

The Hippocampus

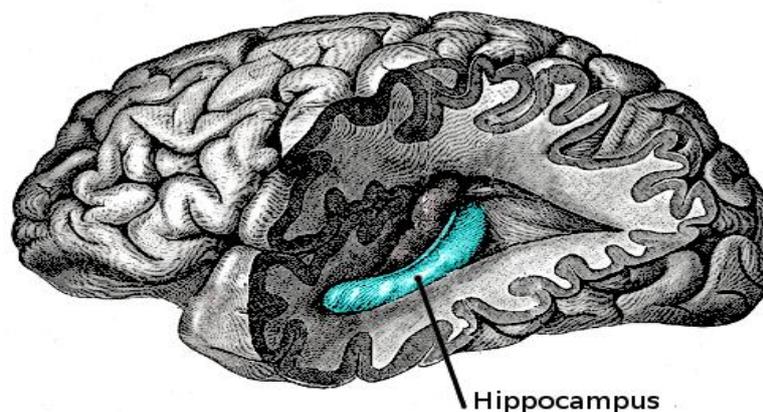
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INTRODUCTION

Hippocampus is a neural structure in the medial temporal lobe of the brain that has a distinctive, curved shape that has been likened to the *sea horse monster* of Greek mythology and the '*ram's horns of Ammon*' in Egyptian mythology. This general layout holds across the full range of mammalian species, from hedgehog to human, although the details vary. For example, in the rat, the two hippocampi look similar to a pair of bananas, joined at the stems. In primate brains, including humans, the portion of the hippocampus near the base of the temporal lobe is much broader than the part at the top. Due to the three-dimensional curvature of this structure, two-dimensional sections such as shown are commonly seen. Neuroimaging pictures can show a number of different shapes, depending on the angle and location of the cut.

The **hippocampus** is a major component of the brains of humans and other mammals. It belongs to the limbic system and plays important roles in long-term memory and spatial navigation. Like the cerebral cortex, with which it is closely associated, it is a paired structure, with mirror-image halves in the left and right sides of the brain. In humans and other primates, the hippocampus is located inside the medial temporal lobe, beneath the cortical surface. In Alzheimer's disease the hippocampus is one of the first regions of the brain to suffer damage; memory problems and disorientation appear among the first symptoms. Damage to the hippocampus can also result from oxygen starvation (hypoxia), encephalitis, or medial temporal lobe epilepsy. People with extensive hippocampal damage may experience amnesia—the inability to form or retain new memories.



Historically, the earliest widely held hypothesis was that the hippocampus is involved in olfaction. This idea was largely motivated by a belief, later shown to be false, that the hippocampus receives direct input from the olfactory bulb. There continues to be some interest in hippocampal olfactory responses, particularly the role of the hippocampus in memory for odours, but few people believe today that olfaction is its primary function. Over the years, three main ideas of hippocampal function have dominated the literature: inhibition, memory, and space. There has been development of a full-fledged theory of the role of the hippocampus in anxiety. The inhibition theory is currently the least popular of the three. The second major line of thought relates the hippocampus to memory. Hippocampal damage and amnesia (caused by accident or disease) have been studied as well, and thousands of experiments have studied the physiology of activity-driven changes in synaptic connections in the hippocampus. There is now almost universal agreement that the hippocampus plays some sort of important role in memory; however, the precise nature of this role remains widely debated. The third important theory of hippocampal function relates the hippocampus to space. As with the memory theory, there is now almost universal agreement that spatial coding plays an important role in hippocampal function, but the details are widely debated.

SPECIFIC ANATOMY

Anatomically, the hippocampus is an elaboration of the edge of the cerebral cortex. It can be distinguished as a zone where the cortex narrows into a single layer of very densely packed neurons, which curls into a tight S shape. The structures that line the edge of the cortex make up the so-called limbic system (Latin *limbus* = *border*): these include the hippocampus, cingulate cortex, olfactory cortex, and amygdala. Paul MacLean once suggested, as part of his triune brain theory, that the limbic structures comprise the neural basis of emotion. Most neuroscientists no longer believe that the concept of a unified "limbic system" is valid, though.

The hippocampus as a whole has the shape of a curved tube, which has been analogized variously to a seahorse, a ram's horn (*Cornu Ammonis*, hence the subdivisions CA1 through CA4), or a banana. It consists of ventral and dorsal portions, both of which share similar composition but are parts of different neural circuits. This general layout holds across the full range of mammalian species, from hedgehog to human, although the details vary. The entorhinal cortex (EC), the greatest source of hippocampal input and target of hippocampal output, is strongly and reciprocally connected with many other parts of the cerebral cortex, and thereby serves as the main "interface" between the hippocampus and other parts of the brain. The hippocampus receives input from the serotonin, norepinephrine, and dopamine systems, and from nucleus reuniens of the thalamus. A very important projection comes from the medial septal area, which sends cholinergic and GABAergic fibers to all parts of the hippocampus. The inputs from the septal area play a key role in controlling the physiological state of the hippocampus. The cortical region adjacent to the hippocampus is known collectively as the parahippocampal gyrus (or parahippocampus). It includes the EC and also the perirhinal cortex, which derives its name from the fact that it lies next to the rhinal sulcus. The perirhinal cortex plays an important role in visual recognition of complex objects, but there is also substantial evidence that it makes a contribution to memory which can be distinguished from the contribution of the

hippocampus, and that complete amnesia occurs only when both the hippocampus and the parahippocampus are damaged.

PSYCHIATRIC SIGNIFICANCE OF THE HIPPOCAMPUS

Aging and Dementia

Age-related conditions such as Alzheimer's disease (for which hippocampal disruption is one of the earliest signs) have a severe impact on many types of cognition, but even normal, healthy aging is associated with a gradual decline in some types of memory, including episodic memory and working memory. Because the hippocampus is thought to play a central role in memory, there has been considerable interest in the possibility that age-related declines could be caused by hippocampal deterioration.

Stress Related Damage, Depression and Post Traumatic Stress Disorder

The hippocampus contains high levels of glucocorticoid receptors, which make it more vulnerable to long-term stress than most other brain areas. Stress-related steroids affect the hippocampus in at least three ways: first, by reducing the excitability of some hippocampal neurons; second, by inhibiting the genesis of new neurons in the dentate gyrus; third, by causing atrophy of dendrites in pyramidal cells of the CA3 region. There is evidence that humans who have experienced severe, long-lasting traumatic stress show atrophy of the hippocampus, more than of other parts of the brain. These effects show up in post-traumatic stress disorder, and they may contribute to the hippocampal atrophy reported in schizophrenia and severe depression.

Epilepsy

The hippocampus is often the focus of epileptic seizures: hippocampal sclerosis is the most commonly visible type of tissue damage in temporal lobe epilepsy. It is not yet clear, though, whether the epilepsy is usually caused by hippocampal abnormalities, or the hippocampus is damaged by cumulative effects of seizures. This may be a consequence of the hippocampus being one of the most electrically excitable parts of the brain. It may also have something to do with the fact that the hippocampus is one of very few brain regions where new neurons continue to be created throughout life.

Schizophrenia

The causes of schizophrenia are not at all well understood, but numerous abnormalities of brain structure have been reported. The most thoroughly investigated alterations involve the cerebral cortex, but effects on the hippocampus have also been described. Many reports have found reductions in the size of the hippocampus in schizophrenic subjects. It is unclear whether hippocampal alterations play any role in causing the psychotic symptoms that are the most important feature of schizophrenia.

REFERENCES

1. Andersen P, Morris R, Amaral D, Bliss T, O'Keefe J. The Hippocampus Book : Oxford Neuroscience Series. Oxford: Oxford University Press ; 2006.