Long Term Consequences of Repeated Brain Injury - A Cadaveric Study

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Abstract

The purpose of this paper was to examine the long term consequences of repeated brain injury through a cadaveric dissection. For this literature review, the limbic system will be the anatomical structure of focus. In particular, this paper will examine the effects of mild and traumatic brain injury. Mild traumatic brain injuries can cause long term damage which can lead to memory loss, fatigue, hormonal imbalances, behavioral issues, and mood inconsistencies. These symptoms all can be linked back to changes within the limbic system, especially when they have occurred more than once. In this review of literature I will discuss the anatomy and physiology of the cerebrum, nervous system, damage to the limbic system and surrounding areas due to a mild traumatic brain injury. I will discuss the symptoms, treatments, and lasting effects of mild and traumatic brain injuries. This study was based on current evidence and is meant to provide and in depth look into how damage to a specific area of the brain, the limbic system, can cause dramatic long lasting effects if proper precautions are not taken directly after injury.

Keywords: Mild Traumatic Brain Injury, Traumatic Brain Injury, Limbic System, Nervous System, Anatomy, Physiology

NERVOUS SYSTEM

WHAT IS IT?

The nervous system is the connection between the brain and the rest of the body, made up of complex networks that send electrical signals, called action potentials, to neurons, that produce a reaction to a stimulus once the action potential is received**.** (The Effects of Nervous System Injury on Sensory and Motor Function, pg 1) Structurally, the nervous system is made up of two components: the central nervous system (CNS) and peripheral nervous system (PNS) and is comprised of neurons which are the basic building blocks of the nervous system. In this section of the literature review will discuss the make up of neurons and provide an in depth look into the CNS and PNS.[2,5,26,88]

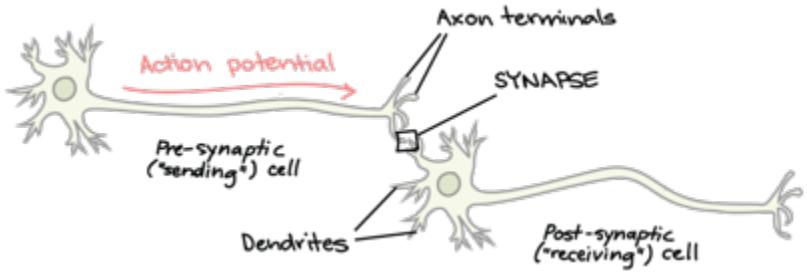
NEURONS

The nervous system is made up of neurons and glial cells. While smaller in number when compared to their glial counterpart, neurons make up the structural and functional units of the nervous system. They are the conducting cells of the nervous system and are responsible for transporting high-speed signals, called nerve impulses, to and from the brain. Each neuron is composed of a cell body, dendrites, and axons. The most central portion of the neuron is called the cell body or soma. The cell body contains a nucleus and cytoplasm as well as organelles surrounding it. It is also the site of synthesis for virtually all neuronal proteins and membranes.[5,14,26,88]

Most neurons have multiple dendrites which extend outward from the cell body. The dendrites are specialized to receive chemical signals from the terminal ends of the axons. More specifically, the dendrites convert the signals received from the terminal axonal ends into small

electric impulses and transmit them inward in the direction of the cell body. Each dendrite has many branches which are referred to as dendritic spines. These spines are extra sensitive and contain signaling systems that are necessary for synaptic function and plasticity.[5,14,26,83,88] Finally, each neuron has a single axon that is a long strand spanning out from the cell body. The axon is connected to the cell body via the axon hillock. The axon hillock is responsible for integrating signals from multiple synapses and also serves to provide a connection between the cell body and axon. Typically, axons carry neural information away from the soma and often undergo extensive branching, which enables them to communicate with many target cells. Finally, at the end of the axon is the axon terminal (see figure 1 below). The axon terminal is responsible for causing the release of neurotransmitter chemicals and also communicates with target neurons.[5,14,26,83,88]

Figure 1. Axon Anatomy



Many axons are covered in a myelin sheath, which is composed of layers of lipid and protein. Because of myelin's composition, axons covered by this substance have increases in the velocity of impulse conduction, which leads to increases in the rate at which nerve impulses travel along the nerve.[14] It is important to note that while the section attempts to describe each anatomical structure in isolation that in fact a single neuron does not act in isolation. Neuronal communication most often depends on the connections that multiple neurons make with each

other. Overall, the nervous system has three different types of neurons, which serve different roles in relaying information throughout the body and they are: afferent, efferent and relay neurons. Afferent neurons function to transmit impulses from the sensory receptor on the periphery to the brain and spinal cord for interpretation. Efferent neurons on the other hand function to transmit impulses from the brain and spinal cord to the periphery. Lastly, a relay neuron is as the name implies most responsible for transmitting impulses between afferent and efferent neurons.[5,14,26,70,83,88]

In between neurons are synapses that form a synaptic cleft. A synapse is a small space between two neurons that allow for information to be sent from one neuron to another.[26] Communication between neurons occurs via a process called neurotransmission. Neurotransmission facilitates interaction between neurons or between neurons and other cell types. It is the fundamental process that drives information transfer between neurons and their targets and occurs at a highly specialized structure known as the synapse. The synapse is a highly specialized contact between a presynaptic and postsynaptic cell built to transmit information with high fidelity. Following action potential generation, large quantities of neurotransmitters are released into the synaptic compartment. The process of conduction, however, begins when the primary motor cortex receives a stimulus which triggers an action potential in a motor neuron. Following the triggering of an action potential an electrical signal is sent causing electrically charged particles (ions) to move across a neuronal barrier. These ions are able to move across a membrane or barrier because of the presence of a neurotransmitter. Neurotransmitters allow a neuron to be stimulated and stimulate the release of acetylcholine that is used to stimulate a response from a stimulus.[5,14,26,83,88]

When an action potential is sent, a series of physiological processes occurs within the membrane. On average the resting membrane potential of a neuron is -70 millivolts (mV). Typically, changes to the resting potential lead to depolarization, repolarization, or hyperpolarization of the membrane. These changes are determined by the ionic flow into and out of the membrane. The standard is to compare the inside of the cell relative to the outside, so the membrane potential is a value representing the charge on the intracellular side of the membrane. Typically, the concentration of Sodium (NA^+) outside of the cell is 10 times greater than the concentration inside. Additionally, the concentration of Potassium (K^+) inside the cell is greater than the outside. Large anions and negatively charged proteins are also circulating inside the cell creating a negative charge. With the ions distributed across the membrane at these concentrations, the difference in charge is measured at -70 millivolts (mV), which is considered the resting state. Because there is a potential difference across the cell membrane, the membrane is said to be polarized. In general, if the membrane potential becomes more positive then that membrane is said to be depolarized. If the membrane becomes more negative than it is said to be hyperpolarized. In order for an electrical signal to be sent, the membrane potential has to change. This process begins with a channel opening for NA^+, because the concentration of NA^+ is higher outside the cell than on the inside by a factor of 10, ions will rush into the cell because they are driven by a concentration gradient. Since NA^+ is a positively charged ion it will change the voltage of the cell, this shift in the membrane potential from a negative state to a more positive state is known as depolarization. The membrane potential during the influx of NA^+ can reach +30mV. As the membrane potential reaches +30mV, other voltage channels begin to open within the membrane. These channels are more specific towards the K^+ ion. As K^+ ions begin to leave

the cell, taking a positive charge with them, the membrane potential begins to move back towards its resting potential state. This process of progressing back towards resting potential is known as the repolarization phase. Hyperpolarization, then, represents the phase when there is a lowered membrane potential which is caused by the efflux of K^+ ions and closing the K^+ channels. It is during this phase that another action potential can be released.[5,14,26,83,88]

Finally, glial cells are supportive cells within the central nervous system. Unlike neurons, glial cells do not conduct electrical impulses. Their major role is to surround neurons and provide support for and insulation between them. Glial cells are by far the most abundant cell types in the central nervous system.[5,14,26,83,88]

FUNCTION OF NERVOUS SYSTEM

SENSORY

The nervous system can be broken up on the basis of its functions. There are three ways that the nervous system is divided based on three functions and they include: sensory, motor integration, and motor systems.. The first major function of the nervous system is sensation. The sensory portion of the nervous system is responsible for receiving information about the environment to gain input about what is going on in the environment. Anatomical structures included in the functional sensory division of the nervous system include taste, smell, touch, sight and hearing. Each of the senses have varying stimuli. For example, taste and smell senses are most often stimulated by chemical substances, touch is most often stimulated by a mechanical stimulus, sight is stimulated by light, and hearing is the perception of sound. Together, these five senses work to receive stimuli from the external environment.[5,14,26,83,88]

The eye contains photoreceptors that allow for sight. Photoreceptors are a specialized type of cell found in the retina of the eye. The human eye contains two types of photoreceptors known as cones and rods, each of these contribute information that is used by the visual system to provide representation of the visual world. Cones provide vision during the day or in bright light environments and assist in allowing us to see finer details, whereas rods are for seeing black and white and aid in night vision. Rods are typically found towards the periphery of the retina and the cones can be found in concentration towards the most center portion of the retina. In general, a lack or deficiency in rods can lead to the development of night blindness and if cones are deficient it can lead to color blindness. These anatomical structures are most important to the nervous system because as stated above they provide information about the external environment.[5,14,26,53,83,88]

This is important because when a mild traumatic brain injury occurs, oftentimes reflexes to stimuli within the visual system are damaged. It has been reported in the literature that following a mild traumatic brain injury (mTBI) patients experience sensitivity to light, visual field deficits, saccadic dysmetria (abnormal eye movements) and impaired distance perception. More specifically, the pupillary light reflex (PLR) is most often compromised following a head injury. The PLR is a visual reflex that regulates the diameter of the pupil, which means it is responsible for controlling the amount of light entering into the retina. In patients with mTBI it has been reported that PLR responses were delayed, slowed and reduced when compared to healthy controls. More will be discussed later in this review of literature in specific sections on mTBIs.[53]

The auditory system is responsible for the sense of hearing. It is divided up into two subsystems: the peripheral auditory system and the central auditory system. The peripheral

auditory system consists of the outer, middle and inner ear. The central auditory system consists of the cochlear nucleus up to the primary auditory cortex. The outer ear of the peripheral auditory system contains the pinna, which are made up of folds of cartilage. These anatomical structures surround the ear canal and function mainly as sound attenuators allowing the brain to determine the location of the sound. From the pinna sound waves travel through the auditory canal, a structure is responsible for amplifying the sound and allowing it to travel to the tympanic membrane. The tympanic membrane serves as the gatekeeper, allowing sound waves to pass from the outer ear to the middle ear. When the sound wave passes from the inner ear to the middle ear it immediately causes the ossicle bones (malleus, incus and stapes) to vibrate. These three bones amplify or increase the pressure of the vibrations. This is important because it is this increase in pressure that leads to the sound wave traveling to the inner ear. Sound waves from the middle ear into the inner ear by way of the oval window. Once the sound wave enters the inner ear the environment shifts from air to an environment that is filled with fluid. It is in the inner ear where sensory information is transformed into neural information. The cochlear duct is the major anatomical structure located in the inner ear and it contains the organ of corti. The organs of corti contain hair-like structures that are responsible for turning the sound wave into an electrical neural signal. The organ of corti lies in the basilar membrane and contains two types of hair cells: inner hair cells and outer hair cells. Inner hair cells distinguish between sound and vibrations through cilia that line the basilar membrane. Outer hair cells act as amplifiers allowing for distinguishing between different frequencies, such as speech and music.[87] The central auditory system takes these sound waves from the cochlear nucleus through cranial nerve VIII to different parts of the brain, specifically the superior olivary process in the pons and the inferior

colliculus in the midbrain. The superior olivary process is the first major converging point of information into the central auditory canal. The inferior colliculus is the main auditory center for the body. The information from the superior olivary process and inferior colliculus end up in the thalamus where it is then passed to the primary auditory cortex for further processing. This is located in the temporal lobe. The portion of the primary auditory cortex that receives sound is the left posterior superior temporal gyrus and within that is the area that processes pitch, sound, and rhythm.[103] The brainstem then receives the signals that were sent via the vestibulocochlear nerve transmitting it to the brain, which will then process the signals registered as sound to a person.[26] In addition to transporting sound waves, the vestibulocochlear nerve is also responsible for transmitting signals used to maintain equilibrium. A brain injury to this area causes deficits in balance and hearing dysfunctions. Damage can cause the inability of knowing the body's position in space. People with this injury often feel as if they are upright when really they are leaning one direction or the other. Orientation in space is controlled by the semicircular canals and when neurons die, stimuli is not properly sent and processed, causing this lack of orientation.[62]

The last primary sensory system is the olfactory system. The olfactory system is a powerful sensory modality that is capable of detecting environmental odors and translating them into perceptions and behaviors. The olfactory system contains sensory receptors which are responsible for the recognition of odors. In general, the nasal passage is made up of a lateral wall, septal wall, roof and floor. Lining the nasal cavity are olfactory receptors that are located in the upper part of the nasal cavity called the mucous membrane. Olfactory receptors bind odor

molecules that allow one to smell. The nasal cavity is covered in mucous and under this mucous lie cilia that also help in detecting smells.[62,103]

Within the nasal cavity are microvilli that line the mucous membrane. The role of these microvilli are to move particles trapped in the membrane out of the nose. The major receptors involved in olfaction are the olfactory nerves. The body for these receptors lies within the olfactory epithelium (see Figure 2 below for anatomical location).[97,106]

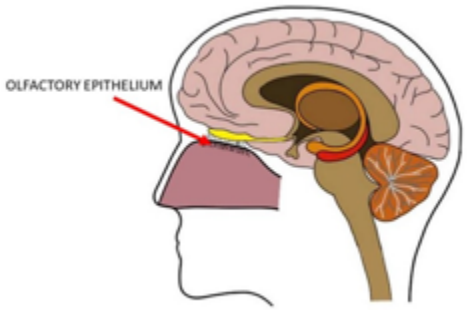


Figure 2. Image of the Olfactory Epithelium

The olfactory nerve travels through the cranium and into the olfactory bulb where this nerve connects to the mitral cells.[26] This nerve sends axons to the brain via the olfactory tract. The olfactory nerve is the shortest cranial nerve within the cranium, making it susceptible to lesions created by blunt trauma. Damage to the olfactory nerve can lead to reduced or absent sense of smell. If however, the olfactory nerve is damaged, pain can still be transmitted via the trigeminal nerve.[93]

INTEGRATION

Sensory integration is a complex process that takes place in the central nervous system that produces task-specific motor output based on selective and rapid integration of sensory information from multiple sources. During integration, sensory input is converted into electrical

signals called nerve impulses that are transmitted to the brain. There all of the signals are brought together to create sensations, produce thoughts, or add to memory. Based on the sensory input and integration, the nervous system then responds by sending signals to muscles (causing them to contract or withdraw) or to glands (causing them to produce secretions). It is this process of combining systems to produce a response that is called integration.[16,56]

MOTOR SYSTEMS

The motor system is responsible for controlling movement of the skeletal muscles. Motor systems are responsible for voluntary movement and the way in which the movements are made. These movements require consistent information coming from proprioceptors in muscles. There are also impulses that come from the frontal lobe and cerebellum that allow for the movement of muscles. A few areas that the motor systems affect are posture, speed at which a movement occurs, and whether the movement is voluntary or involuntary. This means that motor movement is reflexive as well as conscious. The two reflexes relating to skeletal muscles are monosynaptic and polysynaptic.[20,89]

A monosynaptic stretch reflex is also known as a muscle stretch reflex. This reflex allows direct communication between sensory and motor neurons that innervate muscle. The reflex starts inside of the muscle spindle in a muscle. The location of the muscle spindle allows the amount of stretch on a muscle to be determined. When a muscle is stretched sensory signals are sent from the muscle spindle by afferent fibers to the dorsal root of the spinal cord. An example of a monosynaptic reflex would be the patellar reflex.[118]

A polysynaptic reflex is a reflex that uses electrical impulses passed from a sensory neuron to a motor neuron via an interneuron in the spinal cord.[89] A polysynaptic reflex happens when a

stimulus is sent to a specific area signaling the body to move into flexion, such as stepping on a sharp object.[26]

In addition to the monosynaptic and polysynaptic reflexes, there are also groups in the brainstem that play an important function in signal transmission. These groups in the brainstem are called neuronal groups. Neuronal groups send signals to motor neurons signaling the automatic response, whereas the cerebral cortex is used in the more voluntary movements. A tract that is important in sending these signals down the spinal cord to the motor neurons is the pyramidal tract. This pathway doesn't only descend and function in motor movement, but it also can ascend through signal transmission. The pyramidal tract is important because it aids in the ability to have exact voluntary movement. It is mainly made up of axons in the corticospinal tract that descends from the brainstem. This pathway is uninterrupted by synaptic connection, therefore passing directly through from the cerebral cortex to the spinal cord. Most of the fibers from this tract are located in the primary motor cortex, which is where most of the electrical signals are sent allowing for gross motor movement to occur.[26]

PARTS OF NERVOUS SYSTEM

The nervous system is broken up into two main categories: the Central Nervous System (CNS) and the Peripheral Nervous System (PNS). The CNS is made up of the brain and spinal cord, whereas the PNS is broken down further into the autonomic nervous system (ANS) and the somatic nervous system (SNS).[26]

The Somatic Nervous System controls the voluntary processes of the body, such as conscious gross motor movement. The somatic nervous system consists of afferent and efferent nerves. Afferent neurons carry sensory impulses toward the CNS and the brain. Efferent nerves

carry stimuli away from the brain and CNS, toward the muscles for production of movement.[88] Given that the somatic nervous system has both sensory and motor neurons, this portion of the nervous system is capable of producing voluntary movement. A neurotransmitter, known as acetylcholine, is used to produce an excitatory response by the muscles, causing a muscle contraction. This muscle contraction can be seen clearly when a reflex point is triggered.[26,86,88]

The Somatic Nervous System is connected to the reflex arc. The reflex arc is a neural group that contains a sensory neuron that sends a signal, through an action potential pathway, to the spinal cord generating a subconscious muscle contraction known as a reflex. The most common reflex is the patellar reflex, however there are other reflex points as well.[26,86,88]

The ANS is part of the peripheral nervous system that controls the unconscious part of the body, such as heart rate and breathing. There are three divisions of which the ANS can be broken into. These are the sympathetic nervous system (SNS), parasympathetic nervous system (PNS), and the enteric nervous system.[26,88]

The SNS has neurons that are located in lateral horns within the spinal cord. Presynaptic fibers of the nervous system, located in the spinal cord, exit the spinal column through anterior roots of the spinal cord, and enter at the anterior rami of vertebrae T1 through L2, where the spinal nerves are. Anterior roots of the spinal cord are the efferent motor roots of a spinal nerve, and the anterior rami are the anterior portion of the spinal nerves. From the anterior rami, the presynaptic fibers ascend onto the sympathetic trunks by white rami communicantes. Next the presynaptic fibers pass through the inferior paravertebral ganglion, to adjacent anterior spinal nerve rami or it passes the trunk without synapsing and leads straight to the prevertebral ganglia. Paravertebral ganglia are where the preganglionic and postganglionic neurons synapse.[26,59,70,88]

The Sympathetic Nervous System contains afferent and efferent fibers that allow the CNS to receive sensory and motor inputs. Both the SNS and PNS have a preganglionic neuron with a cell body, and a postganglionic neuron with a cell body that aid in the reception of sensory and motor input. However the location of these structures are different. The preganglionic neuron is located in the CNS, while the postganglionic neuron is in the PNS and it innervates specific tissues. When the SNS is activated, a flight or fight response happens. A Flight or fight response occurs when a person is in danger or afraid and the body subconsciously reacts by activating the SNS as a mechanism of protection. This reaction causes a startle reflex, controlled by the cardiac accelerator nerve. The cardiac accelerator nerve produces physical effects within the body. The body's heart rate, blood pressure, and respiratory rate will increase when the SNS is activated. The SNS is always activated, assisting in inspiration and dilating the airways, regulating immunity in the spleen, thymus, and lymph nodes, however the SNS only becomes stimulated in high stress situations. The sympathetic effect is opposite of the PNS.[26,59,70,88]

The Parasympathetic Nervous System is part of the CNS and exits through cranial nerves, specifically III, VII, IX, and X, and through nerve roots S2-4. All of the parasympathetic ganglia are located in the cranium. (The specific nerves are talked about in the section labeled Cranial Nerves) The PNS is controlled by the vagus nerve, CN X, which slows the body's systems down. Cranial Nerve X sends signals to the thoracic and abdominal viscera, as well as the descending and sigmoid colon, and the rectum. There are four cell bodies of the vagus nerve located in the medulla oblongata. These cell bodies are the dorsal nucleus, nucleus ambiguus, nucleus solitarius, and spinal trigeminal nucleus, each having different functions. The dorsal nucleus allows parasympathetic output to the viscera. The nucleus ambiguua creates motor fibers and

preganglionic neurons that innervate the heart. Nucleus solitarius receive afferent sensations of taste from the viscera. Lastly the trigeminal nucleus receives sensations such as touch, pain, and temperature. The vagus nerve, due to its slowing effects, helps in maintaining the body's equilibrium, such as heart rate, blood pressure, and stabilized breathing. The PNS ultimately keeps a person relaxed while at rest. Keeping the body at equilibrium is important because when the body is not in equilibrium the heart rate, breathing, and blood pressure can become to fast, high, slow, or low putting the patient at risk of cardiovascular, pulmonary, or blood pressure issues.[26, 88, 98]

Lastly the Enteric Nervous System (ENS) is made up of two ganglionated plexuses known as the myenteric and the submucosal plexuses. The myenteric plexus is located in between the longitudinal and smooth muscle of the GI tract. The myenteric plexus assists in coordinating the contractility of muscle cells in the gut, helping with peristalsis. Peristalsis is an involuntary movement in the intestines or other canals causing tightening or loosening of those muscles, allowing for movement of the substances in those areas. The submucosal plexus is located within the submucosa. This plexus regulates the movement of water and electrolytes that pass over the intestinal walls.[26,88]

The ENS is a self contained nervous system in that it functions through reflex activity in a specific area, though it does receive information from the SNS and PNS. It also receives input from postganglionic or preganglionic sympathetic neurons. It aids in the movement of substances from the stomach, through the intestines, and out the rectum through motility produced in the reflex circuit of the circular and longitudinal muscles. Although this is part of the nervous system

the primary nervous systems in this paper are the PNS, SNS, and CNS. In this next section the nervous system in relation to the body will be discussed.[26,88]

CENTRAL NERVOUS SYSTEM AND PERIPHERAL NERVOUS SYSTEM IN RELATION TO BODY

The Central Nervous System is made up of the brain and spinal cord.[26] The brain weighs only about three pounds, but is crucial to human function. It controls every function of the body, taking in information from the outside world and processing it, then those signals are sent out for a person to speak, see, feel ,taste, and smell. The brain regulates emotion, intelligence, memory, personality, and other organs and hormone secretions.[78] Its functions are partly due to the way it is shaped structurally. There are many folds on the brain's exterior which increases the surface area for neurons. Neurons allow for communication between different areas of the brain by sending and receiving signals that transfer information to different parts of the brain. This allows for more action potentials to be sent and received, and therefore more information to be transported throughout the body. Most often, communication happens because of the thousands of neurons stored in the brain. These neurons can send and receive signals transferring information to different parts of the brain.[76]

In addition to the brain, the spinal cord has three very specific roles that allow the brain and body to receive signals. First the spinal cord sends messages from the brain through the PNS to the periphery. Second, it transfers signals from the periphery of the body to the brain. Lastly the spinal cord helps to coordinate reflexes that are specific to the spinal cord.[70]

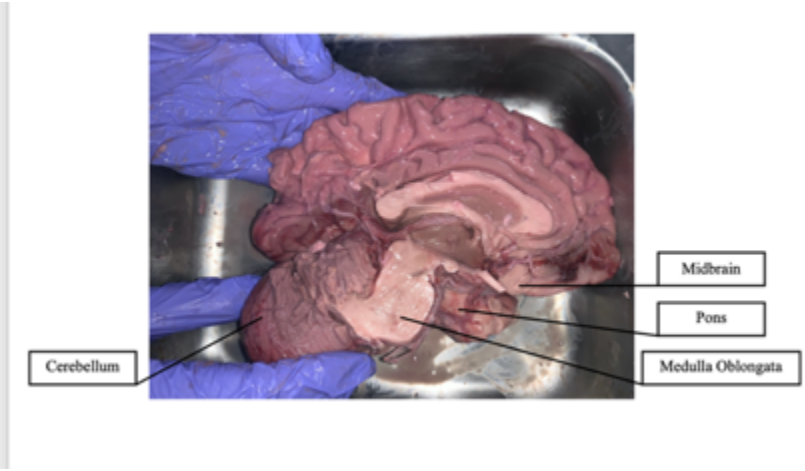
BRAIN/BRAINSTEM

The brain is the most complex part of the body, but surprisingly only weighs about 3-4 pounds. It is made up of 100 billion neurons that are linked by a quadrillion connections between.[26] The brain is also an auto regulator, meaning it controls most of the automatic functions the body performs. For example, 15 percent of the cardiac output is controlled by the brain.[26] Cardiac output is the amount of blood the heart pumps through the circulatory system in one minute.

The brain lies in the cranial cavity within the skull. In the center of the brain there is an anatomical structure called the foramen magnum. The foramen magnum is what houses the vertebral column. The vertebral column, also known as the spinal cord, passes through the foramen magnum connecting to the brainstem at the base of the brain. (see Figure 3 below)[26]

The brain is composed of the brainstem, which is split up into multiple sections. The sections most critical in relation to head injuries are the Pons, Medulla Oblongata, and the midbrain which is composed of the Mesencephalon and Diencephalon. (See section titled Mesencephalon and Diencephalon) The pons communicates with the cerebellum helping regulate respiration. The medulla is a relay center for sensory nerves and contains autonomic centers that help regulate the body automatically. In addition, the brain is connected in such a way that the right side is controlled by the left and left by right. Many of these connections occur in the medulla oblongata. The midbrain controls the visual and auditory centers, maintains

consciousness, and connects the cerebrum with the lower brain and spinal cord.[26]



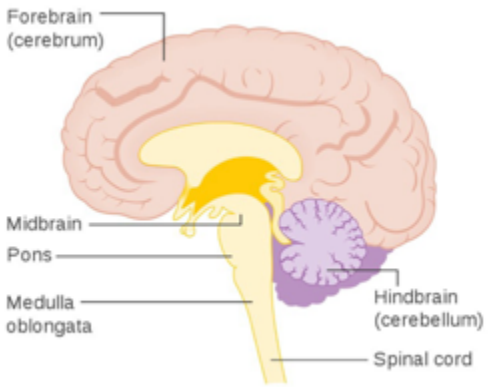


Figure 3. Brainstem and Surrounding Structures

The brain also consists of a covering called the meninges. The meninges are a protective layer that surrounds the brain. Meninges specifically protect blood vessels that innervate nerve tissue containing cerebrospinal fluid. The meninges are made up of three layers called the dura mater, arachnoid mater, and pia mater. Each has a specific function in protecting the brain.

SPINAL CORD

The spinal cord is a long tube-like structure allowing nerves to pass through the full length of the spinal column.[26, 70] The spinal cord consists of grey matter, white matter, interneurons, rootlets, and nerves. Within the spinal cord itself, white matter surrounds the grey matter. Grey

matter and white matter aid in the connection of nerve fibers to each other. A similar structure to this matter is the interneuron. These interneurons connect two nerve fibers together, creating a pathway that an electrical signal can be sent down, when responding to a stimulus. Interneurons are specifically stationed in the spinal cord and will not leave it. Whereas interneurons do not leave the spinal column, rootlets do, allowing for axons to exit the spinal column and retrieve stimuli from the peripheral nervous system, and bring the information to the central nervous system, where it will be processed.[26,70]

There are two kinds of rootlets in the spinal column: dorsal rootlets and ventral rootlets. Ventral rootlets consist of somatic neurons, which control motor function, whereas dorsal rootlets are made up of sensory fibers, controlling sensory information. Ventral rootlets are made up of neurons that are positioned in such a way that somatic neurons face the ventral horn, and the ventral rootlets extend axons out through the body, in order to gather information that will be sent back to the CNS. Similarly, dorsal rootlets consist of neurons that are unipolar bringing in sensory information. The rootlets make up the spinal nerves (making up the CNS) which will then extend out into the body towards the limbs via the peripheral nervous system, retrieve stimuli, and bring it back to the CNS for processing.[26, 70] The way in which the spinal cord and the brain connect is through the vertebral column at the brainstem.

PIA MATER

The pia mater is the innermost layer of the meninges. It covers the spinal cord and the brain. The pia mater is the only layer that connects closely to the brain. The pia mater is a mesh-like layer that covers every depression and sulci of the brain.[26] Having every gyrus (folds/ridges of brain) and sulci (grooves) closely covered by the pia mater allows for blood vessels to

innervate this layer and innervate the external portion of the brain.[26] The pia mater is loosely attached to the arachnoid layer of the brain. This attachment creates a small space called the subarachnoid space that is filled with Cerebrospinal fluid. The CSF travels the full length of the CNS filling in the spinal column and spaces in the brain, such as the subarachnoid space. Cerebrospinal fluid is vital because it provides the brain with a protective barrier and functions as a shock absorber. Cerebrospinal fluid also filters nutrients and chemicals in the blood and removes any waste products from the brain.[9,10,20,24-25]

ARACHNOID MATER

The arachnoid mater is the middle layer of the meninges. It covers the brain and spinal cord, however it is only loosely attached, unlike the pia mater. The arachnoid layer takes the shape of the depressions, fissures, and sulci of the brain.[26] The arachnoid layer is made up of a spider web like texture containing simple squamous epithelium. Simple squamous epithelium is a type of skin cells containing flat cells that comes in contact with the basal lamina, which is one or two layers of the basement membrane. The epithelium consists of collagen, which forms elastic fibers that spread between the arachnoid layer and the outer portion of the pia mater.[26] Since the arachnoid layer is loosely attached, it does not create a subarachnoid space between the arachnoid layer and the outermost layer of the brain, the dura mater.[9,10,20,24-25]

DURA MATER

The dura mater consists of a thick dense connective tissue layer that lines the inside of the skull and periosteum. (See figure 4 below) The periosteum is a thick fibrous layer that covers bones. The dura mater's primary function is protecting the brain from excessive movement. The dura mater also forms a sac around the arachnoid layer and assists in carrying blood from the

brain to the heart.[26] The spinal cord has an attachment to the meninges through nerves in the spine and denticulate ligaments that span out from the spinal cord attaching to the arachnoid mater and dura mater.[26] Denticulate ligaments are extensions of the pia mater that connects the spinal cord to the dura mater. Denticulate ligaments run from the pia mater to the dura mater and anchor the spinal cord on each side of the dura mater. The dura mater also supports the dural sinuses which are venous channels between the periosteum and the dura mater that drain blood in the central nervous system into the jugular vein and out through the body.[9,10,20,24-25]

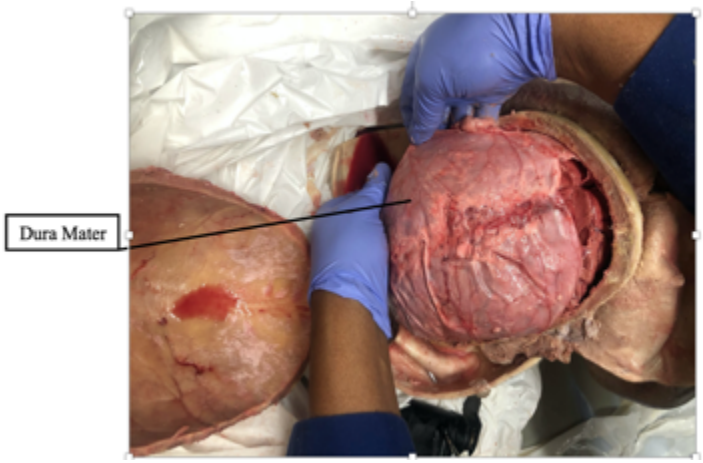


Figure 4. Dura Mater

CEREBRAL SPINAL FLUID

Cerebral Spinal Fluid, also known as CSF, is a clear fluid that is made up of sodium, potassium, and chloride, but contains no protein.[26] Cerebral Spinal Fluid is created by ependymal cells located in the choroid plexus of ventricles in the brain. These ventricles are located in the brain and spinal cord column.[26] On average there is about 150 ml of CSF circulating in the brain and spinal cord. This fluid is replaced about every 8 hours throughout the day, producing an overall amount of 800ml, but only 150ml are consistently in the spinal column. When the CSF is released, the fluid flows through the ventricular system. The ventricular system is the primary

pathway of CSF. Cerebrospinal fluid begins at the lateral ventricle of the brain where it is then passed to the 3rd and 4th ventricles, flows through the cerebral aqueduct, and into the interventricular foramen. The interventricular foramen is where absorption takes place, and any excess CSF is drained into the sagittal sinuses, through the arachnoid villi, located near the arachnoid granulation.[26]

Cerebrospinal fluid acts as a cushion from any damage that may be incurred to the spinal column or brain by keeping these structures submerged in CSF. Cerebrospinal fluid also protects against immunological and mechanical issues. It fills all the crevices such as the ventricles, perivascular space, subarachnoid space, and the cisterna.[26] Cerebrospinal fluid has 5 main functions. These functions are: buoyancy, protection, chemical stability, waste removal, and preventing ischemia. In addition CSF creates a pressure gradient between the brain and the spinal cord, allowing for fluid waste exchange to take place between the brain and spinal cord. When the CSF pressure is greater than the venous pressure, the CSF flows to the blood. However, if the CSF pressure is less than the venous pressure, no blood is capable of passing through. Cerebrospinal fluid receives metabolites, which are brought in via the systemic circulation and are sent to the bloodstream. The pressure gradient system is controlled by a one way valve.[26] CSF is an auto regulator for cerebral blood flow. One way this is regulated is through the blood brain barrier. The blood brain barrier contains tight junctions that consist of claudins, specifically occludins. Tight junctions act as clamps keeping any unnecessary chemicals out, therefore maintaining the equilibrium of the CSF. Claudins are a family of proteins that aid in the flow of particles through the intercellular space, between the epithelium. The particles that are kept out are forced to move through active and passive transports via transcellular routes so they do not

pass through the intracellular space.[26] This keeps out any ions or particles from passing into this space and into the CSF, preventing against a change in the composition of the CSF or plasma in this space. The blood brain barrier also protects against bacterial infections, which could be lethal if infection were to occur in the brain or spinal cord.[9,10,20,24-25]

CELLS OF BRAIN

GLIAL CELLS

There are two major categories of cells that make up the brain. These are neurons and glial cells. Glial cells support neurons and the tasks they carry out. Glial cells are smaller than neurons, therefore there is about a 3:1 ratio of glial cells to neurons. Glial cells do not have axons or dendrites attached to them.[24]

Glial cells have 5 main functions. These functions are to maintain the ionic equilibrium within nerve cells, control the rate of nerve signaling, control the synaptic actions by monitoring the uptake of neurotransmitters, such as acetylcholine, scaffolding neural development, and helping in the recovery of neural injury. [24]

Glial cells fall under the category of neuroganglia.[26] This means that they are non-neuronal cells that make up the CNS. There are three categories of nonneuronal cells. These are macroglia, microglia, and ependymal cells.

Macroglia come from the neural tube and are made up of three types of cells as well: protoplasmic astrocytes, fibrous astrocytes, and oligodendrocytes. Protoplasmic astrocytes have three main functions. They support neurons in the grey matter, cover the capillaries in the CNS, and form a barrier called the subplial barrier. The subplial barrier surrounds the perivascular space, which is deep to the pia mater.[26] Whereas, microglia come from the hematopoietic stem

cells in bone marrow. Stem cells help to remove any debris within the cells, similar to the job of macrophages in the immune system. After incurring a brain injury, hematopoietic stem cells rush to the area that has been damaged. They can proliferate from microglia already present in a specific region, others come from the macrophages when an injury happens.[22,24]

Fibrous astrocytes are located in white matter and are very similar to the astrocytes. They help maintain the chemical environment within the CNS.[26] Also, oligodendrocytes make up the myelin sheath that surrounds the axon, dendrite, and cell body of a neuron. The myelin sheath increases the speed at which an impulse is sent. Oligodendrocytes are contained in the CNS. And, ependymal cells make up the simple cuboidal epithelium lining of the central canal of the spinal cord as well as the ventricles of the brain. They help form the choroid plexus, which is made up of tissue that will then go on to make CSF. [26] The peripheral nervous system consists of nerves that branch out from the brain and spinal cord. The PNS contains cells that create the myelin sheath around the axons. These cells are called Schwann cells. They cover the unmyelinated axons laying down lipid myelin which will speed up the transfer of neuronal signals called action potentials, which go from one neuron to the next.[26]

COMPOSITION OF BRAIN MATTER

The brain is made up of two different kinds of matter: grey matter and white matter. Grey matter consists of nerve cell bodies that are grouped in sheaths, such as the cerebral cortex, as well as smaller bodies, like the nucleus.[26] These cell bodies are unmyelinated containing glial cells and dendrites. Grey matter and white matter are often layered. For example, in the cerebellum and cerebrum white matter is in the deeper layers, and grey matter covers the white

matter. Structures such as the basal ganglia, which contain grey matter, are surrounded by white matter. Grey matter and white matter are different from each other, however.[9,10,20,24-25]

First white matter has very few neuronal cells compared to grey matter. In addition, white matter is myelinated whereas grey matter is not. When a neuron is myelinated it increases the speed at which action potentials are sent and received. This myelination allows for electrical signals to be passed through, providing both hemispheres of the brain the ability to send signals back and forth.[26]

There are two neuron groups: those whose axons leave the CNS such as principal cells, and interneurons which are located only in the CNS. Interneurons relay information from one group of neurons to another, similar to how an action potential travels along an axon, whereas principal cells are motor neurons and can control both the autonomic nervous system and somatic nervous system. Grey matter contains regions for muscle control, which is where motor neurons are located, as well as areas controlling sensory perception. Sensory perception consists of speech, emotions, hearing, memory, sight, smell, and taste.[26,88]

In addition to grey matter, the brain consists of white matter. White matter contains axons that are myelinated connecting various grey matter to white matter. White matter is contained in bundles of two different sizes. Fasciculi are small bundles, and funiculi are large bundles, usually formed as tracts or capsules. In addition, axons that cross the midline and attach to the other side are called commissures. Commissures provide interconnections between lobes allowing for sensory perceptions to occur. Axons positioned vertically as well as horizontally and cross the midline are called decussate. This term is used for the point at which the crossover happens.[26]

Axons and neurons not only send and receive signals within the brain, but many signals that are transmitted within the brain originate from the spinal cord (CNS) or PNS. The spinal cord receives input from the PNS, the extremities, and then relays the information to the brain for processing. In this next section the anatomy and physiology of the spinal cord is discussed.

ANATOMY AND PHYSIOLOGY OF THE BRAIN AND SPINAL CORD

SPINAL CORD

The spinal cord is a bundle of nerve tissues that run from the brain stem through the vertebral column, to the superior border of the second lumbar vertebra (L2). As the spinal cord runs distally from the brain stem, it decreases in thickness except in two places where there are intumescences. Intumescences are bump-like protrusions that extend off of the cervical and lumbar vertebrae, supplying the extremities with sensory and motor nerves. An example of this is the brachial plexus. The brachial plexus begins in the spinal column, specifically the cervical spine, and crosses under the pectoralis to the axillary.[23]

Within the vertebrae are where the spinal nerves are housed. There is a circular hole in the vertebrae called the intervertebral foramina where the 31 spinal nerves pass through and attach to various portions of the body. There are 8 cervical nerves, 12 thoracic, 5 lumbar, 5 sacral, and 1 coccygeal nerve. Therefore, the number of nerves do not coincide with the number of vertebrae. Connecting to the vertebrae are nerves that make up the CNS, and branching out from the CNS is the PNS.[23]

Along the spinal cord, both anteriorly and posteriorly, there is a fissure that allows vessels of the spinal cord to embed. The spinal cord has neurons that consist of axons. These axons act as a line of communication between the central nervous system (CNS) and other areas of the

body, such as the limbs or brain. The CNS's primary function is to make sense of sensory information that is being brought in, and responding in a way that will allow for the best overall reaction of the body. An example is signaling reflexes in a person who has been startled, signaling the knee to extend when tapped with a hammer.[23]

The peripheral nervous system (PNS) contains nerves, whose nerve roots branch out towards the extremities of the body. Within the PNS there are rootlets that connect to nerve roots that are either ventral or dorsal. Ventral roots contain efferent nerves whereas dorsal roots contain afferent nerves. Efferent neurons are motor neurons that carry neural impulses away from the CNS, whereas afferent neurons are sensory neurons that carry impulses toward the CNS. The dorsal roots have a raised portion that is called the spinal ganglion, which houses the cell bodies of the sensory axons. Together the ventral and dorsal roots make up the nervous spinalis (spinal nerves).[23]

BRAINSTEM

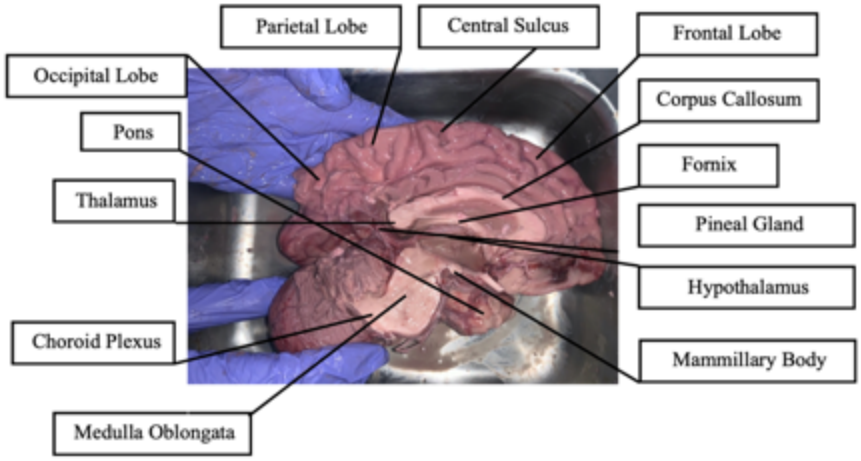
The brain stem consists of the proximal portion of the spinal cord. It has different sections in the superior portion that are separated. The inferior portion, which is most anatomically similar to the spinal cord, has a much more complex arrangement of sections.

The brain stem is split up into four main sections. These sections are the medulla oblongata, pons, mesencephalon (midbrain), and the diencephalon. (See figure 5 below) The brain stem functions as a relay station between the body and cerebral cortex. It contains all the cranial nerves except for the first. These nerves help with hearing, eye movement, facial movement, taste, swallowing, neck and shoulder movements, and tongue movement.

The spinal cord has a fissure that connects to the longitudinal sulcus of the medulla oblongata. The sulcus ends at the base of the pons where pyramids of the sulcus begin extending out on both sides of the sulcus. These pyramids come from a pyramidal tract that help send signals from the cerebral cortex to the spinal cord. This tract is made up of axons making up the pyramids.[24, 25]

MEDULLA OBLONGATA

The medulla oblongata's primary function is to join the brain and the spinal cord as well as regulate breathing, heart rate, blood pressure, and swallowing. It consists of four cranial nerves. These nerves are the Glossopharyngeal (9), Vagus (10), Accessory (11), and Hypoglossal (12).[98] The glossopharyngeal nerve innervates the pharynx with sensory and motor fibers that signal the swallowing reflex. The vagus nerve is similar to the glossopharyngeal nerve except it innervates the larynx with sensory and motor fibers. Accessory nerves are located lateral to the medulla.[98] The cervical spine supplies many of its fibers beginning in the cranial cavity and exiting the skull alongside the glossopharyngeal and vagus nerves. The primary function of the vagus nerve is to innervate the sternocleidomastoid and upper trapezius in the neck. The hypoglossal nerve has its roots between the olive (large nucleus) and the pyramid. It innervates the tissues of the tongue with efferent fibers allowing for movement of the tongue. These four cranial nerves are what make up the medulla oblongata.[98]



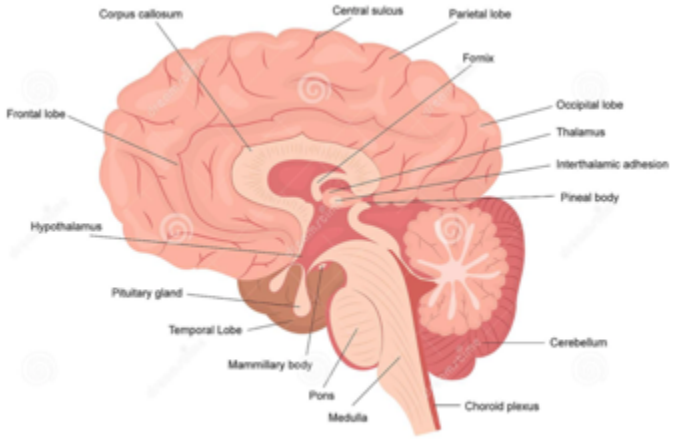


Figure 5. Limbic System

PONS

At the top of the brain stem a bulging prominence makes up the pons. (See image 5 above) It has fibers consisting of pontine nuclei that run transversely across the top of the pons and end at the cerebellum. There are four cranial nerves that make up the pons. These are cranial nerves five to eight. In order these nerves are Trigeminal, Abducens, Facial, and Vestibulocochlear. The trigeminal nerve is the largest cranial nerve consisting of a larger and smaller piece. The large piece contains sensory fibers that control the face, compared with the smaller section that innervates the masticatory muscles via motor fibers. These muscles allow for chewing to occur.

There is a thinner nerve on either side of the pons that is called the abducens. It controls eye movements through motor fibers that connect to the external portion of the extraocular muscles. The nerve that innervates facial muscles and controls facial expression is called the facial nerve. The facial nerve also consists of motor neurons. The last nerve in the pons is the vestibulocochlear nerve. The vestibulocochlear nerve controls the equilibrium in the ears, aiding in balance, as well as hearing. The vestibulocochlear nerve uses sensory impulses sent from sensory organs that signals the semicircular canals when the equilibrium is skewed. Semicircular canals are located in the inner ear and are the center in which balance is controlled.[24, 25, 29,40,98]

MESENCEPHALON

The mesencephalon is located in front of the pons. The mesencephalon contains only two cranial nerves. The oculomotor (III) and trochlear (IV) nerve. There is a fissure that runs between the crura, and in that space is where the oculomotor roots are stored. Cranial nerve III sends motor signals to the eye muscles, aiding the eye in specific movements. These movements include dilation of the pupil and the curvature of the lens. These muscles are both striated and smooth. Striated fibers are fibrous fibers seen in muscles. Smooth muscles have a smooth appearance and make up vessels and arteries.[98]

In addition, the mesencephalon includes colliculi. Colliculi are spherical prominences on the posterior side of the mesencephalon that are divided into superior (visual center) and inferior (auditory center) colliculi. They have nuclei that help with these reflexes. The trochlear nerve is the only nerve that is on the posterior side of the brain stem. It innervates the extraocular muscles with motor neuron fibers to aid in eye movement.[24, 25, 98]

DIENCEPHALON

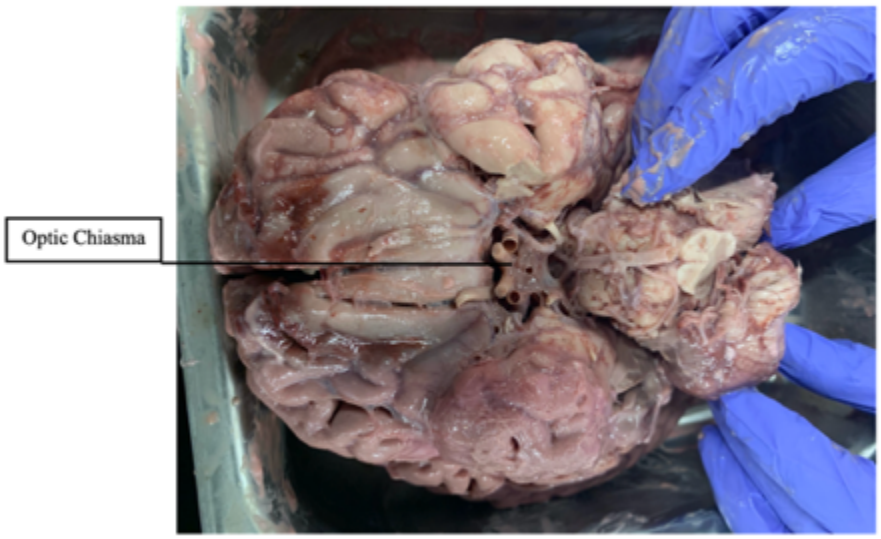
The diencephalon does not consist of specific boundaries, unlike some of the others did. The diencephalon contains multiple structures within it. These structures are the thalamus, hypothalamus, and pituitary gland.[24, 25, 30]

The thalamus is located on either side of the third ventricle of the brain. The thalamus is the center where signals are sent and received through distal parts of the CNS to the cerebral cortex. The thalamus also aids in attention, alertness, and sensation.[25]

The white matter of the internal medullary lamina consists of three nuclei. These are the medial thalamic nucleus, anterior thalamic nucleus, and lateral thalamic nucleus. There is also one bigger nucleus in the pulvinar. The pulvinar covers two more nuclei called the lateral geniculate body and the medial geniculate body. These are centers that relay visual and auditory stimuli to the brain.[24]

There is one main nerve in the diencephalon called the optic nerve. The optic nerve has its nerve ending in the lateral geniculate body, which is the visual center of the brain.[98] Below the diencephalon is where the optic nerves cross, creating an optic chiasma. (See Figure 6 below)

Figure 6. Optic Chiasma



The optic chiasma is found directly inferior to the hypothalamus. It is superior to the sella turcica, which contains the pituitary gland. One of the 12 nerves called the optic nerve, contains axons of retinal ganglion cells (RGC), which originate in the outer retina. From the retina the RGC's move through the optic canal where the lesser wing of the sphenoid bone resides. The optic tract begins where the intracranial part of the optic nerve ends. From there the RGC fibers cross within the optic chiasm. Moving beyond the optic chiasm, the RGC fibers (also known as optic tract at this point) will synapse into one of six layers of the lateral geniculate nucleus, which is located in the thalamus. The path does continue and the optic fibers leaving the lateral geniculate nucleus, called optic radiations, end in the striate visual cortex.[65]

The optic chiasma is a visual structure that helps in processing visual information. The pathway starts at the retina, transferring gross visual impulses to the brain through the optic nerve (cranial nerve II), to the optic chiasma, optic tract, lateral geniculate bodies, and lastly, the

visual cortex of the brain for interpretation. The optic chiasma aids in binocular vision by contributing to processing visual information from one side of the visual field in the contralateral visual cortex. Nasal fibers from both eyes cross at the optic chiasma. This crossing causes information to the right visual field to be projected onto the nasal retina of the right eye, therefore projecting the right visual field information onto the temporal lobe of the left eye, causing the information to leave on the left optic tract.[65]

There is another part of the diencephalon that is anterior and inferior to the thalamus. That is the hypothalamus. The hypothalamus controls the autonomic nervous system including the organs and vessels.[16] (See section titled Parts of the Nervous System) Just like the thalamus is part of the third ventricle, so is the hypothalamus. The hypothalamus has many functions such as regulating the body's temperature, breathing, everyday physiological cycles, and hormonal regulation.[16] The hypothalamus contains a very important gland called the pituitary gland. The pituitary gland has two lobes: the anterior and posterior lobe. The posterior lobe stems from the CNS and the anterior stems from the roof of the mouth. The posterior portion of the hypothalamus aids in elevating blood pressure, pupillary dilation, and shivering or body heat conservation. The anterior pituitary secretes the hormones that promote the onset of puberty. The anterior pituitary also regulates other bodily functions such as stress levels from the hormone cortisol, and growth from growth hormone secretion. The pituitary gland is positioned under the hypothalamus.[16]

CEREBELLUM

The cerebellum is the portion of the brain that is just below the occipital lobe in the posterior cranial fossa, behind the 4th ventricle, pons, and medulla oblongata. (See figure 8

below) It is the largest part of the hindbrain. This portion is highly concentrated with neurons that are arranged in dense cell layers. About 80% of the brain's neurons are in the cerebellum.[104] The cerebellum is separated from the cerebrum by a membranous layer called the tentorium cerebelli. The cerebellum is composed of 2 hemispheres that are connected by a vermis. The vermis is the rounded lobes that are seen in between the 2 hemispheres, and are made up of folia, which are tiny folds. The vermis controls movement of the trunk, neck, shoulders, thorax, abdomen, and hips and is divided into 3 lobes: the anterior, posterior, and flocculonodular.[104] The anterior and posterior lobes are separated by a V shaped fissure, and the posterior and flocculonodular lobes are separated by the posterolateral fissure. The flocculonodular lobe is separated by 2 fissures. A horizontal fissure separates the superior and inferior area of the cerebellum. The cerebellum also consists of an intermediate zone. This zone is what controls the distal extremities. It is located next to the vermis. The lateral part of the cerebellum controls the planning of movement in a sequence, and the awareness of errors in movement.[24, 104]

It has also been reported that the cerebellum consists of nuclei and is split into grey and white matter which come together to form the arbor vitae. The arbor vitae surrounds the nuclei which lie within the cerebellum. Arbor vitae are branched white matter. The deepest nuclei are the fastigial, which are then broken into dentate (the largest), globose, and embofilium. These all exit the cerebellum through the superior Cerebellar peduncle, except for the fastigial, which exit through the inferior Cerebellar peduncle.[104]

Additionally, the cerebellum consists of the Cerebellar cortex which is a thin layer consisting of folds at the midline that contains white matter, covered by grey matter. The grey matter of this anatomical structure is divided into three layers. These layers are the molecular

outer layer, Purkinje middle layer, and the granular inner layer. The Molecular layer is made up of 2 kinds of cells called stellate cells and inner basket cells. These cells connect to the intracellular nuclei via axons that pass through the white layer where they become myelinated. In the middle layer, the Purkinje cells make up the Purkinje layers. They have dendrites that reach the molecular layer allowing for the axons to pass through to the white matter. There are also climbing and mossy fibers that are made up of aspartate and glutamate, which excite the Purkinje fibers. These climbing and mossy fibers are the main source through which input is sent to the cerebellar cortex. The granular layer is the innermost layer of the cerebellar cortex.[104]

There are three nerves that attach to the brainstem from the cerebellum. These are the superior, middle, and inferior peduncles. Peduncle nerves are connected to the pons and transport nerve impulses from the cortex and brainstem to the lower portion of the CNS. These peduncle nerves connect to efferent and afferent fibers attaching to the brainstem and cerebellum, allowing the peduncles to connect to the rest of the nervous system.[104]

CEREBRAL CORTEX

The cerebral cortex is made up of billions of neurons and glia that make up the surface of the cerebellum. The cerebral cortex contains superficial layers of grey matter, and deeper layers of white matter. Grey matter makes up the cerebral cortex, and below that is the white matter. There are gyri and sulci (folds and grooves) which give the cerebral cortex more area to fit in the brain.[28] There is also a longitudinal fissure which divides the right and left hemispheres.[5] The two main sulci are the central sulcus and the lateral sulcus. The central sulcus begins at the midbrain and runs horizontally, whereas the lateral sulcus begins posteriorly dividing the brain into four lobes. These lobes are the parietal, temporal, frontal, and occipital lobes.[28] The lobes are each

divided by sulci. The temporal lobe is split by the Sylvain fissure from the frontal and parietal lobe. The central sulcus divides the frontal and parietal lobe. Another sulcus, called the pario-occipital sulcus, separates the parietal from the occipital. Lastly a calcarine sulcus splits the occipital lobe into two parts- the cuneus from the lingual gyrus. These four lobes are the centers for visual, motor, and somatosensory function.[5, 28]

A region called the thalamus is in charge of relating somatosensory information to the primary Somatosensory cortex in order for the information to process the signal. On the other hand, the motor cortex is primarily located in the frontal lobe, in front of the central sulcus. This includes the primary and premotor cortex which start and monitor voluntary movement. The occipital lobe primarily functions as the brain's visual center. This will be explained in detail under the function of the lobes section.[5, 28]

HEMISPHERES OF BRAIN

The brain is divided into two main hemispheres- the left and the right. The right side controls nonverbal and spatial awareness while the left controls language and speech. However, in ⅓ of left handed people, the right hemisphere controls language and speech. Both sides of the brain work together and are connected by the corpus callosum. Research shows that the left side of the brain controls the right and the right controls the left via a fibrous band known as the corpus callosum. The next section will go in detail about what the corpus callosum is.[25]

CORPUS CALLOSUM

The corpus callosum is what connects the right and left hemispheres together, allowing for transmission of information between both hemispheres. It is made up of white matter tracts which runs between the left and right hemispheres.[56]

The Corpus Callosum is made up of four parts: rostrum, genu, body, and splenium. Each of these connects to distinct parts of the hemispheres. In between the trunk and the splenium, in the posterior aspect of the cortex is the isthmus.[56] The isthmus primarily functions in transmitting visual information in the posterior area of the brain.

The corpus callosum connects the brain in many ways. Beginning with the genu, this region crosses over to forceps minor which connects between regions of the frontal cortices via the genu. Next, the body fibers form the corona radiata and other white matter allowing for messages to be sent and received. The splenium is posterior and connects to the forceps major allowing for a connection between the occipital lobes. The splenium mainly aids in auditory transmission to the posterior area of the brain. Lastly an area of the frontal lobe, called the orbital region is connected by rostral fibers.[56]

The brain contains ventricles, their primary function being to produce CSF and keep the brain healthy. The corpus callosum acts as a physical barrier separating these ventricles.[9]

The main function of the corpus callosum, however, is to integrate and transfer information from both hemispheres in order for visual, sensory, motor, and high cognitive signal information to be processed.[56]

FRONTAL LOBE

The frontal lobe is the largest of the four lobes. (See Figure 8 of the Lobes below) It controls voluntary movement, speech, intellect, and behavior.[9]

The frontal lobe is divided into 3 main areas: the primary motor cortex and prefrontal cortex, and the premotor cortex.[9] The primary motor cortex controls primarily movement production and is located in the post precentral sulcus.[68]

The prefrontal cortex also controls memory as well as intelligence, concentration, temper, personality. The premotor cortex guides eye and head movement and one's sense of orientation.[9] The frontal lobe is divided further into sections by superior and inferior sulci. These are further divided into superior, middle, and inferior gyri. The frontal lobe is separated from the parietal lobe by the central sulcus whereas the temporal lobe is separated by the lateral sulcus.

This frontal lobe is a common area that develops dementia (specifically the frontotemporal portion which includes cells from both the frontal lobe and temporal lobe). This is because the frontal lobe controls higher executive functions such as emotional regulation, planning, and reasoning or problem solving.

An important area of the frontal lobe is Broca's area. This is located in the posterior inferior frontal gyrus. Its primary function is speech production and comprehension. There are two portions of Broca's area: anterior and posterior.[99] The anterior part aids in semantics, the meaning of words. The posterior portion deals with phonology, which is how words sound. Broca area is important in language repetition, gesture production, sentence grammar, and fluidity. It is also involved in interpreting others' actions.[99]

PARIETAL LOBE

The parietal lobe is posterior to the frontal lobe and superior to the temporal lobe. An important section of the parietal lobe is the primary sensory cortex. This is located near the postcentral gyrus.[68](See Figure 7 below)

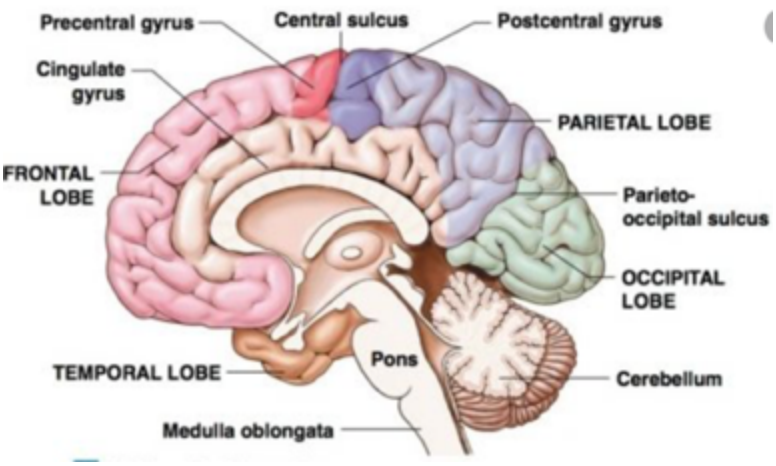


Figure 7. Postcentral Gyrus and Surrounding Limbic System

It is the section of the brain that receives information from the thalamus. It senses pain, touch, temperature, and pressure.[14] The posterior parietal lobe is divided into 2 sections. The superior parietal lobe and the inferior parietal lobe. The superior parietal lobe is important in motor planning actions where the inferior portion helps integrate outputs that have a higher motor function.[99]

Generally the parietal lobe plays a major role in sensorimotor planning, learning, language, spatial recognition, and stereogenesis. Stereogenesis is the ability to tell the difference between size and shapes of objects.

TEMPORAL LOBE

The temporal lobe is posterior to the frontal lobe and inferior to the parietal. It contains 2 surfaces: lateral and medial. There is also a superior temporal sulcus that contains three gyri. These are the superior, which has the dorsal and lateral surface, middle, and inferior temporal gyri.[68] The temporal lobe has several specific roles, primarily hearing, language, and memories. Different areas of the temporal lobe control these functions.[14]

The primary auditory cortex is located in the dorsal surface, within Heschi's gyrus.[99] This is right next to Wernicke's area. Wernicke's area is used in phonological representation, the pronunciation of words based on tone and sound from a previously learned sound.[99] The lateral surface contains the secondary auditory cortex.[99] This section receives auditory information from the ears and other secondary areas and translates and processes the information into something that we hear as sounds.[14]

A portion of the temporal lobe is specific to visual processing allowing complex visual information to be made sense of. This is located in the inferior temporal gyrus.[114] These visual images consist of facial perception containing ventral visual pathways.[114] This pathway carries information from the primary visual cortex to the temporal lobe in order for visual content to be determined and processed.[114]

The middle temporal gyrus has four regions: anterior, middle, posterior, and sulcus. This is where memory is located in the medial temporal lobe. It also contains the hippocampus which controls memory, learning, and emotions.[14]

There are different kinds of memory that this lobe can process. These include declarative memory, semantic memory recognition, which has recollection and familiarity, and episodic memory.[14]

Declarative memory is a long term memory of concepts or ideas and events that happened or have been learned throughout life. There are two subcategories of declarative memory: semantic memory and recognition. Semantic memory pertains to thoughts and objects and semantic control. Semantic control is putting meaning to words or sounds which requires previous stored knowledge and a mechanism of semantic control. Recognition is divided into

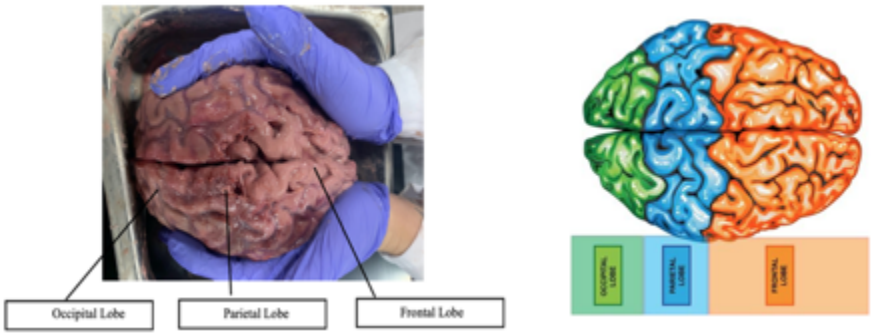
recollection and familiarity. Recollection is memories of objects and the specific details relating to those objects such as time and place. Familiarity is memory of the object, but not the details about that object.[95] Lastly, episodic memory is the memory of events and details associated with those events. Each of the four regions discussed above control these different kinds of memories. Declarative memory is commonly affected after a head injury. Many people cannot remember the accident they were in, or they have a hard time remembering events, day, names, etc for a while after the injury. The most common memory deficit is that of recognition. [95]

The anterior portion is specific to sound recognition and semantic retrieval. The middle portion is used in semantic memory. The posterior is specific to the classical sensory language area. Lastly the sulcus is used in decoding gaze direction and in speech as well, not so much memory.[95]

OCCIPITAL LOBE

This is the smallest of the four lobes. It controls vision and interpretation of visual images.[114] It is divided into 5 areas, however for the purposes of this paper the primary visual cortex is of greatest concern. The primary visual cortex receives visual information from the thalamus, located around the calcarine sulcus.[114] This cortex receives, processes, and interprets information. From there the information is sent to other regions to be further analyzed. This area also helps determine, recognize, and compare objects, as well as perception of depth, distance, and location.[95, 114]

Figure 8. Lobes of the Brain



Blood Flow is important to the body because when the heart pumps out blood, the blood leaves carrying oxygen on the red blood cells. The blood is circulated through the body bringing oxygen to areas such as the brain. There are many different arteries and veins, but the ones listed in Table 1 are the main arteries and veins pertaining to the brain.[12,66]

BLOOD FLOW OF BRAIN [3,11-12,15,17,46-52,63-64,66,69,71,73,81,84,90-92,94,116-118]

Table 1. Venous Blood Flow of Head and Neck

Name	**Location**	**Importance**
Superior Sagittal Sinus	Midline vein that doesn't have any valves or tunica muscularis. Originates at the frontal and ethmoid bone running posteriorly.	Largest dural venous sinus making it very susceptible to injury. It runs along the falx fabri and drains multiple cerebral structures around it.

Inferior Sagittal Sinus	Another part of the superior dural venous sinuses. Begins above the anterior body of the corpus callosum and receives blood from medial cerebral hemispheres, falx cerebri, corpus callosum, and cingulate gyri before draining into the vein of Galen.	Drains superficial cerebral hemispheres.
Great Vein of Galen	It is located in the quadrigeminal cistern and is formed by the connection of two internal cerebral veins and the basal vein.	Large blood vessels in the skull that drain into the cerebrum of the brain.

Straight Sinus	Area in the skull beneath the brain that receives venous blood. Straight sinus gets blood from superior Cerebellar veins and Inferior sagittal sinus draining into the merging of sinuses.	Receiving link of many veins,allowing blood to be sent inferiorly out posteriorly.
Torcular Herophili	This is where the superior sagittal sinus, straight sinus, and occipital sinus connect. It is located deep in the occipital protuberance of the skull.	Blood coming into this area will then drain into the left and right transverse sinuses.

Occipital Sinus	Located on the occipital bone and on the margins of the falx cerebelli. There is usually only one, however two is possible.	Smallest of the dural venous sinuses.
Anastomotic Vein of Labbe	Crosses the temporal lobe between the Sylvian fissure and the transverse sinus, connecting the superficial middle cerebral vein to the transverse sinus.	This is the largest channel that crosses the temporal lobe.

External Jugular Vein	Located in the anterior portion of the neck beginning at parotid and runs down the neck vertically posterior to the sternocleidomastoid.	Receives a larger portion of blood from the outside portion of cranium and deep portion of face. It is formed by the posterior part of the retromandibular vein and posterior auricular vein.
Internal Jugular Vein	Originates from jugular foramen and joins the subclavian vein. Lies anterolateral to the carotid artery. Lies deep to sternocleidomastoid.	Drains blood from brain, face, and neck.

Great Anastomotic vein of Trolard	Channel between superior sagittal and transverse sinuses as well as the superficial middle cerebral vein. Border the temporal lobe.	Brings blood to cerebral hemispheres and around the temporal lobe.
Internal Cerebral Vein	There are two internal cerebral veins and they are located near the interventricular foramina and located on the thalamus.	Has a large role in the diagnosis of deep tumors, such as lesions in the third ventricle.
Basal Vein	Begins at the orbital cortex and in the sylvian fissure. It then runs around the temporal lobe joining the straight sinus.	Supplies medial portion of the frontal lobe.

Intercavernous Vein	Anterior, Posterior, and inferior border of the sella turcica.	Supplies blood to stellar region. Prone to bleeding during surgery of the stellar region.
Cavernous Sinus	One of the dural sinuses of the head. A network of veins sitting in the cavity. The carotid siphon of the internal carotid artery, and cranial nerves III, IV, V, and IV pass through this space.	It's importance is due to its close connection to cranial nerves and the internal carotid artery.

Basilar Plexus	Has many venous channels between the dura mater over the basilar portion of the occipital bone. It connects two inferior petrosal sinuses with the anterior vertebral venous plexus.	Innervates the dura mater providing venous blood supply.
Pterygoid Plexus	Venous plexus that is located between the temporalis muscle and lateral pterygoid muscle.	Joins the maxillary vein, temporal vein, and retromandibular vein lying within the parotid gland. It is a relatively large vein.
Inferior Petrosal	Two small sinuses located on the inferior border of the petrous portion of the temporal lobe. There is one on each side.	Receives internal auditory veins as well as veins from the medulla oblongata, pons, and inferior portion of the cerebellum.

Superior Petrosal	Located on the petrous part of the temporal bone, one on each side.	Receives blood from the cavernous sinus and passes backward and laterally draining blood and CSF into the transverse sinuses at the base of the skull.

Common Facial Vein	Connects with the anterior branch of the retromandibular vein forming the common facial vein. It crosses the external jugular vein and enters at the internal jugular vein below the hyoid bone. Begins at medial angle of eye and descends posteriorly to the masseter, over the mandible, entering the neck.	Collects deoxygenated blood from the forehead, eyelids, nose, lips, masseter, and more.

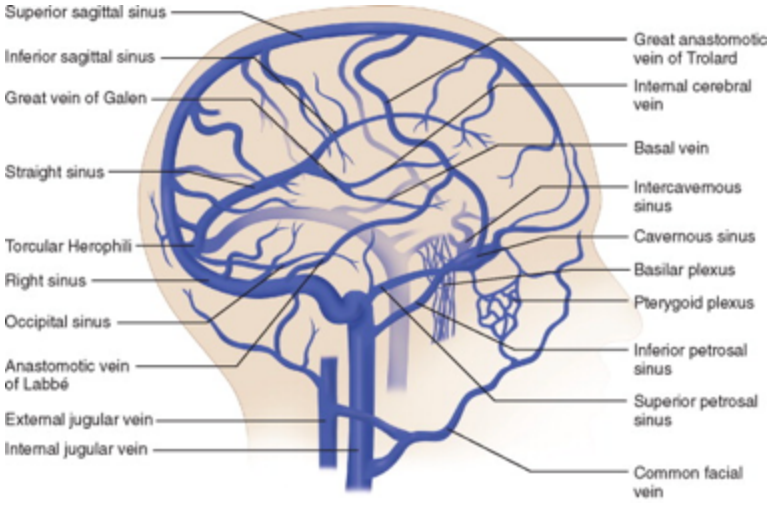


Figure 9. Venous Blood Flow [3,11-12,15,17,33,46-52,63-64,66,71,73,81,84,90-92,94,116-118]

Table 2. Arterial Blood Flow of Head and Neck (cerebrovascular abnormalities)

Name	**Location**	**Importance**
Anterior Cerebral Artery	Branches off of internal carotid (part of Circle of Willis)	Supplies superior medial parietal lobes and some of the frontal lobes with blood
Posterior Communicating Artery	Lower portion of circle of Willis connecting to three other arteries on same side passing backward above the oculomotor nerve	Provides blood supply to medial thalamic surface and walls of third ventricle

Middle Cerebral Artery	Supplies anterior portion of internal capsule and some of basal nuclei (branching from internal carotid) Also spans out to lateral surface of cerebral hemisphere at the insula of the lateral sulcus giving off cortical branches to the temporal, frontal, and parietal lobe.	Provides blood flow to the basal nuclei, temporal, frontal, and parietal lobes.
Posterior Cerebral Artery	Supplies the occipital lobe, inferior portion of temporal lobe, and parts of the limbic system, such as the thalamus, and posterior portion of the internal capsule.	Supplies blood to vision centers in occipital lobe and connects the internal carotid arteries on both sides of basilar arteries.

Superior Cerebellar Artery	Originates from basilar artery supplying the superior surface of the cerebellum and portions of the midbrain.	Splits into various branches leading to the pineal body, anterior medullary velum, and to tela choroidea of the 3rd ventricle.
Anterior Inferior Cerebellar Artery	Originates at the basilar artery of the brainstem. It branches into three vessels- internal auditory, medial branch, and lateral branch.	Provides oxygenated blood to cerebellum.
Posterior Inferior Cerebellar Artery	Largest branch of vertebral artery.	One of three vessels providing blood to cerebellum. Blockage can result in lateral medullary syndrome, a type of stroke.

Internal Carotid Artery	Terminal branch of common carotid artery around C-4 and bifurcation into the external carotid artery.	Begins around C-4 through foramen magnum at base of skull and splitting to innervate areas of the cerebrum.
External Carotid Arteries	Major artery of the head and neck. It comes from the common carotid, which splits into internal and external carotid arteries.	Supplies blood to the face and neck**.**
Common Carotid Artery	There is a left and right carotid artery innervating the head and neck and then divides into external and internal carotid arteries.	Supplies the head and the neck with oxygenated blood.

Subclavian Artery	Supplies blood to thorax, head, neck, shoulder, and arms. May originate on an aortic arch on the left or brachiocephalic trunk on right. These arteries branch to vertebral arteries.	Carry oxygenated blood to the brain from the base of the neck.
Brachiocephalic Artery	Supplies blood to the head, neck, and right arm branching off of aortic arch. It will divide into common carotid and subclavian.	Brings oxygenated blood to the neck, brain, and right arm.
Vertebral Artery	Originate from subclavian arteries alongside the neck, and connecting to the skull to connect to the midline basilar artery.	Supplies neck and base of brain with oxygenated blood.

Basilar Artery	Supplies brain and nervous system. It begins where the vertebral arteries connect at the base of the skull.	Carries oxygenated blood to the cerebellum, brainstem, and occipital lobes.
Circle of Willis	Joins at multiple arteries at the bottom and side of brain. The internal carotid arteries branch into smaller arteries.	The circle of Willis supplies 80% of the oxygenated blood to the cerebrum.
Anterior Communicating Artery	Connects left and right anterior cerebral arteries.	Brings blood to parts of the ventromedial frontal lobes such as corpus callosum, anterior cingulate gyrus, fornix, and basal forebrain. It is a very common site for aneurysms.

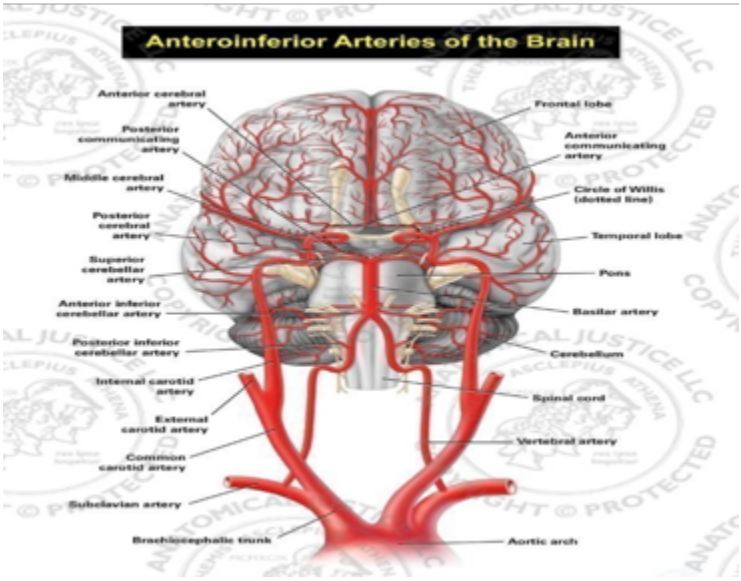


Figure 10. Arterial Blood Flow

CRANIAL NERVES [16,34,62,98]

The brain is made up of thousands of neural pathways, however there are 12 key nerves known as the cranial nerves that control a number of functions in the body (see Figure 11 below). In general these nerves arise from the brain with cranial nerves I-II arising from the cerebellum and cranial nerves III-XII arising from the brain stem. In general each cranial nerve contributes to sensory, motor or a combination of both (see Figure 1 below for nerve function).

Table 3. **Cranial Nerves**

Nerve	**Function**	**Modality**	**Damage** **Effects**

Olfactory (I)	Smell	Sensory	Inhibits sense of smell and therefore taste because smell is connected to taste due to the fact that they both use chemoreceptors.
Optic Nerve (II)	Sight	Sensory	If the optic nerve is damaged blindness can occur because the optic nerve is what allows a person to see.

Oculomotor (III)	Extraocular Movement Intrinsic Movement (i.e. iris sphincter and ciliary muscle) Eyelid Movement	Motor	The oculomotor nerve controls oculomotor mobility which is eye movement. Pupillary function may also be inhibited meaning that the pupils will not contract or dilate properly or one pupil may be larger than the other.

Trochlear (IV)	Superior Oblique Movement (i.e. internal rotation, and downward movement)	Motor	The trochlear nerve is connected to downward eye movement. If this nerve is damaged downward eye movement may be weak or nonexistent. Diplopia, otherwise known as double vision, may occur when the trochlear nerve is damaged. Diplopia is normally only

Trigeminal (V)	Touching of Face Chewing	Mixed	Central nuclear and supra nuclear lesions may result in ipsilateral sensory or motor deficits meaning that if there is a lesion on that specific region of the body there may be sensory and motor issues pertaining to the side that has the lesion. Damage to the trigeminal nerve may also result in trigeminal

Abducens (VI)	Lateral Rectus Movement (i.e. lateral movement)	Motor	The abducens controls eye movement toward the outside therefore If the abducens is damaged loss of peripheral vision may occur. Diplopia most commonly will occur in the lateral regions of the eye if at all. This is due to the fact that the abducens nerve controls lateral eye

Facial (VII)	Eyelid Closing Facial Expression Taste to Front ⅔ of Tongue	Mixed	If the facial nerve is damaged it results in facial paralysis as well as a loss of taste because the nerve controls both facial expression and ⅔ of the front of the tongue.

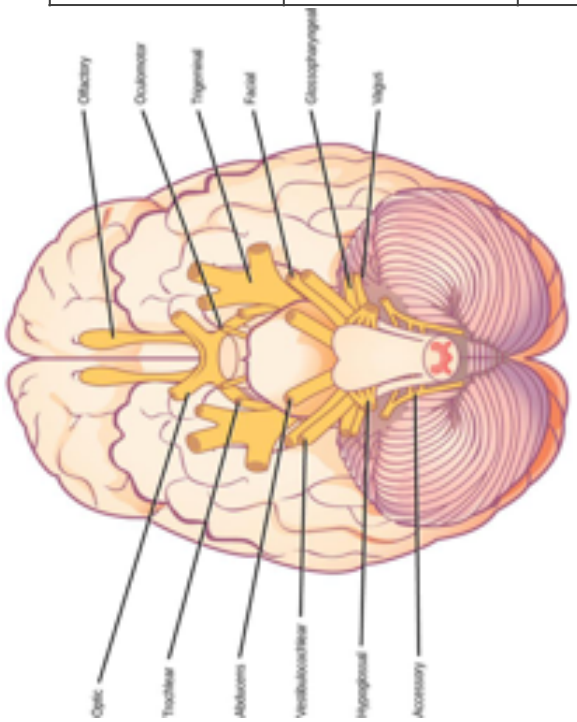
Vestibular (VIII)	Hearing, Balance	Mixed	When the vestibular nerve is damaged it is common for there to be sensorineural hearing loss. This means that hearing loss is due to sensory nerve damage.

Glossopharyngeal (VIIII)	Taste Sensation of Back ⅓ of Tongue Swallowing BP Salivary Glands	Mixed	Damage to the glossopharyngeal nerve causes the inhibition or impaired ability to swallow Loss of taste on the posterior ⅓ of tongue is also common due to the fact that this nerve controls taste. An increase or decrease in blood pressure may also occur since damage to this nerve also affects blood

Vagus (X)	Heart Lungs Abdominal Organs	Mixed	When the vagus nerve is damaged dysphagia may occur. Dysphagia is the inability or reduced ability to swallow. Dysarthria causes the muscles for speech to become weak or a person may even have difficulty controlling their speech. Uvula deviation

Accessory (XI)	Neck Shoulder Muscles	Motor	Damage to the accessory nerve may cause paralysis to the sternocleidomastoid leading to the inability to rotate the head, as well as inhibiting shoulder shrugging movements/ trapezius movement

Hypoglossal (XII)	Tongue Movement	Motor	Damage to the hypoglossal nerve causes weakness of ipsilateral tongue movement, such as the inability to stick the tongue straight out of one's mouth.



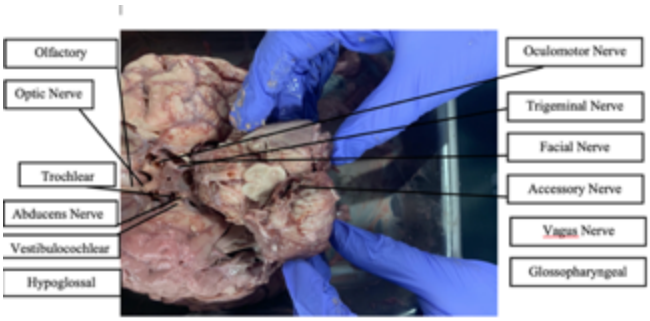


Figure 11. Cranial Nerves

Cranial nerves are either purely afferent (sensory), efferent (motor), or mixed sensory motor. They are composed of neural processes that are associated with distinct brainstem nuclei and cortical structures within the brainstem itself.[98] There are posterior and lateral nuclei which are generally related to sensory, and anterior nuclei that are related to motor function.[98]

Cranial nerves I, II, and VIII are afferent. Nerves III, IV, VI, XI, X are efferent and V, VII, VIIII, and X are mixed sensory motor.[98] Damage to any of these nerves will result in dysfunction to the areas they are connected to (see figure above). Cranial nerves I, III, IV, VI, and VII were most commonly damaged, however when more than one nerve was damaged CN VIII became commonly injured. See Table 3 for in depth details.[34]

The olfactory nerve (CN I) uses chemoreceptors within the mucosal lining to bind to molecules containing a scent. It then sends a signal through the cribriform plate to the olfactory bulb. There are some fibers that run through the olfactory trigone to the septal area as well as laterally to the amygdala and piriform cortex.[98] The primary olfactory cortex is where conscious odor scent is processed. Olfaction also plays a nonconscious role in activating the limbic system.[98] The olfactory bulb has receptors that deliver messages to areas such as the limbic

system. Once the limbic system receives this information, memories, and emotions relating to that information may be triggered.

Cranial Nerve II conveys somatic afferent visual information from rods and cones to the thalamus, particularly the lateral geniculate nucleus and superior colliculus. The optic nerve is made up of ganglion cells that have central projections. This nerve runs from the optic canal to the cranium to the optic chiasm (lateral field). The medial visual fields go posteriorly and do not cross the optic chiasm. The branches of neurons run centrally and innervate the superior colliculus. This causes a pupillary light reflex and pulvinar in the thalamus and is responsible for unconscious optic input (blindsight.)[98]

Cranial Nerve III and IV go through the common tendinous ring which attaches in the posterior orbit to four extra recti muscles. Cranial nerves III, IV, and VI innervate the extraocular muscles and unilaterally travel to the brainstem to the calvarium to the superior orbital fissure. CN IV innervates the superior oblique muscle of the eye. Cranial nerve VI innervates the lateral rectus muscle used for eye gaze.[98]

Cranial nerve III innervates most eye muscles and is split into superior and inferior parts innervating three recti muscles, the inferior oblique, and levator palpebrae superioris. The general visceral efferent neurons also originate from the accessory oculomotor nucleus. These fibers travel with CN III to the ciliary ganglion in orbit. Post ganglionic sympathetic fibers of the ciliary ganglion go through the sclera and innervate the pupillary sphincter and ciliary smooth muscle. This is used for pupillary constriction and lens accommodation.[98]

Cranial nerve V is responsible for somatic sensory innervation of the face through the ophthalmic (V1), maxillary (V2), and mandibular (V3) nerves. Cranial nerve via V3 is

responsible for motor innervation of mastication, anterior digastric, mylohyoid, and tensor palatini, and tensor tympani. Parasympathetic nerves mix with the cranial nerves to innervate lacrimal, parotid, submandibular, and sublingual glands.[98]

Cranial nerve VII has both motor and autonomic fibers containing somatosensory components. This nerve contains visceral efferent motor innervation that is linked to muscles used in facial expression. They exit the skull through the stylomastoid foramen. There are 2 different types of visceral efferent neurons: general visceral efferents (GVE) and special visceral efferents (SVE). They both exit via the brainstem, however components of the GVE from the superior salivary nucleus are responsible for PNS innervation of facial glands and mucosae.[98]

Cranial nerve VII is also related to taste. Taste fibers move more central as the chorda tympani nerve sends signals to the cell body before synapsing in the solitary nucleus.[98]

There are two other nerves whose functions are mixed sensory and motor. These are cranial nerves IX and X. IX is responsible for motor innervation of the stylopharyngeus and pharyngeal constrictor muscles by the nucleus ambiguous. Inferior salivary nucleus fibers have GVE allowing innervation to the parotid, buccal, and labial glands.[98]

There are also 2 kinds of afferents that play a role here too. These are visceral afferents and sensory afferents. Visceral afferents receive sensory information from the carotid body and carotid sinus as well as taste from the posterior ⅓ of the tongue. This allows synapsing on the solitary nucleus. Sensory afferents bring information from the skin over the tongue, oropharynx, middle ear cavity, and auditory canal. This allows for the senses to be perceived by the brain and processed into perceptions.[98]

Cranial nerve X has parasympathetic efferent fibers running from the dorsal vagal nucleus to the thoracic and abdominal viscera. From there it runs to the splenic flexure of the colon representing the major neural component. This component forms the comprehensive plexus that travels along the esophageal serosa to the visceral.[98]

Motor output from the nucleus is ambiguous to the pharyngeal and soft palate muscles as well as intrinsic laryngeal muscles via the superior and recurrent laryngeal nerves.[98]

Somatic and Visceral afferents are used here as well. For CN X nerve, somatic afferents supply the posterior cranial dura as well as portions of the ear, such as the external auditory canal epithelium. Visceral afferents coming from the pharynx, larynx, aorta, thoracic spine, abdominal viscera, and taste buds synapse on the solitary nucleus as well.[98]

ANATOMY OF SKULL, EYES, EARS, AND NOSE

SKULL

The cranium, also referred to as the skull provides support for the face and provides protection to the brain. In an adult skull, there are 22 bones, 21 of which are immobile and come together to form one single unit. Eight of the bones are cranial bones and include the frontal bone, two temporal bones, two parietal bones, a sphenoid bone, an ethmoid, and an occipital bone. Additionally, there are also 14 facial bones which include two nasal conchae, two nasal bones, two maxilla, two palatine bones, two lacrimal bones, two zygomatic bones, the mandible, and vomer bone. In general each of these bones plays a vital role in providing structure and protection to the brain and surrounding structures. In addition to the bones providing structure and protection to the brain, the muscles also serve to create movement about the face. The

muscles of the skull and face along with primary function can be located in Table 2. Cranial nerves V, VI, and VII work together to control facial movement and sensation.[10]

Table 4. Facial Muscles [92,119]

Facial muscles control movement of the face. When a brain injury occurs nerves may become damaged causing paralysis of the facial muscles. This is commonly seen when an individual has a stroke. Generally one side of the face will droop and sometimes this can be reversed, and other times the individual is paralyzed on one side for life. Please see table below for a list of facial muscles that may become compromised following a head injury.

Muscle	**Function**
Orbicularis Oris	Shapes lips during speech
Temporalis	Mastication Closes mouth; pulls lower jaw in under upper jaw
Medial Pterygoid	Mastication Elevates (adducts) and protrudes mandible
Lateral Pterygoid	Mastication Opens mouth; pushes lower jaw out under upper jaw; moves lower jaw side-to-side
Masseter	Mastication Elevates (adducts) and protrudes mandible

Depressor Supercilli	Depresses Eyebrows
Orbicularis Oculi	Acts as the orbital sphincter Palpebral portion gently closes Orbital portion tightly closes
Nasalis	Elevates sides of nose
Levator Labii Superioris	Elevates upper lip
Superioris Alaeque Nasi	Elevate side of nose
Depressor Labii Inferioris	Draws lower lip downward
Procerus	Depresses medial eyebrow angle
Auriculars	Moves ears anteriorly and posteriorly
Zygomaticus Major	Draws angle of mouth upward and laterally smiling
Zygomaticus Minor	Elevates and everts upper lip
Buccinator	Allows chewing to occur without biting cheeks/ aids in blowing out air
Occipitofrontalis	Belly 1: Raises eyebrows Belly 2: Depresses Eyebrows
Corrugator Supercilli	Draws eyebrows medially Downward frowning
Risorius	Draws angle of mouth laterally

Depressor anguli oris	Opening mouth and sliding lower jaw left and right
Mentalis	Elevates and protrudes lower lip and skin of chin
Depressor septi nasi	Depression of nasal septum

The face is very vascular due to the amount of blood supply it receives from arteries and veins. This can be problematic when a head injury occurs because a significant amount of blood can be lost or even worse the blood can accumulate in the brain leading to Cerebral Vascular injuries. (See Table 5 below)

Table 5. Arterial Blood Supply of Face [18,27,47-52,63-66,84,92,94,97,100,106,116]

Name of Arteries	**Location of Arteries/ Blood Supply**
Carotid Artery	Branches up side of neck and superficially feeds the skull and facial structures
Facial Artery	Goes across face (transversely) to the lateral mandible to the side of mouth
Angular Artery	Travels from mouth to the side of the nose
Inferior/Superior Labial Arteries	Branches to supply upper, lower lip and mouth

Maxillary Artery	Branches from carotid and supplies maxilla region
Superficial Temporal Artery	Branches near ear and supplies forehead region

Table 6. Venous Blood Supply of Face [18,27,47-52,63-66,84,92,94,97,100,106,116]

Name of Veins	**Location of Veins/ Blood Supply**
Angular Vein	Connection of supratrochlear and supraorbital veins

Facial Vein	Angular vein connects to the facial vein which goes into the jugular vein in neck Function: allows drainage of the eyes, nose, lips, cheeks, and mental region Drainage: happens because of lymph nodes Submental Submandibular Preauricular Parotid

EYES

The eyes are the structure that allow for light, dark, and color to be seen. The eyes are located in a bony socket called the orbit. It is made up of six extraocular muscles: the superior rectus, inferior rectus, lateral rectus, medial rectus, superior oblique, and inferior oblique. The superior and inferior oblique aid in circular motion of the eye. Cranial nerves III, IV, and VI control the movement of the eyes as well as opening and closing the eyelids.[53,98]

The extraocular muscles connect to the sclera, which is the white portion of the eye. A layer called the conjunctiva covers the surface of the eye and inner eyelids as is protected by the tear film which has three layers. Those three layers are the lipid layer (oil), aqueous layer (water) and the mucin layer (mucus).These tear film layers have several important roles within the eye: (1) to protect the eyes from infection, (2) to lubricate the eye, (3) wash away foregin products and (4) to keep the surface of the eye clear. These lubricants, specifically the water based layer, are secreted from lacrimal glands which are located in the upper lateral region of each orbit in the lacrimal fossa. Lacrimal glands secrete lacrimal fluid creating a lubricant for the conjunctiva and retina.[53,97-98,106,119]

The next layer of the eye is the cornea. The cornea is like a window that is responsible for focusing entry light into the eye. It is dome shaped and is the most outermost portion of the eye. Behind the cornea is a fluid filled space called the anterior chamber. The anterior chamber is filled with aqueous humor, which is always being produced, and is drained periodically to maintain homeostasis of pressure within the eye. Located just posterior to the anterior chamber is the iris. This is the colored portion of the eye that contains the pupil and is responsible for controlling the diameter and size of the pupil. Surrounding the pupil are pupillary sphincter muscles which when contracted causes pupillary vasoconstriction based on the amount of light that is traveling to the eye. As we continue to travel deep into the eye from the pupil, the next anatomical structure is the lens.The lens is the second part of the eye that helps focus light as it travels towards the back of the eye and changes shape depending how far away an object is. Finally, a vitreous cavity lies between the lens and the back of the eye. This cavity is filled with

vitreous humor and is responsible for keeping the eye nourished and maintaining the eye shape.[53,97-98,106,119]

Finally, the most posterior anatomical structure of the eye is the retina. The retina is located relatively close to the optic nerve and is essentially responsible for receiving light that the lens has focused and converting that light into neural signals that can then be interpreted by the brain. There are two parts of the retina: the macula and peripheral retina. The macula allows for detailed vision and is responsible for providing clarity in our vision, whereas the peripheral retina is responsible for peripheral vision and plays a major role in nighttime vision as well. Finally, the retina contains photoreceptors, which are cells that are responsible for converting light into energy that will get interpreted in the brain. There are two kinds of photoreceptors located within the eye and they are the rods and cones. As noted before in the section labeled Cranial Nerves, rods are responsible for vision in lowlight conditions and such as black and white or night vision, whereas cones are more active in high light conditions and allow the sight of color and visual acuity. The pathway of light through the retina begins as light being changed to electrical impulses through the optic nerve. From there the optic nerve passes the impulses to the brain where the impulses are transmitted to the visual cortex, which is responsible for sight.[53,97-98,106,119]

NOSE

The nose is the organ which is responsible for sense of smell but also functions as part of our respiratory system. The nose is made up of the external meatus, external nostrils, septum, nasal bone, ethmoid, maxilla, palentine, sphenoid, greater alar cartilage, and sinuses. The sinuses

contain four mucus membranes called the ethmoid, maxillary, frontal, and sphenoid sinuses.[97-98,106]

The ethmoid membrane bridges the nose and is present from birth. The maxillary membrane runs transversely under the cheeks and is also present from birth. The frontal sinuses are located in the forehead region and begin to show around age seven. Lastly the sphenoid membrane lays deep behind the nose and does not begin to develop until the teenage years.[97-98,106]

There are several nasal muscles that control movement of the nose. These are the nasalis which has a compressor and dilator, the procerus, depressor septi, levator labii superioris alaeque nasalis, and orbicularis oris. The nose is innervated by cranial nerve VII, allowing for facial sensation, and cranial nerve I which senses smell.[97-98,106]

The lower nasal cavity is covered in hair and the upper nasal cavity contains epithelium and mucous cells. As air enters the nasal cavity the hair and cells filter and clear out any of the debris that passes through. As the air travels up toward the epithelium the air begins to humidify and warm to body temperature for the body to take in and use.[97-98,106] As the air reaches the epithelium, they begin sweeping away any particles that may have gotten through, but were not caught by the hair. In addition, mucous lines these surfaces acting as a protected barrier against pathogens.

The other function of the nose is olfaction. In order for olfaction to occur, air particles containing odor must be transported to the olfactory epithelium located at the “apex of the nasal cavity.” [97] The odorous particles become trapped in the mucous and bind to proteins that make the particles soluble. The particles then attach to olfactory receptors on the cilia and are

transmitted through the cribriform plate to nerves in the olfactory bulb that will then transmit the signals to cranial nerve I and bring the signals to the brain for higher processing.[97]

A component of the limbic system called the thalamus allows for the integration of sensory information. The sensory information is then sent to other areas of the cortex, allowing for the sensation of smell and taste to be interconnected.[97-98,106]

EARS

The ears allow for hearing, and also play a role in proprioception. The ears are composed of an external, middle and inner portion. The external ear contains the pinna/auricle and the auditory canal. It is responsible for bending sound waves that are transmitted to the middle ear, allowing sounds to be heard.[8,103,120]

The connection between the external ear and internal ear is the auditory canal. A membrane, known as the tympanic membrane, or eardrum, divides the external ear from the middle ear.[8,103,120]

The middle ear is known as the tympanic cavity. The middle ear is made up of three bones known as the malleus, incus, and stapes. There is an eustachian tube that links the middle ear with the posterior portion of the nose. The eustachian tube is important because it helps equalize pressure in the middle ear allowing for the transfer of sound waves to the cochlea. There are two muscles in the middle ear that contract in response to loud noise. These are called the tensor tympani and stapedius.[8,103,120]

The inner ear contains the cochlea, vestibule, and semicircular canal. The cochlea is fluid filled, and contains vestibulocochlear nerves that allow for hearing. The vestibule has receptors for balance. Lastly, the semicircular canals contain receptors that aid in balance.[8,103,120]

The pathway of hearing starts with the outer ear which transports sound waves to the external auditory canal. From there these sound waves are transferred to the eardrum which vibrates and is sent through the malleus, incus, and stapes, amplifying the sound. The sound waves are then sent through the fluid filled cochlea which creates electrical impulses that are sent to the nerves and then the brain. Cranial nerve VIII controls hearing and balance of the ear.[8,103,120]

PARTS OF THE LIMBIC SYSTEM

HYPOTHALAMUS

The limbic system is important because it plays a major role in the regulation of emotions, memories, and motivation. Without the limbic system emotional stability, self control, drive to accomplish goals, and the emotions that come with memories would not be possible. This section will discuss the ways in which injury to the anatomical structures within the limbic system can lead to permanent damage of these abilities.[16,30,74-75]

The limbic system consists of many individual anatomical landmarks of the brain. The first is the hypothalamus. The hypothalamus is a bilateral connection of nuclei that is separated into three areas around the third ventricle and mammillary bodies. (See figure 12 below)

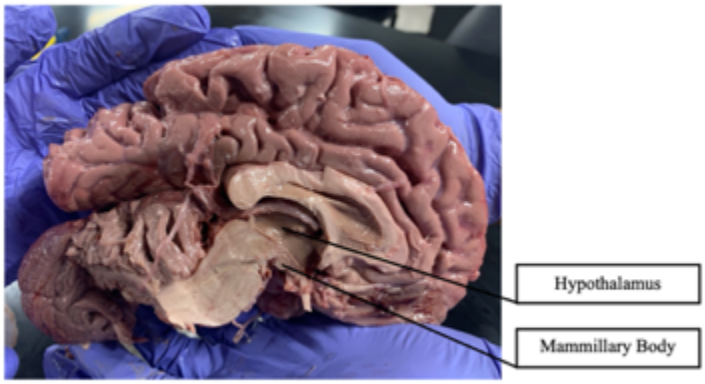


Figure 12. The Hypothalamus

These three areas are known as the periventricular, medial, and lateral zones. The periventricular zone regulates the endocrine system, whereas the medial and lateral zones control the autonomic system and somatic behavior.[16,30,74-75]

The hypothalamus is centrally located in the brain. It is a central connection to many areas of the brain and brainstem. Specifically, the hypothalamus is connected to the brainstem, cerebral cortex, hippocampus, amygdala, thalamus, pituitary gland, and retina. Many of these anatomical landmarks are located within the limbic system such as the hypothalamus, thalamus, amygdala, and hippocampus.[16,30,74-75]

The hypothalamus is attached to the brainstem via the dorsal longitudinal fasciculus, descending fiber group that begins at the hypothalamus and ends at the autonomic nuclei of the pons and medulla. The cerebral cortex is connected via the median forebrain bundle which is also a group of fibers passing through the hypothalamic region, containing fibers from the basal olfactory region. The fornix, which is also located in the limbic system, attaches the hypothalamus to the hippocampus acting as an output system of information from the hippocampus to mammillary bodies and the anterior nucleus of the thalamus. The amygdala is connected via stria terminalis, a band of fibers along the lateral portion of the surface of thalamus, and the thalamus via the mammillothalamic tract. The mammillothalamic tract begins at the mammillary bodies and continues to the thalamus and fornix. There are two more structures in which the hypothalamus is connected. These are the pituitary via the median eminence, a part of the hypothalamus where hormones are released, and the retina via the

retinohypothalamic tract, which sends information regarding how much light there is. These seven anatomical components are the attachments for the hypothalamus.[16,30,74-75]

The hypothalamus consists of a highly sensitive sensory integration and motor area making it the center for homeostasis regulation. Specifically, the hypothalamus regulates the endocrine, autonomic, and somatic systems. The hypothalamus contains homeostatic receptors that sense circulating hormones allowing for internal stimuli to be received. The hypothalamus can also sense external stimuli via the spinothalamic tract. The spinothalamic tract is a pathway that ascends from the spinal cord, and is very important to the sensory pathways. Since the hypothalamus is part of the limbic system, it works closely with other components of the limbic system in the area of sensory integration. This is done via the fornix and has a connection to the amygdala as well. There is a retinohypothalamic tract that carries light signals to the suprachiasmatic nucleus, which controls circadian rhythms. This aids in regulation of hormone release. The hypothalamus consists of multiple ways input can be integrated, allowing for the regulation of homeostasis.[16,30,74-75]

As stated earlier, the hypothalamus mainly regulates the endocrine system, autonomic system, and somatic behavior. There are 11 nuclei, inferior to the thalamus, that each have a different role being played in regulating these systems.[16,30,74-75]

First, the paraventricular and supraoptic nuclei produce the hormones oxytocin and antidiuretic hormone (ADH) that are then released from neuronal axons into capillaries of the posterior pituitary. These hormones regulate the body's functions and act as neurotransmitters, which signal neurotransmission to begin.[16,30,74-75]

Oxytocin is a hormone that controls uterine contractions during labor. Oxytocin as well as prolactin aid in the production of milk in a woman immediately after giving birth. When prolactin is not being produced it is inhibited by dopamine.[16,30,74-75]

ADH is a hormone that works to retain water in the renal system when the body becomes dehydrated. Oxytocin and ADH hormones share a common peptide that allows them to work together through pair bonding. Sharing a common peptide means that when oxytocin is in excess, it can activate the receptors of ADH.[16,30,74-75]

There are preoptic, anterior, and posterior nuclei that regulate body temperature by decreasing sympathetic tone of skeletal muscle, which is indirectly related to the effect the nuclei have on skin. Sympathetic tone of the skin, the condition of muscle controlled by impulses from the SNS, is increased by dilating capillaries, causing vasodilation, and improving heat exchange.[16,30,74-75]

The suprachiasmatic nucleus controls the secretion of hormones and behavior based on light input from the eyes. Cortisol is one example of this. The highest levels of cortisol peak in the morning, increasing blood pressure. Cortisol is lowest at night when it is dark, but this is when growth hormone peaks. [16,30,74-75]

The ventromedial nucleus regulates feeding behavior. When this area gets damaged hyperphagia or satiety can occur depending on the injury. The lack of satiety can cause aggression, which is controlled by the dorsomedial nucleus. This nucleus controls rage behavior. The lateral hypothalamus regulates the perception of hunger increasing the need to eat. Damage to this area leads to anorexia.[16,30,74-75]

The arcuate nucleus produces releasing hormones that are secreted by the axon terminals into the hypothalamohypophyseal venous system. This tract controls the release of the anterior pituitary hormone called adrenocorticotropic hormone (ACTH). Adrenocorticotropic hormone signals the production of cortisol, which is present during a stress response.[16,30,74-75]

Another hormone that is released by the hypothalamus, specifically the anterior pituitary, is thyroid stimulating hormone (TSH). Thyroid stimulating hormone is released when the thyrotropin releasing hormone is stimulated by a change in the metabolic system. When levels in the metabolic system increase or decrease, a signal is sent to the anterior pituitary, which stimulates TRH to create TSH. Thyroid stimulating hormone is released and corrects the discrepancy within the metabolic system.[16,30,74-75]

The hypothalamus contains receptors of the hormone leptin. Leptin senses energy stores within the body. When the body is in low reserves, leptin receptors signal the hypothalamus to slow metabolism by decreasing TRH which will thereby decrease TSH.[16,30,74-75]

There are several hormones released by the hypothalamus that regulate reproductive levels. These are gonadotropin releasing hormone (GnRH), luteinizing hormone (LH), and follicle stimulating hormone (FSH).[16,30,74-75]

Gonadotropin releasing hormone increases LH and FSH levels, however continuous production of GnRH decreases LH and FSH. Luteinizing hormone stimulates the release of testosterone and estrogen. When there is a surge in LH, ovulation occurs. Follicle stimulating hormone functions in the production of male spermatogenesis and female oocyte maturation. These hormones are crucial during puberty. Luteinizing hormone and follicle stimulating hormone levels begin to rise during puberty. This causes the eggs in women to mature and form a

fluid layer around the egg called the follicle. During the first day of a woman's menstrual cycle, estrogen levels are low. The hypothalamus is signaled and stimulates GnRH to produce LH and FSH and release these hormones to increase estrogen levels. The follicle of the egg begins growing, causing estrogen levels to rise. By day seven of a woman's cycle, estrogen levels peak inhibiting the production of FSH causing small follicles to die off. This is when ovulation happens and the surge in LH occurs. (UCSF)[16,30,74-75]

The hypothalamus produces a hormone known as growth hormone releasing hormone (GHRH). This is a receptor that, when stimulated, releases growth hormone. Growth hormone stimulates tissue growth and metabolism. Growth hormone has an inhibitor called somatostatin, and when released, it decreases growth hormone levels, and opposes GHRH.[16,30,74-75]

The mammillary nucleus contributes to the limbic system as part of the Papez Circuit. The Papez circuit is a neural circuit that is closed , meaning it begins and ends in the hippocampus. It aids in memory formation, and controls exploratory behavior. When a person has bilateral lesions, known as Wernicke's Karkaroff, anterograde amnesia and likely retrograde amnesia occur.[16,30,35,74-75,95]

The hypothalamus sits atop of the motor hierarchy which includes the cerebral cortex, limbic system, brainstem, and spinal cord motor neurons. The hypothalamus combines internal and external information about the hormone levels within a person, and monitors these levels closely in order to maintain homeostasis.[16,30,74-75]

The cerebral cortex contains a sensory area that provides complex sensory perceptions. The limbic system is the primary emotional regulation center. The spinohypothalamic tract senses pain and temperature. The hypothalamus uses all the stimuli received in the cerebral cortex and

brainstem and sends signals through the central nervous system (spinal cord), to the peripheral nervous system (appendices), where the motor neurons activate muscles to produce a movement.[16,30,74-75]

THALAMUS

Another component of the limbic system is the thalamus. The thalamus is centrally located lying above the midbrain allowing for nerve fiber connections, in every direction, between the cerebral cortex. The medial surface of the thalamus forms the upper and lateral walls of the third ventricle of the brain. The third ventricle is lined with ependymal cells, which aid in the production of CSF.[102,108]

The thalamus is composed of mostly grey matter within the diencephalon. There are some white matter areas known as the stratum zonale. The stratum zonale contains external and internal medullary laminae. Internal laminae are divided into three groups called the anterior, posterior, and lateral groups. The external laminae cover the lateral surface of the thalamus. This white matter coats the neurons in myelin aiding in faster transmission of stimuli between neurons.[102,108]

The thalamus is connected to many components of the limbic system. The primary connections are the hippocampus, mammillary bodies, and the fornix via the mammillothalamic tract. Since the thalamus is connected to anterior nuclei through the limbic system, there are many functions of the thalamus. The roles connected to the limbic system are aiding in learning and episodic memory and controlling sleep and wakefulness. The thalamus' primary function is relaying signals from the exterior portions of the body, to neurons in the thalamus, then to the

cerebral cortex for processing. The thalamus processes sensory information from taste, touch, sight, and sound. Olfaction is the only sense that is not processed by the thalamic nucleus.[102,108]

Like the hypothalamus, the thalamus contains different nuclei that aid in relaying signals of motor function, sensory function, alertness, and consciousness. These nuclei are formed by excitatory and inhibitory neurons. The thalamocortical neurons receive sensory or motor information from the body and transport the stimuli via the thalamocortical nerve fibers to be processed in the cerebral cortex.[102,108]

There are five major nuclei in the thalamus. These nuclei are the ventricular and intralaminar nuclei, sensory nuclei, effector nuclei, associative nuclei, and limbic nuclei. The nuclei of the thalamus each have different roles.[102,108]

The effector nuclei work in processing language, associative nuclei aid in cognitive function, and limbic nuclei control mood and motivation.[80,102,108]

The thalamus is divided into anterior, medial, and lateral portions. The anterior portion contains thalamic nuclei made up of input and output fibers. The input fibers are mammillary nuclei, which are important to memory, the cingulate gyrus, involved in processing of emotions and regulating behavior, and the hypothalamus. The output fibers are the cingulate gyrus and hypothalamus.[102]

The medial portion of the thalamus contains the dorsomedial nucleus. The dorsomedial nucleus sends fibers to the prefrontal cortex, hypothalamus, and thalamus. Dorsomedial nuclei send and receive information from other nuclei of the thalamus.[102]

The lateral portion of the thalamus contains a dorsal and ventral tier. The dorsal tier contains a lateral dorsal nucleus, which receives input from subdivisions of the visual cortex, and

a lateral posterior pulvinar sends output efferent connections from projections in the visual cortex. These have connections with nuclei of the thalamus, parietal lobe, occipital, and temporal lobe.[102] The ventral tier nucleus contains the ventral anterior, ventral lateral, and ventral posterior nucleus. This group of nuclei receive input and are arranged in such a way that signals can flow bidirectionally.[102,108]

Ventral anterior nuclei receive input information from the cerebral cortex and redirect it back to cortical areas, known as association areas. These nuclei contain the reticular formation, substantia nigra, corpus striatum, and premotor cortex. They all have important roles, and when damaged, cause substantial inhibition of motor function, emotions, consciousness, and sleep regulation.[28-30]

The reticular formation regulates sleep and consciousness, and if this region is damaged consciousness may be lost and sleep cycles may become disrupted.[82]

The substantia nigra and the corpus striatum are important for motor movement and reward. They contain dopaminergic neurons allowing for the feeling of validation and reward. When these structures are damaged movement of any body part may become inhibited, and the dopaminergic neurons can become depleted, decreasing the feeling of well being and reward.[102,108]

The premotor cortex also plays a large role in motor movement. It allows the body to have precise movements, from both external and internal cues.[102,108]

The ventral lateral nuclei contain the same components as the ventral anterior nucleus, but also include the cerebellum and red nucleus. The ventral lateral nuclei are important in

coordination and the planning and learning movement.[102,108] When these nuclei are damaged coordination is often severely decreased and learning movement becomes difficult.

The ventral posterior nucleus is subdivided into three sections. These sections are the ventral posteromedial nucleus, ventral intermediate nucleus, and ventral posterolateral nucleus. The ventral posterior nucleus uses the spinothalamic tract pathway, which sends signals for pain, temperature, and touch from neurons in the spinal cord to the ventral posterolateral nucleus for processing. Posterolateral nuclei contain medial and spinal lemnisci containing the anterior and lateral spinothalamic because the spinal lemnisci is where the two merge.[102,108]

The posteromedial nucleus receives sensory information from the trigeminal nerve of the face. The posteromedial nucleus contains tegmental and gustatory fibers that act as a pathway from the cerebellum to the thalamus. The ventral intermediate nucleus correlates to motor function and pathologic tremors when injury occurs to this nucleus.[28-30]

The ventricular nucleus is located in the ventral portion of the thalamus and forms a capsule laterally around the thalamus. The ventricular nucleus does not send signals to the cerebral cortex. It uses other thalamic nuclei to process the information it receives. The ventricular thalamus also receives disinhibitory input from the globus pallidus. The globus pallidus allows for voluntary movement to occur.[28-30]

The intralaminar nuclei are located in the medullary lamina. Similar to the ventral posterior nuclei, the intralaminar nuclei receive fibers from the spinothalamic and trigeminothalamic tracts and send efferent fibers to other nuclei. The trigeminothalamic tract is a pathway from the spinal nucleus of the trigeminal nerve to the thalamus.[82] The level of consciousness is controlled by intralaminar nuclei. Intralaminar nuclei receive information from the reticular formation and

control activity in other thalamic nuclei. The thalamic nuclei control overall activity of the cortex.

There are two more nuclei, lateral geniculate nuclei and medial geniculate nuclei, that process visual and auditory information. The lateral geniculate nucleus receives visual information from the retina and sends this information to the visual cortex in the occipital lobe for processing. The medial geniculate nucleus receives auditory information from the inferior colliculus, which is the primary midbrain nucleus of the auditory pathway receiving input from the brainstem nuclei and auditory cortex. The auditory information is then sent to the auditory cortex in the temporal lobe where it will be processed.[28-30,102,108]

There are reticular nuclei that are located between the external medullary lamina and posterior limb of the capsule. They receive fibers from the reticular formation and cerebral cortex, sending efferent fibers to other nuclei.[28-30,102,108]

When head injuries occur, damage to the thalamus is common. The thalamus is considered a main structure for regulating consciousness because of the amount of sensory input the thalamus receives. Since the thalamus has a significant role in consciousness, it is common for a person to become unconscious when an injury occurs to this portion of the brain. Since the thalamus is the center of consciousness, it is common for a person to become unconscious when an injury occurs. When damaged, the sensory function of the thalamus can be disturbed creating a loss of sensation as well as motor disturbances. Lesions on the thalamus may damage the ventral posteromedial and posterolateral nuclei leading to complete sensory loss. Sensory loss includes touch, pain, joint, and muscle sensations to the opposite side of the body from where the lesion is.[28-30,102,108]

AMYGDALA

The amygdala is another structure within the limbic system. It is a paired structure with one portion in each hemisphere. These structures lie anterior to the hippocampus. The amygdala's primary functions are regulating emotion, particularly the fear response, some cognitive processes, such as decision making, attention, memory, and appetitive learning, such as being able to link positive and negative emotion with a memory. Appetitive learning occurs in the pathway between the amygdala and ventral striatum.The ventral striatum plays a major role in decision making, and when damaged it inhibits this action. The amygdala integrates emotions, emotional behavior, motivation, and drive, through the limbic system, which can influence responses. These responses can be learned, which is where associative learning takes place. When the amygdala becomes stimulated, fear and aggression are projected.[74,75]

There are two main pathways within the amygdala, and these pathways are further divided into subpathways. The ventral amygdalofugal pathway and stria terminalis are the largest pathways through which efferent fibers leave the amygdala. The amygdala also has direct connections to the hippocampus, entorhinal cortex, dorsomedial thalamus, and brainstem. The entorhinal cortex is important in memory, navigation, and time perception.[74,75]

The amygdala consists of inputs and outputs, otherwise known as afferent and efferent fibers. The amygdala receives all inputs from senses and visceral inputs. The visceral inputs are received from the hypothalamus, septal area, orbital cortex, and parabrachial nucleus. Parabrachial nuclei aid in autonomic control and help regulate respiratory rate. Sensory input such as olfaction is received from the olfactory bulb. Auditory, visual and somatosensory input are received from the temporal and anterior cingulate cortices.[45,74,75]

The amygdala has five output pathways known as the ventral amygdalofugal pathway, stria terminalis, hippocampus, entorhinal cortex, and the dorsomedial nucleus of the thalamus.

The ventral amygdalofugal pathway is one of the output efferent pathways. This pathway continues from the amygdala to the anterior olfactory nucleus, anterior perforated substance, piriform cortex, orbitofrontal cortex, anterior cingulate cortex, and ventral striatum. The anterior perforated substance plays a significant role in blood supply of the deep grey matter. It is located in front of the optic tract. The piriform cortex helps with the sense of smell. It is located in a part of the cerebrum called the rhinencephalon. The orbitofrontal cortex is located in the frontal lobe and helps with cognitive processing and decision making. The anterior cingulate cortex is the front portion of the cingulate cortex. Its primary function is controlling emotions.[45,74,75]

The ventral amygdalofugal pathway connects to the hypothalamus and septal nucleus and has a major connection through the stria terminalis carrying output from the central and basal nuclei.[74,75]

The ventral striatum includes the caudate, putamen and nucleus accumbens septi. The caudate is located near the basal ganglia, and is important in how the brain learns and stores information. The putamen is located at the base of the forebrain in an area called the telencephalon. It aids in regulating movements and different types of learning. The putamen sends neurotransmitters out to aid its functions. The nucleus accumbent is located near the basal forebrain. It is important for processing and analyzing rewarding and reinforcing stimuli as well as sleep regulation. When these landmarks are damaged learning, memory, sleep regulation, and processing can all become impaired. This striatum has projections that are linked in a basal ganglia circuit. These projections are important for stimuli responses to associative learning.[74,75]

The stria terminalis is another output that is similar in form, function, and structure to the fornix. The stria is only connected to subcortical structures. It overlaps with the ventral amygdalofugal pathway connecting to septal nuclei and the hypothalamus, forming a loop. The stria terminalis has precommissural and postcommissural branches leading to the anterior commissure. The anterior commissure is a tract containing white matter that connects two temporal lobes across a midline. It links the hemispheres of the brain aiding in memory, emotion, speech, and hearing. The precommissural branch leads to the septal area and the postcommissural branch leads to the hypothalamus, specifically the lateral nucleus and ventral medial nucleus. Some of the fibers of the stria terminalis cross the anterior commissure to the contralateral side. This is how the amygdala from each hemisphere, both having the same function, communicates with one another, through the anterior commissure. The stria even projects to the habenula and part of the epithalamus.[74,75,104]

Similar to the thalamus and hypothalamus, the amygdala has nuclei that have different functions in receiving and sending signals in order to process stimuli. The central nucleus functions through output pathways by producing autonomic components of emotion to the lateral hypothalamus and brainstem. The central nucleus also functions as conscious perception of emotion through the ventral amygdalofugal pathway leading to the anterior cingulate cortex, orbitofrontal cortex, and prefrontal cortex. The amygdala has significant connections to the prefrontal cortex, septal area, and hypothalamus.[19,74,75,104]

The amygdala also comprises a group of nuclei called the basolateral complex. These are the largest clusters in the middle and lateral part of the amygdala. The basolateral nuclei include lateral basal nuclei and accessory basal nuclei. Lateral basal nuclei and accessory basal nuclei are

output nuclei that send signals to the cerebral cortex for further processing. Their function is to regulate cognitive functions such as decision making, attention, and memory. When drug abuse occurs, reinforcing stimuli in the basolateral complex contributes to the feeling of being high. The basolateral complex activates the emotional learning area of the amygdala. Basolateral nuclei regulate memories related to emotional events. The basolateral complex also acts as a pathway to the central nucleus, carrying inhibitory neurons called intercalated masses. Intercalated masses have inhibitory control over the amygdala by transporting the input and output of fear.[19,74,75,104]

The amygdala receives information from the prefrontal cortex, particularly the anterior cingulate cortices, orbitofrontal cortices, insula, hippocampus, and rhino cortices. Projections to the prefrontal and sensory cortices, hippocampus, and rhino cortices allow for attention memory formation and decision making to occur. When injuries occur these anatomical landmarks are at risk of being damaged, which inhibits the center's ability to make decisions and recall memories.[19,74,75,104]

Lateral nuclei are important input receptors from sensory information. Auditory stimuli are transported directly from the subcortical area where the medial geniculate nucleus is located in the thalamus. Cortical and medial nuclei form the corticomedial group, which is where olfactory stimuli, from the olfactory bulb, and the piriform cortex flow into. Olfactory stimuli in the corticomedial group mediate emotion.[19,74,75,104]

HIPPOCAMPUS

The hippocampus is a complex brain structure that is divided into two lobes and is embedded deep into the temporal lobe. It is a paired structure, with mirror-image halves in the

left and right side of the brain. In general the hippocampus functions significantly in the formation, organization, and storage of new memories. The hippocampus connects certain memories to sensations, such as a scent triggering a memory. The hippocampus consists of the Papez circuit which controls learning, memory, emotion, and social behavior. The Papez circuit is the anatomical substrate of emotion. When the hippocampus is damaged, amnesia occurs, affecting explicit memories, such as names, dates, and events.[35]

The hippocampus has two major pathways of communication in and out of the brain. These are the fornix and entorhinal cortex. The fornix is a C-shaped tract beginning as a bundle of fibers called the alveus. The alveus is white matter that has myelinated afferent and efferent neurons. The fibers of the alveus travel posteriorly combining medially to form the fimbria of the fornix. Fimbria is the fringe of the hippocampus becoming thicker as the fringe moves posteriorly, until it splits off forming the crus of each hippocampus. The crua meet, forming the hippocampal commissure, providing one of the two pathways through which the hippocampi communicate. At the end of the hippocampal commissure is where the fornix is located, and it continues to the anterior commissure. The anterior commissure is important because this is where the fornix splits into three sections, in three directions.[19,74.75,104]

The fornix begins by splitting into the precommissural fornix, which branches to the septal nuclei, ventral striatum, and cingulate cortex. (See Figure 14 below) Some fibers pass through the anterior commissure to the contralateral hippocampus forming the second of the two major pathways of communication between hippocampi. The third split occurs after the anterior commissure. This division is called the postcommissural fornix and branches to the mammillary bodies of the hypothalamus and the anterior nuclei of the thalamus.[19,35,74,75,104]

The precommissural branch of the fornix connects to the septal nuclei, preoptic nuclei, ventral striatum, orbital cortex, and anterior cingulate cortex. The hippocampus receives input through the precommissural branch of the fornix from the nucleus basalis and part of the septal nuclei.[19,74,75,104]

The postcommissural branch of the fornix connects to the anterior nucleus of the thalamus and the mammillary bodies of the hypothalamus. The input through the postcommissural branch is sent from the mammillary bodies of the hypothalamus. The mammillothalamic tract travels from the anterior thalamic nucleus of the hippocampus to the posterior hypothalamus. This connection allows the hippocampus to have effects on the hypothalamus and the thalamus.[19,74,75,104]

The anterior thalamic nuclei connect to the cingulate cortex, which projects back to the entorhinal cortex of the parahippocampal gyrus, making up the Papez circuit. The hippocampus has direct connections to the entorhinal cortex and the amygdala. The entorhinal cortex is the second major input pathway. The entorhinal cortex is made up of the cingulate cortex, temporal lobe cortex, amygdala, orbital cortex, and olfactory bulb. The entorhinal cortex projects to the cingulate cortex, which is affected by the anterior thalamic nuclei. The cingulate cortex projects to the temporal lobe cortex, orbital cortex, and the olfactory bulb. All of these anatomical structures can be affected by the hippocampus because they are inputs through the entorhinal cortex.[19,74,75,104]

The hippocampus contains two major anatomical landmarks. These are the dentate gyrus and cornu ammonis. The dentate gyrus is important because it receives inputs from the entorhinal cortex. The dentate gyrus processes information that is passed through the hippocampus. The

hippocampus and dentate gyrus are considered a cortex, although they only have three layers instead of six. The cerebral cortex is made up of six layers, therefore, the hippocampus and dentate gyrus are being compared to the number of layers of the cerebral cortex. The cortex is located between the neocortex and diencephalon. The cortices, known as the paleocortex, are a type of cortical tissue that has three layers of cortical laminae (neuronal cell bodies). The paleocortex contains structures in the limbic system such as the hippocampus and cingulate gyrus. Each layer consists of different cells. The inside layer is known as the superficial molecular layer, the middle layer of the hippocampus is the pyramidal layer, and the outermost layer is the deep polymorphic layer. The dentate gyrus is also divided into layers, however the only difference is the middle layer which is made up of granular cells as opposed to pyramidal cells. The molecular layer of the hippocampus faces the dentate gyrus. The polymorphic layer contains the alveus which form the fimbria fibers that are the gateway to and from other regions of the brain. There is one anatomical structure that lies between the entorhinal cortex and the cornu ammonis 1, called the subiculum. This structure is a transition layer that aids in passing information through the entorhinal pathways.[19,74,75,104,114]

There are three pathways that are critical to communication. The first is known as the perforant pathway from the entorhinal cortex to the granule cells of the dentate gyrus. There is a mossy fiber pathway from the granule cells of the dentate gyrus to the pyramidal cells of the cornu ammonis 3 (CA3) region of the hippocampus. Lastly there is a collateral pathway from the CA3 region of the hippocampus to the cornu ammonis 1. All these pathways work to transport and receive information to and from the hippocampus to other areas of the brain. When head injury occurs these pathways become damaged, causing communication between these

pathways to be lost, inhibiting the transmission and reception of information in the hypothalamus.[19,74,75,104,114]

The cornu ammonis is a subfield located between the dentate gyrus and the subiculum. There are three distinct layers known as the cornu ammonis 1, 2, 3 (CA 1, 2, 3) . The polymorphic layer is considered cornu ammonis 4. Cornu ammonis 3 contains pyramidal cells, perforant pathways, and Shaeffer collaterals. Cornu ammonis 4 is the primary layer of communication. Cornu ammonis 3 borders the dentate gyrus and CA2. Cornu ammonis 1, 2 contain pyramidal cells. Cornu ammonis 2 borders with CA 3 and CA 1. CA 1 borders with CA 2 and the subiculum.[114] **SEPTAL REGION**

The septal region is made up of the cortical septal area and subcortical septal nuclei. The septal nuclei are a group of telencephalic nuclei wrapped around the inferior, superior, and anterior aspects of the anterior commissure. The anterior commissure is the anterior boundary for the hypothalamic nuclei. Septal nuclei are made up of several nuclei that have widespread connections to and from the limbic system. These nuclei are divided into medial and lateral septal groups.[1]

The lateral septal group contains afferent neurons. The lateral group consists of the nucleus basalis and nucleus accumbens. The nucleus accumbens is responsible for creating biological drives for survival and reproduction. The nucleus basalis are significant in the function of memory. The lateral group are the main input nuclei.[1]

There are many areas of the brain that project towards nuclei in the septal region. (See figure 13 below) Cerebellar fastigial nuclei, amygdalar nuclei, lateral hypothalamus, cingulate gyrus, mammillary body, and the substantia nigra all project to the lateral septal region.[1,97-98]

The medial septal group is the primary source of efferent fibers. This medial group contains the nucleus of the diagonal band of Broca's area. The medial group also contains the bed nucleus of the stria terminalis, anterior commissure, and the septofimbrial nucleus. This group of nuclei contains many cholinergic neurons. This means that the way in which stimuli is sent and received is through the neurotransmitter acetylcholine. The medial septal group is the primary output.[1,97-98]

There are many afferent projections from the brainstem to the septal region. These include the periaqueductal gray region, the nucleus of locus coeruleus, ventral tegmental nuclei, and raphe nucleus. The nucleus of coeruleus is nonadrenergic, which means when nerve impulses are sent, norepinephrine is used in the transmission of signals. Ventral tegmental nuclei are dopaminergic meaning dopamine is used as the neurotransmitter. Raphe nuclei are serotonergic meaning serotonin is the neurotransmitter used among these nuclei.[1,97-98]

The septum is divided into two structures. These structures are the septum pellucidum and septum verum. The septum pellucidum is a thin, transparent membrane that passes through the middle of the brain from the corpus callosum to the fornix. It is an anatomical barrier that has connections to the hippocampus and hypothalamus. The septum pellucidum is also a relay station. It acts as a division between portions of the lateral ventricles forming walls of the anterior region of lateral ventricles. The septum pellucidum is a thin two layered structure that consists of white matter, neurons, fiber bundles, and blood vessels. The septum pellucidum is surrounded by neurons that make up the septum verum, which contains septal nuclei.[1,97-98]

The septal region has many different functions. Septal nuclei are part of the limbic system receiving afferent connections from other limbic structures. Septal nuclei also send projections to

the hippocampus, habenula, thalamus, ventral tegmental area, and hypothalamus. The habenula is a pair of nuclei above the thalamus. It is important in the sleep-wake cycle, reproduction, behavior, and mood, such as depression. When the habenula is damaged it can greatly affect sleeping behavior as well as emotions, leading to depression and anxiety. Neurons in the septal nuclei are strongly connected with the hippocampus and have a significant role in learning and memory. In addition, septal nuclei also aid in social behaviors and the expression of fear. Neurons in the septal nuclei give rise to axons that travel in the medial forebrain bundle. This is important in reward systems because it causes the stimulation of dopamine receptors. The septal area has a strong connection to the limbic system because of the role it has on social connectedness and bonding. The septal area also creates positive feelings toward one another, such as unconditional trust and empathy. Since the septal region has such an important role, significant effects occur when this region is damaged. For example, when damage occurs to nuclei in this area, the onset of bipolar, depression, and schizophrenia increase. The septal area is very important in mental illness because it contains the subcortical region that has strong correlation to emotion centers in the brain making depression more likely after an incident. This is due to the inability to produce positive emotions. Head injuries cause the loss of myelination on neurons and when this happens, specifically in the septal area, emotional regulation becomes inhibited often leading to depression and mental health issues.[1,97-98]

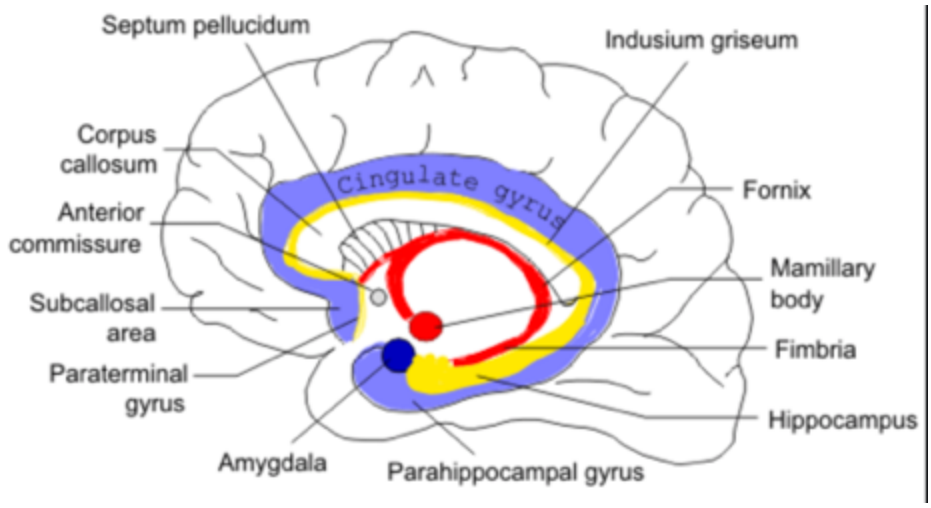


Figure 13. The Septal Area

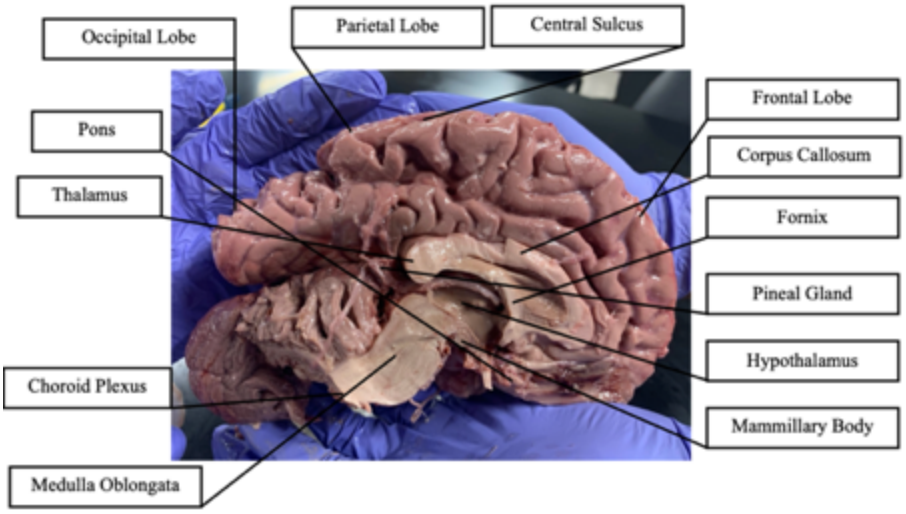


Figure 14. Closeup View of Limbic System

HOW PARTS OF LIMBIC SYSTEM WORK TOGETHER

The limbic system contains many anatomical structures and nuclei that are interconnected and located in the telencephalon and diencephalon. These structures work together to produce and regulate emotion. Most of these structures control self preservation. They regulate the

endocrine and autonomic system, particularly with emotional stimuli. There is a set level of arousal involved in motivation and reinforcement behaviors. Many of the structures play a critical role in memory as well. Some structures are closely attached to the olfactory system, triggering memory and emotion, as well as involvement with certain senses. The anatomical structures referenced above are stored in two particular areas: cortical and subcortical regions.

The cortical component contains the hippocampus, cingulate gyrus, and parahippocampal gyrus, creating a rim around the corpus callosum. (See figure 14 above) The subcortical structures include the olfactory bulb, hypothalamus, amygdala, septal nuclei, and certain thalamic nuclei, such as the anterior thalamic nuclei.[30]

Certain structures within the limbic system aid in the input of information and processing. These structures are the amygdala and hippocampus. Others send signals outward such as the septal nuclei and hypothalamus. All of the structures in the limbic system are connected by pathways that allow for signals to be transmitted to and from different areas. For this reason, even though structures may not be directly connected, there is still an indirect effect on the structures within the limbic system.[30]

HOW THE LIMBIC SYSTEM IS AFFECTED BY HEAD TRAUMA

The limbic system covers a large portion of the brain. This puts the limbic system at a greater risk of being compromised when head trauma occurs. When a traumatic brain injury (TBI) happens, cognition, behavior, emotion, motor skills, sensory abilities, and somatic behavior are all areas that may be affected.[80,96]

Similarly, all of these systems are related to the limbic system. For example, following a TBI, the primary symptoms include difficulty with decision making, loss of memory, mood

disturbance, aggression, anger, loss of coordination and balance, vision and hearing disturbances, and difficulty sleeping.[96]

Most of these symptoms are controlled by the amygdala, thalamus, and occipital lobe. Anger and aggression is controlled by the amygdala. Memory is controlled by the hippocampus. Sensory information is relayed through the hypothalamus. This is where the olfactory bulb is located. The hippocampus and hypothalamus work closely with memory and smell allowing for a scent to trigger a memory. When a TBI occurs this pathway can be damaged. The limbic system is important to many critical functions of the brain, and when damaged by a TBI, significant disturbances of one's ability to function normally decreases significantly.[96]

HEAD TRAUMA AND HOW IT AFFECTS THE BRAIN

Head injuries are much more common than one would expect. About 30 million combined head injury related ER visits, hospitalizations, and deaths occur each year. Sixteen percent are diagnosed with Traumatic Brain Injury (TBI) as being their secondary diagnosis, and ⅓ of the head injury deaths were directly related to TBI as being the underlying cause. As of 2010, 2.5 million TBI cases occurred, which is a 56% increase from three years prior. These statistics do not account for the people who did not seek medical care following the accident. The population at highest risk for incurring a TBI is that of males who are injured by falls, objects, or a motor vehicle incident.[79,96]

When a head injury occurs from a fall, motor vehicle incident**,** or object often a concussion has been sustained. A concussion is “a type of TBI caused by a bump, jolt, or blow to the head or a hit by a body that causes the head to move rapidly back and forth. Movement to the

brain causes the brain to bounce or twist in the skull. This causes chemical changes or stretching and damage to the brain cells." [79,96]

One example of a chemical change is when shear force disrupts the neural membranes, more K+ is sent into the extracellular space, suppressing neural activity. The sodium potassium pumps restore balance in the cells, but increase energy and decrease blood flow, leading to disruption of the autonomic nervous system.[93]

Concussions have many mechanisms of injury, however the most common are sports related, particularly in soccer, hockey, and football due to the amount of body contact that occurs in these sports. Concussions and TBI's can also occur in motor vehicle accidents and in falls which is more common in the larger population, whereas sports related is the most common among the younger population, specifically ages 10-25.[93]

A study was done using varsity soccer athletes who had a previous history of concussions. There were three categories of symptoms: somatic, neurophysiologic, and cognitive. One main point that was gathered from this study was the concern for repeated concussions and the long term effect. Once one concussion has been sustained these athletes had an increased fear that it would happen again. After the first concussion a person is four to six times more likely to sustain a second concussion. Each concussion after the first causes worsened symptoms and a delayed recovery. If an athlete has sustained a concussion, but goes back before it is fully healed, second impact syndrome (SIS) can occur. This is where an athlete goes back to play while the brain is still healing and gets hit again causing the brain to swell very quickly leading to a serious disability or even paralysis depending on the person and the stage of healing the brain was in. Usually the hit that they incurred was very minor and to the trunk, but

because the brain was still healing the body uses the swelling to protect itself, but ends up doing more damage.[62,79,93,96,110-111]

When a head injury happens there are different motions in which the head can move. These are contact and inertial casual forces. These happen during impact loading where the head is struck or it strikes something. Inertial forces occur from impulsive head motions, such as the absence of the head striking something. Inertial loading happens at the moment of impact. There are two types of forces that occur during inertial loading- linear acceleration and rotational acceleration.[62,79,93,96,110-111]

Linear Acceleration, the biomechanical way in which the brain is moved during impact, showed that pressure during impact had a correlation between peak acceleration and peak pressure. An internal response of brain pressure and an external input of linear acceleration led to the effects of pressure being studied. A small increase in pressure causes neurologic dysfunction, with a level of dysfunction correlating to peak pressure being achieved.[62,79,93,96,110-111]

Rotational acceleration is common during impact or impulsive head loading. Brain tissue deforms more readily in response to shear force as compared with other tissues. When rapid head rotation occurs, it generates shear force throughout the brain. This shear force causes the brain to have a high potential for having shear force induced tissue damage. Shear deformation that is caused by rotational acceleration is the primary mechanism of injury in a concussion. The severity depends on the amount of brain tissue injured. Tissue deformation is influenced by applied rotational acceleration, intracranial partitioning membranes, and material properties of brain tissue. Patterns of strain are different depending on which plane the force is applied. Lateral (coronal) force produces most of the damage in humans.[62,79,93,96,110-111]

When damage occurs generally a transfer of energy from external input to the brain and tissue has occurred causing the damage. How this acceleration moves and deforms brain tissue, as well as its effect on living tissue and neural network, is key in understanding concussions. Knowing the biomechanics of how internal responses combine with external responses, helps scientists study how concussions work.[62,79,93,96,110-111]

Damage can be done to the brain in such a way where the glutamate receptors can become damaged. Glutamate receptors are located on membranes of neuronal and glial cells. Glutamate receptors are important in glutamate mediated postsynaptic excitation of neural cells and aid in neural communication, memory formation, regulation, and learning. Glutamate receptors affect neurotransmission and plasticity**,** so when these become damaged the brain loses its ability to remain plastic and struggles to send certain neuronal signals. Brain plasticity is the brain's ability to adapt after an injury. Neurons become myelinated, improving brain function and resulting in healing of the brain injury. Inhibitory synaptic receptors function can be altered with physical force showing the importance of excitation/inhibition coupling. Physical injury can lead to the activation of different neuronal death pathways with physical coupling glutamate receptors, which explains the activation.[31,58,77,79]

DEGENERATIVE BRAIN DISEASES

Degeneration is caused by the decline and death of nerve cells. The brain is a soft, fragile organ that when damaged, is susceptible to degeneration. Chronic Traumatic Encephalopathy (CTE) is the term used to describe brain degeneration caused by repeated head trauma. A diagnosis of CTE can only be made during autopsies. Chronic Traumatic Encephalopathy has connections to post concussion syndrome and second impact syndrome later in life. The

symptoms begin to show years to decades after the injury occurred. Chronic Traumatic Encephalopathy is most commonly found in people who play contact sports as well as the military personnel who have been exposed to explosions. As of now there is no cure for CTE. People who have CTE may show signs of ALS, Alzheimer's, or Parkinson's disease. In CTE the brain wastes away becoming deformed and these diseases are connected with the neurodegenerative disorders such as the ones listed above. The most common symptoms associated with CTE are difficulty thinking, impulsive behavior, short term memory loss, difficulty planning, substance misuse, suicidal thoughts, and emotional instability. The best way to prevent developing CTE is by minimizing the amount of MTBI and SIS athletes obtain.[34,38,109-111]

In addition to CTE there are also progressive degenerative disorders that affect the brain. These are Alzheimers, Dementia, Parkinsons, and Huntington's Disease. Progressive diseases cause an increase in death of nerves over time decreasing intellectual function of speech, memory, and spatial skills. Alzheimer's disease affects memory whereas dementia affects thought and causes behavioral changes. Huntington's disease affects the ability to walk and Parkinson's impairs movement. About ⅓ of adults are diagnosed with a progressive disease in their lifetime. These diseases can affect balance, movement, speech, breathing, and cardiovascular function as well. The most common causes of progressive diseases are genetics, alcohol, drugs, tumors, strokes, toxins, chemicals, and viruses. Most of these diseases do not have a cure as of now.[109-111]

Alzheimers have microtubule associated proteins called tau that is a major component of filaments that form the neurofibrillary tangles of disease. Similarly, Parkinson's has a component

called alphasynuclein that is important to the Lewy bodies which is an aggregate of Parkinsons.[38,109-111]

NONDEGENERATIVE DISEASES AND HEAD INJURIES

There are many different kinds of nondegenerative conditions including concussion, bleeding due to a TBI, meningitis, encephalitis, septicemia, drug and alcohol abuse, and vitamin deficiency.

CONCUSSION

Concussions are non degenerative brain injuries that are caused due to a blow to the head from an outside source. Headache, loss of memory, dizziness, and mood changes are all common symptoms of a concussion. Loss of consciousness may occur, but it is rare for a mild to moderate concussion to last more than a few minutes to hours. A concussion may lead to temporary or permanent damage to areas of the basin specifically cognitive function, physical abilities, or psychological problems. Assessment of a concussion is generally to get a CT scan, and sometimes an MRI of the brain. Treatment of a concussion usually consists of bed rest, so time off of work and school, chiropractic adjustments, and pain medication, such as NSAIDs.[62,79,93,96,109-111]

BLEEDING CAUSED BY TBI

A traumatic brain injury occurs either by a significant blow to the head or by a penetrating object and the damage is much more severe than a concussion due to the likelihood of a brain bleed. Symptoms may be mild to moderate depending on the pathology of the injury. Two types of brain bleeds can occur. These are a subarachnoid hemorrhage and a hematoma.[6,109-111]

A subarachnoid hemorrhage is bleeding in the area around the brain that normally contains CSF, but now is filled with blood. Surgery may be necessary to eliminate the blood.[109-111]

A hematoma is caused by ruptured blood vessels forming clots. These clots may be small or large and may be located in various parts of the brain depending on where the damage occurred. The body may absorb the clots during healing or surgery may be required.[109-111]

MENINGITIS

Traumatic Brain Injuries are commonly thought of direct blows to the head, however this is not the only injury that can cause a TBI. Severe diseases can also affect the brain similarly to how a direct hit to the brain does. Meningitis is a bacterial or viral infection inflammation of the meninges that presents with headache, fever, sensitivity to light, and muscular rigidity, which may cause convulsions, delirium, and death.[109-111]

Treatment of bacterial meningitis is through intravenous antibiotics and sometimes corticosteroids. Corticosteroids are used to reduce the risk of brain swelling and seizures. A doctor may also drain infected sinuses or mastoids.[109-111]

Viral meningitis has no antibiotic cure and treatment mainly consists of bed rest, fluids, pain medications, corticosteroids for swelling, and anticonvulsant for seizures.[109-111]

ENCEPHALITIS

Encephalitis is inflammation of the brain generally caused by a viral infection. Symptoms tend to be flu-like such as fever and headache. Some people have no symptoms, whereas others have seizures, confused thinking, movement, vision, or hearing impairment. Assessments for encephalitis include MRI, CT, spinal tap, brain biopsy, or EEG. An EEG is a test where

electrodes are placed on the skull, and are set to measure electrical activity in the brain. Treatments that are used for encephalitis are generally antiviral medications since the swelling of the brain is commonly caused by a virus. Prescribing antiviral medications helps get rid of the virus, allowing from the brain to decrease in swelling and return to normal function thereafter.[32,44,109-111]

SEPTICEMIA

Septicemia occurs when a bacterial infection in the lungs, kidneys, bladder, or abdomen spreads to the bloodstream causing blood poisoning. This condition may lead to sepsis if not treated properly. Symptoms of septicemia are chills, fever, increased heart and respiration rate. Treatment of septicemia is only antibiotics which are used to kill the bacterial infection.[109-111]

DRUG AND ALCOHOL ABUSE

Many addictive drugs, such as narcotics, target the reward system of the brain which is located in the prefrontal and cerebral cortex. When drugs are taken dopamine floods the brain giving the sensation of a “high.” As the brain becomes used to the increase in dopamine, higher dosage is required to feel the same feeling. The increase in drug use causes judgement issues, decision making, memory, and the ability to learn. Alcohol has a similar effect by causing a person to forget the negative feelings they had when sober. The absence of those feelings while under the influence is what causes the addiction to grow stronger. Alcohol damages the brain as well as the liver and other organ systems, such as the brain. Drinking excessively can cause the neurons in the brain to die off, causing vision and speech impairments, balance and walking inhibition, and anger management issues. Alcohol and drugs age people beyond their years, and take years off their life. Treatment for drug and alcohol abuse is psychological therapeutic

rehabilitation, generally in an inpatient facility. As alcohol remains absent from the body, the brain can begin to reverse the shrinkage that occurred from excessive drinking, by myelinating new neural pathways, however the brain may not return to full capacity. The longer a person has been an alcoholic, the more permanent the brain damage is.[7,76,101,09-111]

VITAMIN DEFICIENCY

Although vitamin deficiency may not seem significant enough to classify under a TBI, the damage that can occur from certain vitamin deficiencies can have similar symptoms to that of a TBI. There are many types of vitamin deficiency such as vitamin D, B12, and folate. The most common symptoms of vitamin deficiency are fatigue, breathlessness, memory issues, balance problems, loss of coordination, and weakness in the body. Vitamin deficiencies can generally be treated by taking a certain amount of that vitamin per day, however sometimes they can be chronic in which case a physician will need to monitor the levels periodically to make sure it is not dangerous to the person.[109-111]

Most of the non degenerative conditions can be cured or healed whether it be from bed rest, pain medication, antibiotics, surgery, occupational therapy, or physical therapy.[109-111]

Symptoms of the conditions listed above may appear similar to schizophrenia, depression, or psychosis so it is important to rule these psychological issues out as well before moving forward with any treatments.[109-111]

A TBI results from an external physical force to the head or another form of displacement causing damage that is either focal or widespread. Damage can result from either primary or secondary injury. Primary injury is the initial injury that occured, such as the blow to the head. The secondary injury involves systematic and intracranial effects after the injury, such as

hypoxia or seizures. The severity of a TBI is based on the extent and mechanism of injury, duration of level of consciousness, post traumatic amnesia, and the extent of confusion.[113]

A Mild Traumatic Brain Injury has a loss of consciousness of up to 30 minutes or confusion and disorientation lasting 24 hours with a CT scan presenting as normal. This would be classified as a mild concussion.[39,109-111,113]

A moderate TBI has a loss of consciousness for more than 30 minutes, but less than 24 hours. Confusion and disorientation may last up to seven days, and presents with an abnormal CT scan. A severe TBI includes loss of consciousness lasting more than 24 hours. . In some cases a person may not experience loss of consciousness for 24 hours, however this is typical of a severe TBI. Memory loss will last up to seven days or more. A structural brain image will be taken and usually presents as abnormal, though in some cases it may be seen as normal. A penetrating TBI is an open head injury in which the scalp, skull, and dura mater have been penetrated. This usually occurs from high velocity projectiles, however a low velocity projectile such as a knife or bone may cause a penetrating wound as well. There is also a specific grading scale that is used, called the Glasgow Coma Scale, that is used to measure the amount of consciousness a person has directly after injury. It is graded by points. The more alert a person is, the higher their score will be. An alert patient scores between 13-15 and it decreases down to fully unconscious, which is 3 points. See Table 8.[109-111,113]

Table 8. Glasgow Coma Scale [62,79,93,96,109-111,113]

Eye Opening	**Observed**	**Rating**	**Score**
Open before stimulus	————————	Spontaneous	4

After Spoken or shouted request	————————	To sound	3
After finger tip stimulus	————————	To pressure	2
No opening at any time and no interfering factor	————————	None	1
Closed by local factor	————————-	None testable	NT
Verbal Response	————————		
Correctly gives name, place, and event	————————	Oriented	5
Not oriented, but communicates well	————————	Confused	4
Intelligible single words	————————-	Words	3
Only moans and groans	————————-	Sounds	2

No audible response and no interfering factor	————————	None	1
Factor interfering with communication	————————	None testable	NT
Best Motor Response			
Obey 2-part request	————————-	Obeys command	6
Brings hand above clavicle to stimulus on head	————————	Localising	5
Bends arm at elbow rapidly, but features are not abnormal	————————	Normal Flexion	4

Bends arm at elbow and features abnormal	——————-	Abnormal Flexion	3

Extends arm at elbow	——————-	Extension	2
No movement in arms and legs and no interfering factor	———————	None	1
Paralysed or other limiting factor	——————-	None Testable	NT

The most common cause of a TBI, other than sports, is falls and motor vehicle accidents. Falls account for 52% of TBI's whereas motor vehicle accidents make up about 20%. Aside from accidents, self harm, such as suicide, is the leading cause of death related to TBI due to the high prevalence of guns used as suicide. Self harm accounts for 33% of deaths from a TBI. The most common age pertaining to TBI ranges from 15-44 and 75+. These age ranges are most likely to have TBI's from motor vehicle accidents, crashes, falls, violence, and suicide.[62,79,93,96,109-111,113]

There is a minimal amount of diverse treatments related to TBI's because the brain needs rest and time to heal itself. In a sense, rest is a type of treatment, although not the typical kind many think of when they think of 'treatment.'The neurons and myelin covering the axons need to regenerate because when an accident occurs, cell and neuron death occurs. Treatment such as chiropractic, physical therapy, and fish oil or other supplements can help the patient return to function to where they can perform activities of daily living (ADL) on their own.[62,79,93,96,109-111,113]

There are two types of rehabilitation that can assist in this. These Rehabilitation techniques are restorative and compensatory. Restorative is direct therapy used to help rehabilitate the person to being able to perform ADL's on their own, back to how they used to be able to function. Compensatory rehabilitation helps the person adapt to their deficits and learn how to work around them so that they can be independent again.[8]

STROKE

A stroke is a sudden interruption in blood supply to the brain. A stroke affects the arteries leading to and within the brain. The most commonly affected arteries are the middle cerebral artery, internal carotid arteries, forming the anterior circulation, and the vertebral basilar arteries that supply the posterior circulation of the brain. The entire area of the arteries is known as the Circle of Willis. The Circle of Willis is a ring of communication between the basilar artery and the internal carotid arteries. Stroke is the fifth leading cause of death in the United States and a leading cause of disability. A stroke occurs when a blood vessel carrying oxygen and nutrients becomes blocked or ruptured. When a blood clot occurs, it causes decreased flow of blood and oxygen to the brain, causing cell death.[4,41,42,78]

There are two main types of strokes: ischemic and hemorrhagic. An ischemic stroke happens when there is obstruction of blood flow to the brain. A hemorrhagic stroke occurs when a blood vessel ruptures, preventing blood from flowing to the brain. One less significant kind of stroke is called a transient ischemic attack (TIA). A TIA is caused by a temporary blood clot in the brain, often resolving itself relatively quickly.[4,41,42,78]

A stroke's effect depends on the location of the obstruction, and how much brain tissue was affected. There are many areas in which a stroke may damage the brain. A stroke can occur in the left or right hemisphere. When a stroke occurs in the left hemisphere, damage will take place on the right side. Damage to the right side of the brain may cause paralysis of that side, speech or language may be inhibited, development of a slow, cautious behavioral style is common, as well as memory loss. A person may also have trouble seeing the right visual field. Their may be an inability to do math and organize, as well as an increased inability to read and write.[4,41,42,78]

When a stroke occurs in the right hemisphere, paralysis to the left side can occur as well as vision issues. There may be an inability to see the left visual field. A person might become quick and inquisitive, but also have memory loss. A person may have reduced insight; denial is also common. Decreased spatial awareness and depth perception is normal when damage to the right hemisphere occurs. Impulsiveness and inappropriateness is also very common.[4,41,42,78]

A stroke occurring in the cerebrum can cause impairment of movement and sensation, speech, eating and swallowing, vision, cognition, perception, self care, bowel and bladder control, emotional control, and sexual ability. The cerebrum's main functions are to provide sensation, speech, thought, reasoning, memory, vision, and emotion. When this area is affected

by a stroke, the nerves that originally processed that information, have now become damaged or deceased, creating deficits in signal production between neurons.[4,41,42,78]

When the cerebellum is affected by a stroke, there are four main symptoms that occur. These symptoms include the inability to walk, dizziness, nausea, and a headache. The cerebellum is a less common origin of a stroke.[4,41,42,78]

The last commonly affected area, due to stroke, is the brainstem. When a stroke occurs in the brainstem the regulatory functions of the body often become impaired. Breathing, heart rate, body temperature, weakness, chewing, swallowing, and speaking are all at risk of damage. When a stroke occurs in the brainstem death is a possibility because of its connection to the spinal column.[4,41,42,78]

Up until now the primary focus has been on specific areas of the brain that are susceptible to serious injuries. Moving forward we will discuss the systems of the brain and how they are interconnected.

INJURIES THAT AFFECT THE LIMBIC SYSTEM

When the hypothalamus is affected by head injury many different hormone insufficiencies may occur. A small gland, called the pituitary gland, is often damaged when the hypothalamus is injured. The pituitary gland releases thyroid, adrenal, and reproductive hormones. When the pituitary gland is damaged, insufficient hormone levels occur.[21,30,74-75]

The most commonly affected hormones are adrenocorticotropin (ACTH), aldosterone (ADH), follicle stimulating hormone (FSH), growth hormone (GH), prolactin, and thyroid stimulating hormone (TSH). Soon after a TBI, it is common for the patient to have adrenal insufficiencies due to injury of the hypothalamus or pituitary gland. Adrenal insufficiencies can

lead to diabetes insipidus, and hypernatremia. Diabetes Insipidus occurs when there is not enough ADH. This causes a person to urinate frequently, as well as drink extreme amounts of water, due to extreme thirst. Hypernatremia causes a discrepancy in the balance of salt and water. This may result in headache, fatigue, vomiting, and confusion.[21,30,74-75]

Months after a TBI has occurred, hypothyroidism, hypogonadism, growth hormone imbalances, and hyperprolactinemia may be seen. Hypothyroidism occurs when TSH levels are abnormally low. Hypothyroidism presents itself through feeling fatigued, constipation, weight gain, irregular menstruation in women, and lower body temperature. Hypogonadism stops menstruation in women and causes a person to lose body hair. In men, hypogonadism causes sexual dysfunction, breast enlargement, loss of body hair, and muscle. Growth hormone increases fat, decreases muscle and bone density, and decreases energy. In minors, imbalances in growth hormone may cause growth issues. Hyperprolactinemia causes irregular menstruation and nipple discharge in women, while men experience erectile dysfunction.[21,30,74-75]

Another possible problem arising from a damaged pituitary gland is hyperpituitarism. Hyperpituitarism is a biochemical deficiency, in at least one endocrine axis, caused by the instability to release or supply hypothalamic releasing hormones. The pituitary gland lies within a bony enclosure called the sella turcica and is supplied by the hypophyseal vessels. Primary injury, hypoxia, brain swelling, hypotension, anemia, hemorrhage, and critical illness can cause pituitary dysfunction. Basal skull fracture and fracture of the sella turcica can damage the hypothalamus, especially when rotational or shearing impact occurs. The anterior pituitary is more susceptible to damage because long hypophyseal vessels and portal capillaries supply this portion of the brain. Different patterns of hormonal insufficiency, with deficiency of those

hormones, can be seen in gonadotropin hormone and gonadotropin levels. This is because somatotrophic and gonadotropic hormones are located in the lateral pituitary, which is susceptible to ischemic damage. When there is a lack of blood flow to the brain, nerves die damaging specific areas, and creating irreversible nerve repair and brain damage.[67]

THALAMUS

Seventy seven percent of patients, in a study of 228 participants, sustained TBI's related to thalamic and basal ganglia hemodynamic impairments. Many symptoms of TBI and mTBI occur because of damage to the thalamus.[57]

The thalamus plays a vital role in regulating sleep and wake cycles. When the thalamus is damaged, it is common for a person's sleep to become abnormal. When loss of consciousness occurs with an mTBI, it is common for insomnia to onset as a result of the injury. The sleep cycle is controlled by neuronal systems in the thalamus, as well as the hypothalamus, brainstem, and basal forebrain. The thalamus is the first relay station, in which afferent signals are blocked at the onset of sleep. This blockage prevents the cerebral cortex from receiving peripheral stimuli, which aid in the sleep/wake rhythm. Thalamic degeneration, involving the anterior nucleus or dorsal medial nucleus, decreases the ability of creating a sleep pattern. The thalamic midline and intralaminar nuclei receive signals from the brainstem and reticular formation relaying information to the ventral anterior nucleus. The reticular formation contains fibers connecting the thalamus to the cerebral cortex. The cerebral cortex is thought to correlate activity of the thalamic neurons, creating spindle rhythms during sleep.[36,37,57,68,82]

The thalamus also plays a significant role in memory, executive function, and attention. When the thalamus is damaged, it is susceptible to losing reticular nuclei neurons. This may

result in the onset of attention deficit issues, however research shows that attention and processing speeds are not directly related to any specific structure in the thalamus. This finding shows that inattention can occur with any damage to thalamus, not just one particular structure.[54,57,82]

Damage to the anterior nucleus, dorsal medial nucleus, midline, and intralaminar structures contribute to amnesia. Executive functioning deficits are only seen when in correlation with the ventral internal medullary lamina and ventral dorsal medial nucleus. Executive functioning is largely controlled by the prefrontal cortex (PFC), however the mediodorsal nucleus of the thalamus is strongly connected to the PFC.The exact way in which the mediodorsal nuclei are connected to the PFC is yet to be determined. When a moderate to severe TBI has been sustained, grey matter density is seen to be decreased in the thalamus, as well as hippocampus, basal forebrain, and parts of the neocortex. Decreased grey matter density is consistent with deficits in sustained attention, associative learning, and reaction time.[54,57,82]

When an mTBI or TBI is sustained, one of the most common symptoms is headache or migraine. Head pain is associated with the thalamus. When one complains of a migraine, the thalamus and thalamocortical circuits are commonly involved. A thalamocortical circuit synapses on dendrites of pyramidal cells in the cortex. They then synapse back onto thalamic neurons. The thalamocortical circuit is regulated by sensory input. On a xenon CT scan it can be seen that hemodynamic changes to the thalamus, basal ganglia, and cerebral cortex during a migraine occur. There are links between the thalamocortical processing centers, vestibular nuclei, and trigeminal system. These connections may provide the basis for pathophysiological models of migraines in relation to vertigo.[57,82]

Fatigue is another common symptom of a head injury that relates to thalamic injury. Central fatigue causes a lack of physical and mental tasks requiring self motivation. Central fatigue is related to non motor output channels in basal ganglia. Neurons of basal ganglia are involved in higher motor cognition, as well as other functions through connections related to the cortex and limbic structures. A predisposition to fatigue may occur when there is an interruption of striatocortical fibers or a change in the thalamic activity causing a suppression of cortical activation via the striatothalamocortical loop. Striatocortical fibers make up parts of the basal ganglia. They have many function, however they are best known for aiding in voluntary movement. The striatothalamocortical loop has connections between the cortex, basal ganglia, thalamus, and returns back to the cortex. Neural circuits pass through this loop sending and receiving information.[57,82]

Many patients who had sustained a moderate to severe TBI had smaller thalamic volumes than those who only had mild to moderate trauma. Patients who had visible non thalamic lesions had less thalamic volume than those with no lesions. When lesions are present, the thalamus may be susceptible to transneuronal degeneration. Transneuronal degeneration occurs when neurons die because of a disruption in input or output to other neurons. Thalamic damage in moderate to severe cases, shows neuronal loss in the dorsal medial nucleus and ventral posterior nucleus. Dorsal medial neuronal loss may be the basis of predicting the outcome of patients and their recovery because when neurons are visibly lost in a portion of the brain that automatically shows that there will be some sort of disruption of function to that part of the brain. Knowing this, can lead to more area-specific treatments that would help in replenishing lost neurons.[55,57,82]

AMYGDALA

Brain injuries are notorious for changing the way people feel or act. Many people experience emotions quickly and intensely, though generally have little lasting effects. These changes in emotion are related to damage of the amygdala. The amygdala is the emotional center of the brain. When damage occurs, a person may feel happy one minute, then sad the next, and then angry. This progression is known as emotional lability. People may experience sudden bursts of crying and laughing unrelated to any situation. There are generally no specific events that cause this outburst. It is usually strictly dysregulation of the amygdala due to injury.[19,43,74]

Anxiety is a common emotion that surfaces after a brain injury. Anxiety is the feeling of fear or nervousness that is more extreme than the situation poses. Being rushed, in crowds, or changes of plans can be difficult after an injury. Panic attacks may surface due to PTSD of the accident, particularly replays of the incident. Problems with reasoning and concentrating makes it difficult to solve problems. It is very common for a person to feel overwhelmed when making decisions. Anxiety occurs, in part, when too many demands are put on an injured person. These emotional instabilities are related to damage of the amygdala because the amygdala controls the fear, anger, and emotional center of the brain. Treatments for anxiety are reducing environmental demands and unnecessary stressors, giving the person reassurance, adding in structured activities to their daily life, and offering medications and psychotherapy as options if the natural remedies do not appear helpful.[19,43,74]

Depression is another very common onset after a head injury. The feelings of sadness, frustration, anger, and loss are also common. The feeling of worthlessness, changes in sleep or appetite, difficulty concentrating, seeming withdrawn from people, loss of interest in pleasurable

activities, and lethargy are all symptoms of depression. These feelings are common right after an injury occurs, but if any of these symptoms last for months most likely the person is depressed. Depression occurs when the amygdala is injured either physically or chemically, disrupting the biochemical levels. Biochemical levels may be affected due to damage of the adrenal glands, pituitary gland, or other hormone centers in the brain. Damage to these hormone secreting glands can deplete the amount of hormones being produced, causing levels to be too low. An increased amount of hormone secretion causes an excess amount of hormones in the body. Having too little or too much hormone secretions drives the body out of a state of equilibrium, leading to potential medical issues. Treatments for depression are manifold, setting a daily routine, eating healthy, and exercising regularly can help reduce symptoms. Medications and psychotherapy are also available and proven to help.[19,43,74]

Another symptom related to damage of the amygdala is temper regulation problems and irritability. Frustration due to life changes is common after an injury also. The feeling of depression, tiring easily, pain, and difficulty concentrating can all lead a person to feel angry. After a head injury, it is common for a person to have a short fuse due to damage of the limbic system, causing disruption of emotional regulation. After a TBI it is common to have less emotional stability during the healing process. Up to 71% of people dealing with a TBI report feeling irritable. Expression through yelling, explicit language, throwing, slamming, threatening, or harming people is common. Treatment for anger problems include decreasing stress and irritation by removing triggers, anger management skills, and medications. Family can be of help by understanding that a person's behavior is most likely related to their injury, and learning what they can do to help is essential. Learning how to communicate well, using effective calming

techniques, and giving the person space are all helpful tools when dealing with an upset, injured person.[19,43,74]

HIPPOCAMPUS/SEPTAL AREA

Neurological injury to the hippocampus can result from primary or secondary injury. Primary injury occurs from mechanical forces, like shearing and compressing, at the time of impact. Secondary injury occurs as a subsequent cascade of pathological events that occurs minutes to days after injury. Such events include hypoxia/ischemia, edema, increased intracranial pressure, excitotoxicity release through glutamate release, inflammation, and cell death. Excitotoxicity release is neuronal cell death from the release of the excitatory amino acid called l-glutamate. When too much glutamate is activated it can cause neurons to die, which is known as excitotoxicity release through glutamate release. Knowing what kind of secondary injury occurred is important for therapeutic considerations that can be altered with the goal of preventing injury or protecting brain tissue that may be able to heal itself. Certain biomarkers are important for diagnosing an MTBI early on. These biomarkers are glutamate, glucose, and lactate. Glutamate decreases in the acute phase after sustaining an injury to the temporal cortex and neocortex.[13,55,77]

There is increasing evidence that cognitive and memory dysfunction are related to physiological changes in the hippocampus that impact the phenotype of recovery. GABA receptor subunits change, reducing the inhibitory postsynaptic currents, and increasing the excitatory currents. GABA receptors are connected to K+ channels, and when these channels become activated GABA receptors decrease the amount of Ca2+ that is being produced by inhibiting the production of cAMP (used in intracellular signal transduction, derivative of ATP.)

Irregular levels of GABA may lead to impairment in the hippocampal synaptic transmission, and cause long term cognitive impairment. The regulation of gene transcription affects the proteins involved in neurotransmission and the synthesis of neurons. TBI is connected to hippocampal neuronal damage and death, making it very important to create therapeutic ways to protect the young neurons, and enhance neurogenesis.[13,55,77]

Neurogenesis is driven by forced overexpression of IGF 1 and transplantation of synthetic human progenitor cells that rush to the hippocampus after TBI. IGF-1 stands for insulin-like growth factor that is a hormone that helps bones and tissues have normal growth and development. The liver and skeletal muscles produce IGF-1 when growth hormone is sensed. Progenitor cells are similar to stem cells in that they can be used as different cells depending on where they are needed. They are very specific and become a target cell. The severity of TBI determines the degree of post traumatic neurogenesis in the hippocampus. Mild traumatic brain injury has no effect on neurogenesis, moderate TBI has neural stem cell proliferation, but does not increase neurogenesis, and severe TBI increases neurogenesis. In severe TBI, neurogenesis in the dentate gyrus may be induced.[13,55,77]

There are electrical changes which may occur after a TBI. These electrical changes affect the neural activity playing a role in the consequences of TBI. Electrophysiologic structures show changes occuring in the hippocampal circuit after a TBI. Moderate to severe TBI's are associated with neuronal cell loss in the hippocampal regions, as well as changes to cell homeostasis. Mild traumatic brain injuries only have slight changes in the firing patterns. Any disruption in the firing patterns of the brain leads to cognitive exhaustion.[13,55,77]

Many people experience memory loss after a head injury. This is due in part to damage of the hippocampus. The hippocampus and mesial temporal structures are the most vulnerable to head injury. When the mesial temporal lobe is damaged seizures may occur. The structures within this lobe include the hippocampus and amygdala, so emotional dysfunction may also occur when the mesial temporal lobe is damaged. The hippocampus is critical in the formation of declarative memories. In Vivo MRI it can be seen that moderate to severe TBI patients have a high volume of atrophied hippocampi. The atrophy is what causes long term memory problems.[13,55,77]

In addition to memory problems, there can be second effects on concentration and attention. Hippocampal learning deficits can last weeks to months depending on the severity of the injury. Atrophied hippocampi causes cells and synapses to be lost. This is generally progressive, however some synapses may recover. Atrophy is usually bilateral and even involves the fornix, which results in deefferanation. Certain parts of the hippocampus are more vulnerable to damage. These parts are the dentate hilar neurons, CA3 pyramidal cells, and new neurons in the inner layer of the dentate.[13,55,77]

EFFECTS OF TBI ON LIFE

PHYSICAL

Following a TBI there are many physical effects that play a negative role in the daily life of an individual. Individuals report frequent headaches lasting up to a few months post injury. Some people experience vertigo which is characterized by dizziness due to injury of the cerebellum. In more severe cases, people may begin developing seizures in the early stages of recovery or even years later. Recurrent seizures are known as post traumatic epilepsy. There may

be a buildup of cerebrospinal fluid in cerebral ventricles increasing pressure and swelling in the cranium. Penetrating wounds are susceptible to infection when the skull is fractured because bacteria can enter the brain. If not treated properly, infection can spread to the rest of the nervous system. Blood vessels are susceptible to damage as well, which can lead to blood clots or strokes.[109]

Damage to cranial nerves can cause long lasting physical effects. Depending on which nerve is damaged, paralysis of the facial muscles can occur as well as a loss of facial sensations. If the olfactory nerve is damaged, sense of smell can be affected. Taste is also commonly inhibited if the glossopharyngeal or vagus nerve is damaged. Loss of vision or double vision occurs when the optic nerve is injured. People may also have difficulty swallowing after experiencing a TBI. Dizziness is affected when the cerebellum is injured and hearing loss can be affected by a TBI when there is damage to the temporal lobe.[109]

COGNITIVE

In the time following a TBI, the patient's thinking skills may be compromised. Most often it becomes more difficult to focus and takes longer to process thoughts. Memory, learning ability, reasoning, judgement, attention, and concentration may become more difficult or inhibited, depending on the severity of the TBI because of damage to the limbic system. Short term and working memory tend to be the most affected portion of memory. It can become difficult to recognize faces and remember names, comprehension is harder , and learning new things is slower. Executive function may also become difficult, specifically problem solving, multitasking, organization, planning, decision making, and starting or competing tasks.[109-111]

Communication becomes more difficult which leads to increased frustration, conflict, and misunderstanding. Understanding speech and writing is a challenge as well. Difficulty speaking and writing is also common. The inability to organize thoughts and ideas as well as follow along in a conversation and participate can be challenging. Taking turns and topic selection becomes more difficult. Some people find it difficult to understand nonverbal communication and reading body language. People may experience language loss such as receptive or expressive. Receptive language loss makes it difficult to make sense, whereas expressive aphasia affects the ability to find words. Damage to Broca's area, located in the frontal lobe, causes speech dysfunction. Other portions of the frontal lobe control organization and writing. Any damage to the frontal lobe will cause these issues.[109-111]

BEHAVIORAL

Many people struggle with behavior after sustaining a TBI. They may have a hard time with self control, impulsiveness, and verbal or physical outbursts. Some underestimate or overestimate their abilities, getting them into trouble. Some have difficulty in social situations. There is a high percentage of people who have outbursts and aggression after a TBI. This affects not only them, but their relationships too.[109-111]

EMOTIONAL

The most common issues that individuals with head injury report are depression and anxiety. These are extremely normal after sustaining a head injury. When an individual sustains a TBI it can be life changing due to the headaches, memory loss, confusion, disorientation, emotional dysregulation, and more , making it easy to become depressed. Many individuals with head injuries experience mood swings, irritability, lack of empathy, anger, and even insomnia

due to damage to the limbic system. Some people have a hard time falling asleep for hours and others sleep for hours on end. Both are normal, but take a toll on the person. Sleeping hours on end also makes it very easy to become depressed.[109-111]

SENSORY

When a patient experiences a head injury they most often report signs and symptoms that are sensory related. These symptoms include: tinnitus, known as ringing in the ears, whereas others have damage to vision nerves, causing different vision impairments. Tinnitus following a head injury is caused by damage to CN VIII. Damage to CN I, III, IV, and VI, will cause different impairments depending on the nerve damaged. See Table 3 for more information. Other signs and symptoms that patients report due to damage of CN I are difficulty recognizing objects, impaired hand eye coordination, and blind spots or double vision. Making sense of pictures and shapes, drawing, and recognizing objects, such as faces may be difficult. Issues with taste and smell are possible if the olfactory and glossopharyngeal or vagus nerves are damaged. Many people have lingering symptoms of impaired balance and dizziness. This is very common, lasting for weeks or even months.[109-111]

TREATMENTS

There are many treatments that are used following a head injury to manage the patients signs and symptoms but also to return them to baseline in a timely fashion. This review of literature will focus on the following treatments: medications, surgery, homeopathy and physical therapy. This section will also provide an in depth explanation of the mechanisms by which these treatments work. The majority of treatments following head injury typically are relatively passive

in an attempt to give the brain time to rest making the main sources of relief for head injury over the counter pain medication, rest, and at home monitoring.

MEDICATIONS

Medications are commonly used following a head injury to help monitor seizures, emotional dysregulation, and pain to list a few. Medications can be helpful for limiting secondary damage to the brain. Diuretics are commonly prescribed because they decrease the amount of fluid in tissues and increase the urine output. If a diuretic is given intravenously, it can help reduce the pressure in the brain. Another common medication used is an anti seizure drug. Anti seizure medications may be given to avoid any brain damage that causes seizures. Anti seizure medications will only be continued if seizures continue to occur. In severe cases coma inducing medications may be given. Doctors induce comas in patients when their brain is not receiving enough oxygen. When the body is asleep, the brain does not use as much oxygen as when a person is awake. Coma inducing medications are useful when blood vessels have become compressed from an increase in pressure in the brain, limiting the supply of nutrients and oxygen to the brain cells. Antidepressants are given to help regulate the secretion of serotonin. Many people become depressed after a brain injury because the injury damages the limbic system, and PTSD is common, which causes depression as well. Pain medication may also be given to help with headaches, or other areas of the body that may be affected as well. Pain medication ranges from ibuprofen and tylenol to opiates depending on the severity of the pain.[109-111]

SURGERY

Following traumatic brain injury surgery may be necessary to relieve pressure on the brain if in fact internal bleeding occurs. Two main types of brain bleeds can occur following the injury:

an epidural or subdural hematoma. An Epidural hematoma occurs when blood accumulates in the space between the skull and the dura mater. Epidural bleeds occur when a skull fracture or blow to the skull causes an arterial bleed. These injuries are medical emergencies and typically require a craniotomy to relieve pressure. On the other hand, a subdural hematoma occurs when blood accumulates between the brain's surface and the dura mater. Subdural bleeds most often are as a result of stretching and tearing of veins on the surface of the brain. This most often happens when the head is unexpectedly jolted or shaken, which often happens in a mild and traumatic brain injury. Some brain bleeds will heal on their own, but some need to be cauterized, in which case a neurosurgeon must go in and reattach the vessels.[44]

HOMEOPATHY

Homeopathy is a type of treatment that uses natural remedies to heal. Headaches are of the most commonly reported symptoms following a head injury. There are several homeopathic treatments that have been proposed to relieve headaches following a head injury and they include: lavender oil, basil oil, feverfew, and flaxseed. Lavender oil works in reducing anxiety, depression, and insomnia related to head injury. Basil oil is similar to lavender oil, however it also reduces fatigue levels. Feverfew acts as an anti-inflammatory, aiding in the reduction of swelling in the brain post injury. Flaxseed aids in reducing blood pressure and are high in Omega 3 fatty acids. Omega 3's help begin myelination of the neurons that were damaged. It has also been reported that homeopathic agents also help with attention problems that result from head injuries as well. A few agents that are used frequently to assist patients who have attention deficits following head injury are stramonium, cina, and hyoscyamus. Homeopathic remedies

work through the idea of "like cures like." When these herbs are strongly diluted they bring on a small amount of similar symptoms and that eases the issue, in this case the ADD/ADHD.[61]

Another commonly reported symptom following a head injury are memory deficits. Ambra grimes, anacardium orientale, hellebores niger, lycopodium coloratum, nux moschata, phosphoricium acidum, and sulphur have all been reported to improve memory in patients following a head injury. Additionally, chamomile has been used to help with sleep and to reduce pain, while St. Ignatius Bean has been used to treat anxiety, depression, and seizures, in those who suffer from head injury. Ignatius bean has the poisons strychnine and brucine. When these poisons reach the brain and muscle nerve impulses, it calms down the symptoms of depression as well as muscle spasms and seizures. Chamomile works in a similar way in that the chemicals it contains aid in the reduction of pain and ability to sleep.[61]

Other homeopathic remedies are acupressure and acupuncture. Acupressure affects the flow of Qi and relieves imbalances that are slowing the flow of Qi by removing the blockage of Qi and allowing it to flow throughout the whole body. This will slowly restore the neural pathways that have been damaged. Acupressure releases neuropeptides that activate the opioid system in the brain, and helps modulate the autonomic nervous system aiding in the decrease in respirations, heart rate, and blood pressure.[61]

Acupuncture includes the penetration of pressure points by thin solid needles. This practice is known to reduce pain, stress, swelling, mental fog, and improve memory to name a few. Many people find relief through this form of homeopathic medicine.[61]

PHYSICAL THERAPY

Ten to thirty percent of individuals with a head injury do not fully recover within seven to ten days. Therefore, it becomes important to identify treatments that have been successful in improving systems and decreasing the number of days a patient suffers from systems post injury. One such treatment is general physical therapy (PT). Active rehabilitation promotes neuroplasticity in the brain, contributing to symptom resolution. Gradual exercise training, through physical therapy, can be beneficial for brain adaptation. Physical therapy works well for headaches, dizziness, and balance issues because PT establishes goals and treatment to address the issues and functional limitations that exist following a head injury.[107]

CHIROPRACTIC

Chiropractic treatment is commonly used with patients who have suffered from a musculoskeletal injury, as it relates to patients suffering from head injury, these patients typically receive treatment from a neurologic chiropractor. Chiropractic neurologists are relatively new in healthcare and are medical professionals who have received an additional certification in functional neurology training. Functional neurology doesn't just focus on manual manipulation but also encompasses treatment that involves stimulating the vestibularchoclear and proprioceptive systems. Unlike a traditional chiropractic treatment which mainly focuses on relieving headaches, nerve pain, spinal pressure and mobility, functional neurology treatment includes: balance and eye tracking exercises to stimulate the somatic, vestibular and ocular systems. Chiropractic neurologists may use specific vision exercises to strengthen the vision centers in the occipital lobe. The same can be done for memory and mood. They may give a patient memory exercises to help improve their memory. Mood will improve as treatments

progress, mainly through adjustments and release of pressure in the brain. Cold laser is another treatment that is used by chiropractors that helps reduce inflammation in any muscle or joint. This is very helpful for reducing the inflammation from whiplash, which may be causing some of the headaches. Tight muscles in the neck increases the pressure of headaches.[39,121]

COGNITIVE BEHAVIORAL THERAPY

Cognitive behavioral therapy is a short term and goal oriented treatment that helps teach problem solving of behavior and ways of thinking. Cognitive behavioral therapy helps people achieve their goals or change their way of acting, feeling, or thinking. It focuses on the current issue a person is having and provides a solution in helping people have more control over their life. Cognitive behavioral therapy is a good treatment for people who have post traumatic stress from the incident. Prolonged exposure, cognitive processing, and EMDR are the most common methods of helping with PTSD. In this therapy patients will discuss their traumas and behavioral difficulties with a professional and learn ways of coping, in healthy ways, with any behavioral issues, ADD/ADHD, depression, anxiety, PTSD, eating disorders, and more.[120]

Eye Movement Desensitization and Reprocessing (EMDR) is a form of psychotherapy that has been used following a head injury to help reduce PTSD and emotional distress, which lead to disruptions of activities of daily living. EMDR focuses on the physical trauma of the head injury but also addresses the emotional component which is present in the majority of patients following the initial head injury. It has been reported that patients who undergo EMDR therapy tend to have quicker resolution of symptoms when compared to those patients who go through CBT.[120]

SPEECH PATHOLOGY

After a head injury individuals may continue to have trouble producing speech because of damage to Broca's area. Speech language pathology therapy focuses on communication between the muscles of the face, throat, and mouth. There are many specific kinds of speech therapy which include: Therapies of Dysarthria, Therapies of Apraxia, Memory Therapy, Social Language Functions, and Cognitive Communication Skills. Each therapy will be discussed below.[107]

THERAPIES OF DYSARTHRIA

Therapies of Dysarthria are used when injury to the brain leads to damage of CN V, VII, VIII, VIIII, X, XII which are responsible for controlling speech, phonation, resonance, and swallowing. Following a head injury some patients suffer from speech impairments which may present as speech that is often slower, softer in pitch, or muffled. Therapies that are used include exercises that help coordinate lip and tongue movements. Common exercises are saying phrases 20 times through, and having to slowly practice saying the words and enunciating clearly to regain muscle strength in the facial region.[88,107]

THERAPIES OF APRAXIA

Following a head injury patients continue to have difficulty producing sounds and syllables due to damage of Broca's area.[99] Apraxia is the inability to conduct movements when asked to. The person may understand what is being asked, but they cannot produce the movement. Therapies of Apraxia are used when the patient is having difficulty with sounds and syllables. They may have issues with sequencing words or forming words. The main goals of apraxia therapy is to slow the rate of speech and to help the patient pronounce words properly. This is

most often done in therapy with the use of memory aids. Memory aids include using a memory log, calendar, documented schedules, and logs of important addresses.[99]

SOCIAL LANGUAGE THERAPIES

Following a head injury patients continue to have issues understanding nonverbal cues and facial expression due to damage in any of the following areas: temporal lobe, orbitofrontal lobe, insula, and amygdala. Social language therapy is used to help the patient relearn how to interpret nonverbal signals such as body language and facial expressions. It is possible for the patient to return to having normal conversations. Therapists may have the patient work in small groups to help build social language functions.[107]

Improving cognitive communication skills helps increase cognitive processing that may have been damaged after an injury. Speech therapists help with any sequencing of sentences to help the patient regain their speech processing and verbalizing. They do this by using internal memory strategies or spaced retrieval training used to regain memory function.[107]

CONCLUSION

Brain injuries have a major effect on individuals' lives. From memory loss, depression, seizures, and speech dysfunction, there are a range of symptoms and severity of injury that may occur. Any portion of the brain is susceptible to damage, however some regions are more at risk than others. The limbic system is one of the most vulnerable regions because the structures within the limbic system are interconnected. The interconnection of structures means if one is damaged it will have an affect on many of the other structures connected to it. The limbic system is located deep in the midbrain, but between the number of small structures, and the interconnections of these structures, makes this system high risk of significant damage. The

limbic system contains the hypothalamus, thalamus, amygdala, hippocampus, and septal region.[30,74-75]

The hypothalamus is the body's regulatory system. It controls heart rate, breathing, hunger and thirst signals. The hypothalamus is also where the pituitary gland is located. The pituitary gland secretes hormones important for reproductive regulation. In women it secretes estrogen and in males it secretes testosterone. When this structure is damaged hormone secretion may increase or decrease causing women's menstrual cycle to become irregular, and in men, cause erectile dysfunction. Other hormone levels may be affected from injury as well. The most commonly affected hormones are adrenocorticotropin (ACTH), aldosterone (ADH), follicle stimulating hormone (FSH), growth hormone (GH), prolactin, and thyroid stimulating hormone (TSH). Insufficient levels of these hormones can lead to diabetes insipidus, hypernatremia, hypothyroidism, hyperthyroidism, hypogonadism, growth hormone imbalances, and hyperprolactemia. (More information can be seen in the section Injuries Affecting the Limbic System)[16,67]

The thalamus is important in regulating sleep-wake cycle, episodic memory, and learning. When the thalamus is damaged, individuals may develop hypersomnia or insomnia. Patient's may also have trouble with long term memory, and struggle to learn new things. This can affect work, school, and daily life. Most commonly, when grey matter is decreased these symptoms will occur. Grey matter contains most of the neuronal cell bodies in the brain, and when injured the brain loses the neurons. Decreased grey matter may also lead to fatigue because the body needs energy to regenerate the lost neuronal cell bodies.[102,108]

The amygdala is the emotional regulation center of the brain. It sends and receives signals of fear, and aids in the feelings of motivation and drive. It also has some role in cognitive processing such as decision making, attention, memory, and appetitive memory. When this structure is damaged, individuals affected may have difficulty controlling their anger, they may feel more fearful or paranoid, depression and anxiety may onset if the individual is not already affected. Impulsiveness is also a common issue when an individual has sustained injury to the amygdala. Impulsiveness is generally associated with the frontal lobe, but the frontal lobe and amygdala are interconnected. This can cause dysfunction to both structures if one is damaged.[19,74]

The hippocampus has two lobes one on either side of the temporal lobe, located in the right and left hemisphere. The hippocampus is important in linking memories to smells. It also contains the Paper Circuit which controls learning, memory, emotion, and social behavior. If this structure is damaged amnesia may occur, especially affecting the remembrance of names, dates, and events. The hippocampus has direct connections to amygdala, allowing the Paper circuit and the amygdala to work as emotional regulation centers of the brain. Damage to the hippocampus affects neurogenesis, the production of neural cells.[75,114]

The septal region receives afferent connections from other areas of the limbic system, such as the hypothalamus, thalamus, and hippocampus. The connection between the septal region and the hippocampus leads to the role of learning and memory. The septal region also aids in social behavior and fear expression. It is also important in reward systems because this structure will stimulate the release of dopamine when a reward is sensed. It is important to have an

understanding of the anatomy and physiology of the limbic system in order to determine which treatments and therapies will be used to heal the damaged brain.[30,74,75]

There are many different types of brain injuries ranging from diseases such as meningitis and encephalitis to a severe concussion and bleeding in the brain. Given the range of injuries, there are also a variety of treatments. Medications may be given for pain, viruses, inflammation, and seizures to name a few. Surgery may be necessary if an individual sustained a skull fracture, had a stroke or a brain bleed that needs to be contained. Some injuries occur from a penetrable object in the skull. This requires surgical removal and repair of the skull. Some patients may not want to take medicine, so they may use homeopathic remedies. These include diluted oils and herbs that produce similar symptoms, but antagonize the symptoms the individual is experiencing.[4,32,41,42,44,61]

Therapies are another common type of treatment used. Physical therapy, speech therapy, chiropractic, and cognitive behavioral therapy are the most common.[60,107,120,121]

Physical Therapy is active rehabilitation that promotes neuroplasticity in the brain, contributing to symptom resolution. Gradual exercise training, through physical therapy, can be beneficial for brain adaptation. Physical therapy uses physical exercises to regain muscle strength, balance, and coordination. After a brain injury individuals may lose their ability to walk well because of damage to the cerebellum, coordination is regularly impaired, and muscle weakness is common as well.[107]

Speech therapy is commonly used to help individuals learn to use their facial muscles again, enunciate words clearly, and slow speech down. When damage to Broca's area, located in the frontal lobe, occurs speech becomes impaired. Different types of speech therapies are used

depending on the damage incurred. Therapies of Apraxia deal with difficulty producing sounds and syllables. Therapies of Dysarthria helps with individuals struggling to produce sounds other than muffled, soft pitch ones.[88,99,107]

Chiropractic therapy is used to realign the spine, releasing pressure that leads to headaches. Chiropractors use different techniques that can aid in the recovery of vision problems, such as using their finger and the individual must follow it. That strengthens the vision center in the occipital lobe.[39,121]

Cognitive behavioral therapy (CBT) is used when individuals have emotional struggles that they need help working through. This therapy is common for individuals struggling with anxiety, depression, anger, impulsiveness, and post traumatic stress disorder to list a few. These symptoms are common after a TBI has been sustained. In CBT the therapist teaches the patient how to problem solve, and cope with the issues they are dealing with.

Sustaining a head injury can be a lifelong injury. Many of the effects can be treated and improved, but many individuals continue to struggle physically, emotionally, cognitively, and behaviorally long term. It has been reported that many following a head injury, patients experience lasting depression, anxiety, and PTSD. Some even go on to suffer from permanent damage which could present as deficits in speech, balance, hearing, and/or vision. Additionally, cognitive functions such as memory and organization may also be compromised.[31-32,34-35,38-39,41-44,58,60,62,67,77,96,109-111]

A head injury is a traumatic injury with life long consequences. The purpose of this paper was to provide insight into the anatomy and physiology of the limbic system and other surrounding anatomical structures. To discuss the effects of different head injuries on patients

who suffer from them, and to provide a brief discussion on treatment options available to those suffering from a head injury. My hope is that by educating individuals the anatomy and long term consequences of head injury that individuals will take more precautions and will also know what treatments to seek in the event that they are recovering from a head injury.

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