

NEUROSCIENCE COURSE
MODULE 1

Module 1 :

FUNDAMENTAL CONCEPTS

For centuries, the brain's functions were attributed to the heart. Today, however, thanks to scientific and technological progress, we know a great deal more about the brain and the nervous system. Nevertheless, we are only just beginning to understand how they function, hence the growing interest in neuroscience, an area of study that relates to the organization and functioning of the nervous system.

It is impossible to talk about neuroscience without mentioning the nervous system. If we were to describe it, we could refer to it as the 'ultimate processor'. It is thanks to the nervous system that we are born, and that we can eat, breathe, move, think and love. It is also what puts an end to our existence by 'switching off' all our organs.

Medical and technological progress can allow us to survive even if several vital organs fail. It is now possible to replace a heart, liver, lungs, kidneys and limbs. This is not without constraints, but the person who receives the transplant remains alive. However, once the nervous system stops working, the person stops living.

Welcome to this course on neuroscience. This area of study that falls within medicine, psychology and biology is, as you can imagine, quite vast. As such, we have decided to only address cognitive neuroscience and its application, because its impact on everyday life is much more tangible.

Before we get to the heart of the subject, we're going to focus on the nervous system as a whole. How does it work? What are the functions of each of its organs? How are all these elements synchronized? How does their environment influence how they function? There are many questions to address. Let's begin by studying the neuroanatomy of the nervous system.

🌟 Neuroanatomy of the nervous system

The nervous system (NS) is composed of two parts:

- ◆ The central nervous system (CNS);
- ◆ The peripheral nervous system (PNS).

The nervous system controls the entire body through nerve impulses.

The central nervous system

The central nervous system is the information processing center. It is made up of four structures:

- ◆ the brain;
- ◆ the cerebellum;
- ◆ the brainstem, made up of the midbrain, the pons (formerly known as the annular protuberance) and the medulla oblongata (formerly known as the spinal bulb);
- ◆ the spinal cord.

There is another way of classifying the parts of the central nervous system. We refer to the cerebrospinal axis, which is made up of:

- ◆ the encephalon, composed of the cerebellum, brain and brainstem;

Module 1 :

FUNDAMENTAL CONCEPTS

◆ the spinal cord.

This is the best protected part of the nervous system. The encephalon is housed in the skull, while the spinal cord is found in the vertebral canal.

The central nervous system is protected by:

◆ the cerebrospinal fluid (CSF) located in the subarachnoid space;

◆ an envelope with three layers (membranes) called *meninges*:

- ❖ the dura mater, the outermost, resistant membrane,
- ❖ the arachnoid mater, the middle membrane,
- ❖ the pia mater, the inner membrane, which is thin and in direct contact with the surface of the encephalon and has a primarily nourishing role.

◆ the blood-brain barrier (BBB), a specialized cell system that lines the blood vessels in the brain; the BBB prevents the majority of the substances present in the blood from entering the brain.

If we were to compare the human body to a computer, the brain would be the hard disk. It is responsible for managing all the bodily functions directly or indirectly. It regulates the coordination of the different parts of the nervous system and all the organs, as well as communications with the outside world.

★ The encephalon

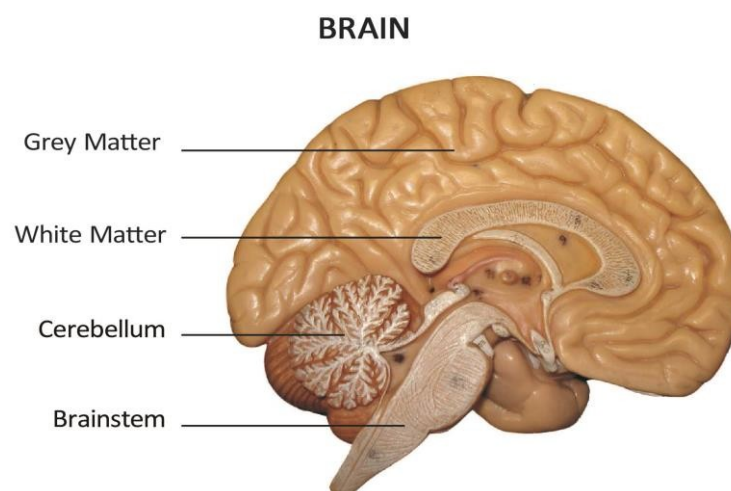
The encephalon is made up of several parts:

◆ the two hemispheres that form the telencephalon (the brain);

◆ the diencephalon, which is located in the center and groups together a set of structures;

◆ the cerebellum;

◆ the brainstem.



The encephalon controls all intentional behaviors, including:

◆ sleep;

Module 1 :

FUNDAMENTAL CONCEPTS

- ◆ thought;
- ◆ language;
- ◆ planning of projects or events;
- ◆ decision making;
- ◆ learning.

However, control of these functions is not localized to one single place. The brain is divided into two hemispheres, left and right, connected by a band of nerve fibers called the *corpus callosum*. It is also made up of several layers, just like the cerebellum and the spinal cord.

The first layer is known as the *cortex*. Also known as *gray matter*, this structure is made up of neuron bodies to which it owes its color. The surface of the cortex is increased thanks to its multiple convolutions, which increases its capacities considerably.

The hemispheres are not functionally symmetrical:

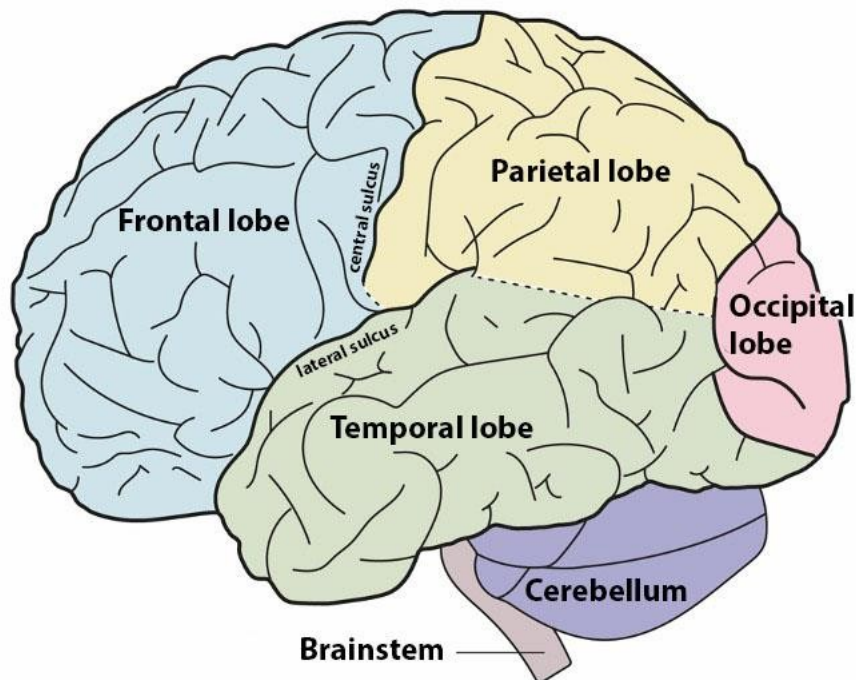
- ◆ The right hemisphere is more intuitive and emotional; it has better 3D perception than the left, and musical and artistic sensitivity.
- ◆ The left hemisphere is concerned with memory and symbolic (or abstract) thought; it is the center of logic and analytical and sequential reasoning.

Each hemisphere projects onto the opposite side of the body (contralateral) and is divided into several lobes:

- ◆ **The parietal lobe:** its functions are primarily somatosensory. The right parietal lobe is involved in coordinating spatial awareness, while the left lobe is more involved in understanding language (written and spoken).
- ◆ **The occipital lobe** (or visual center): this is where recognition of shapes, curves and colors takes place.
- ◆ **The frontal lobe:** this is responsible for many important functions. It is where the motor speech area (Broca's area) is located, and where many voluntary movements (of the skeletal muscles, ocular muscles) are controlled. It is also involved in higher-level cognitive tasks, like planning.
- ◆ **The temporal lobe:** this is involved in auditory processing and processing of certain visual information, more specifically in the recognition of objects, shapes and people. This lobe regulates the processes linked to short-term memory, and some language processing (for example comprehension, supported by Wernicke's area), hearing, sight, taste and emotions.

Module 1 :

FUNDAMENTAL CONCEPTS



We also distinguish between two internal lobes:

- ◆ **The limbic lobe:** which is the center of memory and certain emotions, including appetite, desire, survival instincts and sensations of pleasure.
- ◆ **The insular cortex:** which also plays an important role in regulating emotions and in homeostasis control phenomena.

It is also important to mention other structures that play a crucial role in ensuring the body functions properly. For example, the basal ganglia coordinate sensory information moving towards the cortex (this is true of the thalamus). One of these ganglions, the hypothalamus, is also responsible for controlling functions like sleep, appetite, and reproductive and defense processes.

The mesencephalon, or midbrain, mainly manages the auditory and visual reflexes, and is responsible for transferring these types of stimuli towards the thalamus. The neurons that control all the mechanisms related to mood and psychological rewards are located in the mesencephalon. It also manages vital functions, for example regulating the respiratory and cardiovascular centers, as well as involuntary motor functions. It also acts as a relay center, particularly with the cerebellum.

Also known as the hindbrain, the rhombencephalon is made up of the cerebellum, the annular protuberance (or pons) and the medulla oblongata (formerly known as the spinal bulb). This structure is primarily responsible for managing cognitive processes linked to coordination. It also regulates the heart rate and respiratory rate. This is also the area where Pavlovian responses are trained, more specifically in the cerebellum.

🌟 The spinal cord

The spinal cord is an extension of the brain, a set of nerve cells whose main function is to transmit nerve impulses from the cerebral cortex towards the peripheral nerves, and from effector organs

Module 1 :

FUNDAMENTAL CONCEPTS

(like the skin) towards the brain. This formation begins at the base of the skull, level with the medulla oblongata, and extends over almost the entire length of the spine, finishing at the second lumbar vertebra.

Around 50 cm long and 1 cm in diameter, it has two convex sections that are similar to the start of the limbs. The spine acts as a support to 31 pairs of spinal nerves. Just like the brain, it is made up of two substances:

- ◆ **Gray matter:** in the center and in the shape of an H: primarily made up of neuron bodies, it includes interneurons (mainly gathered in the dorsal horn) and motor neurons (mainly found in the anterior horn). In the center of the gray matter is a canal known as the ependyma, through which cerebrospinal fluid flows.
- ◆ **White matter:** made up of myelinated axons of neurons, it is responsible for transmitting nerve impulses. Its white color comes from the myelin that surrounds the axons.

The spinal cord is surrounded by three envelopes known as *meninges*, the main function of which is to protect it. It acts as an intermediary; it transmits information and nerve impulses not only from the brain to the different organs, but also from the outside and from these organs towards the brain. As such, it has two types of pathways:

- ◆ motor pathways;
- ◆ sensory pathways.

There are two motor or descending pathways:

- ◆ the pyramidal tract, which is responsible for voluntary motor functions. It begins at the cerebral cortex, goes through the brainstem and finishes at the end of the spinal cord.
- ◆ the extrapyramidal tract, which is responsible for involuntary/automatic movement regulation

Damage to the nerves involved in these two formations leads to paralysis or sclerotic states.

The sensory or ascending pathways begin level with the spine and finish in the cerebellum and brain. These pathways are divided into three categories:

- ◆ the spinocerebellar pathways, which serve primarily to transfer unconscious proprioceptive nerve impulses from the muscle system to the cerebellum;
- ◆ the extralemniscal pathways, which serve to transmit thermal and painful nerve impulses. They send the information they receive to the brain;
- ◆ the lemniscal sensory pathways, which transmit nerve impulses linked to pallesthesia, baresthesia, fine tactile sensitivity and conscious proprioceptive sensitivity.

The peripheral nervous system

The peripheral nervous system is made up of all the cranial and spinal nerves, as well as glands. It is divided into two parts:

- ◆ the autonomic nervous system;

Module 1 :

FUNDAMENTAL CONCEPTS

✦ the somatic nervous system.

✦ The autonomic nervous system

Also known as the “vegetative system”, the autonomic nervous system controls all the automatic and unconscious functions. As such, it plays a decisive role in ensuring the body functions properly. It governs everything: body temperature, respiration, the different kinds of secretions, digestion, water balance, and many other automatic functions. It is made up of two parallel systems: the parasympathetic system and the sympathetic system.

✦ The parasympathetic system

This controls the body’s involuntary activities when at rest, such as all the processes linked to digestion (stomach, biliary, pancreatic secretions, etc.). It is also responsible for regulating the heart rate, blood pressure and respiration, to name but a few. The centers of the parasympathetic system are located level with the sacral spinal cord and brainstem.

✦ The sympathetic (or orthosympathetic) system

This system has the same functions as the parasympathetic system but, unlike the former, it is mainly active when the body is in a waking state or a state of stress. The sympathetic system is particularly involved in stimulating the organs involved in the body’s defenses. In the event of danger, for example, it accelerates the heart rate, controls the muscles and improves respiration to prepare the body for ‘flight’.

The functions of this system are antagonistic to those of the parasympathetic system. The nerve centers in the sympathetic system are organized in a segmentary manner. It is based on a system with two neurons: the preganglionic neuron, located in the spinal cord, is connected to the postganglionic neuron, which is positioned on the organ tissue, via a synapse.

There is one final system to mention that is exclusively responsible for managing the activities of the digestive system: the enteric nervous system.

Overall, the vegetative system rests on three pillars. At the base are the nerve centers located in the central nervous system. Then come the peripheral ganglia, which are also divided into three categories:

- ✦ The first encompasses the paravertebral sympathetic chain (which extends from the base of the cervical segment to the coccygeal segment of the spine) and the superior, middle and inferior cervical ganglions.
- ✦ The second is made up of previsceral ganglions. Note that the term “ganglions” is not entirely suitable to describe these formations; they are more like ganglionated plexi than simple ganglions. In the neck region, they are found in even numbers: for example, the pharyngeal and carotid plexi. In the pelvis, abdominal and thorax regions, however, they are found in odd numbers: the pulmonary, cardiac, paraaortic and solar plexi.
- ✦ The third category is made up of the terminal ganglia, also known as “visceral ganglia”. They are found on the surface of the organ and mark the end of the chain.

The third pillar of the vegetative system is made up of fibers that act as a connection between the innervated organ and this system’s nerve center. Very often, the nerve fibers in the autonomic

Module 1 :

FUNDAMENTAL CONCEPTS

nervous system are located near those of the somatic nervous system. They are mainly positioned along the blood vessels.

✦ The somatic nervous system

The somatic nervous system acts as a link between the central nervous system and the body's environment thanks to two types of nerve fibers:

- ✦ The afferent nerve fibers (sensory nerve fibers), which receive stimuli through their sensory receptors and transmit information to the central nervous system via the sensory nerves.
- ✦ The efferent nerve fibers (motor nerve fibers), which transport information from the central nervous system to the organs or muscles.

These orders are controlled by a feedback system that enables the central nervous system to be informed of the new state of the organ or muscle in question.

There are two categories of afferent nerve fibers:

- ✦ visceral fibers, which are attached to the viscera;
- ✦ somatic fibers, which are connected to the receptor organs in the skin, muscles and joints.

Note, however, that the nerve fibers in the somatic system are usually mixed, i.e., the nerves are made up of both sensory and motor fibers. It is also not uncommon for these nerves to include nerve fibers from the autonomic nervous system.

Generally, there are two types of somatic nerves:

- ✦ cranial nerves;
- ✦ spinal nerves.

There are twelve cranial nerves and they are either sensory or motor. The sensory nerve category includes:

- ✦ the olfactory nerve (I);
- ✦ the optic nerve (II);
- ✦ the vestibulocochlear nerve (VIII).

The motor nerve category includes:

- ✦ the oculomotor nerve (III);
- ✦ the trochlear nerve (IV);
- ✦ the abducens nerve (VI);
- ✦ the accessory nerve, formerly known as the spinal nerve (XI);
- ✦ the hypoglossal nerve (XII).

Some cranial nerves are made up of both motor and sensory fibers. These nerves include:

- ✦ the trigeminal nerve (V), which includes the ophthalmic, maxillary and mandibular nerves;
- ✦ the facial nerve (VII);

Module 1 :

FUNDAMENTAL CONCEPTS

- ◆ the glossopharyngeal nerve (IX);
- ◆ the vagus nerve (X).

The spinal nerves (which are all mixed) are classified based on the section of the spine to which they are connected. Thus, there are five main groups of spinal nerves:

- ◆ the cervical nerves: eight pairs located between C1 and C7;
- ◆ the thoracic nerves: twelve pairs positioned between T1 and T12;
- ◆ the lumbar nerves: five pairs located between L1 and L5;
- ◆ the sacral nerves: five pairs situated between S1 and S5;
- ◆ the coccygeal nerve: this vestigial nerve is found at the CO.

The spinal nerves transmit nerve information from the spinal cord to the joints, muscles and skin. The cranial nerves act as the connection between the central nervous system and almost all the rest of the entire body (from the head to the internal organs).

The neuron: definition and function

The neuron is the basic unit of the nervous system and is both structural and functional. This cell is responsible for both emitting and transmitting nerve signals. Neurons owe their capacity to transmit and analyze electrical signals to the proteins that regulate the ion channels. Nerve cells can also secrete the neurotransmitters they use to transmit nerve impulses. This secretion is specific: it only targets the cells to which the neurons are connected.

With a few exceptions, neurons are different to the other cells in the body. They are amitotic (apart from in some exceptional cases) and, unlike the majority of cells, display remarkable longevity as a result. Their regeneration process is complex. We recover from an injury easily, however deep it may be, as long as it is not fatal. However, an injury to the nervous system not only has fatal consequences, but will also require specialist care.

Another specific characteristic of neurons is the unmatched speed at which their metabolism functions, which requires a very high supply of oxygen and glucose.

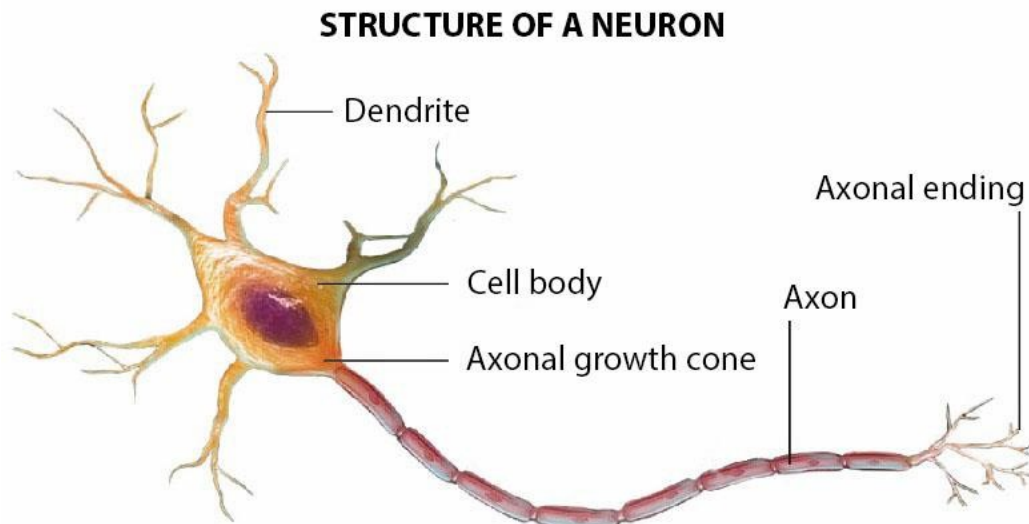
Neurons are made up of three parts:

- ◆ Dendrites: a neuron may have one or several of these. These extensions serve to transmit the nerve impulses from synapses to the cell bodies. Dendrites often have an irregular appearance due to the presence of “dendritic spines” on the surface of this formation.
- ◆ Axon: unlike dendrites, there is always only one axon. However, it can branch out to make contact with other cells. This structure serves to transmit nerve impulses from the cell body to the synapses. Its length can vary from 1 mm to 1 m. Axons are what form white matter. Unlike dendrites, they are smooth in appearance, and have a uniform diameter across their entire length. They are sometimes covered with a myelin sheath.

Module 1 :

FUNDAMENTAL CONCEPTS

◆ Cell body: this is made up of the nucleus and cytoplasm. Note that the neuron is only found within the gray matter. Sometimes several cell bodies form a compact mass that makes up a new structure called a ganglion.



Neurons have two main properties. The first is excitability, as a result of which they can become polarized or depolarized depending on the circumstances. In short, excitability is the capacity to develop an action potential. The second property is conductivity. This is what enables the neuron to transmit or receive information sent to it, and without losing any of it along the way. Information flows in one direction along a neuron, from the dendrites to the axonal endings.

The cell body and dendrites constitute the receptive base of the nerve cell due to the multiple synaptic connections established with other neurons. They receive and process afferent messages and generate electrical signals (postsynaptic potentials) towards other neurons or efferent organs (efferent message) in response.

There are three categories of neurons: afferent (or sensory), efferent (or motor) and associative. Their classification is closely linked to their function.

★ Afferent (or sensory) neurons

Afferent neurons transmit nerve information from the sensory receptor to the central nervous system. The sensory body of this neuron is located outside of the central nervous system, in the ganglion. Its dendrites are always weakly branched and connected to the sensory receptors. The axon, meanwhile, is connected to the associative neuron.

★ Efferent (or motor) neurons

Efferent neurons transmit information from the central nervous system to the effector organ. The cell body of this neuron is always located in the central nervous system. Information flows in one direction along a neuron: from the dendrites to the axonal endings. Unlike the previously mentioned neuron, its dendrites have many branches; they are connected to the associative neuron as well as the effector organ.

Module 1 :

FUNDAMENTAL CONCEPTS

★ Associative neurons

As its name suggests, the associative neuron creates associations between other neurons. It transmits information exclusively within the central nervous system. Like the efferent neuron, the cell body of the associative neuron is found within the central nervous system. Its dendrites are highly branched and are in contact with sensory neurons or other associative neurons. Meanwhile, the axons are linked to motor neurons or other associative neurons.

Neuromodulators and neurotransmitters

There are several types of chemical substances that are responsible for transmitting nerve impulses. They are divided into neuromodulators and 'classical' neurotransmitters.

★ Classical neurotransmitters

Neurotransmitters are chemical substances produced by the body and that serve to facilitate the transmission of nerve impulses, either between neurons or from neurons to other cells in the body. Neurotransmitters' action is closely linked to the physiology of the function of the postsynaptic cell. This means that a neurotransmitter provokes different reactions depending on the environment in which it acts.

Chemical substances that have the following properties are considered classical neurotransmitters:

- ◆ must be synthesized in the presynaptic element and stored in the vesicles of its endings;
- ◆ must only be released into the synaptic cleft as a response to excitation of the presynaptic neuron;
- ◆ must have specific postsynaptic ionotropic or metabotropic receptors that act on the transmembrane polarity by modifying it or causing a form of switching;
- ◆ must be able to degrade or be inactivated in the presynaptic space.

There are four categories of classical neurotransmitters:

- ◆ monoamines, derived from amino acids, for example catecholamines are derived from tyrosine; serotonin is produced thanks to tryptophan; GABA is produced by glutamic acid; histamine is synthesized from histidine;
- ◆ amino acids, including glycine and glutamic acid;
- ◆ other chemical substances, like adenosine or acetylcholine.

It is important to note that some hormones can play the role of neurotransmitters. Conversely, some neurotransmitters can behave like hormones. Substances in this final category are called neurohormones.

★ Neuromodulators

Neuromodulators are chemical messengers that do not directly transmit nerve impulses. Instead, they modulate the strength, probability, or timing of synaptic transmission across broader networks of neurons. They are released by neurons (and sometimes glia), often outside the classic synaptic cleft, and act via slower, longer-lasting pathways (commonly G-protein-coupled receptors).

Module 1 :

FUNDAMENTAL CONCEPTS

can be elements that are completely foreign to the human body. Also note that the system for transmitting information is different to that of neurotransmitters.

In this instance, the chemical substance found in the endings starts to act after the neuron has been depolarized and is completely annihilated once its action is completed. Furthermore, these substances always act on several groups of neurons, and not in a selective manner, like neurotransmitters do.

In short, neuromodulators are not directly involved in transmitting nerve impulses. Rather, their primary function is to cause classical neurotransmitters to be synthesized, inhibited or recaptured. The list of examples of neurotransmitters and neuromodulators that follows is, of course, not exhaustive.

Examples of neurotransmitters and neuromodulators

★ Acetylcholine

Acetylcholine was the first neurotransmitter to be identified, in the early 20th century. It acts on a host of neurons in the central nervous system in an excitatory or inhibitory manner. Acetylcholine is synthesized from acetyl coenzyme A and choline, in the axonal endings. It acts primarily on the muscle cells.

In addition, this neurotransmitter plays a significant role in regulating sleep, memory, sexuality, thirst and attention. It is also a very common excitatory neurotransmitter that causes muscle contraction and stimulates the excretion of certain hormones. The elimination of acetylcholine is performed by acetylcholinesterase and takes place in the synaptic cleft.

★ Amino acids

Also known as the body's 'building blocks', amino acids are at the heart of the synthesis of many different proteins. Those that also fulfil the functions of neurotransmitters include GABA (gamma-aminobutyric acid), glycine and glutamic acid.

◆ GABA (gamma-aminobutyric acid)

In the adult brain, GABA plays a primarily inhibitory role. In the immature brain, however, it has a more excitatory function. It mainly acts on the neurons in the cortex and is involved in motor control of vision and several cortical functions. This amino acid is the target for benzodiazepines and increases their inhibitory action. The same is true of anticonvulsant drugs.

◆ Glycine

This chemical substance is found in all the body's tissues. It is synthesized from serine. It acts on two groups of receptors: receptors with a pentameric structure and NMDA receptors. It is involved in both the peripheral nervous system and the central nervous system. Glycine is what contributes to the relaxation of the antagonistic muscles, for example.

◆ Glutamic acid

Module 1 :

FUNDAMENTAL CONCEPTS

This is one of the most important excitatory neurotransmitters in the human body. Its action is restricted to the central nervous system. It is part of the family of amino acids that are a component of proteins. The body's production of this amino acid decreases considerably with age.

★ Biogenic amino acids

These substances synthesized by decarboxylation, amination or hydrolysis are involved in many bodily functions. Out of all the biogenic amino acids, the most important neurotransmitters are histamine, serotonin and tryptamine.

◆ Serotonin

This substance is found in a particularly high concentration in the brain and blood platelets. It has a significant impact on sleep quality, appetite, sexuality and emotional states (depression, anxiety).

◆ Tryptamine

This substance is mainly found in trace amounts in the body. Its scope of action is restricted to the central nervous system.

◆ Histamine

This biogenic amino acid acts as both a neurotransmitter and a hormone. It regulates sexuality, sleep and the immune system, and controls certain functions of the digestive system.

★ Catecholamines

These chemical substances constitute a subcategory of biogenic amino acids. They include noradrenaline, adrenaline and dopamine.

◆ Dopamine

This neurotransmitter is found in extremely high levels in the central nervous system, and more specifically in three neural circuits: the endocrine, dopaminergic and nerve circuits. Dopamine has a significant impact on sleep, mood and the process of natural motivation. It is also involved in coordination of movements.

◆ Adrenaline

This biogenic amino acid is both a hormone and a neurotransmitter with a specific action. This chemical substance is secreted in the brain by the chromaffin cells and acts on the androgenic receptors. It is almost always produced in response to a state of stress. It increases the body's physical capacities to facilitate its reaction (rapid increase in blood pressure as a result of an increase in heart rate, lung expansion, etc.).

◆ Noradrenaline

Like dopamine, there is a high concentration of noradrenaline in the central nervous system. Its action extends to both the central and peripheral nervous system. It is involved in regulating functions linked to sleep, alertness, learning, awareness, emotions and libido, but is primarily connected to learning and memory. As such, a decrease in the concentration of noradrenaline has disastrous repercussions on learning abilities.

Module 1 :

FUNDAMENTAL CONCEPTS

★ Hormones

Very often, the endocrine system is just as important for cell communication as the central and peripheral nervous systems. However, unlike the latter two systems, it relies on hormones to play the role of neurotransmitters. In addition, hormones also act like neurotransmitters outside of the endocrine system. These chemical substances have a vast scope of action. They are involved in:

- ◆ learning;
- ◆ sexuality (ovulation, erection, etc.);
- ◆ attention;
- ◆ weight gain or loss;
- ◆ activation of the immune system;
- ◆ pain;
- ◆ energy metabolism;
- ◆ the memorization process;
- ◆ emotional regulation.

This is not an exhaustive list. Adrenaline, oxytocin, serotonin and dopamine are all hormones that are involved in the functioning of the body.

★ Neuropeptides

Neuropeptides are chemical substances secreted by neurons and fulfil the role of neurotransmitters. There are more than one hundred neuropeptides, which are classified into several broad categories:

- ◆ calcitonins (CGRP);
- ◆ tachykinins (neurokinins A, B and K, and substance P);
- ◆ inhibiting and releasing hormones from the hypothalamus (corticoliberin or CRH, gonadoliberin or GnRH, somatoliberin or GHRH, somatostatin, thyrotropic hormone or TRH);
- ◆ hypothalamic hormones (vasopressin, oxytocin);
- ◆ VIP-glucagon (GLP-1, PACAP, VIP);
- ◆ neuropeptide Y (NPY, PYY, PP);
- ◆ opioid peptides (dynorphin, leu-enkephalin, met-enkephalin);
- ◆ various neuropeptides (ARP, bradykinin, melanin-concentrating hormone or MCH, cholecystokinin, neurotensin, galanin, orexin, orphanin FQ).

Each of these peptides has a particular mechanism of action. However, it is important to recognize that the function of some of them remains a little unclear. This is true, for example, of the opioid peptides: several studies have sought to clarify the mechanism of action of opioids to assist the development of new therapeutic medicines.

For others, the mechanism of action is no longer in doubt. Substance P, for example, is a stimulator that plays an important role in our perception of pain. The action of endorphins and enkephalins is

Module 1 :

FUNDAMENTAL CONCEPTS

also linked to pain regulation. They are natural analgesics that act on the central nervous system to inhibit the sensation of pain. They are also referred to as endogenous opioids.

★ Gases and atypical neurotransmitters

Generally speaking, these substances are not stored in the presynaptic vesicles. They pass through the membranes by simple diffusion to act on the neurons. The most common are:

- ◆ carbon monoxide (CO);
- ◆ nitric oxide (NO).

Carbon monoxide acts in both the central nervous system and the peripheral nervous system. In the former, it is responsible for regulating the emission of hormones from the hypothalamus. In the latter, it acts as an inhibiting agent on the cells of the intestinal smooth muscle.

Nitric oxide is mainly active in the autonomic peripheral system. It is involved in smooth muscle relaxation (gastrointestinal tract, airways). It also plays an important role in the erection process. Indeed, it is one of the active principles of Viagra. The latter inhibits the action of phosphodiesterase E5 (PDE5), an enzyme that is responsible for the degradation of cyclic guanosine monophosphate (cGMP), a second intracellular messenger of nitric oxide (NO).

Add to these the trophic factors, secondary messengers and lipid messengers:

- ◆ Trophic factors are small proteins that are synthesized in the nerve cells. They act locally on specific receptors.
- ◆ Lipid messengers are substances synthesized from lipids found in the cell membranes. They have an extremely powerful but short-lived effect. There is a second category of lipid messengers with an inhibitory action, which act primarily on the immune system.
- ◆ Secondary messengers are molecules that convert the signal coming from outside the cell to the inside or surface of the latter.

Generation and formation of nerve connections

We are not looking to discuss neurogenesis in minute detail here. It is simply about understanding the main features of this process in order to better grasp how the central nervous system functions, and to see how to deal with, or at least mitigate, developmental disabilities, injuries and other conditions affecting the central nervous system.

Nowadays, a large number of studies are carried out to understand how to help people suffering from spinal cord injuries. Valuable information is obtained through these studies to help improve the neural capacities and, by the same token, the functioning of the brain.

★ Nerve connections

The mechanism of neurogenesis occurs relatively late. It only begins after the regionalization stage. Formation takes place as follows: first, we observe the release of neurons, followed by axonal navigation. The multiple axons of each neuron are programmed to establish precise connections. We refer to axons in the plural because each neuron emits as many axons as possible.

Module 1 :

FUNDAMENTAL CONCEPTS

To ensure the operation is successful, each axon has a growth cone at its tip that attracts the target cell and repels the inappropriate cell. After contact has been established, next comes the maturation stage for the circuits generated. This process is regulated by a strict pattern of connections.

To avoid the occurrence of errors, the embryo sends guidance signals to help the neurons select the right target. They are either repulsive or attractive. There are two main categories of guidance signals: chemotropic signals and chemoaffinity signals.

Each chemotropic signal has a receptor. UNC and DDC receptors only react to netrins. Plexins and neuropilins are sensitive to semaphorins. Robo receptors respond to Slit signals. The Slit proteins (Slit1, Slit2, Slit3), discovered in 1993, have been historically described for their key role in the development of the nervous system. There are also several factors described as morphogenetic, to which a large number of receptors react.

Chemoaffinity signals have a different mechanism because the guidance cells are located on the cell membranes. They are also more powerful than chemotropic signals. The two main signals of this type are ephrins and semaphorins. The former act on ephedrine receptors, while the latter act on plexins.

Neurons maximize connections by sending axons towards as many targets as possible. This mechanism is known as the *initial exuberance phenomenon*. Neurons create far more connections than are necessary for the body to function in an optimal manner. Unnecessary connections are then eliminated gradually. This process takes place during the embryonic stage and continues after birth.

As such, during the embryonic stage, we witness a cellular remodeling process. This is a destruction mechanism during which we observe a weakening of the excess axons and their cytoskeleton. At birth, babies have a much higher number of synaptic connections than adults. After the learning process begins, the body eliminates the excess connections and enhances the important connections.

✦ Adult neurogenesis: myth or reality?

As we gain a better understanding of the process of neurogenesis in adults, hopes are being raised in the scientific community. Indeed, if the nervous system is able to make new cells after birth, this means that many illnesses that are currently incurable (like degenerative diseases) could be treated.

Prior to the mid-20th century, no scientist would have dared to question the axiom that neurogenesis only occurs in embryos. In the 1960s, however, new studies began to cast doubt over what had seemed to be a given. Studies conducted by Joseph Altman hinted at the possibility that neurogenesis phenomena even occurred in adults.

His hypothesis was supported in 1980 by the work of Fernando Nottebohm. His studies, conducted on adult birds, demonstrated clearly that the process was far from being over at birth. In the 1990s, Elizabeth Gould's experiments carried out on rodents corroborated earlier research. All these studies triggered a revolution in the scientific world. Many people hoped that adult neurogenesis could be activated by antidepressants.

Studies conducted by Fred Gage and Jonas Frisén in the early 2000s strengthened this hope. They found that adult neurogenesis did not only occur in animals, but also in humans. However, all these studies are far from ideal, and many people have detected errors and discrepancies in them. That being said, they seem too minute to be taken into consideration.

Module 1 :

FUNDAMENTAL CONCEPTS

In a study conducted by Arturo Alvarez-Buylla and published in the journal *Nature*, one sentence caused a scandal; it stated that “hippocampal neurogenesis drops sharply in children to undetectable levels in adults”. This sentence alone contradicted all previous findings.

This researcher reached the conclusion that the neurogenesis process remains active in children, and even in adolescents, but is not detectable in adults; and even if it did take place, it would be virtually insignificant and would only exist in the form of traces that would not be worth considering.

Unlike earlier studies, those conducted by Arturo Alvarez-Buylla were extremely meticulous and it is hard to question their findings. However, this doesn't mean that we should abandon the idea of adult neurogenesis definitively. Analysis techniques are far from perfect, and it is not impossible that future studies might produce completely opposing results.

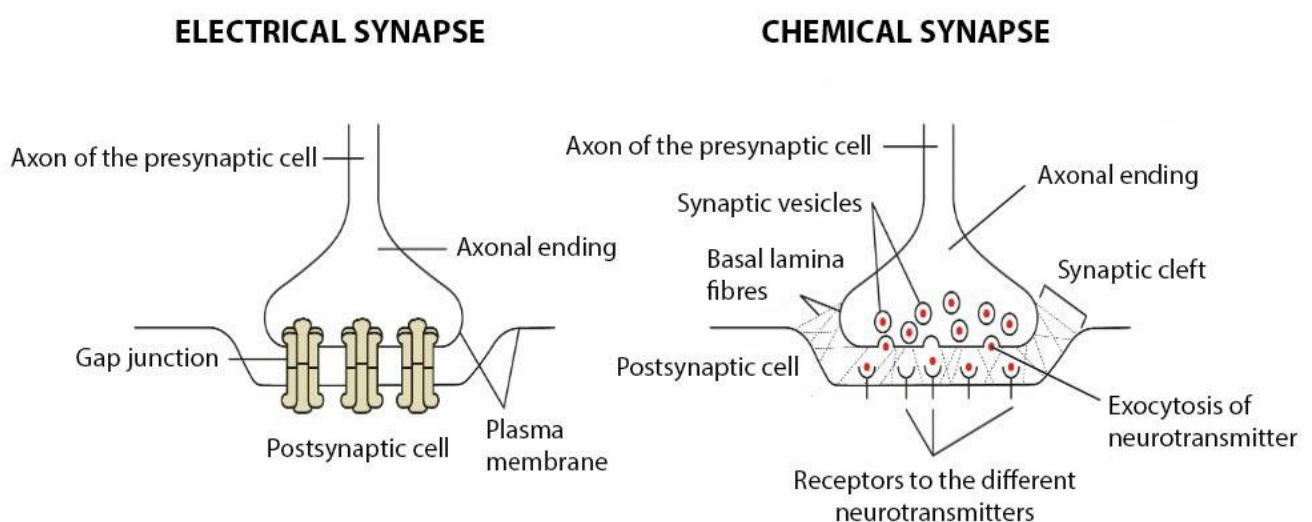
Adult neurogenesis has now been clearly demonstrated in a number of mammals. A recent article unequivocally noted the presence of adult neurogenesis (“Adult hippocampal neurogenesis is abundant in neurologically healthy subjects and drops sharply in patients with Alzheimer's disease”, *Nature Medicine*, vol. 25, p. 554-560, 2019).

Another study has shown that many cells are produced in the hippocampus in adults, and that this occurs throughout individuals' lives (“Dynamics of hippocampal neurogenesis in adult humans”, *Cell*, vol. 153, no. 6, p. 1219-1227, 2013).

As such, adult neurogenesis is neither a myth nor a reality, but rather something that should be followed closely for new developments.

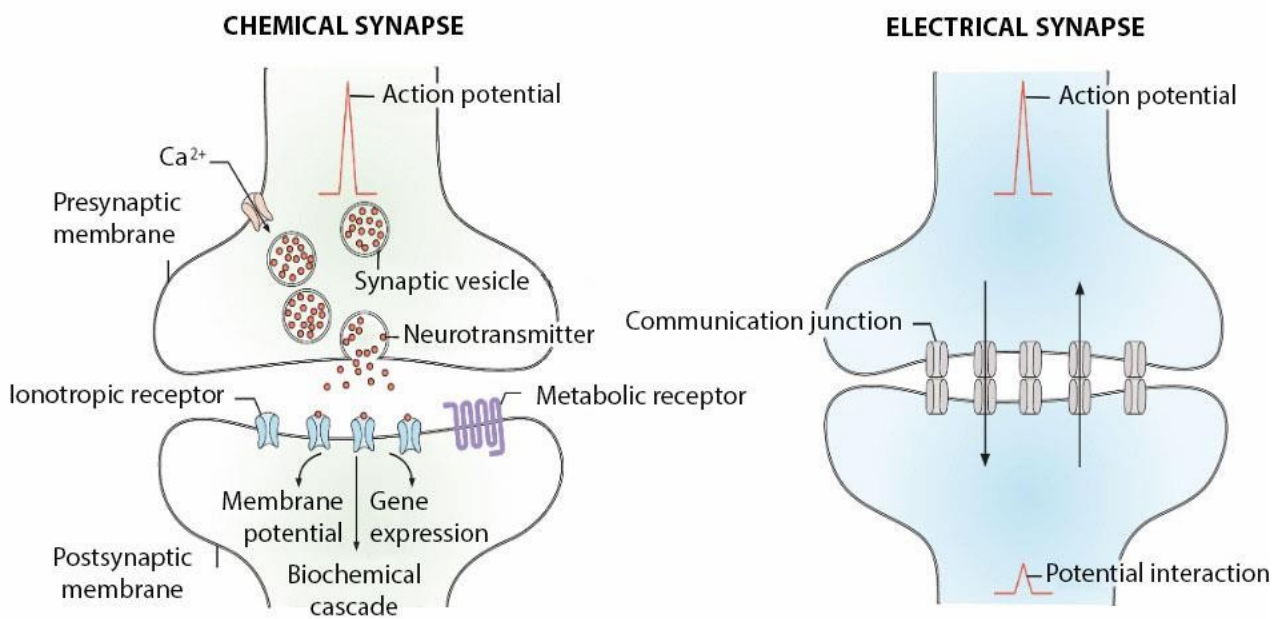
★ Concept of synapses and the different types of synapses

The transmission of nerve impulses requires the movement of said information from one cell to another. The neuron that disperses the information is described as presynaptic, and the neuron that receives it is the postsynaptic neuron. Synapses are not points of contact. A few examples of this do exist, but they are relatively rare; the only synapses that are in physical contact are electrical synapses.



Module 1 :

FUNDAMENTAL CONCEPTS



In most cases, synapses are split into two categories:

- ◆ electrical synapses;
- ◆ chemical synapses.

✦ Electrical synapses

Electrical synapses are contact surfaces through which nerve impulses are transmitted. On these synapses, we see the ion channels of the two connected neurons: the pore of one ion channel is adjacent to that of one ion channel on the other neuron. Thus, the two pores fuse to form just one. Together, they constitute a communication junction. These junctions can open and close, like all ion channels.

These communication junctions have the advantage of being remarkably efficient: information is transmitted from one cell to another at a very high speed, and without the slightest fatigue. However, they have one major drawback: electrical synapses are primarily bidirectional.

This is why, in most cases, their primary function is to synchronize the activity of the different neurons. Let's take the synapses involved in managing the respiratory rate and brain rhythm as an example. In all vertebrates, including humans, the percentage of these synapses is very low.

✦ Chemical synapses

Here, transfer of information takes place through chemical substances or, to be more precise, neurotransmitters. The latter influence the postsynaptic neurons to ensure data is transferred. In fact, neurotransmitters do not act directly on the neurons, but rather on the surrounding cells. Chemical synapses can be:

- ◆ **axodendritic**, when they connect one axon to one dendrite;
- ◆ **axoaxonic**, when they connect two axons;

Module 1 :

FUNDAMENTAL CONCEPTS

- ◆ **axoextracellular**, if the connection takes place between the axon and an extracellular environment;
- ◆ **axosomatic**, when they connect the axon to the cell body of a different neuron;
- ◆ **axosecretory**, when neurotransmitter secretion takes place in the blood with the aim of acting on a specific organ. For example, the pituitary gland controls the production of growth hormone (which stimulates growth) or those that control sexual development.

The notion of plasticity

Plasticity, or more precisely neuroplasticity, is the brain's ability to adapt to the environmental conditions to which it is exposed. There are two types:

- ◆ synaptic plasticity;
- ◆ compensatory plasticity.

Classification is also performed based on the adaptation mechanism. Thus, we distinguish between experience-dependent and experience-expectant neuroplasticity. Let's have a few reminders before getting to the key point.

At birth, the nervous system is regulated by reflexes. Babies cry to show their fear and suffering or to draw attention to their needs. Gradually, children learn to recognize their family and those around them, and then to move around, speak, etc. Learning is closely linked to the information they receive, but also to the environment they live in.

Ultimately, it doesn't matter if the adult child does not use all the information received previously. Even if it becomes obsolete, it will still have contributed towards sculpting their brain. During childhood, all the phases of learning contribute towards synapse formation; the more information to remember, the greater the number of synapses.

But what happens in adulthood? The principle remains the same. The nervous system receives new information and adapts. However, a problem arises: neurogenesis. Many theorists rely on this concept to argue that neuroplasticity is colossal.

There is no doubt that neurons regenerate in children. However, things become more complicated in adults. Renewal of their nerve cells is not an absolute certainty, so it is impossible to guarantee that neuroplasticity in the latter depends partly on neurogenesis. Thus, we rely solely on the brain's ability to adapt.

Nevertheless, it is important to understand that the process of neuroplasticity is not exclusively associated with the growth of the synaptic network; it is also linked to eliminating obsolete connections.

★ Synaptic plasticity

This type of plasticity has generally been described in changes on the pre- and postsynaptic levels. The principle is simple: every time the brain needs to store a new type of information, it constructs the appropriate neuronal connections. The more information there is, the more connections it has to create. As such, the behavior of the synapses is similar to that of the muscles. The network

Module 1 :

FUNDAMENTAL CONCEPTS

develops as much as is necessary, as long as the brain employs them actively. Note that the more synapses there are, the easier it is to learn.

Let's take a simple example. You listen to a tune you've never heard before for the first time. After a few minutes, you listen to it a second time, and the melody is already more familiar to you. If it is played constantly in your environment and you like it, it will only take you a few days to learn this tune by heart, but also, with a little effort, to get to know other pieces of music by the same artist. Synaptic plasticity forms the basis of the brain's malleability.

★ Compensatory plasticity

To be more precise, we can describe this as functional compensatory plasticity. The notion of compensation involves a prior loss. Neurological decline is an inevitable stage that comes with aging. As we age, we become weaker in all senses of the word. Our sight, hearing and muscle strength decline, as does our brain function.

If we look closely at the results of neurocognitive testing, we soon understand that the success rate is by far the highest in young people. However, the human brain always tends to compensate for its weaknesses. As a result, it tries to optimize the neural network and relies on zones that younger people do not need to call upon.

Ultimately, the brain often manages to activate more areas than in young adults, or even both hemispheres at the same time (like children do) to offset the decrease in the capacities of the normal neural pathways. The mechanism of compensatory plasticity is particularly useful for people with neurodegenerative diseases.

★ A few words on postlesional plasticity

The mechanisms of neuroplasticity are very often used to overcome trauma and injuries. It is about tackling problems and restoring the individual's faculties, at least in part.

The progression of medical treatment will depend on the nature of the injuries, their extent and the patient's age. It will also depend on the stage of development of the structure involved and the functional stimuli it can receive, taking into account the notion of the critical period during which the stimuli remain operational.

Generally, we rely on three mechanisms to overcome, or at least reduce, the impact of a trauma and start the recovery process. These are:

- ◆ mechanisms to repair the neural circuits;
- ◆ substitution mechanisms that activate systems that are normally not used or underused;
- ◆ compensatory processes that correspond to the progressive recovery of the 'normal' level of function of the structures under the influence of the damaged area and that are temporarily inactivated.

If we analyze this recovery process from a cellular perspective, we can say that its success is linked to:

- ◆ the reorganization of afferents through axon sprouting and reactive synaptogenesis;

Module 1 :

FUNDAMENTAL CONCEPTS

◆ compensatory neural adaptation through overactivation of the preserved afferents and proliferation of the postsynaptic receptors through denervation hypersensitivity, reactive phenotypic changes.

How to improve neuroplasticity

Training the brain and increasing its capacities is much easier than we might think. Here's a simple exercise to try.

Take two groups of five children aged 2 to 3 years.

Make sure that they don't already know how to count, because the aim is to teach them to count from 1 to 10 as quickly as possible.

★ First group

Each of the children in the first group receives some rods, a sheet of paper, colored pencils and a little piano.

They are asked to associate each number with a note and a colour. The instructor says "One" and places one rod in front of the child. The child then has to do a small drawing with a specific colour, and only this color, then press one of the piano keys while repeating out loud: "One." The process is repeated for the number "two", and so on until they reach the number ten.

★ Second group

The exercise remains the same, but the child only has rods this time. The instructor says "One" and places a rod in front of the child. Then they say "Two", and give them two rods, and so on. The only thing the child needs to do is remember the numbers.

★ Results

The children in the first group will retain the numbers quicker and make fewer mistakes when asked to repeat what they have learnt. Meanwhile, the children in the second group will need more time to retain the same numbers.

We can use the same experiment for learning to dance, sing or play a game and the result will remain the same. The plasticity of the brain is closely linked to the environmental stimuli to which it is exposed.

In the above example, the children in the first group will not only retain the numbers; being exposed to several stimuli pushes their brain to increase the number of connections dealing with the subject, for example '5, the color blue and the note *la*'. The child may eventually forget the number, but the color and note will act as anchors. Thus, it will be easier for the child to remember the information than it will be for a child who only has to listen to what the instructor says.

Another example involves the use of art therapy with children with intellectual disabilities or people with brain defects. Creative activities are not the only kind that can improve neuroplasticity; manual activities and sport also contribute significantly. Note that the things that increase plasticity are not the same for everyone; they are linked to the individual's age and environment. However, this doesn't mean that the inductive environment must always be positive and bright.

Module 1 :

FUNDAMENTAL CONCEPTS

Sometimes the brain is led to improve its neural network and synaptic plasticity in order to acquire the skills and faculties necessary for its survival. In everyday life or as part of conventional therapy, the subject's preferences should always be considered when selecting the inductive technique.

Conclusion

The nervous system in general is an extremely complex structure that still harbors many secrets. Just a century ago, the notion of being able to move an object through the power of thought seemed unthinkable and like something from a work of science fiction. Now, however, this is the exact principle that is used when creating high-quality prostheses. If it is not possible for an individual to have a hand, arm or leg transplant, they receive a bionic limb that they can control as if it were real.

It would have also been impossible to help people with brain injuries just a few years ago. By associating neural imaging capacities to different scales (macroscopic, microscopic, nanoscopic) and static or dynamic, researchers have been able to increase understanding of how the brain functions considerably.

Thus, we cannot begin studying neuroscience without first having a basic reminder about the nervous system and how it functions. We will then go on to examine important elements of cognitive neuroscience, such as memory, attention, language and emotions.