1 Introduction to Nerve Cells and Nervous Systems

The essence of nervous system function is control by means of communication. Unicellular (acellular) organisms, such as *Amoeba* or *Paramecium*, can perform every function necessary to sustain their lives. They can take in nutrients from their external environment, organize their metabolic reactions, excrete waste products and move towards or away from objects in their external environment; that is, they can perform simple behavioural adjustments. These actions are performed without the aid of a nervous system as such. In multicellular organisms more complex than sponges the constituent cells have become specialised into organs and tissues for carrying out specific functions, such as digestion and assimilation of foodstuffs, respiration, circulation of the blood to carry oxygen, metabolites and hormones to and from the tissues, reproduction and so on. In these organisms the nervous system and the endocrine system together carry out the function of control and communication, between the various organs and tissues of the body and between the organism and its external environment.

In this book the structure and function of the vertebrate nervous system will be the subject of most consideration. But invertebrate nerve cells and nervous systems will also be discussed, especially where they illustrate a particularly important principle of neuroscience or where the experimental evidence is compelling. The endocrine system will also be mentioned where appropriate, since there is the closest relationship between nervous and endocrine mechanisms. Some nerve cells function as endocrine cells, and some endocrine cells are modified nerve cells. The main difference in action between nervous and endocrine systems relates to the directness of control.

The Nervous System and Control

The nervous system, along with the endocrine system, controls the animal's internal environment. That is, it controls the composition of its extracellular fluid (ECF) and the supply of oxygen and nutrients to the tissues and the removal of carbon dioxide and metabolites from the tissues. In fact, for the most part, the nervous system controls the endocrine system. Changes in the internal environment are monitored by sensory receptors (sense organs – see Chapter 11) and the appropriate action to bring the altered parameter back within set limits is by controlling the various effector cells of the body: cardiac muscle, gland cells, smooth muscle of visceral organs such as the stomach and spleen and smooth muscle of blood vessels. For example, a fall in arterial blood pressure such as may be caused by an acute loss of blood (haemorrhage) will be monitored by receptors (baroreceptors) in the arterial side of the cardiovascular system and, the information transmitted to the central nervous system (see The General Plan of Nervous Systems, below) and appropriate outputs produced to activate effectors so offsetting the blood pressure drop, including constriction of smooth muscle in arterioles, increased force and rate of contraction of cardiac muscle and secretion of the hormone adrenaline (epinephrine) from the adrenal medulla.

The nervous system also monitors the external environment and, at the simplest level, reacts to any changes so as to maintain the integrity of the animal. The nervous system controls the animal's skeletal (striated) muscle and therefore controls the movement of its body in space. A damaging or threatening stimulus will lead to protective action such as a reflex withdrawal. Interaction with the external environment can lead to complex behaviour, such as may occur in the finding of the next meal or a member of the opposite sex.

In the most complex organisms this interaction with the outside world is further developed. The animal does not just react passively to the environment but explores it actively. Such exploration is well-developed in mammals and probably most highly developed in primate species. Young mammals spend a considerable amount of time playing, which is really an active exploration of their environment. Humans may spend most of their lives playing; for example, in highly developed societies certain sections of the community are rewarded for playing (artists and scientists). This development leads to control over the external environment by humans to a remarkable extent.

An important function of nervous systems that greatly increases the ability of an animal to survive is the capability for learning. Learning and its closely associated function of memory allow an organism to change its behaviour as a result of experience.

The Nervous System and Communication

The nervous system is able to exert control over the internal and external environments because of its remarkable ability to communicate. Nerve cells (or neurons) are the essential communicating elements in the nervous system, signalling to each other and to the muscle and gland cells. Neurons also communicate with the other major cell type in nervous systems, the glial cells. In addition to communication within an individual nervous system and an individual animal, nervous systems also communicate with one another. In both invertebrate and vertebrate species highly organised communication about the state of an individual and about the external environment can occur. Thus animals give behavioural signals about their emotional state, e.g. submissive behaviour by young mammals to their elders, rage reactions expressed by members of the cat tribe, and about the environment, e.g. the well-known "dance" performed by honey bees for describing the distance and direction of a source of pollen or nectar, or the various alarm calls of birds in the presence of a predator.

Communication between members of the same species is very well developed in primate species and especially so in humans. The evolution of language has allowed learned experience to be passed between members of the human race and between members of different generations in contact with one another (some other species can also pass on experience by example). More than this, however, the development of written languages has meant that learning may be passed on to members of the species not yet born. The advances in information transmission brought about by modern electronic technology is transforming global human communications in ways not dreamt of even a couple of generations ago.

Nerve Cells

The active components of nervous systems are the nerve cells or neurons. The human nervous system contains somewhere of the order of 10^{20} neurons. These neurons are the units that communicate with one another and with the various effector organs. The essential aims of neuroscience are to understand

1. how single neurons operate
2. how one neuron communicates with another or with its target (effector) cell
3. how groups of neurons are interconnected to form component parts of the nervous system
4. how neurons within a group interact with one another
5. how groups of neurons interact with one another
6. how nervous systems develop and how the interconnections are made

and ultimately

7. how whole nervous systems operate and control behaviour.

An additional and very important aim is

8. to understand how things can go wrong with each of these sets of functions and to learn how to prevent or ameliorate diseases and disorders of the nervous system.

This book considers the normal anatomy and physiology of nervous systems and in the following chapters we shall consider the first seven aims. Considerable advances in knowledge have been made concerning aims 1–3, some advances in aims 4–6 and rather little as yet in aim 7. Before these items are considered in more detail, some basic background information about the structure and function of nervous systems is presented. An introduction to experimental approaches available for studying the structure and function of single neurons and their interconnections in nervous systems is indicated in Boxes 1.1 and 1.2.

Box 1.1

Experimental Methods for Studying the Structure of Nervous Systems

The microscopical structure of nerve cells may be examined after staining thin sections of fixed nervous tissue with a variety of stains at the level of both the light and electron microscopes. The Nissl method, using basic aniline dyes, stains the ribosomal RNA of the rough endoplasmic reticulum and is useful for examining the sizes, shapes and densities of neuronal somata under the light microscope. Staining with silver salts, e.g. the Golgi method, allows the visualisation, in both light and electron microscopes, of dendrites and the axon with its branches as well as the soma and the synapses in contact with them. Development of histochemical stains and antibody techniques has allowed the visualisation of particular substances in neurons, e.g. transmitters, and also the location of transmitter receptors. Direct injection of a dye into a neuron by means of very fine pipettes (or microelectrodes – see Box 1.2) has allowed the visualisation of neurons from which electrical recordings have been made. The development of confocal microscopy together with fluorescent ion-sensitive dyes has allowed changes in, for example, internal calcium (Ca^{2+}) concentration to be observed and followed over real time in in-vitro preparations.

A variety of experimental anatomical methods has provided important information about the connections between neurons. If an axon is transected its peripheral parts undergo degeneration – anterograde degeneration – and these changes can be seen using particular techniques. Thus the Marchi method stains degenerating myelin, and a variety of methods can demonstrate degenerating axons and terminals, at both the light and electron microscope levels. After axonal section those parts of the neuron proximal to the section also undergo changes – retrograde degeneration – and these can also be demonstrated microscopically. More recently there has been an explosion in our knowledge of neuronal connections due to the development of techniques that utilise a neuron's ability to transport substances both from the cell body to its terminals (anterograde transport) and from its terminals to its cell body (retrograde transport). A large number of substances have been used including radioactive amino acids (detected by exposing the histological slide to a photographic emulsion – autoradiography), horseradish peroxidase, various fluorescent dyes sometimes attached to inert microspheres, various toxins and viruses. The latter, toxins and viruses, may cross synapses and have been used to delineate chains of connected neurons. Finally, electrophysiological methods may be used for neuronal tract tracing. Thus if a recording is made from a neuronal soma, then the location of its axon and terminals may be determined by systematic electrical stimulation in other parts of the nervous system to find those locations from which the neuron may be excited antidromically (backfired). Also, by examining those regions of the nervous system that respond orthodromically (that is, usually trans-synaptically) to electrical stimulation of another part, then neuronal pathways may be delimited. This is the evoked potential method.

Various imaging techniques that may be used in the intact living animal or human have been developed. Methods such as computed tomography (CT) scanning, positron emission tomography (PET) scanning and magnetic resonance imaging (MRI) have all been useful in studies of normal brains and also in the diagnosis of disease. CT scanning allows detailed study of the anatomy of the CNS and is particularly useful for diagnosing the site of a lesion. PET scanning combines the anatomical detail of CT scanning and, in addition, provides dynamic functional data of, for example, localised changes in metabolism or the localisation of particular transmitters following injection of suitable substances intravenously. MRI provides similar data to PET scanning but at a higher resolution.

The Generalised Neuron

In order to carry out their function of communication, neurons need to receive input from other neurons or sensory receptors, to balance (integrate) this input, to produce a signal that reflects this balance, and to send the signal to the neuron's contact points with other neurons (at synapses) or effector

Box 1.2

Experimental Methods for Studying the Function of the Nervous System

Classically there are three techniques for studying neuronal function: by making lesions, by stimulation and by recording. Lesions may be made surgically or by injecting particular chemicals into the nervous system. The animal's behaviour is then examined. Any behavioural deficits following such lesions are usually interpreted to mean that the lesioned part had a role to play in the behaviour. However, there are difficulties in interpreting such experiments. It is the remaining ability of the nervous system that is being tested under such circumstances. Stimulation, by either electrical or chemical means, has also been much used and has been important in human studies (the brain can be stimulated in conscious patients under local anaesthesia) as well as in animal preparations. The original recognition and demarcation of motor areas in the cerebral cortex was determined in this way. Undoubtedly the most powerful technique for studying the behaviour of neurons has been to record their electrical activity. Such techniques range from gross recordings of massed neuronal activity using coarse surface electrodes to recording the activity of a single neuron and even a single membrane channel using fine micropipette or patch electrodes. For recording single-neuron activity microelectrodes may be placed just outside a neuron (extracellular recording) or placed inside a single neuron (intracellular recording). Over the past 10 years or so the powerful techniques of molecular and cell biology have been applied to the nervous system and provided important results in many areas, for example, the control of gene expression, signalling mechanisms especially those utilising second messengers and enzyme cascades, and how the nervous system develops and maintains its integrity.

cells (at neuromuscular or neuroglandular junctions). Figure 1.1 shows a diagrammatic concept of a generalised neuron in which these various functions have been anatomically separated, and compares this generalised neuron with a variety of neuronal types, with one exception, from vertebrates. As may be seen, such anatomical separation is indeed commonly found in some vertebrate neurons, but it is by no means standard in vertebrate nerve cells and is extremely uncommon in inveterbrate neurons (Figs 1.2, 1.3).

Resting Membrane Potential

Like all other cells in an organism, neurons have a cell membrane which separates the contents of the cell from its extracellular environment. There is a separation of electric charge (ions) across this membrane such that the inside of the cell is held at a negative potential, of some tens of millivolts, compared with the outside (which is taken to be at earth – zero – potential). This is the resting membrane potential (see Chapter 2), although in neurons it is very rare to find a true resting potential such as occurs in striated muscle, for example. Much signalling in the nervous system involves changes in the membrane potential of neurons.

Receptive Function

Neurons contact each other at membrane specialisations – gap junctions and synapses (see Chapter 5) – where communication between neurons occurs. This communication can be of several types. Over a short time course of milliseconds to seconds there can be either passage of electrical current (produced by movement of ions) or the release of chemical transmitters from the presynaptic neuron on to the postsynaptic target, producing ionic current flow across the cell membrane and, usually, changes in membrane potential that increase or decrease the cell's excitability. Over a longer time course one neuron may release substances on to another that affect that cell's metabolism and be responsible for altering synaptic efficacy and maintaining synaptic links between the cells. Neurons may also be receptive to substances produced by non-nervous tissue, e.g. to hormones. In order to respond to chemicals released on to it, a neuron must have either appropriate receptor molecules in or on its cell membrane or must allow access into the cell for these molecules. Generally the receptive surface of the (vertebrate) neuron includes the dendrites, soma and also the axon terminals of the cell. For membrane receptors that bind with an outside agent (ligand), it is the nature of the receptor that determines the response of

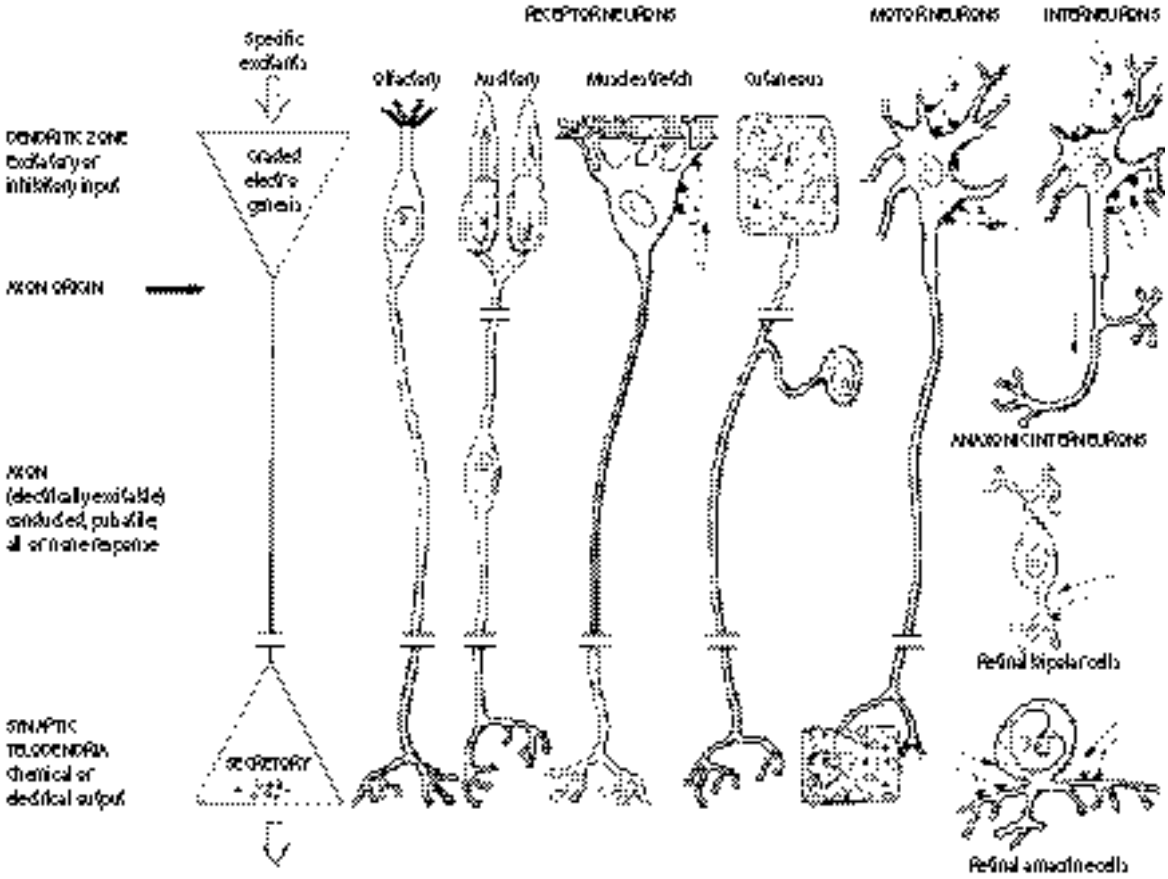


Fig. 1.1. The "generalised" neuron and a variety of neuronal types. On the *left* is a diagram of the generalised neuron that relates structural neuronal components to functional properties. On the *right* is a series of simplified diagrams of the structure of a variety of neurons. Note that the position of the cell body (soma), which contains the nucleus, does not have a constant relationship to the functional geometry of the generalised neuron. Also, note that the muscle stretch receptor neuron is from an invertebrate, all other neurons are from vertebrates. (Reproduced with permission from Bodian 1967.)

the cell (see Chapter 8), which may simply be changes in the cell's permeability to particular ions (ionotropic receptor) or may set in train more complex events involving a series of intracellular enzyme cascades (metabotropic receptor) that may regulate the function of cellular proteins or may regulate the synthesis of such proteins by altering gene expression.

Integrative Function

Neuronal responses to neurotransmitters and similar molecules are generally, in the short term, changes in membrane potential produced by ionic currents across the cell membrane or the clamping of the membrane potential at a particular value by such an ionic current. Such changes may be in the depolarising direction and are then usually excitatory, or may be in the hyperpolarising direction and are then usually inhibitory. These potential changes are summed by the neuron and determine the neuron's output to its target cells. In vertebrate neurons the summing activity takes place within the dendrites and the cell body (see Chapter 9). Some neurons are capable of the self-generation of output (rather like the pacemaker cells of the heart) but even in these cells such rhythmic activity is modulated by input from other neurons.

Impulse Initiation

In many neurons, but by no means all and perhaps only in a minority, nerve impulses are set up if the neuron's membrane potential is depolarised sufficiently to reach a certain threshold level. These impulses are all the same shape and size, under a given set of conditions, and are, therefore, all-or-nothing events (see Chapter 9). In neurons that are capable of initiating impulses the information that

such cells pass on to their targets is in the form of a frequency code.

Conduction

The nerve impulses travel (are conducted) actively along the neuron's axon (see Chapter 3). In those neurons that do not generate impulses the potential change caused by the input is conducted passively to the sites of transmitter release.

Transmission

The term transmission is usually reserved for the relatively short-term actions of one neuron on another. As mentioned above, it may be either electrical or chemical in nature. In electrical transmission one neuron influences another by passive electrical means. In chemical transmission the potential change in one neuron leads to the release of a chemical neurotransmitter (see Chapter 6) that diffuses to the other neuron, combines with specific receptor molecules in its membrane and this ligand–receptor combination leads to either changes in the permeability of the membrane to particular ion species or to changes in the cell's metabolism.

The Anatomy of Neurons

The generalised neuron discussed above is a convenient abstraction. Few neurons bear much resemblance to it. Perhaps the nearest are certain vertebrate nerve cells in the brain and spinal cord (see Fig. 1.2). These neurons consist of a cell body (soma or perikaryon) that contains the nucleus of the cell. From the soma arises a series of branching processes, the dendrites, and also the nerve fibre, or axon (the axon may arise from one of the dendrites). The axon arises from the axon hillock, a part of the soma or dendrite that is free of the protein-synthesising machinery called Nissl substance by classical histologists, and its first part, the initial segment, is usually the site of origin of the nerve impulses generated by the neuron. The dendrites and soma form the receptive surface for incoming messages from other neurons, usually at contacts called synapses, and it is in the soma that the balancing of excitatory and inhibitory actions that produces any output is performed. The axon may be short (a few tens of micrometres) or long (several metres in large animals) but it ultimately breaks up into a series of branches that may divide repeatedly and finally, in their terminal arborisation (telodendria), form synaptic boutons which are the sites of transmission to the next cell in the series. In some neurons the synaptic boutons may receive other synaptic contacts which provide a means for controlling the output of the neuron by, for example, presynaptic inhibition (see Chapter 9).

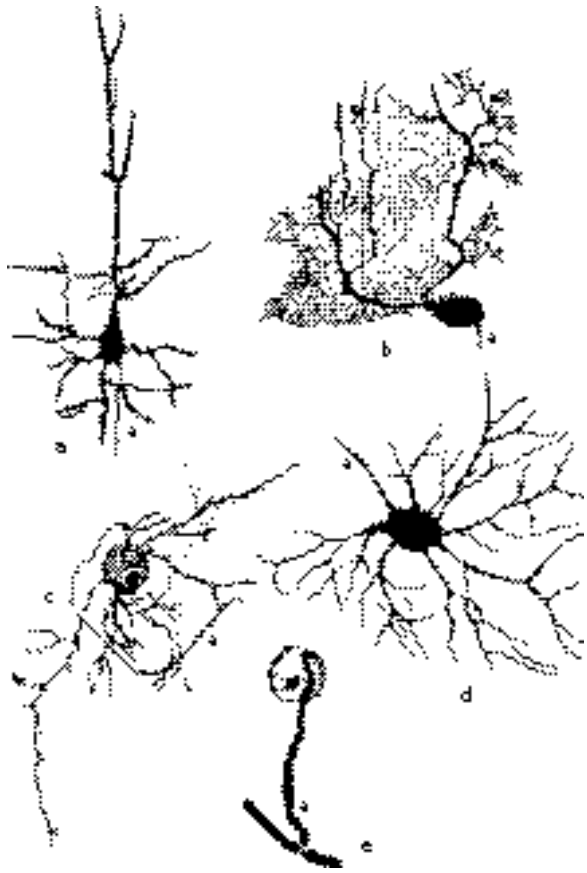


Fig. 1.2. Examples of vertebrate neurons, all as seen in Golgi preparations: **a** A pyramidal cell from the cerebral cortex. The dendrites are covered in spinous processes. In this, and the other parts of the figure, *a* is the axon. **b** A Purkinje cell from the cerebellar cortex. **c** A sympathetic postganglionic neuron. **d** An α-motoneuron from the spinal cord. **e** A dorsal root ganglion cell. Note the absence of dendrites. In all of these drawings the axon is incomplete. (Reproduced with permission from Willis and Grossman 1973.)

The anatomy of vertebrate neurons may depart considerably from this form. There may be no obvious axon or no obvious dendritic tree. Invertebrate neurons (see Fig. 1.3) have a different structure in that the soma is set off from the rest of the neuron and the neuronal processes carry out the receptive, integrative and transmission functions, and in many cases the impulse initiation and conduction functions too.

Fig. 1.3. Examples of invertebrate neurons, taken from the nervous systems of various flies. The numbers indicate different types of cells. Note the cell bodies set off from the rest of the neurons. (Reproduced from Strausfeld 1976.)

Ultrastructure of Neurons

Like all cells, neurons contain the machinery for life (Fig. 1.4). This machinery includes the usual organelles found in cells: a nucleus with a nucleolus, mitochondria, endoplasmic reticulum and Golgi apparatus, lysosomes and a cytoskeleton of tubular structures. Specialised organelles, the synaptic vesicles, are characteristic of neurons and accumulate over their release sites, e.g. in synaptic boutons.

Neurons have a high rate of protein synthesis and in their ultrastructure resemble protein-secreting gland cells. The protein synthesising machinery is the Nissl substance, revealed in the light microscope by aniline dyes, and under the electron microscope observed to consist of free ribosomes (polysomes) arranged in rosettes or attached to the surface of the endoplasmic reticulum.

The cytoskeleton consists of tubular structures, the microtubules, microfilaments and intermediate filaments together with a large number of associated proteins, and is responsible for the shape of the neuron and also for the transport of many substances and organelles from one part of the neuron to

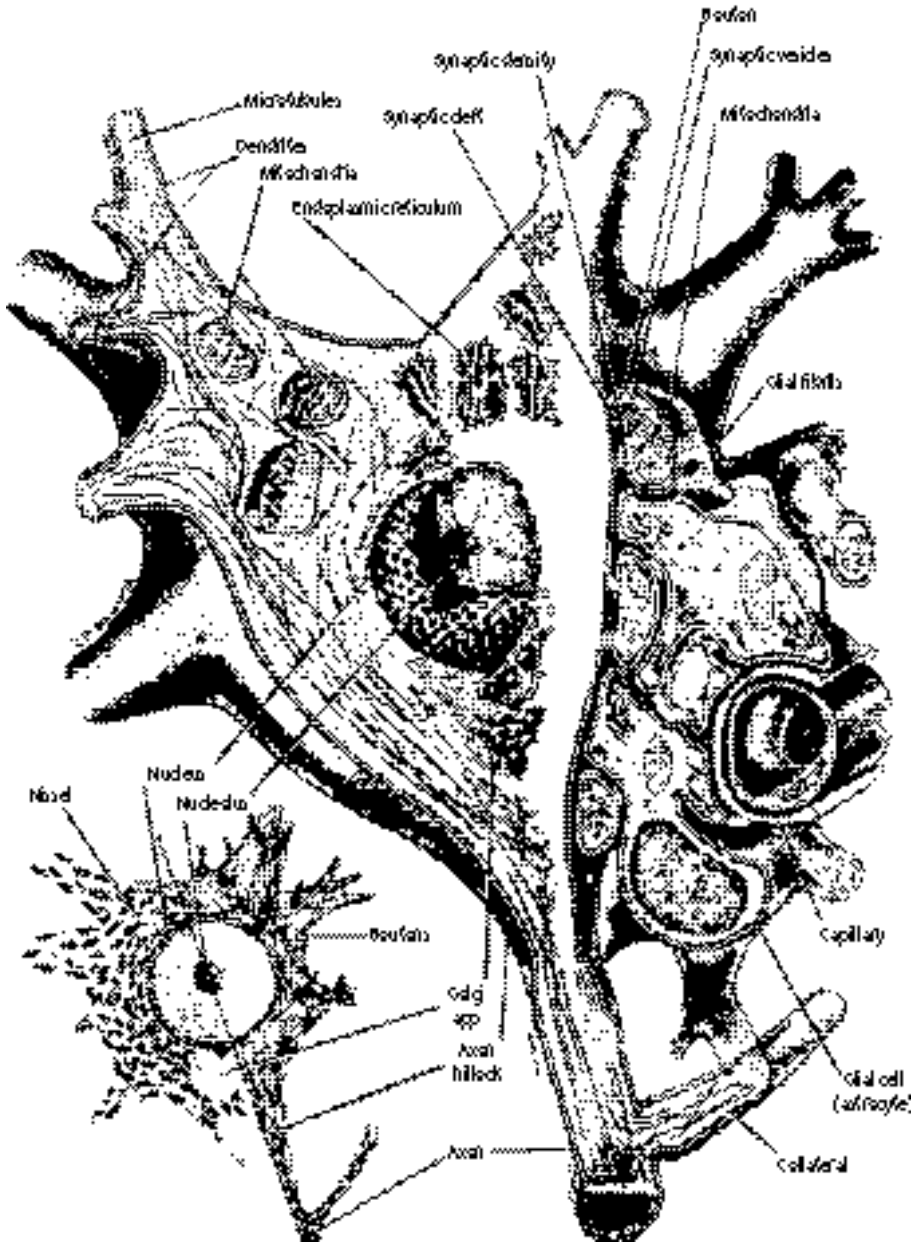


Fig. 1.4. The organelles of a neuron. The smaller drawing (*lower left*) indicates the organelles as seen using light microscopy after staining with basic aniline dyes (to *left* of broken line) or after staining with heavy metals (to *right* of broken line) which also indicates the synaptic boutons from other neurons. The larger drawing shows structures demonstrable with the electron microscope. (Reproduced with permission from Willis and Grossman 1973.)

another (Box 1.3). Microtubules are hollow tubes some 24 nm in diameter and up to several hundred micrometres in length, made up of 12–14 protofilaments of α- and β-tubulin. They are important in determining the shape of a cell and also in intracellular transport. Microfilaments consist of the protein actin in the form of a twisted strand of two filaments some 4–6 nm in diameter and a few hundred nanometres in length. They are concentrated in certain parts of neurons – synaptic terminals, dendritic spines and also in growth cones of growing axons – and appear to have important roles to play in the movement of cytoskeletal and membrane components. Intermediate filaments are solid, rod-like filaments about 10 nm in diameter and up to several micrometres long. They are of several different types and appear to be particular important during development.

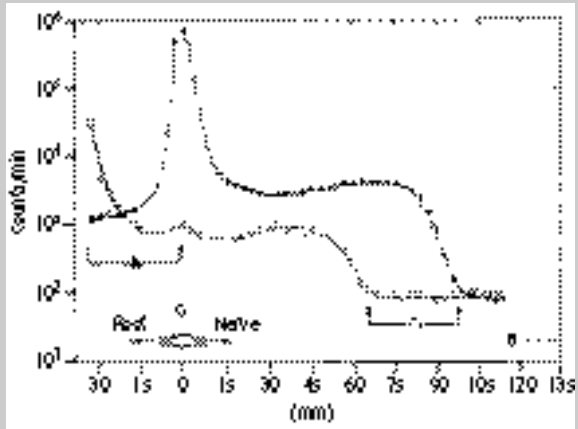
Synaptic vesicles are membrane-bound vesicles filled with transmitter molecules (see Chapter 6). The vesicle proteins are made in the cell body and transported, as transport vesicles, to the sites of release (synapses) by axoplasmic transport on microtubules. At some stage the vesicles are filled with transmitter,

Box 1.3

Axonal Transport

There are both slow and fast transport mechanisms that move substances and subcellular organelles, etc. along axons in both the anterograde and retrograde directions. Slow transport, which may be subdivided into two types, moves the cytosolic components such as cytoskeletal and microtubule proteins, neurofilaments and a variety of polypeptides at rates of a few millimetres a day. Fast transport (Box Fig. 1.3) moves neurotransmitters, neuropeptides and neurotrophic factors at rates of up to 400 mm a day. In fast transport the material moved is associated with membrane-bound vesicles, that is, it is contained within the vesicles. It appears that the mechanisms for fast transport in the anterograde and retrograde directions differ. Several families of molecular motors have now been identified (Brady 1991, Brady and Sperry 1995) which drive transport systems.

The transport of various substances in both the anterograde and retrograde directions by fast transport mechanisms has been used to very good effect by experimental anatomists. Thus the enzyme horseradish peroxidase (HRP) is taken up by nerve terminals, packaged in membrane-bound vesicles and retrogradely transported to the cell body. By injecting the enzyme around nerve terminals,allowing subsequent take-up and retrograde transport, the locations of the cell bodies having axonal projections to the injection site can be determined since the HRP may be easily visualised (for both light and electron microscopy) by straightforward histochemical techniques. Various other substances, including HRP conjugates, plant lectins and fluorescent dyes may also be used for both anterograde and retrograde neuronal pathway tracing. Neurotoxic viruses are also taken up and transported along axons and even across synapses, thus allowing complete pathways to be traced.



Box Fig. 1.3. Fast axonal transport in sensory and motor fibres in the cat. The motoneuronal region of the seventh lumbar segment (*open circles*) and the seventh lumbar ganglion (*filled circles*) were injected with tritiated leucine. After 6h the nerves were removed and the radioactivity sampled. The displacements of the fronts of the crests of activity (*open triangle*) is comparable to the displacement of the locations of the spinal cord segment and the ganglion (*filled triangle*). After 6 h the rate of transport was similar in sensory and motor nerves at about 100mm, corresponding to a rate of 400mm a day. (Reproduced with permission from Ochs and Ranish 1969.)

either close to the release sites (small molecular transmitters such as acetylcholine [ACh], glutamate, γ-amino butyric acid [GABA], glycine, catecholamines, serotonin) or in the soma (peptide transmitters such as substance P, vasoactive intestinal peptide [VIP], the enkephalins). The amino acid transmitters and ACh are contained in small clear vesicles whereas the catecholine and peptide transmitters are contained in dense-cored vesicles of various sizes.

The Neuroglia

The nervous system contains another group of cells in addition to neurons: these are the neuroglia or glial cells. In the mammalian nervous system they are far more numerous that the neurons. They are generally small cells and do not partake in the active generation of signals (impulses) nor do they have a direct role to play in the information processing functions of the nervous system. Some,however, are influenced by neuronal activity and help regulate the ionic environment of the neurons and also remove some transmitters and other substances released by neurons.

The glial cells may be divided into two major classes, the macroglia (astrocytes, oligodendrocytes and ependymal cells) and the microglia, which act as phagocytes. Astrocytes, some but not all of which are star-shaped, have many functions. Some take up excess potassium (K^+) ions from the extracellular space, others are capable of removing neurotransmitters such as γ-aminobutyric acid and serotonin

from the region of the synapse. Oligodendrocytes are responsible for forming the myelin sheath around the axons of certain cells in the central nervous system. In the peripheral nervous system this function is carried out by Schwann cells, which have a different origin from the glia.

The General Plan of Nervous Systems

In all but the simplest multicellular animals the nervous system can be considered to consist of two main parts, the central nervous system (CNS) and the peripheral nervous system. In vertebrates, the CNS consists of the brain within the skull and the spinal cord within the vertebral canal (Fig. 1.5). In invertebrates the CNS consists of a series of collections of neurons (and glia) called ganglia that run in pairs along the length of the animal (Fig. 1.6). In the more complex invertebrates a number of ganglia at the head end of the animals fuse together to form a brain or head ganglion (Fig. 1.6). In all animals the brain or head ganglion is especially concerned with the special sense organs,including those for vision, audition, olfaction, etc., situated on the head. Most of the neuronal processing takes place within the brain, the spinal cord and (in invertebrates) the ganglia.

The peripheral nervous system consists of several elements:

- nerve fibres with cell bodies situated within the CNS and whose axons run to innervate muscles or other neurons outside the CNS
- nerve fibres running from peripheral sense organs and whose cell bodies are usually situated outside the CNS, often in ganglia such as the dorsal root ganglia or cranial nerve ganglia in vertebrates
- nerve cells whose cell bodies and processes are completely outside the CNS.

Thus in mammals the peripheral nervous system consists of three parts: a somatic component, a visceral component and an enteric nervous system. The somatic component is made up of

- afferent (or incoming) nerve fibres, innervating sense organs in the skin, muscles, tendons and subcutaneous tissue, with their somata located outside the CNS in ganglia
- efferent (or outgoing) nerve fibres, innervating skeletal muscle, with their somata located in the CNS.

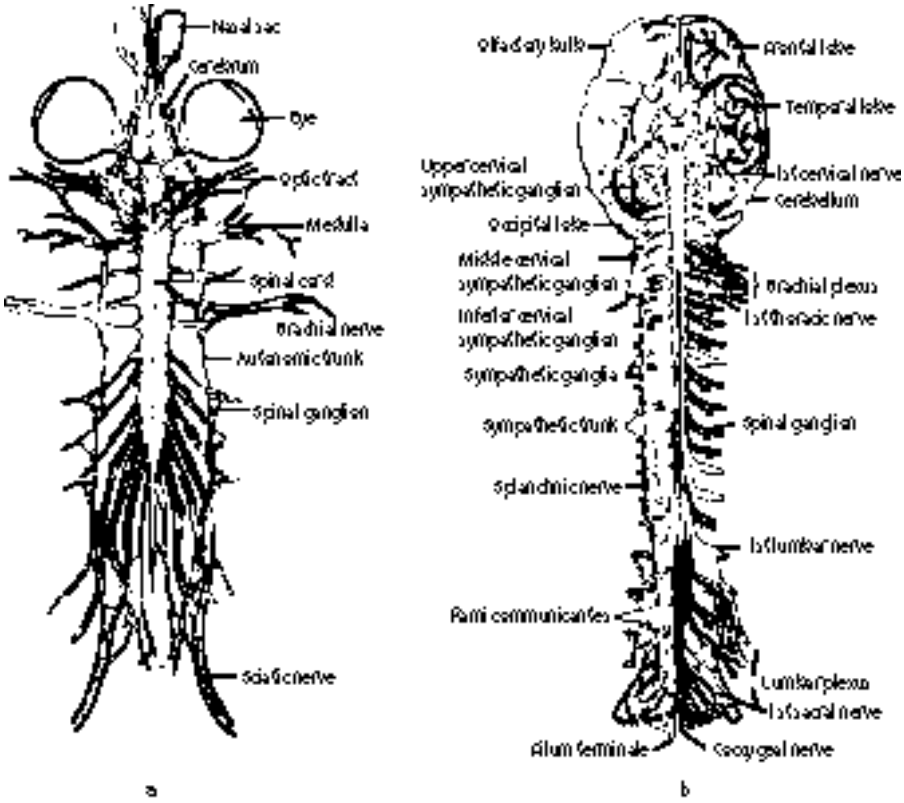
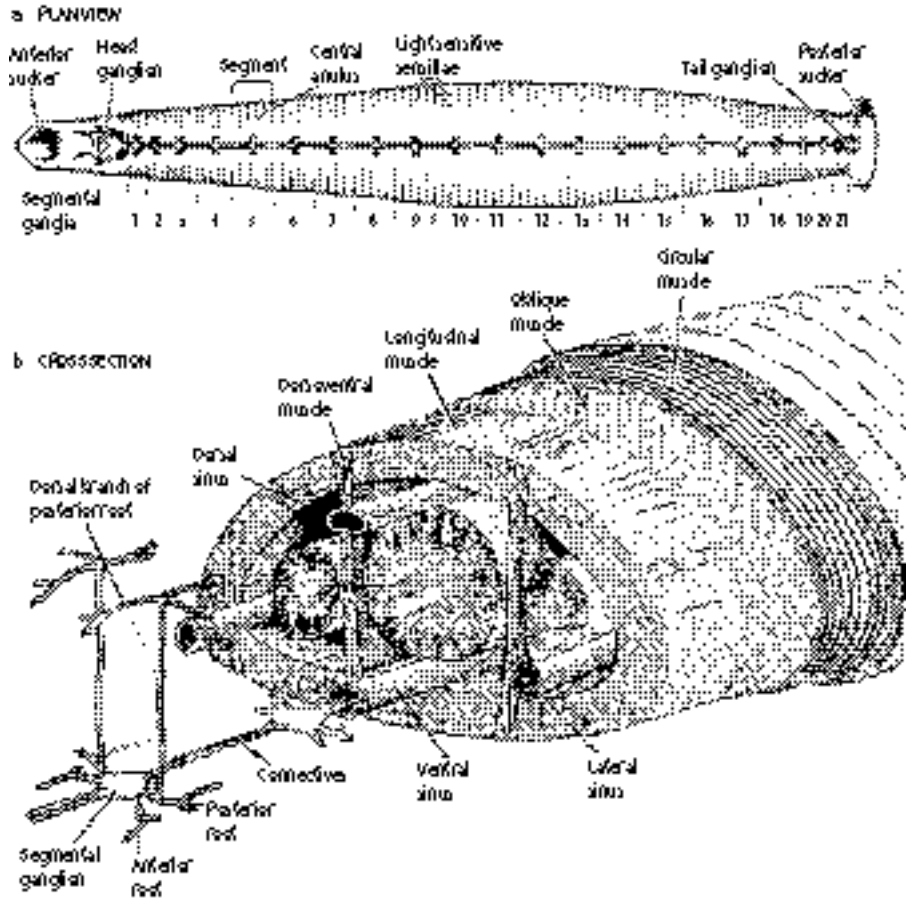
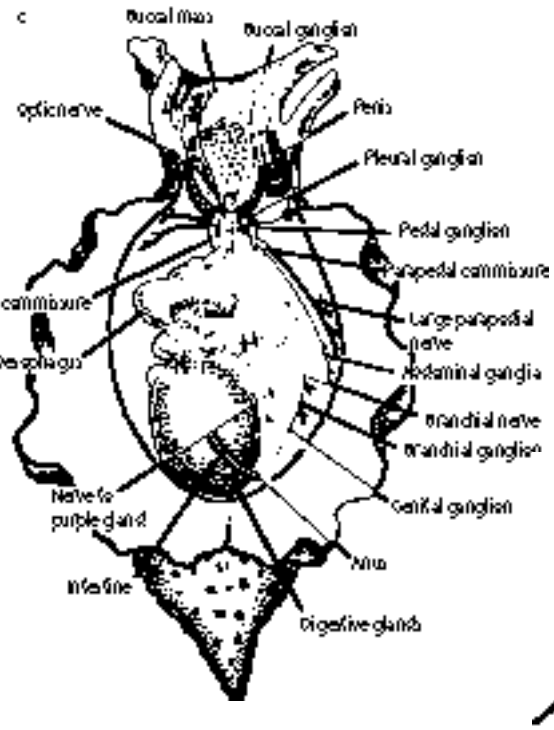
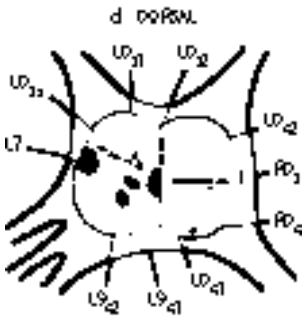


Fig. 1.5. General plan of vertebrate nervous system: **a** frog; **b** human. Both are viewed from the ventral aspect. Note that the peripheral nerves are incomplete. (Reproduced with permission from Eckert and Randall 1978.)







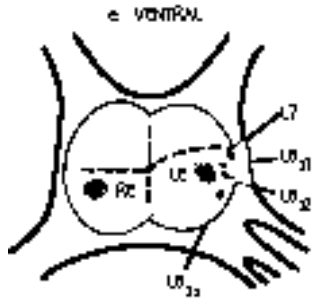


Fig. 1.6. Examples of invertebrate nervous systems: **a**, **b** The leech. **a** the general plan with 21 segmental ganglia, and head and tail ganglia; **b** the ventral nerve cord running between the ganglia. **c–e** The sea snail (*Aplysia*). **c** the general plan of the nervous system; **d, e** indicate identified neurons in the abdominal ganglia. (Reproduced with permission (**a, b**) and modified (**c–e**) from Kuffler et al 1984.)

The visceral component likewise consists of

- a sensory or afferent part running from sense organs in the viscera (the internal organs and tissues such as the heart, stomach, lungs, uterus, etc.) and having somata in ganglia
- a motor or efferent part consisting of nerve fibres with cell bodies either in the CNS or in well-formed ganglia or in the viscera themselves.

The efferent visceral component of the vertebrate peripheral nervous system is also known as the peripheral autonomic nervous system (Fig. 1.7). The enteric nervous system consists of several sets of neurons and their processes in the wall of the gastrointestinal tract and is capable, by itself, of regulating reflex activity of the gut, although it is normally under control from the autonomic nervous system.

Regulation of the External Environment of Neurons

In order for neurons to carry out their functions of communication and control they need to be in a relatively stable environment. They also need an adequate supply of oxygen and metabolites, such as glucose, amino acids and fatty acids, and also need waste products removed from their vicinity. In vertebrates the brain and spinal cord are surrounded by a special fluid – the cerebrospinal fluid (CSF) – formed from blood plasma by active secretory processes in special capillary loops, the choroid plexuses, which protrude into the cavities of the brain, the ventricles (Fig. 1.8). Unlike blood plasma,CSF is almost protein free. The CSF around the brain and spinal cord is in communication with the CSF in the ventricles of the brain and their continuation into the spinal cord,

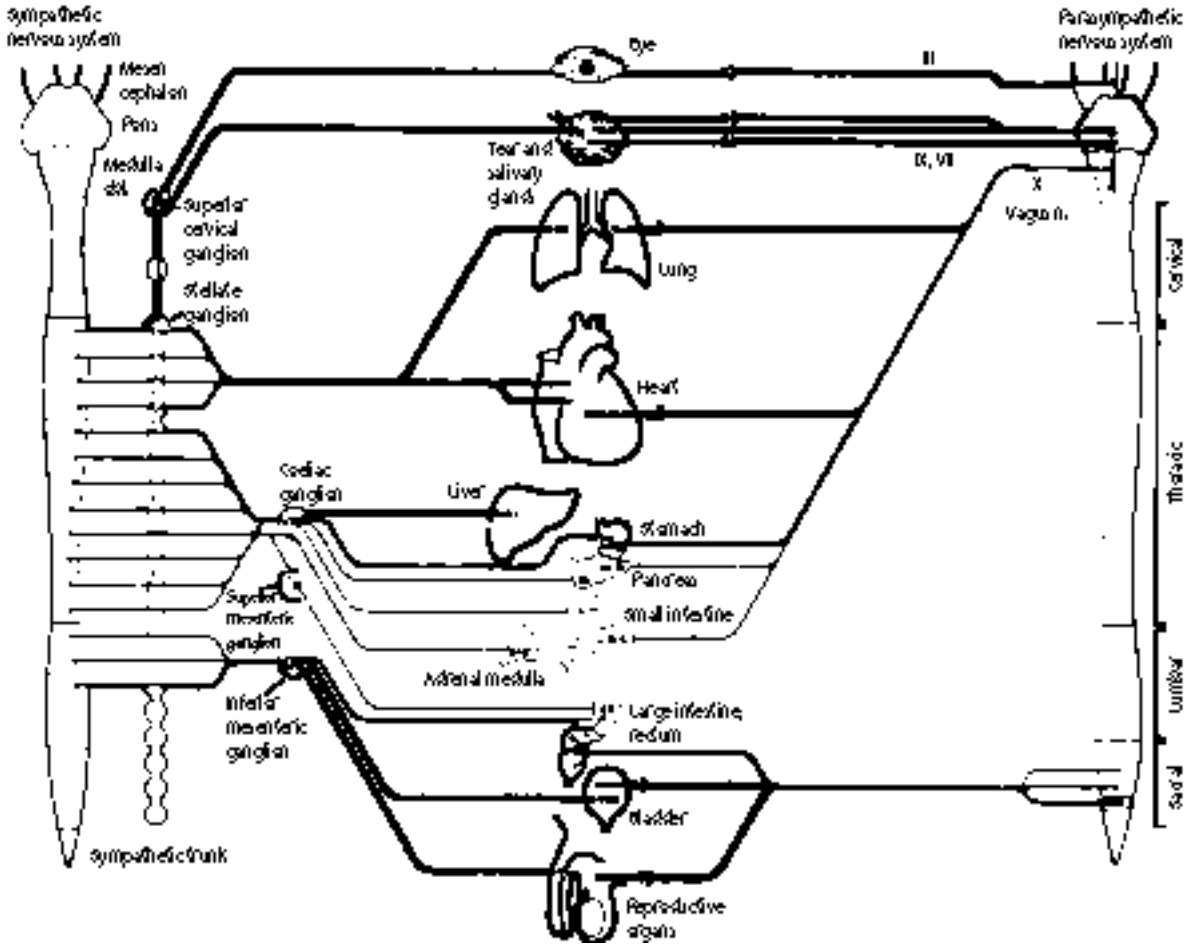


Fig. 1.7. The peripheral autonomic nervous system of mammals. The sympathetic component is on the *left* and the parasympathetic component on the *right*. The sympathetic innervation of blood vessels, sweat glands and piloerectormuscles is not shown. (Reproduced from Schmidt and Thews 1983.)

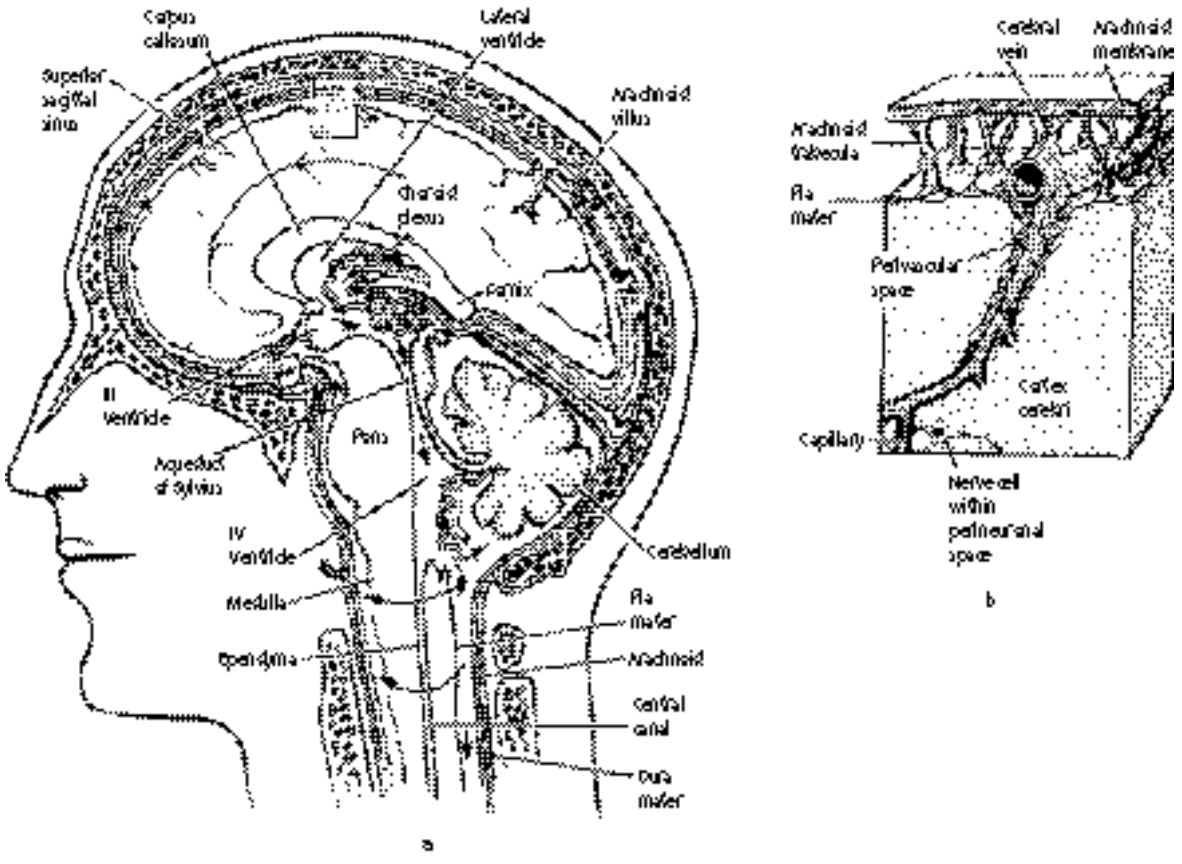


Fig. 1.8. The distribution of CSF. **a** A sagittal section through the human skull. The CSF is formed in the choroid plexus and drains via the arachnoid villi into the venous blood in the sagittal sinus. The *arrows* show the direction of flow of the CSF. **b** an enlarged view of the box outlined in **a**. (Reproduced with permission from Kuffler et al 1984).

the spinal canal.CSF is continually formed and drains back into the blood via the arachnoid villi into the superior sagittal sinus and other venous sinuses of the cranium.

The CSF surrounding the brain and spinal cord is contained within two connective tissue sheets or meninges, an outer, thick, dura mater and an inner, thin, dual sheet, the pia-arachnoid. This outer CSF provides a shock-absorbing system that helps prevent mechanical injury to the CNS during sudden accelerations and decelerations. The major blood vessels supplying the brain and spinal cord run between the two components of the pia-arachnoid (the arachnoid membrane and the pia mater) and give off smaller vessels that run into the CNS carrying a sheath of pia mater and CSF with them (Fig. 1.8b). The CSF does not bathe the neurons and neuroglia but is separated from them by a layer of basement membrane. The ECF of the CNS is contained within very small intercellular clefts. Between the neurons and neuroglia, on the one hand,and the blood in the brain capillaries, on the other, there are (1) the ECF, (2) a basement membrane, (3) the CSF and (4) the endothelium of the capillaries.

There are barriers to the free passage of substances from the blood into the ECF of the brain. It is conventional to consider these as a blood–CSF barrier and a CSF–brain barrier. The endothelial cells of the capillaries in the CNS differ from those elsewhere in the body in that they contain interendothelial tight junctions (zonula occludens) which restrict the passage of solutes between the cells. Another component of the blood–brain barrier is made up of the basement membranes and various cellular components such as astrocytes and the pericytes, which are cells found within the basement membrane structures. These barriers are not complete. In certain areas peptide hormones can gain exit from and access to the brain. This is important in the communication between the endocrine and nervous systems. Infection of the meninges (meningitis) and of the brain (encephalitis) also lead to increased permeability of the

barriers,as may tumour formation in the brain. This increased permeability can aid treatment by allowing drugs, which are normally kept out of the CNS, into the affected parts.

Summary

1. The essence of nervous system function is control by communication. The nervous and endocrine systems together control the internal environment of the animal and allow it to interact with the external environment.
2. The active components of nervous systems are the nerve cells or neurons. Neurons are of many different shapes and sizes but all have receptive,integrative and transmission functions that allow them to communicate with other neurons and with the effector cells – muscle fibres and gland cells. Many neurons are also able to initiate and conduct nerve impulses, allowing them to communicate efficiently over relatively long distances within the animal. Transmission between neurons or between neurons and effector cells may be electrical or chemical, and may have excitatory or inhibitory actions.
3. In addition to neurons there are other cells in the nervous system – the neuroglia. Neuroglia have important functions during the development of the nervous system and following injury, and also play a role in maintaining the ability of neurons to function by controlling their ionic environment and by removing excess transmitters.
4. In all but the simplest multicellular animals, the nervous system consists of central and peripheral components. The CNS of vertebrates consists of the brain and spinal cord. In invertebrates the CNS consists of a chain of paired ganglia, some of which may be fused together at the head end to form a brain. Cell bodies of neurons are generally located in the CNS. The peripheral nervous system consists of nerve fibres (axons) passing to the CNS (afferent fibres) and away from it (efferent fibres). The afferent fibres arise from sensory receptors on the surface and within the body. Their cell bodies are usually outside the CNS in ganglia. The efferent fibres consist of motor fibres supplying the skeletal muscles and other fibres forming part of the peripheral autonomic nervous system and supplying cardiac and smooth muscle (of the heart, viscera and blood vessels) and gland cells. The peripheral autonomic nervous system contains ganglia where connections are made between different neurons and where the cell bodies of (postganglionic) neurons are located. The enteric nervous system in the wall of the gut is a third component of the peripheral nervous system.
5. The ionic environment of neurons is also controlled by a system of barriers that prevents free passage of substances from the blood into the extracellular space of the brain and spinal cord. CSF is formed within the cavities of the brain and also surrounds it and the spinal cord, forming a shock-absorbing system. CSF is formed by epithelial cells surrounding special capillaries (the choroid plexuses),and the cells act as a barrier to certain ions and molecules. Necessary substances are brought to the CNS by arterial blood and waste products are removed in venous blood. The endothelial cells of the brain capillaries and also the astrocytes, basement membrane and its pericytes act as further barriers to the free passage of substances.