3rd Edition

Mental Health Medicines Management for Nurses

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LM Learning Matters

Learning Matters
A SAGE Publishing Company
1 Oliver's Yard
55 City Road
London EC1Y 1SP

SAGE Publications Inc.
2455 Teller Road
Thousand Oaks, California 91320

SAGE Publications India Pvt Ltd
B 1/I 1 Mohan Cooperative Industrial Area
Mathura Road
New Delhi 110 044

SAGE Asia-Pacific Pte Ltd
3 Church Street
#10–04 Samsung Hub
Singapore 049483

Third edition published in 2021

Editor: Laura Walmsley
Senior project editor: Chris Marke
Project management: River Editorial
Marketing manager: George Kimble
Cover design: Wendy Scott
Typeset by: C&M Digitals (P) Ltd, Chennai, India
Printed in the UK

Library of Congress Control Number: 2020949654

British Library Cataloguing in Publication Data

A catalogue record for this book is available from the British Library.

ISBN: 978-1-5264-7361-5
ISBN: 978-1-5264-7360-8 (pbk)

Contents

Chapter 3 Essential anatomy and physiology of the brain related to psychopharmacology

Chapter aims

By the end of this chapter, you should be familiar with:

- the anatomy and physiology of the brain regions relevant to psychopharmacology;
- the role of ion channels and classical neurotransmission;
- neural connectivity and the importance of synapses.

Introduction

The human brain is the result of at least four billion years of evolution and is the most complex object known; it is an electrical and chemical powerhouse that sends messages where needed in a perfectly targeted way. The brain is soft and grey, and weighs about 1.5 kg. It is not only where we experience and manipulate the world, but it is also responsible for the control of our breathing, body temperature, blood pressure and hormones. Unlike the heart or lungs, the brain has no moving parts; and unlike the kidney, liver or spleen, it does not make anything. Unlike the skin or bones, the brain serves no *obvious* purpose, yet we know it is responsible for thoughts, emotions and free will. In short, the simple view of the brain as the most fundamental of all organs may seem rather obvious, but how did we come to such a conclusion? To answer this question, we need to go back into the past and find out what people before us believed about the brain.

In ancient Egypt, the brain was regarded to be a form of 'cranial stuffing' that served no useful purpose. The heart was instead thought of as the seat of intelligence. This belief is best exemplified by the way that ancient Egyptians prepared bodies for mummification, by taking great care in the preparation of organs such as the heart, lungs, liver and stomach, while the brain was simply scooped from the skull. As much as we now know that the brain is the seat of intelligence, colloquial expressions such as 'learning something by heart' or 'suffering from heartache' remain in common use to this day.

Around 450 BC, the Greek physician Alcmaeon was among the first to recognise the brain's importance, but his view was not universally accepted. One hundred years later, Aristotle reasserted the importance of the heart and suggested that the brain was little more than a cooling system for the heart.

From the first century BC, the prevailing view was that of Galen, a Greek doctor who suggested that the heart controlled the four humours: blood, phlegm, yellow bile and black bile. This theory was untrue, of course, but Galen did manage to recognise the link between the brain and memory, as well as emotions and the processing of senses. It was not until the 1800s that progress regarding brain physiology was made.

Thomas Willis (1621–1675), an English neurologist, is largely credited with advancing knowledge about the brain, being the first person to examine the brain with real scientific rigour. After years of research, he published his groundbreaking *Cerebri Anatome*, providing the first complete description of the brain's regions. He correctly linked memory and higher function with the cerebral hemispheres, as well as laying down the basis of brain science terminology. Another breakthrough by Willis was to correctly propose that the liquid-filled spaces deep inside the brain, the ventricles, served no significant purpose, whereas before many believed that the ventricles were the centre of high brain function. Several other scientists contributed to our knowledge of the brain, including Emanuel Swedenborg (1688–1772), Franz Joseph Gall (1758–1828), Pierre Paul Broca (1824–1880) and Carl Wernicke (1848–1905). Most importantly, Santiago Ramón y Cajal (1852–1934) published a textbook regarded by many as one of the greatest scientific texts: *Manual of Normal Histology and Micrographic Technique*. He was the first to suggest that the brain and the nervous system consist of discrete cells called neurons. He described the nervous system and the brain with unparalleled clarity, and for his work he received the Nobel Prize in Physiology or Medicine in 1906. These breakthroughs inspired many surgical techniques and drug discoveries that remedy brain dysfunctions. But the greatest advance of all was observing the activity of the living brain using brain scanning.

Brain scanning

Our knowledge of the brain has been greatly enhanced by scanning techniques. The first major attempt at scanning the human brain was by Hans Berger in 1924. He used an electroencephalogram (EEG) to measure human brainwaves, and this laid the groundwork for future research into computerised axial tomography (CAT/CT) and positron emission tomography (PET). CAT scans use powerful computers to convert two-dimensional X-ray pictures into three-dimensional images for further study. PET scans use a radioactive 'tracer' substance that is injected directly into the human body. This substance gradually accumulates inside the major organs while at the same time emitting positron radiation, which is detected by a sensor. A more recent and non-invasive technique is functional magnetic resonance imaging (fMRI). This technique uses a magnet weighing several tons. It relies on the metal-charged ions in our body, including iron. The magnetic properties of the metal charges change in the presence

of oxygen. A change in oxygen concentration reflects brain activity and a powerful computer processes this information to construct a two- or three-dimensional image of brain activity. This technique allows us to observe the global behaviour of the brain during different types of activities, such as mental arithmetic, reading a book or watching a movie.

In summary, it has taken us centuries to understand even the basic functions of the human brain. Although there is still much that we do not know about the brain, we now have a good knowledge of the basic anatomy and physiology of each region of the brain.

Brain regions

In neuroscience, the brain is considered to have at least six main regions: the cerebral hemispheres, the diencephalon (thalamus and hypothalamus), the midbrain, the cerebellum, the pons, and the medulla oblongata. Each brain region has a complex internal structure.

The brainstem

This is the stalk-like part of the brain connecting to the spinal cord and the forebrain, and it is made up of the pons, the medulla oblongata and the midbrain (see Figure 3.1). The brainstem functions as an important relay station for every electrical impulse that passes between the brain and the spinal cord to allow the body to function normally.

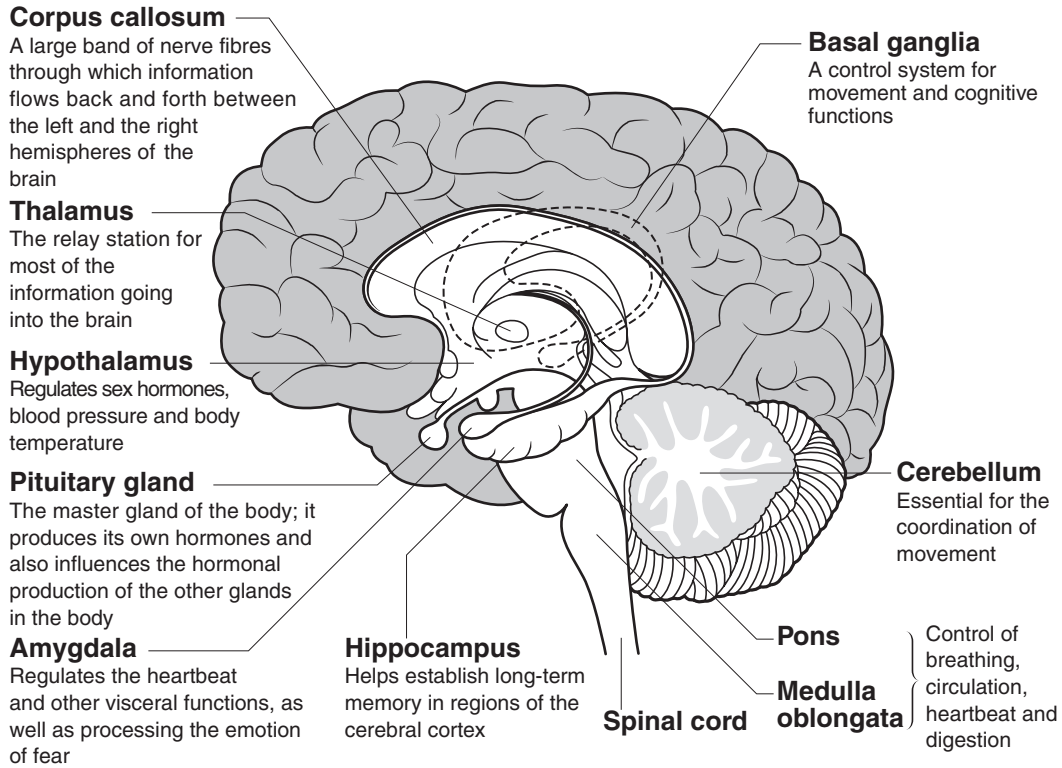

Figure 3.1 A cross-section of the brain showing the major regions and their functions

The medulla oblongata controls the unconscious or autonomic parts of bodily function, such as blood pressure, heart rate and muscle tone. It also plays a part in regulating other reflexive functions, such as sneezing, coughing and vomiting.

The pons is situated between the midbrain and the medulla oblongata. The pons' function is to relay signals from the cortex to assist in the control of movement, and it is also involved in the control of sleep and arousal. The pons also plays an important part in fine-tuning motor messages as they travel from the motor area of the cerebral cortex down to the cerebellum. The midbrain is positioned between the hindbrain and the forebrain. It forms part of the brainstem and connects the brainstem to the forebrain, and it is mainly responsible for controlling sensory processes. Before you read further, undertake Activity 3.1.

Activity 3.1 Critical thinking

If a person is pronounced to be 'clinically dead', what part of the brain plays an important part in coming to this conclusion, and why?

An outline answer is provided at the end of the chapter.

The cerebellum

The cerebellum, or 'little brain', is found behind the brainstem, to which it connects. It is split into two hemispheres and it has a convoluted surface that makes it look somewhat like a giant walnut (see Figure 3.1). It is one of the earliest brain regions to evolve and the human version is comparatively like that of other mammals. The cerebellum fine-tunes and smooths out movements, especially those necessary for quick changes in direction. For example, when a person reaches out to catch a moving object, the cerebellum is involved in the timing of movement.

As the motor systems of mammals became more sophisticated, there was a need to coordinate increasingly accurate movements, such as those of the eyes, hands and fingers, and this has resulted in the evolution and enlargement of the cerebellum. This is evident in its structure, in which the central part is the oldest and most primitive and the outer part is concerned with functions unique to humans. It has strong connections with the motor parts of the cortex. The cerebellum has two lobes, but – unlike the motor cortex – it controls movements on the same side of the body as itself. When the cerebellum goes wrong, it results in awkward, jerky movements and an impairment of coordination called *ataxia*. Professional boxers are particularly susceptible to slight cerebellum damage, which can result in 'punch-drunk syndrome'. The most common cause of temporary ataxia is consuming alcohol. Now we need to turn our attention to another part of the brain called the diencephalon.

The diencephalon

The diencephalon, or 'interbrain', is part of the forebrain that is located between the cerebral hemispheres and above the midbrain. This region of the brain includes the

thalamus, the hypothalamus, the epithalamus, the prethalamus or subthalamus, the pineal gland, the pituitary gland, and other structures (see Figure 3.1).

The egg-shaped thalamus that is above the hypothalamus consists of two oval-shaped lobes that lie side by side, one in each hemisphere. It is essential for gating and processing sensory information entering the brain. The only exception to this is that it does not process information from the nose. The thalamus processes information and decides whether it needs to be sent to the cortex for conscious consideration. Also, information from the cerebellum and other areas that are involved in movement is sent to the thalamus for processing. Just below the thalamus is the hypothalamus, which controls a multitude of functions.

The hypothalamus is about the size of a pearl or grape, but despite its small size it is the control centre for many autonomic functions, and it connects to almost every other part of the brain. It is the control centre for many autonomic functions of the central and peripheral nervous systems. The hypothalamus influences various emotional responses through its influence on the pituitary gland, the skeletal muscular system and the autonomic nervous system. The hypothalamus directs a multitude of important functions in the body. It is essential to motivation, including seeking out pleasurable rewards. Its connection with structures of the endocrine and nervous systems allows it to play a vital role in maintaining **homeostasis**. Blood vessel connections between the hypothalamus and the pituitary gland allow hypothalamic hormones to control pituitary hormone secretion (see Table 3.1). Some of the physiological processes that the hypothalamus regulates include blood pressure, body temperature, cardiovascular system functions, fluid balance and electrolyte balance.

Table 3.1 Hormones produced by the hypothalamus and their function

Hormone	**Function**
Anti-diuretic hormones	Regulate water levels and influence blood volume and blood pressure.
Corticotropin-releasing hormone (CRH)	Central role is the regulation of stress. It causes release of adrenocorticotropic hormone (ACTH) from the pituitary gland. CRH also acts on many other areas within the brain, where it suppresses appetite, increases anxiety, and improves memory and selective attention. CRH is also produced throughout pregnancy in increasing amounts by the foetus and the placenta, with the effects of increasing cortisol. Ultimately, it is the high levels of CRH, along with other hormones, that are thought to start labour.
Oxytocin	Influences sexual and social behaviour. Its release during labour is triggered by the widening of the cervix and the vagina.
Gonadotropin-releasing hormone	Produced and released into tiny blood vessels in the pituitary gland, where it stimulates the production of follicle-stimulating hormone (FSH) and luteinising hormone (LH), or lutropin.
Somatostatin	Somatostatin from the hypothalamus inhibits the pituitary gland's secretion of growth hormone (GH) and thyroid-stimulating hormone (TSH).
GH-releasing hormone	Stimulates the pituitary gland to produce and release GH into the bloodstream. This then acts on virtually every tissue of the body to control several physical functions and processes.
Thyrotropin-releasing hormone (TRH)	Stimulates the pituitary gland to release TSH, which regulates metabolism, growth, heart rate and body temperature.

The limbic system

In addition to the structures that make up the diencephalon, there are further major brain structures buried deep beneath the folds of the cortical hemispheres: the basal ganglia, the amygdala and the hippocampus (see Figure 3.1), as well as the cingulate gyrus, the fornix, the thalamus, the olfactory cortex, the spinal cord and the cerebrum. These structures and others form the limbic system.

The limbic system, which includes portions of all the lobes of the cerebral hemispheres, is a complex set of three C-shaped structures containing both grey and white matter. It is buried under the cortex and can be located on top of the brainstem. It is one of the more primitive parts of the brain. Limbic system structures are parts of the brain that are most closely associated with emotional expression and motivations, particularly those that connect to our survival. Such emotions include fear and anger, as well as emotions related to sexual behaviour. The system influences both the peripheral nervous system and the endocrine system. Damage to or stimulation of sites within this system may profoundly affect emotional expression, either by causing excessive reactions to situations or greatly reducing emotional response. Clinical conditions involving the limbic system include epilepsy, congenital syndromes, dementias and various psychiatric disorders, as will be seen in later chapters. Here, we describe key structures that are important to mental health pathology and treatment.

Basal ganglia

Connected to the cortex and the thalamus are swollen structures called the basal ganglia (see Figure 3.1). The basal ganglia consist of substructures, including the caudate nuclei, the putamen, the nucleus accumbens, the olfactory tubercle, the globus pallidus, the ventral pallidum, the substantia nigra and the subthalamic nucleus. In general, the basal ganglia structures receive most of their input from the cortex and are responsible for the coordination of fine movement. Parkinson's disease provides an excellent example of what happens when there is damage to the basal ganglia through the progressive destruction of dopamine neurons. This destruction leads to a decrease in the activity of other structures within the basal ganglia. A related movement disorder, tardive dyskinesia, may result from long-term use of antipsychotic medication (see Chapter 11).

Nucleus accumbens

A part of the basal ganglia that deserves special consideration is the nucleaus accumbens. It is a paired structure (one in each hemisphere) located near the amygdala and is part of a group of structures that form the dopamine pathway originating from the brainstem (upper pons), terminating in the frontal cortex. The nucleus accumbens itself is separated into two anatomical components: the shell and the core. These two connecting areas have overlapping connections but make different contributions to its

function. The most widely accepted role of the nucleus accumbens is in the 'reward circuit' of the brain. When we do anything that we consider rewarding (e.g. eat food, have sex, take drugs), dopamine neurons (along with other types of neurons) in the ventral tegmental area (VTA) of the brain are activated, increasing dopamine levels in the nucleus accumbens (see Chapter 10). However, this theory is under challenge as new insights seem to suggest that dopamine levels also increase when we experience unpleasant events (Volman et al., 2013).

Amygdala

The term 'amygdala' comes from the Greek word for 'almond' and is a reference to its size and shape. The amygdala is found below the hypothalamus, deep in the temporal lobe (see Figure 3.1). Despite its relatively small size, the amygdala plays an important part in generating emotional responses, such as fear, anger and desire, and it is responsible for the way we relate to the world and those around us. The amygdala is also responsible for determining what memories to store and where to store them in the brain. The decision of what memory to store is believed to be based on how big an emotional response an event invokes in us. Scientific studies of the amygdala have led to the discovery of neurons that are responsible for fear conditioning – an associative learning process where we learn through repeated experiences to fear something (see Chapter 10). Our experiences can cause brain circuits to change and form new memories. For example, when we hear an unpleasant sound, the amygdala heightens our perception of the sound. We then consider this heightened perception as distressing and we form memories associating the sound with unpleasantness. If the noise surprises us, we have an automatic fight or flight response. This response involves the activation of the sympathetic division of the peripheral nervous system. In turn, the activation of the nerves of the sympathetic division results in an accelerated heart rate, dilated pupils, an increase in metabolic rate, and an increase in blood flow to the muscles. The amygdala coordinates this activity and allows us to respond appropriately to danger.

Hippocampus

Close to the amygdala is the hippocampus (see Figure 3.1), which takes its name from its seahorse-like shape. It is a paired structure, with one hippocampus located in each hemisphere. It is particularly important in creating new memories and connecting emotions and senses, such as smell and sound, to memories. It acts as a memory indexer by sending memories out to the relevant part of the cerebral hemisphere for long-term storage and retrieving them when necessary. It is also here that experiences turn into neural pathways that are then stored for future reference. People who experience damage to this structure have difficulty in storing new information, and Alzheimer's disease is a prime example.

Alzheimer's disease severely affects the hippocampus first, before other parts of the cortex, so memory is usually the first thing to falter (i.e. the ability to make new

memories). The hippocampus also seems to be involved in severe mental illnesses such as schizophrenia and some severe depressions, where it appears to shrink. Accumulating evidence also suggests that the hippocampus undergoes significant alteration because of stress or post-traumatic stress disorder (PTSD). Before you proceed further, consider Activity 3.2.

Activity 3.2 Critical thinking

The hypothalamus is part of a collection of brain tissues called the diencephalon, and it is connected to every part of the brain. What may cause hypothalamic dysfunction?

An outline answer is provided at the end of the chapter.

The cerebral cortex

The crowning achievement of brain evolution in many respects must be the cerebral cortex (see Figure 3.2). This is a rippling outer layer that gives the human brain most of its unique powers. The cortex grew a lot during a relatively short evolutionary period, and to accommodate its growth it became increasingly folded. It is estimated that the human cortex has an area of about 1.5 m^2 and is 4 mm thick. The grey surface of the cortex is due to a vast network of specialised neurons, six layers of which travel down towards the underlying white matter. In the white matter region, the same neurons form a vast number of connections with other neurons. This vast matrix allows for swift intercommunication, facilitating our powers of thought.

The cortex is not a homogeneous region as it is divided into many areas (Gibb, 2012). First, it is divided into two hemispheres (left and right), which are themselves divided by deep grooves into four major areas called 'lobes': the frontal, parietal, occipital and temporal lobes (see Figure 3.2).

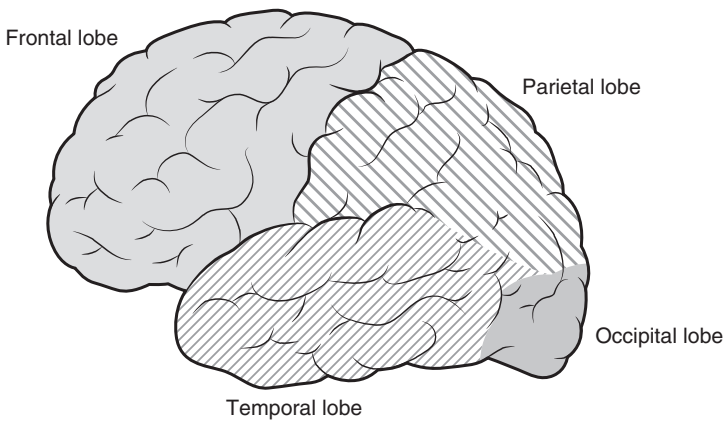

Figure 3.2 The four lobes of the cerebral cortex

The frontal lobe lies directly beneath the forehead and is involved in what are collectively termed 'higher functions'. These higher functions include attention, planning, language and movement. It is like a master control unit that helps to integrate information and govern what the rest of the brain does. Behind the frontal lobe and at the top of the head is the parietal lobe, which processes sensory information, allowing us to perceive the world and our place within it. At the back, the occipital lobe deals primarily with vision, and it is here that signals from the eyes become transformed into useful visual representations. Finally, the temporal lobes are located on each side of the brain, and they mainly process sound and language. Because they connect to the hippocampus, they are also concerned with memory formation and retrieval.

The corpus callosum

A bundle of tissue called the corpus callosum holds the brain's hemispheres together. The corpus callosum is the largest bundle of nerve fibres in the brain and it is also the main channel through which information flows from one side of the brain to the other. If there is damage to the corpus callosum, this can give rise to illnesses such as epilepsy. Now turn your attention to Activity 3.3.

Activity 3.3 Research

The cerebral cortex is a highly evolved part of the brain. Name the subregions of the cerebral cortex and their functions.

An outline answer is provided at the end of the chapter.

Table 3.2 A summary of the parts of the brain and their functions

Part	**Function**
Frontal lobe	Memory, consciousness, motor activities, judgements, controls emotional response and language.
Parietal lobe	Visual attention, touch perception, goal-directed voluntary movements, manipulation of objects, integration of different senses.
Occipital lobe	Vision.
Temporal lobes	Hearing ability, memory, visual perceptions, object categorisation.
Midbrain	Connects the brainstem to the forebrain, controls sensory processes.
Pons	Relays signals from the cortex, involved in sleep arousal.
Thalamus	Processes sensory information entering the brain.
Hypothalamus	Connected to every part of the brain, important in motivation and seeking reward.
Cerebellum	Controls movement.

The neural network

The nervous system consists of the brain, the autonomous nervous system (ANS) and the central nervous system (CNS). It is made up of specialised cells that communicate with each other and with other cells in the body. These specialised cells are called neurons, or nerve cells in common parlance, and the human brain consists of approximately 200 billion of them.

There are three main classes of neurons: sensory neurons, motor neurons and interneurons. Each neuron links with thousands of other neurons through small spaces called synapses. The brain has trillions of these specialised connections. Sensory or afferent neurons carry messages to the central nervous system from sensory receptors in the the skin, eyes, nose, and so on, as well as some organs, muscles and joints. The brain and at times the spinal cord interpret these messages and send appropriate responses through motor or efferent neurons, which cause sensory organs (muscles, glands, etc.) to respond. For example, a sensory neuron from the ear will detect a loud bang and send messages to the brain. The brain will interpret the message, and in turn send information to the motor neurons of the neck muscles and eyes to act. Interneurons are located within the CNS and work to bridge communication between the sensory and motor neurons.

When neurons malfunction, this can result in behavioural symptoms (Stahl, 2013). We can correct the malfunction of neurons through medicines that work on these neurons to relieve behavioural symptoms. The following section will describe the function of a normal neuron as a first step for understanding mental health disorders, and – as you will see in later chapters – this helps us to understand how psychotropic medicines work.

The structure of the neuron

Many textbooks portray the neuron with a generic structure, but the reality is that many neurons have unique structures. They vary so much in shape that it is not possible to describe a 'typical' one, but they have three major features in common. All neurons have a cell body called the *soma*, which contains a *nucleus* and an extension called the *axon*. The soma receives information from other cells and the axon transmits electrical impulses to other cells. It also determines the overall shape and behaviour of the neuron by producing protein in accordance with instructions that the **deoxyribonucleic acid (DNA)** issues. The third major feature of neurons is one or more tree-like branching extensions called *dendrites*, which make connections with other neurons (see Figure 3.3).

When activated, neurons transmit a wave of electrochemical charge called an *impulse*. The starting point of an impulse can be a sensory organ, such as the skin, an eye or an ear, as mentioned in earlier sections, or it can be at a dendrite that has received a message from another neuron.

The dendrites collect information and send it to the neuron's control centre, which is the *cell body* (see Figure 3.3). The cell body pools together the data from each branch of the dendrite to create an overall signal. The signal then passes to an area called the *axon hillock* (see Figure 3.3), which serves as an electrical integrator. Here, the axon hillock decides whether to fire an electrical impulse in response to incoming electrical information or not. If the overall charge from the dendrites reaches a threshold, the neuron fires a signal. The axon propagates chemical signals within the internal cell matrix, but it also propagates these electrical signals travelling along the membrane to the presynaptic zone.

The firing of an electrical impulse down an axon is less straightforward than the flow of electrons down a copper wire (Gibb, 2012). However, just as in copper wire, which is often insulated with plastic, many axons are insulated with a fatty substance called the *myelin sheath*, which reduces the risk of short circuits caused by nearby axons. The **myelin** sheath also helps to speed up electrical impulses, which jump from one node of Ranvier to the next (see Figure 3.3), a process called *saltory conduction*.

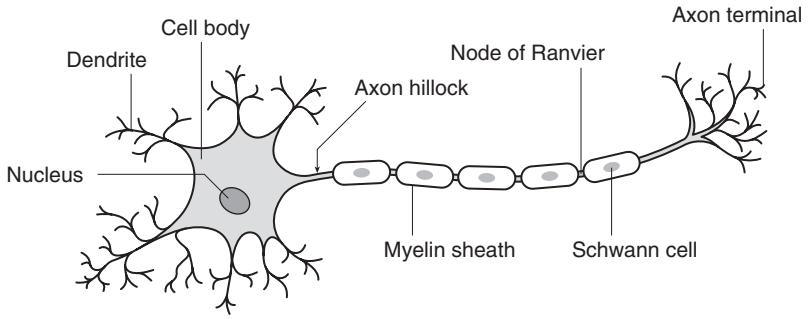

Figure 3.3 The structure of a neuron, showing dendrites, the cell body axon and the myelin sheath

When the electrical impulse reaches the end of the neuron, it causes the activation of the *synaptic vesicles*, which contain chemical substances called *neurotransmitters*. These neurotransmitters amplify or modulate electrical signals being passed to the neighbouring neuron. We will look at neurotransmission in more detail in later sections.

In the human brain, each neuron makes thousands of synapses with other neurons to create an estimated 1 trillion chemically neurotransmitting synapses. Synaptic communication between all of these neurons is chemical (via neurotransmitters), not electrical. Finally, neurotransmission continues in the postsynaptic neuron either by converting the chemical information back into an electrical impulse or remaining unchanged. Later sections describe the action of neurotransmitters in more detail. Meanwhile, turn your attention to Activity 3.4 to test your understanding.

Activity 3.4 Evidence-based practice and research

Search the internet and find out what illnesses are associated with a dysfunction of the following regions of the brain:

- cerebral cortex;
- amygdala;
- hippocampus;
- pons;
- substantia nigra.

Outline answers are provided at the end of the chapter.

Neural development

As previously discussed, it is not possible to overstate the importance of understanding how the brain develops. It is another necessary step towards understanding how psychotropic medicines work. This section will discuss the basic concepts of neural development. Initially, the section will focus on describing the anatomical basis of neurotransmission, before discussing how neurons migrate, form synapses and demonstrate plasticity.

Time course of neural development

The understanding of human neural development is changing at an extremely fast pace thanks largely to stem cell research and advances in forms of brain imaging techniques. The process of neural development starts when the egg fuses with the sperm and a process of cell division (mitosis) commences.

Cells differentiate into immature neurons, and those that are selected migrate to different parts of the brain and differentiate into different (specialised) types of neurons. The formation of new neurons, or *neurogenesis*, continues throughout adult life in some parts of the brain, particularly in the hippocampus. The hippocampus is an area that appears to be particularly sensitive to the effects of stress, ageing and disease. Learning, psychotherapy, exercise and even certain types of psychotropic medicines can stimulate neurogenesis of the hippocampus. Neurogenesis may also occur in other brain areas, including the substantia nigra, the striatum, the amygdala and the neocortex, and several new potential sites of neurogenesis have been described in recent years. We also know that a neuron may fail to develop during childhood, either because of a developmental disease or a lack of appropriate neural or environmental stimulation (Stahl, 2013). Part of neural development takes the form of neural migration.

Neural migration

As much as it is surprising that the production of neurons occurs in the mature adult brain, it is also surprising that periodically, under specific conditions, neurons can kill themselves. We call this form of cell suicide *apoptosis*, and up to 90 **per cent** of the neurons that the brain makes during foetal development commit apoptosis. The reason for apoptosis is that there is an excess of neurons during the prenatal stage of neural development and only a few neurons will be selected for migration. Some of these neurons are healthy and others are defective. In normal brain development, only healthy neurons migrate and the defective neurons commit apoptosis. However, if there is a neurodevelopmental disorder, some defective neurons may migrate, and this will cause neurological or psychiatric disorders in later life.

Scenario

A 46-year-old mother with a son suffering from schizophrenia informed a nurse that while she was seven months pregnant with her son, she contracted a viral infection that lasted three weeks.

Trauma or infection to the mother during pregnancy can have profound effects on the neural development of the unborn child. There is a robust link between viral infection during the third trimester of pregnancy and schizophrenia (Blomstrom et al., 2015; Khandaker et al., 2013). It is possible that via the immune system, microbial agents interfere somewhat with the process of neural selection, whereby defective neurons are selected for migration.

As has been previously discussed, in addition to selecting the correct neurons for migration, the neurons must migrate to the right parts of the brain. Incorrect migration of neurons can dispose an individual to a neurodevelopmental disorder such as epilepsy, schizophrenia or attention deficit hyperactivity disorder (ADHD). We will now turn our attention to another process that involves the formation of the synapse: synaptogenesis.

Synaptogenesis

Once neurons settle down in their respective areas, they specialise and form synapses (see Figure 3.4). A synapse is the space between two dendritic neurons. It is a structure that permits a neuron to pass an electrical or chemical signal to another cell.

During normal development, neurons from different parts of the brain are appropriately directed to their target dendrites to form correct synapses with other neurons.

Therefore, synaptogenesis is the formation of synapses between neurons in the nervous system. Although it occurs throughout a healthy person's lifespan, an explosion of synaptic formation occurs during early brain development, known as *exuberant synaptogenesis*. In abnormal neural development, the wrong dendrites will form synapses with the wrong neurons, resulting in incorrect wiring. In later life, this could lead to abnormal information transfer, which affects neural communication and the ability of neurons to function normally under certain conditions. We now turn our attention to the concept of neural plasticity.

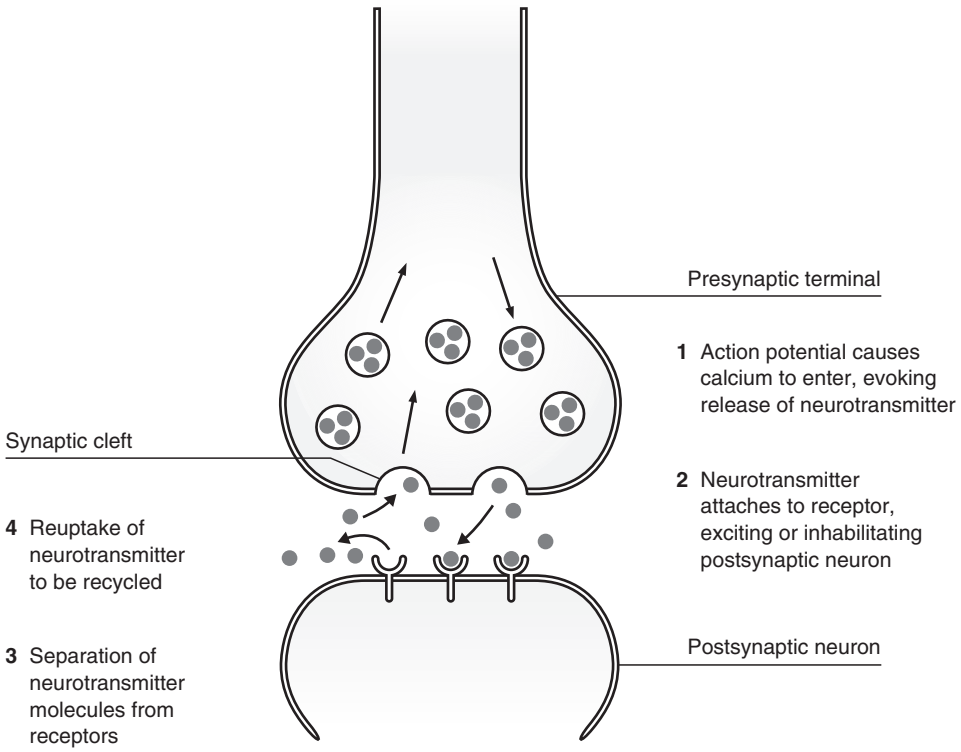

Figure 3.4 A synapse with neurotransmitters

Neural plasticity

The synapses can form on any part of the neuron and not just on the dendrites. Synapses that form on any part of the neuron other than the dendrites are called *asymmetrical*. Once a synapse forms, it remains a dynamic area of intense molecular activity, and in many ways a synapse is under constant revision if it is functional, with molecular maintenance and alterations constantly taking place to respond to changing conditions. For example, the surface area of the pre- and postsynaptic membrane can increase to accommodate numbers and types of receptors that facilitate communication. An increase in neurotransmission may lead to an increase in the number of postsynaptic receptors, or in some cases whole axons can develop. Also, if the brain

stays active, this preserves neurons, and new ones can even form, but if it is not active the neural connection becomes weak and may be 'pruned off'.

As life proceeds, some neural connections get stronger and some get weaker, and the brain can even form new ones. This is how practising a new activity makes us better. In other words, our experiences of repeating interaction with the outside world transform into a strengthened neural interaction or connection between the relevant neurons inside our brain. For example, after one lesson of learning how to administer medicines, little will probably happen in our brain to keep that knowledge intact. However, as we continue to stimulate the neural pathway responsible for learning how to administer medicines, our neurons will eventually reach a critical threshold and the neurons will physically change. The synaptic connections between the neurons become firmer and new synaptic connections can form.

In summary, the dendritic tree of a neuron not only sprouts new branches; it grows and establishes a multitude of new synaptic connections throughout its life, and can also remove, alter, trim or destroy such connections when necessary.

Now that you have read about the mechanism of neural plasticity, undertake Activity 3.5 to test your understanding.

Activity 3.5 Critical thinking

In a group or as an individual, find out the typical age of onset for psychosis.

- How does this period of onset relate to neural pruning?

An outline answer is provided at the end of the chapter.

Chemical neurotransmission

We can define neurotransmission as the passing of signals from nerve cell to nerve cell through chemicals. Chemical neurotransmission constitutes the cornerstone of neuroscientific principles, and the concept has been in existence in various forms since early Greek civilisation. However, it was not until 1877 that the German physiologist Emil du Bois-Reymond (1818–1896) suggested that there might be substances in the body, electrical in nature, responsible for neurotransmission (Lopez-Munoz and Alamo, 2009). We now call these substances *neurotransmitters*. In 1904, the neurotransmission phenomenon was postulated by Thomas Renton Elliott (1877–1961) and his mentor John Newport Langley (1852–1925).

Neurotransmitters are chemicals that the body uses to transmit messages from one neuron to the next across synapses. They are relatively low molecular weight amines that

originate from dietary amino acids. We find neurotransmitters at the axon terminal end of neurons, where they stimulate the muscle fibres or other neurotransmitters. To classify these chemicals as neurotransmitters, they must meet the following criteria:

- they must be present within a neuron;
- they must be released in response to neuron stimulation;
- they must have a postsynaptic receptor present.

Neurotransmitters can be excitatory or inhibitory. *Excitatory neurotransmitters* are the nervous system's 'on switches', increasing the likelihood of sending a signal that excites a neuron. They are like the accelerator of a car: when we press it, it makes the car move or move faster. In other words, excitatory transmitters act as the body's natural stimulants, generally serving to promote wakefulness, energy and activity. An example of an excitatory neurotransmitter is glutamate or adrenaline (see Table 3.3).

Table 3.3 Classical neurotransmitters and their postsynaptic effects

Neurotransmitter	**Location**	**Function postsynaptic effect**
Acetylcholine	Can be found in the parasympathetic nervous system, spinal cord and cortex.	Excitatory
GABA	Most of the brain and spinal cord.	Inhibitory
Glutamate	Brain and spinal cord.	Excitatory
Dopamine	Limbic system and basal ganglia.	Excitatory/inhibitory
Serotonin	Brainstem and most of the brain.	Excitatory/inhibitory
Adrenaline	Brain neurons and adrenal cortex.	Excitatory
Noradrenaline	Spinal cord and limbic system, targeted organ of the sympathetic nervous system.	Excitatory

Inhibitory neurotransmitters are the nervous system's 'off switches'. They decrease the likelihood of sending an excitatory signal. They are like the brakes of a car: when we press them, they slow the car down or stop it moving. In other words, inhibitory neurotransmitters act as the body's natural tranquillisers, generally serving to induce sleep, promote calmness and decrease aggression. The main inhibitory neurotransmitter is gamma-aminobutyric acid (GABA) (see Table 3.3).

It has been proposed that there may be several hundred to several thousand neurotransmitters in the body, but only half a dozen or so are pharmacologically relevant, and these are acetylcholine, serotonin, noradrenaline, adrenaline, dopamine, glutamate and GABA. These neurotransmitters are sometimes referred to as the classical neurotransmitters. In the long term, we may discover many more neurotransmitters, and many more will become pharmacologically important as we discover new medicines.

Classical neurotransmitters

As previously discussed, neurotransmitters mediate neuron-to-neuron communication in the nervous system. Although these neurotransmitters show great diversity in many of their properties, they are all stored in small pockets called *synaptic vesicles* in the axon terminals. During neurotransmission, the synaptic vesicles fuse with the cell membrane and release their contents (neurotransmitters) into the extracellular space or synapse. The action of neurotransmission ends when the presynaptic terminal or surrounding **glial cells** reuptake or reabsorb the neurotransmitters (see Figure 3.4). Specialised proteins called transporters aid the reabsorption process, and the density and availability of these transporter proteins determine the speed of the reuptake process. In certain instances, enzymes destroy the neurotransmitters instead of being reabsorbed back into the presynaptic neuron, a process we call *catabolism*.

Acetylcholine

Acetylcholine was the first neurotransmitter to be identified. It is a neurotransmitter we find in both the peripheral and central nervous systems in many living species, including humans. It is the only neurotransmitter used in the motor division of the somatic nervous system. In the autonomic nervous system, acetylcholine is the neurotransmitter in the preganglionic sympathetic and parasympathetic neurons. It activates muscles in the peripheral nervous system and is a major neurotransmitter in the autonomic nervous system. Inside the brain, acetylcholine acts as a neuromodulator, thus a chemical that alters the way other brain structures process information, rather than a chemical used to transmit information from point to point (neurotransmitter). Additionally, the brain contains several acetylcholine (cholinergic) pathways, each with specific functions. They play an important role in arousal, attention and motivation. There are three acetylcholine pathways in the CNS:

- pons to thalamus and cortex;
- magnocellular forebrain nucleus to cortex;
- septohippocampal.

Because of its role in muscle activation of the autonomic nervous system, as well as in brain function, many important medicines exert their effects by altering acetylcholine transmission. Also, many venoms and toxins from plants, animals and bacteria (e.g. black widow spider venom, nerve gas) can cause harm by inactivating or hyperactivating muscles via their influences on the neuromuscular junction.

There are two types of acetylcholine receptors. First, there are the muscarinic receptors, which have wide distribution throughout the brain, especially in the cortex, the thalamus, the hippocampus, the mesolimbic system and the basal ganglia. They play important roles in cognitive and motor functions, as well as opiate reward. The muscarinic receptors that we find in the VTA regulate the release of dopamine in the nucleus accumbens. The other acetycholine receptor subtype is the nicotinic receptors,

which we find in all muscle cells at neuromuscular junctions. When acetylcholine binds to these receptors, they control calcium channels, which leads to muscle contraction.

Adrenaline

Adrenaline, also known as epinephrine, is an excitatory neurotransmitter and a hormone essential for the breakdown of fat. Adrenaline originates from the compound noradrenaline (norepinephrine). As a neurotransmitter, adrenaline regulates attentiveness and mental focus. As a hormone, it is secreted along with noradrenaline, mainly in the medulla of the adrenal gland directly above the kidneys. An increase in the secretion of adrenaline can occur in response to fear or anger, and will result in an increase in heart rate and the breakdown of glycogen to glucose. We commonly refer to this reaction as the 'fight or flight' response, and it prepares the body for strenuous activity. It is an evolutionary adaptation that allows the body to react to danger quickly. When an individual encounters a potentially dangerous situation, the hypothalamus in the brain signals to the adrenal glands to release adrenaline and other hormones directly into the bloodstream. The body's systems react to these hormones within seconds, giving the person a nearly instant physical boost. Both strength and speed increase, while the body's ability to feel pain decreases. We often refer to this hormonal surge as an 'adrenaline rush'.

We use adrenaline medicinally as a stimulant in cardiac arrest, as a vasoconstrictor in shock, as a bronchodilator and antispasmodic in bronchial asthma, and to counteract anaphylaxis. Commonly, adrenaline levels will be low due to adrenal fatigue (a pattern in which the adrenal output is suppressed due to chronic stress). Therefore, symptoms can present as fatigue with low adrenaline levels. Low levels of adrenaline can also contribute to weight gain and poor concentration. An increase in the levels of adrenaline can be one of the factors that contribute to restlessness, anxiety, sleep problems or acute stress.

Noradrenaline

Like adrenaline, noradrenaline (norepinephrine) is a hormone, as well as an excitatory neurotransmitter, that is important for attention and focus. Noradrenaline is made from *dopamine*. The levels of adrenaline in the CNS are only about 10 per cent of the levels of noradrenaline. The brain produces noradrenaline in closely packed brain cell neurons, and the most important of these nuclei is the *locus coeruleus*, found in the pons. They form an excitatory pathway to the cortex called the **reticular activating system (RAS)**. Noradrenaline binds to several different receptor subtypes that control widely different functions.

As a neurotransmitter, noradrenaline functions in the sympathetic nervous system by stimulating alpha- and beta-adrenergic receptors (both adrenaline receptors). The stimulation of alpha-adrenergic receptors causes vasoconstriction of the radial smooth

muscle of the iris, arteries, arterioles, veins, urinary bladder and the sphincter of the gastrointestinal tract. Stimulation of the beta-1-adrenergic receptors causes an increase in heart contraction, heart rate, automaticity and atrioventricular (AV) conduction, while stimulation of the beta-2-adrenergic receptors leads to the breakdown of glycogen in the liver (hepatic glycogenolysis) and the pancreatic release of glucagon, which increases plasma glucose concentrations.

Noradrenaline functions mainly in the sympathetic nervous system near the spinal cord or in the abdomen. The adrenal glands release noradrenaline directly into the bloodstream. Regardless of how and where it is released, noradrenaline acts on target cells by binding to and activating noradrenergic receptors located on the cell surface. The noradrenergic system is most active when an individual is awake, which is important for focused attention. An increase in noradrenaline activity seems to be a contributor to anxiousness. Also, brain noradrenaline turnover increases in conditions of stress. Interestingly, *benzodiazepines*, which are the primary anxiolytic medicines, decrease the firing of noradrenaline neurons. This may partly explain why benzodiazepines induce sleep. Noradrenaline is rapidly removed from the synapse by two processes: reuptake and metabolism. The noradrenaline transporter protein in the synapse facilitates the transportation of noradrenaline back to the presynaptic axon terminal (reuptake). The enzyme monoamine oxidase (MAO) then facilitates the metabolism of the remaining noradrenaline.

Dopamine

Dopamine is an excitatory and inhibitory neurotransmitter, depending on the dopamine receptor type to which it binds. The dopamine D_2 type tends to show inhibitory effects while the D_1 type promotes excitatory effects (Keeler et al., 2016). It is formed from the dietary amino acid *tyrosine*. It is also the precursor to noradrenaline and adrenaline, which are all *catecholamines*, a group of amino acids. Dopamine has many functions but plays a large role in the pleasure/reward pathway, affecting addiction thrills, memory and motor control. In this respect, dopamine acts as an excitatory neurotransmitter. Like noradrenaline and adrenaline, it is stored in vesicles in the axon terminal. Dopamine plays a significant role in the cardiovascular, renal, hormonal and central nervous systems. Dopaminergic neurons have dendrites that extend into various regions of the brain, controlling different functions through the stimulation of adrenaline (adrenergic) and dopamine (dopaminergic) receptors. The key dopamine pathways in the brain are mesolimbic, mesocortical, nigrostriatal and tuberoinfundibular (see Chapter 8). Common symptoms with low dopamine levels are loss of motor control, addictions, cravings, compulsions and loss of satisfaction. When there is an increase in dopamine levels, symptoms may manifest in the form of anxiety, hyperactivity or psychosis. After use, the dopamine transporter protein quickly removes dopamine from the synapse back into the presynaptic axon terminal, where it integrates back into vesicles for reuse. In some intances, the enzyme MAO facilitates the breakdown or catabolism of dopamine.

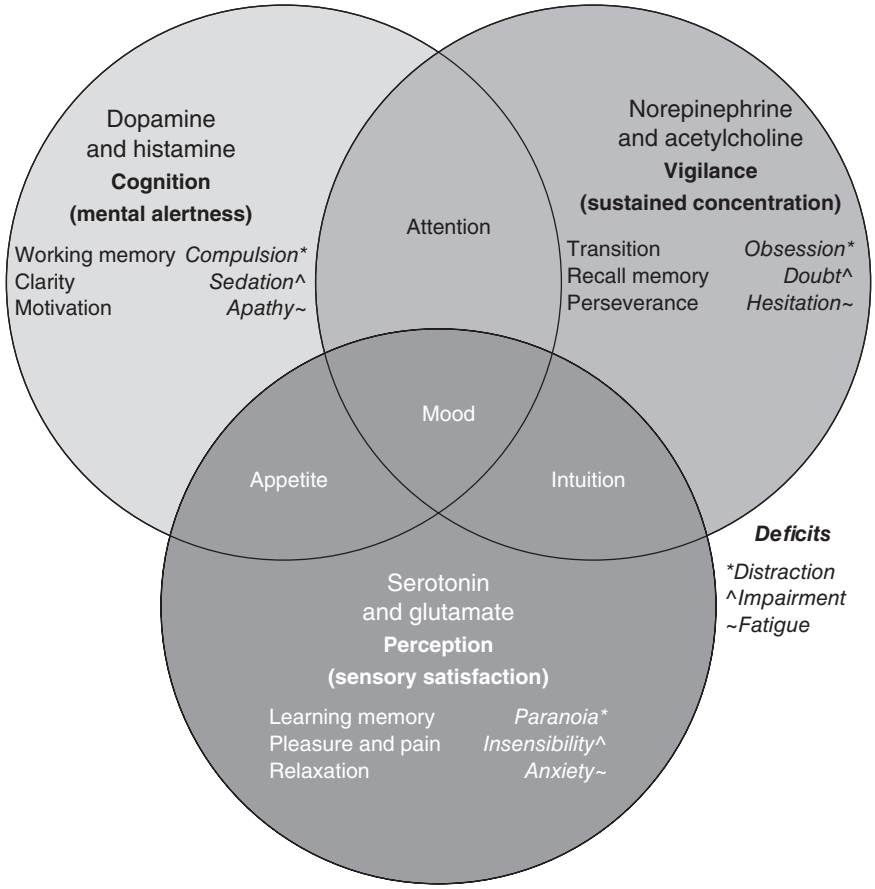

Figure 3.5 Classical neurotransmitters and function

Serotonin

Serotonin, or 5-hydroxytryptamine (5-HT), is a monoamine neurotransmitter made from tryptophan, a compound we primarily find in the gastrointestinal tract, blood platelets and the CNS. Approximately 80 per cent of the human body's total serotonin is in the gut, where its main use is to regulate intestinal movements. The remainder is made in serotonin neurons in the CNS, with the neurons of the raphe nuclei being the principal source of serotonin release in the brain. Because serotonin cannot cross the blood–brain barrier, the brain can only use serotonin that it produces inside itself. Depending on the receptor type, serotonin is both an excitatory and inhibitory neurotransmitter, and it targets for various functions. These include the regulation of mood, appetite and sleep. Serotonin also has some cognitive functions, including memory and learning. We believe that the control of serotonin at synapses is the major action of several classes of antidepressants.

The action of serotonin is terminated by transporting it from the synapse back to the presynaptic neuron. The serotonin reuptake transporter (SERT), a monoamine transporter, plays an important role in this regard. Various biochemical compounds can

inhibit serotonin (5-HT) reuptake. These compounds include dextromethorphan and various classes of antidepressants, and there is comprehensive coverage of this in Chapter 5. Like dopamine and noradrenaline, the body can quickly degrade serotonin into its metabolites (5-hydroxyindoleacetic acid) using the enzyme MAO. The amount of 5-hydroxyindoleacetic acid is used as an indicator for serotonin activity. Dysregulation of serotonin can result in symptoms such as low mood, compulsions, anxiousness and headaches, as well as affecting appetite, sleep, muscle contraction and some cognitive functions, including memory and learning. Table 3.4 shows the effects of 5-HT receptor subtypes in relation to serotonin toxicity.

Table 3.4 Some serotonin receptor subtypes and their function

5-HT receptor	**Main action relating to serotonin toxicity**
5-HT_{1A}	Neuronal inhibition, regulation of sleep, feeding, thermoregulation, hyperactivity associated with anxiety, hypoactivity associated with depression.
5-HT_{1D}	Locomotion, muscle tone.
5-HT_{2A}	Neuronal excitation, learning, peripheral vasoconstriction, platelet aggregation.
5-HT_{2B}	Stomach contraction.
5-HT_{3}	Nausea and vomiting, anxiety.
5-HT_{4}	Gastrointestinal motility.

Glutamate

Glutamate is the most abundant excitatory neurotransmitter in the human nervous system, and it is necessary for memory and learning. Excitatory neurotransmitters increase the activity of signal-receiving neurons and play a major role in controlling brain function. Glutamate is made from glutamine, an abundant non-essential amino acid that we find in fish, eggs and dairy products. Approximately 70 per cent of the fast-excitatory CNS synapses use glutamate as a transmitter. In large quantities, glutamate can be neurotoxic and can lead to cell death.

Glutamate exerts its effects on cells, in part, by binding to at least four neuroreceptors: the kainite receptors, the alpha-amino-hydroxy-5-methyl-4-isoxazolepropionic acid receptors (AMPARs), the N-methyl-D-aspartate receptors (NMDARs) and the metabotropic glutamate receptors (mGluRs) receptors. Of these, the NMDARs play a particularly important role in controlling the brain's ability to adapt to environmental and genetic influences, which is important for learning and memory. The NMDARs have been studied extensively, especially when it was discovered that they play an important role in synaptic plasticity. These receptor types also play an important role in the origin of epilepsy. It is believed that this happens through the process of kindling, whereby repeated sub-threshold electrical stimuli of NMDARs in the limbic system leads to spontaneous seizure activity. When the person responds to stimuli with generalised convulsions, this signals the development of a permanent epileptic condition.

Therefore, activation of NMDARs, as well as their levels of function, is critical in kindling epilepsy. Selective NMDAR antagonists slow down kindling development, and at higher concentrations have an anticonvulsant effect.

The AMPARs are responsible for quick excitatory transmission within the central nervous system. AMPAR antagonists are anticonvulsant in nature.

Glutamate is also capable of exciting the mGluRs, of which there are currently eight subgroups that have been identified. Activation of mGluRs has been implicated in a variety of CNS functions, including different forms of synaptic plasticity, excitotoxicity and the release of other neurotransmitters.

Overall, an event or process that dramatically increases the activity of glutamate often increases the degree of neuronal excitation, and in extreme cases can induce the death of neurons. We believe that such a scenario takes place in conditions such as ischaemia, trauma, hypoxia, **hypoglycaemia** and hepatic encephalopathy. Milder but chronic dysfunction of glutamate systems may play an important role in many neurodegenerative diseases, such as Huntington's disease, Parkinson's disease, Alzheimer's disease, vascular dementia, and Tourette's and Korsakoff's syndromes. The **excitatory amino acid transporter (EAAT)** and **vesicular glutamate transporter (VGLUT)** facilitate several reuptake mechanisms responsible for the removal of glutamate from the synapse. We find these transporter family proteins (EAAT and VGLUT) either on the presynaptic axon terminal or the surrounding glial cells. Alterations in the function and/or expression of these carriers is implicated in a range of psychiatric and neurological disorders. For example, alteration in EAATs is implicated in cerebral strokes, epilepsy, Alzheimer's disease, HIV-associated dementia, Huntington's disease, **amyotrophic lateral sclerosis (ALS)** and malignant glioma, while alteration in VGLUTs is implicated in schizophrenia. Turn to Activity 3.6 to test your understanding of what you have read in this section.

Activity 3.6 Reflection

Name the classical neurotransmitters that are excitatory and inhibitory.

An outline answer is provided at the end of the chapter.

Gamma-aminobutyric acid

Gamma-aminobutyric acid (GABA) is the major inhibitory neurotransmitter of the brain, occurring in 30–40 per cent of all synapses. GABA concentration in the brain is 200–1,000 times greater than that of the adrenaline, noradrenaline, dopamine, serotonin or acetylcholine neurotransmitters. Essentially, GABA is made from the amino acid glutamic acid (glutamate) in the presynaptic neurons. The synaptic vesicles store the neurotransmitter until its release into the synapse during inhibitory neurotransmission.

GABA helps to induce relaxation and sleep, as well as balancing the brain by inhibiting over-excitation of the neurons, contributing to motor control, vision and many other cortical functions. GABA is one of several neurotransmitters that regulate anxiety, and some medicines that increase the level of GABA in the brain are used to treat epilepsy and to calm the trembling of people suffering from Huntington's disease.

GABA also stimulates the anterior pituitary, leading to higher levels of human growth hormone (HGH), a hormone that contributes significantly to muscle growth and prevents the creation of fat cells. The presynaptic GABA transporter or reuptake pump (GAT) terminates synaptic action, and the enzyme GABA transaminase (GABA-T) terminates GABA into an inactive substance by breaking down GABA to succinic semialdehyde. To fully understand the role of neurotransmitters, we now need to turn our attention to their connection to receptors and ion channels.

Receptors and ion channels

After release into the synaptic gap, a neurotransmitter diffuses towards the postsynaptic membrane, where there are receptor sites made of specific proteins or chains of amino acids. Receptors have specific molecular structures, which determines which substance (neurotramsmitter) can temporarily bind to them. When a neurotransmitter binds to postsynaptic receptors, this alters the permeability of the postsynaptic membrane to ions. Ions are atoms or molecules that possess negative or positive electrical charges, and they can move through ion channels. The principal function of ion channels is to allow the movement of ions (gating) across the cell membrane (see Figure 3.6). Gating refers to the opening or closing of these ion channels. It is the movement of ions in and out of cells through ion channels that creates an electrical signal essential for cell-to-cell communication.

There are two major classes of ion channels: voltage-gated ion channels and ligand-gated ion channels, and we will discuss these next (see Figure 3.6). We will look at voltage-gated, or ionotropic, ion channels first as they are involved in the generation of an action potential.

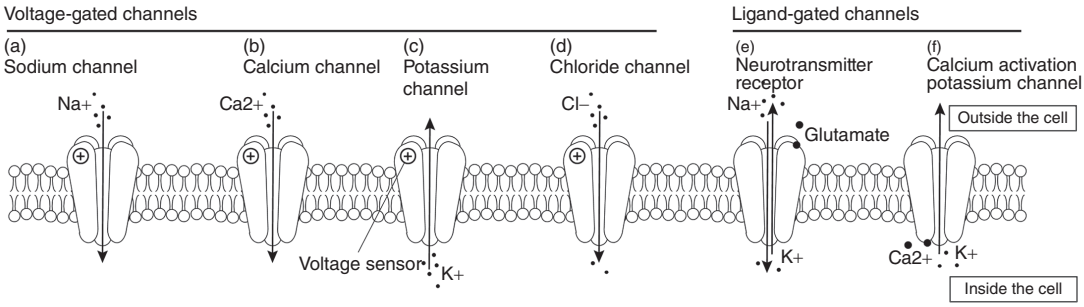

Figure 3.6 Voltage-gated ion channels (examples of voltage-gated ion channels include sodium, calcium, potassium, magnesium and chloride channels)

Voltage-gated ion channels, action potential and neurotransmission

Examples of voltage-gated ion channels are sodium, potassium, chloride, calcium and magnesium ions, and these are involved in classical neurotransmission. Voltage-gated ion channels are a class of channels we find across cell membranes (transmembranes) made from proteins. We find these along the axon and at the synapse, and they play a fundamental role in the generation and propagation of the nerve impulse (action potential). The difference in electrical charge between the inside and the outside of the cell membrane causes electromotive forces to drive ions inside or outside of the cell.

When a cell is in an unstimulated state, the concentration of sodium ions is greater outside the cell than inside. Simultaneously, the concentration of potassium ions is greater inside the cell than outside. We call this unstimulated state the *resting potential* of the cell, and its voltage is approximately −70 millivolts (mV). When a neuron cell is at its resting potential, it is *polarised* and its ion channels are closed (see Figure 3.6). This situation changes when we stimulate the neuron.

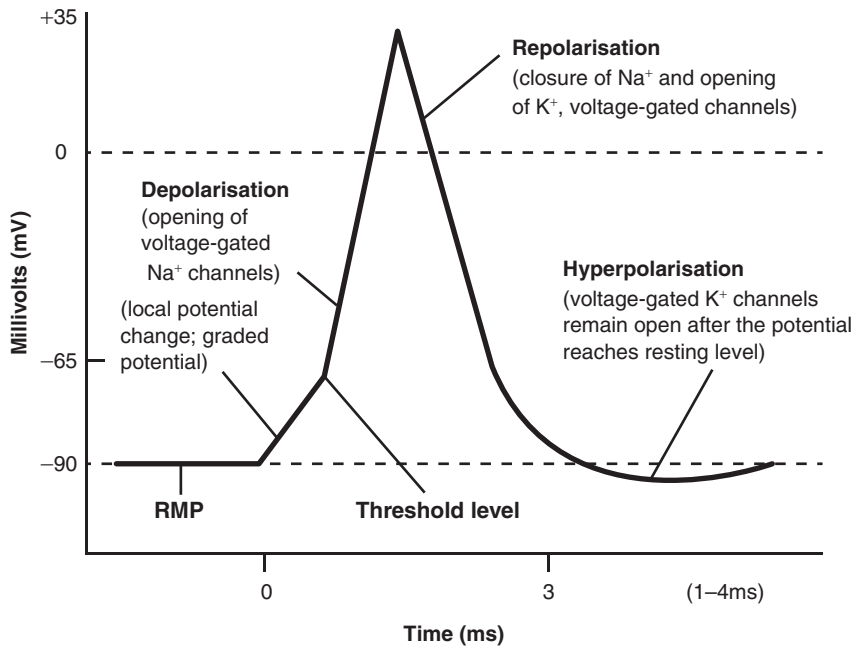

Figure 3.7 The generation of an action potential in a neuron

The stimulation of a neuron above a threshold will result in the opening of sodium channels, allowing positively charged sodium ions to rush inside the neuron, causing a brief positive charge. At this point, the electrical *membrane potential* (see Figure 3.7)

of the cell rapidly rises and falls, and we call this spike an *action potential*. The sodium channels then close; simultaneously, potassium channels open, allowing positively charged potassium ions to move out of the cell, therefore causing the membrane potential to go back to normal. The cell is now said to be *repolarised*. The potassium channels then close.

Before the membrane potential stabilises at −70 mV, there is a small undershoot called the *refractory period*. During this period, the neuron cannot fire another action potential. At this resting state (−70 mV), the excess sodium and potassium ions will slowly diffuse away from the membrane and the neuron is ready to fire another action potential. Once fired, the action potential quickly spreads along the axon like a wave until it reaches the axon terminal, where chemical neurotransmission begins.

When an electrical impulse or action potential reaches the axon terminal, it causes the cell membrane to change its permeability and allows calcium ions (Ca^{+}) to enter the axon terminal. Calcium ion entrance into the axon terminal causes the neurotransmitter vesicles to migrate to the cell membrane and fuse. This results in the conversion of the original electrical message to a chemical message in the neurotransmitter. The amount of neurotransmitter released in the synapse depends on how many calcium ions enter the axon terminal. A more intense stimulation of the neuron allows more calcium ions to enter, resulting in the release of more neurotransmitters. The neurotransmitters then travel to the postsynaptic neuron, where they bind to a receptor and initiate an action potential.

Ligand-gated ion channels, action potential and neurotransmission

The location of ligand-gated ion channels is on postsynaptic receptors, where the binding action of a neurotransmitter on to a receptor triggers the opening or closing of these ion channels. This transforms a presynaptic chemical message to a postsynaptic action potential (electrical message). In contrast to voltage-gated ion channels, where voltage differences initiate action, in ligand gated ion channels it is the binding action of neurotransmitters to a receptor that is the initiator. Examples of ligand-gated receptors are GABA, serotonin ($5\text{-}HT_3$), nicotinic acetylcholine and some of the glutamate family of receptors. Since these ligand-gated ion channels are also receptors, we sometimes call them ionotropic receptors or ion-channel-linked receptors. Some drugs, medicines and proteins can cause the ion channel to open to its maximum, allowing the maximum possible postsynaptic signal transduction. By contrast, other chemicals or drugs can cause the ion channel to slow down and open infrequently, and some can put the ion channel into a closed and inactive state. Now that you have read this section, test your understanding by working on Activity 3.7.

Activity 3.7 Evidence-based practice and research

In a group or alone, research psychiatric illnesses that are a result of a shortage of one of the excitatory neurotransmitters. For each illness, list the neurotransmitter that is implicated.

An outline answer is provided at the end of the chapter.

Chapter summary

Contrary to popular belief, the brain is not an organ. It is the most complex structure in our body; and although our knowledge of the brain has increased thanks to new technology, there is a great deal we still do not know about this important structure. Currently, we know that the brain is divided into two hemispheres, which in turn are divided into the frontal, parietal, occipital and temporal lobes. In addition, the brain has two layers, namely the grey and white matter.

Neurons are the basic cells of the brain, and these are of many different shapes and sizes. They are involved in cell-to-cell communication, but at times the cells miscommunicate. The reason for this miscommunication is partly due to the wrong types of neurons making the wrong connections during a period of neural migration at the prenatal development level. Neural miscommunication can result in neurodevelopmental conditions or psychiatric symptoms.

Neural communication is aided by chemicals at the synapse called neurotransmitters. There may be thousands of different types of these in the body, but only seven are currently of pharmacological importance: acetylcholine, GABA, glutamate, dopamine, serotonin, adrenaline and noradrenaline. Most medicines used to treat mental health problems work on these neurotransmitters.

Activities: brief outline answers

Activity 3.1 Critical thinking (page 82)

If there is no electrical activity in the brainstem, it is possible to pronounce someone as clinically dead. The brainstem relays nerve impulses to the rest of the body. In particular, the medulla oblongata part of the brainstem is responsible for maintaining reflexes such as blood flow pressure, heart rate and breathing. If this is not happening, the individual is clinically dead.

Activity 3.2 Critical thinking (page 86)

Some of the causes of hypothalamic dysfunction include anorexia, bleeding, bulimia, genetic disorders, tumours, head trauma, infections and swelling (inflammation), malnutrition, radiation, and excess iron.

Activity 3.3 Research (page 87)

The cerebral cortex is divided into hemispheres, which in turn are divided into lobes:

- *Frontal lobe*: higher order functioning, critical thinking, memory including attention, planning, language and movement.
- *Parietal lobe*: processing of sensory information.
- *Occipital lobe*: vision.
- *Temporal lobes*: sound and language.

Activity 3.4 Evidence-based practice and research (page 90)

Illnesses associated with dysfunction of different areas of the brain are:

- cerebral cortex: depression, Huntington's disease, mania;
- amygdala: depression;
- hippocampus: Alzheimer's disease, mania;
- pons: sleep disturbance;
- substantia nigra: Parkinson's disease.

Activity 3.5 Critical thinking (page 93)

Most psychosis, especially schizophrenia, starts in the late teens and early adulthood. This coincides with higher rates of neural pruning, whereby new connections are being made at various synapses in the brain.

Activity 3.6 Reflection (page 100)

- Excitatory: glutamate, dopamine, serotonin, adrenaline, noradrenaline, acetylcholine.
- Inhibitory: dopamine, GABA, serotonin.

Activity 3.7 Evidence-based practice and research (page 104)

- Dopamine: depression/psychosis.
- Adrenaline: depression.
- Serotonin: depression/personality disorder/aggression.
- Glutamate: psychosis.

Further reading

Gibb, B. (2012) *The Rough Guide to the Brain*. New York: Rough Guides.

This is an accessible introduction to how the brain evolved and how it works.

Useful websites

www.neurogenesis.com/Neuroscience/index.php

This is a useful website that explains in very simple terms the concept of neural development.

www.neuroskills.com/brain.shtml

This is a useful website that explains in more detail the different parts of the brain and their function. It has useful colour diagrams.

www.waiting.com/brainanatomy.html

This is another useful website that explains brain anatomy and has very clearly annotated diagrams.