Neuroanatomy

1

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1.1 Overview

The nervous system is made up of two parts: the central nervous system (CNS) and the peripheral nervous system (PNS). The brain and spinal cord form the majority of the CNS. The CNS integrates, processes, and coordinates incoming sensory data and outgoing motor functions that alter the activities of the end organs or muscles. The brain is also the part of the body where higher cognitive activities occur, while the cranial and spinal nerves form the majority of the PNS. The PNS delivers sensory information to the CNS and carries motor commands from the CNS to the peripheral tissues and systems. The two systems are in close communication with each other. And when one of the two systems is altered in any fashion, the other one may be affected. This chapter will review the significant anatomical considerations in each of the two systems (Fig. 1.1).

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1.2 Central Nervous System

1.2.1 Brain

The brain can be divided into the supratentorial and the infratentorial compartments. The supratentorial compartment contains the cerebral hemispheres and the diencephalon (thalamus and hypothalamus). The infratentorial compartment is made up of the brain stem and the cerebellum.

1.2.1.1 Supratentorial Compartment

Cerebrum

The cerebrum makes up the largest part of the brain. It is made up of a right and left hemisphere. The hemispheres are made up of numerous sulci or fissures and gyri or folds. The two sides of the brain are connected via the corpus callosum, which is a collection of white matter fibers. Based on functional differences, the cerebrum is divided into four lobes: frontal, parietal, temporal, and occipital lobes. The frontal lobe is separated from the parietal lobe via the central sulcus (Rolandic fissure). The frontal lobe is separated from the temporal lobe via the lateral sulcus (Sylvian fissure). The frontal and parietal lobes are separated from the temporal lobe via the lateral sulcus. And finally, the parieto-occipital sulcus divides the parietal lobe from the occipital lobe.

The cerebrum is made up of numerous functional areas that each provide a particular activity

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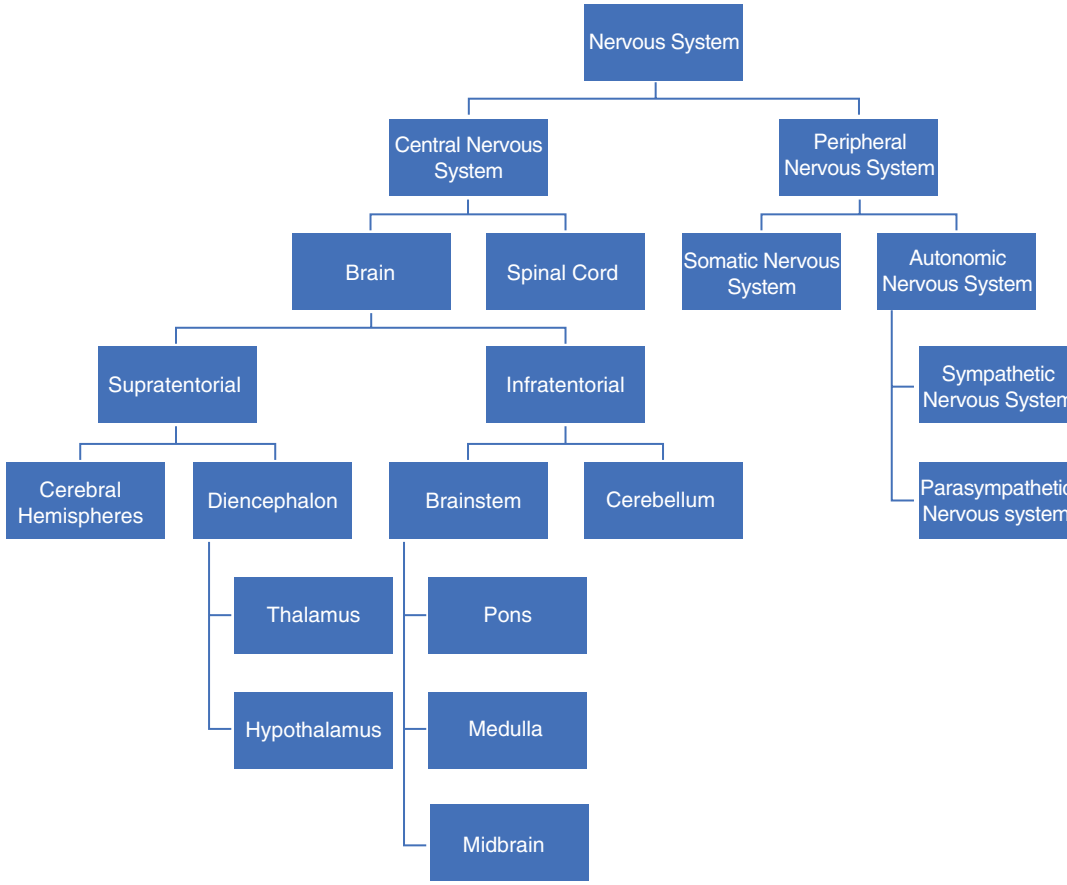

Fig. 1.1 Overall anatomical organization of the nervous system

essential to survival. The frontal lobe, which is made up of primary motor cortex, executes actions. Adjacent to this cortex is also the premotor cortex and other supplementary motor areas, which are involved in selecting voluntary movements. There are also sensory areas within the cortex, which help integrate the different stimuli from the senses. These areas work closely with the thalamus. Each of the hemispheres receives information about the contralateral side of the body. The primary somatosensory cortex located in the lateral parietal lobe, which integrates the touch signal, is often illustrated as a homunculus. The homunculus is a deformed human, where there are different sized body parts reflecting the relative density of their innervation. Areas with lots of innervation such as the fingertips and lips require more cortical processing compared to other areas. Also, within the cerebrum are Broca's and Wernicke's areas, which are responsible for speech and comprehension. Broca's area is located in the frontal lobe, while Wernicke's is located at the temporoparietal junction. These two areas are closely linked by arcuate fibers. Damage to any one of these parts can cause problems either with speech or comprehension. The cerebrum also works closely with the hippocampus to form memories. Neurodegenerative diseases such as Alzheimer's affect the cerebrum.

Cortex

The outermost surface of the cerebrum is the cortex that has a grayer appearance and, as a result, is called gray matter. The cortex is a folded structure, and each one of these folds is referred to as a gyrus. Each one of the grooves is called a

sulcus. These folds allow the brain to occupy a smaller cranial volume and store increased functional areas [1]. Below the cortex are myelinated axons, which give the characteristic appearance and often referred to as white matter.

Limbic System

The limbic system is the medial portion of the temporal lobe. It is vital in forming memories, emotions, and behaviors. The limbic system coordinates actions between different parts of the brain including the cortex, brain stem, thalamus, and hypothalamus. The limbic system is made up of the amygdala, hippocampus, fornix, mammillary bodies, cingulate gyrus, and parahippocampal gyrus. These structures communicate with each other via the Papez circuit. The amygdala is a collection of the nuclei that receives multiple sensory nerve signals. The amygdala integrates this information, ignores some stimuli, and creates outputs via the hypothalamus, thalamus, hippocampus, brain stem, and cortex. The amygdala also plays a role in mediating emotional responses associated with memories particularly the fear response [2]. The hippocampus is most important to memory formation, particularly declarative memory. Declarative memory is the ability to recall previous life events. Overtime, certain declarative memories can be independently recalled without the hippocampus [3]. The hippocampus is also important in learning [4].

Basal Ganglia

The basal ganglia (or basal nuclei) are made up of the caudate nucleus, putamen, globus pallidus, nucleus accumbens, olfactory tubercle, ventral pallidum, subthalamic nucleus, and substantia nigra [5]. The basal ganglia work with the motor cortex, premotor cortex, and motor nuclei of the thalamus. It modulates voluntary movements, procedural learning, and routine behaviors or habits [6]. The substantia nigra forms the dopamine necessary for basal ganglia function. The subthalamic nucleus is the only part of the basal ganglia to produce the excitatory neurotransmitter glutamate. A number of motor-related diseases have pathology in the basal ganglia, including Parkinson's and Huntington's disease.

Diencephalon

The diencephalon is made up of the thalamus, epithalamus, subthalamus, and hypothalamus.

Thalamus

The thalamus integrates sensory and motor inputs and transmits the information to the ipsilateral cerebral cortex. There is reciprocal feedback that projects to the thalamic subnuclei. It receives significant inputs from all the senses except for smell. The thalamus may also serve as a filter, trying to simplify the information received and process it to convey the best overall impression. There are a number of nuclei in the thalamus that play key roles in the functioning of the body. The anterior thalamic nuclei work closely with the limbic system, which is also connected with the cingulate gyrus and mammillary bodies. Medial nuclei are associated with the frontal association cortex and premotor cortex. Ventral anterior and lateral nuclei have inputs from the globus pallidus and project to the motor cortex. Ventral posteromedial and ventral posterolateral nuclei function as sensory transmitters associated with the face and body, respectively. Another part of the thalamus is the medial and lateral geniculate bodies, which process auditory and visual information [7]. Finally, the thalamus is also the primary entrance through which additional information from the reticular formation reaches the cerebral cortex. Animals with a damaged thalamus often suffer in a permanent coma.

Epithalamus

The epithalamus connects the limbic system to the rest of the brain. The pineal gland is a part of the epithalamus. The pineal gland secretes melatonin, which is involved in the regulation of the circadian rhythm.

Subthalamus

The subthalamus has efferent connections to the striatum (caudate nucleus and putamen), dorsal thalamus, substantia nigra, and red nucleus. It also has afferent connections from the substantia nigra and striatum. It is often involved in movement control.

Hypothalamus

The hypothalamus mediates the endocrine, autonomic, visceral, and homeostatic functions. It is the highest center for regulation of visceral functions. The hypothalamus connects the nervous system to the endocrine system via the pituitary gland. The hypothalamus is made up of a number of nuclei, each of with particular nuclei that function to regulate the body. Anterior nuclei include preoptic, supraoptic, and paraventricular. Anterior nuclei function in thermoregulation via sweating or panting, vasopressin release, oxytocin release, thyroid-releasing hormone release, and corticotropin-releasing hormone release. Middle nuclei include infundibular, tuberal, dorsomedial, ventromedial, and lateral. They function in the regulation of blood pressure, heart rate, gastrointestinal stimulation, satiety, growth hormone-releasing hormone release, and feeding. Posterior nuclei include supramammillary, mammillary, intercalate, and posterior. They function in arousal, learning, memory, energy balance, and sleep. Lateral nuclei are the location where hypocretin is released, which functions in arousal, temperature regulation, blood pressure, hunger, and wakefulness. Anterior and medial nuclear groups provide parasympathetic control, whereas sympathetic control is performed by the posterior and lateral nuclei. The hypothalamus is also connected with other areas in the brain to help coordinate different functions.

Pituitary

Pituitary gland is located below the hypothalamus at the base of the brain. The hypothalamus works closely with the pituitary to initiate endocrine responses. The pituitary regulates the majority of body functions, including blood pressure, water balance, thyroid levels, breast milk production, sexual organ function, and growth. The pituitary has three parts: anterior, intermediate, and posterior. The anterior pituitary synthesizes and secretes prolactin, growth hormone, adrenocorticotropic hormone, thyroid-stimulating hormone, luteinizing hormone, and follicle-stimulating hormone. The anterior and intermediate pituitary together release melanocyte-releasing hormone. The posterior pituitary does not synthesize but secretes antidiuretic hormone and oxytocin.

1.2.1.2 Infratentorial Compartment

The infratentorial compartment is the area under the tentorium cerebelli. The primary component is the cerebellum. Nerves C1–C3 innervate this area.

Cerebellum

The cerebellum is made up of tightly folded layer of the cortex, with several deep nuclei embedded in the white matter underneath and a fluid-filled ventricle in the middle. Signals in the cerebellum flow in a unidirectional fashion. The cerebellum plays a major role in motor functions, in particular coordination, posture, and balance [8]. Damage to the cerebellum leads to motor disturbances. There is decreased muscle tone ipsilateral to the lesion site. The cerebellum is an anatomically distinct portion from the cerebrum. It is made up of fine grooves, with several different types of neurons in a very regular distribution. The most important types of cells in the cerebellum are the Purkinje and granule cells. All of the output from the cerebellum passes through a couple of small deep nuclei lying within the white matter.

The three lobes of the cerebellum are flocculonodular lobe, anterior lobe, and posterior lobe. The latter two lobes are also split into the midline cerebellar vermis and lateral cerebral hemispheres. The flocculonodular lobe regulates balance and eye movements. It receives vestibular input from both the semicircular canals and the vestibular nuclei and sends fibers back to the medial and lateral vestibular nuclei. It also receives visual input from the superior colliculi and from the visual cortex.

The cerebellar vermis and paravermis regulate body and limb movements. It receives proprioception input from the dorsal columns of the spinal cord and trigeminal nerve, as well as visual and auditory systems. It also sends fibers to the deep cerebellar nuclei which in turn project to both the cerebral cortex and brain stem, thus providing modulation of the descending motor systems. This area also has sensory maps because it

receives data on the position of various body parts in space. This information is also used to anticipate the future position of the body (also known as "feed forward").

The lateral hemispheres are involved in the planning movement and evaluating sensory information for action. It receives input from the cerebral cortex particularly the parietal lobe via the pontine nuclei and dentate nucleus and sends fibers to the ventrolateral thalamus and red nucleus. This area is also involved in planning the movement that is about to occur.

Blood Supply

Cerebral blood flow to the brain makes up about 15% of cardiac output. The brain is vulnerable to factors that acutely decrease perfusion; as a result the brain has many safeguards including autoregulation and redundancy within the blood supply. Autoregulation is the phenomenon of maintaining a constant blood flow despite a change in perfusion pressure. The consequence of a compromise in blood flow, which is known as a stroke, can be devastating [9]. The arterial blood supply is divided into anterior and posterior portions. The anterior part is via the left and right internal carotid arteries, while the posterior portion is the vertebrobasilar artery. The anastomosis of these systems forms the circle of Willis and helps to create a redundant system of blood supply to help protect against ischemia. However, it is important to note that the system doesn't always protect against ischemia and is not completely redundant. Once the internal carotid arteries enter the cranial vault, they branch into the anterior cerebral artery (ACA) and eventually form the middle cerebral artery (MCA). The anterior cerebral arteries are connected via the anterior communicating artery (ACOM). The ACA supplies the majority of the midline portions of the frontal and superior medial parietal lobes. The MCA supplies most of the lateral portions of the hemispheres. The ACA, MCA, and ACOM form the anterior circulation of the circle of wills. The posterior circulation begins when the basilar artery, which is formed from the right and left vertebral arteries, branches into the left and right posterior cerebral artery (PCA). The vertebral arteries are formed from the subclavian artery. The posterior communicating arteries (PCOM) connect the PCAs and also connect to the anterior circulation. The PCA supplies most of the blood to the occipital lobe and inferior portion of the temporal lobe [7].

Three arteries perfuse the cerebellum: superior cerebellar arteries (SCA), anterior inferior cerebellar artery (AICA), and posterior inferior cerebellar artery (PICA). The SCA branches off the lateral portion of the basilar artery, just inferior to its bifurcation into the posterior cerebral artery. It also supplies blood to the pons before reaching the cerebellum. The SCA supplies blood to most of the cerebellar cortex, the cerebellar nuclei, and the superior cerebellar peduncles. The AICA branches off the lateral portion of the basilar artery, just superior to the junction of the vertebral arteries.

Symptoms associated with infarctions vary based on the artery infarcted in the brain and the area of the brain supplied by that particular artery. MCA infarctions or strokes are the most common. MCA infarctions present with sensory and motor disturbances of the contralateral face, arm, and leg. They can also present with aphasias if the dominant hemisphere is affected. If the ACA is infarcted, it can present with leg weakness more than arm weakness. If the PCA is infarcted, then it presents with visual field abnormalities. Lacunar strokes present with pure sensory or pure motor abnormalities. Vertebrobasilar infarctions present with brain stem dysfunction, which can include vertigo, ataxia, and dysphagia.

The venous drainage system helps remove the blood from the brain. It is made up of two parts: the superficial and deep sinuses. The superficial system is composed of the sagittal sinuses and cortical veins that are located on the surface of the cerebrum. The most prominent of these sinuses is the superior sagittal sinus, which is located midline along the fal x cerebri. The deep venous drainage system is composed of the lateral sinuses, sigmoid sinuses, straight sinus, and draining deep cerebral veins. All the veins in the deep venous drainage system combine to form the vein of Galen. Both of these systems combine to drain into the internal jugular veins.

Brain Stem

The brain stem is considered the most ancient part of the brain. It is made up of three parts: the medulla oblongata, pons, and midbrain. The brain stem primarily provides motor and sensory innervation to the face and neck via the cranial nerves. It also plays a key role in connecting the motor and sensory systems of the brain, which includes the corticospinal tract, posterior column-medial lemniscus pathway, and the spinothalamic tract. Finally, the brain stem plays a key role in the regulation of cardiac and respiratory function. It also regulates the CNS helping to maintain consciousness and regulating the sleep cycle [10].

Medulla Oblongata

The medulla oblongata is a structure that is located superior to the cervical spinal cord. On the external surface, the prominent structure is the anterior median fissure. On either side of this are the medullary pyramids. The pyramids are made up of the corticospinal and corticobulbar tracts originating from the spinal cord. At the caudal part of the medulla, these tracts cross over to form the decussation of the pyramids. The anterior external arcuate fibers lie on top of this. The area between the anterolateral and posterolateral sulcus is the olivary bodies. These bodies are formed by the inferior olivary nuclei. The posterior medulla contains the gracile fasciculus and the cuneate fasciculus. Together, they make up the posterior funiculi. Just above these tubercles is the triangular fossa, which forms the lower floor of the fourth ventricle. The fossa is bound by the inferior cerebral peduncle, which connects the medulla to the cerebellum.

The medulla plays an important role in controlling the autonomous nervous system. The medulla regulates respiration via interaction with the carotid and aortic bodies. These receptors detect changes in pH; thus, if the blood is acidic, the medulla sends signals to the respiratory musculature to increase the respiratory rate to reoxygenate blood. The medulla also plays an important role in regulating the parasympathetic and sympathetic nervous systems, which play a key role in the cardiovascular system [11]. It also plays as a baroreceptor. And finally, the medulla is important in managing the reflex centers of vomiting, coughing, sneezing, and swallowing [12].

Pons

The pons is located between the medulla and midbrain. The pons contains the tracts that carry signals that travel from the cerebrum to the medulla and on to the cerebellum. It also contains the tracts that carry important sensory signals up to the thalamus. Posteriorly, there are cerebellar peduncles that connect the pons to the cerebellum and midbrain. The pons also has the respiratory pneumotaxic center and apneustic centers, which are vital in maintaining respiration and transitioning from inspiration to expiration. The pons also has the nuclei that coordinate with sleep, swallowing, respiration, and bladder control. The pons also coordinates the activities of the cerebral hemispheres. It also plays an important role in control of cranial nerves of 5–8, which includes hearing, equilibrium, taste, and facial sensations.

Midbrain

The midbrain is made up of four parts: tectum, cerebral peduncles, tegmentum, and cerebral aqueduct. The tectum forms the upper border of the midbrain. It is comprised of the superior and inferior colliculi. The inferior colliculi are the principal midbrain nuclei of the auditory pathway. Above the inferior colliculi are the super colliculi, which are involved in vision, in particular the vestibulo-ocular reflex. Together they form the corpora quadrigemina. These structures help to decussate the fibers of the optic nerve. Of note, the trochlear nerve comes out of the posterior midbrain below the inferior colliculi. The dorsal covering of the cerebral aqueduct is also part of the midbrain.

The tegmentum, which forms the floor of the midbrain, is made up of several nuclei, substantia nigra, and reticular formation. The ventral tegmentum is composed of cerebral peduncles, which serve as the transmission axons of the upper motor neurons. The reticular formation is a large area of the midbrain that has multiple regulatory functions. It plays a key role in arousal,

sleep-wake cycling, and maintaining consciousness [13, 14]. It also contains the locus coeruleus, which is involved in alertness modulation and autonomic reflexes. Serotonin is also made in the reticular formation, which is a key regulator of mood. The reticular formation also plays a key role in regulation of the cardiovascular system, along with the medulla. Finally, the reticular formation is important in habituation, which is the process by which the brain begins to ignore repetitive meaningless stimuli, but remains vigilant to new sounds. The red nucleus is closely involved in motor coordination. Another important part of the tegmentum is the substantia nigra, which is closely associated with the basal ganglia. Dopamine produced in the substantia nigra and ventral tegmental area plays a role in excitation, motivation, and habituation. Dysfunction is associated with Parkinson's disease.

The cerebral aqueduct is involved with the movement of CSF. It is surrounded by gray matter, which is known as the periductal gray. In this area, there are neurons involved in the pain desensitization pathway that interact with the reticular activating system. When the neurons here are stimulated, they cause activation of the nucleus raphe magnus. The neurons project into the posterior gray column of the spinal cord and prevent pain sensitization transmission [15].

Development

In utero, the brain starts to develop at the beginning of the third week as the ectoderm forms the neural plate. By the fourth week, the neural plate has widened to give a broad cephalic end and a narrower caudal end. The swellings represent the beginning of the forebrain, midbrain, and hindbrain. Neural crest cells make up the lateral edge of the plate at the neural folds. By the end of the fourth week, the neural plate folds and closes to form the neural tube, which brings together the neural crest cells. Cells at the cephalic end give rise to the brain, while cells at the caudal end give rise to the spinal cord. With time the tube flexes giving rise to the crescent-shaped cerebral hemispheres. These cerebral hemispheres first appear on day 32. During this fourth week, the cephalic part bends forward forming the cephalic flexure, which becomes the forebrain. The forebrain divides into two parts: the telencephalon and diencephalon. The telencephalon goes on to form the cerebral cortex, basal ganglia, and other structures. The diencephalon forms the thalamus and hypothalamus. The hindbrain goes on to develop into the metencephalon and myelencephalon. The metencephalon forms the cerebellum and pons. The myelencephalon forms the medulla oblongata [7]. The developing brain is more vulnerable to injury in comparison to the developed or adult brain. When the development of the brain is delayed by an external influence or toxin, there is virtually no regeneration or repair. This can lead to lifelong disability. As a result, minimizing exposures to a developing brain is vital.

One of the most defining features of the brain is the gyri that define the outer surface. In womb, the brain starts off smooth, but with time the fissures start to form. The fissures form because of the rapidly growing hemispheres, which rapidly increase in size due to the expansion of the gray matter. The underlying white matter does not grow at the same rate as the hemispheres [7].

1.2.1.3 Spinal Cord

The spinal cord is a bundle of nervous tissue that extends from the medulla oblongata in the brain stem to the lumbar region of the vertebral column. The spinal cord connects the brain to the peripheral nervous system. The spinal cord is encased in a bony shell made up of the cervical vertebrae. The spinal cord transmits nerve signals from the motor cortex to the musculature and from the afferent fibers of the sensory neurons to the sensory cortex. The spinal cord also plays a key role in coordinating reflexes and contains numerous reflex arcs (ankle jerk, knee jerk, biceps jerk, forearm jerk, triceps jerk). The spinal cord is made up of 31 segments; at each level there are 1 pair of sensory nerve roots and 1 pair of motor nerve roots.

The spinal cord and brain are covered by three protective layers of the meninges. The dura mater is the outermost layer and forms a tough protective coating. Between the vertebrae and dura mater is the epidural space. The epidural space is

made up of adipose tissue and has numerous blood vessels. The arachnoid mater is the middle layer that is located underneath the dura mater. The arachnoid mater is named for its open, spiderlike appearance. The space between the arachnoid mater and pia mater is the subarachnoid space. The subarachnoid space has cerebrospinal fluid (CSF), which is accessed in neuraxial anesthesia. The CSF is made in the brain's lateral ventricles and flows through the foramen of Monro into the third ventricle and through the cerebral aqueduct to the fourth ventricle. It passes into the subarachnoid space through three openings in the roof of the fourth ventricle. The two lateral openings are the foramen of Luschka and a median opening called the foramen of Magendie. The CSF then flows through the subarachnoid space around the brain and drains into the superior sagittal sinus through the arachnoid granulations [7].

The pia mater is tightly adhered to the spinal cord. The cord is stabilized within the dura mater by connecting denticulate ligaments, which extend from the enveloping pia mater laterally between dorsal and ventral roots. The dural sac ends at the level of the second sacral vertebrae.

Spinal Cord Segments

The gray column (matter) at the center of the spinal column is shaped like a butterfly and consists of cell, bodies of interneurons, motor neurons, neuroglia cells, and unmyelinated axons. The gray matter consists of longitudinal columns of cells, with a segmental relationship to the spinal nerve fibers. These columns are grouped into the dorsal (posterior) horn, ventral (anterior) horn, and intermediate gray. The dorsal roots are afferent fascicles, receiving sensory information. The roots terminate in dorsal root ganglia, which are made up of the respective cell bodies. The ventral nerve roots are made up of efferent fascicles that arise from motor neurons whose cell bodies are found in the ventral horns of the spinal cord [7]. The ventral horn also includes interneurons, which are involved in the processing of motor information. The intermediate gray contains the interneurons for primitive connections.

The white matter is located adjacent to the gray matter and is made up of myelinated motor and sensory axons. The columns of white matter carry information up or down the spinal cord [7]. The white matter is made up of the dorsal white matter, ventral white matter, and lateral white matter. The dorsal white matter has the ascending tracts, while the ventral white matter has the descending tracts. The dorsal column below T6 has the gracile fasciculus, which has input from the lower body. And above T6, there is both input from the lower body and upper body, which is also known as the cuneate fascicle. The lateral white matter has both and is mainly involved with pain and movement. The absolute amount of white matter decreases as you progress caudally through the spinal cord. Lesions at the dorsal and ventral roots present as strictly sensory or motor deficits; while lesions at the peripheral nerves more often present with deficits in both the sensory and motor pathways.

The spinal cord terminates at the conus medullaris, while the pia mater continues via the filum terminale, which anchors the spinal cord to the coccyx. The cauda equina is a collection of nerves below the conus medullaris that travel in the vertebral column to the coccyx. The cauda equina forms because the spinal cord stops elongating at about age 4, even though the vertebral column continues to lengthen until adulthood.

There are 31 spinal cord segments in the spinal cord – 8 cervical segments, 12 thoracic segments, 5 lumbar segments, 5 sacral segments, and 1 coccygeal segment. In the fetus, vertebral segments correspond with spinal cord segments. In adults, the spinal cord ends around the L1/L2 vertebral level, which corresponds to the conus medullaris. As a result, the spinal cord segments do not correspond with the vertebral segments especially in the lower spinal cord. The cervical enlargement, stretching from the C5 to T1 vertebrae, is the location for the sensory and motor output associated with the arms and trunk. This enlargement corresponds with the brachial plexus. The lumbar enlargement, located between L1 and S3, handles sensory input coming from and going to the legs. This corresponds with the lumbosacral enlargement [7].

Development

There are four stages of spinal cord development: neural plate, neural fold, neural tube, and spinal cord. At the end of the third week, the ectoderm located at the midline of thickens to form the neural plate. Slowly, the lateral edges of the neural plate began to move dorsally and medially. When the edges meet, they form the neural tube. As the neural tube begins to develop, the notochord begins to secrete sonic hedgehog (SHH) [16]. This helps to establish the ventral pole in the developing fetus [16]. As a result, the floor plate also begins to secrete SHH, which induces the basal plate to develop motor neurons. During the maturation of the neural tube, lateral walls thicken and form the longitudinal groove of the sulcus limitans. This extends the length of the spinal cord into dorsal and ventral portions. At the same time, the ectoderm secretes bone morphogenetic protein (BMP). These two opposing gradients help the cells divide along the dorsal ventral axis [17]. This release of the BMP also induces the roof plate to secrete BMP, which leads to the formation of the sensory neurons. Simultaneously, the lumen of the neural tube begins to narrow to help form the central canal of the spinal cord. Further, the floor plate secretes netrins. The netrins act as chemoattractants, which lead to the decussation of pain and temperature sensory neurons in the alar plate across the anterior white commissure. These fibers ascend toward the thalamus. Once the caudal neuropore and formation of the brain's ventricles with the choroid plexus is completed, the central canal of the caudal spinal cord is filled with CSF. Closure of the neural tube progresses both cranially and caudally. Malformations of the neural tube closure can lead to abnormal development of the central nervous system. Failure of the cranial tube to close completely at the cranial end may manifest as exencephaly, anencephaly, or cranioschisis. The complete closure of the lumbar region of the neural tube may lead to rachischisis or myeloschisis, which is where the spinal cord is exposed to the outside. More mild defects may present as spina bifida, which is the result of an incomplete vertebral arch.

Over the course of the cell division process, groups of cells break off from the neural plate and become a part of the mesoderm. Slowly, these neural crest cells migrate away from the neural tube and form a number of different tissues including the neurons of the dorsal root ganglion and postsynaptic cells of the sympathetic and parasympathetic nervous systems. When these cells fail to appropriately migrate, it forms diseases such as Hirschsprung's disease. Hirschsprung's occurs when there is a portion of the digestive system that can't perform peristalsis.

Blood Supply

The blood supply of the spinal cord is made of three longitudinal arteries, which are the anterior spinal artery, right posterior spinal artery, and left posterior spinal artery. The anterior spinal artery provides blood flow to the anterior 2/3 of the spinal cord [7]. These arteries travel in the subarachnoid space and send branches into the spinal cord. They form connections via the anterior and posterior segmental medullary arteries, which enter the spinal cord at various points. The blood flow through these arteries provides sufficient blood supply primarily to the cervical spinal cord. Beyond that region, the spinal cord derives much of its blood supply from the anterior and posterior radicular arteries, which run into the spinal cord alongside the dorsal and ventral nerve roots. The largest of the anterior radicular arteries is the artery of Adamkiewicz, which usually arises between L1 and L2. Impaired blood flow to these radicular arteries can result in spinal cord infarction and paraplegia [18].

Somatosensory Organization

The somatosensory system is primarily concerned with transmitting the sensory information from the integumentary and musculoskeletal systems of the body. This system can be divided into the dorsal column-medial lemniscus (DCML) and the anterolateral system (ALS). The DCML plays the main role in the touch, proprioception, and vibration, while the ALS plays the key role in pain and temperature. Both sensory pathways use three different nerves to transmit the information from the sensory receptors in the periphery to the

cerebral cortex. In both pathways, the primary sensory neuron cell bodies are found in the dorsal root ganglion and their central neurons project into the spinal cord.

In the DCML, a primary neuron's axon enters the dorsal column of the spinal cord. If the primary axon enters below level T6, the axon travels in the fasciculus gracilis, which is the medial part of the cord. If the primary axon enters above level T6, it travels in the fasciculus cuneatus, which is located more lateral. Through both these pathways, the primary axon ascends to the caudal medulla, where it leaves the fasciculi and synapses with a secondary neuron in one of the dorsal column nuclei, either the nucleus gracilis or nucleus cuneatus, respectively. The first processing of discriminative touch information occurs in the caudal medulla. The secondary axons synapse with these nuclei. These secondary axons are known as the internal arcuate fibers. The internal arcuate fibers decussate and ascend as the contralateral medial lemniscus. Axons from the medial lemniscus terminate in the ventral posterolateral nucleus of the thalamus. In the thalamus, neurons synapse with tertiary neurons, which eventually ascend in the posterior limb of the internal capsule to the primary sensory cortex. Further, the axons that enter the dorsal columns also give rise to collaterals that terminate in the spinal cord. These collaterals play an important role in modulating simple motor behaviors.

The ALS has a different anatomical pathway compared to the DCML. The primary axons of the ALS enter the spinal cord and ascend 1–2 levels ipsilaterally before synapsing with the substantia gelatinosa. Once synapsing, the secondary axons decussate in the ventral white commissure and ascend as a part of the anterolateral spinothalamic tract. This tract travels through the medulla and eventually synapses in the thalamus and further similar to the DCML. In syringomyelia with pathologic cavitation, there is often bilateral loss of pain and temperature sensations in the dermatomes at the level of the lesion because of the proximity of the ventral white commissure to the central canal of the spinal cord.

It is important to note that some of the pain fibers in the ALS deviate away from this pathway to the reticular formation in the midbrain. The reticular formation is connected with the hippocampus to create memories and centromedian nucleus to create diffuse non-specific pain sensation. Further, the ALS axons help inhibit the initial pain signal via projections to the periaqueductal gray in the pons and nucleus raphe magnus.

Motor Component

The corticospinal tract is the motor pathway for the upper motor neurons (UMN) coming from the cerebral cortex and from the primitive brain stem motor nuclei. The cortical upper motor neurons originate from Brodmann areas 1, 2, 3, 4, and 6. Majority originate from Brodmann area 4, which is premotor frontal area. They descend down the posterior limb of the internal capsule, into the cerebral peduncles, and then into the medullary pyramids, where about 90% of axons cross to the contralateral side at the decussation of the pyramids. Then the neurons descend as the lateral corticospinal tract. The axons synapse with lower motor neurons (LMN) in the ventral horns. Most of the axons will cross to the contralateral side of the cord before they synapse. The midbrain nuclei include four motor tracts that send UMN axons down the spinal cord to LMN. These four tracts are the rubrospinal tract, vestibulospinal tract, tectospinal tract, and reticulospinal tract. Damage to the UMN of the corticospinal tract can lead to paralysis, paresis, hypertonia, hyperreflexia, or spasticity.

The LMN have two divisions: the lateral corticospinal tract and the anterior corticospinal tract. The lateral tract contains fibers that are involved with distal limb control. Thus, these neurons are only found at the cervical and lumbosacral enlargements. There is no decussation of the lateral corticospinal tract after decussation at the medullary pyramids. The lateral corticospinal tract forms the majority of connections in the corticospinal tract. The anterior corticospinal tract descends ipsilaterally in the anterior column and synapses ipsilaterally in the ventromedial nucleus. These nerves control the large postural muscles of the trunk and axial skeleton.

Spinocerebellar Tract

Proprioceptive information, which are the stimuli that affect muscle joints or other deep tissues, travel in the spinal cord via three tracts based on the spinal cord level. These receptors are responsible for the perception of motion and position of the body. They carry unconscious proprioceptive information about the body position from the periphery to the cerebellum. Above T1, proprioceptive primary axons enter the spinal cord and ascend ipsilaterally until synapsing in the accessory cuneate nucleus. The secondary axons pass into the cerebellum via the inferior cerebellar peduncle, where they synapse with the cerebellar deep nuclei. This is part of the cuneocerebellar tract [19]. From the levels of T1–L2, proprioceptive information enters the spinal cord and ascends ipsilaterally until synapsing with Clarke's nucleus (nucleus dorsalis). Below the level of L2, proprioceptive information travels via the fasciculus gracilis and DCML, until reaching Clarke's nucleus. Neurons within Clarke's nucleus give rise to second-order sensory fibers that ascended the ipsilateral dorsal part of the lateral funiculus of the spinal cord. At the medulla, these fibers enter the cerebellum via the inferior peduncle. Lesions or deficits to the cerebellum manifest with ataxia of the extremities on the same side of the lesion. It is often hard to damage just the spinocerebellar tracts.

1.2.1.4 Peripheral Nervous System

The peripheral nervous system (PNS) is made up of the nerves and ganglia that are located outside of the brain and spinal cord. The primary function of the peripheral nervous system is to connect the CNS to the limb and organs. However, unlike the CNS, the PNS is not protected by the vertebral column and skull or by the blood-brain barrier. Thus, the nerves are more exposed to toxins, mechanical injuries, and other pathological processes. The peripheral nervous system is divided into the somatic nervous system and autonomic nervous system. The somatic nervous system is involved with voluntary control of the muscles. Of note, the sensory nervous system is part of the somatic nervous system. In the somatic system, the cranial nerves are part of the PNS except for the optic nerve. The optic nerve is considered a tract of the diencephalon [5]. However, the remaining ten cranial nerves extend outside of the brain and are considered a part of the PNS. The autonomic nervous system is involved in involuntary self-regulation via the sympathetic and parasympathetic nervous systems. The sympathetic and parasympathetic systems are antagonists.

1.2.1.5 Somatic Nervous System

The somatic nervous system (SoNS) is made up of the sensory and somatosensory nervous system. The SoNS is made up of afferent neurons (sensory) and efferent nerves (motor). The afferent nerves relay information from the body to the CNS, while the efferent nerves are responsible for stimulating muscle contraction. The efferent nerves include all the non-sensory neurons connected with the skeletal muscles and skin. The efferent SoNS involves an initial signal that begins in the upper cell bodies of motor neurons within the precentral gyrus. Stimuli from the precentral gyrus are transmitted down the corticospinal tract to control the skeletal muscles. These stimuli are conveyed from the upper motor neurons (UMN) through the ventral horn of the spinal cord and across synapses to be received by the sensory receptors of alpha motor neuron, which are large lower motor neurons, of the brain stem and spinal cord. UMN release acetylcholine from their axonal terminal knobs, which are received by the nicotinic receptors of the lower motor neurons. These signals are further relayed to the end organ. In contrast to this pathway, the SoNS is also made up of reflex arcs. The reflex arc is a shorter neuronal circuit creating direct connections between the sensory input and a specific motor output. Reflex arcs have various levels of complexity; some involve just two nerves, while others have three nerves, with the addition of an interneuron. Some of the reflexes are protective, while others contribute to regular behavior [10]. This leads to a shorter response time.

In the head and neck, 12 cranial nerves carry somatosensory data. Ten of the cranial nerves originate from the brain stem and also control the anatomic functions in the head. The nuclei of the

Table 1.1 Cranial nerves

Cranial nerve	Location of exit	Structures supplied
I: Olfactory nerve	Cribriform plate	Olfactory mucosa
II: Optic	Optic foramen	Rods and cones of the retina
III: Oculomotor	Superior orbital fissure	Superior rectus, medial rectus, inferior rectus, inferior oblique, and sphincter oblique
IV: Trochlear	Superior orbital fissure	Superior oblique
V: Trigeminal	Superior orbital fissure, foramen rotundum, foramen ovale	Muscles of mastication, tensor tympani, tensor palati
VI: Abducens	Superior orbital fissure	Lateral rectus
VII: Facial	Internal auditory canal	Posterior external ear canal, anterior 2/3 of the tongue, facial muscles, salivary glands, lacrimal glands
VIII: Vestibulocochlear	Internal auditory canal	Cochlea and vestibule of the inner ear
IX: Glossopharyngeal	Jugular foramen	Posterior 1/3 of the tongue (sensory and taste), middle ear, carotid body/sinus, stylopharyngeus, parotid gland
X: Vagus	Jugular foramen	External ear, aortic arch/body, epiglottis, soft palate, pharynx, larynx, lungs
XI: Accessory	Jugular foramen	Trapezius, sternocleidomastoid
XII: Hypoglossal	Hypoglossal canal	Muscles of the tongue

olfactory and optic nerves lie in the forebrain and thalamus. The vagus nerve receives sensory information from the organs in the thorax and abdomen. The cranial nerves are summarized in Table 1.1.

1.2.1.6 Cervical Spinal Nerves (C1–C4)

Spinal nerve C1 (suboccipital nerve) provides innervation to the nerves at the base of the skull. C2 and C3 form many nerves in the neck, providing both motor and sensory controls. These nerves include greater occipital nerve, lesser occipital nerve, greater auricular nerve, and lesser auricular nerve. The phrenic nerve is a nerve, which arises from C3, C4, and C5, that is vital to survival by supplying the thoracic diaphragm enabling breathing. It is important to note that if the cervical spine is transected above C3, then the patient will not be able to spontaneously breathe.

1.2.1.7 Brachial Plexus (C5–T1)

The brachial plexus, which is made up of the last four cervical nerves (C5–C8 and T1), innervates the upper limb and upper back. It is made up of five roots, three trunks, six divisions (three anterior and three posterior), three cords, and five branches [20]. The five roots come together to form five trunks (superior trunk, middle trunk, and inferior trunk). The dorsal scapular nerve comes from the superior trunk and innervates the rhomboid muscles which retract the scapula. The subclavian nerve, which branches from C5 and C6, innervates the subclavius muscle that lifts the ribs during respiration. The long thoracic nerve, which originates from the C5, C6, and C7, innervates the serratus and is vital in lifting up the scapula [20].

The trunks split into divisions and then form cords, which are named in relation to their positon with the axillary artery. The three cords are the posterior, lateral, and medial cords. The cords lead to the formation of the terminal branches. The terminal branches are musculocutaneous nerve, axillary nerve, radial nerve, median nerve, and ulnar nerve. Because both the musculocutaneous and median nerve originate from the lateral cord, they are well connected. The musculocutaneous nerve innervates the skin of the anterolateral forearm along with the brachialis, biceps brachii, and coracobrachialis [20]. The median nerve innervates the skin of the lateral 2/3 of the hand and the tips of digits 1–3. It also innervates the forearm flexors, thenar eminence, and lumbricals of the hand 1–2 [20]. The axillary nerve innervates the sensory portion of the lateral shoulder and upper arm and also plays a role innervating the deltoid and teres minor muscles [20]. The radial nerve innervates the sensory portion of the

posterior lateral forearm and wrist. It also innervates the triceps brachii, brachioradialis, anconeus, and extensor muscles of the posterior arm and forearm [20]. The ulnar nerve innervates the skin of the palm and medial side of the hand and digits 3–4. It also innervates the hypothenar eminence, some forearm flexors, the thumb adductor, lumbricals 3–4, and the interosseous muscles [20]. Brachial plexus injuries affect the cutaneous sensation and the muscular motions depending on the nerve that has been affected.

1.2.1.8 Lumbosacral Plexus (L1-Coccygeal Nerve)

The lumbosacral plexus is made up of three key parts: lumbar plexus, sacral plexus, and pudendal plexus. Often times bone injuries in the pelvic region can affect these nerves.

1.2.1.9 Autonomic Nervous System (ANS)

The ANS controls involuntary responses to regulate physiologic functions, in particular those that have smooth muscle [21]. This includes the heart, bladder, and other exocrine or endocrine organs via ganglionic neurons [21]. The ANS is always active. Depending on the situation, either the sympathetic or parasympathetic system dominates. This leads to the release of neurotransmitters, which affect the organs in different ways. The other division of the ANS is the enteric nervous system [22]. The enteric nervous system surrounds the digestive tract and, as a result, allows for local control of the gastrointestinal system [22]. However, the sympathetic and parasympathetic provide input.

The sympathetic system is involved in "flight or fight," which is a stress response mediated by norepinephrine and epinephrine [21]. This often occurs when the body feels that it is under great stress. The norepinephrine and epinephrine increase the heart rate and blood flow to certain areas such as the muscles while also decreasing the activities of noncritical functions such as digestion [22].

The parasympathetic system is in many ways the opposite of the sympathetic system. The primary neurotransmitter involved is acetylcholine, which allows the body to "rest and digest." As a result of the parasympathetic system, there is decreased heart rate and other sympathetic response, while there is increased digestion, urination, and defecation. Humans have some control over the parasympathetic system.

1.3 Conclusion

The nervous system is made up of two key parts: CNS and PNS. The relationship and interaction between the two are as important as each individual part. Damage to one area can be minor or devastating for the welfare of the individual. Disturbances during development in utero can be particularly profound affecting a number of different areas of the nervous system. Anatomy plays a key role in determining function and pathology. Clearly identifying the different structures and function can help predict the deficiency found upon damage.

Key Points

- The nervous system is made up of two parts: the central nervous system and peripheral nervous system. The two systems work closely together to coordinate function.
- Pathology in one portion can lead to dysfunction in the end organs. Stresses or dysfunction during development can lead to diffuse debility.
- Some of the pathological changes are amenable to correction, while others are not.

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