



ROLE OF ASTROCYTES IN NEUROPHARMACOLOGY

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ABSTRACT

Astrocytes are a heterogeneous class of neuroectodermally derived glial cells that arise from the neural crest and are present in the central nervous systems of all vertebrates. Although the subtypes of astrocytes described above, namely fibrous, protoplasmic and Layer-1 astrocytes, are widely found in mammalian brains, there are at least two specific subtypes for human or other primates. Astrocytes (from Ancient Greek *ἄστρον*, *ástron*, "star" and *κύτος*, *kútos*, "cavity", "cell"), also known collectively as astroglia, are characteristic star-shaped glial cells in the brain and spinal cord. Astrocytes regulate metabolic homeostasis through synthesizing glycogen and supplying neurons with energy substrates. Astrocytes define the cytoarchitecture of the grey matter by tiling the latter and by forming contacts with the vasculature by vascular end feet and by glial sheets at all surfaces of the brain. Astrocytes contribute to the maintenance of the health and function of the central nervous system (CNS). Thus, it is not surprising that these multifunctional cells have been implicated in the onset and progression of several neurodegenerative diseases. Astrocytes actively respond to neurotransmitters through changes in calcium ion levels. Astrocytes react to glutamate, GABA, acetylcholine, ATP, and endocannabinoids by releasing glutamate, GABA, D-serine, and ATP to influence activity of neighbouring neurons. As such, astrocytes maintain tight control of local ion and pH homeostasis, deliver glucose and provide metabolic substrates. Astrocytes also clear neuronal waste, including not only metabolic by products but also neurotransmitters released during synaptic transmission, which are sequestered through active uptake.

KEYWORDS: Glial cell, synapse, neurotransmitter, neurohormone, white matter, gray matter, astrocytes, spinal cord.

INTRODUCTION

The correlation between proportional makeup and intelligence suggests that astrocytes, which were first discovered by **Rudolf Virchow** [13 October 1821 – 5

September 1902] and later **Camillo Golgi** [7 July 1843 – 21 January 1926], in the late 1800's, may be more involved in sophisticated neural processes than previously considered.

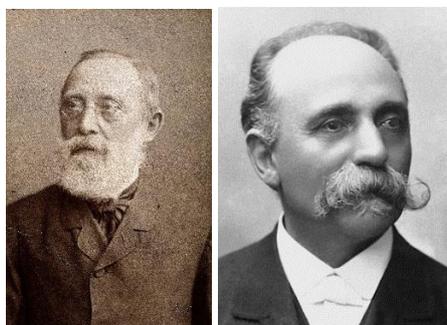


Figure 1: Discovery [Rudolf Virchow & Camillo Golgi].

Astrocytes are a subtype of glial cells that make up the majority of cells in the human central nervous system (CNS). They perform metabolic, structural, homeostatic,

and neuroprotective tasks such as clearing excess neurotransmitters, stabilizing and regulating the blood-brain barrier, and promoting synapse formation. The

functions performed by astrocytes are, among others, to control the sleep process, form the extracellular matrix, serve as a support, build and regulate the blood–brain barrier, maintain the balance of extracellular ions, control the production of neurotransmitters, and modulate the

synapse. In healthy neural tissue, astrocytes play critical roles in many functions, including regulation of blood flow, homeostasis of extracellular fluid, ions and transmitters, energy provision, and regulation of synapse function, and synaptic remodelling.^[1]

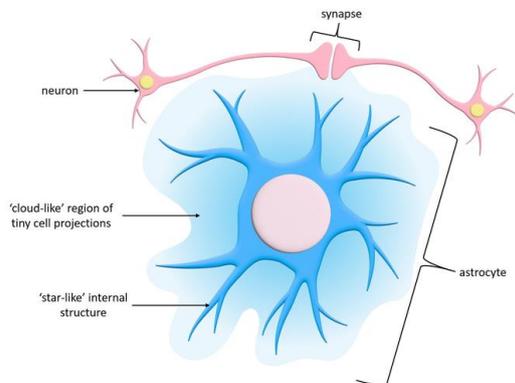


Figure 2: Astrocytes.

Function: Glial cells are an integral part of the human nervous system. The functions of glial cells include helping to support and nourish nerve cells, or neurons. Several types of glial cells exist. Glial cells are the “glue” of the nervous system, engaging in many activities to support typical brain function. They do this by facilitating communication between neurons, regulating inflammation and forming the blood-brain barrier. Each glial cell type has a specific role in supporting the central and peripheral nervous systems.

Therefore, dysfunction in glial cells can play a role in developing certain neurological conditions. The function of glial cells found in the CNS. The central nervous system (CNS) consists of the brain and spinal cord, the body’s main control center. Glial cells are of utmost importance in this region, as they regulate vital functions, such as metabolism, ion balance — or pH balance — and neurotransmission. Neurotransmission refers to how neurons communicate either between themselves or with muscle fibers.^[2]

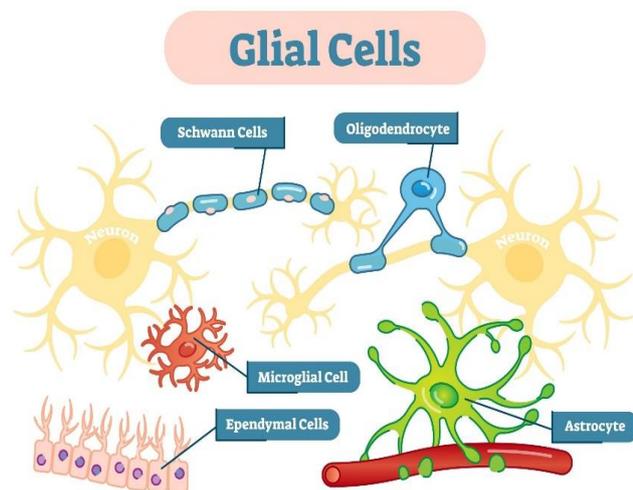
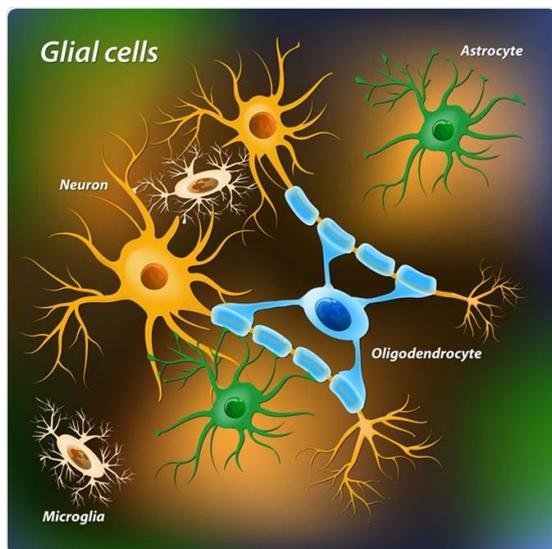


Figure 3: Glial cells.

Astrocytes: The astrocyte is the most abundant Trusted Source type of glial cell in the CNS. They have numerous projections that form a star shape, hence their name.

Although astrocytes exist in different places, they perform similar roles, including.

1. Regulating neurotransmitters, which are chemical messengers responsible for cell-to-cell communication.

2. Forming the blood-brain barrier, a crucial layer of protection for the brain.

3. Cleaning up the remains of dead neurons and excess potassium ions.

4. Controlling blood flow to the brain and ensuring that active regions get enough blood.

5. Synchronizing axon activity so that nerves can communicate properly.

6. Regulating brain metabolism by storing blood sugar, or glucose, to fuel neurons.

Dysfunction of astrocytes has links to some neurological conditions, such as Alzheimer's disease.^[3]



Figure 4: Oligodendrocytes.

Oligodendrocytes: These cells create a fatty material that wraps around a portion of the nerve cell — called the axon — to insulate them and enable faster electrical conduction. Faster electrical conduction means impulses, or messages, can travel more efficiently along the neurons. Oligodendrocytes are essential for proper nerve conduction. They play an important role in certain neurological diseases, such as multiple sclerosis.

Microglia: Microglia is small, star-shaped cells that help protect the CNS. They are the brain's resident immune cells and serve as the first line of defence against invading pathogens or disease-causing agents. Constantly patrolling, these immune cells search for atypical or damaged cells. When the microglia encounter something atypical, they engulf and destroy it with toxic chemicals. Additionally, microglia helps clear out dead cells and debris from the CNS. This process is known as phagocytosis.



Figure 5: Microglia.

Ependymal cells: Ependymal cells develop in the ventricles and fluid-filled compartments of the CNS. They provide the lining for these fluid-filled spaces and help form and transport cerebrospinal fluid (CSF). The CSF carries chemical messengers, hormones, nutrients, and waste from the brain to the spinal cord and vice versa.

signals to and from the CNS. Glial cells play an important role in maintaining the health of peripheral nerves and ensuring proper communication between them and the CNS.

The function of glial cells in the PNS: The peripheral nervous system (PNS) consists of the nerves outside the brain and spinal cord. It is responsible for carrying

Two main types of glial cells develop in this region: Schwann cells and satellite cells.^[4]

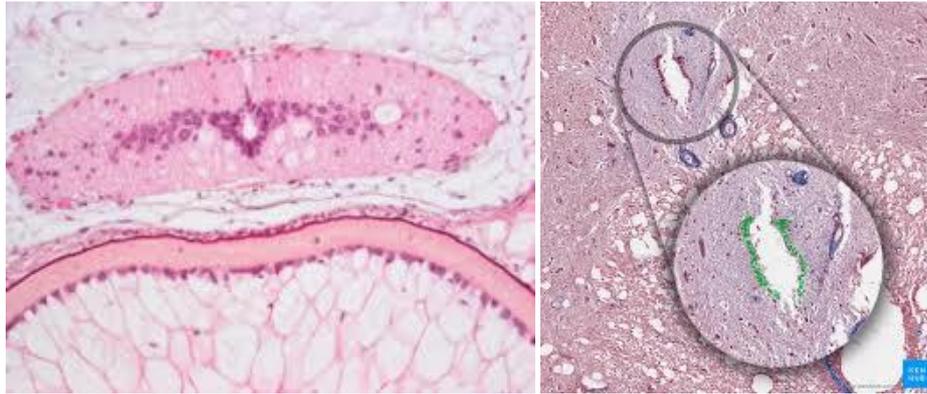


Figure 6: Ependymal cell.

Schwann cells: Schwann cells are a type of satellite cell that function similarly to oligodendrocytes in the CNS. They create a myelin sheath around nerves, which helps insulate them for faster conduction. Additionally, these

cells help repair damaged axons and can even regenerate them. Stimulating the regeneration of new axons may require the release of growth factors.

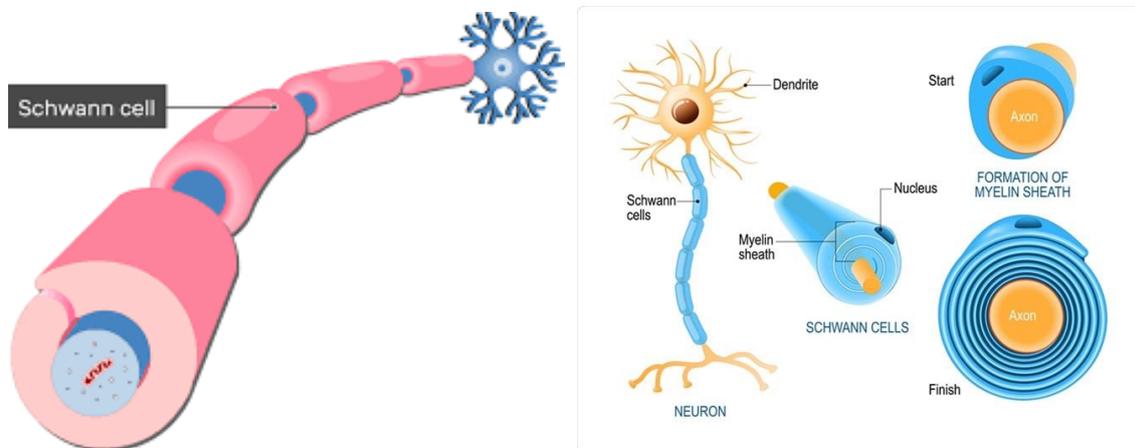


Figure 7: Schwann cell.

Satellite cells: Satellite cells help maintains the health and activity of neurons in the PNS. They provide support and nutrition to peripheral nerves and regulate their calcium levels. These factors are important for proper nerve conduction.

In addition, satellite cells release neurotrophic factors that help protect neurons from degeneration or death. They are essential for developing, maintaining, and repairing peripheral nerves.^[5]

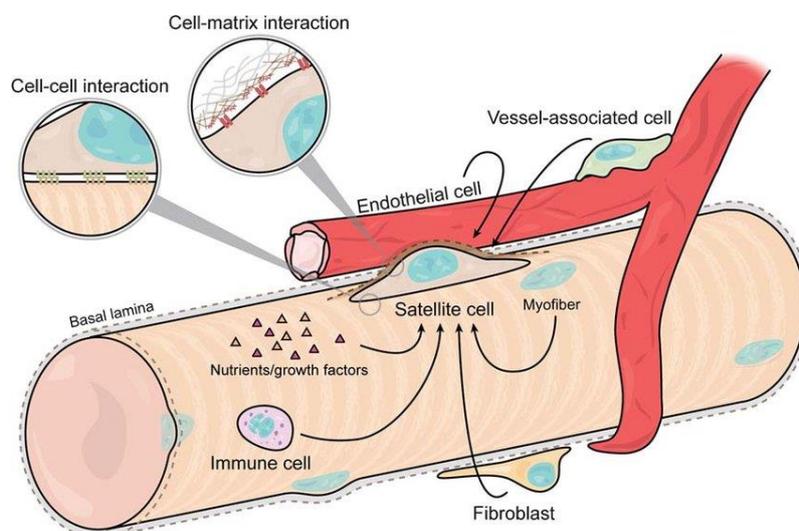


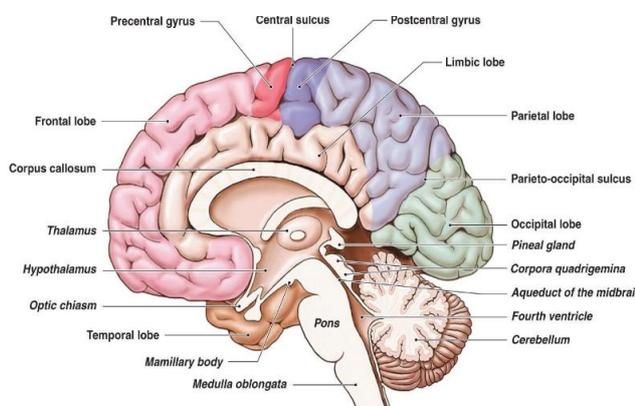
Figure 8: Satellite cells.

Glial cells help support, connect, and protect the neurons of the central and peripheral nervous systems. They come in many shapes, sizes, and types, each performing specialized functions. In the CNS, glial cells regulate neurotransmission and help form the blood-brain barrier. They also clean up dead neurons, synchronize nerve impulses, and regulate brain metabolism. In the PNS, Schwann cells create a myelin sheath for faster conduction. Additionally, satellite cells provide nutritional support for neurons. The central nervous system consists of the brain and spinal cord. The central nervous system controls thought, movement, and emotion, as well as breathing, heart rate, hormones, and body temperature. The central nervous system (CNS) is referred to as “central” because it combines information from the entire body and coordinates activity across the whole organism. This article briefly overviews the CNS. It looks at the types of cells involved, different regions within the brain, spinal circuitry, and how the CNS can be affected by disease and injury.^[6]

The CNS consists of the brain and spinal cord. The brain is the most complex organ in the body and uses 20% of the total oxygen we breathe. The brain consists of an estimated 100 billion neurons connected to thousands more. The brain can be divided into four main lobes: temporal, parietal, occipital, and frontal. What is the central nervous system?

The CNS consists of the brain and spinal cord.

The brain is protected by the skull (the cranial cavity) and the spinal cord travels from the back of the brain, down the center of the spine, stopping in the lumbar region of the lower back. The brain and spinal cord are housed within a protective triple-layered membrane called the meninges. The central nervous system has been thoroughly studied by anatomists and physiologists, but it still holds many secrets; it controls our thoughts, movements, emotions, and desires. It also controls our breathing, heart rate, the release of some hormones, body



temperature, and much more. The retina, optic nerve, olfactory nerves, and olfactory epithelium are sometimes considered to be part of the CNS alongside the brain and spinal cord. This is because they connect directly with brain tissue without intermediate nerve fibers.

The brain: The brain is the most complex organ in the human body; the cerebral cortex (the outermost part of the brain and the largest part by volume) contains estimated 15–33 billion neurons, each of which is connected to thousands of other neurons. In total, around 100 billion neurons and 1,000 billion glial (support) cells make up the human brain. Our brain uses around 20% of our body’s total energy. The brain is the central control module of the body and coordinates activity. From physical motion to the secretion of hormones, the creation of memories, and the sensation of emotion. To carry out these functions, some sections of the brain have dedicated roles. However, many higher functions — reasoning, problem-solving, creativity — involve different areas working together in networks.^[7] The brain is roughly split into four lobes.

Temporal lobe (green): important for processing sensory input and assigning it emotional meaning. It is also involved in laying down long-term memories. Some aspects of language perception are also housed here.

Occipital lobe (purple): visual processing region of the brain, housing the visual cortex.

Parietal lobe (yellow): the parietal lobe integrates sensory information including touch, spatial awareness, and navigation. Touch stimulation from the skin is ultimately sent to the parietal lobe. It also plays a part in language processing.

Frontal lobe (pink): positioned at the front of the brain, the frontal lobe contains the majority of dopamine-sensitive neurons and is involved in attention, reward, short-term memory, motivation, and planning.

The Major Portions of the Brain Include the Cerebrum, Cerebellum and Brain Stem

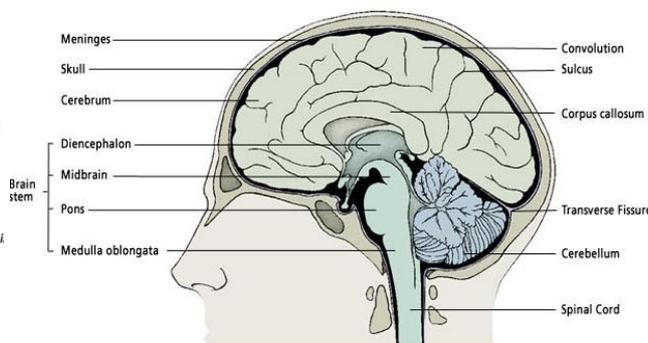


Figure 9: Brain lobes.

BRAIN REGIONS

Basal ganglia: involved in the control of voluntary motor movements, procedural learning, and decisions

about which motor activities to carry out. Diseases that affect this area include Parkinson’s disease and Huntington’s disease.

Cerebellum: mostly involved in precise motor control, but also in language and attention. If the cerebellum is damaged, the primary symptom is disrupted motor control, known as ataxia.

Broca's area: this small area on the left side of the brain (sometimes on the right in left-handed individuals) is important in language processing. When damaged, an individual finds it difficult to speak but can still understand speech. Stuttering is sometimes associated with an underactive Broca's area.

Corpus callosum: a broad band of nerve fibers that join the left and right hemispheres. It is the largest white matter structure in the brain and allows the two hemispheres to communicate. Dyslexic children have smaller corpus callosums; left-handed people, ambidextrous people, and musicians typically have larger ones.

Medulla oblongata: extending below the skull, it is involved in involuntary functions, such as vomiting, breathing, sneezing, and maintaining the correct blood pressure.^[8]

Hypothalamus: sitting just above the brain stem and roughly the size of an almond, the hypothalamus secretes a number of neurohormones and influences body temperature control, thirst, and hunger.

Thalamus: positioned in the centre of the brain, the thalamus receives sensory and motor input and relays it to the rest of the cerebral cortex. It is involved in the regulation of consciousness, sleep, awareness, and alertness.

Amygdala: two almond-shaped nuclei deep within the temporal lobe. They are involved in decision-making, memory, and emotional responses; particularly negative emotions.

Spinal cord: The spinal cord, running almost the full length of the back, carries information between the brain and body, but also carries out other tasks. From the brainstem, where the spinal cord meets the brain, 31 spinal nerves enter the cord. Along its length, it connects

with the nerves of the peripheral nervous system (PNS) that run in from the skin, muscles, and joints. Motor commands from the brain travel from the spine to the muscles and sensory information travels from the sensory tissues — such as the skin — toward the spinal cord and finally up to the brain.

The spinal cord contains circuits that control certain reflexive responses, such as the involuntary movement your arm might make if your finger was to touch a flame. The circuits within the spine can also generate more complex movements such as walking. Even without input from the brain, the spinal nerves can coordinate all of the muscles necessary to walk. For instance, if the brain of a cat is separated from its spine so that its brain has no contact with its body, it will start spontaneously walking when placed on a treadmill. The brain is only required to stop and start the process, or make changes if, for instance, an object appears in your path.^[9]

White and Grey matter: The CNS can be roughly divided into white and gray matter. As a very general rule, the brain consists of an outer cortex of gray matter and an inner area housing tracts of white matter. Both types of tissue contain glial cells, which protect and support neurons. White matter mostly consists of axons (nerve projections) and oligodendrocytes — a type of glial cell — whereas gray matter consists predominantly of neurons. Below are the major causes of disorders that affect the CNS.

Trauma: depending on the site of the injury, symptoms can vary widely from paralysis to mood disorders.

Infections: some micro-organisms and viruses can invade the CNS; these include fungi, such as cryptococcal meningitis; protozoa, including malaria; bacteria, as is the case with Hansen's disease (leprosy), or viruses.

Degeneration: in some cases, the spinal cord or brain can degenerate. One example is Parkinson's disease which involves the gradual degeneration of dopamine-producing cells in the basal ganglia.

Structural defects: the most common examples are birth defects; including anencephaly, where parts of the skull, brain, and scalp are missing at birth.

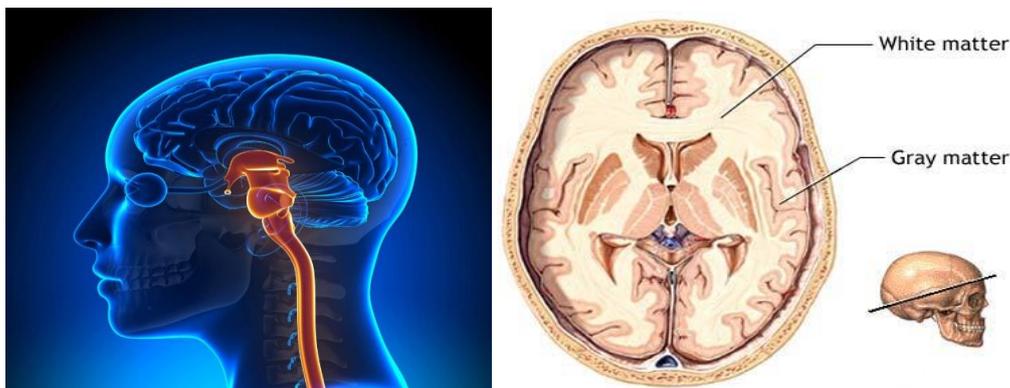


Figure 10: White Matter & Gray Matter.

Tumors: both cancerous and noncancerous tumors can impact parts of the central nervous system. Both types can cause damage and yield an array of symptoms depending on where they develop.^[10]

Autoimmune disorders: in some cases, an individual's immune system can mount an attack on healthy cells. For instance, acute disseminated encephalomyelitis is

characterized by an immune response against the brain and spinal cord, attacking myelin (the nerves' insulation) and, therefore, destroying white matter.

Stroke: a stroke is an interruption of blood supply to the brain; the resulting lack of oxygen causes tissue to die in the affected area.

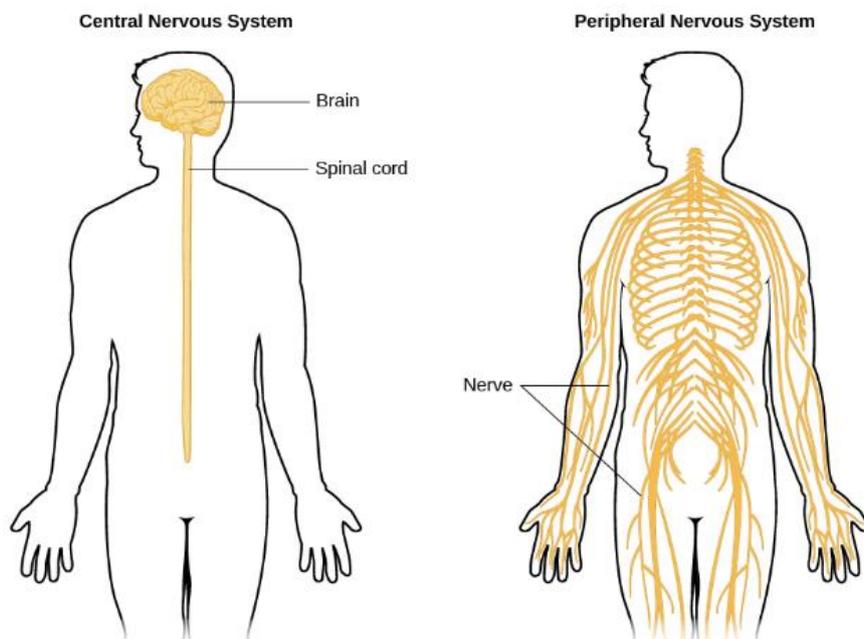


Figure 11: Central Nervous System and Peripheral Nervous System.

Difference between the CNS and peripheral nervous system

The term peripheral nervous system (PNS) refers to any part of the nervous system that lies outside of the brain and spinal cord. The CNS is separate from the peripheral nervous system, although the two systems are interconnected. There are a number of differences between the CNS and PNS; one difference is the size of the cells. The nerve axons of the CNS — the slender projections of nerve cells that carry impulses — are much shorter. PNS nerve axons can be up to 1 meter long (for instance, the nerve that activates the big toe) whereas, within the CNS, they are rarely longer than a few millimetres. Another major difference between the CNS and PNS involves regeneration (regrowth of cells). Much of the PNS has the ability to regenerate; if a nerve in your finger is severed, it can regrow. The CNS, however, does not have this ability. The components of the central nervous system are further split into a myriad of parts. Below, we will describe some of these sections in a little more detail.^[11]

The following diagram illustrates the different ways cranial nerves impact the brain:

I. Olfactory nerve: The olfactory nerve transmits information regarding a person's sense of smell to the brain. When an individual inhales fragrant molecules,

olfactory receptors within the nasal passage send the impulses to the cranial cavity, which then travel to the olfactory bulb. Specialized olfactory neurons and nerve fibers meet with other nerves, which pass into the olfactory tract. The olfactory tract then travels to the frontal lobe and other areas of the brain that have a role in memory and the notation of different smells.

II. Optic nerve: The optic nerve transmits information to the brain regarding a person's vision. When light enters the eye, it hits the retina, which contains rods and cones. These are photoreceptors that signals from light into visual information for the brain. These cones sit within the central retina and have a role in color vision. Conversely, the rods in the peripheral retina are responsible for noncolor vision. The photoreceptors carry signal impulses along nerve cells to form the optic nerve. Most of the fibers of the optic nerve cross into a structure called the optic chiasm. The optic tract then projects to the primary visual cortex in the occipital lobe at the back of the brain. The occipital lobe is where the brain handles visual information.^[12]

III. Oculomotor nerve: The oculomotor nerve helps control muscle movements of the eyes. The oculomotor nerve provides movement to most of the muscles that move the eyeball and upper eyelid, known as extraocular muscles.

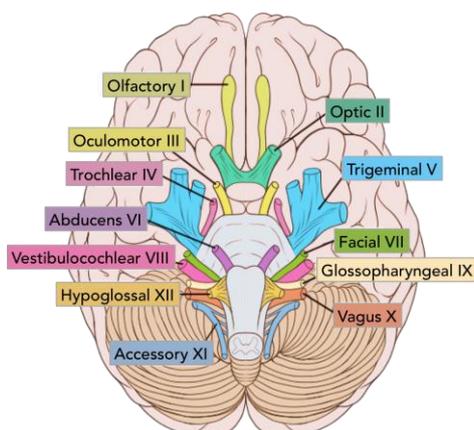


Figure 12: Nerve of brain.

The oculomotor nerve also helps with involuntary functions of the eye. For example, the sphincter pupillae muscle automatically constricts the pupil to allow less light into the eye in bright light conditions. When it is dark, the muscle relaxes to allow more light to enter. Another function is when the ciliary muscles help the lens adjust to short-range and long-range vision. This happens automatically when a person looks at near or far objects.

IV. Trochlear nerve: The trochlear nerve also has a role in eye movement. The trochlear nerve, like the oculomotor nerve, originates in the midbrain. It powers the contralateral superior oblique muscle that allows the eye to point downward and inward.^[13]

V. Trigeminal nerve: The trigeminal nerve is the largest cranial nerve and has both motor and sensory functions. Its motor functions help a person to chew and clench the teeth. It also gives sensation to muscles in the tympanic membrane of the ear. Its sensory division has three parts that connect to sensory receptor sites on the face:

The ophthalmic part gives sensation to parts of the eyes, including the cornea, mucosa in the nose, and skin on the nose, the eyelid, and the forehead.

The maxillary part gives sensation to the middle third of the face, side of the nose, upper teeth, and lower eyelid.

The mandibular part gives sensation to the lower third of the face, the tongue, mucosa in the mouth, and lower teeth.

Trigeminal neuralgia is a common disorder of the trigeminal nerve that can cause intense pain and facial tics.

VI. Abducens nerve: The abducens nerve also helps control eye movements. It helps the lateral rectus muscle, one of the extraocular muscles, turn the gaze outward. The abducens nerve starts in the pons of the brainstem, enters an area called Dorello's canal, travels through the

cavernous sinus, and ends at the lateral rectus muscle within the bony orbit.

VII. Facial nerve: The facial nerve also has both motor and sensory functions. The facial nerve consists of four nuclei that serve different functions:

1. Movement of muscles that produce facial expression
2. Movement of the lacrimal, submaxillary, and submandibular glands
3. The sensation of the external ear
4. The sensation of taste

The four nuclei originate in the pons and medulla and join together to travel to the geniculate ganglion. Bell's palsy is a common disorder of the facial nerve, which causes paralysis on one side of the face and possibly loss of taste sensation.

VIII. Vestibulocochlear nerve: The vestibulocochlear nerve helps with a person's hearing and balance. This nerve contains two components: the vestibular nerve and the cochlear nerve. The vestibular nerve helps the body sense changes in the position of the head with regard to gravity. The body uses this information to maintain balance.

The cochlear nerve helps with hearing. Specialized inner hair cells and the basilar membrane vibrate in response to sounds and determine the frequency and magnitude of the sound. These fibers combine in the pons and exit the skull via the internal acoustic meatus in the temporal bone.^[14]

IX. Glossopharyngeal nerve: The glossopharyngeal nerve possesses both motor and sensory functions. The sensory function receives information from the throat, tonsils, middle ear, and back of the tongue. It also has a role in the sensation of taste on the back of the tongue. The motor division provides movement to the stylopharyngeus, a muscle that allows the throat to shorten and widen. The glossopharyngeal nerve starts in the medulla oblongata in the brain and leaves the skull

through the jugular foramen, which leads to the tympanic nerve.^[15]

X. Vagus nerve: The vagus nerve has a range of functions, providing motor, sensory, and parasympathetic functions. The sensory part provides sensation to the outer part of the ear, throat, heart, and abdominal organs. It also plays a role in taste sensation.

The motor part provides movement to the throat and soft palate.

The parasympathetic function regulates heart rhythm and innervates the smooth muscles in the airway, lungs, and gastrointestinal tract.

Doctors use vagus nerve stimulation therapy to treat various conditions, including epilepsy, depression, and anxiety. Learn more about the vagus nerve and stimulation therapy.

XI. Accessory nerve: The accessory nerve provides motor function to some muscles in the neck. It controls the sternocleidomastoid and trapezius muscles that allow a person to rotate, extend, and flex the neck and shoulders. The accessory nerve separates into spinal and cranial parts. The spinal component starts in the spinal cord and travels into the skull through the foramen magnum. From there, it meets the cranial component of the accessory nerve and exits the skull along the internal carotid artery. The cranial part of the accessory nerve combines with the vagus nerve.

XII. Hypoglossal nerve: The hypoglossal nerve is a motor nerve that supplies the tongue muscles. It originates in the medulla. Disorders of the hypoglossal nerve can cause paralysis of the tongue, most often occurring on one side.

CONCLUSION

Astrocytes are a subtype of glial cells that make up the majority of cells in the human central nervous system (CNS). They perform metabolic, structural, homeostatic, and neuroprotective tasks such as clearing excess neurotransmitters, stabilizing and regulating the blood-brain barrier, and promoting synapse formation. Astrocytes modulate development and function of synaptic and vascular compartments. Dysfunctional astrocytes characterize several mood disorders. Histone modifying enzymes are expressed in astrocytes.

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