



NEURONS, NEUROTRANSMISSION AND COMMUNICATION

CHAPTER OUTLINE

How the nervous system is organised	2
Cells of the nervous system	3
The neuron	3
Neuroglial cells	7
Information exchange in the nervous system	9
The resting membrane potential	10
The action potential and nerve impulse	10
Summation effects	12
Synaptic transmission	13
The synaptic vesicle	14
Modulation of synaptic transmission	15
Non-synaptic chemical communication	15
Postsynaptic receptors and receptor types	17
Neurotransmitters	18
The amino acids	19
Monoamines	20
Acetylcholine	23
Neuropeptides and neuromodulators	23
Soluble gases	24
Summary	24
Further reading	25
Key questions	25



ESSENTIAL BIOLOGICAL PSYCHOLOGY

The purpose of biological psychology is to elucidate the biological mechanisms involved in behaviour and mental activity. Biological psychologists (sometimes referred to as neuropsychologists) attempt to understand how the neural circuits and connections are formed and put together during the development of the brain, allowing the individual to perceive and interact with the world around them. We cannot answer all of the questions that we would like to, nor do we believe that we have access to the best possible tools for studying the brain, but the questions do stir up curiosity and a better understanding of the biological processes that play a role in behaviour. It can be hard to remember the complicated names of **nerve cells** and brain areas. However, to develop theories of behaviour regarding the brain, a psychologist must know something about brain structure. This chapter will focus on the **nervous system**: its organisation, its cell composition, and the type of chemical signals that make it possible for us to process an incredible amount of information on a daily basis.

HOW THE NERVOUS SYSTEM IS ORGANISED

In **vertebrates**, the nervous system has two divisions: the peripheral nervous system and the central nervous system (Figure 1.1). The central nervous system (CNS), which consists of the brain and spinal cord, is surrounded by another nervous system called the peripheral nervous system (PNS). The PNS gathers information from our surroundings and environment and relays it to the CNS; it then acts on the signals or decisions that the CNS

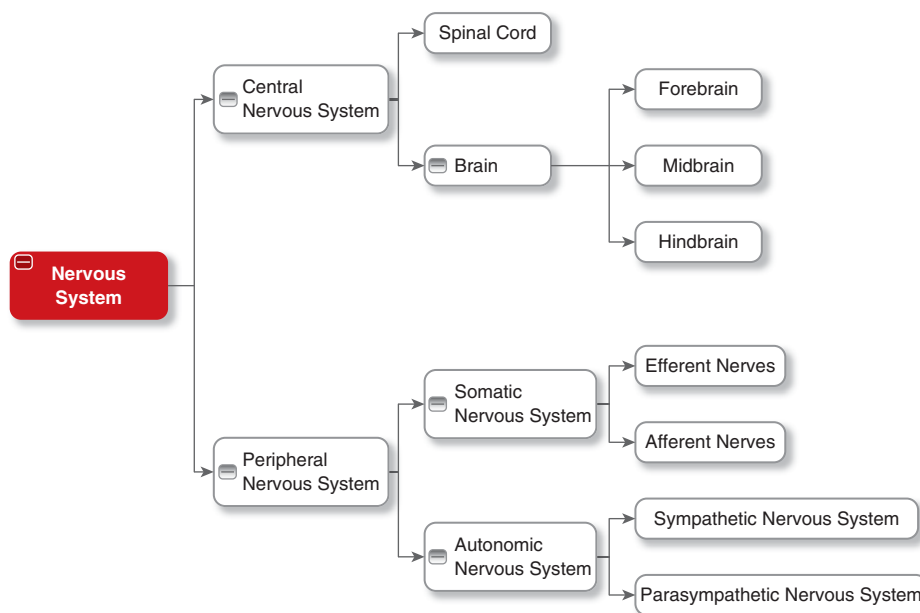


Figure 1.1 Components of the nervous system



returns. The peripheral nervous system itself consists of two parts: the somatic nervous system and the **autonomic nervous system**. The autonomic nervous system is divided into two subsystems: the **parasympathetic nervous system** and the **sympathetic nervous system**. The parasympathetic system is responsible for slowing the heart rate, increasing the intestinal and gland activity and undertaking actions when the body is at rest. Its action can be described as opposite to the sympathetic nervous system, which is responsible for controlling actions associated with the fight-or-flight response. The somatic system contains the sensory **receptors** and motor **nerves** which activate the skeletal muscles, and it is concerned with detecting and responding to environmental stimuli.

CELLS OF THE NERVOUS SYSTEM

THE NEURON

Neurons are the basic information processing structures in the CNS. They are electrically **excitable** cells that process and transmit information around the nervous system. Neurons transmit information either by electrical or by chemical signalling, which as you will see later occurs via **synapses**. Neurons are the core apparatus of the nervous system, and a number of specialised types exist. Neurons are very much like other body cells, possessing common features like the following:

- ❁ Neurons are encased in a cell membrane (also known as a plasma membrane).
- ❁ The nucleus of a neuron contains **chromosomes** and genetic information.
- ❁ Neurons consist of cytoplasm (fluid found within the cell), mitochondria and other organelles.
- ❁ Basic cellular processes occur in a neuron. **Ribosomes** are where **proteins** are produced, and mitochondria are responsible for metabolic activities that energise the cell.
- ❁ Neurons contain a Golgi complex – a network of vesicles that get **hormones** and other products ready to be secreted.

However, neurons or nerve cells are different from other body cells in that:

- ❁ Extensions emanate from the central body of the neuron. We refer to these as **dendrites** and **axons**. Dendrites carry information to the cell body while axons transmit information away from the cell body.
- ❁ Neurons transmit and receive information via an electrochemical mechanism.
- ❁ Neurons have some distinct and specialised structures like the synapse (the junction between one neuron and the next).
- ❁ Neurons synthesise chemicals that serve as neurotransmitters and neuromodulators.





Neuron structure

A typical neuron possesses a cell body (the **soma**), dendrites and an axon. Dendrites are filaments that emanate from the cell body, branch numerous times and give rise to a complex *dendritic tree* (Figure 1.2). An axon is like the wire in an electrical cable. It starts at the cell body at a site called the **axon hillock** and travels to the site in the nervous system where it connects with another nerve cell or different type of cell, such as muscle. The cell body of a neuron frequently gives rise to multiple dendrites, but never to more than one

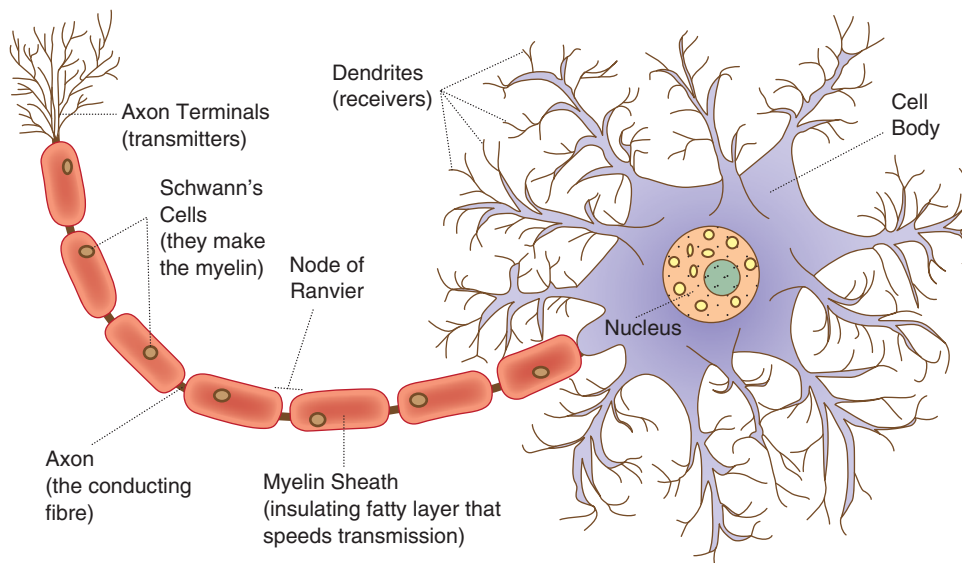


Figure 1.2 *Neuron structure*

Table 1.1 *Differences between axons and dendrites*

Axons	Dendrites
Take information away from the cell body	Bring information to the cell body
Large axons have a distinct swelling called the axon hillock	No hillock
Usually have few or no ribosomes	Usually have ribosomes
Smooth surface	May have rough surface: spiny as in pyramidal cells or non-spiny as in interneurons
Often covered with myelin	Seldom covered with myelin
Generally only one axon or none per cell	Usually many dendrites per cell, each with many branches
May be any length: 1 metre or longer	Usually shorter than axons
Branch further from the cell body	Branch near the cell body

axon. A layer of fatty cells called the myelin sheath segmentally encases the fibres of many neurons that greatly increase the transmission speed of neural impulses. Table 1.1 summarises the differences between axons and dendrites.

Inside the neuron

The inside of a neuron is much like the other cells of the body in many ways, as a neuron has many of the same organelles, including a nucleus and mitochondria. Figure 1.3 shows the following components of a typical animal cell:

- ❁ **Nucleus:** contains genetic material within the chromosomes comprising information for development and maintenance of the cells as well as the production of proteins. The nucleus is covered by a membrane.
- ❁ **Nucleolus:** produces ribosomes, which are essential for translating genetic information into proteins.
- ❁ **Lysosomes:** contain enzymes that reduce chemicals to their individual components.
- ❁ **Centrosome:** this microtubule regulates the cells and the cell cycle.
- ❁ **Cytoplasm:** this is a partially transparent, gelatinous substance that fills the cell.

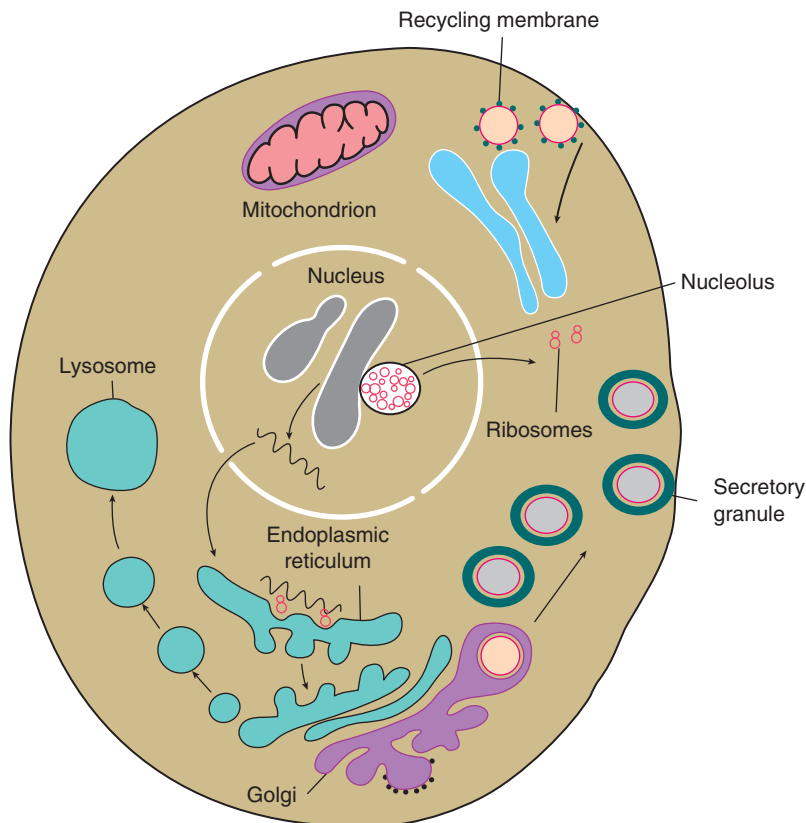


Figure 1.3 Cross-section of animal cell



ESSENTIAL BIOLOGICAL PSYCHOLOGY

- ❁ *Vacuole*: these are compartments bound by membranes that carry out various functions including storage and secretion of neurotransmitters.
- ❁ *Endoplasmic reticulum* (ER): a network of tubes that are used to move materials around the cytoplasm. Endoplasmic reticula which are made from ribosomes are called rough ER, whereas those which have no ribosomes are called smooth ER. ER including ribosomes are vital for protein synthesis.
- ❁ *Golgi body or Golgi apparatus*: a membrane-bound structure that is critical to the process of encasing peptides and proteins into vesicles.
- ❁ *Microfilaments or neurotubules*: the system that moves materials within a neuron. These elements can also be used for structural help.

Neuron classification

The study of the microscopic anatomy of cells and tissues is termed histology (see Box 1.1). As with many things in the nervous system, neurons may be classified in a variety of ways, according to their function (sensor, motor, interneuron), their location (cortical, subcortical), the identity of the neurotransmitter they synthesise and release (**cholinergic**, glutamatergic) and their shape (pyramidal, granule, etc.). One easy way to categorise them is by how their axons and dendrite leave their cell body or soma. This gives three main types of neurons:

- ❁ *Bipolar*: similar to retinal cells, two processes extend from the body of bipolar neurons.
- ❁ *Unipolar*: there are two dorsal root ganglion axons for each unipolar cell. One axon stretches out in the direction of the spinal cord and the other in the direction of the skin or muscles.
- ❁ *Multipolar*: multipolar neurons contain many processes that branch out from the cell body. However, here the neurons each only have one axon (e.g. spinal motor neurons).

Another very basic method for the classification of neurons is by identifying which way they transmit information:

- ❁ *Efferent neurons (motor neurons)*: these direct information away from the brain towards muscles and glands.
- ❁ *Afferent neurons (sensory neurons)*: these transmit information to the central nervous system from sensory receptors.
- ❁ *Interneurons*: found in the central nervous system, these pass information between motor neurons and sensory neurons.



BOX 1.1 Examination of brain tissue: histology

Histology is in fact the microscopic study of tissue, not just brain tissue. In the field of biological psychology the mapping and visualisation of the cellular composition of the brain or its cytoarchitecture are an important complement to the studies of function and gross anatomy. Histology generally refers to the techniques used to prepare tissue for microscopic study. This includes staining brain tissue for light and electron microscopy and also advanced techniques for tracing fibre tracts or classifying receptor types present in a given brain region. There is a wide variety of staining techniques. In neuroscience, perhaps the most familiar is Golgi staining; this method was discovered by Italian physician and scientist Camillo Golgi (1843–1926) in 1873. It stains only a few cell bodies in their entirety, and in so doing allows a detailed visualisation of individual neurons. Other techniques available include myelin stains for visualising fibre bundles and several techniques for cell body staining. Nissl staining is a method which stains the cell body and in particular the endoplasmic reticulum. The Nissl substance, which consists of the rough or granular endoplasmic reticulum, appears dark blue when a dye such as cresyl violet is used.

NEUROGLIAL CELLS

The glial cells are simply the so-called glue (as the name implies) by which the nervous system is held together. Neuroglial cells are the other major cell type in neural tissue; they provide structural integrity and nutrition to the nervous system and maintain **homoeostasis** (Finch, 2002). While some glial cells physically support other cells, others control the internal environment surrounding neurons or nerve cells and provide them with nutrients. Glial cells are also involved in cortical development, the guidance of neurons and the growth of axons and dendrites, and are crucial in the development of the nervous system (Hidalgo, 2003; Howard, Zhicheng, Filipovic, Moore, Antic, & Zecevic, 2008). Because glial cells do not form synapses it was thought that they were merely the housekeepers of the nervous system, required for the maintenance of neurons but not involved in processing information. However, in recent years there have been some changes to this assumption with the discovery that one type of glial cell, the oligodendrocyte precursor cell, is involved in synaptic signalling in the hippocampus (Lin & Bergles, 2004).

Types of glial cell

A number of different types of glial cell exist. Some can be found in the central nervous system and others are essential to the functioning of the peripheral nervous system.



Astrocytes (CNS)

Astrocytes are responsible for maintaining the external chemical environment around nerve cells (Malhotra, Shnitka, & Elbrink, 1990). They do so by disposing of surplus ions, particularly potassium and chloride, and reprocessing and recycling neurotransmitters that were released during synaptic transmission. An additional feature of astrocytes is the formation of end feet; these are small swellings that surround and support the endothelial cells of the blood–brain barrier (BBB). This is a membranous structure of capillary endothelial cells which protects the brain from any harmful substances circulating in the blood while still allowing metabolic function to occur normally (Holash, Noden, & Stewart, 1993).

The brain contains two different kinds of astrocytes: protoplasmic astrocytes and fibrous astrocytes (Miller & Raff, 1984). The grey matter contains the protoplasmic astrocytes, while the white matter of the spinal cord and brain contains fibrous astrocytes. Astrocytes are typically small cells and, even though these cells are the most prevalent glial cells, numbers are found in different areas of the brain.

Oligodendrocytes (CNS)

Oligodendrocytes surround axons in the CNS forming a myelin sheath that insulates the axon and makes it possible for electrical signals to be generated and propagated more effectively (Yamazaki, Hozumi, Kaneko, Fujii, Goto, & Kato, 2010). One oligodendrocyte is capable of coating as many as 50 axons. Myelin, which is white in colour, increases the speed at which **action potentials** are sent along an axon. The sheaths of myelin that cover the axon have gaps between them, referred to as the *nodes of Ranvier*. It is at these gaps that ions can cross the membrane and an action potential occurs. Thus the action potential jumps from one node to the next, enabling action potential to travel along **myelinated** axons quicker than along their **unmyelinated** counterparts. Cognition and behaviour are affected by myelin loss within the CNS, as in the demyelinating disorder of multiple sclerosis (Zeis & Schaeren-Wiemers, 2008).

Schwann cells (PNS)

The cell in the PNS that is functionally equivalent to the oligodendrocytes in the CNS, the Schwann cell, only insulates one discrete axon. Schwann cells are specialised types of glial cell that provide myelin insulation to axons in the peripheral nervous system (Bruska & Wozniak, 1999). Non-myelinating Schwann cells have a role to play in maintaining axons and have a critical role for neuronal survival.

Microglia (CNS)

Microglia are glial cells that serve the CNS immune system and are also specialised **macrophages**. Microglia are important protectors of the central nervous system, and guard and support the neurons of the CNS. Using a process called **phagocytosis**, they actively cleanse the waste from the nervous system. Microglial cells are not derived from ectodermal tissue like other glial cells but instead derive embryologically from haematopoietic precursors, which are multipotent stem cells producing all types of blood cell. Microglia are found in all parts of the brain and spinal cord and they comprise approximately 15–17% of all the cells



of the CNS. Microglia continually sample their surroundings and multiply in response to brain injury. Microglia are thought to be a factor in neurodegenerative disorders like multiple sclerosis, motor neurone disease and Alzheimer's disease. These cells are also responsible for creating the inflammatory response to brain trauma (Dheen, Kaur, & Ling, 2007) and they are the main target cells for the HIV-1 virus in the central nervous system (Erfe et al., 1991).

Radial glial cells (CNS)

Radial glial cells (RGCs) are a temporary cell population present only in the developing central nervous system. They function both as precursor cells and as a scaffolding framework to support neuron migration.

Glial cells and injury





As already suggested, the glial cells react to both central and peripheral nervous system damage, supporting neurons. The debris from injuries in the CNS, like a stroke, is engulfed by astrocytes and digested in the process of phagocytosis. Scar tissue is also formed as astrocytes fill the gaps that occur because of tissue death. Oligodendrocytes in the central nervous system provide support for the axons and create myelin. Schwann cells accomplish the same functions in the PNS.

Gliosis

While neurons cannot undergo cell division in adulthood, glial cells keep that capability. It seems that the mature nervous system cannot replace neurons that have been damaged as a result of a lesion or an injury. However, there is intense proliferation of glial cells, called gliosis, which congregate close to or at the site of the damage. Recently, studies have shown that the 'mature' glia, such as astrocytes, do not maintain the capacity for **mitosis**. It is believed that only oligodendrocyte precursor cells keep this capacity to multiply after the nervous system matures. There is some recent evidence that production of new neurons can occur in a few parts of the mature nervous system such as the subventricular zone and the dentate gyrus of the hippocampus (Seri, García-Verdugo, McEwen, & Alvarez-Buylla, 2001).

INFORMATION EXCHANGE IN THE NERVOUS SYSTEM

Neurons constantly relay information between each other, and also between themselves and their environment. Information is transmitted from cell to cell using the following forms:

-  axon to dendrite – axodendritic exchange
-  axon to cell body – axosomatic exchange
-  axon to axon – axoaxonic exchange
-  dendrite to dendrite – dendrodendritic exchange.





ESSENTIAL BIOLOGICAL PSYCHOLOGY

The cell membrane is sometimes at rest and not receiving information from other neurons; in this state, it is said to be at the **resting membrane potential**.

THE RESTING MEMBRANE POTENTIAL

The resting potential (or resting voltage) of the cell is the membrane potential that is maintained if there are no action potentials or synaptic potentials present. The intracellular fluid of a neuron at rest is more negatively charged than the extracellular fluid, and this polarity difference is termed the resting potential. The resting membrane potential of a neuron is about -70 millivolts (mV); this means that the inside of the neuron is 70 mV less than the outside. The disparity between voltages across the cell membrane is due to the fact that there is a higher concentration of positive ions outside the cell than inside the cell. There is approximately 10 times more sodium (Na^+) on the outside of the cell and approximately 20 times more potassium (K^+) on the inside. This is frequently called the cell's concentration gradient.

The properties of the membrane and the **sodium/potassium pump** are each partially responsible for the distribution of electrically charged ions. As the membrane is semi-permeable, molecules like water, oxygen, urea and carbon dioxide can cross the cell membrane whereas larger or electrically charged ions and molecules generally cannot. Certain ions, like potassium (K^+), chloride (Cl^-) and sodium (Na^+), pass through the membrane at gates formed by **channel** proteins which are located in the membrane and regulate how fast the ions can enter. Though drawn to the negative interior of the nerve cell, the Na^+ gates stay shut until the membrane is depolarised. As a result, there is an increased concentration of Na^+ ions outside the membrane. The greater concentration of K^+ ions on the inside of the membrane can cross the membrane at a regulated rate by passively diffusing out of the cell because they are drawn to a region of lesser concentration; they remain, however, held by the negative interior of the cell. K^+ ions are returned to the inside of the membrane via the sodium/potassium pump which uses an active transport system, with energy supplied by adenosine triphosphate (ATP) molecules. Other ions that have a negative charge, such as chloride, also cross the membrane at a controlled rate; these help in maintaining the negative interior. As a result the resting potential is sustained by Na^+ being held out of the cell, while K^+ diffuses out, only to be brought back into the cell. Three Na^+ ions are actively removed from the cell by the sodium/potassium pump for every two K^+ ions that are allowed to enter.

THE ACTION POTENTIAL AND NERVE IMPULSE

The membrane resting potential is present when a neuron is at rest. However, when our nervous system transmits information, an action potential or a nerve impulse occurs. An action potential is a short-term event in which the electrical **membrane potential** of a cell rapidly increases and falls. Positive ions flowing into the cell will reduce the negative charge and thus reduce the charge across the entire membrane; we refer to this as **depolarisation**. When depolarisation gets to around -55 mV (the tipping point) a neuron will give off an action potential. No action potential will fire if the neuron does not reach the **threshold** level. Once the threshold value is reached, an action potential of a fixed size will always fire; and for any given neuron, the size of the action potential is always the same. Often this is referred to as the **all-or-nothing principle**.

The exchange of ions across the neuron membrane causes nerve impulses or action potentials to take place. A stimulus, for example at the touch receptors, first causes Na^+ channels to open, and because there are many more Na^+ ions on the outside, and the inside of the neuron is negative relative to the outside, Na^+ enters the neuron. Thus, the neuron becomes both more positive and depolarised. Then K^+ channels open (they take a bit more time than Na^+ channels) and K^+ rushes out of the cell, reversing the depolarisation. When Na^+ enters, the membrane potential increases, and when K^+ exits, it drops sharply back down, giving rise to the alternative name for this potential: the spike potential. Na^+ channels then start to go back to their normal closed state, which causes the action potential to revert towards -70 mV (a **repolarisation**). However, the membrane potential actually moves past -70 mV to nearly -80 mV (a **hyperpolarisation**) due to the K^+ channels remaining open just a bit too long. Ion concentrations will steadily return to the resting membrane, and the cell will return to -70 mV.

For a short period in the middle of the action potential, the neuron is totally resistant to additional stimulation. This is known as the **absolute refractory period**, where the neuron cannot make another action potential. The absolute refractory period precedes another brief period, known as the **relative refractory period**, during which the neuron can generate another action potential but the stimulus must be of greater intensity than normal (Figure 1.4).

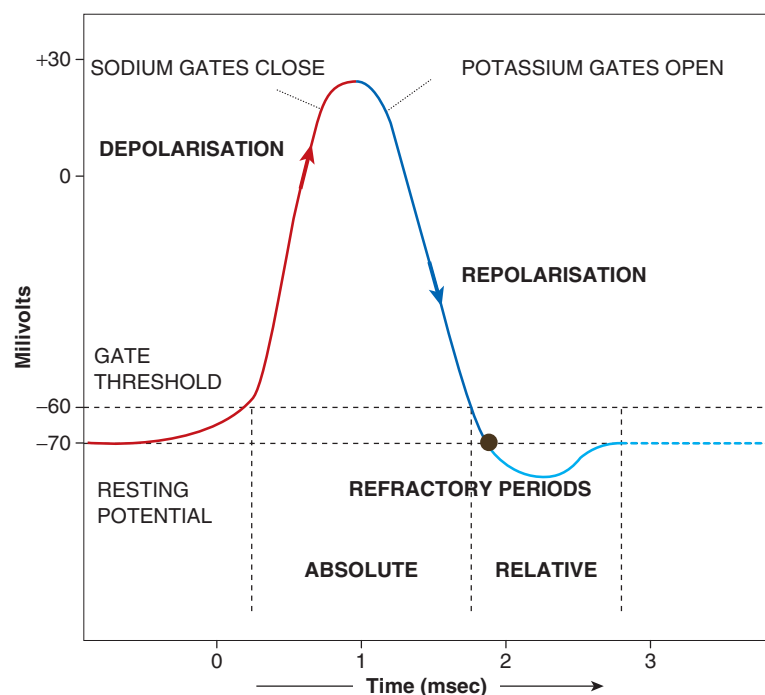


Figure 1.4 The action potential



ESSENTIAL BIOLOGICAL PSYCHOLOGY

One anatomical part of a neuron that connects the cell body to the axon is termed the axon hillock, and it is here that **inhibitory postsynaptic potentials (IPSPs)** and **excitatory postsynaptic potentials (EPSPs)** from various synaptic inputs on the dendrites or cell body accumulate. From the axon hillock an action potential moves along the axon in the form of a nerve impulse. The acceleration of transmission is different in all axons and is separate from stimulus intensity. Actually, the propagation speed is dependent on three things: the measurement of the axon's diameter, whether or not the axon is coated in myelin, and how many synapses there are. If everything else is the same, action potentials are quicker in axons that are larger in diameter, usually travelling at a speed ranging between 10 and 100 m/s. Myelinated axons send information faster than unmyelinated axons, and the number of synapses *en route* will also affect propagation rates: the more synapses, the slower the propagation rate. When an action potential happens, sodium ions travel along the inside of the cell membrane, depolarising the segment of the membrane that lies just ahead. The thicker the axon is, the faster the sodium ions move along the membrane, similar to the way in which water flows faster through a large bore pipe.

Earlier, we discussed how several axons in the nervous system have a myelin coating, which was formed by a specific type of glial cell. The myelinated segments together are better known as the myelin sheath, and the segments are divided by small spaces known as the nodes of Ranvier. These node gaps are the only locations where the cell membrane has any exposure to the extracellular fluid. In addition they also contain **ion channels** where ions can move into and out of the cell and respond to the depolarising stimulus, causing the action potential to jump from node to node. This process of the action potential appearing to jump along the length of an axon while at the same time speeding up the propagation of a nerve impulse is referred to as **saltatory conduction**. Myelinated axons transfer information at a much higher speed, 100 m/s, than unmyelinated axons which normally have an action potential of 1 m/s. Thus the process of saltatory conduction mitigates the necessity of an increase in axon diameters and enables a reduction in the size of the nervous system in organisms.

SUMMATION EFFECTS

Neurons receive multiple excitatory and inhibitory inputs on a continual basis. The determination of whether the axon will fire or not is based on the total effect of all excitations and inhibitions that take place. So, at what point is an action potential produced? The EPSPs and IPSPs received by the dendrites and cell bodies of the neurons are graded potentials. As discussed above, each EPSP results in a depolarisation and each IPSP results in a hyperpolarisation of the postsynaptic membrane. These various EPSP values at different times are added together and produce a combined level of depolarisation, while the IPSPs combine in the same manner to produce a combined level of hyperpolarisation. The method of introducing both positive and negative influences on the cell membrane is called summation. **Spatial summation**

occurs when excitatory potentials from lots of different presynaptic neurons cause the postsynaptic neuron to reach its threshold and fire. **Temporal summation** occurs when a single presynaptic neuron fires many times in succession, causing the postsynaptic neuron to reach its threshold and fire.

SYNAPTIC TRANSMISSION

The discovery that neurons do not physically merge began in the late 1900s when Ramón y Cajal observed a narrow gap separating one neuron from the next. In 1906, Sir Charles Scott Sherrington identified the **synaptic delay** (typically 0.3 to 0.5 ms) and concluded that a certain form of communication occurs at these gaps between nerve cells. He called this point of communication a synapse. Today, these junctions through which the neuronal cells signal to each other and to non-neuronal cells like those found in muscles or glands are still known as synapses. Synapses make it possible for nerve cells in the central nervous system to create interconnected neural circuits or networks. The synapse comprises a synaptic terminal, a nerve cell that transmits information (or the presynaptic ending), a nerve cell that receives the information (the postsynaptic ending), and the gap between them, which is known as the **synaptic cleft** (Figure 1.5).

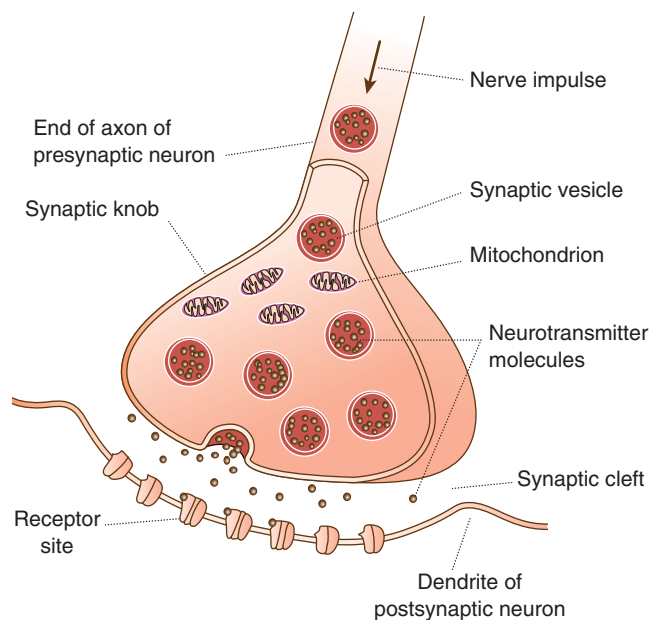


Figure 1.5 The synapse



ESSENTIAL BIOLOGICAL PSYCHOLOGY

Communications across the synapse are facilitated by neurotransmitters – chemicals that are synthesised by neurons and utilised to engage in communications with other cells. The presynaptic ending or synaptic terminal, also known as the **synaptic knob**, bouton or button, holds cell organelles like mitochondria and neurotransmitters. The neuron sending the impulse triggers the migration of vesicles which contain the neurotransmitter to the membrane of the synaptic terminal. The vesicle membrane then fuses with the presynaptic membrane, and neurotransmitter is released into the synaptic cleft (a gap of width approximately 20 nm); it then binds to receptors of the connecting cell and these excite or inhibit electrical impulses. The region of the synapse that releases neurotransmitters is called the active zone. Here, cell adhesion molecules keep the membranes of the pair of neighbouring cells close to one another. The postsynaptic cell may be a muscle cell or a gland, not just another neuron.

One of the most important features of the synapses is that they are the site of action for the majority of psychoactive drugs. Psychotropic medications and neurotoxins can alter neurotransmitter release and reuptake, and the accessibility of receptor binding sites. For example, lysergic acid diethylamide (LSD) interferes with serotonergic synapses, while cocaine blocks reuptake of dopamine and therefore increases its effects. The poison strychnine blocks the inhibitory effects of the neurotransmitter glycine which results in uncontrollable muscle spasms and convulsions.

The synapses discussed so far communicate with other cells via chemical signalling molecules or neurotransmitters, and this is why they are sometimes termed ‘chemical synapses’. Electrical and immunological synapses also exist inside the nervous system; however, unless otherwise designated, the word ‘synapse’ generally refers to a chemical synapse. **Electrical synapses** or gap junctions make it possible for ions to flow directly through protein channels from one nerve cell to another, allowing the fast transmission of information. Because of the rate of transmission, electrical synapses are mainly involved in behaviours and neural processes that require quick responses such as escape mechanisms (Bennett & Zukin, 2004).

THE SYNAPTIC VESICLE

When an action potential arrives at the presynaptic terminal, calcium channels open and Ca^+ ions enter the cell. This calcium influx causes the movement and fusion of secretory vesicles to the cell membrane (a process known as exocytosis). Within the presynaptic cell, vesicles holding neurotransmitters are placed or ‘locked in’ at the synaptic membrane. Proteins in the presynaptic terminal referred to as SNAREs control fusion of the vesicles. The arriving action potential leads to a defined amount (a quantum) of neurotransmitter to be released into the synaptic cleft. The neurotransmitter molecules then travel across the synaptic cleft by **diffusion** to particular receptor sites on the presynaptic membrane, opening ion channels in the postsynaptic cell membrane. This results in ions moving, which consequently modifies the cell’s local transmembrane potential and leads to a change in the potential of the postsynaptic cell or a postsynaptic potential (PSP). Usually



within the nervous system, the result is an excitatory reaction (EPSP) as a result of depolarisation or an inhibitory reaction (IPSP) as a result of hyperpolarisation. The response of a synapse, and whether it is excitatory or inhibitory, is dependent on the type of receptors and neurotransmitters at the synapse.

MODULATION OF SYNAPTIC TRANSMISSION

Various processes affect the amount of the neurotransmitter required for release. One process called **presynaptic inhibition** causes a decrease in the quantity of neurotransmitter released despite an action potential in the presynaptic neuron. This takes place when a neurotransmitter release from one neuron impacts on the release of another neuron through an axoaxonic synapse, resulting in the partial depolarisation of the presynaptic neuron (Wu & Saggau, 1997). Fewer calcium (Ca^+) ions enter the presynaptic membrane as the action potential arrives, which causes less neurotransmitter release. The opposite effect occurs if there is a hyperpolarising release of the neurotransmitter at the axoaxonic synapse; there is an increased amount of neurotransmitter release or presynaptic facilitation.

It is also possible for a neurotransmitter to inhibit its own nerve cell. It sometimes happens that the neurotransmitter not only binds to postsynaptic receptors but also binds to presynaptic receptors, known as autoreceptors. These autoreceptors are located on presynaptic nerve cell membranes and serve as part of a feedback loop in signal transduction. It is possible to deactivate the influence of the neurotransmitter molecules on the postsynaptic membrane through enzymatic degradation, as in the case of **acetylcholinesterase (AChE)** or as with some other neurotransmitters via neurotransmitter reuptake.

NON-SYNAPTIC CHEMICAL COMMUNICATION

While neurotransmitters are released from the terminal buttons and have a local effect, neuromodulators – another communication substance released by neurons – travel greater distances and are dispersed more widely around the nervous system. Most neuromodulators are peptides, which are chains of **amino acids** linked together by peptide bonds. Neuromodulators affect general behavioural states such as vigilance and fearfulness.

Hormones also play a role in the communication of information around our bodies. Hormones are chemical substances that are secreted by cells of the endocrine glands or cells in other organs such as the stomach and kidneys. Most hormones fall into three categories: amino acid derivatives, peptides and proteins, and steroids.

The endocrine system is shown in Figure 1.6. Hormones are released by the endocrine gland into the extracellular fluid and are then distributed through the bloodstream. Specialised receptors for these hormones are located either on the surface of cells or deep within their nuclei. Cells that have these receptors for a particular hormone are called target cells. Many



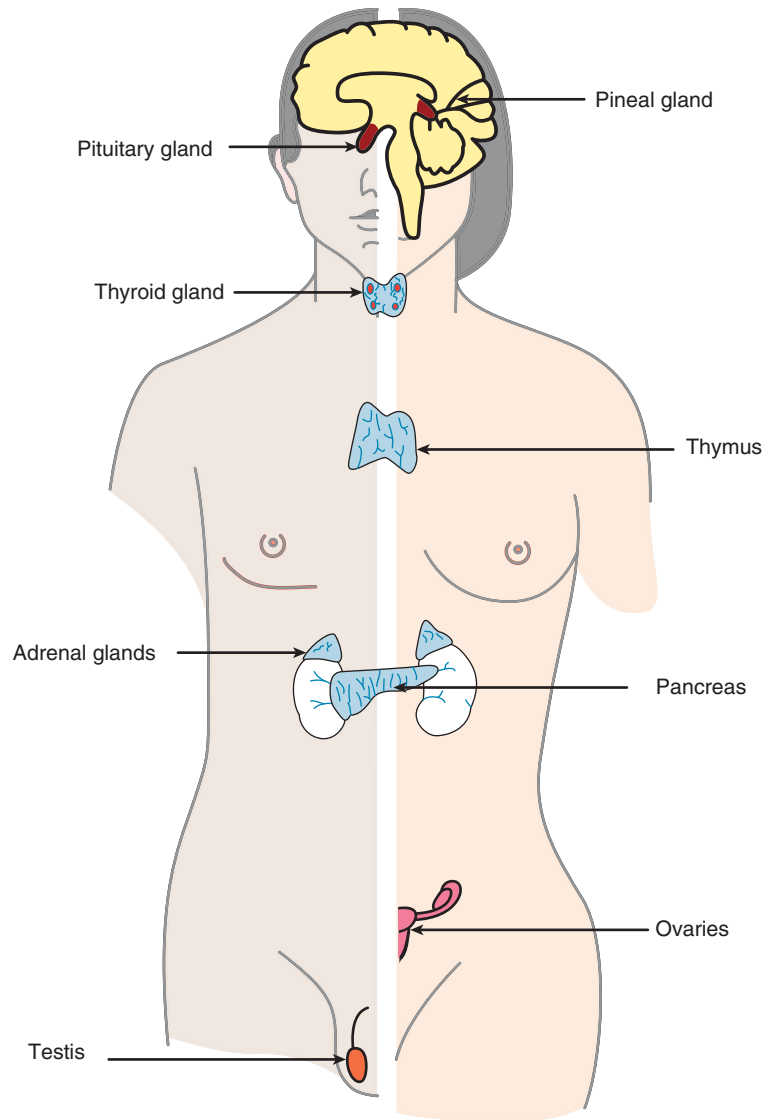


Figure 1.6 *The endocrine system*

neurons contain hormone receptors, so our behaviour is regularly affected by these substances. **Testosterone**, which is a sex hormone for instance, increases the aggressiveness of male animals. The following is a summary of the various glands of the endocrine system:

- ⚙️ *Adrenal glands*: secrete hormones which play a role in the body's reaction to stressful events.
- ⚙️ *Hypothalamus*: controls automatic functions such as regulating sleep; it also plays a major role in hunger and appetite.

- ❁ *Ovaries and testicles*: influence female and male characteristics.
- ❁ *Pancreas*: secretes **insulin**, a hormone that regulates the levels of glucose present in the body.
- ❁ *Parathyroid glands*: maintain calcium levels in the body by secreting a regulatory hormone.
- ❁ *Pineal body*: involved with sleep cycles and the daily biological cycles.
- ❁ *Pituitary gland*: plays a role in regulating other endocrine glands.
- ❁ *Thymus gland*: important in maintaining the body's immune system.
- ❁ *Thyroid gland*: plays a role in the metabolism of the body, including bone growth and heat production.

POSTSYNAPTIC RECEPTORS AND RECEPTOR TYPES

The effects of neurotransmitters is seen on the postsynaptic membrane, where the release of neurotransmitters results in a rapid opening of ion channels, involving a kind of receptor called **ionotropic** receptors or channel-linked receptors. Within this sort of receptor, the ion channel opens directly and the neurotransmitter alone is involved in the information transfer. Metabotropic receptors or G-protein-linked receptors are another type of receptor, and in these the ion channels open indirectly. When the neurotransmitter binds to a metabotropic receptor, another protein that is connected to the inside of the cell membrane becomes activated. This is referred to as a G protein. The G proteins trigger the production of another chemical known as a **second messenger**. This second messenger triggers the opening of the ion channels in the postsynaptic membrane. One of these second messengers is cyclic adenosine monophosphate (**cyclic AMP**), which is synthesised by adenosine triphosphate (ATP). Cyclic AMP is essential to the memory formation process (Jackson & Ramaswami, 2003) and may also play a role in the sedative effects of ethanol (Misra & Pandey, 2003).

The features of ionotropic receptors are:

- ❁ They are sometimes called ligand-gated ion channels.
- ❁ Action is instant and short.
- ❁ The channels in the excitatory receptors are for positively charged ions, otherwise known as cations.
- ❁ Depolarisation is achieved mostly by Na^+ .
- ❁ Hyperpolarisation is achieved by Cl^- influx or K^+ efflux permitting inhibitory action.

Metabotropic receptors are not direct, and can have widespread actions which are often prolonged. An example is muscarinic ACh receptors.

NEUROTRANSMITTERS

We can categorise neurotransmitters into two broad groupings: the ‘classical’ small molecule neurotransmitters, and the larger neuropeptide neurotransmitters (Figure 1.7). Among neurotransmitters in the category of small molecule neurotransmitters there is a group termed the monoamines; these include dopamine, noradrenaline and serotonin, which are often looked upon as a unique group due to their correlation in terms of their chemical makeup.

The criteria for classifying a biochemical substance as a neurotransmitter are:

- ❁ The substance has to be packaged into synaptic vesicles and be present in the presynaptic nerve terminal.
- ❁ On depolarisation or on arrival of an action potential at the presynaptic membrane, the substance must be released from the nerve terminal.
- ❁ Specific receptors for the substance must be available on the postsynaptic membrane.

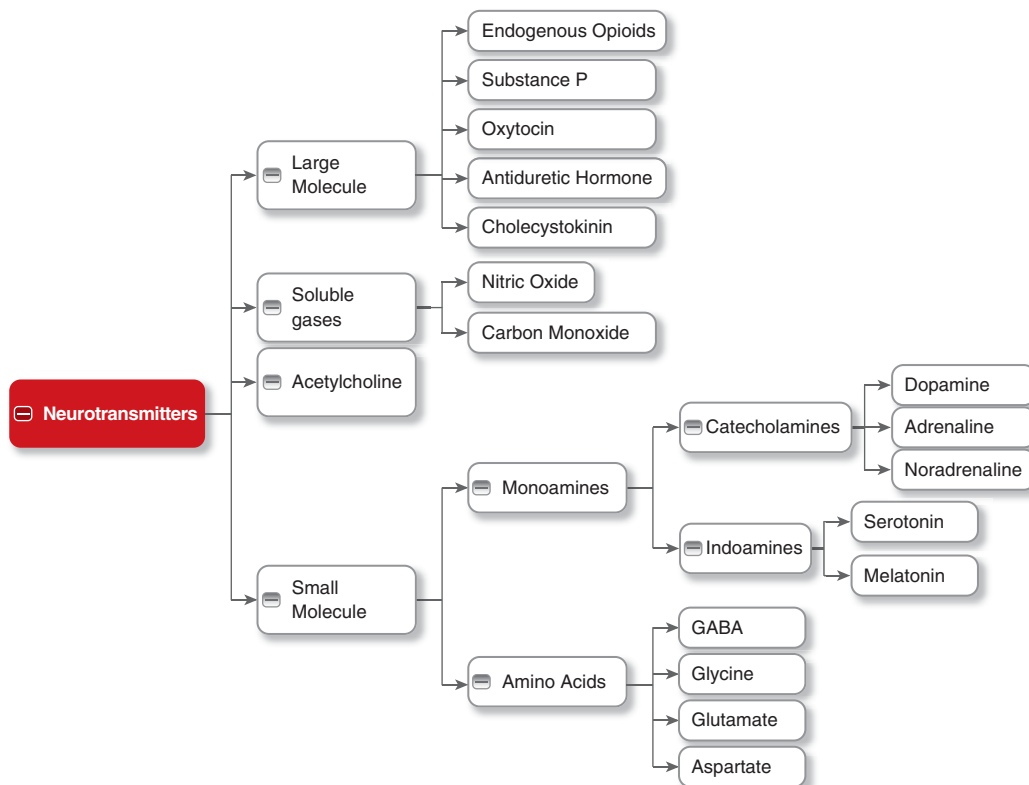


Figure 1.7 Neurotransmitters



Neurotransmitters act in two ways: direct and indirect. In *direct action*, the neurotransmitter opens ion channels by binding to a channel-linked receptor; this causes very fast responses. Examples are amino acids and AChE. In *indirect action*, the action takes place via a G-protein-linked receptor, and when the neurotransmitter binds it causes a cascade of intracellular second messenger systems; this generally has long-lasting effects. Examples are soluble gases such as NO, and neuropeptides.

The major types of neurotransmitter are described in the following sections.

THE AMINO ACIDS

GABA

GABA is the main inhibitory neurotransmitter in the CNS, occurring in 30–40% of all synapses. GABA is located in high concentrations in the substantia nigra and globus pallidus nuclei of the basal ganglia, the hypothalamus, the periaqueductal grey matter and the hippocampus. The concentration of GABA within the brain is 200–1000 times greater than that of the monoamines or **acetylcholine**. Gamma-aminobutyric acid is created from glutamate via the enzyme glutamate decarboxylase. Synapses using GABA are referred to as GABAergic synapses. GABA's activity ends with reuptake, just as with any other amino acid neurotransmitter. GABA A and GABA B are the most analysed of the five types of GABA receptors (Enz, 2001). Several disorders have been connected to GABA receptors; dysfunction with this inhibitory neurotransmitter can cause seizures (Pearl, 2004) and anxiety disorders (see Froestl, 2010 for a review of treatment).

Glycine

Another inhibitory neurotransmitter, found mainly in the spinal cord, **brain stem** and retina, is glycine. This neurotransmitter is only present in vertebrates (Hernandes & Troncone, 2009). It is a simple amino acid in both structure and function. It is formed of an amino group and a carboxyl (acidic) group attached to a carbon atom; when released into a synaptic cleft it binds to receptors, making the postsynaptic membrane more penetrable to Cl⁻ ions. This movement hyperpolarises the membrane, creating less chance for depolarisation. Thus glycine is an inhibitory neurotransmitter. One glycine **antagonist** is strychnine, which can stick to the glycine receptor and prevent the opening of the chloride ion channel, thus stopping inhibition. This disinhibition and consequent spinal hyperexcitability are the very things that make strychnine poisonous (by suffocating or exhausting its victims).

Glutamate (glutamic acid)

Glutamate is the most commonly found excitatory neurotransmitter. The excitatory action of glutamate is stopped by a chloride-independent membrane transport system that reabsorbs glutamate and aspartate into the presynaptic membrane. The **N-methyl-D-aspartate** (NMDA) glutamate receptor is one of the subtypes of the glutamate receptors and is the only receptor known to be regulated by a ligand (i.e. glutamate) and by voltage. NMDA





ESSENTIAL BIOLOGICAL PSYCHOLOGY

receptors have a role to play in the process known as long-term potentiation or LTP. LTP takes place in the hippocampus where an activity-dependent increase in synaptic efficiency occurs, making the process key to some forms of learning and memory (see Chapter 11).

The amygdala and basal ganglia also contain high concentrations of NMDA receptors. Too much of the excitatory neurotransmitter released brings on glutamic acid excitotoxicity. Once glutamate is released into the cleft of a synapse, it is either reabsorbed into nerve cells by way of the ion-exchange transport system or changed by astrocytes into glutamine, which is not involved in excitotoxicity and therefore can be safely returned to the nerve cells to be converted back into glutamate.

Aspartate

Aspartate behaves as an excitatory neurotransmitter, stimulating NMDA receptors (Grem, King, O'Dwyer, & Leyland-Jones, 1988). Aspartate, along with glycine, opens ion channels and is primarily in the **ventral** spinal cord; it is inactivated when reabsorbed into the presynaptic membrane.

MONOAMINES

Serotonin

Serotonin is also referred to as 5-hydroxytryptamine (5-HT). Serotonin is synthesised from the amino acid tryptophan. Serotonin is believed to play an important role in the central nervous system in regulating anger, aggression, mood, sleep, body temperature, sexuality, vomiting and appetite (Folk & Long, 1988). The main source of 5-HT in the brain is the cells in the raphe nuclei which are a cluster of nuclei found in the brain stem. Serotonergic pathways travel widely all over the brain stem, the cerebral cortex and the spinal cord. The serotonin receptors are called 5-HT receptors. The 5-HT₃ receptor is a ligand-gated ion channel; additional 5-HT receptors are G-protein-coupled receptors that depend on intracellular second messenger configuration, as previous explained. Serotonergic action is stopped mainly by the uptake of 5-HT from the synaptic cleft. This action takes place via the 5-HT reuptake transporter on the presynaptic neuron. Selective serotonin reuptake inhibitors (SSRIs) and **tricyclic antidepressants** (TCAs) are used for treating depression. Amphetamine, cocaine and 3,4-Methylenedioxymethamphetamine or MDMA (ecstasy) can all inhibit the reuptake of 5-HT.

Melatonin

Melatonin is derived from serotonin within the pineal gland and the retina. The pineal parenchymal cells secrete melatonin into the blood and cerebrospinal fluid. Melatonin plays a role in the sleep/wake cycle; its synthesis and secretion rise during the dark hours and are maintained at a low level during daylight hours (see Chapter 9). Melatonin also functions as an inhibitor of the synthesis and secretion of other neurotransmitters such as dopamine and GABA.

Noradrenaline

Noradrenergic neurons can be found in the locus coeruleus, the pons and the reticular formation in the brain, and project to the cerebral cortex, midbrain and hippocampus.



Noradrenaline is an excitatory neurotransmitter, and noradrenergic pathways are thought to play a key role in behaviours like attention and arousal. Noradrenergic activity may trigger modifications in several functions including heart rate, blood pressure and digestive processes (Lambert, 2001).

Dopamine

Dopamine also falls under the classification of monoamine neurotransmitters. In the central nervous system, dopamine acts on the five types of dopamine receptors – D1, D2, D3, D4 and D5 – and their variants. Dopaminergic neurons can be found in four dopamine pathways in the brain: the nigrostriatal, the mesocorticolimbic, the mesocortical and the tuberoinfundibular pathways. Dopamine is seen as the reward neurotransmitter, and recent work has shown larger receptor numbers in individuals with a higher social status, suggesting these individuals may experience more pleasure from their experiences. More details can be found in Box 1.2. Dopamine also acts as a hormone and restricts the release of prolactin from the **anterior** lobe of the pituitary.

A shortage of cells that produce dopamine in the substantia nigra contributes to the development of **Parkinson's disease**, while excessive dopamine may be involved in the development of schizophrenia (Stone, Morrison, & Pilowsky, 2007). When used medically, dopamine works on the sympathetic nervous system, resulting in increased heart rate and blood pressure. However, because dopamine cannot permeate the blood–brain barrier, it cannot have a direct effect on the CNS. To increase the level of dopamine in the brains of Parkinsonian patients, **L-DOPA** (levodopa), the precursor of dopamine, is administered because it can pass across the blood–brain barrier and enter into the CNS (Tedroff, 1997).

BOX 1.2 Dopamine receptor density and social status

Background

Previous positron emission tomography (PET) imaging studies in non-human primates had shown that striatal dopamine type 2/3 (D2/3) receptors are associated with social hierarchy in monkeys, and that the more dominant animals exhibit higher levels of D2/3 receptor binding. This study (Martinez et al., 2010) looked at the phenomenon in human participants.

Methods

Healthy volunteers ($N = 14$) were scanned using PET technology to measure D2/3 receptor binding potential (BP). The Barratt Simplified Measure of Social Status (BSMSS) was used to assess social status. Individuals were also assessed on their level of social support using the Multidimensional Scale of Perceived Social Support (MSPSS).

(Continued)



(Continued)

Results

A correlation was seen between social status and dopamine D2/3 receptors, as measured by striatal binding of the PET ligand [11C]raclopride (Figure 1). A similar correlation was seen with perceived social support, where higher [11C]raclopride BP correlated with higher scores on the MSPSS (Figure 2).

Interpreting the findings

The results of this study supported the idea that social status and social support are correlated with D2/3 receptor binding, and suggest that individuals who attain greater social status would be expected to have more rewarding and stimulating experiences in life as they have more receptors for dopamine to act upon within the striatum. This finding may also shed light on the risk for alcoholism among vulnerable individuals, as it suggests that individuals with low D2/3 receptors may be vulnerable to lower social status and other disadvantageous social factors which have previously been found to be associated with alcohol and substance use.

Reference

Martinez, D., Orlowska, D., Narendran, R., Slifstein, M., Liu, F., Kumar, D., et al. (2010). Dopamine type 2/3 receptor availability in the striatum and social status in human volunteers. *Biological Psychiatry*, 67(3), 275–278.

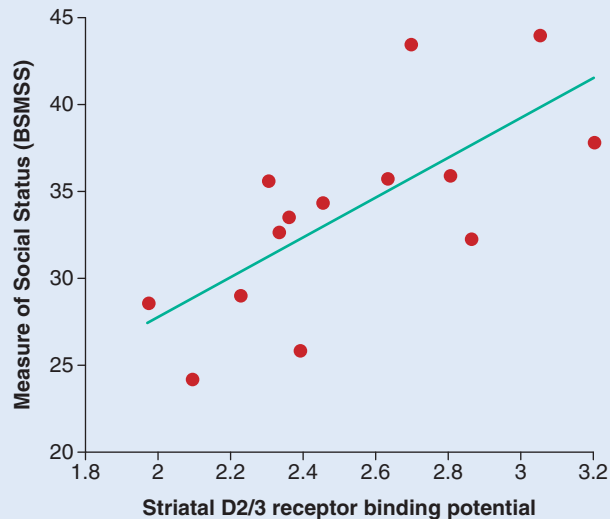
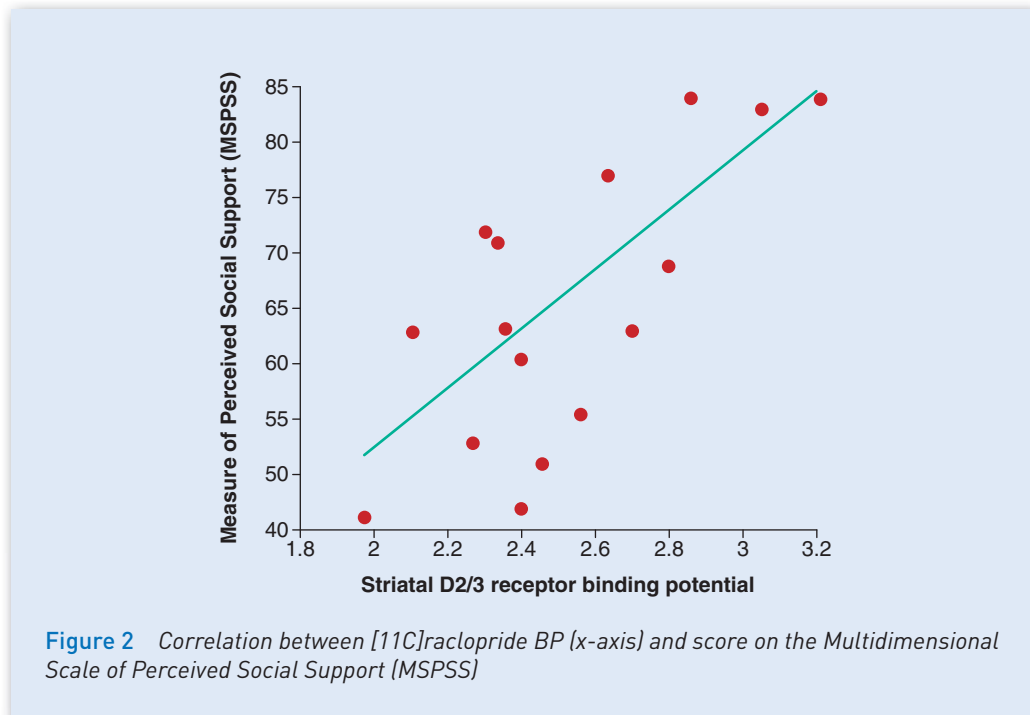


Figure 1 Correlation between [11C]raclopride BP (x-axis) and social status as measured with the Barratt Simplified Measure of Social Status (BSMSS)



ACETYLCHOLINE

Acetylcholine (ACh) was the first neurotransmitter to be identified. We find ACh in both the PNS and the CNS. The common consensus is that cholinergic pathways play a role in cognitive functions, memory in particular. ACh is also a major neurotransmitter of the parasympathetic nervous system, and anticholinergic drugs will modify body functions associated with this part of the nervous system. We see this with some antidepressant medications, where blocking cholinergic receptors and other anticholinergic activity result in side effects like dry mouth. ACh is also associated with Alzheimer's disease, in which patients have a noticeable acetylcholine deficiency (Perry, 1988) (see Chapter 13).

There are two primary kinds of acetylcholine receptors: nicotinic acetylcholine receptors (nAChR) and muscarinic acetylcholine receptors (mAChR). Nicotine, found in cigarettes, stimulates nicotinic receptors, while muscarine, a poison found in mushrooms, activates muscarinic receptors. Almost every receptor in the CNS is muscarinic, while the main centres of nicotinic receptors are located on muscle **motor end-plates** and autonomic ganglia.

NEUROPEPTIDES AND NEUROMODULATORS

Neuropeptides are constructed of short amino acid chains and belong to a class of protein-like molecules which act as neurotransmitters (Yew, Chan, Luo, Zheng, & Yu,



ESSENTIAL BIOLOGICAL PSYCHOLOGY

1999). Neuromodulators, as their name suggests, do not directly excite or inhibit the postsynaptic cell, but increase or reduce the release of neurotransmitter or modify the reaction of postsynaptic cells.

SOLUBLE GASES

Certain soluble gases also act as neurotransmitters. Nitric oxide (NO) is produced by many cells in the body such as the vascular endothelium cells; it is central in the regulation of blood flow and may also play a role in memory and learning. Another soluble gas, carbon monoxide, does not appear to be released in a directed manner but may play a role in the relaxation of blood vessels.

SUMMARY

In this chapter we have discovered that the nervous system has two divisions: the peripheral nervous system (PNS) and the central nervous system (CNS). We have also discussed the various cells of the nervous system and seen that the cell body of the neuron contains all the components that allow the cell to function. Neurons may be classified in a variety of ways, according to their shape, function or location, or the neurotransmitter they synthesise and release. Neurons have an input side called dendrites, which look like the bare branches of a tree, and an output side emerging from the cell called an axon. The thickening of a neuron at its far or distal end is called the terminal bouton; it houses the synaptic vesicles that contain neurotransmitter which is used for communication between the neuron and whatever it connects to via a synapse. The synapse comprises the presynaptic region, the synaptic cleft and the postsynaptic region. We also discussed the concept of non-synaptic chemical communication and detailed the endocrine system. The endocrine system is a collection of glands that produce hormones that regulate your body's growth, metabolism and sexual development and function. The hormones are released into the bloodstream and transported to target cells and organs throughout the body. We have also found that not all the cells in the nervous system are neurons, which represent approximately 50% of the volume of the CNS; the remainder consists of various supporting cells called glial cells which maintain homeostasis in addition to providing support and nutrition. We also discussed the cellular membrane and the presence of a voltage across the membrane when the neuron is at rest. This is called the resting potential and is typically -70 mV. We have also seen how the movement of ions across the membrane produces an action potential which is generated at the axon hillock and conducted along the axon by progressive depolarisation. Finally, we examined the various neurotransmitters in the nervous system which are released from the end of the terminal bouton when the conditions are right. There are different types of neurotransmitter substance and they facilitate the communication between neuron and target cell.



FURTHER READING

Gazzaniga, M.S., Ivry, R.B., & Mangun, G.R. (2008). *Cognitive neuroscience: the biology of the mind* (3rd edn). New York: Norton.

Roger, B., & Barasi, S. (2008). *Neuroscience at a glance*. Chichester: Wiley-Blackwell.

KEY QUESTIONS

- 1 Describe the organisational structure of the nervous system.
- 2 How is information transmitted around the nervous system?
- 3 What are the different types of neurotransmitter?