TOPIC 8: GREY MATTER

For the Edexcel Biology A Level (SNAB)

TOPICS COVERED

- Nervous System and Neurones
- Reflexes
- Action Potentials
- Synapses and Summation
- Plant Coordination: Auxins and Phytochromes
- Vision
- Visual Development
- Evidence for Vision
- Brain Structure and Imaging
- Learning and Memory
- Parkinson's, Depression and MDMA
- Human Genome Project
- Genetic Modification

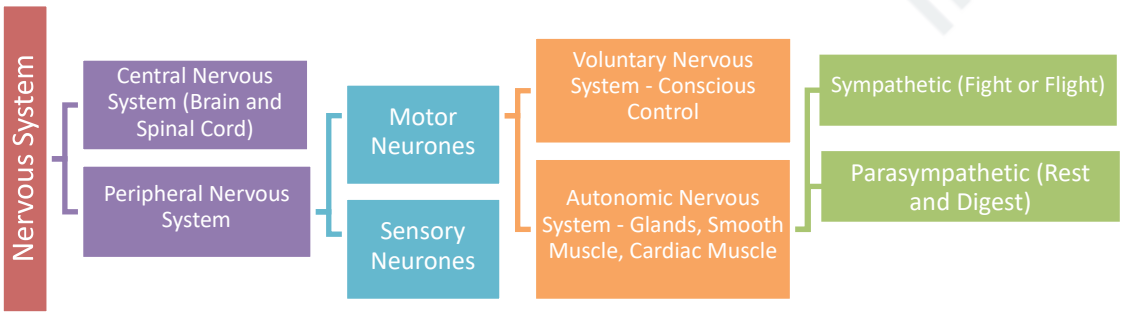
The Nervous System and Impulses

Key Terminology

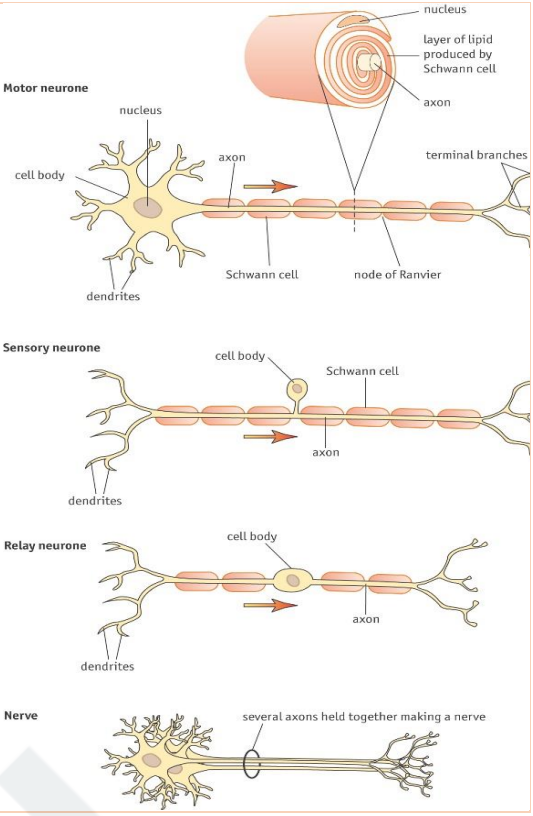
Term	Definition
Stimulus	Any external or internal change detected by the body
Receptor	Organ which detects a stimulus
Co-ordinator	The CNS, which determines a response to the stimulus
Effector	Tissue which carries out the response
Response	Action as a result of the body's response to a stimulus
Axon	Transmits impulse away from the cell body of a neurone
Dendron	Conducts impulse towards cell body
Dendrites	Synapses with receptors or other dendrites, receiving an impulse
Terminal Ends	End of a neurone, at a synapse, muscle or gland
Sensory Neurone	Neurones which carry impulses from receptors
Relay Neurone	Neurones which transmit impulses from one cell to another
Motor Neurone	Neurones which transmit impulses to effectors
Myelin Sheath	Lipid layer around a neurone, giving electrical insulation and increasing transmission speed
Reflex	Autonomous pattern of behaviour which involves a rapid response to a stimulus, preventing harm by bypassing the brain at first
Resting Potential	Difference in electrical charge of -70mV across the membrane of a resting neurone
Depolarisation	Reversal of the potential difference across the cell surface membrane of a nerve cell as a nerve impulse passes along it
Action Potential	The changes which take place across the cell surface membrane of a nerve cell during the passage of an impulse, brought about by the opening and closing of voltage-dependent Na^+ and K^+ gated channels
All-or-Nothing	Action potentials are always the same – as a result, the only way that information about the strength of a stimulus can be carried is by varying the rate of nerve impulses
Hyperpolarisation	Making the potential difference across the cell membrane of a nerve cell more negative
Refractory Period	Period where an impulse cannot be generated
Saltatory Conduction	Conduction of impulses by jumping between nodes of Ranvier
Synapse	Small gap between two neurones
Neurotransmitter	Chemical that is responsible for carrying a nerve impulse across a synapse
Excitatory Synapse	Neurotransmitters released from an excitatory synapse make the postsynaptic membrane more permeable to sodium ions
Summation	Each impulse adds to the effect of others
Inhibitory Synapse	Synapse with a higher depolarisation threshold, decreasing chance of impulse propagation
Endocrine Gland	Location of hormone secretion
Auxin	Plant hormone which causes the elongation of cells in shoots and is involved in regulating plant growth

Nerves

The Nervous System is highly organised, as indicated by the hierarchy on the right. Nerves are complex structures containing a bundle of axons.



Neurones	Sensory	Relay	Motor
Function	Conduct impulse to the CNS	Connect sensory neurones with appropriate motor neurone	Conduct impulse to an effector
Location	Cell body and dendrites outside CNS. Cell body is in the entrance route to the spinal cord	Cell bodies form the CNS	Cell body and dendrites inside CNS, axons outside
Dendrites	Synapse with sensory receptor cells	Synapse with other neurones in CNS	Synapse with other neurones in CNS
Axons	Synapse with other neurones in CNS	Synapse with other neurones	Synapse with effect cells – muscles and glands
Within the neurone, there are thin extensions from the cell body, where the nucleus and organelles are contained in cytoplasm – the dendron carries impulses to the cell body, and the axon carries impulses away from the cell body. The myelin sheath wraps around the axon, providing electrical insulation and increasing neurotransmission speed			



The Reflex Arc

Reflexes – rapid, involuntary responses – help to protect our body by using the spinal cord as the co-ordinator:

Receptor detects a stimulus, generating an impulse which is carried to the CNS along sensory pathway → Sensory neurone synapses with a relay neurone, which formulates a response. Impulse is also sent to the brain → Motor neurone carries impulses to an effector which produces a response to help protect the body

	Light	Dark
Pupil	Constricted	Dilated
Iris	Narrow	Wide
Radial Muscles	Relax	Contract
Circular Muscles	Contract	Relax

An example of a reflex is the **pupil reflex.** This reflex prevents damage to the retina in bright light by rapidly constricting the pupil. In darkness, the pupil dilates to maximise the amount of light reaching the retina.

When high light levels strike photoreceptors in the retina, impulses are sent to the left co-ordinating centre in the midbrain along the optic nerve. Impulses from these cells are sent to the circular muscles of the iris along parasympathetic motor neurones and cause them to contract, while the radial muscles relax. This constricts the pupil. If light is altered in one eye, both pupils see a response.

Resting Potential

All cells have a voltage across their membrane called a resting potential; the inside of a cell is negative relative to the extracellular fluid. This is due to uneven distribution of ions. **The resting potential of a neurone is -70mV**.

- Sodium-potassium pumps carry Na^+ out of the cell and K^+ into the cell by active transport, creating chemical concentration gradients across the membrane
- The membrane is permeable to K^+, and the ions diffuse out of the cell through channel proteins, making the outside of the membrane positive and creating an electrical gradient
- Further outward movement of K^+ is restricted, and since it is attracted to the negative state of the inside of the axon, it is pulled back into the cell
- At -70mV, the chemical and electrical gradients balance and an equilibrium is reached with no net K^+ movement

Action Potential Generation and Conduction

- Neurone stimulation causes depolarisation. Voltage-gated Na^+ channels open, allowing the ions into the axon

- Once the threshold level of -55mV is reached, all of the channels open, causing an immediate influx of ions. This positive feedback means action potentials are all-or-nothing, as there is no way of controlling the degree of polarisation
- At +40mV, voltage-gated Na^+ channels shut. The depolarised membrane causes gated K^+ channels to open, allowing the potassium ions to diffuse out of the cell down the electrochemical gradient. As K^+ flows out, the inside of the cell returns to a negative state during repolarisation
- The high permeability of the membrane to K^+ means that more ions move out of the cell than at resting potential, meaning the potential becomes more negative. This hyperpolarisation causes closing of the K^+ gate, and K^+ diffusion into the cell causes a return to resting potential

When a neurone is stimulated, the action potential is propagated along the axon. After an inflow of Na^+, localised electric currents are generated in the membrane and Na^+ moves to the adjacent resting region causing a change in the potential difference across this part of the membrane, initiating a second action potential. A third action potential is caused by the second, and in this way local electric currents cause the nerve impulse to move along the axon.

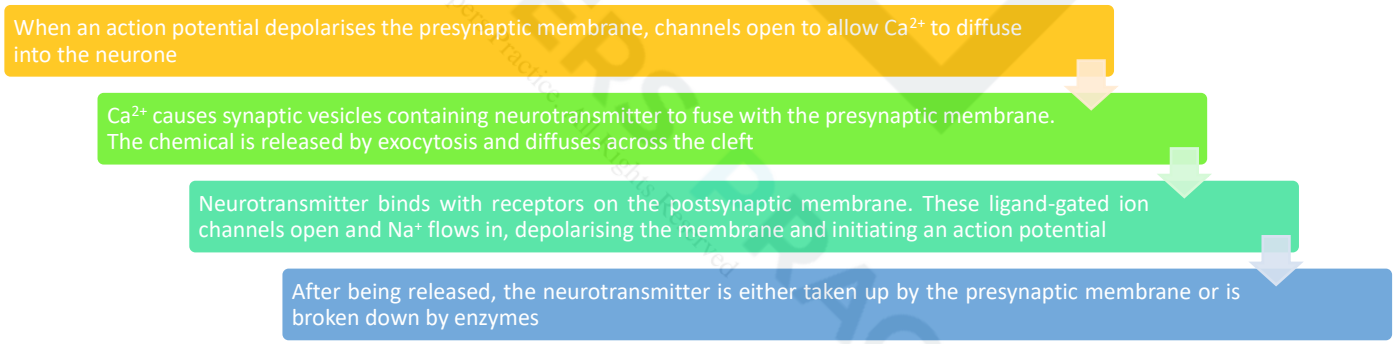
Neurone membranes have a refractory period, which ensures that impulses travel only in one direction. During the absolute refractory period, no new action potentials can be generated as Na^+ permeability is zero. During the relative refractory period, a new action potential can be generated if stimulation is much higher than the -55mV threshold.

The size of a stimulus affects the frequency of impulses and the number of neurones in a nerve that are conducting impulses. If many action potentials are initiated consecutively, high Na^+ concentration is changed by the Na^+/ K^+ pump.

Nervous conduction speed increases with diameter of the fibre. Transmission speed is increased by the myelin sheath. The sheath acts as an electrical insulator along most of the fibre, preventing ion flow. Gaps at the nodes of Ranvier occur between Schwann cells, and are the only places where depolarisation can occur. As ions flow across the membrane at one node during depolarisation, an electrical current is set up which reduces the potential difference of the membrane at the next node, triggering an action potential. This jumping conduction is called saltatory conduction.

Synapses

Neurones meet at a synapse – a gap of around 2-50nm across which impulses are transferred. A common example of a neurotransmitter is acetylcholine.



Synapses have roles in the control of nerve pathways, allowing flexibility of response, and in integration of information from different neurones.

Excitatory synapses make the postsynaptic membrane more permeable to Na^+ as detailed above. Sufficient neurotransmitter release will cause depolarisation. This is controlled by summation – where each impulse adds to the effect of others – of which there are two types:

- Spatial summation – impulses are from different synapses. The number of different sensory neurones stimulated can be reflected in the control of the response
- Temporal summation – several impulses arrive at a synapse having travelled along a single neurone. Combined neurotransmitter release generates an action potential

Inhibitory synapses decrease the likelihood of action potential production. The neurotransmitter from these synapses open Cl^- and K^+ channels, allowing these ions to diffuse into and out of the cell respectively. Movement of these ions produces hyperpolarisation of the postsynaptic membrane with a potential difference of -90mV, making subsequent depolarisation less likely.

Comparing Nervous and Hormonal Control

	Transmission	System	Speed	Effects
Nervous	Electrical	Nervous	Rapid	Temporary, localised changes delivered by specific motor neurones
Hormonal	Chemical	Circulatory	Slower	Longer-term, delivered to all cells but only target organs respond

Plant Coordination

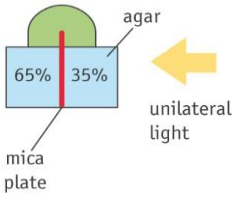
Key Terminology

Term	Definition
Plant Hormone	Chemicals produced in very low concentrations used by plants to coordinate growth, development and responses to the environment
Phototropism	A growth response of a plant to light. Plant shoots show positive growth responses as they grow towards light. Roots exhibit negative phototropism – or positive gravitropism – as they grow away from light
Coleoptile	Protective sheath that covers the first leaf in grasses and cereals
Auxin	Plant hormone which causes the elongation of cells in shoots and is involved in regulating plant growth. The studied example is **indoleacetic acid (IAA)**
Meristem	Actively growing, undifferentiated tissue found in the tips and shoots of a plant
Phytochromes	Blue-green pigment found in plants which regulates various developmental processes
Photoperiod	Length of time each day during which an organism receives illumination
Kinase	An enzyme that catalyses the transfer of PO_4^{3-} from ATP molecules to specific substrates.

Auxins

The plant hormones known as auxins are used to coordinate growth and environmental responses. Having been produced in meristematic tissue, auxins are either transported long distances in the phloem, or travel short distances between cells by facilitated diffusion through carrier proteins.

The most widely studies auxin is indoleacetic acid (IAA), and one of its main functions is to stimulate growth as a result of cell elongation. When a shoot is placed in the presence of unilateral light, auxin passes down the shaded side. The increased auxin concentration increased cell elongation on the shaded side, while the reduced concentration on the illuminated side inhibits cell elongation, causing the shoot to grow towards the light, causing positive phototropism. Similar interactions cause gravitropism, with gravity acting as a stimulus for downwards root growth.

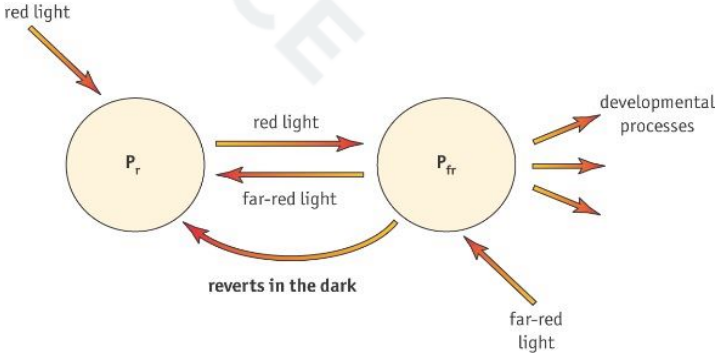


After auxins reach the growth zone, they bind with the protein receptors of cells. This triggers intracellular secondary messenger signal molecules to be released. These, in turn, cause changes in transcription factors of genes coding for metabolic changes leading to cell expansion.

Auxin causes acidification of the cell wall by stimulating proton pumps that move H^+ ions out of the cytoplasm and into the cell wall. The low pH activates expansin proteins, which disrupt H bonds holding cellulose microfibrils and hemicelluloses together. Loosening of the cell wall allows cell expansion. Acidification of the cell wall also increases the potential difference across the membrane, enhancing the uptake of ions by the cell. In turn, water is taken in by osmosis, causing the cell to swell resulting in cell elongation.

Phytochromes

A phytochrome molecule consists of a protein kinase component bonded to a non-protein blue-green light-absorbing pigment. There are two isomers of the pigment: **P_r**, phytochrome red, which absorbs red light (660nm), and **P_{fr}**, phytochrome far-red, which absorbs far-red light. P_{fr} is the active form of phytochrome but is unstable.



These two isomers are photoreversible: plants synthesise phytochromes in the P_r form, and absorption of red light converts P_r to P_{fr}. Absorption of far-red light converts P_{fr} back into P_r. In sunlight, far more red light is absorbed so P_{fr} accumulates during the day. In the dark, P_{fr} reverts slowly back to P_r.

P_{fr} presence is therefore associated with light and is therefore P_r:P_{fr} ratio is used to determine responses such as seed germination, stem elongation, leaf expansion, chlorophyll formation and flowering.

Activated phytochrome activates proteins in the signal pathway. This activates transcription factors that bind to DNA to allow transcription of light-regulated genes. The produced proteins results in the response to light.

- It is well understood that many seeds require light to germinate. In light, P_r is converted to P_{fr}, stimulating responses leading to germination. However, in the dark, no P_r is converted to P_{fr}, and therefore germination is inhibited. The effects of light and dark are reversible
- Plants use P_r:P_{fr} ratio to determine day length: long winter nights allow for all P_{fr} to be converted back into P_r by sunrise; however, in the shorter summer days, some P_r remains. Long-day plants only flower when day length exceeds a critical value, as P_{fr} is needed to stimulate flowering. However, in short-day plants P_{fr} inhibits flowering
- Once a shoot has broken through soil into sunlight, the plant changed in form and biochemistry, undergoing greening. Once in light, phytochromes promote development of primary leaves, leaf unrolling, stem elongation and production of pigments like chlorophyll and more phytochrome.

Vision

Key Terminology

Term	Definition
Photoreceptors	Receptor cells which are stimulated by light, allowing sight
Rhodopsin	Purplish photochemical pigment made of the protein opsin and non-protein component retinal. Rhodopsin which absorbs light, resulting in a chemical change
Dark Adaptation	Once rhodopsin has been broken down, it must be rapidly converted back so that subsequent stimuli can be received
Critical Periods	Periods of time during postnatal development when the nervous system must obtain specific experiences to develop properly
Innate	Natural skills with which we are born

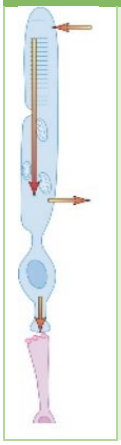
How Light Triggers Impulses

The eye is a sense organ: light enters through the cornea and the lens, which bend and focus light onto the retina respectively. The iris controls the amount of light entering the eye, once this light enters, it passes through the transparent vitreous humour to reach the photoreceptors on the retina.

The human retina contains rods, giving black and white vision in dim as well as bright light, and cones, giving colour vision in bright light only. There are three layers of the retina: the rods and cones, attached to the choroid, synapse with bipolar cells, which in turn synapse with ganglion neurones, whose axons form the optic nerve. Light hitting the retina must pass through the neurone layers before reaching photoreceptors.

Both rods and cones contain rhodopsin. The outer segment of a rod contains layers of flattened vesicles with rhodopsin in their membranes.

Rod Cell Behaviour



In Darkness

- Na^+ flows into the outer segment through non-specific cation channels
- Na^+ diffuses into the inner segment where it is actively pumped out, causing slight depolarisation of -40mV
- This triggers release of glutamate neurotransmitter; since this is an inhibitory synapse, this prevents depolarisation of bipolar cell

In Light

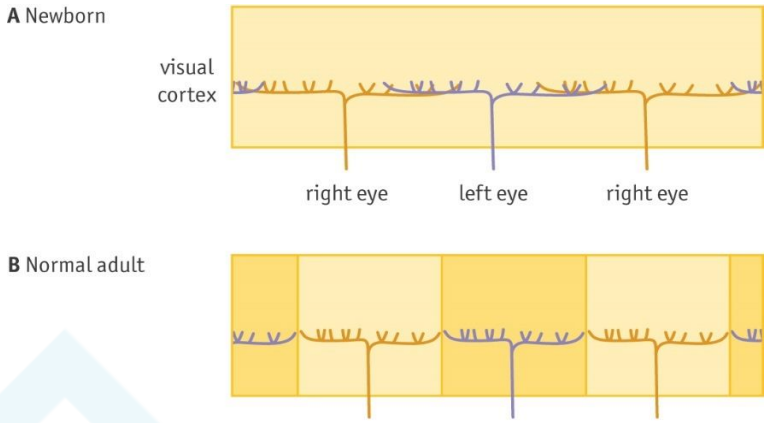
- Light reaches rhodopsin, causing it to break into retinal and opsin, as retinal has changed from its cis to trans form
- Opsin activates a reaction cascade, ending in hydrolysis of a cyclic nucleotide attached to cation channels, leading to their closure
- Influx of Na^+ stops, while inner segment continues to pump out sodium ions, hyperpolarising the cell and preventing glutamate release into synapse
- This causes depolarisation of the bipolar cell and then depolarisation of the ganglion cell

The axons of ganglion cells that form the optic nerve pass out of the eye and extend to the thalamus. The impulses are then sent along further neurones to the primary visual cortex in the occipital lobe where information is further

processed. Before reaching the thalamus, some of the neurones in each optic nerve branch off to the midbrain, where they connect to motor neurones involved in controlling the pupil reflex and eye movement.

Visual Development

A baby is born with roughly 100 billion neurones. The large postnatal increase in brain size is due to axon elongation, synaptogenesis and myelination.



- Axons of the neurones from the retina grow to the thalamus where they form synapses
- Axons then grow towards the visual cortex
- Columns of cells have a very ordered, and genetically determined, arrangement in the occipital lobe. One column receives stimuli from the left eye, the next from the right, in an alternating pattern
- Information from the same area of the retina in the left and right eyes synapse next to each other
- At birth, columns of cells overlap. During the critical period for vision, visual stimulation is needed for refinement
- Axons compete for target cells in the visual cortex
- During the critical period, a cell will receive impulses from the active axon from one eye, strengthening the connection between the neurones as neurotransmitter is received
- Synapses with inactive neurones will be cut off as neurotransmitter is not received. In this way, columns are refined and the visual cortex is developed

Evidence for the Critical Period

Animal Models

In the study of visual development, kittens and monkeys have been used for animal studies.

In a series of studies, Hubel and Wiesel raised monkeys from birth to six months, depriving them of any light stimulus in one eye – monocular deprivation. After six months the eye was exposed to light; the monkeys were blind in the light-deprived eye. Retinal cells did respond to light stimuli, but the cells of the visual cortex did not respond to visual input from the deprived eye. Deprivation for a single week during the critical period produced the same result. Deprivation in adult monkeys had no effect.

Hubel and Wiesel tested kittens for the effects of monocular deprivation at different of development. Since kittens are born blind, early deprivation had no effect, but by three months the critical period had ended and there was no further effect. The critical period occurred at 4 weeks – deprivation for even a few hours caused blindness.

Making Sense of What We See

Visual perception is not simply the creation of an image of what is being viewed, but involved knowledge and experience as the brain interprets the sensory information received from the retina. When we look at an object, we can make a judgement about how far away it is.

- For close objects less than 30m from us, we depend on the presence of cells in the visual cortex that obtain information from both eyes at once. The visual field is seen from two different angles and cells in visual cortex compare the viewpoints. This stereoscopic vision and allows the relative position of objects to be perceived
- For objects more than 30m distant, the images on the two retinas are very similar so visual cues must be used. Relative sizes, overlap of objects, changes of colour, linear perspective and shadows are used to judge depth.

Evidence from the studies below suggests that depth perception could be innate or learnt.

Evidence for Depth Perception being Learned

Cross-Cultural Studies

A culture is a system of beliefs that are shared among a group of people, therefore shaping experience and behaviour. A cross-cultural study observes groups from different cultures. If the outcome is the same then the cause is likely to be nature; if a difference is seen it is likely to be nurture. A large sample, with standardised age and gender, should be used, with the same stimulus material to be responded to and a standardised methodology.

The carpentered world hypothesis suggests that people who live in a world dominated by straight lines and right angles tend to perceive depth cues differently to those who live in a circular culture. Individuals from urban areas are often fooled by the Müller-Lyer illusion, whilst those from a circular culture are rarely fooled.

Newborn Babies

The fact that babies are born with characteristic behaviours such as crying, walking movements and grasping suggests that these are controlled by genes. These innate capacities provide evidence that the brain is wired before birth.

In a classic experiment, babies are encouraged to walk over a table made of glass, below which is a visual cliff. Patterns placed below the glass create the appearance of a sheer drop. If the perception of depth is innate, then babies should be aware of the drop. Young babies were very reluctant to crawl over the cliff, even when encouraged by their mothers. Whilst this would suggest that the behaviour was innate, some perceptual development has taken place after birth and crawling only occurs after several months.

The Brain

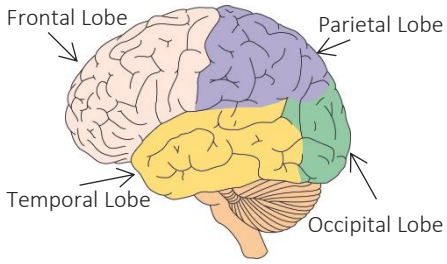
Key Terminology

Term	Definition
Radiology	Use of radiation to produce medical images used to diagnose and treat disease
Cortex	The highly folded outer layer of the brain, formed of grey matter – nerve cell bodies, synapses and dendrites. It is divided into left and right cerebral hemispheres, each of which is composed of four lobes
White Matter	Matter composed of nerve axons, connecting different brain regions and allowing communication between hemispheres
Neural Plasticity	The potential for neurones to change in structure and function, allowing the brain to be flexible and able to respond to environmental changes
Stroke	A sudden interruption in the blood supply of the brain. Ischaemic strokes are caused by clotting in the internal carotid arteries. Haemorrhagic strokes are caused by bleeding into brain tissue when a blood vessel bursts

Brain Structure

The brain acts as the main coordinating centre for nervous activity, receiving information from sensory organs, interpreting it and transmitting responses to effectors. Different regions help us respond to different stimuli.

Looking down onto the brain shows the cortex, grey and highly folded, composed of nerve cell bodies, synapses and dendrites – this is the grey matter. The cortex is positioned over other brain regions, and is divided into left and right cerebral hemispheres, each of which is composed of four lobes.



Frontal Lobe	Higher brain functions – decision making, reasoning, emotions, ideas. Includes motor cortex, controlling and storing movement
Parietal Lobe	Orientation, movement, sensation, calculation, some recognition and memory
Occipital Lobe	Processing information from the optic nerve, including vision, colour, shape, and perspective
Temporal Lobe	Processing auditory information – hearing, sound recognition, and speech in the left hemisphere. Also involved in memory

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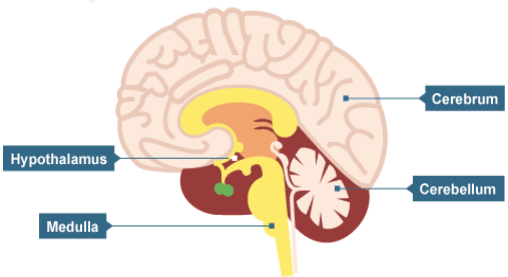
Hypothalamus	Thermoregulatory centre, monitoring core body and skin temperatures. Other centres control sleep, thirst and hunger. Hormones such as ADH, TRH and dopamine are secreted. The hypothalamus is connected to the pituitary gland, which secretes hormones such as FSH and LH, TSH, cortisol and oxytocin.
Cerebellum	Responsible for balance. The cerebellum coordinates movement as it is being carried out, receiving information from the primary motor cortex, muscles and joints, and constantly checks whether the correct motor programme is being used
Medulla Oblongata	Regulates unconscious body processes, such as heart rate, breathing and blood pressure, in the ventilation and cardiovascular centres



Below grey matter lies white matter, composed of nerve axons which connect neurones in different parts of the brain. The two cerebral hemispheres are connected by the corpus callosum, allowing communication. The structures below the white matter have many functions

Other structures include the thalamus (routes incoming sensory information to correct brain region via white matter), the hippocampus (long-term memory), the basal ganglia (selects motor programme) and the midbrain (relays information to cerebral hemispheres)

Brain damage from a stroke can cause issues with speaking, understanding and writing. Some patients recover, showing the potential for neurones to change in structure and function, known as neural plasticity.

Alzheimer's disease is the most common cause of dementia. Symptoms, including memory loss and problems with language and thinking, result from neurone loss. As neurones die, pieces of β-amyloid, a protein from the myelin sheath, clump to form plaques which block signalling at synapses, and also triggering an immune response. Accumulation of the protein is an early sign of Alzheimer's and so patients can undergo a PET scan with an amyloid tracer to visualise protein fibres in order to monitor disease progression.

Deducing the Function of Brain Structures

Historically, brain function was studied using patients in surgery, and particularly individuals with brain damage. If an area has experienced trauma, it is possible to determine the function of the region if a noticeable change has occurred to the individual. Neuroscientists now have a wide range of non-invasive techniques for studying brain function.

Brain Imaging

Technique	How It Works	Advantages	Disadvantages
CT Scans	Uses narrow x-rays to pass through tissue from different angles. Each beam is attenuated according to the density of the tissue. X-rays are detected and are used to produce an image of a thin brain on which different soft tissues can be distinguished.	• Used to detect brain disease and to monitor tissues	• Mutagen x-rays means cannot be used frequently • Only frozen pictures • Limited resolution
MRI	A magnetic field and another field is caused by magnetic component of high-frequency radio waves act. Combined fields cause the direction and spin of the protons in water molecules to change, taking energy from radio waves. When protons return to original alignment, they release the absorbed energy. This energy is detected and signals make an image.	• Different tissues respond differently, producing regions in 3D images • Diagnosis of tumours, strokes, brain trauma and CNS infections • High resolution	• Expensive technique • Metal objects cannot enter scanner so not used for people with stents and pacemakers • Very loud
fMRI	Observes functions of different parts of the brain following uptake of O_2 in active areas. This is possible as deoxyhaemoglobin absorbs the radio waves whereas oxyhaemoglobin does not. Enhanced blood flow in active areas means less signal is absorbed; on the image, areas will light up when they are active.	• Provides information about brain in action • Possible to study memory, emotion and language • Can follow rapidly occurring events	• Expensive technique • Comparisons often required e.g. rest and activity
PET	Isotopes with short half-lives are incorporated into compounds like glucose. Patient is injected with the radiotracer, and as it decays it emits positrons. When a tissue is active, there will be increased blood flow so more radiotracer will be present in the area. In a tissue, when a positron collides with an electron, two gamma rays are emitted and these are picked up by detectors; this is used to produce an image	• Plan heart surgery, monitor cancers and observe treatment effects • Repeating annually allows for change to be followed • Useful in monitoring Alzheimer's	• Can only be done one/twice a year for safety reasons • Very expensive so not used for routine screening

Learning and Memory

Key Terminology

Term	Definition
Habituation	A loss of responsiveness to stimuli that convey little or no information
Sensitisation	Development of an enhanced response to a stimulus
Learning	Any relatively permanent change in behaviour or knowledge that comes from experience

Learning occurs throughout life, and for learning to be effective, you must be able to remember what you have learnt. Throughout life, the memory stores vast amounts of information. Memory is not localised in one part of the brain, but is distributed throughout the cortex with different locations for long- and short-term memory, in addition to the hippocampus, cerebellum and basal ganglia. Memories can be created by altering the pattern of connections or the strength of synapses. Habituation and sensitisation both alter synapse strength.

Habituation increases fitness by allowing an organism's nervous system to focus on stimuli that signal the presence of food or danger instead of wasting energy on other stimuli that do not affect the organism's survival.

Learning by Habituation – Example of a Sea Slug Siphon

i. Water is sprayed onto the sea slug's siphon
ii. Impulses pass along a sensory neurone from the siphon
iii. The sensory neurone synapses with a motor neurone that connects to the gill muscle
iv. Impulses pass along the motor neurone
v. The gill muscle contracts and the gill is withdrawn
vi. With repeated stimulation the calcium ion channels of the presynaptic neurone become less responsive to the changes in voltage associated with action potentials
vii. Fewer calcium ions enter the presynaptic neurone
viii. Less neurotransmitter is released from the presynaptic neurone
ix. Fewer sodium ion channels are opened in the postsynaptic neurone, so there is less depolarisation of the membrane
x. An action potential is not propogated; the gill muscle does not contract and the gill is not withdrawn

Ethics of Animal Use in Medical Research

Reasons For Animal Use	Reasons Against Animal Use
• Utilitarianism: the framework allows certain animals to be used provided the overall expected benefit are greater than the harm • Advancing Research: increases biological knowledge of animal behaviour, development and function • Studying Disease and Developing Medicine: Animals are used as models to understand disease processes and to develop new vaccines and medicines. GM animals, particularly mice, are used to study the role of genes in disease. • Assess Safety of Chemicals: used in toxicological studies to help test the safety of a range of substances that could be harmful to animals, humans or the environment, including household chemicals, fertilisers, and food additives • Strict Licensing: The Home Office licenses use of animals in research if the research allows refinement, reduction and replacement. Where unavoidable, research should reduce suffering, use minimal number of animals without affecting welfare	• Consent: animals are unable to give informed consent, as would be expected from any humans involved • Suffering and Value of Animal Life: experimenting on animals is always unacceptable because it causes suffering • Unknown Benefits: the benefits to human beings are not proven, and any benefits to human beings that animal testing does provide could be produced in other ways. In this case utilitarianism rejects animal testing • Rights: if one accepts that animals have rights, if a test violates these rights, it must be wrong • Absolutism: rejects any use of animals

Problems with Synapses

Key Terminology

Term	Definition
Dopamine	A neurohormone secreted in the midbrain, with a role in reward-motivated behaviour
Serotonin	A neurotransmitter with roles in cognition, reward, learning and memory
MDMA	Commonly known as ecstasy; a psychoactive drug primarily used as a recreational drug
Human Genome Project	An international scientific research project with the goal of mapping the human genome
Single Nucleotide Polymorphism	DNA variations in the genome in at least 1% of the populations. Possessions of certain SNPs may predispose individuals to disease
Genetic Discrimination	Differential treatment as a result of an individual having or perceived to have a gene mutation that causes or increases the risk of an inherited disorder
Transgene	A gene which is artificially introduced into the genome of another organism
Genetic Engineering	The direct manipulation of an organism's genome using biotechnology

Artificial Selection	The intentional selective breeding of organisms in order to produce a desired trait
Marker Gene	A gene, often for antibiotic resistance, used to determine if a transgene has been successfully inserted into the target genome
Micropropogation	Production of plants by growing plantlets in tissue culture and then planting them out

Drugs and Synaptic Transmission

Drugs can affect different stages of synaptic transmission by their effect on neurotransmitters.

Parkinson's Disease

In people with Parkinson's Disease, cells which secrete dopamine in the basal ganglia die. The motor cortexes then receive little dopamine, causing a loss of muscular control, leading to symptoms of stiffness or tremor of muscles, poor balance and slow movement.

Treatments for Parkinson's include:

- L-Dopa, a precursor of dopamine, is able to pass through the blood-brain barrier and increase dopamine levels when converted into dopamine. This is the most common treatment for Parkinson's
- Use of MAO inhibitors, which prevent enzymatic breakdown of dopamine, therefore increasing availability
- Dopamine agonists activate dopamine receptors directly, mimicking the effects of dopamine

Depression

Serotonin is secreted by neurones in the brain set and targets a huge area of the brain. Serotonin has roles in cognition, reward, learning and memory. A lack of serotonin has been linked to depression. Depression is associated with feelings of sadness, anxiety and hopelessness, as well as exhaustion, insomnia and thoughts of death. Depression is likely to be a multifactorial condition, involving several genes in addition to environmental factors such as trauma, stress or other triggers. When someone is depressed, fewer nerve impulses are transmitted around the brain, producing less neurotransmitter. Serotonin pathways may also have abnormalities.

An old treatment for depression was monoamine oxidase inhibitors (MAOIs), which prevented break down of neurotransmitters including serotonin by enzymes. However, due to the many side effects caused, it is now a last line of treatment. Instead, selective serotonin reuptake inhibitors (SSRIs) are prescribed; these drugs prevent reuptake of serotonin from synapses. The high serotonin levels in the synapses increase the rate of nerve impulse transmission through serotonin pathways.

MDMA (Ecstasy)

MDMA affects thinking, mood and memory, and can also cause anxiety and altered perception. The most desired effect is emotional warmth. MDMA causes euphoria and enhanced senses, but has unpredictable side effects including sweating, kidney failure, high heart rate, muscle spasms and hyperthermia. This can all result from a single dose. Insomnia and depression may develop as neurones cannot synthesise enough serotonin to meet heightened demand.

MDMA increases serotonin concentration by binding to molecules in the presynaptic membrane responsible for reuptake, preventing its removal from the synapse. The drug also causes transporting of molecules to work in reverse, further increasing amounts of serotonin.

Human Genome Project

The Human Genome Project was launched in 1990, and the first working draft of the whole human genome was published in 2001. Work continues to produce a sequence with 99.9% accuracy. Using the sequence, biologists aim to identify new genes, consider their control, and discover the proteins they produce.

The human genome is thought to be about 3.2 billion bases in length, containing 20000 – 25000 genes. Coding DNA makes up less than 2% of the genome. The significance of non-coding regions has been a key focus of research, and studies suggest that this DNA is highly conserved, suggesting they play a role in preserving certain useful traits.

- Identification of new genes can occur. Several genes associated with diseases can be found as a result. A candidate gene can be located and screen for mutations in affected individuals. For example, the allele APOE4 increases risk of CVD, as well as increasing risk of Alzheimer's, as the lipoprotein produced causes amyloid plaque formation
- New drug targets can be identified by searching for DNA sequences similar to those for existing target proteins. It is thought that as many as 3000 genes express proteins whose activities could be altered by medicines

Personalised Medicine

- Some drugs are ineffective in some individuals and have major side effects. These responses may be due to variations in genomes, depending on which SNPs individuals possess. Prescribing the best drug for a patient is largely trial and error, but it is hoped that genetic information will enable the prescription of the correct drug at the right dose. The ability to sequence DNA cheaply and accurately allows for SNPs which cause severe side effects with a certain drug to be identified, meaning treatment can be modified for an individual.
- If an individual knew they carried mutations which increased risk of a disease, lifestyle changes or preventative treatment could reduce risk of disease development

Ethical Issues with Genome Sequencing

- Patenting of human DNA poses questions about the use of the data
- The results of genetic predisposition tests need to be secured, and keeping records creates issues surrounding confidentiality. Many initial treatments will be very expensive, with restricted availability.
- Testing for genetic predisposition has many implications, including potential discrimination in employment or insurance. Higher premiums or lack of cover may arise even though having a particular allele does not mean an individual is guaranteed to develop a condition

Genetic Modification

Genetically Modified Microorganisms

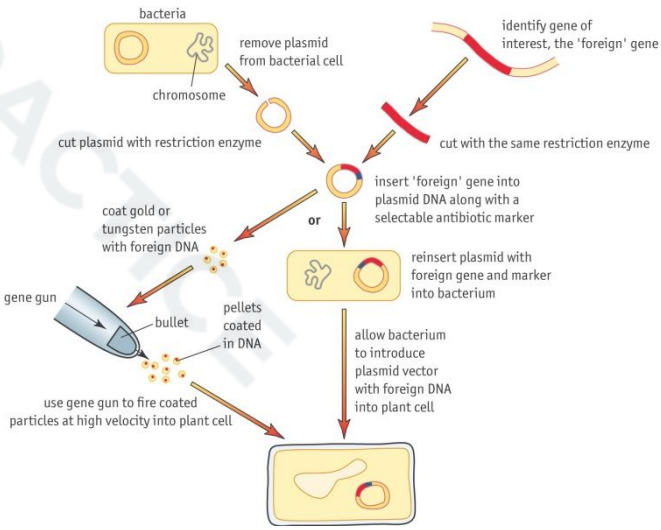
A plasmid is cut using restriction enzymes. This leaves it with sticky ends, strands of unmatched bases. The gene of interest is also cut out using the same restriction enzymes, leaving it with complementary sticky ends to the plasmid. The sticky ends are joined by the enzyme DNA ligase to make recombinant DNA. The vector plasmid is inserted into a bacterium which multiplies in a fermenter, and produces the protein. The protein is extracted and purified, and the bacterial cells destroyed.

Genetically Modified Plants

Artificial selection has occurred throughout history, where farmers selectively breed organisms with desired traits to increase, increasing frequency of alleles which produce the desired trait in the population. In the modern day, new genes can be introduced directly into a plant's DNA. GM crops have the potential to mass produce food and medicine cheaply and efficiently.

Genome Editing of Plants

- A gene of interest is identified and cut out of the original protoplast, a plant cell which has had its cell wall removed, using restriction enzymes.
- A bacterium which invades plant cells has a plasmid removed. The plasmid is cut with the same restriction enzyme, leaving sticky ends. These sticky ends are complementary to those of the gene of interest. The two DNA pieces are joined by DNA ligase to produce recombinant DNA
- The gene can then be introduced into the plant cell in different ways:
    - The plasmid containing the transgene is reinserted into the bacterium with a marker gene, which allows for antibiotic resistance. The bacterium then allowed to introduce the plasmid vector into the plant cell
    - The plasmid can be coated in gold or tungsten particles, then the pellets formed are fired at a high velocity into a plant cell using a gene gun
    - Viruses could also be used, as they insert their DNA or RNA into cells



- The transgene is incorporated into the plant chromosome, which transforms the plant cell. Plant cells are grown on an agar containing nutrients and the antibiotic used to check if gene insertion has been successful. If the plant survives, then insertion has been successful as the marker gene, which was inserted alongside the transgene, has been transcribed, allowing for antibiotic resistance.

- Surviving plans are then cultured on a sterile agar containing sucrose, amino acids, inorganic ions and growth substances. This micropropogation can multiply a single cell to form a callus, which then differentiates to form plantlets then eventually new transgenic plants – every cell in these plants will contain the transgene.

Genetically Modified Animals

DNA can be introduced into animal cells by methods including gene therapy (Topic 2). GM animals can also be produced by injection of DNA into a fertilised ovum, which is then implanted. Retroviruses have also been used to introduce new genes into fertilised eggs, as it incorporates its DNA into the host's DNA.

Concerns About Genetic Modification

GM organisms are used to ensure food security with increasing populations and climate change, and remove the need for pesticide use. For example, GMO Golden Rice synthesises β-carotene, a Vitamin A precursor, and is sold in areas in the world where deficiency of this vitamin leads to 670000 deaths a year. GM organisms are also used extensively in research and medicine. Despite the potential benefits, there are some risks associated with use.

Health

- *Transfer of antibiotic resistance genes to microorganisms* – marker genes often code for antibiotic resistance. This gene could potentially give resistance to pathogenic microbes, perhaps resulting in infection of humans. There is no evidence that dietary DNA can be integrated into the genome of bacteria, but since the marker genes do not benefit anyone after effectiveness of gene insertion is checked, they can be removed

- *Formation of harmful products by new genes* – extraction and purification of proteins from GMOs can be difficult. It is difficult to guarantee that such proteins have no risk with use, and despite there being no reported cases of illness resulting from GMO consumption, it is conceivable that biochemical changes to oils and proteins could result in toxic compounds being produced

- *Transfer of viruses from animals to humans* – concerns that new viruses may be transferred to humans from GMOs

Environmental and Social Issues

Potential of gene transfer to non-target species - cross-pollination can occur over wide distances. Some crops are related to wild plants and can ross with them meaning genes from GM crops may inevitably and irrevocably spread to conventional crops. Although any transgenic crops may be presumed to disappear, there is a chance that the transgene may provide a selective advantage. There is also the possibility of breeding herbicide-resistant superweeds; this risk is not unfounded, given invasive species such as rhododendrons. One solution to GM superweeds would be to ensure that outcrosses are infertile. Opponents of GM argue that GM crops will end up causing us to use more chemicals to control resistant weeds than we would have otherwise done.

It is also difficult to decide how GMOs are legally protected. Biotech companies patent new gene editing techniques. Smaller farmers in less developed areas may struggle to invest in GM seeds.