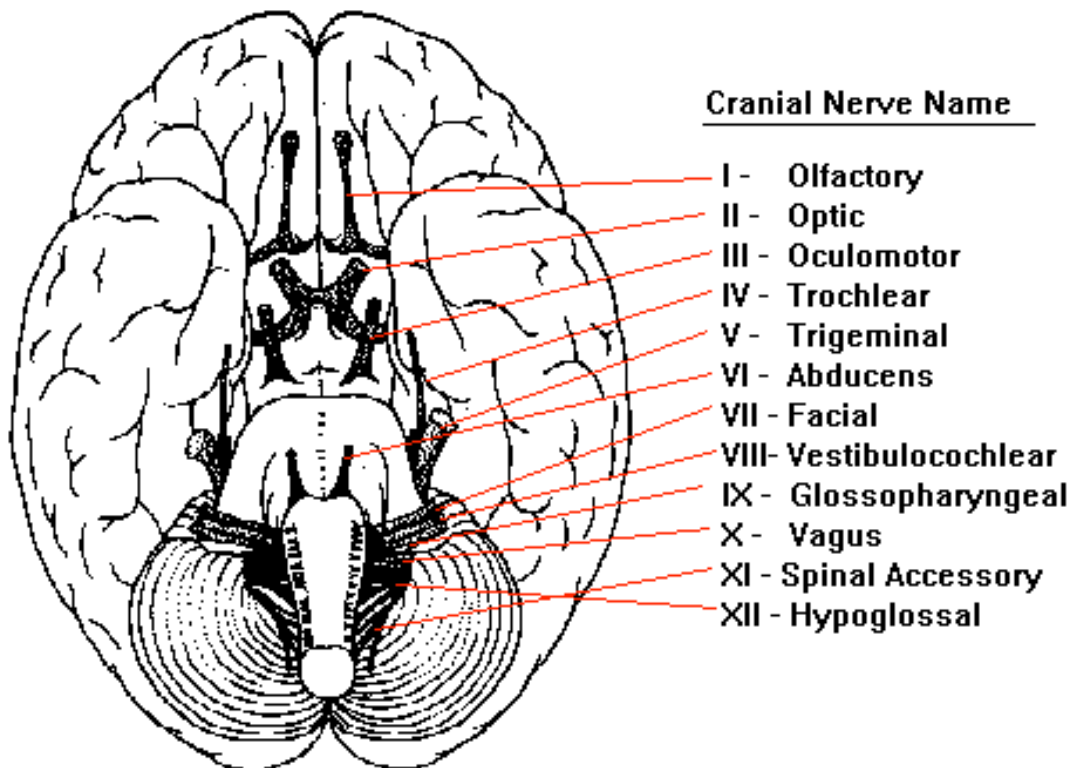**FORENSIC NEUROPATHOLOGY**
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CRANIAL NERVES O AND I

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GENERAL INFORMATION

Cranial nerves (CN) are those nerves, which arise from the brainstem with the exception of **CN I** and **II**, the nuclei (site of origin) of which are located in the forebrain and thalamus respectively. The forebrain consists of the cerebrum, thalamus, hypothalamus and the limbic system. Also the **CNs** are not considered part of the central nervous system **(CNS)** but are part of the **peripheral nervous system (PNS)** with the exception of **CN I** (**olfactory nerve**) and **CN II** (**optic nerve**). The primary function of the PNS is to connect the **CNS** (**brain and spinal cord**) with the 11 major organ systems of the body (Nervous, Reproductive, Respiratory, Skeletal, Urinary/Excretory, Cardiovascular, Digestive, Endocrine, Integumentary, Muscular, and the Lymph and Immune System).

Cranial Nerve Name

I - Olfactory
II - Optic
III - Oculomotor
IV - Trochlear
V - Trigeminal
VI - Abducens
VII - Facial
VIII - Vestibulocochlear
IX - Glossopharyngeal
X - Vagus
XI - Spinal Accessory
XII - Hypoglossal

The **CNs** are numbered traditionally **I** through **XII** in a rostral caudal direction. The term rostral refers to the front or anterior surface, whereas caudal refers to the hind end (tail) or posterior surface. Their primary function, with the exception of **CNs X** and **XI**, is to provide the motor and sensory systems of the head and neck. The motor system controls all voluntary movements via a two-neuron system consisting of upper motor neurons in the primary motor cortex and lower motor neurons in the anterior horns of the spinal cord. The sensory system is that part of the nervous system responsible for processing sensory information. It consists of sensory receptors, neural pathways and parts of the brain involved in sensory perception. The sensory system includes vision, hearing, touch (somatic sensation), taste and smell (olfaction). **CNs X (vagus)** and **XI (spinal accessory)** are mixed but largely autonomic nerves.
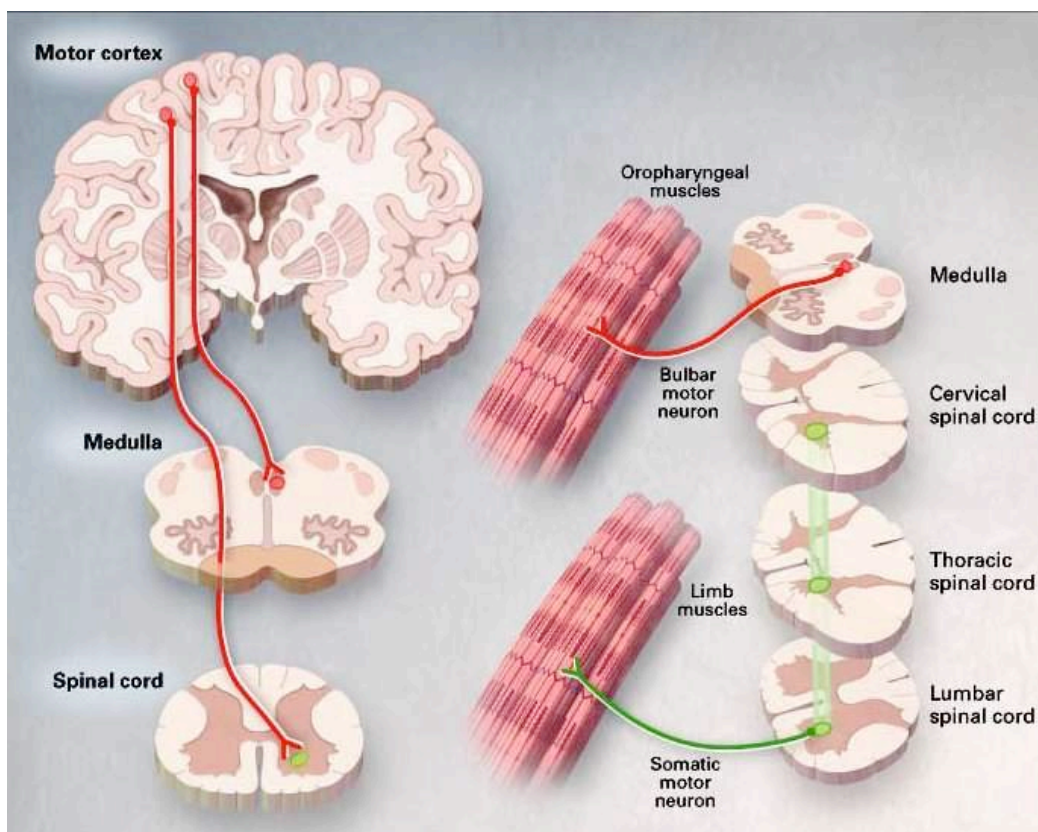
Mixed nerve consists of sensory nerves and motor nerves. The sensory nerves consist of sensory fibers (mechanoreceptor fibers), which sense body movement and pressure against the body and nociceptor, which sense tissue injury. Sensory nerves are afferent

Sensory Pathways
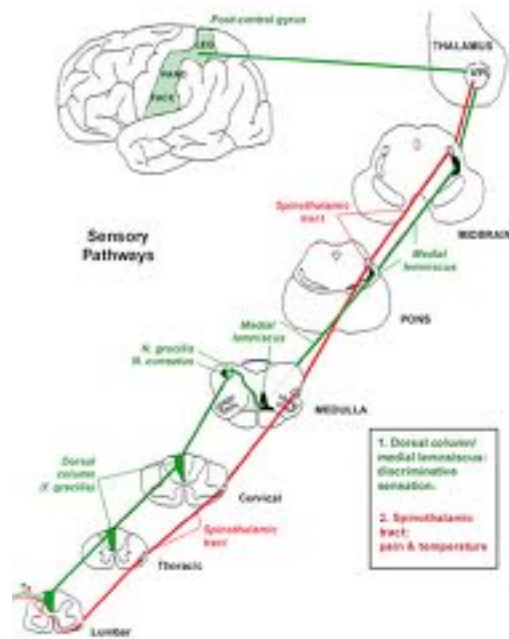
nerves, in that they convey nerve impulses from sensory receptors to the brain. Motor nerves carry impulses from the brain to skeletal muscles to allow for motion of a body-part and to branchial muscles, which control the muscles of the face and neck, hence they are efferent nerves. Another way to look at a mixed nerve is it contains both afferent and efferent axons.

Autonomic nerves (autonomic nervous system) are part of the PNS, which controls the visceral functions (i.e. function of internal organs, including the gastrointestinal tract).
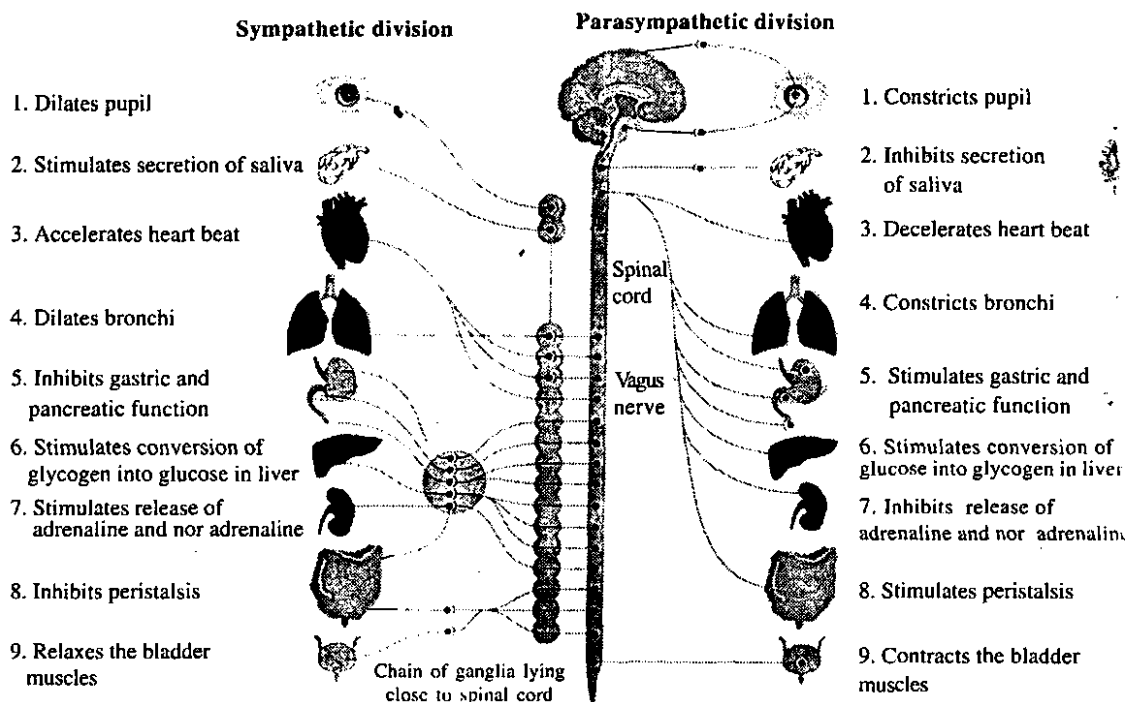

Sympathetic division

1. Dilates pupil
2. Stimulates secretion of saliva
3. Accelerates heart beat
4. Dilates bronchi
5. Inhibits gastric and pancreatic function
6. Stimulates conversion of glycogen into glucose in liver
7. Stimulates release of adrenaline and nor adrenaline
8. Inhibits peristalsis
9. Relaxes the bladder muscles

Parasympathetic division

1. Constricts pupil
2. Inhibits secretion of saliva
3. Decelerates heart beat
4. Constricts bronchi
5. Stimulates gastric and pancreatic function
6. Stimulates conversion of glucose into glycogen in liver
7. Inhibits release of adrenaline and nor adrenaline
8. Stimulates peristalsis
9. Contracts the bladder muscles

Spinal cord

Vagus nerve

Chain of ganglia lying close to spinal cord

Fig 3.7.1 : Autonomous nervous system showing the antagonistic effects of the sympathetic and parasympathetic divisions.

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The nerves involved in the **ANS** are often referred to as **splanchnic nerves (SNs),** which are paired nerves in that they contain fibers of the ANS (visceral efferent fibers) and sensory fibers from the organs (visceral afferent fibers). The splanchnic nerves consist primarily of sympathetic fibers with the exception of the pelvic splanchnic nerves, which consist of parasympathetic fibers. Fundamentally the sympathetic system stimulates cardiac muscle, smooth muscle or glandular tissue where as the parasympathetic system inhibits these same structures.
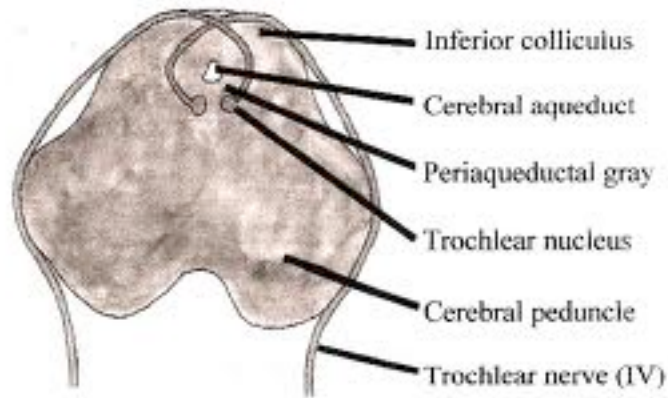
 CN X receives visceral sensory information from the thorax and abdomen (respiratory, cardiovascular, and gastrointestinal organs down to the level of the transverse colon); it does not supply the organs in the pelvis. The visceral afferent fibers from the descending
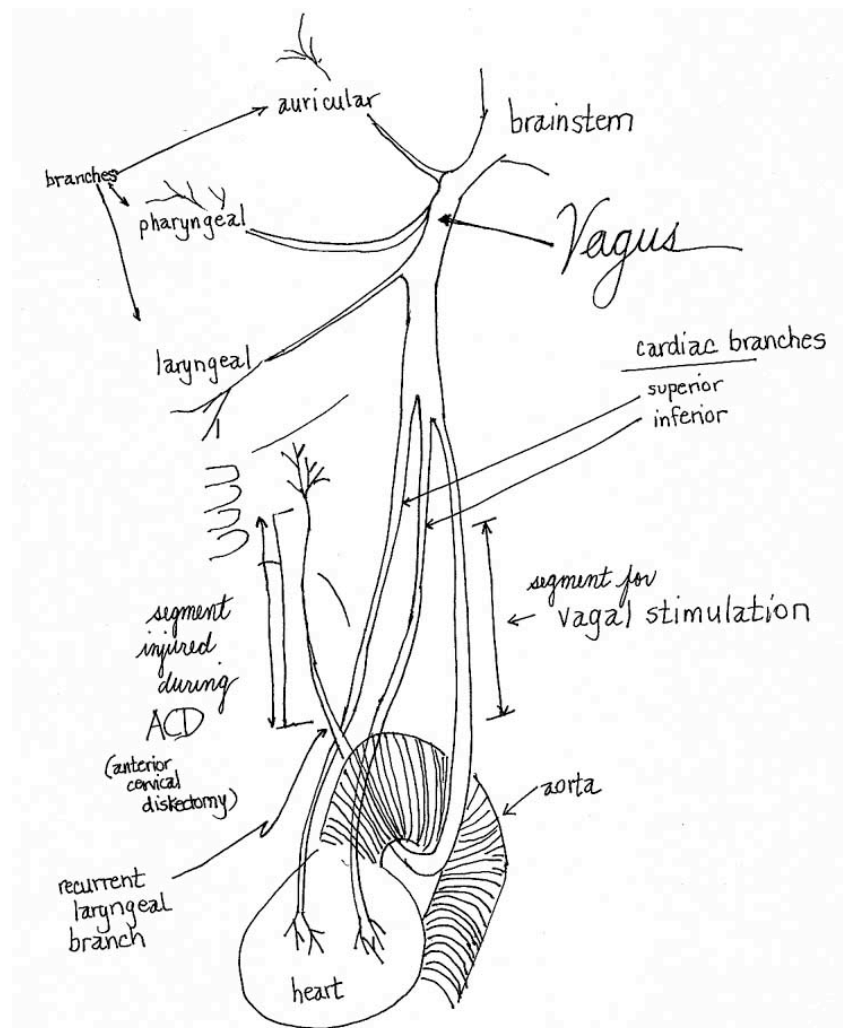
colon, rectum, bladder and accessory genital organs pass by way of the pelvic nerves and enter the spinal cord through the second, third and fourth sacral dorsal roots. Visceral sensory fibers from the bladder also enter the spinal cord through the lower thoracic and lumbar spinal nerves (**T12 to L2**). **CN XI** receives visceral information from the neck, such as information on blood oxygen and pressure from the carotid sinus body. Also, **CN XI** innervates the sternocleidomastoid and trapezius muscles, which are not limited to the head. Remember, **CN XI** arises from the higher cervical motor rootlets; hence it is referred to as the **spinal accessory nerve**. Typically **spinal nerves** provide the sensory and motor function for a specific body part; **CNs** provide innervation to a far larger anatomic region as compared to the **SNs**.
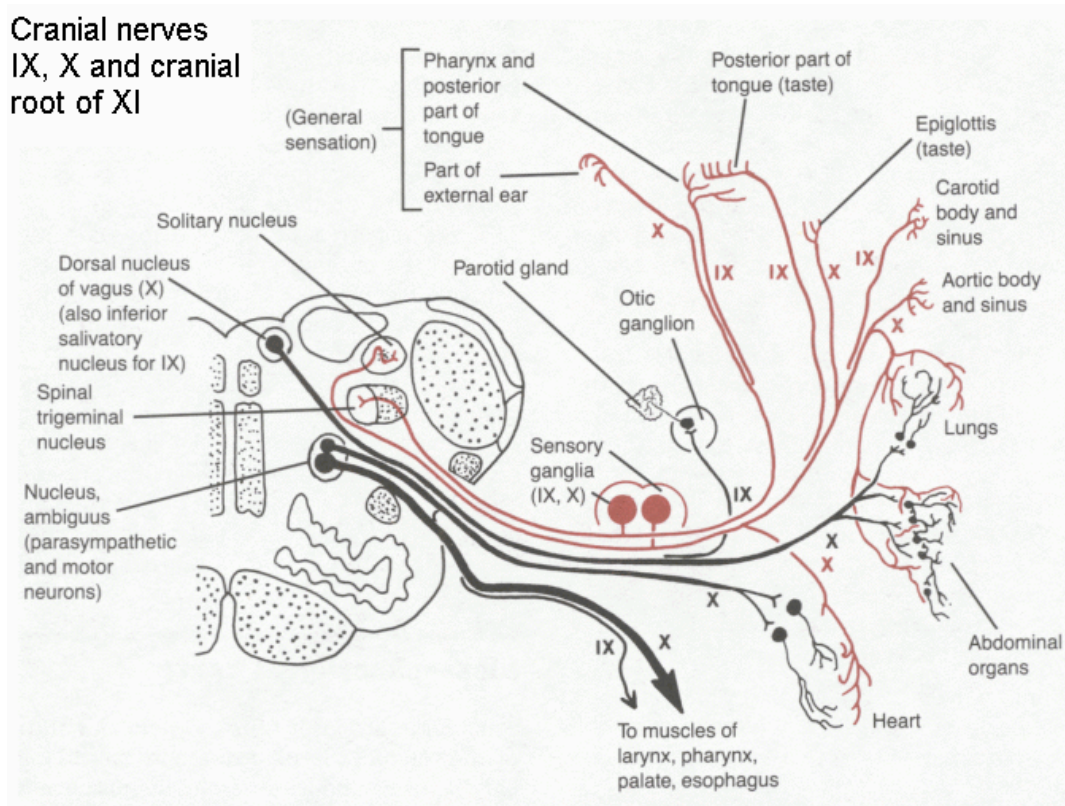

Understanding the function of each of the **CNs** is important, for detection of an abnormality can point to the anatomic site of injury. Each **CN** exits the brainstem in a finite location with all except **CN IV (trochlear)**, leaving the brainstem on its anterior surface. **CN IV** exits the brainstem on the dorsal (superior) surface of the midbrain,

Inferior colliculus
Cerebral aqueduct
Periaqueductal gray
Trochlear nucleus
Cerebral peduncle
Trochlear nerve (IV)

proceeding around the lateral surface of the brainstem joining **CN III (oculomotor)** and **CN VI (abducens)** all of which are involved in coordinating eye movements. **CN IV** has the longest intracranial course of the **CNs**, thus, when there is an increase in intracranial pressure (ICP), it is typically the first **CN** affected resulting in the eye on the same side (ipsilateral) as the affected **CN IV** not being able to abduct (cannot turn laterally).

CNs V (trigeminal), **VII (facial)**, **IX (glossopharyngeal)** and **X (vagus)** have both sensory and motor function.

Another important feature to remember when evaluating potential injuries to the **CNs** is that they exit the skull in groups, doing so through specific foramena (perforations in the base of the skull); consequently, they are typically injured in groups. The **CNs** involved with orbital sensation and movement of the eyes (**CNs III, IV, VI,** and the **ophthalmic division of the trigeminal nerve, CN V**) all course through the cavernous sinus, which is located in the lateral aspect of the sella turcica, and leave the skull through the superior orbital fissure.
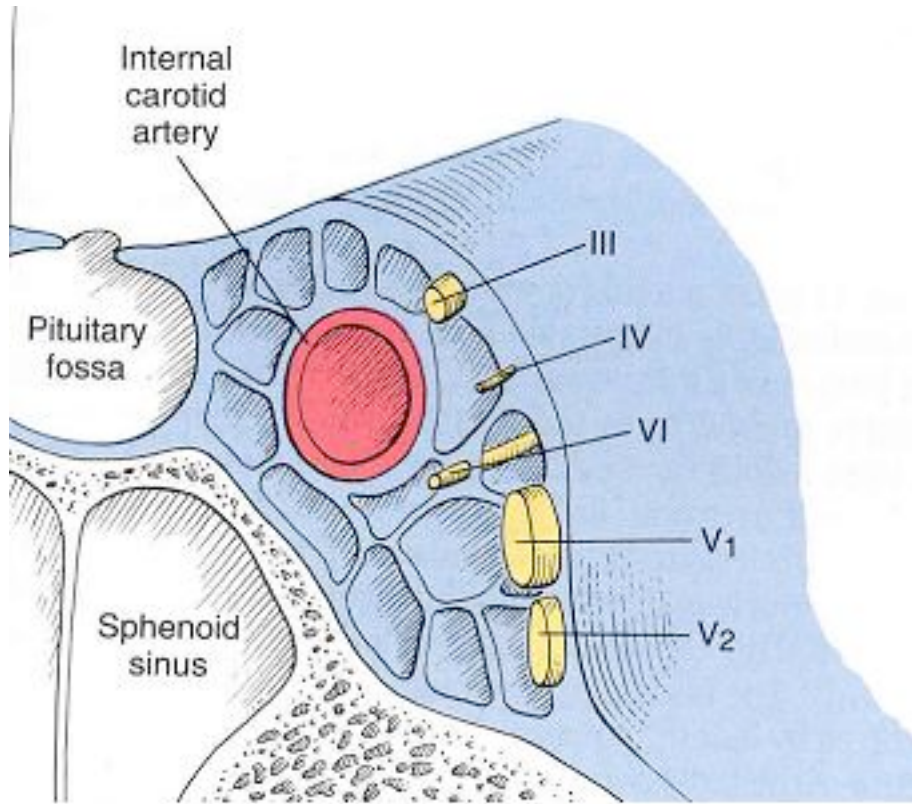
Cavernous Sinus

CNs VII and **VIII (vestibulocochlear)** leave the brainstem at the cerebellopontine angle, which is the anatomic space between the cerebellum and the pons.
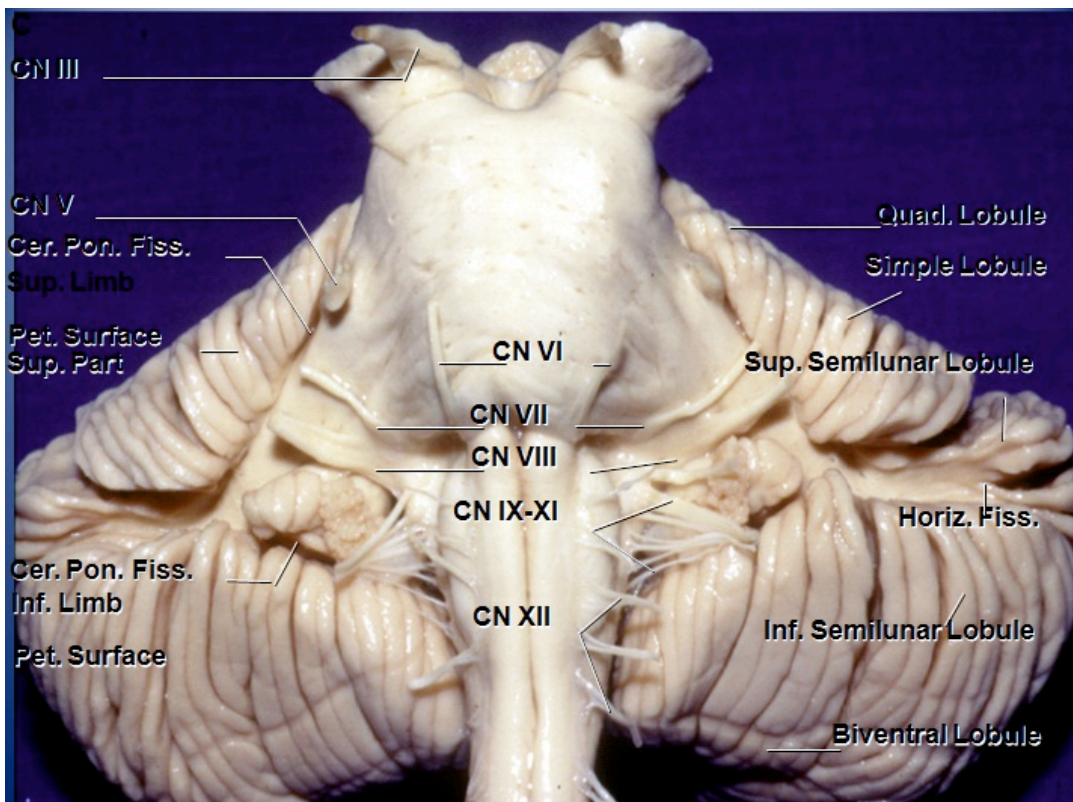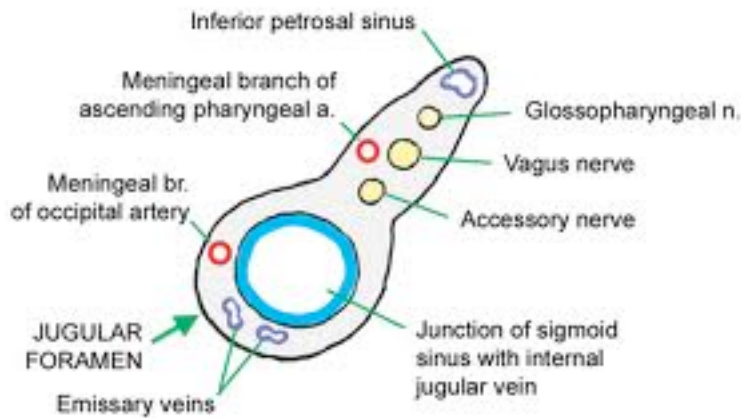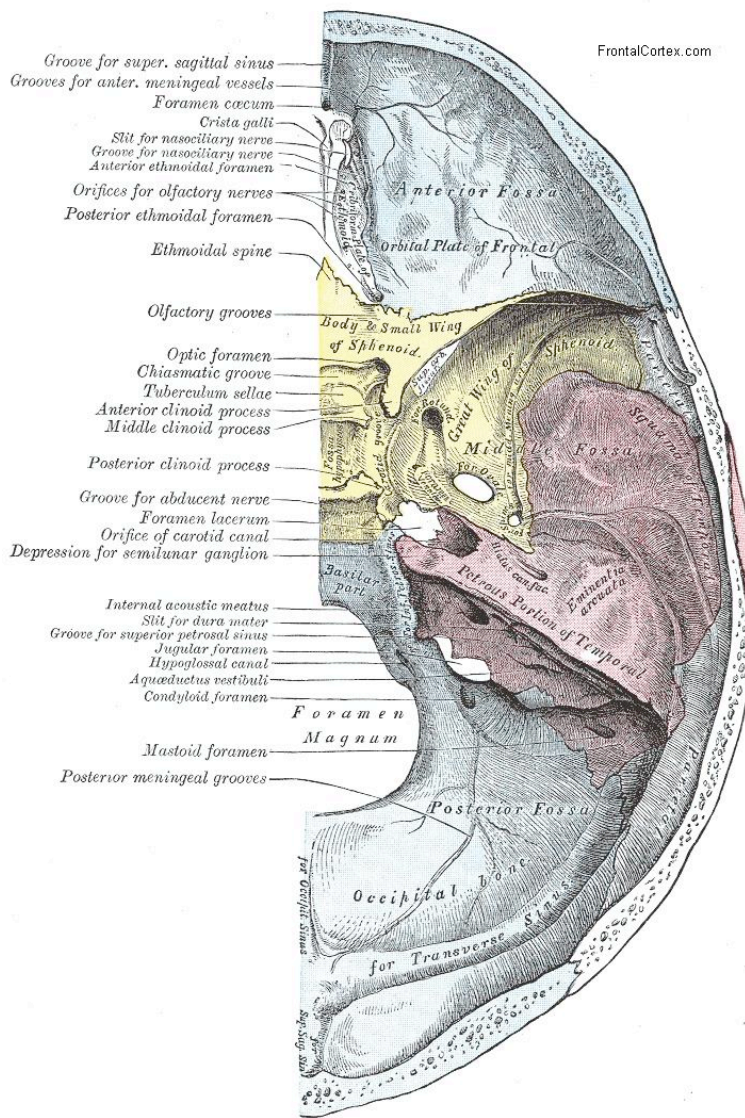
There is a tumor called "vestibular schwannoma," which formerly was referred to by the incorrect term "acoustic schwannoma/neuroma" that arises within the vestibular division of **CN VIII**, but also can press on **CN V** near its site of emergence from the middle cerebellar peduncle as well as compressing the cerebellar hemisphere or its peduncles on the same side as the lesion, giving rise to clumsiness on the same side as the lesion (ipsilateral).

The middle cerebellar peduncle is the largest of the three fiber bundles (superior, middle and inferior cerebellar peduncles which connect the brainstem to the cerebellum) and links the cerebellum with the pons. Through the middle cerebellar peduncle the cerebellum receives information for muscle movement that the pyramidal tract is carrying down to the lower motor neurons in the anterior horns.
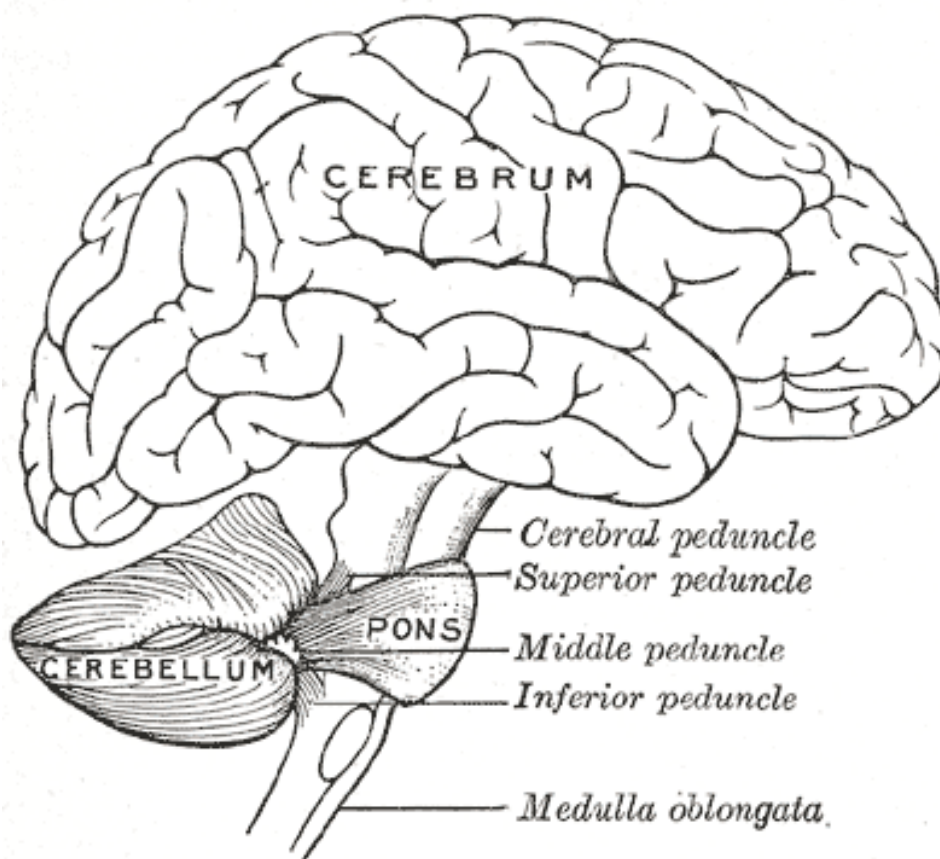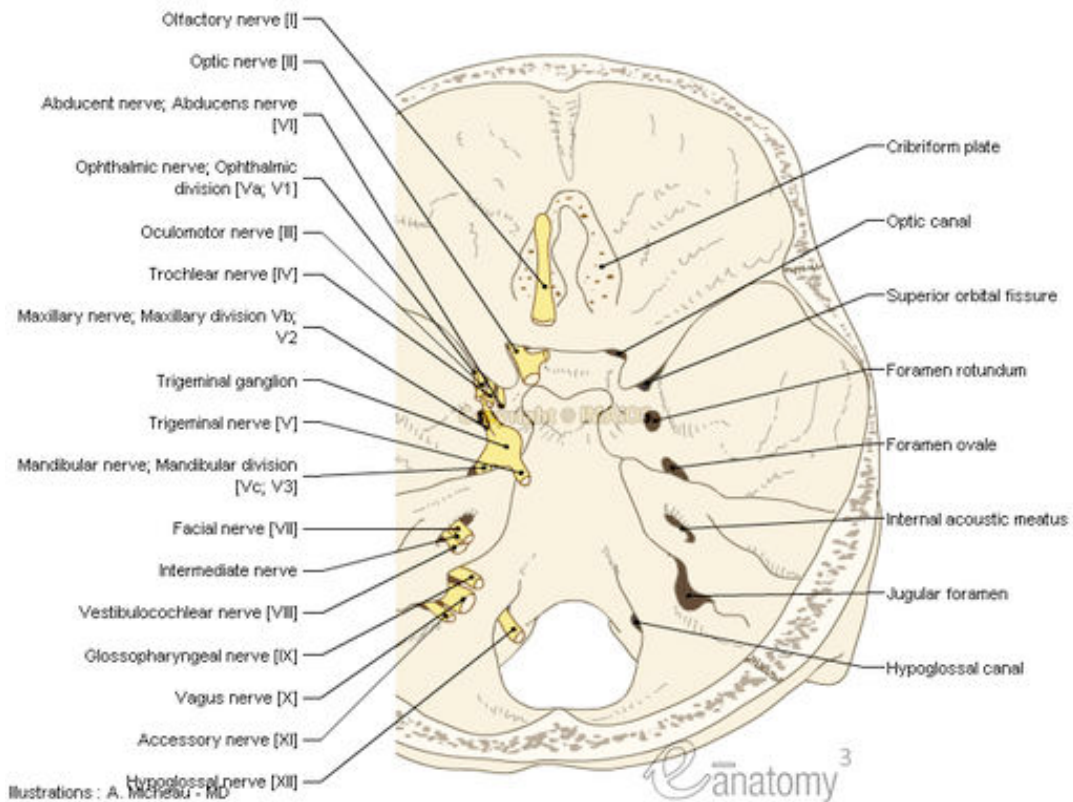

The lower **CNs (IX, X,** and **XI)** are all-vulnerable to compression by tumors as they exit through the jugular foramen. The jugular foramen is a perforation in the base of the

Groove for super. sagittal sinus
Grooves for anter. meningeal vessels
Foramen cœcum
Crista galli
Slit for nasociliary nerve
Groove for nasociliary nerve
Anterior ethmoidal foramen
Orifices for olfactory nerves
Posterior ethmoidal foramen

Ethmoidal spine

Olfactory grooves

Optic foramen
Chiasmatic groove
Tuberculum sellae
Anterior clinoid process
Middle clinoid process

Posterior clinoid process

Groove for abducent nerve
Foramen lacerum
Orifice of carotid canal
Depression for semilunar ganglion

Internal acoustic meatus
Slit for dura mater
Groove for superior petrosal sinus
Jugular foramen
Hypoglossal canal
Aquæductus vestibuli
Condyloid foramen

Mastoid foramen

Posterior meningeal grooves

FrontalCortex.com

Anterior Fossa

Orbital Plate of Frontal

Body & Small Wing of Sphenoid.

Great Wing of Sphenoid

Middle Fossa

Basilar part

Petrous Portion of Temporal

Eminentia arcuata

Foramen Magnum

Posterior Fossa

Occipital bone

for Transverse Sinus

Inferior petrosal sinus

Meningeal branch of ascending pharyngeal a.

Glossopharyngeal n.

Vagus nerve

Meningeal br. of occipital artery

Accessory nerve

JUGULAR FORAMEN

Junction of sigmoid sinus with internal jugular vein

Emissary veins

skull, located behind the carotid canal; the petrous portion of the temporal bone forms its anterior border; posteriorly it is formed by the occipital bone.

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CN XII (hypoglossal) exits the base of the skull through the hypoglossal foramen, which is located in the anterior margin of the foramen magnum of the occipital bone. Typically the hypoglossal nerve is not involved unless there is a fracture through the anterior wall of the foramen magnum or there is a large tumor, which is compressing **CN IX, CN X**, and **CN XI**, but also **CN XII**. If you see compromise of **CN IX** and **CN X**, but no involvement of **CN XI**, than the injury is located within the brainstem and not the jugular foramen.

Olfactory nerve [I]
Optic nerve [II]
Abducent nerve; Abducens nerve [VI]
Ophthalmic nerve; Ophthalmic division [Va; V1]
Oculomotor nerve [III]
Trochlear nerve [IV]
Maxillary nerve; Maxillary division Vb; V2
Trigeminal ganglion
Trigeminal nerve [V]
Mandibular nerve; Mandibular division [Vc; V3]
Facial nerve [VII]
Intermediate nerve
Vestibulocochlear nerve [VIII]
Glossopharyngeal nerve [IX]
Vagus nerve [X]
Accessory nerve [XI]
Hypoglossal nerve [XII]
Illustrations : A. Micheau - MD

Cribriform plate
Optic canal
Superior orbital fissure
Foramen rotundum
Foramen ovale
Internal acoustic meatus
Jugular foramen
Hypoglossal canal

CRANIAL NERVE O

As previously stated, **CNs** are traditionally numbered **I** to **XII**. There is however an additional **CN,** whose existence in humans, and for that matter primates, is quite controversial; this cranial nerve is referred to as **CN O.** Cranial nerve 0 was originally discovered by a German Scientist Gustav Fritsch in 1878 in the brains of sharks. It was first identified in humans in 1913. Further study has demonstrated **CN 0** is a common finding in the adult human brain. It projects from the nasal cavity, entering the brain in the region of the inferior aspect of the frontal lobes, just medial to the olfactory bulb and

tract, as a microscopic plexus of unmyelinated peripheral nerve fascicles. This nerve is often not identified at the time of autopsy due to the fact it is very fragile and thin, thus it is easily torn when the brain is removed from the floor of the skull. It is not connected to the olfactory bulb. This anatomical feature suggest the nerve is either vestigial or may be related to the sensing of pheromones. This hypothesis is supported by the fact that **CN 0**
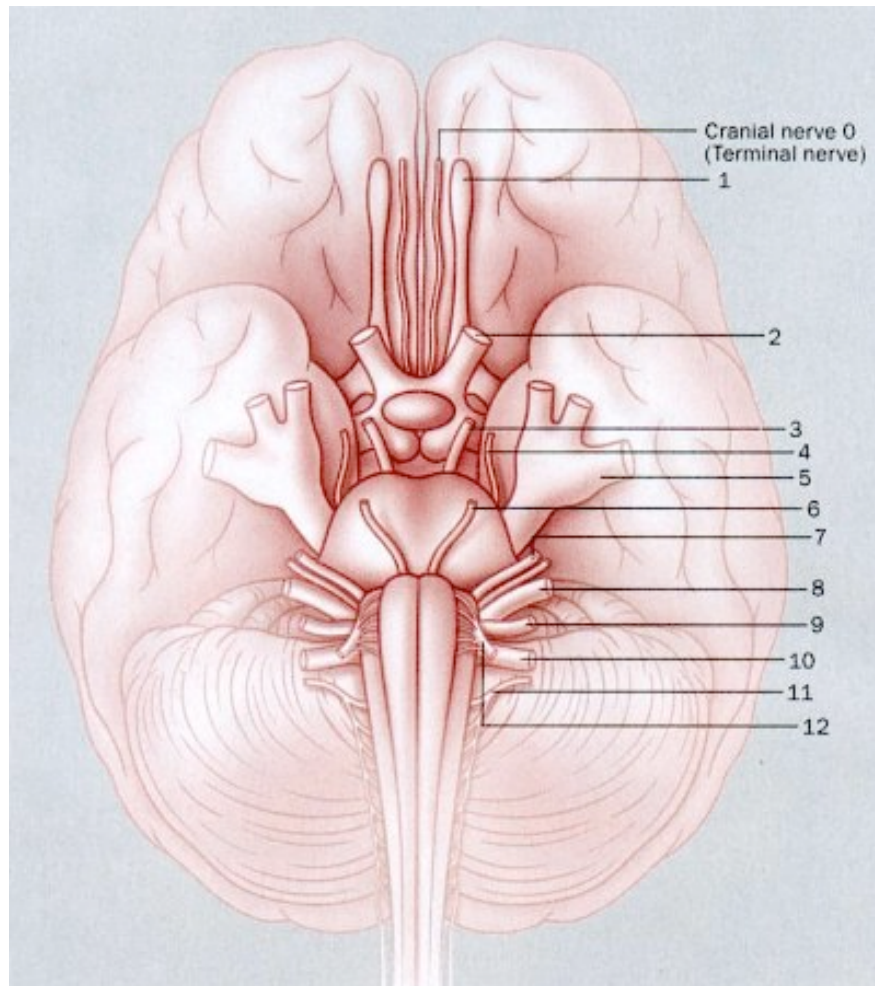
projects to the medial and lateral septal nuclei, and the preoptic areas (limbic system). The limbic system includes the subcallosal, cingulated and parahippocampal gyri, the hippocampal formation, dendate gyrus, and subcortical nuclei, such as the amygdaloid complex, septal nuclei, hypothalamus, eipthalamus, anterior thalamic nuclei and parts of the basal ganglia. A point to remember is that there is a finite difference between limbic system and limbic lobe. The limbic lobe consists of the subcallosal, cingulated and parahippocampal gyri, as well as the underlying hippocampal formation and dendate

gyrus. The limbic system is far more inclusive, including all that constitutes the limbic lobe and more.

The limbic system conveys its influence through the endocrine system and the autonomic nervous system. The monosynaptic connection with the limbic system is made with the amygdala, which is that part of the brain concerned with sexual and aggressive behavior. The amygdala in turn sends impulses to another part of the limbic system, the hypothalamus, which activates the sympathetic nervous system. In addition, the amygdala sends impulses to the thalamus, frontal cortex and causes the release of norepinephrine from the locus coeruleus and acetylcholine from the laterodorsal tegmental nucleus. The locus coeruleus is a nucleus in the pons involved with physiologic responses to stress and panic. The laterodorsal tegmental nucleus extends from the midbrain tegmentum to the pontine tegmentum. Its acetylcholine projections are believed to be involved in modulating sustained attention or in mediating alerting response.

These limbic projections in most mammals is specialized to the point of having its own receptors, which are called the vomeronasal organ and a specific anatomical region within the olfactory bulb called the **accessory olfactory bulb**. The vomeronasal organ is a bilateral, elongated tubular structure in the nasal septum. **CN O** appears to arise from chemosensory cells located within the vomeronasal organs and communicate both with the oral and nasal cavities. The central processes of the vomeronasal chemosensory cells, but not the chemosensory cells of **CN 0**, project to the accessory olfactory bulb. These projections are in the form of fine unmyelinated nerves. The neurons within the accessory bulb in turn send fibers to the amygdala, which sends fibers to the hypothalamus.   The vomeronasal organ and its projections are referred to as the **accessory olfactory system** due to the fact it has no connections with the thalamus or neocortical regions.

The function of the chemosensory cells of **CN 0,** as previously indicated, is the sensing of **pheromones**, which are chemical substances that have evolved in all animal phyla, to signal sex and dominance status, and are responsible for stereotypical social and sexual

behaviour among members of the same species. In mammals, these chemical signals are believed to be detected primarily by the vomeronasal organ, a chemosensory organ located at the base of the nasal septum. The vomeronasal organ is present in most amphibia, reptiles and non-primate mammals but is absent in birds, adult catarrhine monkeys and apes. An active role for the human vomeronasal organ is disputed; the vomeronasal organ although present in the fetus, appears to be vestigal or absent in adults.   This is one of the anatomic facts that has created the controversy as to the actual existence of **CN 0** in adults.

CRANIAL NERVE I (Olfactory Nerve)
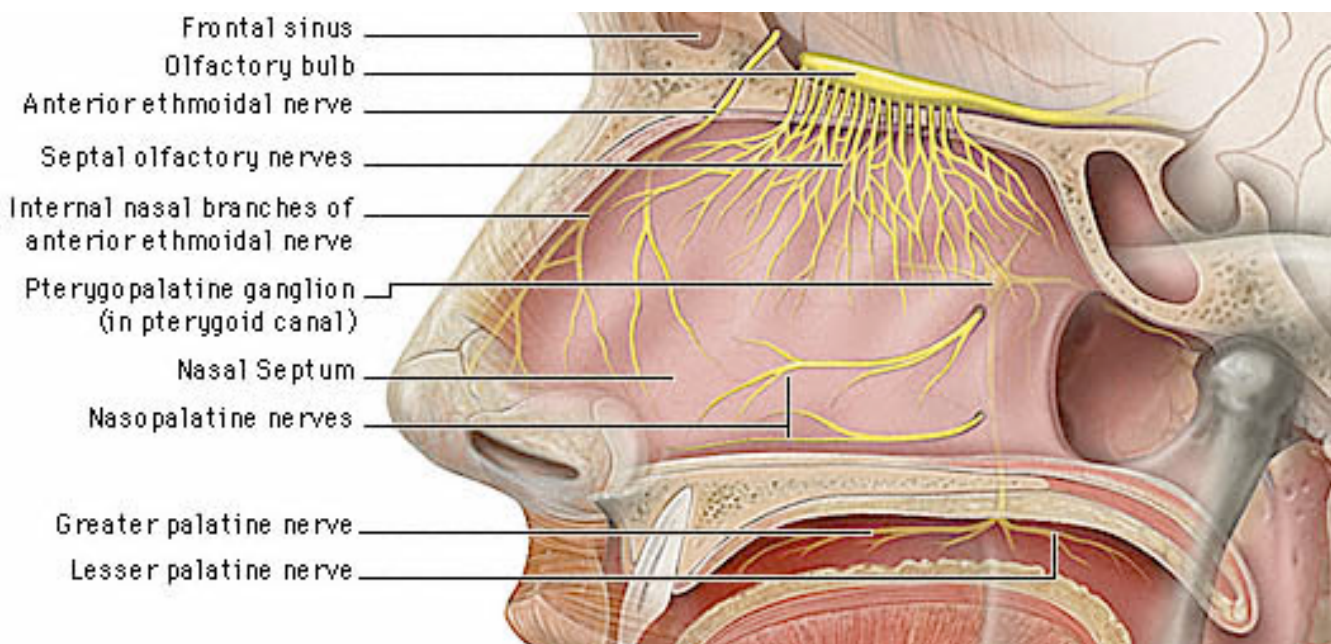
CN I arises from **olfactory sensory neurons** located in the olfactory epithelium in the upper posterior part of the nasal cavity. The **olfactory sensory neuron** is a bipolar nerve cell, which has two projections from its cell surface. From the tip of this neuron, also called its apical surface, it sends a projection called a dendrite, to the epithelial surface, which forms a knob of fine delicate projections called cilia. From the base of the olfactory cell its sends a single projection called an axon, which passes from the nasal cavity through perforations in the cribiform plate of the ethmoid bone, to the **olfactory bulb**. The olfactory bulbs rest in the olfactory sulci on the inferior surface of the frontal

lobes; their medial border is the gyrus rectus and the lateral border is the medial orbital gyrus. It is the axons, which represent the central processes of the bipolar cells in the
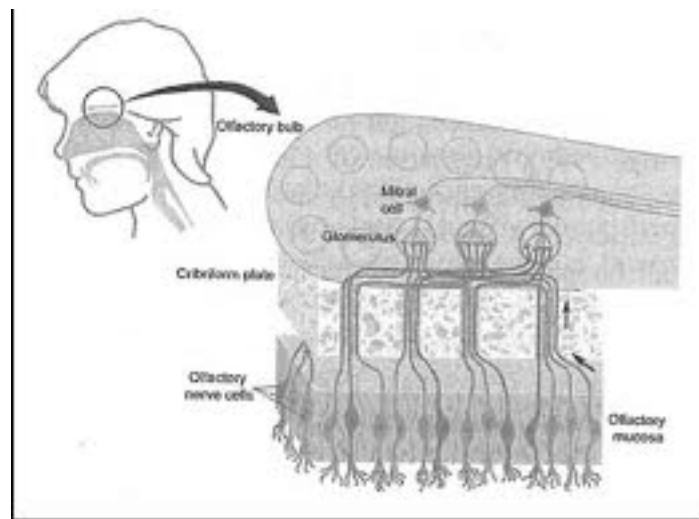

olfactory epithelium that are collectively referred to as the **olfactory nerve**.

Within the olfactory bulb, the axons of the olfactory sensory neurons form synapses with the olfactory bulb neurons that in turn relay signals to the **olfactory cortex**.
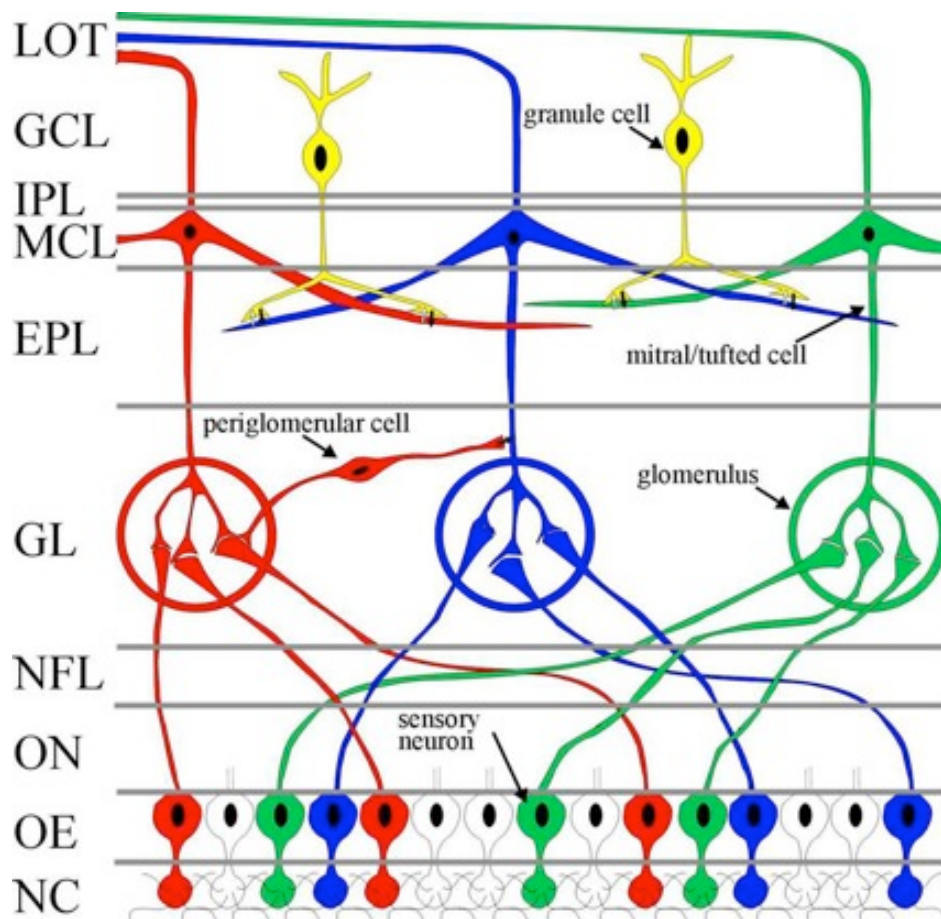
Anatomically the olfactory bulbs consist of multilayered structures composed of 5 layers, which from the outside in are: **glomerular layer, the external plexiform layer, mitral cell layer, internal plexiform layer** and the **granule cell layer**. The principal neuron within the olfactory bulb is the **mitral cell**, the axons of which form the predominant output of the olfactory bulb, the **lateral olfactory tract**. Most of the dendrites of the mitral cells terminate in the granule cell layer, with the exception of the apical dendrite,
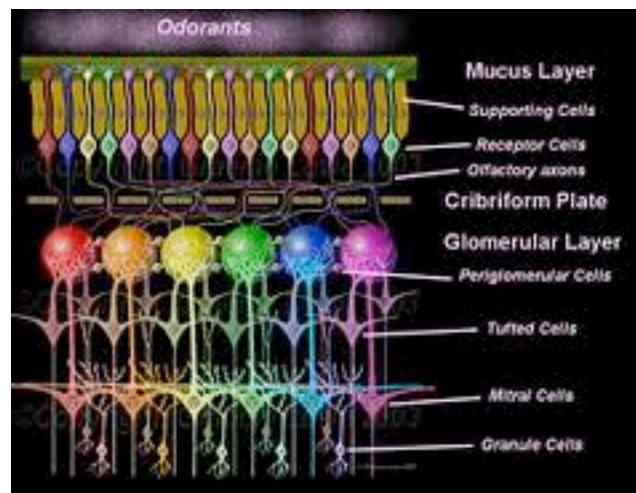
which terminate in the glomerular layer within structures called **glomeruli**. Each glomerulus is formed by synapses between the olfactory nerve and the apical dendrites of the mitral cell. The number of olfactory nerve axons participating in the formation of each glomerulus is much larger than the contribution made by each mitral cell, thus suggesting convergence of impulses from the olfactory epithelium. In humans there are approximately twenty-five thousand axons synapsing on about one hundred mitral cells, with each mitral cell projecting to multiple glomeruli. Each mitral cell however responds to different sets of odorants, thus each odorant typically stimulates many different glomeruli. It has also been demonstrated that the sensory neurons within the olfactory epithelium expressing different odorant receptors will form synapses with glomeruli, which respond to only one receptor. Thus, it appears each glomerulus receives input from only one type of receptor. It is interesting to note that the glomeruli, which receive input from a specific type of receptor, have the same locations in the olfactory bulbs of

different animals. Consequently, at the level of input to the olfactory bulb, a stereotyped spatial map of sensory information is formed by sensory neurons expressing different odorant receptors projecting to different glomeruli.

Mitral cells also project to periglomerular cells and granule cells that in turn inhibit the mitral cells, which is called lateral inhibition. In addition, granule cells mediate inhibition and excitation of mitral cells through pathways from centrifugal (corticofugal) axons and
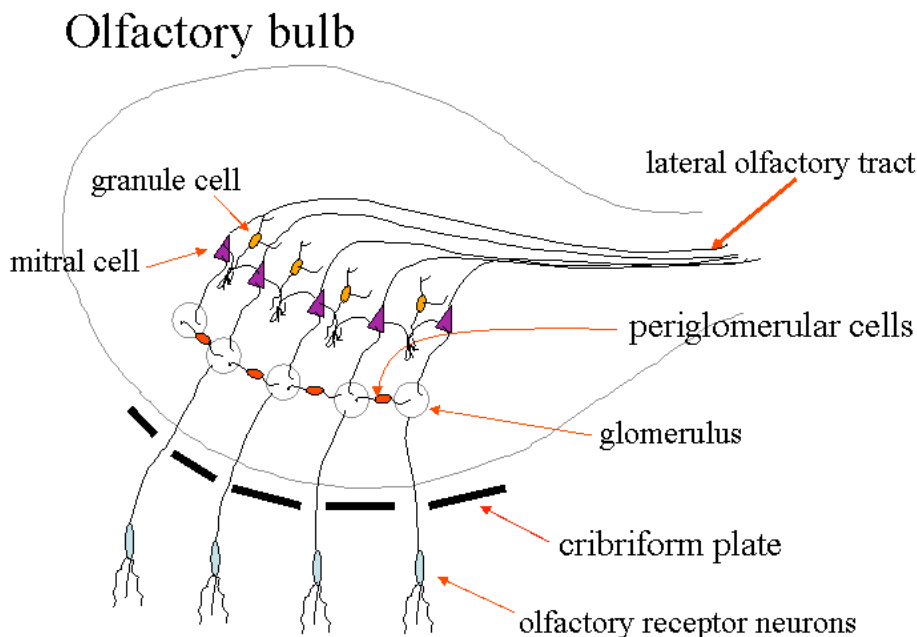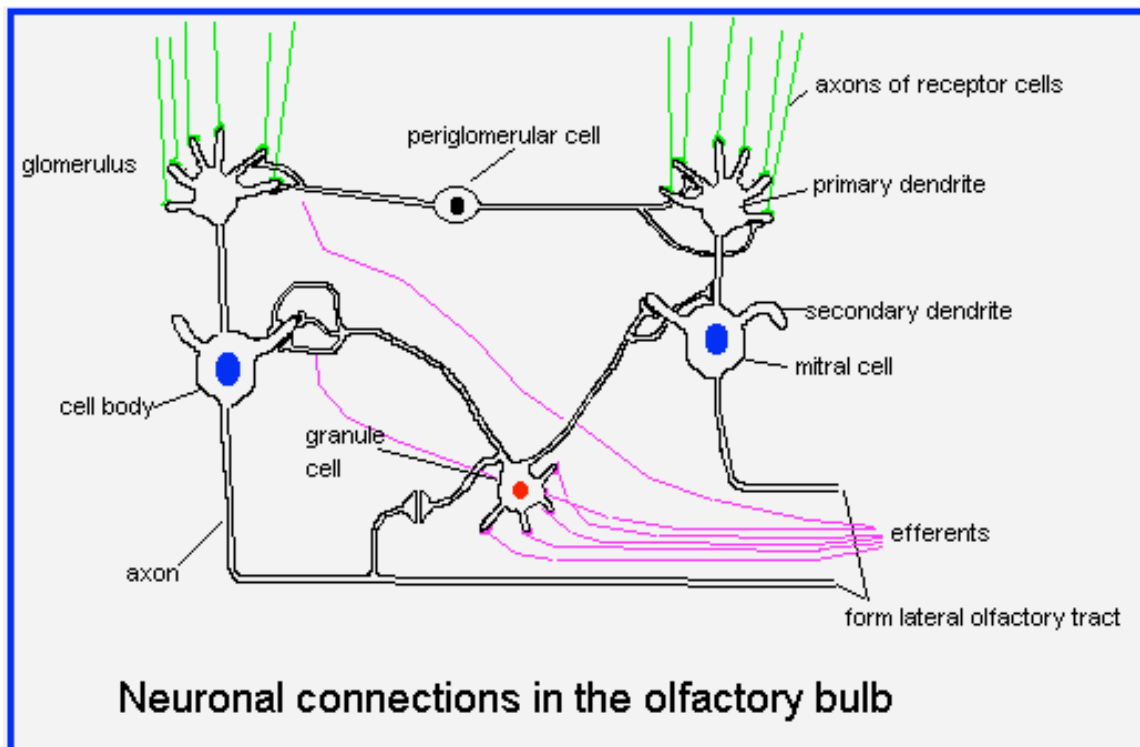
Olfactory bulb

the axons of the anterior olfactory nuclei.

Centrifugal (corticofugal) fibers arise from all regions of the cerebral cortex, i.e. neocortex; these projections convey impulses concerned with motor function, modifications of muscle tone and reflex activity, modulation of sensory input and alterations of awareness and state of consciousness. Centrifugal fibers, originating largely from the deeper layers of the cerebral cortex, can be grouped under the following designations: corticospinal, corticoreticular, corticopontine, corticothalamic, corticostriate and corticonuclear. The latter consist of a composite grouping of fibers that project to

brainstem nuclei at different levels (e.g., corticosubthalamic, corticorubral, corticotectal and projections to various sensory and cerebellar relay nuclei).

In fish the centrifugal fibers to the olfactory bulb originate in the telencephalic hemisphere (telencephalon refers to the embryonic structure which gives rise to the cerebral hemispheres. The telencephalon and the diencephalon together form the forebrain), the diencephalon and the contralateral olfactory bulb, passing through both the medial and lateral olfactory tracts, and form synaptic contacts with the dendrites in the granule cell layer of the olfactory bulb. In mammals, the centrifugal fibers originate in the anterior olfactory nuclei on both sides, and in the ipsilateral horizontal limb of the diagonal band, pass through both the medial and lateral olfactory tract, and terminate on the dendrites of the granule cells and periglomerular cells.

There is a third cellular component, which participates in the formation of the glomeruli called periglomerular cells. These cells are within the glomerular layer and encircle the

Neuronal connections in the olfactory bulb

glomeruli forming synapses between and within glomeruli. They form dendrodendritic synapses with mitral cell dendrites within the glomerulus as well as adjacent glomeruli. It is believed the olfactory nerve axons form excitatory synapses with both the apical

dendrites of the mitral cell and the dendrites of the periglomerular cells; the dendrites of the periglomerular cells however are believed to be inhibitory to the apical dendrite of the mitral cell. Thus, the periglomerular cells provide a mechanism by which information from other glomeruli could influence the signals transmitted from the mitral cells.

The granule cells have only dendrites, which terminate in the external plexiform layer, forming numerous connections with the lateral dendrites of the mitral cells, thus forming another layer of horizontal interaction in the olfactory bulb through their dendro-dendrite synapses with the mitral cells. The dendro-dendrite synapses between mitral and granule cells are unusual in that both sides of the synapse release a neurotransmitter. The mitral cells release the excitatory neurotransmitter glutamate thus stimulating the granule cell. The granule cells release the inhibitory neurotransmitter gamma-aminobutyric acid, which in turn inhibits the mitral cell. Thus, the dendro-dendritic synapse can cause mitral cells to inhibit themselves (auto-inhibition), as well as neighboring mitral cells (lateral inhibition). In addition to the granule cells forming synapses with collaterals of the mitral cell axons, they also form synapses with centrifugal (corticofugal) fibers from other parts of the brain. Consequently, there is a pathway by which the activity of a given mitral cell can be influenced by that of other mitral cells, granule cells, and periglomerular cells and by descending influences from the neocortex, the latter of which appears to be inhibitory.

The short axon cells are found in the same layer as the granule cells and form synapses within the external plexiform layer and the granule cell layer. Little is known about the function of these cells, although it is believed to be inhibitory. The periglomerular cells, along with granule cells and the short axon-cells represent the olfactory bulb intrinsic neurons, i.e. their cell processes are confined to the olfactory bulb. They are excited by the basal dendrites of the mitral cells and in turn inhibit these mitral cells.

There is another cell referred to as the tufted cell, which many consider displaced mitral cells or smaller versions of mitral cells found in the external plexiform layer and the periglomerular region. Recent research has suggested that the sphere of influence of these cells, while qualitatively similar to the mitral cells, is centered only on a few

glomeruli. Like the mitral cell they are subjected to the same inhibition from the interneurons (periglomerular cells, granule cells and short-axon cells). The axons of the mitral and tufted cells form the principal projections of the olfactory bulb represented by the lateral olfactory tract, which pass ipsilaterally to the olfactory cortex. The tufted cells appear to project primarily to the anterior olfactory nucleus and the olfactory tubercle. The mitral cells within the olfactory bulb project to the five different regions of the olfactory cortex via the lateral olfactory tract: the anterior olfactory nucleus, which innervates the contralateral olfactory bulb; the olfactory tubercle; the piriform cortex; and parts of the amygdala and entorhinal cortex. From the latter four areas information is projected to the orbitofrontal cortex via the thalamus; however, the olfactory cortex also sends direct projections to the frontal cortex; the mitral cells within the accessory olfactory bulb project only to the amygdala. The amygdala in turn sends olfactory information to the hypothalamus and the entorhinal area to the hippocampus.
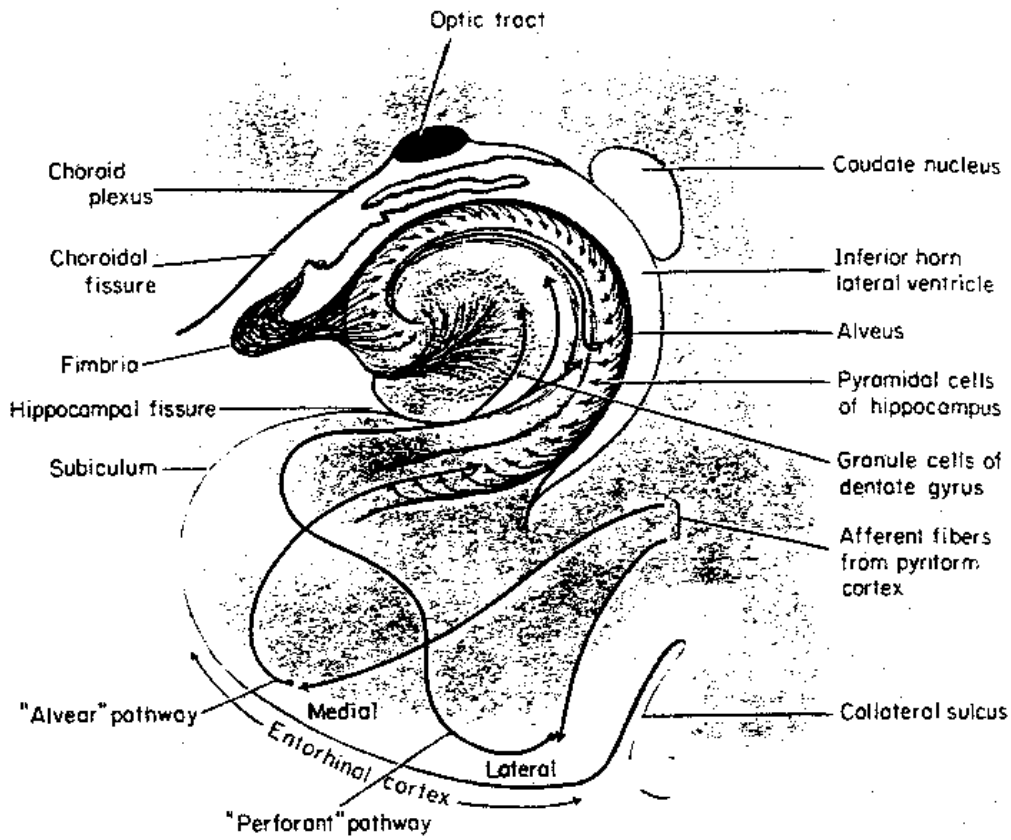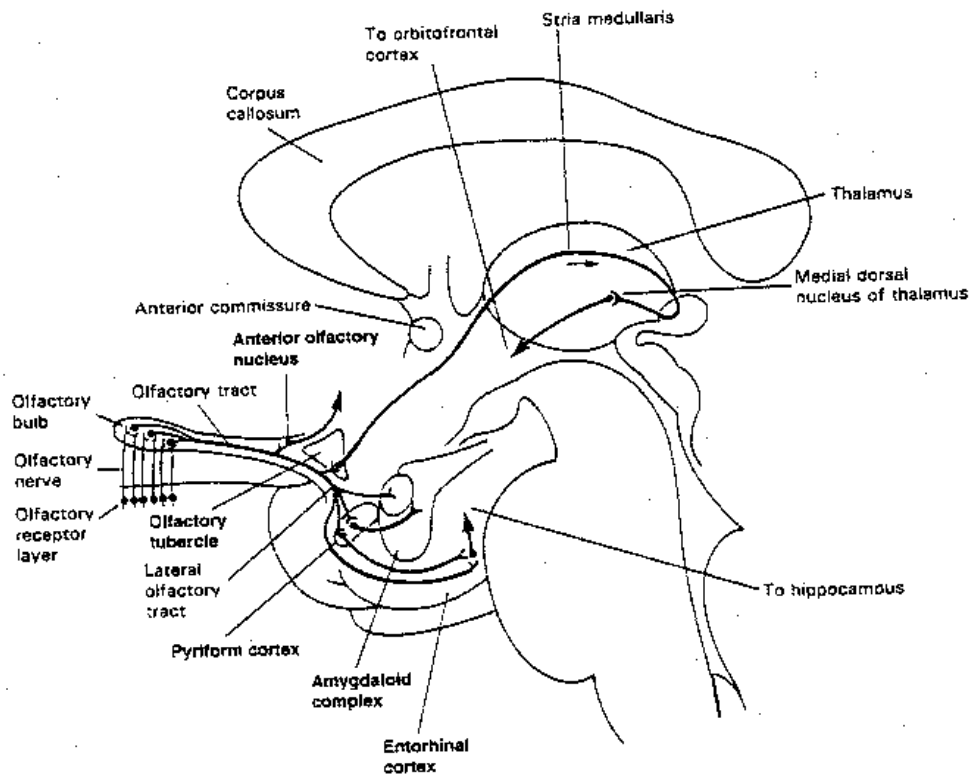

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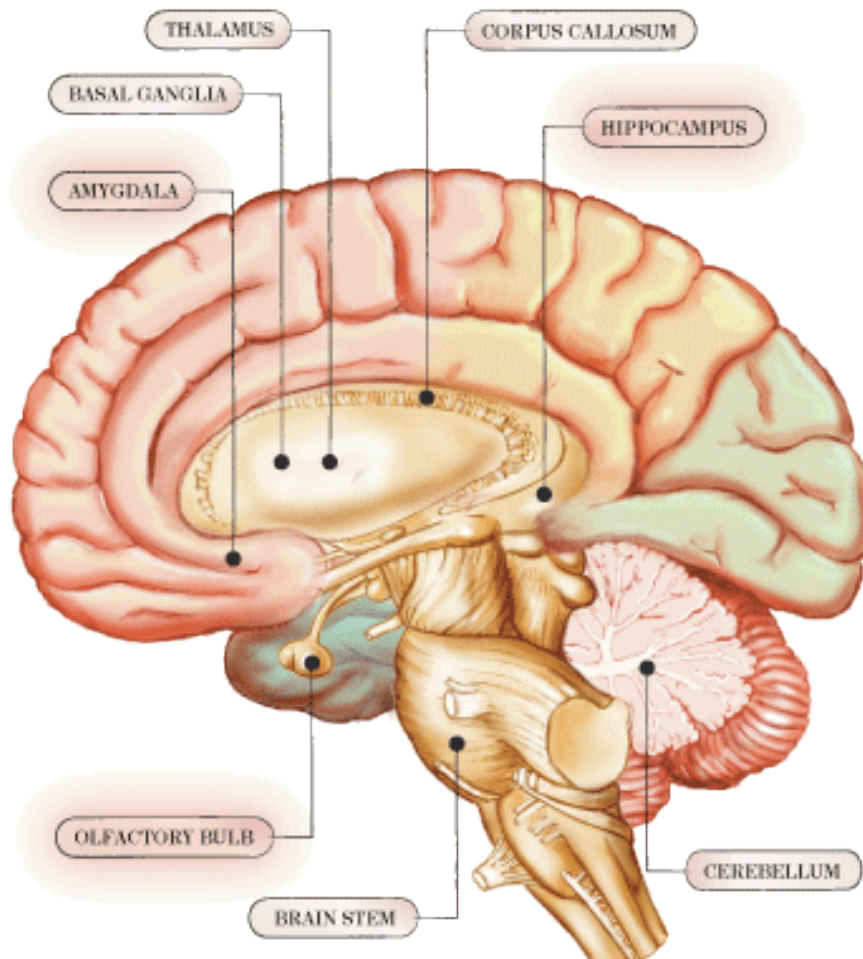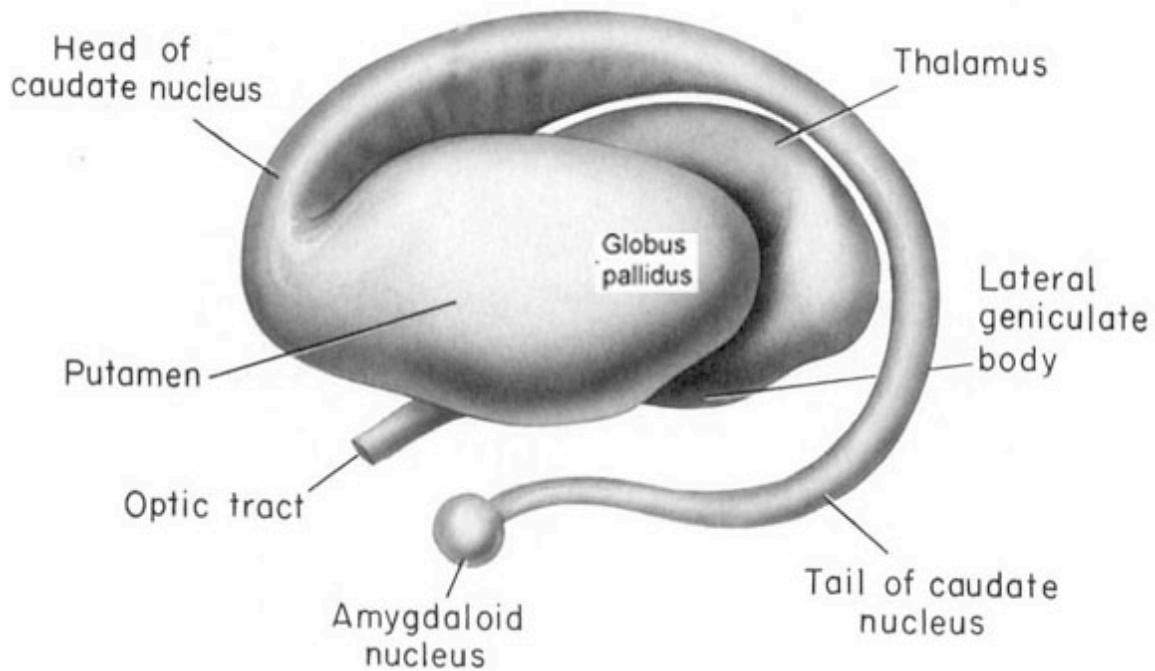
The amygdala, which lies just rostral to the hippocampus, is involved in analyzing the emotional or motivational significance of sensory stimuli and in coordinating the actions of a variety of brain systems to allow an individual to make an appropriate response. It receives input directly from the major sensory systems. In turn, it projects back to the neocortex, to the basal ganglia, the hippocampus, and a variety of subcortical structures including the hypothalamus. Through its projections to the brainstem the amygdala can modulate somatic and visceral components of the peripheral nervous system and thus orchestrate the body's response to a particular situation. Responses to danger, the sense of fear and the change in heart rate and respiration that result are mediated by the amygdala and its connections.
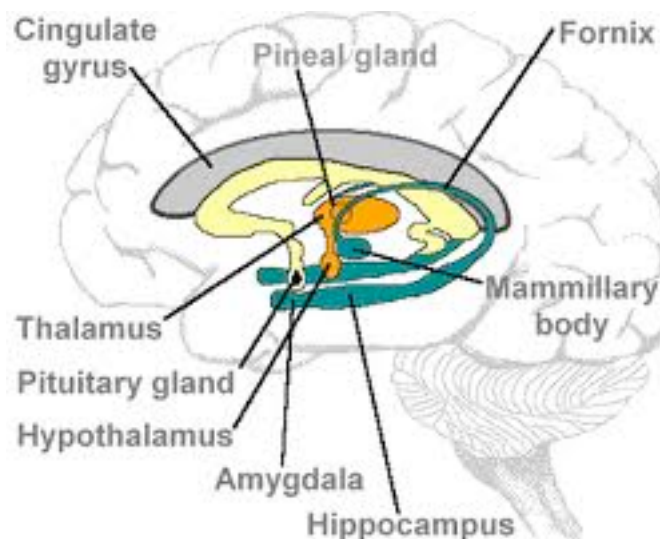
The hippocampus and associated cortical regions form the floor of the temporal horn of the lateral ventricle. Together these structures are responsible for the formation of long

Optic tract

Choroid plexus

Choroidal fissure

Fimbria

Hippocampal fissure

Subiculum

"Alvear" pathway

Medial

Entorhinal cortex

Lateral

"Perforant" pathway

Caudate nucleus

Inferior horn lateral ventricle

Alveus

Pyramidal cells of hippocampus

Granule cells of dentate gyrus

Afferent fibers from pyriform cortex

Collateral sulcus

term memories about our daily experiences. The hippocampus is not the permanent storage of memories. Damage to the hippocampus causes people to become unable to form new memories but does not significantly impair old memories.

To orbitofrontal cortex

Stria medullaris

Corpus callosum

Thalamus

Anterior commissure

Medial dorsal nucleus of thalamus

Anterior olfactory nucleus

Olfactory tract

Olfactory bulb

Olfactory nerve

Olfactory receptor layer

Olfactory tubercle

Lateral olfactory tract

To hippocampus

Pyriform cortex

Amygdaloid complex

Entorhinal cortex

Caudal to the olfactory bulb and within the olfactory tract are a group of neurons that form the anterior olfactory nucleus. These neurons are believed to be mitral cells. Dendrites of these cells pass among the axons of the olfactory tract (mitral and tufted cell axons) with which they form synapses, thus receiving impulses from these neurons. Axons of the cells of the anterior olfactory nucleus pass caudally and cross in the anterior part of the anterior commissure entering the contralateral olfactory tract and communicating with the neurons of the contralateral **anterior olfactory nucleus** and the neurons of the olfactory bulb. It appears the anterior olfactory nucleus modulates information between all participants involved in olfaction.
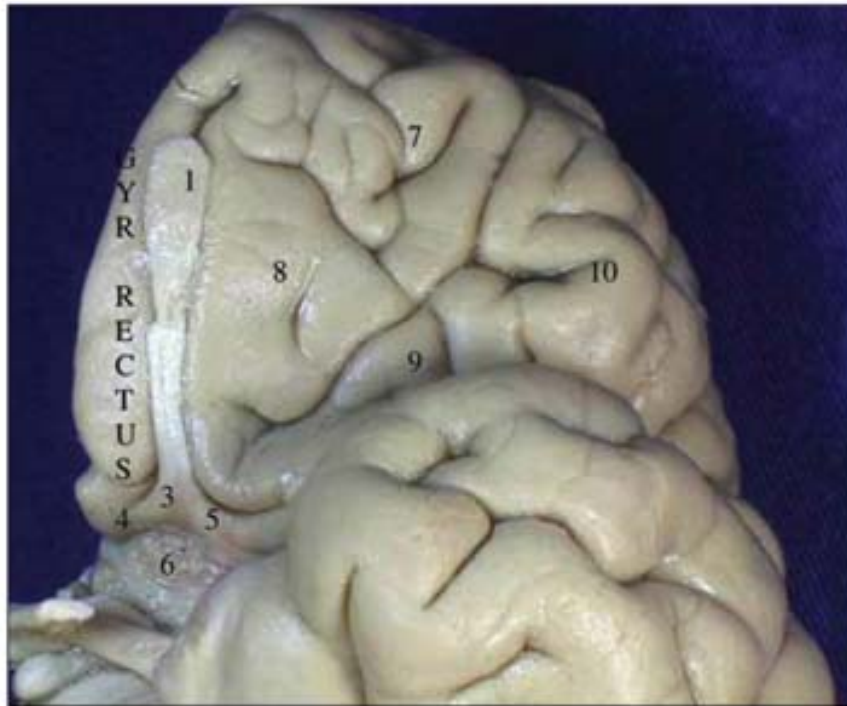
Fig 1. The olfactory nerve is divided in the olfactory bulb (1), olfactory tract (2), olfactory trigone (3) and medial (4) and a lateral (5) olfactory stria in front of the anterior perforated substance (6) in a frontal lobe basal view. The orbital surface is lateral to the olfactory tract, it is divided in the anterior orbital gyri (7), the medial orbital gyri (8), the posterior orbital gyrus (9) and lateral orbital gyri (10).

Initially the olfactory tract passes caudally in the olfactory sulcus and just rostral to the anterior perforating substance it divides into the **lateral** and **medial olfactory striae**. The neurons in the olfactory bulb, which give rise to the lateral olfactory stria, give collaterals to the anterior olfactory nucleus and the **anterior perforating substance**. These axons pass along the lateral margin of the anterior perforating substance terminating in the **prepiriform cortex** and the **amygdaloid nuclear complex**.

The prepirform cortex is a portion of the rhinencephalon consisting of the paleocortex. Technically, the paleocortex is a layer of the cerebral cortex intermediate phylogenetically between the neocortex and the archicortex. The neocortex is the outer layer of the cerebral heispheres, composed of six layers involved in higher functions such as sensory perception, generation of motor commands, spatial reasoning, conscious thought and language. The archicortex is a portion of the cerebral cortex that, with the
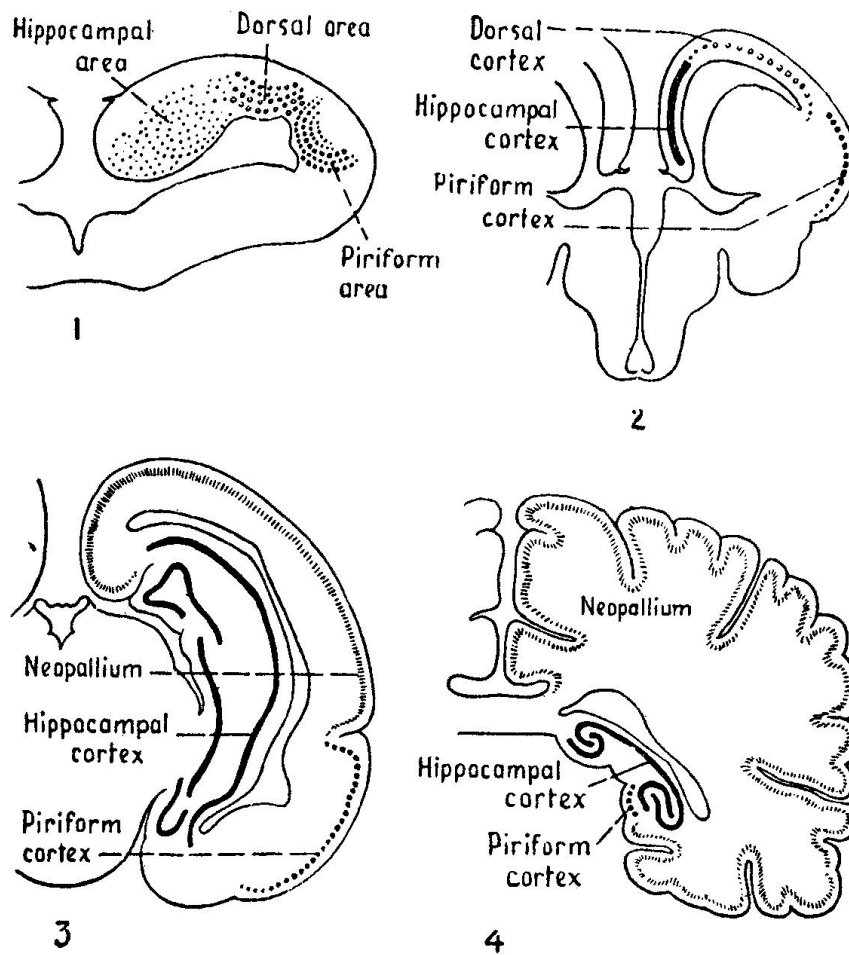
paleocortex, develops in association with the olfactory system, and which is phylogenetically older than the neocortex, lacking its six layers. In actuality, the archicortex is any cortex with fewer than six layers, specifically the three layered hippocampal cortexes. The embryonic archicortex corresponds to the cortex of the dentate gyrus and as stated above, the hippocampus in mature mammals. Since it is part of the limbic system, it has functions related to emotions and formation of memory. The rhinencephalon is that part of the brain involved in olfaction. One definition of the rhinencephalon is that it includes the olfactory bulb, olfactory tract, anterior olfactory nucleus, anterior perforated substance, medial olfactory stria, lateral olfactory stria, parts of the amygdala and prepyriform area Some references classify other areas of the brain related to perception of smell as rhinencephalon, but areas of the human brain that receive fibers strictly from the olfactory bulb are limited to those of the paleopallium (in humans, the paleopallium consists of the parahippocampal gyrus, and the primary and secondary olfactory cortex). As such, the rhinencephalon includes the olfactory bulb, the

olfactory tract, the olfactory tubercle and striae, the anterior olfactory nucleus and parts of the amygdala and the piriform cortex.
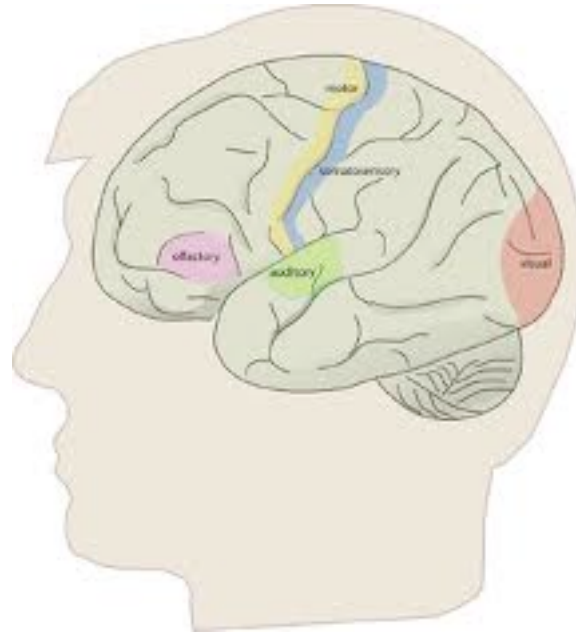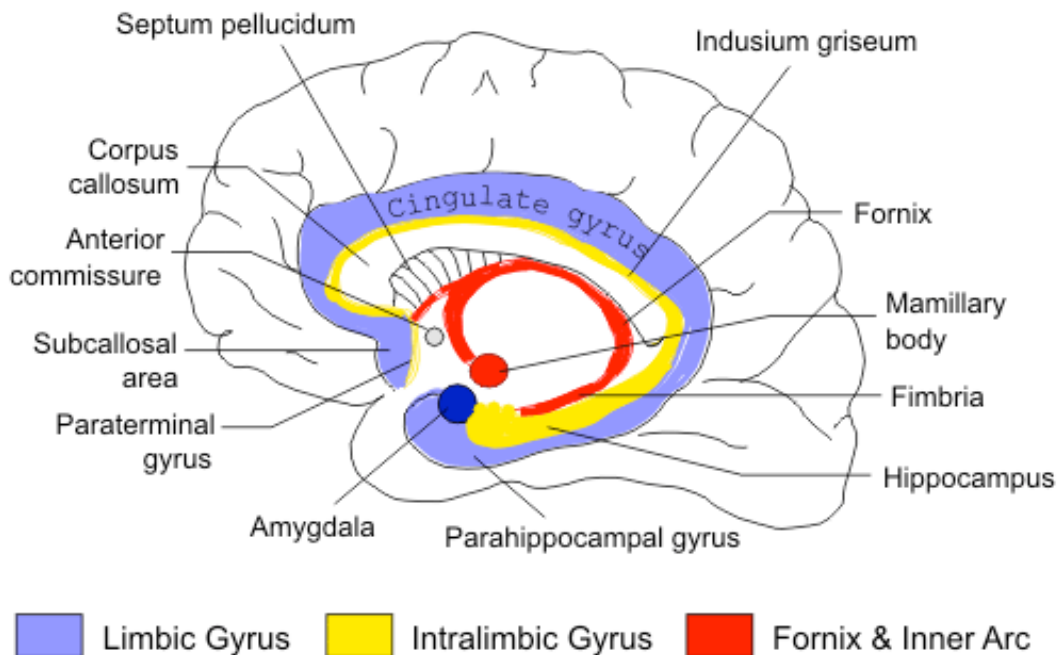

The prepiriform cortex and the amygdaloid nuclear complex constitute the **primary olfactory cortex**.

The prepiriform cortex is often referred to as the lateral olfactory gyrus. It extends along the lateral olfactory stria to the rostral amygdaloid region. It is considered an olfactory relay center. Impulses in this system are somewhat unique as compared to the other sensory systems in that they do not form relays within the thalamus before passing on to the cortex.

As indicated above, immediately caudal to division of the olfactory tract into the medial and lateral olfactory striae, and deep within the sylvian fissure there is an area called the anterior perforated substance. The anterior perforated substance **(APS)** is so named because it contains numerous perforations made by delicate perforating arteries from the internal carotid, anterior choroidal, and anterior and middle cerebral arteries to the basal ganglia, anterior portion of the thalamus, anterior limb, genu, and posterior limb of the internal capsule. It is also the exit site for the inferior striate veins. Posteromedially it is bordered by the optic tract, posterolaterally by the anteromedial surface of the uncus, and

laterally by the limen insulae. Medially, the **APS** extends above the optic chiasm to the interhemispheric fissure.   Along its posterior border is a smooth band, the **diagonal band of Broca** the fibers of which arise from the anterior perforating substance along with fibers from the **parolfactory area (subcallosal area)** and the **subcallosal gyrus**. These fibers course backward in the longitudinal striae to the dentate gyrus and the hippocampal region. This is a cholinergic bundle of nerve fibers , which interconnects the paraterminal gyrus in the septal area with the hippocampus and lateral olfactory area. The paraterminal gyrus (subcallosal gyrus, peduncle of the corpus callosum) is a narrow lamina on the medial surface of the hemisphere in front of the lamina terminalis, behind

The Limbic System

Septum pellucidum

Indusium griseum

Corpus callosum

Cingulate gyrus

Fornix

Anterior commissure

Subcallosal area

Mamillary body

Paraterminal gyrus

Fimbria

Amygdala

Parahippocampal gyrus

Hippocampus

Limbic Gyrus   Intralimbic Gyrus   Fornix & Inner Arc

the parolfactory area, and below the rostrum of the corpus callosum. It is continuous around the genu of the corpus callosum with the supracallosal gyrus.
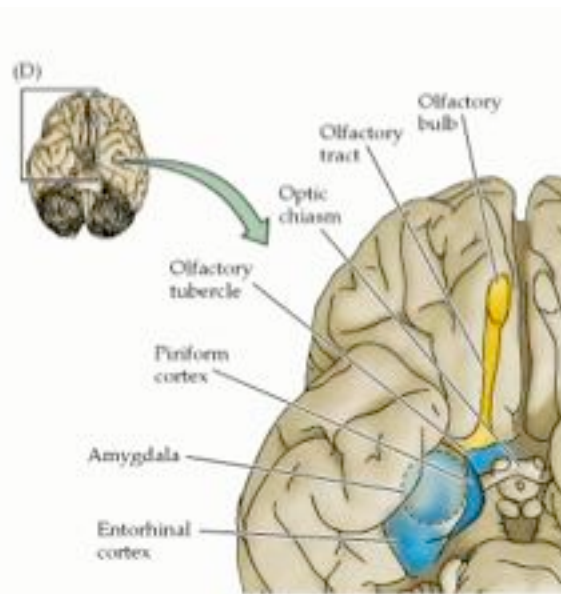
In the rostral (anterior) portion of the anterior perforating substance are rudiments of the
olfactory tubercle in humans. The olfactory tubercle receives axons from the olfactory
bulb, the anterior olfactory nucleus, the amygdaloid nuclear complex and the **temporal
neocortex.** It projects axons into the **stria medullaris** and the **medial forebrain bundle**.
The stria medullaris also contains efferent fibers from the septal nuclei, which will be
described later, lateral preoptico-hypothalamic region, and anterior thalamic nuclei. The
stria medullaris axons terminate in the **habenula**. The habenula is involved in pain
processing, reproductive behavior, nutrition, sleep-wake cycles, stress responses and
learning. There is some evidence to suggest it is also involved in reward processing. The
medial forebrain bundle is part of the reward system in that its stimulation creates a
sensation of pleasure.

The medial olfactory stria extends medially and becomes continuous with the **subcallosal
area (parolfactory area)**, located beneath the rostrum of the corpus callosum. It is
separated from the subcallosal gyrus (paraterminal gyrus) by the posterior parolfactory
sulcus.

The subcallosal area and the subcallosal gyrus constitute the **septal area (paraterminal
body)**. Within the septal area are two nuclei, the **medial** and **lateral septal nuclei**, which
are located just anterior to the anterior commissure. The septal nuclei are involved in
reward and reinforcement along with the nucleus accumbens, which plays a role in the
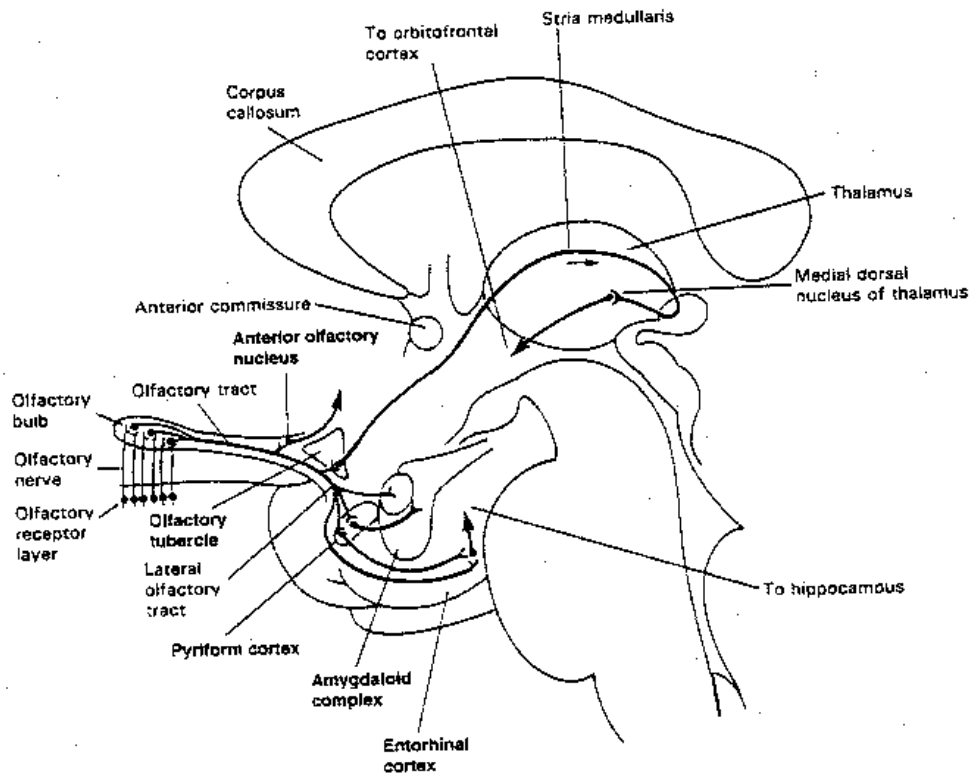feeling of pleasure, as well as fear and addiction to drugs.
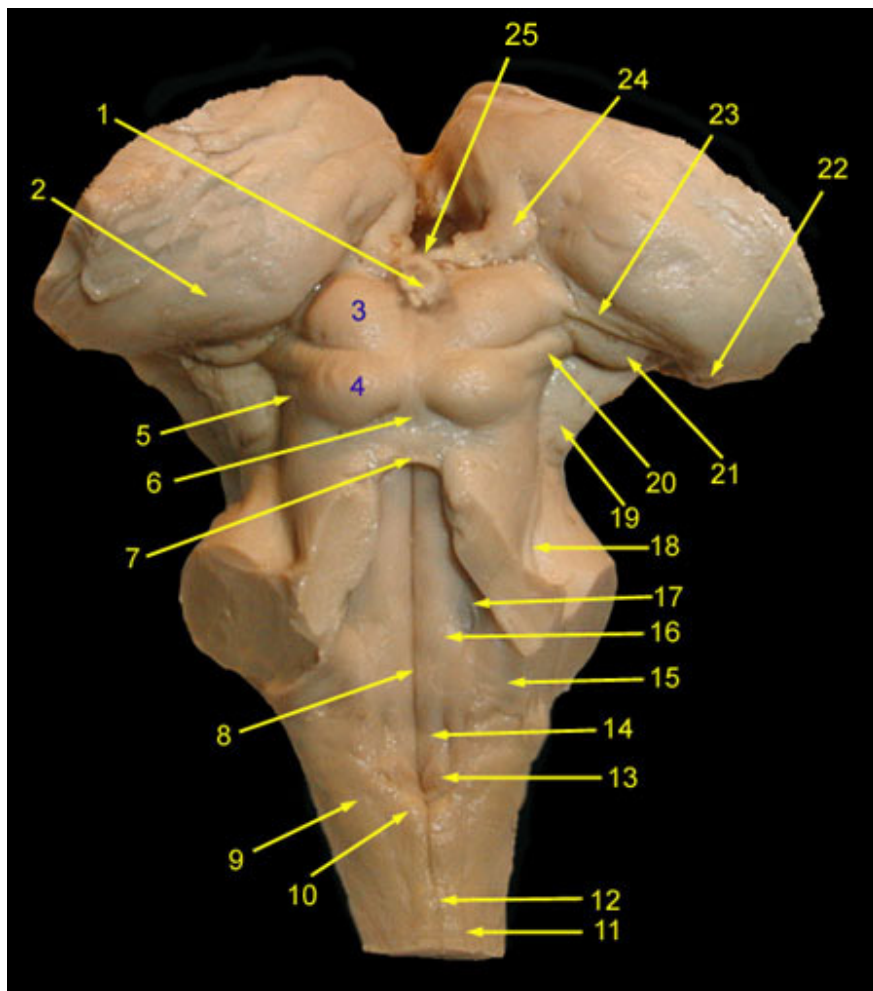
Posterior view of the brain stem

(1. Pineal gland, 2. Thalamus (Pulvinar), 3. Superior colliculus, 4. Inferior colliculus, 5. Lemniscal trigone, 6. Frenulum veli, 7. Superior medullary velum, 8. Median sulcus, 9. Gracile tubercle, 10. Cuneate tubercle, 11. Posterior intermediate sulcus, 12. Posteromedian sulcus, 13. Vagal trigone, 14. Hypoglossal trigone, 15. Striae medullares, 16. Facial colliculus, 17, Locus coeruleus, 18. Parabrachial recess, 19. Crus cerebri, 20. Inferior collicular brachium, 21. Medial geniculate body, 22. Lateral geniculate body, 23. Superior collicular brachium, 24. Habenula, 25. Habenular commissure**)**

The medial septal nucleus becomes continuous with the **diagonal band of Broca** and thus establishes connections with the amygdaloid nuclear complex. The lateral septal nucleus appears to be continuous over the anterior commissure with scattered neurons of the septum pellucidum. The septal nuclei receive a large number of afferent projections and sends efferent projections to the hippocampal formation via the fornix and the

amygdaloid complex. The medial septal nucleus also receives and sends fibers to the reticular formation of the midbrain. The septal nuclei are also believed to participate in reciprocal connections with the olfactory bulb, hypothalamus, habenula, cingulated gyrus and the thalamus.

The **piriform lobe** consists of the **lateral olfactory stria**, the **uncus** and the **anterior**

To orbitofrontal cortex

Stria medullaris

Corpus callosum

Thalamus

Anterior commissure

Medial dorsal nucleus of thalamus

Anterior olfactory nucleus

Olfactory tract

Olfactory bulb

Olfactory nerve

Olfactory receptor layer

Olfactory tubercle

Lateral olfactory tract

To hippocampus

Pyriform cortex

Amygdaloid complex

Entorhinal cortex

part of the **parahippocampal gyrus**. The piriform lobe is divided into several regions, which include **prepiriform**, the **periamygdaloid** and the **entorhinal** areas. The prepiriform area, often referred to as the lateral olfactory gyrus, extends along the lateral olfactory stria to the rostral (anterior) amygdaloid region. Since its afferent fibers are derived from the lateral olfactory stria, it is regarded as an olfactory relay center. The periamygdaloid area is a small region anterior and above the amygdaloid nuclear complex and is very closely related to the prepiriform area. The entorhinal area is the most posterior part of the piriform lobe, which corresponds to area 28 of Brodmann and constitutes a major portion of the anterior parahippocampal gyrus. The entorhinal cortex

does receive direct projections from the olfactory bulb. Information from the olfactory bulb and tract is also conveyed to the entorhinal cortex through synapses in the prepiriform cortex. The entorhinal cortex projects to the amygdala and is involved in emotional and autonomic responses to odor. It also projects to the hippocampus and is involved in motivation and memory. Odor information is stored in long-term memory
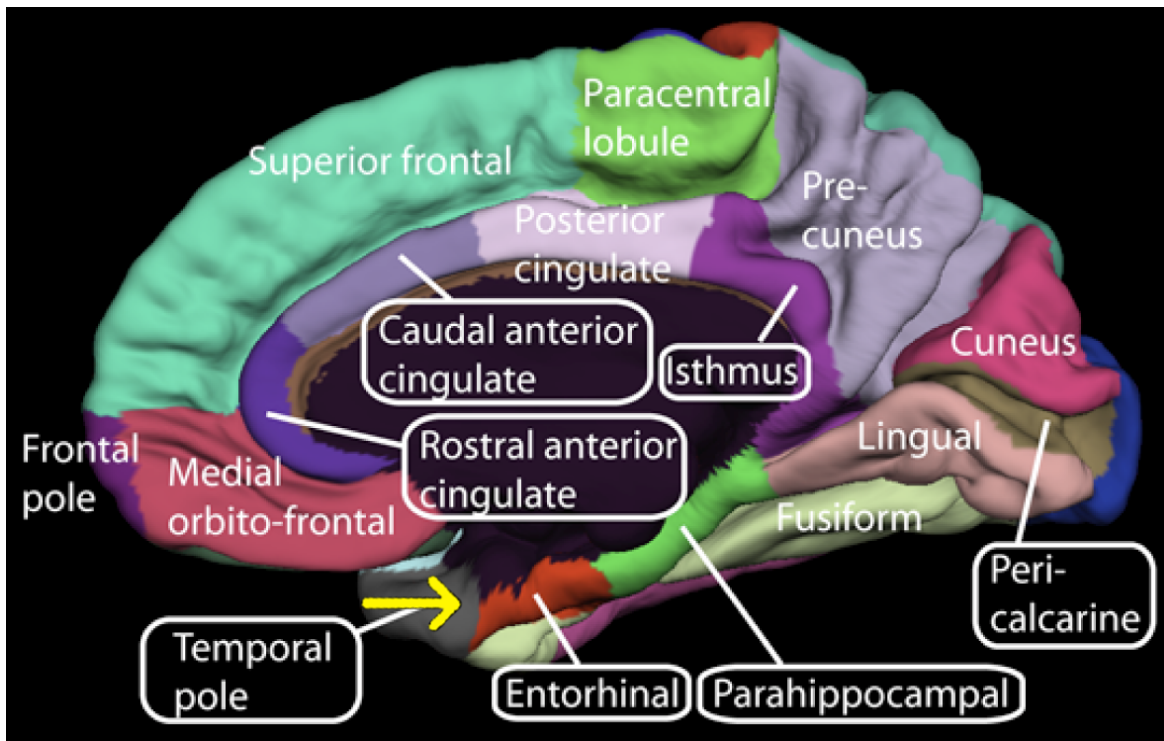

and has strong connections to emotional memory.

The prepiriform cortex sends axons to the entorhinal cortex, the basal and lateral amygdaloid nuclei, the lateral preoptic area, nucleus of the diagonal band of Borca, the medial forebrain bundle and to parts of the dorsomedial nucleus of the thalamus. The dorsomedial nucleus of the thalamus then projects to the orbitofrontal cortex.

The orbitofrontal cortex, which mediates conscious perception of odor, receives projections from four general areas via the thalamus: the piriform cortex; parts of the amygdala; the olfactory tubercle and part of the entorhinal cortex. The afferent pathways through the thalamus to the orbitofrontal cortex are thought to be responsible for the
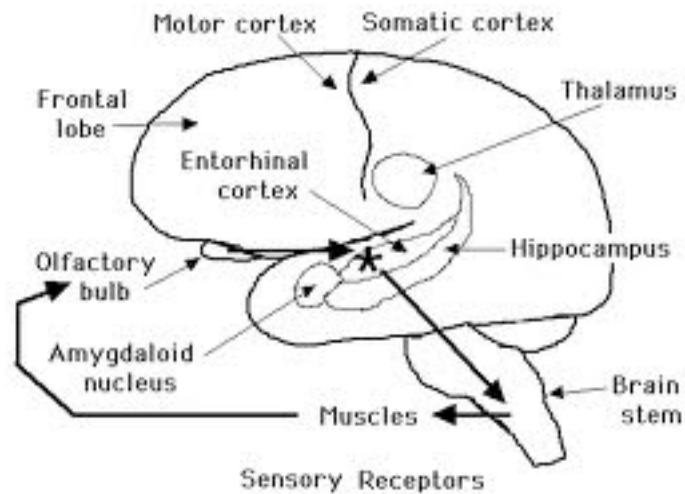
perception and discrimination of odors, because people with lesions of the orbitofrontal cortex are unable to discriminate odors.

The orbitofrontal cortex is that part of the brain involved in cognitive thinking or to put it another way information processing. The orbitofrontal cortex gets its name due to the fact it is that portion of the frontal lobe, lying on the orbital plates of the frontal bones, which form the bony roof of the orbits. It is also defined as that part of the prefrontal cortex, which receives projections from the mediodorsal thalamus.   Although the

Orbitofrontal
cortex

Figure 11.8
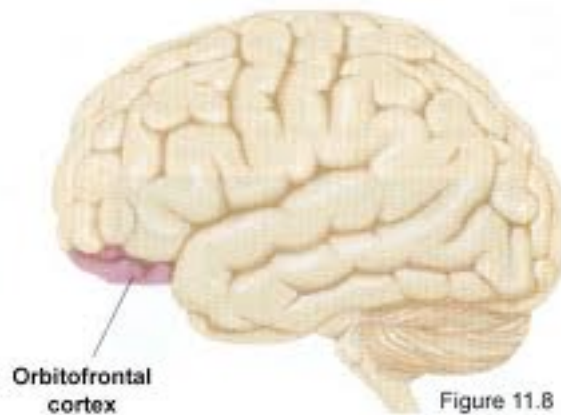
orbitofrontal cortex receives much of its information through the thalamus it also receives direct projections from the olfactory cortex.

The **entorhinal cortex** is regarded as a **secondary olfactory cortical area**. Although, this aspect of the entorhinal cortex has nothing to do with olfaction, it is an important fact that should not be forgotten; the entorhinal cortex is one of the first areas to be affected in Alzheimer's disease, with the first symptom being an impaired sense of direction. This is related to the fact that the entorhinal cortex has a neural map of the spatial environment. Projections from the olfactory cortex to the amygdala and from the amygdala to the hypothalamus are believed to be involved in the emotional and motivational aspects of smell as well as many of the behavioral and physiological effects of odors. It is because of the orbitofrontal cortex involvement of emotion and the behavior of pleasurable effects that it is considered part of the limbic system.
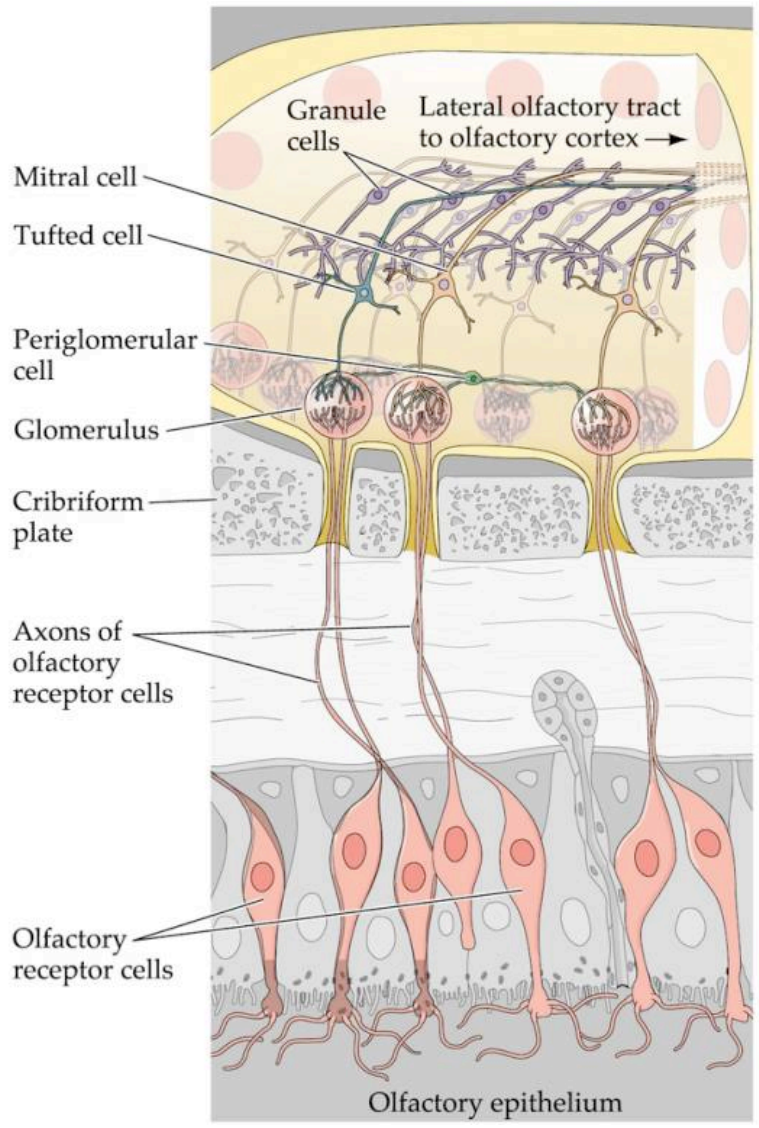
Motor cortex Somatic cortex

Frontal lobe

Thalamus

Entorhinal cortex

Olfactory bulb

Hippocampus

Amygdaloid nucleus

Brain stem

Muscles

Sensory Receptors

Molecular Considerations

The ability of the olfactory system to discriminate thousands of different odors is well known. It appears that molecules of odorants are dissolved or in some fashion processed in the mucus coating the olfactory epithelium. The processed molecules are recognized by olfactory receptors located on the dendrites of the olfactory sensory neurons. The process of the binding of the processed odorant molecules to a receptor leads to the synthesis of cAMP through the stimulation of adenyl cyclase via a G protein called GcAMP. This in turn opens a cyclic nucleotide-gated channel, which causes an influx of calcium ion along with some sodium ion into the cell, giving rise to a degree of depolarization. The influx of calcium ions opens a calcium ion-activated channel, which in turn leads to an efflux of chloride ion, which further depolarizes the cell, giving rise to an action potential. It appears that the identification of a particular molecule is accomplished through a process of encoding by receptors, which recognize certain structural features of the molecule. It is also believed; each receptor may serve as one component of the code for many odorants, thus allowing for the discrimination of a large number of different odorants. Thus the stereotyped spatial map of sensory information in each olfactory bulb may not be so much based on different odors, of which there are seven primary odors, but rather on different molecular features, each of which may be shared by a variety of odorants.

The seven primary odors (i.e. camphoraceous, musky, floral, pepperminty, ethereal (ether-like), pungent and putrid) are considered to be equivalent to the three primary colors, because every known odor can be produced by appropriate mixtures of the primary odors. Molecules with the same primary odor appear to have particular configurations, and these configurations are thought to fit appropriately shaped receptors in olfactory nerve endings. Some molecules may fit more than one receptor in different fashions and these are considered to signal a complex odor. Linda B. Buck and Richard Axel, for which they received the Nobel Prize in 2004, developed this concept of odorant molecules being recognized by specific receptor proteins

Functional Considerations

While the olfactory nerves are rarely the seat of disease, they frequently are involved by disease or injury of adjacent structures. The most common traumatic injury of the olfactory nerve occurs in head injury, usually of the acceleration-deceleration type as occurs in motor vehicular accidents. Fractures of the cribriform plate of the ethmoid bone or hemorrhage at the base of the frontal lobes may cause tearing of the olfactory nerves. The most common chief complaint of patients with olfactory nerve injury is not loss of smell but a decrease in their ability to taste. The olfactory nerve plays a key role in the perception of taste because of the volatile substances in many foods and beverages. The olfactory nerves may be involved as a consequence of meningitis, neuritis (inflammation of the olfactory nerves, bulbs or tracts) or abscess of the frontal lobe, which can give rise to an impaired sense of smell. Diabetes mellitus can also give rise to an impaired sense of smell through its underlying causation of infarction to these structures.

The olfactory bulb and tract may be contused or lacerated in head injuries, such as in fractures of the cribiform plate of the ethmoid bone and the body of the sphenoid bone. These injuries may give rise to a total loss in smell (anosmia) due to bilateral injuries to the olfactory nerves and/or olfactory bulbs or tracts or a transient loss with smell returning in approximately 2 weeks.

Unilateral anosmia may be of important diagnostic significance in localizing intracranial neoplasms, especially meningiomas of the sphenoidal ridge or olfactory groove or when hypophysial tumors extend above the sella turcica. Sometimes patients with injuries to the olfactory bulb or tract will experience parosmia, which is not a loss in the ability to smell, but rather is a perversion in the sense of smell. In these patients they can smell an odor present, but they misrepresent it. Often the odor they describe is unpleasant such as decaying fish, garbage etc.

 Olfactory hallucinations (phantosmia) frequently are a consequence of lesions involving the parahippocampal gyrus, the uncus or adjoining areas around the amygdaloid complex. Phantosmia, in contradistinction to parosmia, is a symptom, which manifest by the

patient smelling an odor that is not present, whereas in parosmia the patient misrepresents the odor that is present. What is important to remember is that these olfactory hallucinations may precede a generalized convulsion. Such seizures are referred to as "uncinate fits."

Lastly, there is a syndrome called the Foster-Kennedy syndrome in which there is homolateral (unilateral, ipsilateral) anosmia and blindness with atrophy of the olfactory and optic nerves, and contralateral (opposite side) papilledema due to tumors at the base of the frontal lobe. This presentation is due to a tumor compressing the ipsilateral optic and olfactory nerve, bulb or tract giving rise to atrophy of these structures but also leading to an increase in intracranial pressure, thus causing contralateral papilledema.