Neurulation

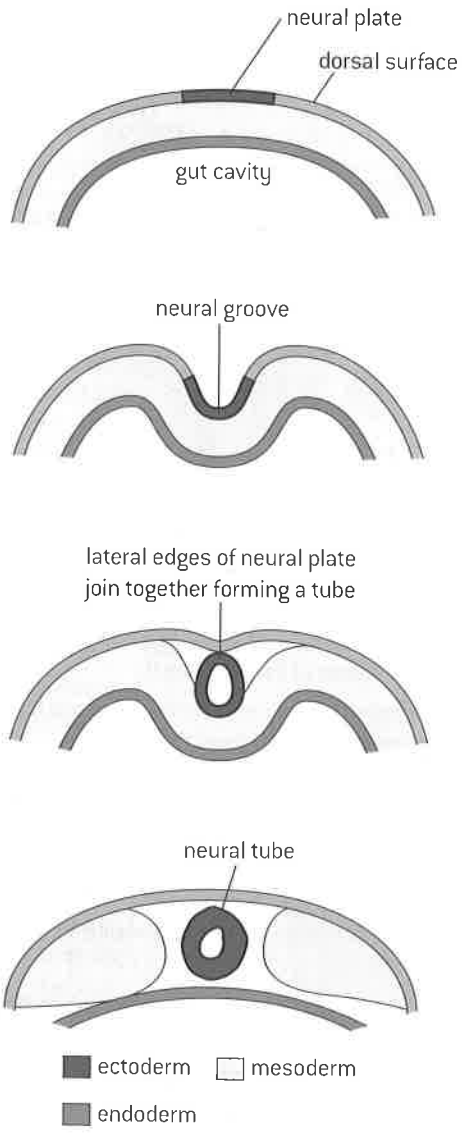
NEURULATION

Humans are in the phylum Chordata. All animals in this phylum develop a dorsal **nerve cord** at an early stage in their development. The process is called **neurulation** and in humans it occurs during the first month of life. The dorsal nerve cord develops from **ectoderm**, which is the outer tissue layer. An area of ectoderm cells on the dorsal surface of the embryo develops differently from the rest of the ectoderm and becomes the neural plate.

The cells in the neural plate change shape and this causes the plate to fold inwards forming a groove along the back of the embryo and then separating from the rest of the ectoderm. This forms the **neural tube**, which develops into the **nerve cord**.

NEURULATION IN XENOPUS

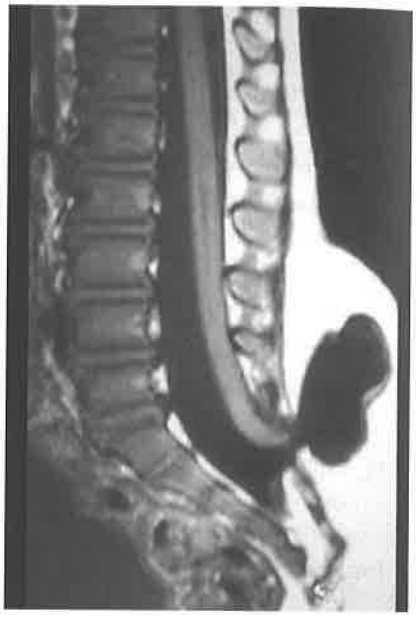
The diagrams below show how neurulation takes place in *Xenopus* (African clawed frog). This species is an ideal model for research into neurulation because the embryo is transparent.



SPINA BIFIDA

In vertebrates there are a series of bones called vertebrae. Each of these has a strong centrum that provides support and a thinner vertebral arch, which encloses and protects the spinal cord. The centrum develops on the ventral side of the neural tube at an early stage in embryonic development. Tissue migrates from both sides of the centrum around the neural tube and normally meets up to form the vertebral arch.

In some cases the two parts of the arch never become properly fused together, leaving a gap. This condition is called **spina bifida**. It is probably caused by the embryonic neural tube not closing up completely when it is formed from the neural groove. Spina bifida is commonest in the lower back. It varies in severity from very mild with no symptoms, to severe and debilitating.



USING ANIMAL MODELS

Neuroscience is the branch of biology concerned with neurons and nervous systems. The aim of research in developmental neuroscience is to discover how nervous systems are formed as animals grow from an embryo into an adult. The aim of many neuroscientists is to understand and develop treatments for diseases of the nervous system, but most experiments are impossible to perform in humans for ethical reasons. Also, research into other animal species is usually easier because development of the nervous system is more rapid, less complex and is easier to observe because the embryo develops externally rather than in a uterus.

For these reasons, even when researchers are trying to make discoveries about humans, they work with other species. A relatively small number of species is used for most of this research and these species are known as animal models:

- *Caenorhabditis elegans* (flatworm)
- *Drosophila melanogaster* (fruit fly)
- *Danio rerio* (zebrafish)
- *Xenopus laevis* (African clawed frog)
- *Mus musculus* (mouse).

Xenopus embryos

Development of the nervous system

DEVELOPMENT OF NEURONS

Cell division in the neural tube produces large numbers of cells that gradually differentiate into neurons. Some immature neurons migrate from where they are produced in the neural tube to a final location.

Axons grow out from each immature neuron. They are stimulated to do this by chemical stimuli. In some cases the axon grows out of the neural tube to other parts of the embryo and the neuron develops into a sensory or a motor neuron.

Developing neurons produce connections with many other neurons, called **multiple synapses**, but not all of them persist. Synapses that are not used are removed, following the principle 'use it or lose it'.

There is also a process of removing entire neurons that are not being used. This is called **neural pruning**. This is an example of the plasticity of the nervous system – throughout life it can change with experience.

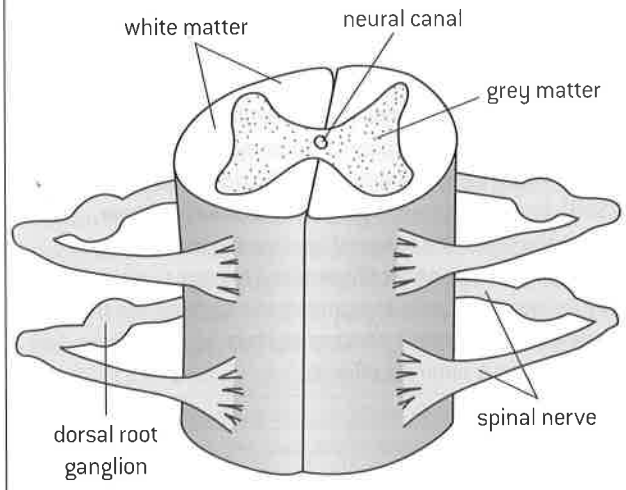
DEVELOPMENT OF THE CNS

The nervous system has two main parts:

- the **peripheral nervous system** consisting of nerves and sensory receptors,
- the **central nervous system** (CNS) consisting of the spinal cord and brain.

Both the brain and spinal cord develop from the neural tube.

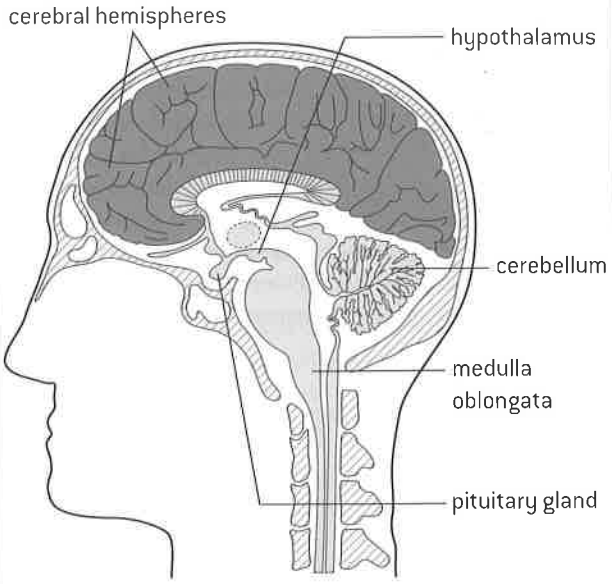
As the embryo grows, the neural tube elongates. The anterior part of the neural tube develops into the brain and the rest thickens to form the spinal cord. The channel at the centre of the neural tube persists as the very small neural canal in the middle of the spinal cord.



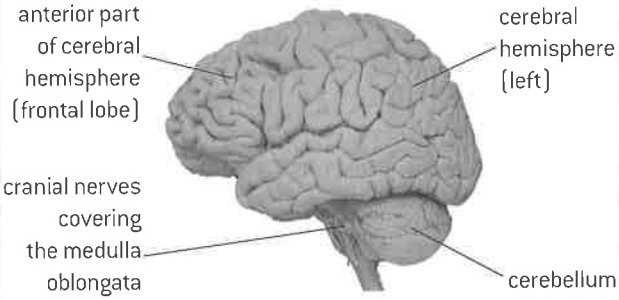
Far more neurons are needed than are initially present in the embryonic neural tube, so cell proliferation continues in both the developing spinal cord and brain. Although this ceases before birth in most parts of the nervous system, there are parts of the brain where extra neurons are produced during adulthood.

STRUCTURE OF THE BRAIN

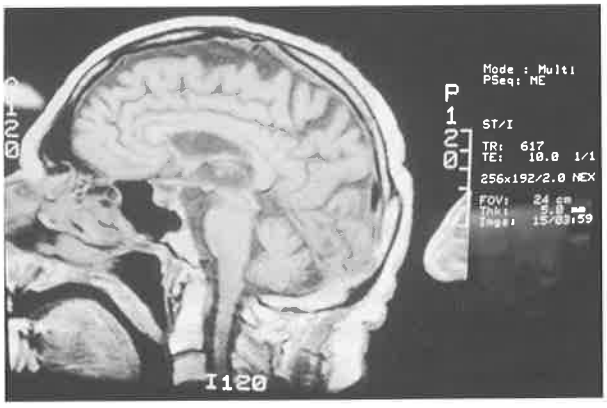
The brain has a complex structure with distinctive parts, which are shown in the vertical section below.



Photographs of the exterior of the brain show the cerebral hemispheres and cerebellum, with the spinal cord connected to the hindbrain (lower part of brain).



MRI and CAT scans reveal the internal structure of the brain and are widely used to investigate health problems. The image below is a CAT scan.



Functions of the brain

METHODS OF BRAIN RESEARCH

Various approaches have been used to identify the roles of parts of the brain.

Lesions and autopsy

A **lesion** is a region of damage or injury to an organ. An **autopsy** is dissection after death of an animal or human body. Brain lesions can be caused by tumours, strokes or accidental damage. Many lesions have been investigated by carrying out an autopsy and relating its position to changes that had been observed to behaviour or capabilities. There are some famous cases from the 19th century including that of Phineas Gage and those investigated by Jean-Martin Charcot.

Animal experiments

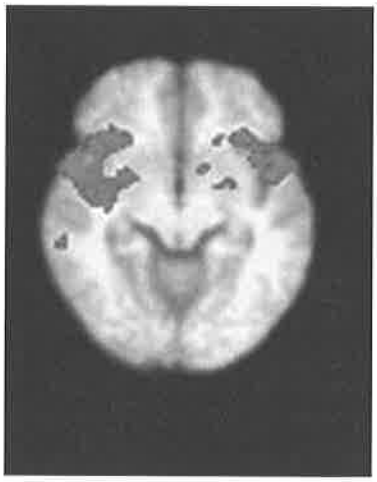
Although lesions due to natural causes have revealed much about the brain, more can be learned using animals. Removal of parts of the skull gives access to the brain and allows experimental procedures to be performed. The effects of local stimulation or surgery to a specific part of an animal's brain can be observed.

There are widespread objections to such research, because of the suffering caused to the animal and because at the end the animal is often sacrificed. Neuroscientists have argued that these experiments can increase our understanding of conditions such as epilepsy, Parkinson's disease and multiple sclerosis. There are now strict regulations in most countries to ensure that the benefits of the research justify any harm caused to the animals used.

Functional MRI (fMRI)

Magnetic resonance imaging is used to investigate the internal structure of the body, including looking for tumours or other abnormalities in patients. A specialized version of MRI, called **functional MRI (fMRI)** allows parts of the brain that have been activated by specific thought processes to be identified. Active parts of the brain receive increased blood flow, often made visible by injecting a harmless dye, which fMRI records.

The subject is placed in the scanner and a high-resolution scan of the brain is taken. A series of low-resolution scans is then taken while the subject is being given a stimulus. These scans show which parts of the brain are activated in the response to the stimulus.



fMRI scan of endometriosis pain

FUNCTIONS OF PARTS OF THE BRAIN

The brain has easily distinguishable parts which have different roles.

The **medulla oblongata** controls automatic and homeostatic activities such as swallowing, digestion, vomiting, breathing and heart rate. Three examples are explained below.

The **cerebellum** coordinates unconscious functions, such as movement and balance.

The **hypothalamus** is the interface between the brain and the pituitary gland, controlling the secretion of pituitary hormones.

The **pituitary gland** secretes at least ten hormones that regulate many body functions.

The **cerebral hemispheres** have many different functions. They are explained on the next page.

THE AUTONOMIC NERVOUS SYSTEM

The peripheral nervous system has two parts: the voluntary and autonomic nervous systems. The autonomic nervous system controls unconscious processes using centres in the **medulla oblongata**.

Swallowing

In the first phase of swallowing food is passed from the mouth cavity to the pharynx. This is voluntary and controlled by the cerebral cortex. The food then passes down the esophagus to the stomach by involuntary muscle contraction, coordinated by the swallowing centre of the medulla oblongata.

Breathing

Two centres in the medulla control the rate and depth of ventilation in response to changes in blood pH, which is monitored by **chemoreceptors** in blood vessels and in the medulla. The depth and rate of inspiration are increased if blood pH falls, as this indicates an increase in CO_2 concentration. They are decreased if blood pH rises.

Heart rate

The cardiovascular centre of the medulla regulates the rate at which the heart beats. It increases or decreases the heart rate by sending impulses to the heart's pacemaker (SAN). Impulses carried by **sympathetic nerve fibres** cause the heart rate to speed up; impulses carried by **parasympathetic nerve fibres** cause the rate to slow down. The sympathetic and parasympathetic systems are the two parts of the **autonomic nervous system**. In many cases, like this, they have opposite effects.

STROKES

A **stroke** is a disruption of the blood supply to part of the brain, caused either by a blockage or by bleeding. Brain tissue is deprived of oxygen for a time and is often damaged. Patients frequently recover from minor strokes, even though a part of the brain is no longer able to function as it did before. This shows that there can be reorganization of certain functions and that not all functions are invariably carried out by one part of the brain. Scans of the brain show that some activities involve many different areas and there may be alternative ways to carry them out.

EVOLUTION OF THE CEREBRAL CORTEX

The **cerebral cortex** is the outer layer of the cerebral hemispheres. Although it is only between two and four millimetres thick, it consists of up to six layers of neurons with a complex architecture. It forms a larger proportion of the brain and is more highly developed in humans than other mammals.

Over millions of years of evolution the human cerebral cortex has become immensely enlarged, principally by an increase in total area. There is extensive folding, without which the cerebral cortex could not be accommodated within the cranium.

FUNCTIONS OF THE CEREBRAL HEMISPHERES

The cerebral hemispheres act as the integrating centres for higher order functions such as learning, memory and emotions. As with other parts of the brain, specific functions are carried out by specific parts of the left and right cerebral hemispheres.

The **somatosensory cortex** receives sensory inputs. The left hemisphere receives sensory inputs from the right side of the body and vice versa for the right cerebral hemisphere.

The **motor cortex** controls voluntary muscle contractions by skeletal (striated) muscles. The left cerebral hemisphere controls muscle contraction in the right side of the body, and vice versa for the right cerebral hemisphere.

The **visual cortex** processes visual stimuli detected by light-sensitive rod and cone cells in the retina. In the eye the visual field (the area of vision) is divided into left and right halves. Impulses generated by the right half of the visual field in both eyes are passed to the left cerebral hemisphere and impulses from the left half of the visual field of both eyes are passed to the right cerebral hemisphere. This allows stimuli from the two eyes to be combined, so distance and relative size of objects can be judged. Analysis in the visual cortex also includes pattern recognition and judging the speed and direction of moving objects.

Broca's area is a part of the left cerebral hemisphere that controls the production of speech. If there is damage to this area an individual knows what they want to say and can produce sounds, but they cannot put sounds together into words that have meaning. For example, if we see a horse-like animal with black and white stripes, Broca's area allows us to say 'zebra', but a person with a damaged Broca's area knows that it is a zebra yet cannot say the word.

The **nucleus accumbens** in each of the cerebral hemispheres act as the pleasure or reward centres of the brain. A variety of stimuli including food and sex cause the release of the neurotransmitter dopamine in the nucleus accumbens, which causes feelings of well-being, pleasure and satisfaction. Cocaine, heroin and nicotine are addictive because they also cause release of dopamine in the nucleus accumbens even when nothing has happened in a person's life to justify these feelings.

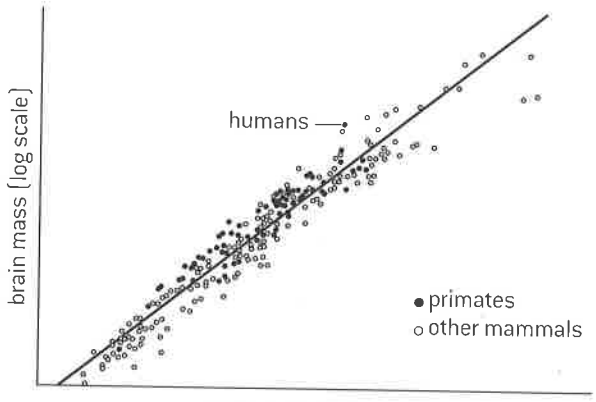
SENSORY AND MOTOR HOMUNCULI

Models of the human body can be made with the size of each part of the body proportional either to the area of the somatosensory cortex that receives inputs from that part (right), or to the area of the motor cortex that controls muscles in that part of the body (below) These types of model are called sensory and motor homunculi.

There are striking differences between the proportions of both homunculi and actual human bodies. Hands appear disproportionately large for example, as they contain a relatively large number of sensory receptor cells and many small muscles.

BRAIN AND BODY SIZE

The graph below shows the relationship between brain mass and body mass in animal species.



The correlation coefficient for the data in the graph is 0.75, so there is quite a strong positive correlation between brain and body mass. Humans do not have the largest brain size of any animal – species with a larger body mass such as blue whales and elephants have larger brains. However, the data point for humans is further above the correlation curve than any other species, indicating that humans have a larger brain in relation to their body mass than other animals. The graph also shows that most but not all primates have relatively large brains in relation to their body mass.

Perception of stimuli

DIVERSITY OF SENSORY RECEPTORS

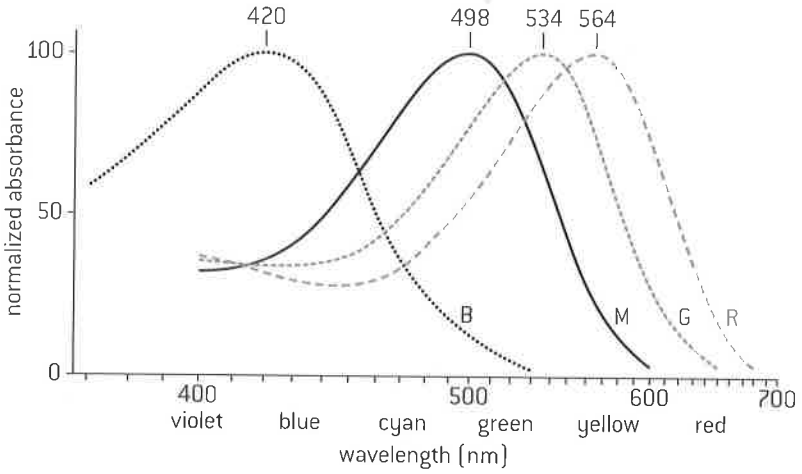
Sensory receptors detect changes in the environment. The change detected by a receptor is a **stimulus**. In humans there are four types of sensory receptor, which together can detect a wide range of stimuli.

Type	Stimulus	Example
Mechanoreceptors	Mechanical energy in the form of sound waves Movements due to pressure or gravity	Hair cells in the cochlea of the ear Pressure receptor cells in the skin
Chemoreceptors	Chemical substances dissolved in water (tongue) Chemical substances as vapours in the air (nose)	Receptor cells in the tongue Nerve endings in the nose
Thermoreceptors	Temperature	Nerve endings in skin detect warm or cold
Photoreceptors	Electromagnetic radiation, usually in the form of light	Rod and cone cells in the eye

PHOTORECEPTORS

The photoreceptors of the eye are contained in the retina. There are two types of photoreceptor cell – **rod cells** and **cone cells**. The diagram of the retina on the next page shows the structure of rod and cone cells. These cell types both absorb light and then transmit messages to the brain, via the optic nerve. They are different in these ways:

1. Rod cells are more sensitive to light than cone cells, so they function better in dim light, for example at night. Rod cells become bleached in bright light, for example in daylight, but cone cells function well in high light intensities.
2. All rod cells contain the same pigment, which absorbs a wide range of wavelengths of light, so they do not distinguish between different colours and only give monochrome vision. There are three types of cone cell, each of which contains a different pigment. These pigments absorb different ranges of wavelength, with peaks of absorbance in blue, green and red light. Cone cells can therefore distinguish between light of different wavelengths and so give colour vision.



The graph shows the absorbance of wavelengths of light by the three pigments in cone cells (B, G and R) and the pigment in rod cells (M).

OLFACTORY RECEPTORS

The sense of smell (olfaction) is due to **olfactory receptor cells** located in the epithelium inside the upper part of the nose. These cells have cilia which project into the air in the nose. In the membrane of these cilia are the **receptors**, which are proteins that can detect specific chemicals in the air.

Only chemicals that are volatile and can pass through the air can be detected (smelled). Odorants from food in the mouth can pass through the air in the mouth and nasal cavities to be detected in the nose.

Each olfactory receptor cell has just one type of odorant receptor in its membrane, but there are many different types of receptor, each of which is encoded by a different gene and detects a different group of odorants.

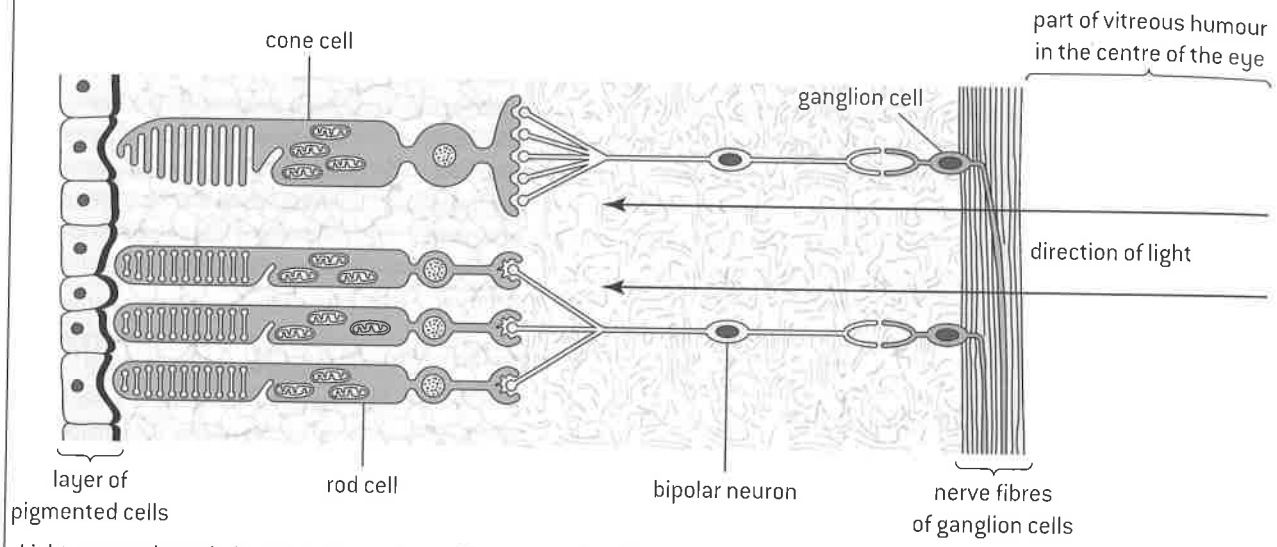
In some mammals such as mice there are over a thousand different receptors, but humans have fewer. Using these olfactory receptors a large number of chemicals in the air can be distinguished.

RED–GREEN COLOUR-BLINDNESS

The photoreceptor pigments in blue, green and red cone cells are all members of a group of proteins called **opsins**. There is a separate gene coding for each of the three pigments. The genes for the pigments in both red and green cones are located on the X chromosome. Red–green colour-blindness is a common inherited condition. It is due to a lack of functioning pigment in either red or green cone cells. Whichever pigment is missing, light with the wavelengths in the green to red part of the spectrum cannot be distinguished. As genes for both pigments are on the X chromosome, red–green colour-blindness is sex-linked, whether it is the green- or red-detecting pigment that is missing. The normal alleles of both genes are dominant and the alleles that cause red–green colour-blindness are recessive. Red–green colour-blindness is therefore much commoner among males than females and males inherit the allele that causes the condition from their mother.

Vision in humans

STRUCTURE AND FUNCTION OF THE RETINA



Light passes through the nerve fibres of **ganglion cells** and the layer of **bipolar cells** in the outer part of the retina until it reaches the rod and cone cells. When rod or cone cells absorb light they pass impulses to bipolar cells, which pass them on to ganglion cells. Groups of up to two hundred rod cells pass impulses to the same bipolar cell, whereas as few as one cone cell may pass impulses to a single bipolar cell, so cone cells give greater visual acuity. Impulses from rod and cone cells are processed in bipolar and ganglion cells and are then transmitted to the brain in the nerve fibres of ganglion cells, which are located in the **optic nerve**.

ASSESSING BRAIN DAMAGE USING THE PUPIL REFLEX

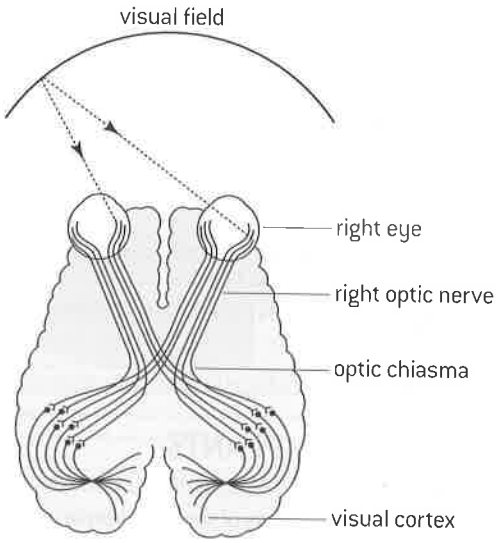
Muscle cells in the iris control the size of the pupil of the eye. Impulses carried to radial muscle by neurons of the sympathetic system cause them to contract and dilate the pupil; impulses carried to circular muscle by neurons of the parasympathetic system cause the pupil to constrict. The pupil reflex occurs when bright light suddenly shines into the eye. Photoreceptive ganglion cells in the retina perceive the bright light, sending signals through the optic nerve to the mid-brain, immediately activating the parasympathetic system, which stimulates circular muscle in the iris to constrict the pupil, reducing the amount of light entering the eye and protecting the delicate retina from damage. The mid-brain is part of the brain stem – the region of the brain that is adjacent to the spinal cord.

Doctors sometimes use the pupil reflex to test a patient's brain function. A light is shone into each eye. If the pupils do not constrict at once, the brain stem is probably damaged. If this and other tests of brain stem function repeatedly fail, the patient is said to have suffered brain death. It may be possible to sustain other parts of the patient's body on a life support machine, but full recovery is extremely unlikely.

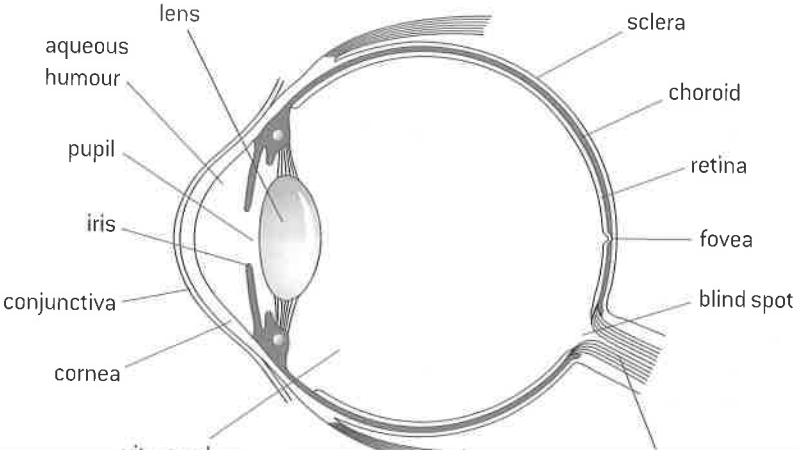
OPTIC NERVES

The diagram below shows how information from the left field of vision reaches the right visual cortex and vice versa.

Nerve Fibres cross over at the optic chiasma so that impulses from the left field of vision in both eyes go to the right side of the visual cortex and vice versa for the right field of vision.



STRUCTURE OF THE HUMAN EYE

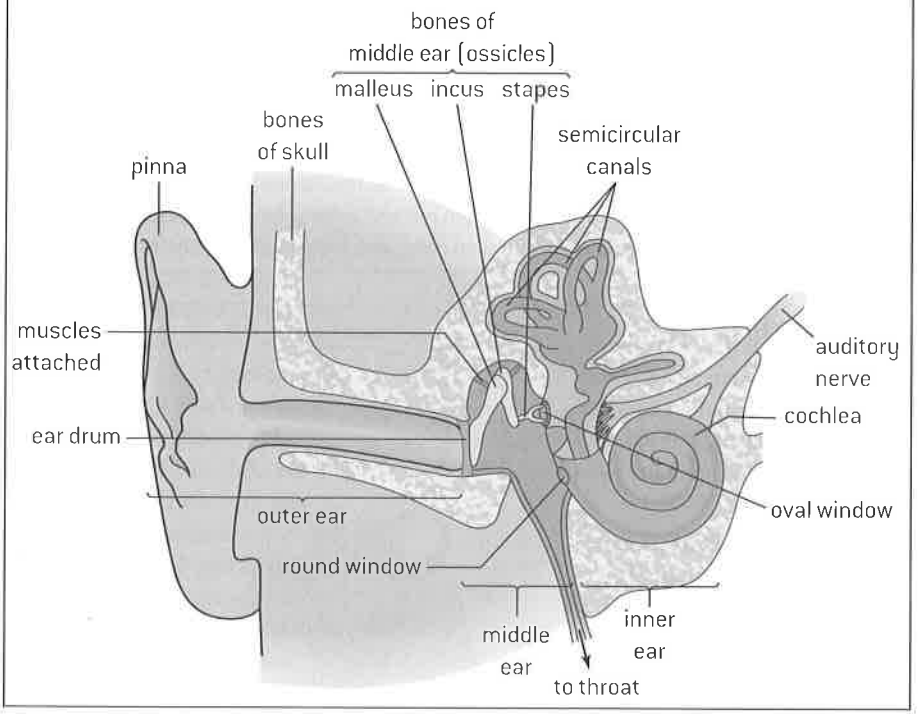


Hearing in humans

FUNCTIONS OF THE MIDDLE EAR

When sound waves reach the eardrum at the end of the outer ear, they make it vibrate. The vibration consists of rapid movements of the eardrum, towards and away from the middle ear. In the middle ear is a series of very small bones called **ossicles**, which are shown in the diagram below. The **malleus** is attached to the **eardrum** and makes contact with the **incus**, which in turn makes contact with the **stapes**. The stapes is attached to the **oval window**. The ossicles therefore **transmit** sound waves from the eardrum to the oval window. They also act as levers, reducing the amplitude of the waves, but increasing their force, which **amplifies** sounds by about 20 times. Both the eardrum and the oval window are thin layers of tissue that can readily vibrate. The oval window is much smaller than the eardrum. This helps to amplify sounds. Muscles attached to the ossicles protect the ear from loud sounds by contracting, which damps down vibrations in the ossicles.

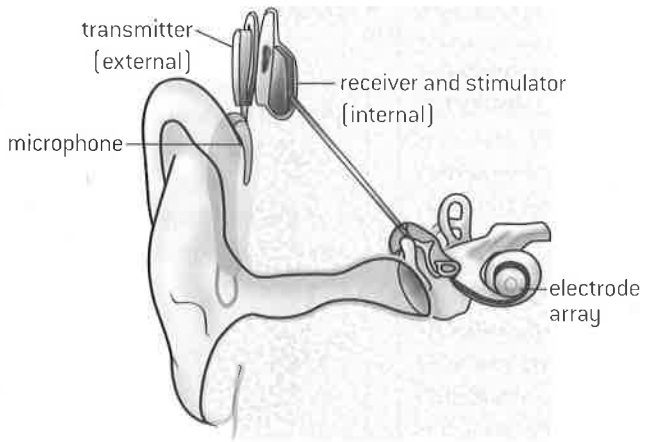
STRUCTURE OF THE HUMAN EAR



COCHLEAR IMPLANTS

Research from the 1950s onwards led to the development of **cochlear implants**, which can help give some sense of sound to people with non-functional cochlear hair cells. The external parts are a microphone to detect sounds, a speech processor to filter out frequencies apart from those used in speech and a transmitter.

The internal parts are implanted in bone behind the ear. They consist of a receiver that picks up sound signals from the transmitter, a stimulator to convert the signals into electrical impulses and an array of electrodes to carry the impulses to the cochlea. The electrodes stimulate the auditory nerve directly and so bypass the non-functional hair cells.



FUNCTION OF THE SEMICIRCULAR CANALS

There are three fluid-filled semicircular canals in the inner ear. Each has a swelling at one end in which there is a group of sensory hair cells, with their hairs embedded in gel.

When the head moves in the plane of one of the semicircular canals, the stiff wall of the canal moves with the head, but due to inertia the fluid inside lags behind. There is therefore a flow of fluid past the hairs, stimulating the hair cells to send impulses to the brain.

The three semicircular canals are at right angles to each other, so each is in a different plane. They can therefore detect movements of the head in any direction. The brain can deduce the direction of movement by the relative amount of stimulation of the hair cells in each of the semicircular canals.

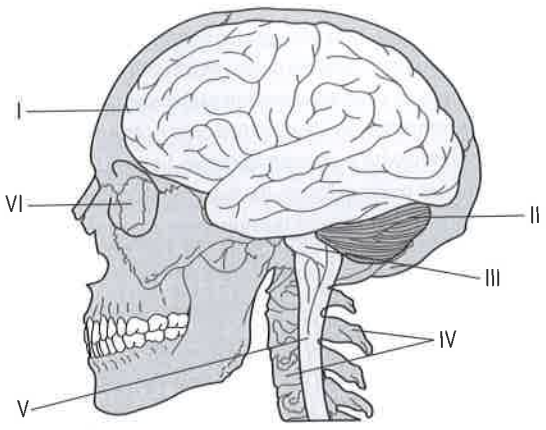
FUNCTION OF THE COCHLEA

The cochlea consists of a spiral fluid-filled tube. Within the tube are membranes with receptors called **hair cells** attached. These cells have hair bundles, which stretch from one of the membranes to another. When sound waves transmitted by the oval window pass through the fluid in the cochlea, the hair bundles vibrate.

Gradual variations in the width and thickness of the membranes allow different **frequencies** of sound to be distinguished, because each hair bundle only resonates with particular frequencies. When the hair bundles vibrate, the hair cells send messages to the brain via the **auditory nerve**.

Questions – neurobiology and behaviour

1. The diagram shows part of the CNS.



a) State the name of structures I to V. [5]

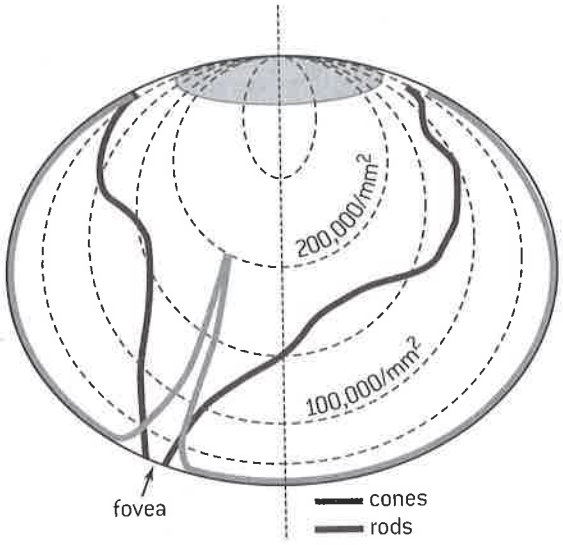
b) Outline the functions of structures I to III. [6]

c) Explain the development of structure V in an embryo. [3]

d) Outline the types of receptor in the organ occupying the position marked VI. [3]

e) State three types of procedure that are used to investigate the functions of parts of structure I. [3]

2. The graph below shows the density of rods and cones across the retina.



a) Distinguish between the distribution of rod and cone cells across the retina. [3]

b) Distinguish between the roles of rods and cones. [4]

c) Compare and contrast processing in the retina of visual stimuli in rods and cones. [3]

3. A pedestrian who uses cochlear implants to help with deafness is waiting to cross a road. Vehicles are approaching from the right.

a) Explain which side of the brain is responsible for

(i) the pedestrian seeing approaching vehicles [2]

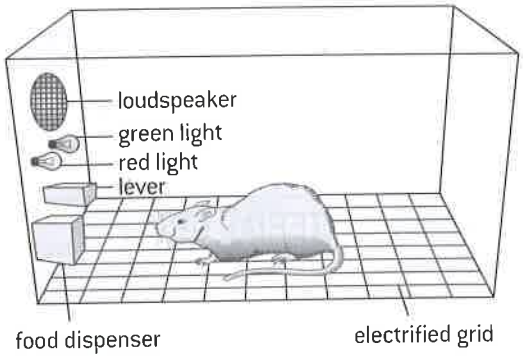
(ii) the pedestrian hearing approaching vehicles. [2]

b) The pedestrian turns their head to the right. Explain how this movement is detected by sensory receptors, apart from those in the eye. [2]

c) A garbage truck drives past the pedestrian. Explain how the smell of the garbage is detected. [2]

d) Explain how the cochlear implants help the pedestrian to hear. [4]

4. (HL) The diagram shows a rat in a Skinner box.



a) State two names for the type of learning that was investigated using Skinner boxes. [2]

b) Outline the role in this type of learning of

(i) the food reward [2]

(ii) pressing the lever. [2]

c) Design an experiment into operant conditioning involving three labelled structures within the Skinner box. [6]

5. (HL) To investigate the effects of MDMA (ecstasy), healthy human volunteers were given one of three different drugs:

- citalopram (which inhibits reuptake of serotonin from synapses into pre-synaptic neurons and reduces secretion of serotonin from them),
- ketanserin (which binds to serotonin receptors and blocks them), or
- haloperidol (which binds to dopamine receptors and has opposite effects to dopamine).

The volunteers were then given 1.5 mg/kg of MDMA.

Citalopram markedly reduced most of the subjective effects of MDMA, including positive mood, increased extroversion and self-confidence. Haloperidol selectively reduced MDMA-induced positive mood. Ketanserin selectively reduced MDMA-induced perceptual changes and emotional excitation.

a) Subjective effects can only be perceived by the person who takes a drug. Suggest difficulties of investigating the subjective effects of drugs. [2]

b) List three subjective effects of MDMA. [3]

c) State the evidence from this research for the subjective effects of MDMA being mediated through serotonin and dopamine metabolism. [5]

6. (HL) a) Outline what is studied by ethologists. [2]

b) Using the examples of migration in blackcaps and feeding on cream from milk bottles by blue tits,

(i) discuss whether patterns of behaviour are learned or genetic. [3]

(ii) deduce whether behaviour patterns spread through populations faster if learned or genetic. [2]

c) Explain the advantages of synchronized oestrus in female lions. [4]