subset of these are crucial for understanding the brain basis of human emotion, cognition, and biological psychiatry, so this survey would not be complete without another look at the human brain with these components in view.

In the accompanying video, our focus will be on localizing the amygdala and the hippocampus in the medial temporal lobe. Here in this tutorial text, we will provide a brief overview of the limbic forebrain and discuss some of the known major functions associated with the major collections of cortical and subcortical structures associated with this complex ventral-medial rim ("limbus") of forebrain.

Anatomy of the limbic forebrain

Attempts to understand the control of emotional behavior have a long history. In 1937, James Papez first proposed that specific brain circuits are devoted to emotional experience and expression. In seeking to understand what parts of the brain serve this function, he began to explore the medial aspects of the cerebral hemisphere. In 1878, Paul Broca used the term "limbic lobe" (*le grand lobe limbique*) to refer to the part of the cerebral cortex that forms a rim ("limbus" is Latin for rim) around the corpus callosum and diencephalon on the medial face of the hemispheres. Two prominent components of this region are the **cingulate gyrus**, which lies above the corpus callosum, and the **parahippocampal gyrus**, which lies in

[1] Visit **BrainFacts.org** for *Neuroscience Core Concepts* (©2012 Society for Neuroscience) that offer fundamental principles about the brain and nervous system, the most complex living structure known in the universe.

the medial temporal lobe. For many years, these two structures, along with the olfactory bulbs, were thought to be concerned primarily with the sense of smell. Indeed, Broca considered the olfactory bulbs to be the principal source of input to the limbic lobe. Papez, however, speculated that the function of the limbic lobe might be more related to emotions. He knew that the **hypothalamus** influences the expression of emotion; he also of course knew that emotions reach consciousness and that higher cognitive functions affect emotional behavior. Ultimately, Papez showed that the cingulate cortex and hypothalamus are interconnected via projections from the mammillary bodies (part of the posterior hypothalamus) to the anterior nucleus of the thalamus, which projects in turn to the cingulate gyrus; the cingulate gyrus (like many other cortical regions) projects to the **hippocampus**. Finally, he showed that the hippocampus (actually, the *subiculum*, a division of the hippocampal formation) projects via the **fornix** (a large fiber bundle) back to the hypothalamus and septal region. Papez suggested that these pathways, which became known as the "Papez circuit," provide the connections necessary for cortical control of emotional expression.

Figure 1. Medial view of the human brain sectioned along the midsagittal plane. In this view, several components of the limbic forebrain are visible, but other important components are not. Refer to the terms in bold typeface in the main text and see if you can locate them in this image. You should also note the location (by reference to the accompanying video) of those structures highlighted in bold that are not visible in this image. You should review tutorials in Unit 1 as needed if you are not confident in your ability to localize these anatomical structures that are associated with the limbic forebrain.

Over time, the concept of a forebrain circuit for the control of emotional expression has been revised to include parts of the **orbital and medial prefrontal cortex**; ventral portions of the basal ganglia—most importantly, the **nucleus accumbens**; the **mediodorsal nucleus of the thalamus** (a different thalamic nucleus than the one Papez emphasized); and the **amygdala**, a large nuclear mass in the temporal lobe anterior to the hippocampus. This set of structures, together with the parahippocampal gyrus and cingulate cortex, is generally referred to as the "limbic system" (see **Figure 1**). However, this so-called system (so-called primarily for historical reasons) is not unimodal, as the term 'system' implies. Rather, the limbic 'system' is involved in the regulation of visceral motor activity, emotional experience and expression, olfaction, and memory, to name some of its better understood functions. Furthermore, some of the structures that Papez originally described (the hippocampus, for example) now appear to have little primary role in emotional processing, whereas the amygdala, which Papez hardly mentioned, clearly plays a major role in the experience and expression of emotion[2].

In order to know which groups of structures in the limbic forebrain are associated mainly with particular aspects of sensation and cognition, it is helpful to recognize three basic groupings or divisions:

- an ***olfactory division***, concerned with the encoding of olfactory signals and engaging behaviors motivated by air-borne stimuli;
- a ***parahippocampal division***, centered in the medial temporal lobe, that is mainly concerned with explicit representation and the acquisition and retrieval of declarative (episodic) memory;
- an ***amygdala/orbital prefrontal division*** encompasses a network of telencephalic and diencephalic structures with the amygdala and related sectors of the orbital and medial prefrontal cortex as key nodes; this division is primarily concerned with implicit representation, which becomes manifest in the experience and expression of emotion and emotional behavior.

Thus, it is the amygdaloid/orbital prefrontal division that is most germane for understanding the brain basis of emotion and motivated behavior. Through an illuminating history of empirical findings and clinical observations in both experimental animals and humans, it is now clear that the amygdala mediates neural processes that invest sensory experience with emotional significance in a form of associative learning, particularly when the sensory experience signals threat. Indeed, it is not too much of a stretch to characterize the amygdala (and its telencephalic and diencephalic connections) as an "early warning system" being especially well-tuned to social cues and environmental stimuli that signal threat.

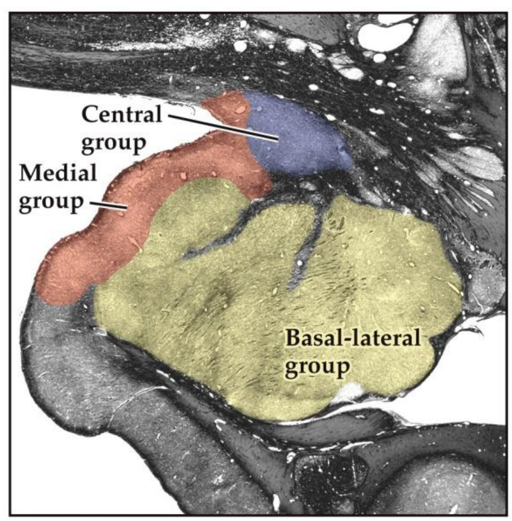

Figure 2. The human amygdala in histological section. View of the temporal lobe in a coronal section that was stained with silver salts to reveal the presence of myelinated fiber bundles, which subdivide major nuclei and cortical regions. Three major groups of subdivisions can be recognized: a basal-lateral group, a medial group, and a central group. (image courtesy of J.L. Price and L.E. White)

[2] Many authors now advocate dismissal of the term "limbic system" as an outmoded and misleading concept, and rather emphasize the diverse functions associated with the various components of an expansive constellation of structures in the ventral-medial forebrain.

Neuroanatomically, the amygdala is a complex mass of gray matter buried in the anterior-medial portion of the temporal lobe, just rostral to the hippocampus (**Figure 2**). It comprises multiple, distinct subnuclei and cortical regions that are richly connected to nearby cortical areas on the ventral and medial aspect of the hemispheric surface. The amygdala (or amygdaloid complex) can understood in terms of three major functional and anatomical subdivisions, each of which has a unique set of connections with other parts of the brain. The *medial group* of subnuclei has extensive connections with the olfactory bulb and the olfactory cortex. The *basal-lateral group*, which is especially large in humans, has major connections with the cerebral cortex, especially the orbital and medial prefrontal cortex and the associational cortex of the anterior temporal lobe (**Figure 3**). These cortical territories associate information from every sensory modality (including information about visceral activities) and can thus integrate a variety of inputs pertinent to moment-to-moment experiences. In addition, the basal-lateral group projects to the thalamus (specifically, to the mediodorsal nucleus), which projects in turn to these same cortical areas. This same group also innervates neurons in the nucleus accumbens that receive the major cortico-striatal projections from the prefrontal cortex and parahippocampal gyrus. Lastly, the *central group* of nuclei is characterized by connections with the hypothalamus and brainstem, linking the amygdala with autonomic, neuroendocrine and somatic effector systems.

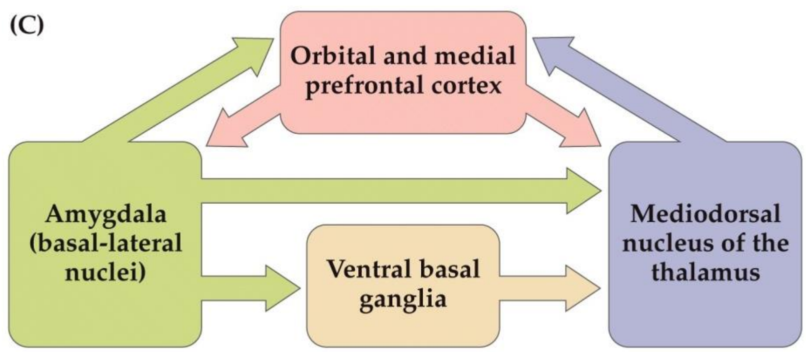

Figure 3. The amygdala (specifically, the basal-lateral group of nuclei) participates in a "triangular" circuit linking the amygdala, the thalamic mediodorsal nucleus (directly and indirectly via the ventral parts of the basal ganglia), and the orbital and medial prefrontal cortex. These complex interconnections allow direct interactions between the amygdala and prefrontal cortex, as well as indirect modulation via the circuitry of the ventral basal ganglia.

Considering all these seemingly arcane anatomical connections, the amygdala emerges as a key node in a network that links together the cortical and subcortical brain regions involved in emotional processing and the expression of emotional behavior. More generally, the amygdala and its connections to the prefrontal cortex and basal ganglia are likely to influence the selection and initiation of behaviors aimed at obtaining rewards and avoiding punishments (recall that the process of program selection and initiation is an important function of basal ganglia circuitry). The parts of the prefrontal cortex interconnected with the amygdala are also involved in organizing and planning future behaviors. Thus, the amygdala may provide emotional input to overt (and covert) deliberations of that bias decision-making in prefrontal networks.

Finally, it is likely that interactions between the amygdala, the neocortex and related subcortical circuits account for what is perhaps the most enigmatic aspect of emotional experience: the highly subjective "feelings" that attend most emotional states. Although the neurobiology of such experience is not understood, it is reasonable to assume that emotional feelings arise as a consequence of a more general cognitive capacity for self-awareness. In this conception, feelings entail both the immediate conscious experience of implicit emotional processing (arising from amygdala–neocortical circuitry) and the explicit processing of semantically based thought (arising from hippocampal–neocortical circuitry). It is plausible to conceptualize feelings as the product of an 'emotional working memory' that sustains neural activity related to the processing of these various elements of emotional experience. Given the evidence for working memory functions in the prefrontal cortex, this portion of the frontal lobe—especially the orbital and medial sector—is the likely neural substrate where such associations are maintained in conscious awareness.

STUDY QUESTION

Which of the following statements best differentiates the hippocampus from the amygdala?

A. The hippocampus is anterior to the amygdala in the medial temporal lobe.
B. The amygdala is involved in implicit representation, and the hippocampus is involved in explicit representation.
C. The amygdala is a cortical structure, and the hippocampus is a subcortical structure.
D. The hippocampus forms the floor of the temporal horn of the lateral ventricle, and the amygdala forms the medial wall of the third ventricle.
E. The amygdala communicates with the hypothalamus via the fornix, and the hippocampus communicates with the hypothalamus via the anterior commissure.