Brief Overview about Anatomy of Hippocampus & Cerebrum

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Abstract

Background: The cerebrum is the brain's largest component, consisting of two cerebral hemispheres joined by the corpus callosum, a mass of white matter. Each cerebral hemisphere extends from the frontal to occipital bones over the anterior and middle cranial fossae, as well as posteriorly above the tentorium cerebelli. A deep gap, the longitudinal fissure, separates the hemispheres, through which the falx cerebri projects. The hippocampus is a key component of human and other animal brains. The hippocampus is a component of the limbic system that aids in the consolidation of information from short-term to long-term memory as well as spatial memory. Hippocampi are two structures in the brain that are found on opposite sides of the brain in humans and other mammals. The hippocampus is C-shaped in frontal section, and its outline resembles a Ram's horn, hence the name Ram's horn. It is also called Ammon's Horn after an Egyptian deity with a ram's head. Its anterior extremity is elongated, with a few grooves and ridges between them. It's called pes hippocampi (pes = foot) because it looks like an animal's paw. The hippocampus narrows as it travels backward, eventually ending beneath the splenium of the corpus callosum.

Keywords: Hippocampus, Cerebrum, Anatomy

Introduction

The cerebrum is the brain's largest component, consisting of two cerebral hemispheres joined by the corpus callosum, a mass of white matter. Each cerebral hemisphere extends from the frontal to occipital bones over the anterior and middle cranial fossae, as well as posteriorly above the tentorium cerebelli. A deep gap, the longitudinal fissure, separates the hemispheres, through which the falx cerebri projects **(1)**.

Saladin (2) stated that each hemisphere's exterior surface is highly convoluted, with a series of folds, or gyri, divided by sulci. About 2500 cm2 is the surface area of the gyri in the cerebrum. The extent of folding in the human brain is one of the greatest differences between it and other mammals with relatively smooth surfaces.

In addition, **Sinnatamby (3) and Standring (4)** stated that there are three surfaces on the cerebral hemisphere: the superolateral, the medial, and the inferior. The superolateral surface of the hemispheres follows the shape of the skull and is convex. The medial surfaces of either hemisphere lie flat against the falx cerebri and are less irregular than the inferior surfaces. The stem of the lateral sulcus divides the inferior surface into orbital and tentorial areas. The orbital part is concave and is located above the nasal and orbital roofs in the anterior cranial fossa. The tentorial portion is located in the middle cranial fossa, above the tentorium cerebelli, and separates it from the cerebellum.

Furthermore, **Saladin (2)** added that each hemisphere of the brain is divided into lobes. According to the names of the skull bones covering them, they are the frontal, temporal, parietal, and occipital lobes. The insula, the fifth part of the cerebrum, is not visible from the surface of the brain because it lies deep in the frontal, parietal, and temporal lobes.

Gross anatomy of the hippocampus:

The hippocampus is a key component of human and other animal brains. The hippocampus is a component of the limbic system that aids in the consolidation of information from short-term to long-term memory as well as spatial memory. Hippocampi are two structures in the brain that are found on opposite sides of the brain in humans and other mammals. The name "hippocampus" meaning "sea horse", is derived from its appearance in coronal section **(5)**.

Fig. (I): The hippocampus is a neural structure in the medial temporal lobe of the brain that has a distinctive curved shape that resembles the shape of a sea horse **(6).**

The limbic system is called a "primitive brain," located deep within the brain. The hippocampus is the posterior part of the limbic lobe, whereas the amygdala is the frontal part. Human adults have a hippocampus volume of 3-3.5 cm3 on each side of the brain, compared to a cortex volume of 320-420 cm3. Therefore, the hippocampus has a 100-fold smaller volume than the cerebral cortex **(7).**

The hippocampal region, hippocampal formation, and hippocampus are three different anatomical terms. The hippocampal region consists of two main structures: the hippocampal formation (HF) and the parahippocampal region (PHR) **(7).**

Wright (8) stated that the hippocampus proproius, dentate gyrus (DG), subiculum proprium, pressubiculum, parasubiculum, and region entorhinal cortex are the six structures that make up the hippocampal formation.

The hippocampus is C-shaped in frontal section, and its outline resembles a Ram's horn, hence the name Ram's horn. It is also called Ammon's Horn after an Egyptian deity with a ram's head. Its anterior extremity is elongated, with a few grooves and ridges between them. It's called pes hippocampi (pes = foot) because it looks like an animal's paw. The hippocampus narrows as it travels backward, eventually ending beneath the splenium of the corpus callosum **(5)**.

The hippocampus is located above the subiculum and medial parahippocampal gyrus, forming a curving elevation along the floor of the inferior horn of the lateral ventricle that is roughly 5 cm long. Its frontal end is enlarged and may present two or three shallow grooves that provide a paw-like shape, the pes hippocampi. DG is a scalloped cortex band that is related medially to the fornix fimbria, laterally to the hippocampus proprius, and inferiorly to the subiculum. Between DG and Cornu Ammonis, the hippocampal sulcus appears. Cornu Ammonis is divided into CA1, CA2, CA3, and CA4. The entorhinal cortex connects the subiculum to the hippocampus **(4)**.

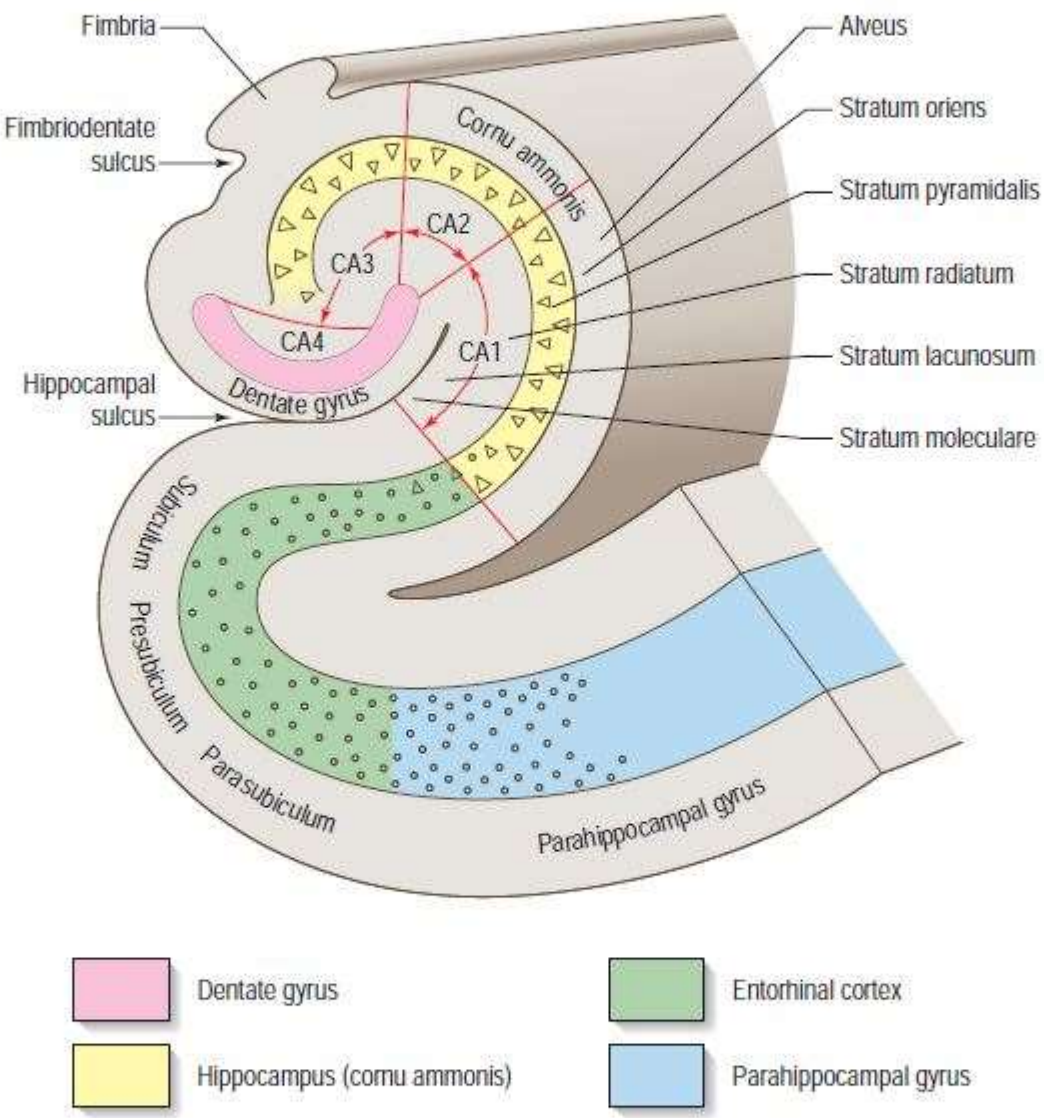

Fig. (II): The hippocampal formation in humans shows the deposition of varying cell fields **(4)**.

The limbic system is the emotional and learning centre of the brain. It is a ring of cortex that encircles the corpus callosum and thalamus on the medial side of each hemisphere. The cingulate gyrus, which arches over the top of the corpus callosum in the frontal and parietal lobes; the hippocampus in the medial temporal lobe; and the amygdala directly rostral to the hippocampus, also in the temporal lobe, are the most physically significant components. There are still differences of opinion on what structures to consider as parts of the limbic system, but these three are agreed upon. The mammillary bodies and other hypothalamus nuclei, some thalamic nuclei, parts of the basal nuclei, and parts of the frontal lobe known as the prefrontal and orbitofrontal cortex are among the other components. The components of the limbic system are linked by a complex loop of fibre tracts, allowing for circular patterns of feedback between their nuclei and cortical neurons. All of these structures are bilaterally paired; each brain hemisphere has its own limbic system **(2)**.

Meninges, cerebrospinal fluid, and ventricular system:

1-Meninges:

Three protective membranes surround the brain and spinal cord, called meninges. From the inside out, these are: pia mater, arachnoid mater, and dura mater. They protect the brain while also providing a structural framework for arteries, veins, and dural venous sinuses **(9)**.

The dura mater is a thick fibrous membrane with two layers: an outer periosteal layer and an inner meningeal layer. Except for where they enclose dural venous sinuses, the two layers are fused together. Through sutures and the foramina of the skull, the outer layer of dura is connected to the periosteum on the outer surface of the skull and supplies sheaths for cranial nerves, which merge with the epineurium. The inner meningeal layer is actually the dura mater proper, which surrounds the brain and joins the dura mater enclosing the spinal cord at the foramen magnum. As the meningeal layer folds on itself, it forms the dural folds. Dural folds divide the cranial cavity into compartments in which different parts of the brain are located **(5)**.

There is a transparent membrane between the dura and the pia matter called the arachnoid membrane. It is separated from the pia by the subarachnoid space. The subdural space separates it from the dura above in some areas. The subarachnoid space encloses the blood vessels of the cerebral surface **(2)**.

The pia mater encircles the central nervous system from the surface to the deepest fissures and sulci. It is made up of thin vascular fibrous tissue that can be removed from the surface of the brain. As it extends over the cranial nerves and spinal nerve roots, it is fused with their epineurium, and it enters the substance of the brain through the entering cerebral arteries **(3)**.

2-CSF and ventricular system:

In the brain, there are four ventricles: two lateral ventricles, one third ventricle, and one fourth ventricle. The ventricular system's major component is the two lateral ventricles, one in each cerebral hemisphere. They occupy a considerable part of the cerebral hemisphere and are separated from each other by the septum pellucidum, which extends between the corpus callosum and the fornix. The third ventricle is an elongated, slit-like cavity located in the diencephalon. Through the interventricular foramina of Monro, the two lateral ventricles are connected to the third ventricle. The cerebral aqueduct of the midbrain connects the third ventricle with the fourth ventricle, which is a cavity within the hindbrain. Similarly, the fourth ventricle is continuous with the spinal cord's central canal **(5)**.

There is cerebrospinal fluid (CSF) present in the ventricular system, which is mainly secreted by the choroid plexuses located in the lateral, third, and fourth ventricles **(4).)**. The cerebrospinal fluid (CSF) is a clear, colourless liquid that is present in the ventricles and canals of the brain and bathes the external surface of the CNS. About 500 mL of CSF are produced per day by the brain, but the fluid is continuously reabsorbed at the same rate, so only 100 to 160 mL are present at one time. The lateral ventricles' CSF enters the third ventricle via the interventricular foramina, then travels via the cerebral aqueduct to the fourth ventricle **(2)**.

Gross anatomy of the rat cerebrum

The laboratory rat is an essential component of biomedical research today. A well-known model in various fields, such as cancer research, neurobehavioral research, and toxicological research. The use of animal models is a powerful tool for understanding human disease and basic biology **(10)**.

Concerning the anatomy of the rat, the central nervous system is composed of the brain and spinal cord and covered by three layers of meninges. The dura is the most outer, folding between the two brain hemispheres to produce the falx cerebri. It also separates the cerebrum from the cerebellum by the tentorium cerebelli. The innermost one of the meninges is the pia mater, which is adherent to the brain and the spinal cord. Between the two previous layers is a network of thin fibers known as the arachnoid **(11)**.

The most obvious variations are that rodent brains are tiny (2.0g in rats) and have little white matter. They are considered a lissencephalic species, which means that they do not have sulci or gyri. Thus, it is impossible to demarcate specific regions of the rodent cerebrum on the basis of surface topography. The main ventral attribute that differs between rodents and humans is the prominence of the olfactory bulbs and tracts. Due to the importance of smell as the main sensory modality in rodents, the olfactory bulbs are extremely large **(12)**.

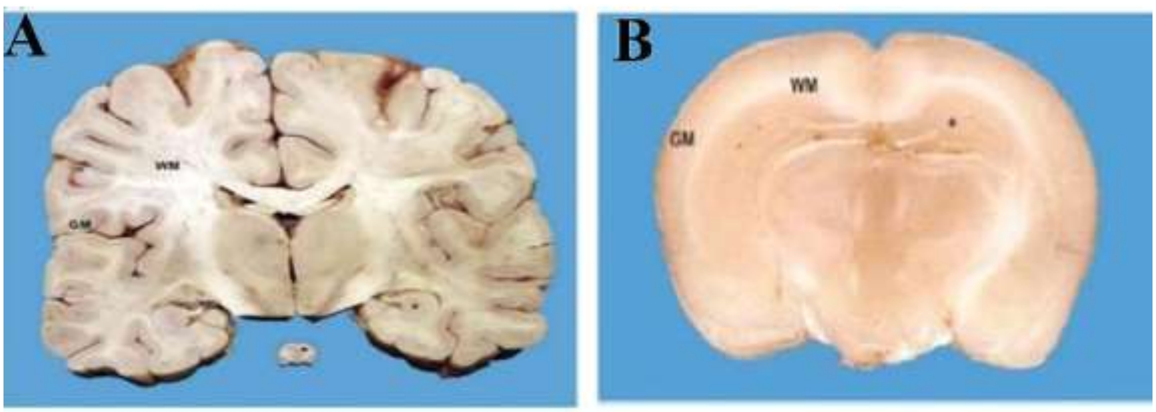

Fig. (III): Coronal brain slices from rodents and humans demonstrating the marked differences in organ size and organization. A) Human; B) Rodent. Gray matter (GM) White matter (WM) **(12)**.

In the median sagittal plane of the rat brain, there is a prominent corpus callosum, which is a white band of fibers connecting the two cerebral hemispheres. The rostral (anterior) commissure is a very small white fiber tract that lies anterior to the corpus callosum. Also recognizable are the crura cerebri, which are thickened fiber masses that are found on the floor of the brain and connect the fore- and hindbrains **(13)**.

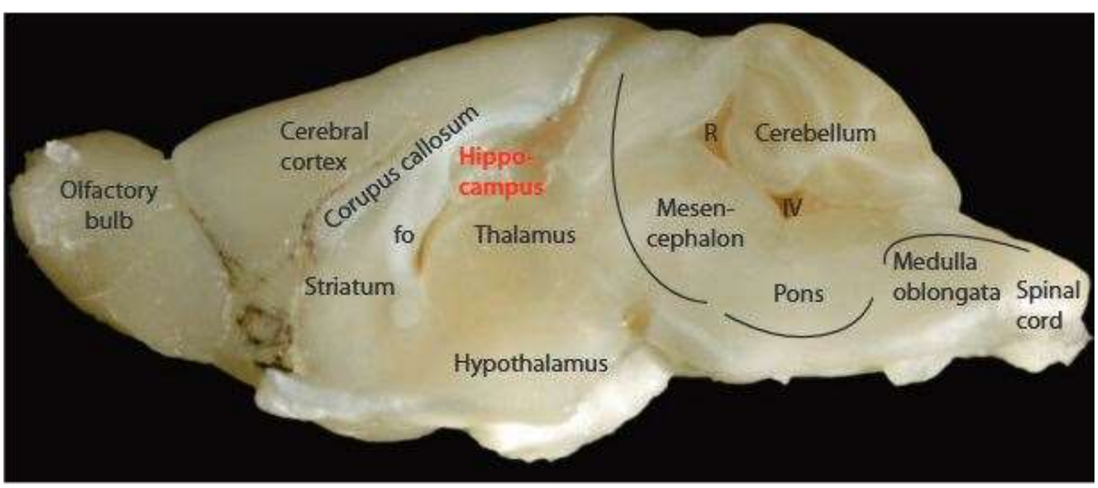

Fig. (IV): Midsagittal view of the mouse brain **(14).**

The ventricular system of the rat consists of one central ventricle, which is the third ventricle, which is connected with two lateral ones, and the fourth, which is caudal to them. Through the interventricular foramen, the two lateral ventricles are connected to the third one. Connecting the third and fourth ventricles is the cerebral aqueduct, which is about 3mm in length. The ventricular system communicates with the cerebral subarachnoid space only through two lateral holes. CSF is secreted from the choroid plexus within the lumen of all ventricles **(11)**.

Gross anatomy of the rat hippocampus:

In terms of anatomical structure and function in memory formation, the hippocampus region of the brain is identical in humans and rats. The rat's hippocampus, like that of humans, develops age-related changes and degenerations in its circuits. The human hippocampus is 100 times larger than the rat's **(12)**.

The hippocampus in the laboratory rat is placed more dorsally within the cerebrum, whereas it is oriented more ventrally in the human brain **(12)**.

The hippocampus is a paired structure with mirror-image halves on the right and left sides of the brain; it is located beneath the cortical surface in the medial temporal lobe **(15).**

Histological aspect of the cerebrum

There are two major types of nerve cells in the nervous system. These are the nerve cells that are called neurons and the support cells that are called neuroglia. A neuron is a functional and structural unit of the nervous system. In a nerve cell, you have three components: the cell body, also called the cell soma, the cytoplasmic processes (the dendrites), and the axon **(16).**

Structure of the neuron:

Neurons are highly polarized cells that include a soma, or cell body, from which cytoplasmic processes arise. The nerve fibers, known as processes, can be as large as 1.5 meters in length. The processes conveying impulses towards cell bodies are dendrites, while a single process conveying impulses away from cell bodies is an axon **(17)**.

In the CNS, the cell soma may take various shapes and sizes, but it tends to be polygonal in shape. This consists of a nucleus surrounded by cytoplasm. Most nerve cells have a large spherical, euchromatic (pale-staining) nucleus with a prominent nucleolus. Also, it contains a highly developed rough endoplasmic retinaculum arranged as a collection of parallel cisternae. In the cytoplasm between the cisternae, there are numerous polyribosomes. Under a light microscope, RER and free ribosomes appear as clumps of basophilic material called Nissl bodies or chromatophilic substances **(16).**

Ovalle & Nahirney (17) stated that nissl bodies differ in quantity depending on the type of neuron and are particularly abundant in large nerve cells like motor neurons. The Golgi apparatus is specialized to the cell body, but mitochondria can be found anywhere within the cell, and they are commonly found in axon terminals. Both the cell body and the processes contain intermediate filaments. These filaments are called neurofilaments in nerve cells. Nerve cells also contain microtubules similar to those found in other cells. Sometimes pigmented material is found in nerve cells, for example, lipofuscin.

Types of neurons in the nervous system:

Based on the number of processes extending from the cell body, neurons can be classified. There are three types: unipolar, bipolar, and multipolar. The most common neurons in the adult brain are the pseudounipolar (unipolar) neurons, which have only one process from the cell body. This process is divided into two long axonal branches. Unipolar neurons are mostly sensory neurons located close to the CNS. The dorsal root ganglia and the cranial nerve ganglia contain the cell bodies of unipolar neurons. Bipolar neurons have only one dendrite and one axon. They are sensory neurons found in the retina, olfactory epithelium, and inner ear. Multipolar neurons are the most common type of neurons in the CNS. They have multiple dendrites and only one axon on the opposite side. They include motor neurons and interneurons of the cerebrum, cerebellum, and spinal cord **(18)**.

Types of neuroglial cells:

Mescher (19) stated that neuronal survival and activity are supported by glial cells. They are ten times more abundant than neurons in the mammalian brain. In the CNS, glial cells surround both the neuronal cell bodies, which are often larger than the glial cells, and the processes of axons and dendrites occupying the spaces between neurons. Astrocytes, oligodendrocytes, microglia, ependymal, and Schwann cells are six types of glial cells. The first four types are found in the CNS, and the last two in the PNS.

The astrocytes are responsible for supporting the nervous system. They are star-shaped and have many fine dendrites. The ends of processes have small swellings called foot-processes **(5)**. Both fibrous and protoplasmic types of cells make up these foot-processes. The fibrous type has long processes and is found in white matter. While the protoplasmic one has short processes and is found in the grey matter **(5)**.

Eroschenko (18) stated that oligodendrocytes are smaller and have fewer processes than astrocytes. Oligodendrocytes found in the CNS originated in the neural tube. They are responsible for myelination of the axons that are found in the CNS, and they are able to surround and myelinate several axons. Also, they protect the axons from electrical current.

Mescher (19) added that the microglia are small active cells that are evenly distributed throughout the gray and white matter. Unlike other glial cells, microglia migrate, scanning the neuropil and removing damaged synapses. They also play an important role in immune defense in the CNS by removing microbial invaders and secreting a number of immunoregulatory cytokines. By light microscopy, the nuclei appear as dense, small, elongated structures, in contrast to the pale, large spherical nuclei of other supporting cells, which are stained by haematoxylin and eosin (H&E).

Ependymal cells are simple cuboidal or low columnar epithelial cells that line the ventricles of the brain and the central canal in the spinal cord. They contain cilia and microvilli at their apices. There are cilia that facilitate the movement of CSF through the spinal canal, while microvilli are thought to have some absorption functions **(18).**

Organization of cerebral cortex layers:

In the cerebral cortex, there are six layers, each with its own neuron morphology, size, and density. They merge with one another rather than being sharply demarcated. The first is a molecular layer, in which cortical neurons make synaptic connections with one another; the nuclei are sparse and are those of neuroglia and horizontal Cajal cells. The external granule is the second layer and consists of many small pyramidal cells and stellate cells, which have many axons and dendritic connections. An external pyramidal layer is the third layer, which contains moderate-sized pyramidal cells and Martinotti cells. The fourth layer is the internal granular, which consists mainly of densely packed stellate cells. The fifth layer is an internal pyramidal layer that contains large pyramidal cells and smaller stellate cells and cells of Martinotti **(20).**

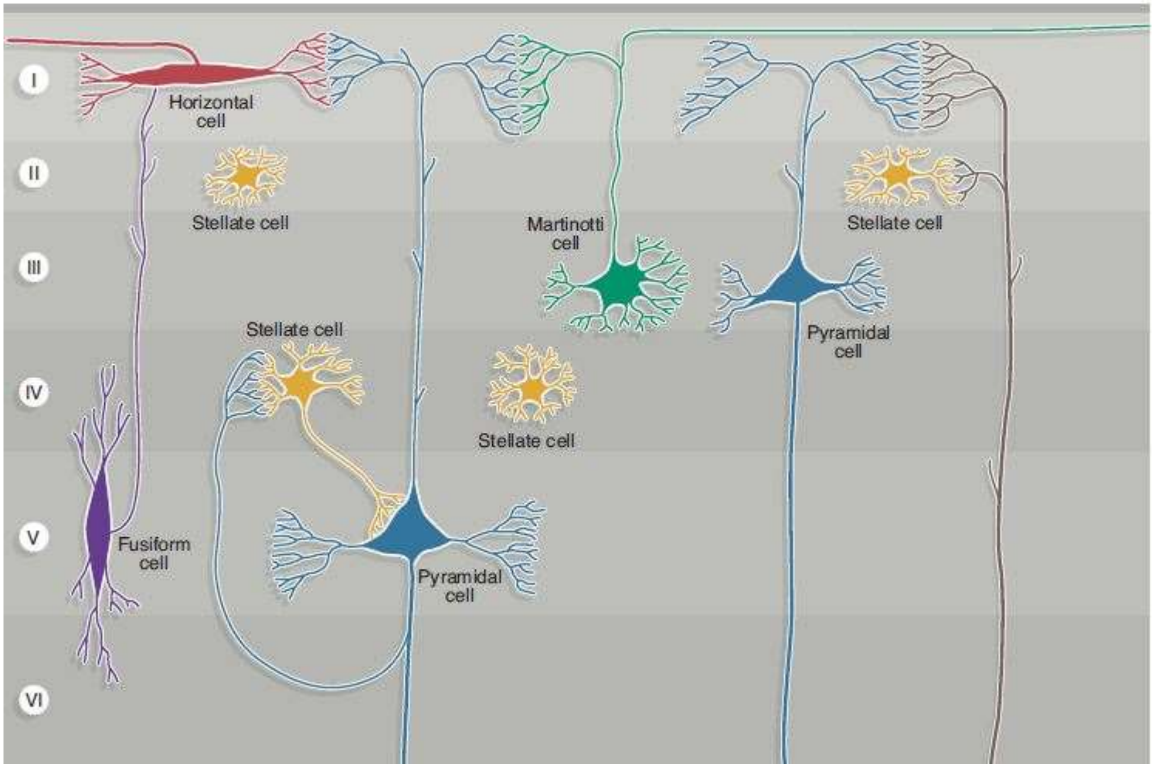

Fig. (V): Diagram of neuronal cell types **(20).**

<u>Histological structure of rat cerebrum:</u>

The parenchyma of the nervous system is composed of neurons and neuroglia. A neuroglia cell is composed of astrocytes, oligodendrocytes, microglia, and ependymal cells. In the adult rat brain, astrocytes are the most abundant glial cells. This star-shaped cell has multiple radially arranged cytoplasmic processes that are not easily seen by H&E staining. Under the electron microscope, astrocytes feature packed bundles of intermediate filaments (8 nm in diameter) and pale cytoplasm. Oligodendrocytes provide the myelin sheath in the CNS. They are recognized by their small, spherical, densely stained nuclei, and under the electron microscope, oligodendrocyte cytoplasm is electron-dense and rich in microtubules and organelles, especially RER and mitochondria. Microglia cells are responsible for the mechanisms of immune defence in the CNS. Ependymal cells form an epithelium that lines ventricular cavities within the brain **(13)**.

The rat cerebral cortex consists of six layers, arranged horizontally as in humans. Layer I (the molecular layer), the most superficial layer, contains scattered and small glial cells and fusiform-shaped neurons. Layer II (the external granular layer) contains densely packed, small pyramidal or stellate neurons. Layer III (the external pyramidal layer) is characterized by small and medium-sized pyramidal neurons. Layer IV (the internal granular layer) contains densely packed small granular cells. Layer V (the internal pyramidal layer) consists of large pyramidal neurons. Layer VI (the multiform layer) contains a few large pyramids and many small spindle-like pyramids and multiform (ovoid, triangular, or fusiform) neurons **(12,21)**.

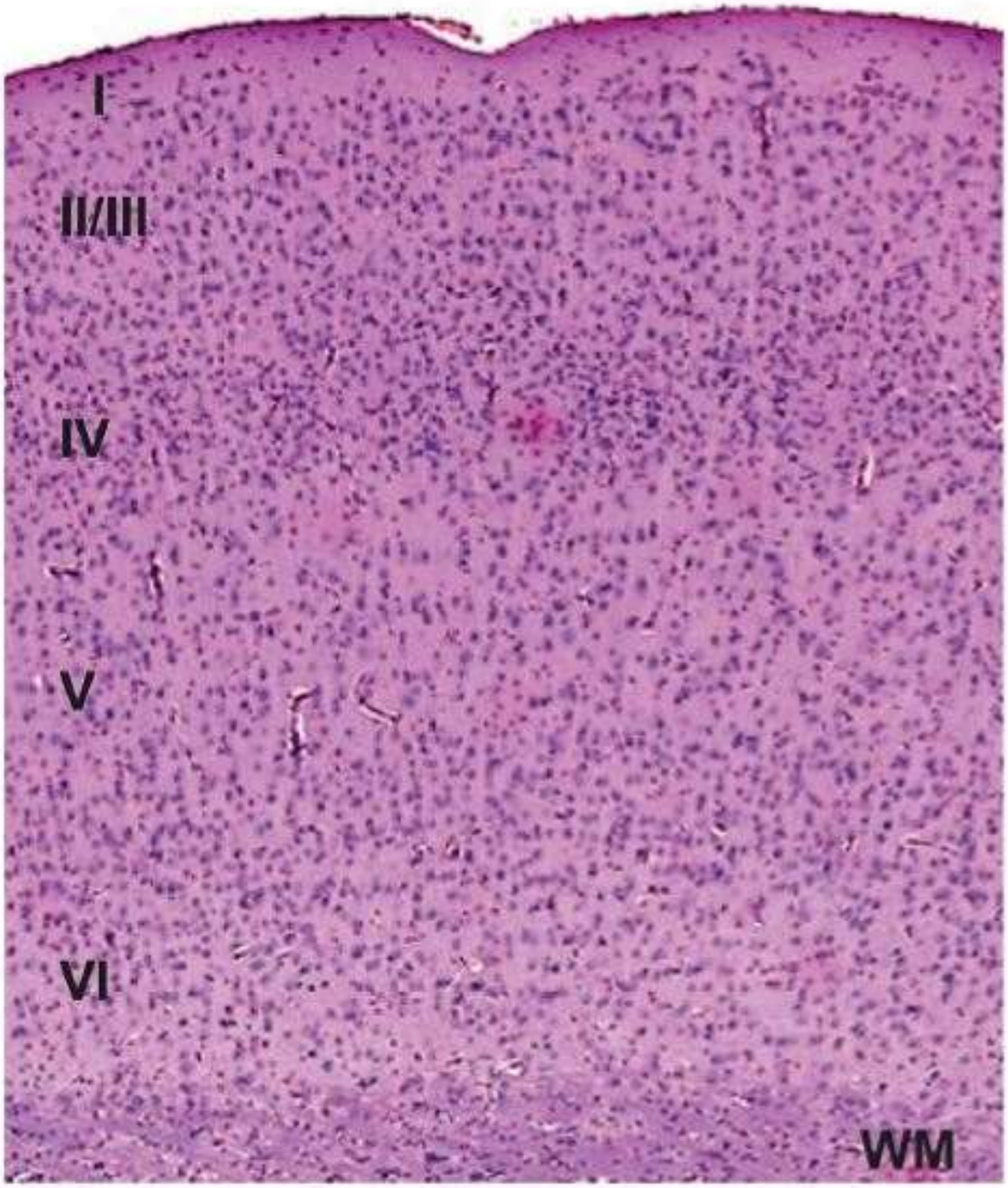

Fig. (VI): Neuronal organization in the cerebral cortex of the mouse. The typical six layers from pia to white matter (WM) are: **I** molecular layer, **II** external granular layer, **III** external pyramidal layer, **IV** internal granular layer, **V** internal pyramidal layer, and **VI** multiform layer **(12)**.

Cytoarchitectural organization of the hippocampus:

The trilaminar archicortex of the hippocampus is made up of a single layer of pyramidal cells sandwiched between plexiform layers. CA1, CA2, and CA3 are the three separate fields. At one end, field CA3 borders the hilus of the dentate gyrus, and at the other, field CA2. The biggest pyramidal cells in the hippocampus are field CA3 pyramidal cells, which receive mossy fibre input from dentate granule cells on their proximal dendrites. In this field, the entire pyramidal cell layer is around 10 cells thick. The line separating CA3 and CA2 isn't always clear. The pyramidal cell layer in the CA2 field is the most densely packed **(4)**.

CA regions are made up of three distinct layers: **Polymorphic layer**: contains pyramidal neuron axons, inhibitory basket cell bodies, horizontal trilaminar cells, and basal dendrites of pyramidal cells. **Pyramidal layer**: contains the pyramidal neurons' cell bodies, which are the hippocampus's primary excitatory neurons. This layer contains synapses from mossy fibers in the CA3 region (projections from the dentate gyrus granule cells to CA3). **Molecular layer**: contains septal and commisural fibers, Schaffer collateral fibers (the projection from CA3 to CA1), apical dendrites of pyramidal cells, some interneurons, and perforant path fibers (fibers from superficial layers of the entorhinal cortex superficial layers) **(6).**

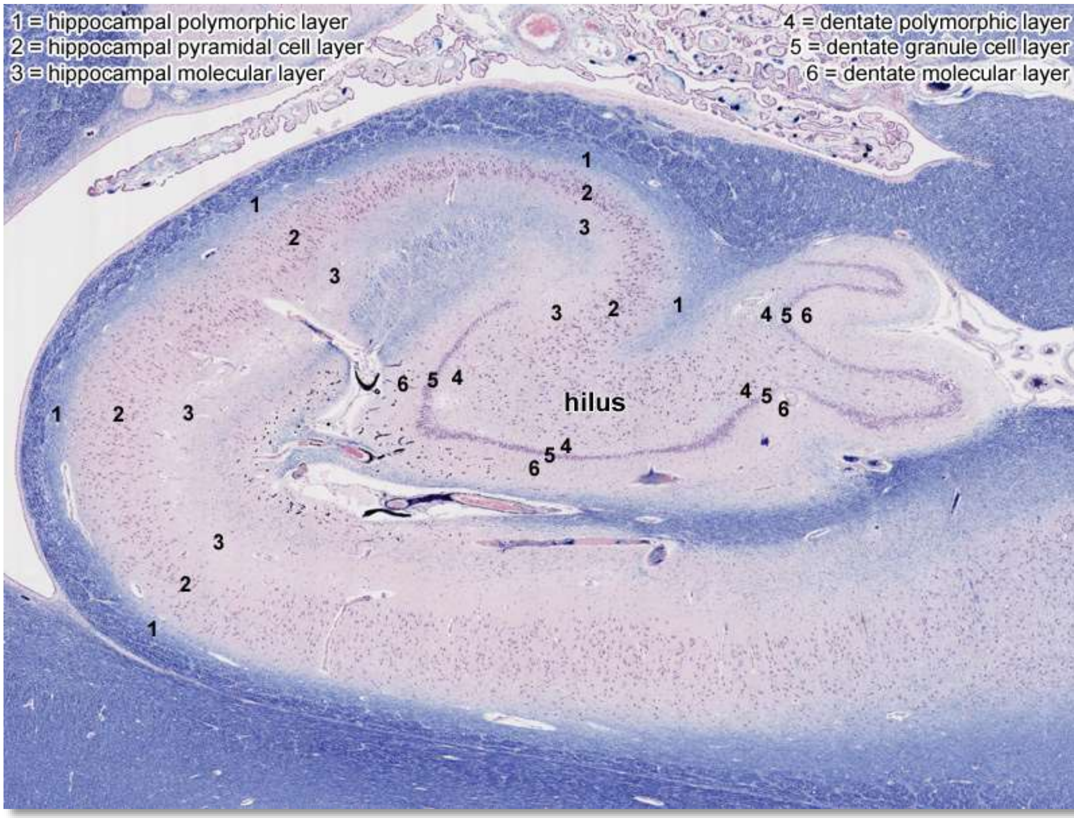

Fig. (VII): The Cytoarchitectural Organization of the Hippocampus **(22).**

The pyramidal cell is the most common type of neuron in the hippocampus and makes up the majority of neurons in the pyramidal cell layer. The hippocampus proper has a basal dendritic tree that extends into stratum oriens and an apical dendritic tree that extends to the hippocampal fissure. The pyramidal cell layer is characterized by pyramidal-shaped cells and nuclei with prominent nucleoli, intermingled with glial cells. The cytoplasm of neurons contains RER (rough endoplasmic reticulum), also known as Nissl substance. The number of Nissl granules is higher in large-sized neurons than in small-sized neurons. The RER is mostly restricted to the cell body but may also extend into the axonal hillock. The pyramidal cells have a basal dendritic tree that extends into the stratum oriens and an apical dendritic tree that extends to the hippocampal fissure. There is a narrow, relatively cell-free layer deep in the pyramidal cell layer called the stratum oriens. This layer is composed of pyramidal dendrites and multiple types of interneurons. In the proximal part of these dendrites, the commissural afferents from the contralateral hippocampus are terminated **(23)**.

Alveus lies in the deep part of stratum oriens and contains the myelinated axons of hippocampal pyramidal neurons in parallel with the stratum pyramidale, fibers of the alveolar tract from the entorhinal cortex, and projections from the septum. The stratum lucidum is a slight cellular zone located in the CA3 field but not in the CA2 or CA1 fields. It is presented just above the pyramidal cell layer and is occupied by the mossy fibers of DG . Superficial to the stratum lucidum in CA3 and just above the pyramidal cell layer in CA2 and CA1, the stratum radiatum is located. This layer contains primary shafts of pyramidal neurons in both the superior and inferior halves of Ammon's horn **(24).**

The stratum lacunosum is composed of branched apical dendrites of pyramidal neurons. This layer is the end of the perforant path that emerges from the entorhinal cortex. The stratum moleculare is formed by terminal branches of apical dendrites from the stratum pyramidale **(14).**

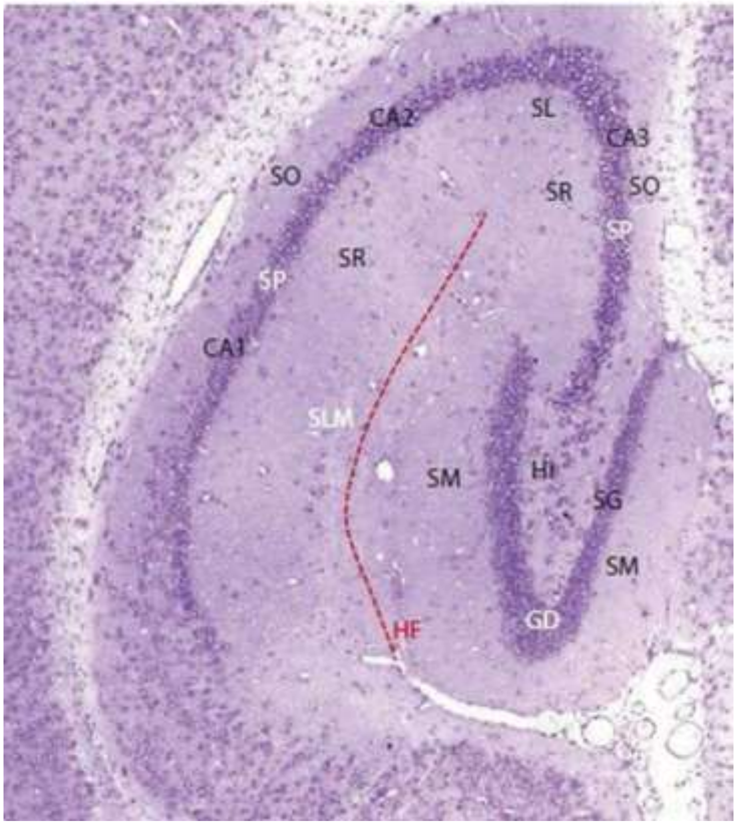

Fig. (VIII): Section of mouse hippocampal formation indicating the different layers of the Cornu Ammonis **(CA)** and the Gyrus dentatus **(DG). CA**: From external to internal, the stratum oriens **(SO)** with the axons of the pyramidal cells in the stratum pyramidale **(SP)** is followed by the stratum radiatum **(SR)** and the stratum lacunosum-moleculare **(SLM).** The stratum lucidum **(SL)** is only present in the CA3 region. **GD**: the stratum moleculare harbours the dendrites of the granule cells in the stratum granulare **(SG).** The axons of the granule cells, the mossy fibers, leave the SG via the hilus **(H)** or stratum multiforme. Hippocampal fissure **(HF) (14).**

The dentate gyrus consists of three layers: molecular, granular, and polymorphic. These layers are organized in a U or V form, with the open portion towards the fimbria. The molecular layer of the dentate gyrus is continuous with that of the hippocampus in the depth of the hippocampal fissure. It comprises commissural fibres from the contralateral DG and inputs from the medial septum, both of which terminate on the proximal dendrites of the granule cells. The main cell layer (granule cell layer) is a densely packed layer that is four to eight granule cells thick and lies deep under the molecular layer. The third layer of the dentate gyrus is made up of polymorphic cells **(12)**.

The molecular layer is mainly occupied by the dendrites of the granule, basket, and many polymorphic cells, as well as terminal axonal arbours from several sources. It is divided into the outer molecular layer (OML), the middle molecular layer (MML), and the inner molecular layer (IML). At least two types of neurons can be found in the molecular layer **(25)**.

The cell body of the dentate granule cell is elliptical, having a width of about 10 μm and a height of around 16 μm. Each granule cell is closely apposed to neighbouring granule cells, and there is usually no glial sheath between them. The granule cell has a very characteristic cone-shaped tree of spiny dendrites with all of the branches directed towards the superficial portion of the molecular layer; most of the distal tips of the dendritic tree end just at the hippocampal fissure or at the ventricular surface **(26)**.

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