Nervous system

Components

Figure 1 The nervous system.

The nervous system is the central nervous system (CNS) - the brain and spinal cord, and the peripheral nervous system (PNS) - nerves connecting to the CNS and serving the body.

The PNS is divided into the somatic system that coordinates voluntary activities (conscious control) and the autonomic system that coordinates involuntary (automatic) activities.

Functions

The nervous system controls the activity of the bulk of the body's muscular and glandular systems. Neurones coordinate rapid responses through electrical signalling. Changes in membrane potential generate an all or nothing code, using electrical spikes called action potentials.

Neurones receive, process, code and transmit information from one part of the body to another.

- Some are associated with or form sensors (receptors) capable of detecting stimuli (changes in the external or internal environment).
- Some convey information from sensors about changes to which the body must respond.
- Others process information and coordinate responses by relaying signals to effectors - muscles may be stimulated to contract or to relax and glands to start or stop secreting.

Activity may be voluntary or involuntary, for example, an object in the throat may cause an automatic cough or a person may deliberately cough to dislodge it.

Not all responses are under voluntary control, for example, movement of food through the gut by peristalsis or change in heart rate are involuntary actions. The autonomic nervous system controls activities in internal organs. It is divided into the sympathetic and parasympathetic systems:

- Sympathetic nerves tend to excite or speed up responses, for example by increasing breathing or heart rate, dilating bronchioles or stimulating sweat production.
- Parasympathetic nerves tend to inhibit responses, for example by decreasing breathing or heart rate, constricting bronchioles or decreasing blood pressure.

Key mechanisms

Neurones

Neurones are highly specialised nerve cells which transmit electrical impulses. They have a cell body, which contains the nucleus and the bulk of the organelles, attached to various cytoplasmic extensions. Cell bodies occur in grey matter in the CNS and in swellings called ganglia.

In the brain, neurones tend to have numerous short extensions and connect with large numbers of other neurones. In the peripheral nervous system, neurones usually have extensions which form single long fibres to transmit impulses over distances between structures. Fibres are collected into bundles and surrounded by protective sheaths of connective tissue to form nerves.

- Impulses are transmitted in one direction only.
- Dendrons and dendrites (short) are extensions which transmit impulses towards the cell body.
- Axons transmit impulses away from cell bodies.

- Bulb-like swellings at the end of axons form synaptic knobs.
- Synaptic knobs transmit a signal to target cells by releasing a chemical transmitter into a gap called the synapse.

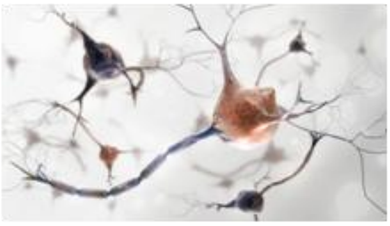


Figure 2 Neurones are able to transmit electrical pulses.

Neurones may be:

- sensory (or receptor or afferent) neurones – transmit impulses from sensors to the CNS;
- motor (or effector or efferent) neurones – transmit impulses from CNS to muscles and glands;
- relay (also called connector neurones) – link sensory and motor neurones within the CNS.

The simplest type of response is controlled by a reflex arc. A stimulus causes an impulse to be generated in a sensory neurone that is transmitted to the CNS, where it stimulates an impulse in a relay neurone. This connects to a motor neurone so that an impulse passes to an effector.

In this way a specific stimulus will cause an automatic and rapid response in an effector. Many reflexes are designed to protect the body from harm. For example, touching a hot object causes a flexor muscle to bend the arm and move the hand before any pain is felt – much more rapidly than could occur with a voluntary, conscious response. Other reflexes include sneezing and blinking.

The nervous impulse

A nervous impulse is not the passage of electrons. It is a wave of depolarisation which passes along the nerve cell membrane.

Resting potential

Cell membranes have a resting potential. They maintain a difference in the relative numbers of cations and anions in the intracellular fluid and extra cellular fluid. The potential difference across the cell membrane can be measured in millivolts (mV).

Nerve cells and muscle cells are excitable, that is they are capable of producing rapid, transient changes in their membrane potential.

The ions mainly responsible for the generation and maintenance of the resting potential are Na^+, K^+ and large negatively charged proteins. The table shows the unequal distribution of ions.

Ion responsible for resting membrane potential in a neurone	Concentration / mmol dm^{-3}		Relative permeability
	extracellular	intracellular	
Na^+	150	15	1
K^+	5	150	50-75
Protein, A^-	0	65	0

- Protein carrier molecules act as Na^+-K^+ pumps to actively transport 3 Na^+ out of the cell in exchange for each 2 K^+ which enters the cell.
- The cell membrane is impermeable to large proteins, so these remain inside the cell.
- As there are many more passive K^+ protein channels than Na^+ channels, the membrane is about 50 to 75 times more permeable to K^+.
- K^+ diffuses outwards along the concentration gradient much more rapidly than Na^+ diffuses out.

The inside of the cell is more negative than the outside, a resting potential of about – 70 mV.

Action potentials

An action potential is a brief, rapid change in membrane potential during which the potential in a small area of the inside of the cell reverses and becomes more positively charged than the outside:

- action potentials initiate with slow depolarisation from −70 mV to around −50 mV,
- at this threshold potential a rapid change takes place to peak at +30 mV, reversing polarisation,
- there is then a rapid return to resting potential, usually after some hyperpolarisation to −80 mV.

The action potential (or 'spike') is the rapid change from threshold to peak and lasts for 1 ms.

The mechanism is all or nothing − if the threshold potential is not reached there will be no action potential. If it is reached an action potential will occur and will always be generated in full.

The action potential is generated by an initial rapid influx of Na^+, which occurs when the threshold potential is reached and voltage-gated Na^+ channels open. This is followed by a rapid efflux of K^+. The Na^+ gates return to their original starting structures, with K^+ gates being slightly too slow to close, leading to hyperpolarisation. The Na^+-K^+ pump then restores resting potential.

Propagation

The generation of an action potential in a localised area of membrane initiates depolarisation in the neighbouring membrane – a series of action potentials spread through the whole membrane, travelling along dendrites and axons to reach synaptic knobs.

As new action potentials are generated, the signal does not weaken as it travels. Nervous impulses can therefore travel, for example, down the whole length of the human leg without fading.

Schwann cells can wrap certain neurone fibres in myelin sheaths as they develop. These are multi-layered coatings of phospholipid with small gaps at nodes between them where voltage gated channels are concentrated. The rate of transmission of action potentials by myelinated neurones is greatly accelerated, as they skip from node to node.

Synapses

Neurones do not connect directly together. Action potentials reach synaptic knobs which have a presynaptic membrane about 20 nm from the postsynaptic membrane of the target cell.

Arrival of action potentials causes vesicles of a transmitter substance (neurotransmitter) to fuse with the presynaptic membrane releasing the chemical into the synapse.

- Neurotransmitter diffuses rapidly over the short distance to bind with receptor molecules in the post synaptic membrane, causing it to depolarise.
- At the postsynaptic membrane the transmitter is broken down or removed (for example acetyl choline is hydrolysed by the enzyme cholinesterase).
- If enough transmitter is released sufficiently rapidly, threshold depolarisation occurs and a new action potential will be generated in the target cell.
- The need for a more than one action potential to generate a new action potential is called summation.
- Products diffuse to the presynaptic membrane, transmitter is reformed and repackaged into vesicles for reuse.

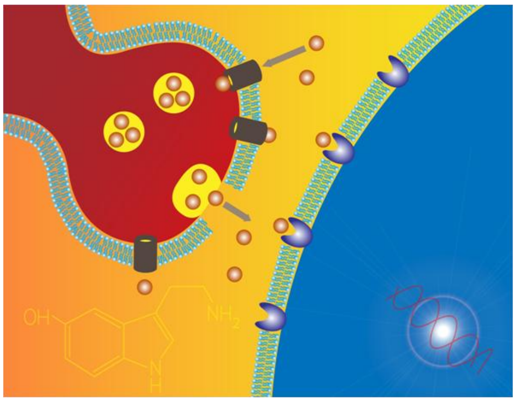


Figure 3 Movement of neurotransmitter at a synapse.

Transmitter can only be released from the synaptic knobs, so transmission is in one direction only.

Synapses increase the sophistication of the control mechanisms used by the body. Different transmitter substances are used (for example noradrenaline, dopamine, serotonin) and responses at the postsynaptic membrane can vary. Some synapses are inhibitory.

Role in homeostasis

By detecting changes inside and outside the body and causing appropriate action to be taken the nervous system is central to the maintenance of a constant internal environment. Responses may be automatic, for example to alter breathing rate to eliminate carbon dioxide at a rate that will stabilise the pH of body fluids. Other responses may be voluntary and some may be based on experience, for example seeking shade on a hot day. Learning from experience has made humans more efficient at exploiting their environment and improving conditions for survival.

Examples of what can go wrong

Drugs and the nervous system

Most drugs that affect the nervous system interfere with synaptic mechanisms. They may be used to block undesirable effects or to enhance desirable ones.

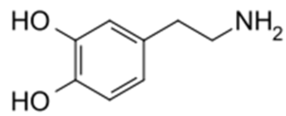
Effects include:

- altering the synthesis, storage or secretion of a neurotransmitter;
- modifying neurotransmitter interaction with the postsynaptic receptor;
- affecting neurotransmitter breakdown or reuptake;
- using molecules that mimic or replace neurotransmitters.

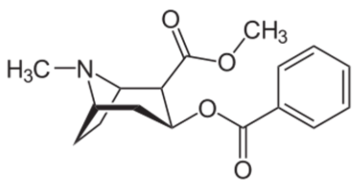
Cocaine addiction

Cocaine binds competitively with reuptake transporters in the presynaptic membrane for the neurotransmitter dopamine. Dopamine therefore remains longer in the synaptic cleft and continues to interact with the postsynaptic membrane receptors to generate additional action potentials. Neural pathways that use dopamine as a neurotransmitter include emotional responses, such as pleasure.

Cocaine causes changes in the synapses so that they no longer transmit normally. Pleasure responses no longer occur and higher doses of the drug become necessary to achieve them. The user is now addicted to using the drug.



Dopamine



Cocaine

Figure 4 Cocaine causes the displacement of dopamine in the synaptic cleft.

Parkinson's disease

Gradual destruction of dopamine producing cells in part of the brain responsible for the coordination of slow sustained movements and the suppression of unnecessary movements leads to Parkinson's disease. Symptoms develop slowly as dopamine activity reduces, and include involuntary tremors at rest.

Dopamine itself cannot be administered as it cannot cross the blood-brain barrier. However, L-dopa (L-3,4-dihydroxyphenylalanine) can enter the brain from the blood and

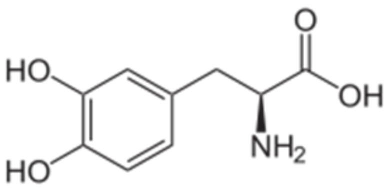


Figure 5 L-dopa can be converted into dopamine in the brain.

be converted into dopamine. This greatly relieves symptoms of Parkinson's, but after prolonged use becomes less effective and side-effects develop.

An alternative approach using GDNF, a factor that maintains neurones, appeared to stop the ongoing loss of dopamine secreting cells in the brains of experimental animals. But Amgen have recently (2011) halted human trials after concerns about the safety of its use.

There is hope that stem cell research will allow the development of cell lines that can be used to test new drugs or replace dopamine secreting nerve cells in affected individuals.

Finding out

In terms of their action on the nervous system, what are agonists and what are antagonists?

Find examples and describe the effect of drugs that act on:

- the central nervous system;
- the somatic nervous system;
- the autonomic nervous system.