Republic of Iraq
Ministry of Higher Education and Scientific Research
The Islamic University college
AL-Najaf Al-Ashraf
College of Dentistry

NERVE TISSUE & THE NERVOUS SYSTEM

BY
T.A. Hawra'a F. AL. Baghdady

2022

INTRODUCTION

The human nervous system is by far the most complex system in the body histologically and physiologically and is formed by a network of many billion nerve cells (neurons), all assisted by many more supporting glial cells. Each neuron has hundreds of interconnections with other neurons, forming a very complex system for processing information and generating responses. Nerve tissue is distributed throughout the body as an integrated communications network. Anatomists divide the nervous system into the following:

1- Central nervous system (CNS) : consisting of the brain and spinal cord .
2- Peripheral nervous system (PNS) : composed of the cranial, spinal, and peripheral nerves conducting impulses to and from the CNS (motor and sensory nerves respectively) and ganglia which are small groups of nerve cells outside the CNS.

The general organization of the nervous system.

The major anatomical division of nervous tissue is as components of the central and peripheral nervous systems.

- The CNS includes all parts of the brain, including the large cerebrum and cerebellum, and the spinal cord, which are protected by the bones of the cranium and spinal column respectively.
- The PNS includes nerves, which contain both long nerve processes (fibers) growing from motor neurons whose cell bodies are within the spinal cord and processes of sensory neurons which are grouped in a series of ganglia outside the spinal cord. Motor nerves are efferent, carrying impulses away from the CNS; Sensory fibers are afferent, carrying impulses to the CNS. Another group of peripheral neurons, fibers, and ganglia comprises the more dispersed autonomic nervous system. Both central and peripheral nerve tissue consists of two cell types: nerve cells, or neurons, which usually show numerous long processes; and various glial cells ,which have short processes, support and protect neurons, and participate in neural activity, neural nutrition, and defense of cells in the central nervous system.

Neurons respond to environmental changes (stimuli) by altering the ionic gradient that exists between the inner and outer surfaces of their membranes. All cells maintain such a gradient, also called an electrical potential. Neurons react promptly to stimuli with a reversal of the ionic gradient (membrane depolarization) that generally spreads from the place that received the stimulus and is propagated across the neuron's entire plasma membrane. This propagation, called the action potential, the depolarization wave, or the nerve impulse, is capable of traveling long distances along neuronal processes, transmitting such signals to other neurons, muscles, and glands. By creating, analyzing, identifying, and integrating information in such signals, the nervous system continuously stabilizes the intrinsic conditions of the body (eg, blood pressure, O_2 and CO_2 content, pH, blood glucose levels, and hormone levels) within normal ranges and maintains behavioral patterns (eg, feeding, reproduction, defense, interaction with other living creatures).

DEVELOPMENT OF NERVE TISSUE

The nervous system develops from the outer embryonic layer, the ectoderm, beginning in the third week of human embryonic life.

NEURONS

The functional unit in both the CNS and PNS is the neuron or nerve cell. Most neurons consist of three parts :

1- The cell body, or perikaryon, which is the synthetic or trophic center for the entire nerve cell and is receptive to stimuli.
2- The dendrites, many elongated processes specialized to receive stimuli from the environment, sensory epithelial cells, or other neurons.
3- The axon, which is a single process specialized in generating and conducting nerve impulses to other cells (nerve, muscle, and gland cells).

Axons may also receive information from other neurons, information that mainly modifies the transmission of action potentials to those neurons. The distal portion of the axon is usually branched as the terminal arborization. Each branch terminates on the next cell in dilatations called end bulbs (boutons), which interact with other neurons or nonnerve cells at structures called synapses. Synapses initiate impulses in the next cell of the circuit.

Neurons and their processes are extremely variable in size and shape. Cell bodies can be very large, measuring up to 150 µm in diameter. Other cells are among the smallest cells in the body; for example, the cell bodies of granule cells of the cerebellum are only 4–5 µm in diameter. Neurons can be classified according to the number of processes extending from the cell body .

1- Multipolar neurons : which have one axon and two or many dendrites.
2- Bipolar neurons : with one dendrite and one axon.
3- Unipolar or pseudounipolar neurons : which have a single process that bifurcates close to the perikaryon, with the longer branch extending to a peripheral ending and the other toward the CNS.

1- Cell Body (Perikaryon)

The cell body, or perikaryon, is the part of the neuron that contains the nucleus and surrounding cytoplasm, exclusive of the cell processes.Most nerve cells have a spherical, unusually large, euchromatic (pale-staining) nucleus with a prominent nucleolus. Bi-nuclear nerve cells are sometimes seen in sympathetic and sensory ganglia.

Cell bodies often contain a highly developed rough ER organized into aggregates of parallel cisternae. In the cytoplasm between the cisternae are numerous polyribosomes, suggesting that these cells synthesize both structural proteins and proteins for transport and secretion. When appropriate stains are used, RER and free ribosomes appear under the light microscope as clumps of basophilic material called chromatophilic substance (often called Nissl bodies). The amount of chromatophilic substance varies according to the type and functional state of the neuron .The Golgi apparatus is located only in the cell body, but mitochondria can be found throughout the cell and are usually abundant in the axon terminals. Intermediate filaments are abundant both in perikarya and processes and are called neurofilaments in this cell. Neurofilaments become cross-linked with certain fixatives and when impregnated with silver stains, they form neurofibrils visible with the light microscope. The neurons also contain microtubules identical to those found in other cells.

2- Dendrites

Dendrites are usually short and divide like the branches of a tree. They are often covered with many synapses and are the principal signal reception and processing sites on neurons. Most nerve cells have numerous dendrites, which considerably increase the receptive area of the cell. The arborization of dendrites makes it possible for one neuron to receive and integrate a great number of axon terminals from other nerve cells. It has been estimated that up to 200,000 axonal terminations establish functional contact with the dendrites of a single large Purkinje cell of the cerebellum. Unlike axons, which maintain a constant diameter, dendrites become much thinner as they subdivide into branches. The cytoplasmic composition of the dendrite base, close to the neuron body, is similar to that of the perikaryon but is devoid of Golgi complexes. Most synapses impinging on neurons are located on dendritic spines, which are usually short blunt structures 1 to 3 μm long projecting from dendrites, visible with silver staining methods . These spines occur in vast numbers, estimated to be on the order of 1014 for cells of the human cerebral cortex, and serve as the first processing locale for synaptic signals arriving on a neuron. The processing apparatus is contained in a complex of proteins attached to the cytosolic surface of the postsynaptic membrane, which is visible under the transmission electron microscope (TEM). The morphology of such spines is based on actin filaments and can be highly plastic; dendritic spines participate widely in the constant changes that make up neuronal plasticity which underlies adaptation, learning, and memory.

3- Axons

Most neurons have only one axon, a cylindrical process that varies in length and diameter according to the type of neuron. Axons are usually very long processes. For example, axons of the motor cells of the spinal cord that innervate the foot muscles may have a length of up to 100 cm (~40 inches). The plasma membrane of the axon is often called the axolemma and its contents are known as axoplasm.. Several types of ion channels are localized in the initial segment and these channels are important in generating the action potential. In contrast to dendrites, axons have a constant diameter and do not branch profusely.

Occasionally, the axon, shortly after its departure from the cell body, gives rise to a branch that returns to the area of the nerve cell body. All axon branches are known as collateral branches. Axoplasm contains mitochondria, microtubules, neurofilaments, and some cisternae of smooth ER. The absence of polyribosomes and rough ER emphasizes the dependence of the axon on the perikaryon for its maintenance. If an axon is severed, its peripheral parts quickly degenerate. There is a lively bidirectional transport of small and large molecules along the axon. Retrograde transport in the opposite direction carries certain other macromolecules, such as material taken up by endocytosis (including viruses and toxins), from the periphery to the cell body. Retrograde transport can be used to study the pathways of neurons.

4- Membrane Potentials

Many integral membrane proteins of neuronal cell membrane act as pumps and channels that transport or allow diffusion of ions into and out of the cytoplasm. The axolemma or limiting membrane of the axon pumps Na^+ out of the axoplasm, maintaining a concentration of Na^+ that is only a tenth of that in the extracellular fluid. In contrast, the concentration of K^+ is maintained at a level many times greater than that in the extracellular environment. This produces a potential difference across the axolemma of about –65 mV with the inside negative to the outside. The duration of these local events is very short, only about 5 milliseconds.

However, the action potential propagates along the axonal membrane, producing the nerve impulse. The electrical disturbance opens neighboring sodium channels and, in sequence, potassium channels. In this way the action potential propagates at a high speed along the axon, with several occurring per second. When an action potential arrives at the nerve ending, it promotes discharge of stored neurotransmitter that stimulates or inhibits another neuron or a non-neural cell, such as a muscle or gland cell.

Synaptic Communication

The synapse is responsible for the transmission of nerve impulses from neuron to another cell and insures that transmission is unidirectional. Synapses are sites of functional contact between neurons or between neurons and other effector cells. The function of the synapse is to convert an electrical signal (impulse) from the presynaptic cell into a chemical signal that acts on the postsynaptic cell. Most synapses transmit information by releasing neurotransmitters during this signaling process. Neurotransmitters are chemicals that bind specific receptor proteins to either open or closed ion channels or initiate second-messenger cascades. A synapse has the following structure:

1- Presynaptic axon terminal (terminal bouton) from which neurotransmitter is released,
2- Postsynaptic cell membrane with receptors for the transmitter and ion channels or other mechanisms to initiate a new impulse,

20–30 nm wide intercellular space called the synaptic cleft separating the presynaptic and postsynaptic membranes. synaptic vesicles containing neurotransmitters, numerous mitochondria, and smooth ER as a source of new membrane. Some neurotransmitters are synthesized in the cell body and then transported in vesicles to the presynaptic terminal

GLIAL CELLS & NEURONAL ACTIVITY

Glial cells are 10 times more abundant in the mammalian brain than neurons. In the CNS glial cells surround most of the neuronal cell bodies, which are usually much larger than glial cells, and the processes of axons and dendrites that occupy the spaces between neurons. Except around the larger blood vessels, the CNS has only a very small amount of connective tissue or ECM. Glial cells (Table 7–1) furnish a microenvironment ideal for neuronal activity. A dense network of fibers from processes of both neurons and glial cells fills the interneuronal space of the CNS and is called the neuropil.

Table 7–1 Origin and principal functions of neuroglial cells.

Glial Cell Type	Origin	Location	Main Functions
Oligodendrocyte	Neural tube	Central nervous system	Myelin production, electric insulation
Neurolemmocyte	Neural crest	Peripheral nerves	Myelin production, electric insulation
Astrocyte	Neural tube	Central nervous system	Structural support, repair processes Blood-brain barrier, metabolic exchanges
Ependymal cell	Neural tube	Central nervous system	Lining cavities of central nervous system
Microglia	Bone marrow	Central nervous system	Immune-related activity

1- CENTRAL NERVOUS SYSTEM

The principal structures of the CNS are the cerebrum, cerebellum, and spinal cord. It has virtually no connective tissue and is therefore a relatively soft, gel-like organ. When sectioned, the cerebrum, cerebellum, and spinal cord show regions of white (white matter) and gray (gray matter), differences caused by the differential distribution of myelin. The main components of white matter are myelinated axons and the myelin-producing oligodendrocytes. White matter does not contain neuronal cell bodies, but microglia are present. Gray matter contains abundant neuronal cell bodies, dendrites, the initial unmyelinated portions of axons, astrocytes, and microglial cells. This is the region where
synapses occur. Gray matter is prevalent at the surface or cortex of the cerebrum and cerebellum, whereas white matter is present in more central regions. Aggregates of neuronal cell bodies forming islands of gray matter embedded in the white matter are called nuclei. Neuroscientists recognize six layers in the cerebral cortex with most neurons arranged vertically. The most abundant neurons are the efferent pyramidal neurons which come in many sizes .

Cells of the cerebral cortex function in the integration of sensory information and the initiation of voluntary motor responses . The cerebellar cortex, which coordinates muscular activity throughout the body, has three layers : an outer molecular layer, a central layer of very large neurons called Purkinje cells, and an inner granule layer.

White matter is peripheral and gray matter is internal and has the general shape of an H . In the center is an opening, the central canal, which develops from the lumen of the embryonic neural tube and is lined by ependymal cells. The gray matter forms the anterior horns, which contain motor neurons whose axons make up the ventral roots of spinal nerves, and the posterior horns, which receive sensory fibers from neurons in the spinal ganglia (dorsal roots). Spinal cord neurons are large and multipolar, especially the motor neurons in the anterior horns

Meninges

The skull and the vertebral column protect the CNS. Between the bone and nervous tissue are membranes of connective tissue called the meninges. Three meningial layers are distinguished:

A- DURA MATER

The dura mater is the thick external layer consisting of dense, fibroelastic connective tissue continuous with the periosteum of the skull. Around the spinal cord the dura mater is separated from the periosteum of the vertebrae by the epidural space, which contains a plexus of thin-walled veins and areolar connective tissue. The dura mater is always separated from the arachnoid by the thin subdural space. The internal surface of all dura mater, as well as its external surface in the spinal cord, is covered by simple squamous epithelium of mesenchymal origin

B- ARACHNOID

The arachnoid has two components:

1- A sheet of connective tissue in contact with the dura mater and
2- A system of loosely arranged trabeculae containing fibroblasts and collagen.

This trabecular system is continuous with the deeper pia mater. Surrounding the trabeculae is a large, sponge-like cavity, the subarachnoid space, filled with CSF. This space forms a hydraulic cushion that protects the CNS from trauma. The subarachnoid space communicates with the ventricles of the brain. The connective tissue of the arachnoid is said to be avascular because it lacks nutritive capillaries, but larger blood vessels run through it. Because the arachnoid has fewer trabeculae in the spinal cord, it can be more clearly distinguished from the pia mater in that area. The arachnoid and the pia mater are intimate associated and are often considered a single membrane called the pia-arachnoid.
In some areas, the arachnoid perforates the dura mater and protrudes into blood-filled venous sinuses within the dura mater. These CSF-filled protrusions, which are covered by vascular endothelial cells, are called arachnoid villi. Their function is to transport CSF from the subarachnoid space into venous sinuses.

C- PIA MATER

The innermost pia mater is lined internally by flattened, mesenchymally derived cells closely applied to the entire surface of the CNS tissue, but this layer does not directly contact nerve cells or fibers. Between the pia mater and the neural elements is a thin limiting layer of astrocytic processes, which adheres firmly to the pia mater. Together the pia mater and glial layer form a physical barrier at the CNS periphery. This barrier separates the CNS tissue from the CSF in the subarachnoid space Blood vessels penetrate the CNS through tunnels covered by pia mater—the perivascular spaces. The pia mater disappears when the blood vessels branch to the smallest capillaries. However, these capillaries remain completely covered by expanded perivascular processes of astrocytes

2- PERIPHERAL NERVOUS SYSTEM

The main components of the peripheral nervous system are the nerves, ganglia, and nerve endings. Nerves are bundles of nerve fibers (axons) surrounded by glial cells and connective tissue.

Nerve Fibers

Nerve fibers consist of axons enclosed within a special sheath of cells derived from the embryonic neural crest. Like tracts within the CNS, peripheral nerves contain groups of nerve fibers. In peripheral nerve fibers, axons are sheathed by Schwann cells, also called neurolemmocytes . The sheath may or may not form myelin around the axons, depending on their diameter. Axons of small diameter are usually unmyelinated nerve fibers.Progressively thicker axons are generally sheathed by increasingly numerous concentric wrappings of the enveloping cell, forming the myelin sheaths. These fibers are known as myelinated nerve fibers

A- MYELINATED FIBERS

As axons of large diameter grow in the PNS, they are engulfed along their length by many undifferentiated neurolemmocytes and become myelinated nerve fibers. The plasma membrane of the covering neurolemmocyte (Schwann cell) fuses around the axon and becomes wrapped around the nerve fiber as the glial cell body moves around and around the axon many times . The multiple layers of Schwann cell membrane unite as a layer myelin, a whitish lipoprotein complex whose abundant lipid component is partly removed by standard histologic

procedures, as in all cell membranes . With the TEM the myelin sheath can appear as a thick electron-dense cover in which individual membrane layers are seen .
Membranes of Schwann cells have a higher proportion of lipids than do other cell membranes and the myelin sheath serves to protect axons and maintain a constant ionic microenvironment required for action potentials. Between adjacent Schwann cells the myelin sheath shows small nodal gaps along the axon, also called nodes of Ranvier Interdigitating processes of Schwann cells partially cover each node . The length of axon covered by one Schwann cell is called the internodal segment and may be more than 1 millimeter. Unlike oligodendrocytes of the CNS, Schwann cells only form myelin around a portion of one axon.

B- UNMYELINATED FIBERS

The CNS is rich in unmyelinated axons which are not sheathed at all but run free among the other neuronal and glial processes. However in the PNS, even all unmyelinated axons are enveloped within simple folds of Schwann cells . In this situation the glial cell does not form multiple wrapping of itself as myelin. Unlike their association with individual myelinated axons, each Schwann cell can enclose portions of many unmyelinated axons with small diameters. Adjacent Schwann cells along unmyelinated nerve fibers do not form nodes of Ranvier.

Nerves

In the PNS nerve fibers are grouped into bundles to form nerves. Except for very thin nerves containing only unmyelinated fibers, nerves have a whitish, glistening appearance because of their myelin and collagen content. Axons and Schwann cells of nerves are enclosed within connective tissue layers. Externally is a dense, irregular fibrous coat called epineurium, which continues more deeply to also fill the space between bundles of nerve fibers. Each such bundle or fascicle is surrounded by the perineurium, a sleeve of specialized connective tissue formed by layers of flattened epithelial-like cells. The cells of each layer of the perineurium are joined at their edges by tight junctions, an arrangement that makes the perineurium a barrier to the passage of most macromolecules and has the important function of protecting the nerve fibers and helping maintain the internal microenvironment. Within the perineurial sheath run the Schwann cell–covered axons and their enveloping connective tissue, the endoneurium . The endoneurium consists of a sparse layer of loose connective tissue that merges with an external lamina of type IV collagen, laminin, and other proteins produced by the Schwann cells.