# Topic 8: Grey Matter

**SPECIFICATION**

Students should:

8.1 Know the structure and function of sensory, relay and motor neurones including the role of Schwann cells and myelination.

8.2 i) Understand how the nervous systems of organisms can cause effectors to respond to a stimulus.

ii) Understand how the pupil dilates and contracts.

8.3 Understand how a nerve impulse (action potential) is conducted along an axon including changes in membrane permeability to sodium and potassium ions and the role of the myelination in saltatory conduction.

8.4 Know the structure and function of synapses in nerve impulse transmission, including the role of neurotransmitters, including acetylcholine.

8.5 Understand how the nervous systems of organisms can detect stimuli with reference to rods in the retina of mammals, the roles of rhodopsin, opsin, retinal, sodium ions, cation channels and hyperpolarisation of rod cells in forming action potentials in the optic neurones.

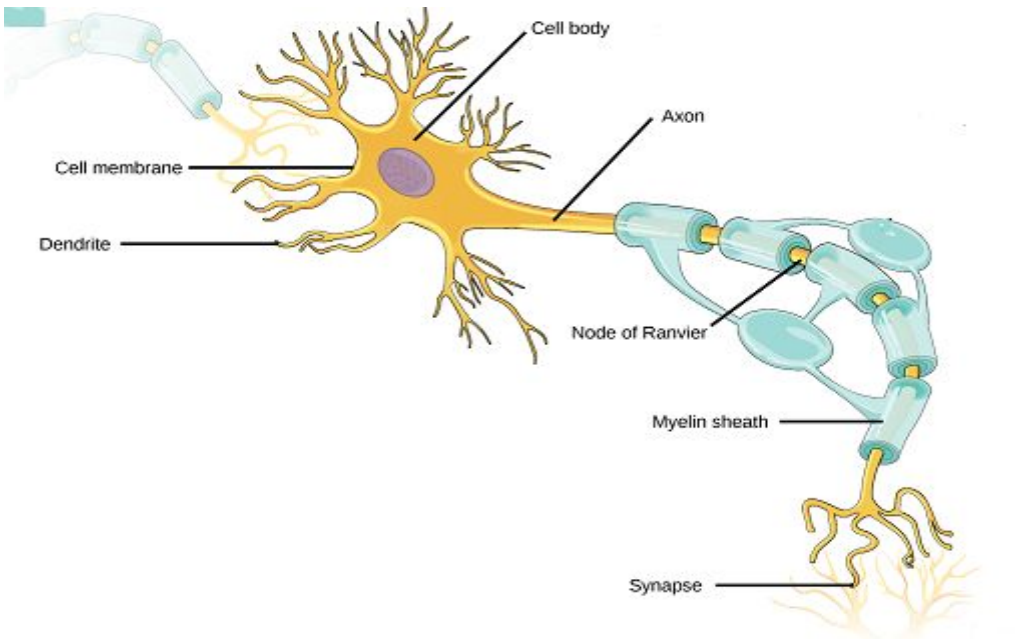
8.6 Understand how phytochrome and IAA bring about responses in plants to environmental cues, including their effects on transcription.

8.7 Understand how coordination is brought about through nervous and hormonal control in animals.

8.8 Know the location and functions of the cerebral hemispheres, hypothalamus, cerebellum and medulla oblongata in the human brain.

8.9 Understand how magnetic resonance imaging (MRI), functional magnetic resonance imaging (fMRI), positron emission tomography (PET) and computed tomography (CT) scans are used in medical diagnosis and the investigation of brain structure and function.
8.10 Understand what happens during the critical period so that mammals can develop their visual capacities to the full.
8.11 Understand the role animal models have played in the research into human brain development and function, including Hubel and Wiesel's experiments with monkeys and kittens.
8.12 Be able to discuss moral and ethical issues relating to the use of animals in medical research from two ethical standpoints.
8.13 Understand how animals, including humans, can learn by habituation.
8.14 Understand how imbalances in certain, naturally occurring brain chemicals can contribute to ill health, including dopamine in Parkinson's disease and serotonin in depression, and to the development of new drugs.
8.15 Understand the effects of drugs on synaptic transmissions, including the use of L-Dopa in the treatment of Parkinson's disease and the action of MDMA in Ecstasy.
8.16 Understand how the outcomes of genome sequencing projects are being used in the development of personalised medicine and the social, moral and ethical issues this raises.
8.17 Know how drugs can be produced using genetically modified organisms (plants, animals and microorganisms).
8.18 Understand the risks and benefits associated with the use of genetically modified organisms.
8.19 Understand the methods used to investigate the contributions of nature and nurture to brain development, including evidence from the abilities of newborn babies, animal experiments, studies of individuals with damaged brain areas, twin studies and cross-cultural studies.

- **The nervous system** of an organism consist of specialised cells called **neurons**, which have three main parts: **cell body, dendrites** and **axon**.
- A **cell body** consist of a nucleus and other cell organelles.
  **Dendrites (multiple)**: Receives signals from other neurons and send them to cell body.
  **Axon (single)**: Sends signal away from cell body to other neurons.




Structure of a typical neuron
Source : cnx.org

- Some axons are covered by a protective sheath called **myelin sheath** (made of lipids and proteins). This sheath helps in speeding up the conduction of nerve impulses. In PNS (peripheral nervous system) Schwann cells produce the myelin sheath.

On the basis of the **function** there are three types of neurons:

- **Motor Neurons**: They carry nerve impulses from CNS to the effector cells.
  They have short dendrites and a long axon.

- **Sensory Neurons**: They carry nerve impulses from receptor cell (eye) to the CNS.
  They have one long dendron and one short axon.

- **Relay Neurons**: These neurons are connection between sensory and motor neurons.

**Response of effector to stimulus**:

- **Effectors** are cells (eye, muscle, etc.) that produce response to a stimulus. Receptor cells on the effectors detect the stimulus.
- Sensory neurons carry electrical impulses which when reaches at its end releases chemicals called **neurotransmitters** that take information to the next neuron, which then sends electrical impulses to CNS that processes it and send to the effectors via motor neurons in the form of electrical impulses.
- **Example:** Response of eye to stimulus (dim and bright light).

**Dilation of pupil**

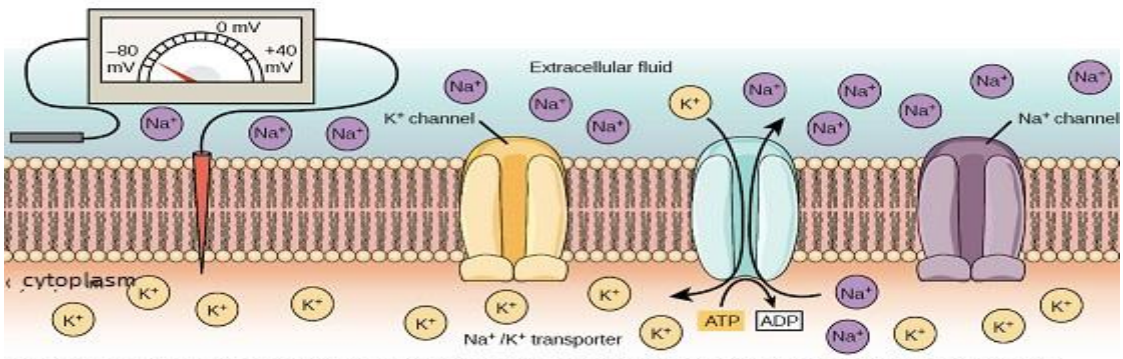
- In dim light, light receptors in eyes detect lack of light and send electrical impulses to CNS via sensory neurons.
- CNS processes the information and send response in the form of electrical impulses via motor neurons to the radial muscles in iris which contract to dilate the pupil.

**Constriction of pupil**

- In bright light, light receptors in eyes detect the bright light and send electrical impulses to CNS via sensory neurons.
- CNS processes the information and send response in the form of electrical impulses to the circular muscles in the iris, which contract to constrict the pupil.

**Nerve impulse conduction (action potential)**

- At **resting state** neural cell membrane are **polarised** due to difference of charge inside and outside of membrane.
- Neuron cell membrane has:
  **Sodium potassium ion exchange pump**: It allows movement of **three sodium** ions outside the membrane in exchange of **two potassium** ions (active transport).
  **Potassium ion channel**: It allows diffusion of potassium ions freely outside the membrane.
- This results in more positive charge outside the membrane as compared to inside.

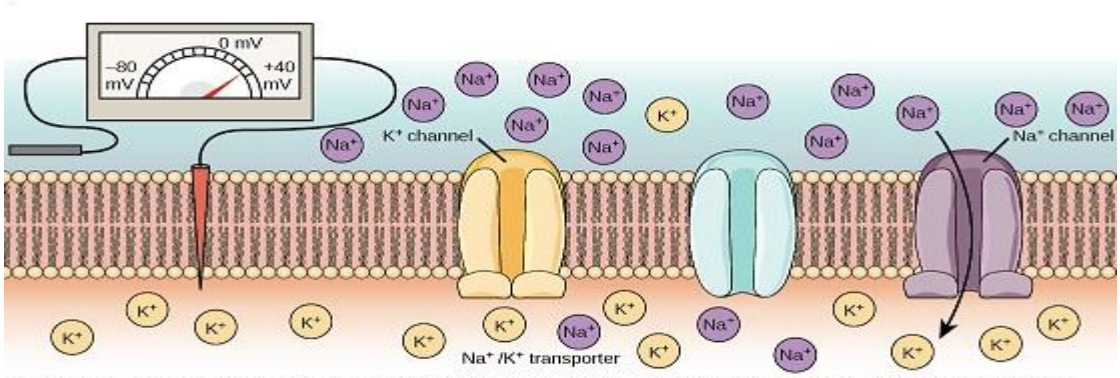



At the resting potential, all voltage-gated $Na^+$ channels and most voltage-gated $K^+$ channels are closed. The $Na^+/K^+$ transporter pumps $K^+$ ions into the cell and $Na^+$ ions out.

At resting state neuron is polarised
Source :- cnx.org

## Depolarisation of neural membrane on getting stimulus

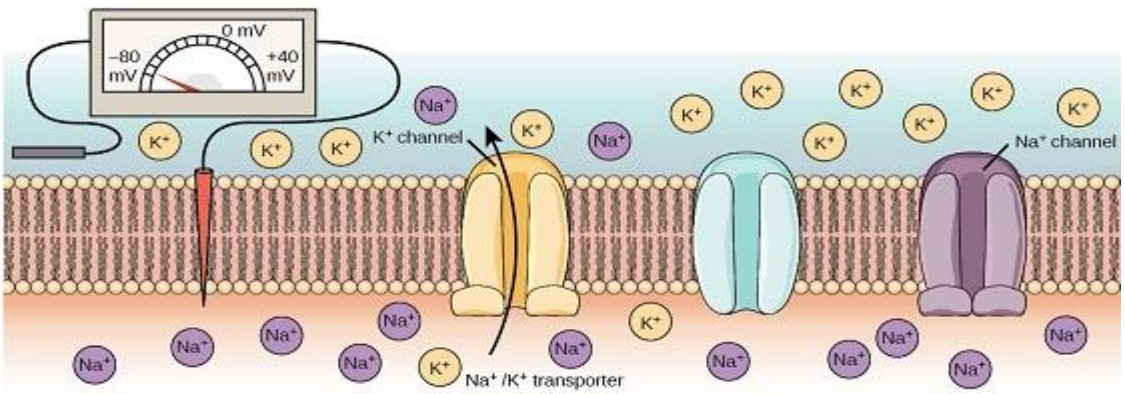
- **Action potential:** The sequence of events that occur when a neural membrane is stimulated and change in potential difference occur is called action potential.
- When neural membrane gets stimulated,other ion channel like sodium ion channels Opens and allow more and more sodium ions to diffuse into the membrane. This makes **inside less negative and change in potential difference occurs.** When this change reaches threshold, more sodium ions diffuse inside membrane.This is called **depolarisation.**




In response to a depolarization, some $Na^+$ channels open, allowing $Na^+$ ions to enter the cell. The membrane starts to depolarize (the charge across the membrane lessens). If the threshold of excitation is reached, all the $Na^+$ channels open.

Depolarisation of Neural membrane on getting stimulus
Source: cnx.org

- When potential difference reaches around +30 mV sodium ion channels closed and potassium ion channels open getting back the membrane to resting potential again. This is called **repolarisation.**
- The potential difference becomes more negative than the resting potential because potassium ions close slowly.This is called **hyperpolarisation.**
- At end the membrane again come to resting potential with the help of sodium ion pumps.




At the peak action potential, $Na^+$ channels close while $K^+$ channels open. $K^+$ leaves the cell, and the membrane eventually becomes hyperpolarized.

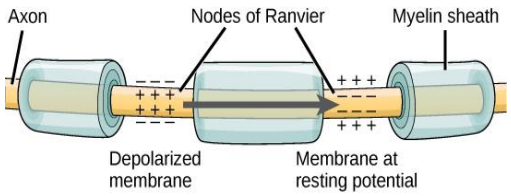
Hyperpolarisation of neural membrane
Source: cnx.org

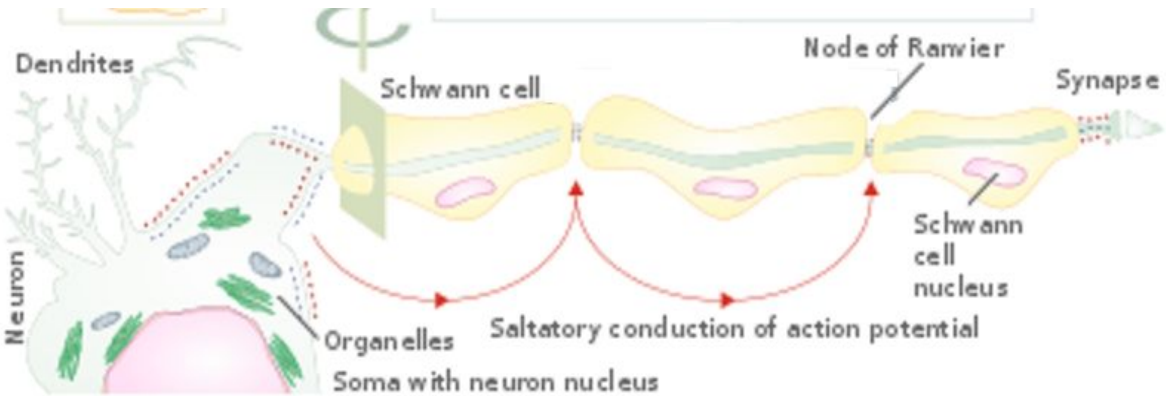
## Action potential move along the neuron

- During depolarisation of membrane the action potential move along the membrane as a **wave of depolarisation**.
- During depolarisation, some of the sodium ions diffused inside the membrane move sideways.This causes sodium ion channels of next region to open and create an action potential there. In this way, a wave of depolarisation moves from one region to the next.

## Action potential in myelinated neurons (saltatory conduction)

- In myelinated neurons, the impulse conduction is very fast.
- Myelinated neurons are covered by myelin sheath and the regions where sheath is absent is called node of Ranvier.
- Node of Ranvier are rich in sodium ion channels therefore depolarisation occurs at nodes only.
- In myelinated neurons impulse jumps from one node to next. This is called **saltatory conduction**.



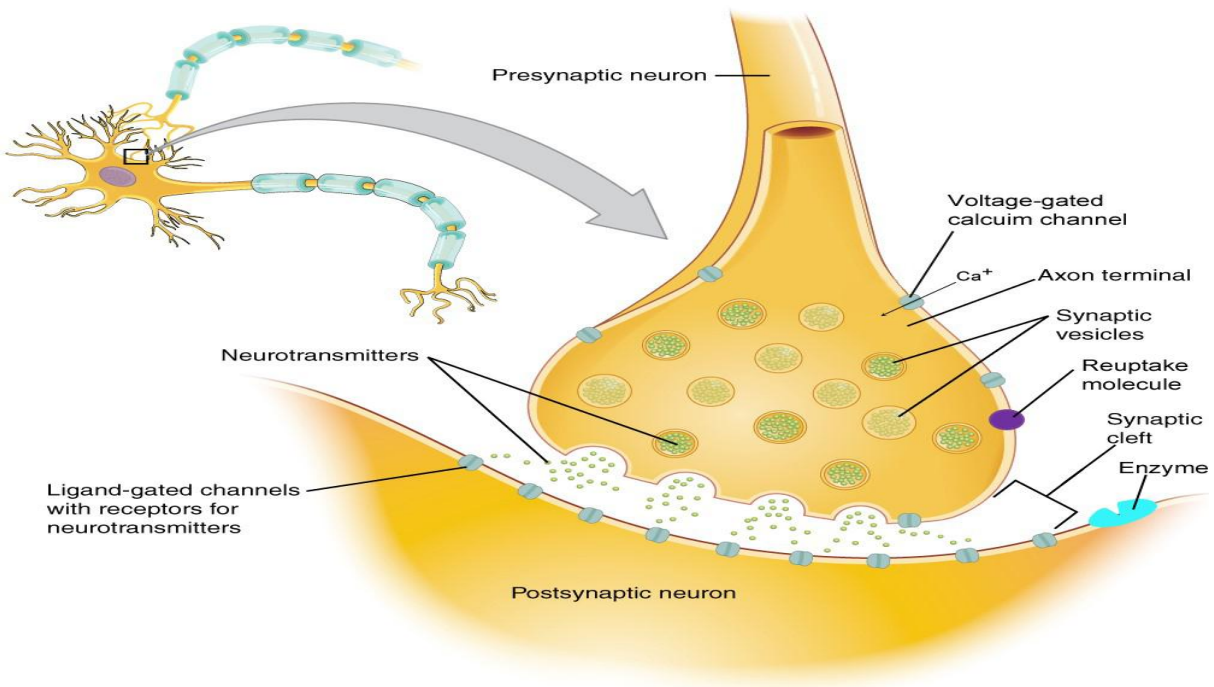

Saltatory conduction in myelinated neurons
Source: wikipedia, cnx.org

## Synapses

- Synapse is junction between the two or more neurons or between a neuron and the effector cell.
- Intercellular space at the synapse is called synaptic cleft.
- There is a swelling called synaptic knob in the presynaptic neurons which contains synaptic vesicles filled with neurotransmitters.
- When a stimulus reaches the end of neuron, neurotransmitter gets released in synaptic cleft where they bind to receptors on postsynaptic neurons and trigger action potential.
- **Function of synapse** is to disperse the information to different parts of body information **(synaptic convergence**) and to amplify the information **(synaptic convergence).**

## Action of neurotransmitter

- Action potential reaches synaptic knob and stimulates voltage gated calcium ions to open. Calcium ions diffuse into knob. This stimulates synaptic vesicles to fuse with presynaptic membrane and release neurotransmitter into synaptic cleft.
- Neurotransmitter binds to receptor on postsynaptic membrane and stimulates the opening of of sodium ion channels.The influx of sodium ions cause depolarisation and when the threshold is reached action potential is generated.




Structure of synapse and action of neurotransmitter
Source: cnx.org

**Role of photoreceptors in the eye**

- Photoreceptors are cells in the eye that detect light. They are located in the retina (fovea region) of the eye.
- Light sensitive pigments in the photoreceptors absorbs the light entering the brain via optic nerve and cause a chemical change that results in generation of nerve impulse along the bipolar neuron.
- Bipolar neuron carry the nerve impulse to the brain.
- **Types of photoreceptors:**
  **Rods** : Found in peripheral parts of retina and gives information in black and white.
  **Cones** : Found packed together in fovea and gives information in colour. Cones are red, green and blue sensitive.

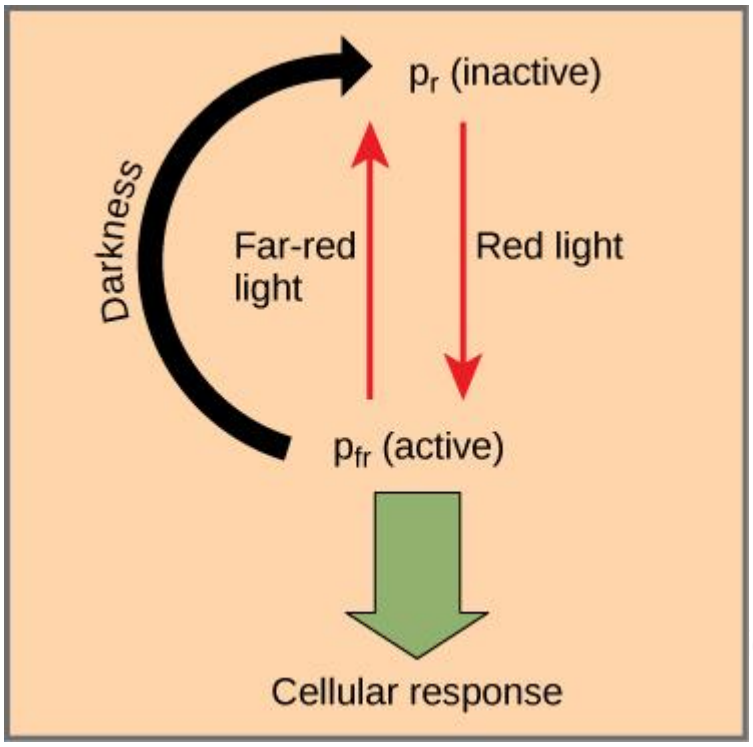
**Hyperpolarisation of rod cells:**

- Rhodopsin is a light sensitive pigment present in rods. It is made up of retinal and opsin.
- **In the dark,** rod cells are **not stimulated** because sodium ions are pumped out of the cell actively and also diffuse back in the cell through sodium channels. So inside of the cell is slightly negative leading to depolarisation of cell membrane and release of neurotransmitter, which inhibit bipolar neuron and no action potential reaches brain.

- **In the light,** rod cells are **stimulated** because rhodopsin break into retinal and opsin.This results in closure of sodium ion channels due to which sodium ions are actively transported out but not diffuse back.The cell membrane gets hyperpolarised and does not release neurotransmitters, no inhibition of bipolar neurons occur and action potential reaches the brain.

**Response of plants to external stimulus**

- Plants also produce response to the stimulus.
- In plants, there are some chemicals (growth factors) that speed up or slow down the growth e.g. auxin, cytokinin, gibberellin etc.
- **Auxins** helps in growth and cell elongation. E.g **IAA(Indole Acetic Acid).**
- IAA gets distributed unevenly in different parts of plant and leads to uneven growth of plant.
- **Phytochromes** are the photoreceptors by which plants **detect light**.
- Phytochromes exist in two states: **Pr** (absorbs red light at wavelength of **660 nm**)
  **Pfr** (absorbs far red light at wavelength of **730 nm**)
- Phytochromes are **interconvertible** when exposed to light.

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- Phytochrome controls response (flowering) by regulating transcription of genes.
- High level of Pfr (in summer) stimulate flowering in some plants by transcribing the genes involved in flowering.

## Coordination through nervous and hormonal control in animals

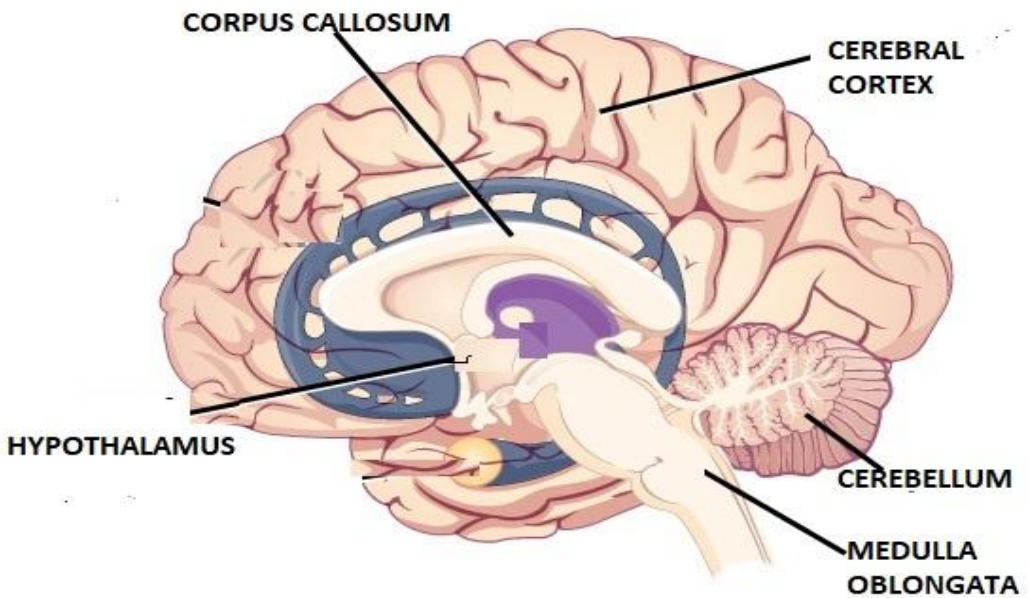
- **Hormones** are the chemicals that are secreted by the glands.They are secreted when a gland is stimulated by change in amount of specific substance or by electrical impulses generated by the nervous system.
- Examples of some hormones are **insulin** and **progesterone**.
- Hormones are secreted by the glands into the bloodstream.
- There are specific receptors on the target cells where a particular hormone binds and response is produced.
- **Example:** When the concentration of glucose is low in the blood, the pancreas releases the hormone glucagon in blood that bind to specific receptors on target cell (liver). Glucagon convert glycogen into glucose and release it into blood increasing the concentration of glucose.

## Structure and function of the brain

The brain has four important regions.

### Cerebrum

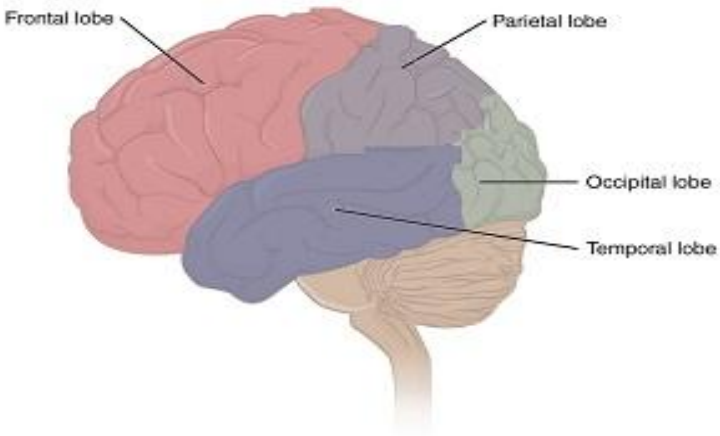
- **Largest** part of the brain and is divided into two halves known as **right and left hemispheres.**
- The outer layer of cerebrum called **cortex** is highly **folded.**




Structure of Brain

Source: cnx.org

Cerebrum has four areas:
**Frontal lobe:** Involved in thinking.
**Parietal lobe:** Involved in sensation of temperature
pain etc.
**Temporal lobe:** Process memory and hearing information.
**Occipital lobe:** Involved in vision.




Source: cnx.org

**Cerebellum**

- **Second largest** part of the brain, located at the back of the skull.
- Helps to control the equilibrium of body, coordination of muscular activities.

**Medulla oblongata**

- It is the **lowest part** and is interconnected with the help of the spinal cord.
- It helps in controlling heart rate, blood pressure.

**Hypothalamus**

- It is present just beneath the thalamus.
- It performs function like **temperature regulation** and **secretes neurohormones**, which control secretions of the pituitary gland.

**Scanners used to visualise the brain**

**CT scanner (Computed Tomography)**

- It is used to investigate the structure and function of brain and also to diagnose the diseased or damaged part of brain.
- X-rays are used by the scanner to form cross-section images of the structure.
- CT scanner can only be used to find the function of diseased structure, not the normal one.
- Example: If some blood vessels of the brain get damaged due to accident or stroke then a CT scanner will show a lighter colour in the scan due to different density of the blood as compared to normal tissues. As a result, the location of damaged blood vessels can be diagnosed and also the functions affected.

**MRI (Magnetic Resonance Imaging)**

- It is also used to investigate the structure and function of brain and also to diagnose the diseased or damaged part of brain but it gives better quality images and better resolution picture as compared to CT scan.
- Magnetic field and radiowaves are used by MRI scanners to form the cross-section image of the brain.
- Example: In the case of a brain tumour (an abnormal mass of cells), MRI scanners will show a lighter colour in the scan because brain tumour cells respond differently to the magnetic fields than healthy cells. The scanner shows the location and exact size of the tumour.

**fMRI (Functional Magnetic Resonance Imaging)**

- These scanners are used to investigate the detailed, high resolution structure of the brain like MRI scanners but they can also be used to show changes in brain activity as they happen.
- Example: If during fMRI, the patient is asked to move their right hand, then the areas of the brain involved in that function or activity get highlighted in red.
- fMRI scanners can also be used to diagnose the diseased areas of brain e.g.: If an epileptic patient undergoes a fMRI scan before and during a seizure, then the scanner can help to know which part of brain is not doing its function properly and needs treatment.

**PET (Positron Emission Tomography)**

- These scanners are used to investigate the structure and function (activity) of the brain like fMRI scanner, but it uses radioactive material in place of magnetic field.
- Radioactive tracer is introduced in the body and the scanner builds up a map in the body. e.g.: Glucose metabolism can be traced by using radioactively labelled glucose.
- PET can also be used to diagnose the diseased areas of the brain which changes brain activity. E.g.: In phenylketonuria, metabolism in certain areas of the brain is reduced.

**Role of critical period**

- Critical period is the period in early life of animals (including humans) when, for the proper development of visual cortex, exposure to visual stimuli is critical.
- Baby mammals have lots of neurons (synapses) in the visual cortex, which needs to be properly organised to process visual information.
- Synapses that do not receive the visual signal during the critical period are destroyed and the rest retained, developing visual cortex properly**.**
- **Example:** If a human baby has cataracts, then it is important to remove them in early life otherwise the visual cortex will not develop because it will not receive visual signals necessary for visual cortex development. This does not happen in the case of adults if they have cataracts because their visual cortex has already developed earlier in life. If cataracts are removed, they can see normally.

**Development of Visual Cortex**

- Cerebral cortex has an area named **visual cortex** (having lot of neurons), which receives and process the visual information.
- Visual cortex consists of right and left ocular dominance columns (group of neurons) that receive information from right and left eye respectively.

**Hubel and Wiesel experiments to study development of the visual cortex**

- They experimented first on very **young kittens**.
- They stitched shut one eye of each kitten and were kept like this for several months.
- On unstitching the eye, they found that the eye was blind because the ocular dominance columns for the stitched eye was not normal (smaller) as compared to the open eye.
- They repeated the same experiment with monkeys and found the same results.

**Results of experiments: They concluded that ocular dominance columns remain normal for both eyes if both eyes are stimulated early in life.**

**Moral and ethical issues regarding use of animals in medical research**

- **Arguments against the animals use in research**
  Everybody has a right to live peacefully and not to be disturbed so animals also have the right not to be experimented on because it also cause pain and discomfort.
  Drugs tested on animals can show different results in humans because both are different.

- **Arguments in favour of the animals use in research**
  Humans have a more complex brain so some think that humans have more right to live compared to animals. Animals must be looked after properly during or after Experiments, they must be given painkillers to reduce pain.
  Animals have much similarity with humans so drugs can be tested on them. Also the previous results of drug testing on animals are very good.

**Habituation: Learning Behaviour**

- All the animals including human beings respond to the external stimuli for their survival. But it is not important to respond to every stimuli because some stimuli are unimportant and it wastes energy to respond to them all.
- Animals learn to ignore **unimportant stimuli** if they are repeated over time.This reduced response to unimportant stimuli which has no effect on us is called **habituation**.
- **Example:** Prairie dogs warn others of predators by using their alarm calls but they don't use alarm calls when they see humans because they get habituated that humans are not harmful.

**Disorders due to imbalance of neurotransmitters**

**Parkinson's disease**

- It is a **brain disorder** caused by a **lack of neurotransmitter dopamine**, which is produced by neurons that control movement.
- Less dopamine is available for binding to receptors on postsynaptic membrane. As a result, few sodium ion channels open and fewer action potential produced.
- This leads to **symptoms** like **slow movement** and **shaking fingers or limbs.**
- **Drugs** like **L-dopa** are used for treatment.

**Depression**

- **Depression** is also a **brain disorder** due to low level of neurotransmitter serotonin, which is produced by neurons that control mood.
- Symptoms of depression includes loss of appetite, confidence, less social involvement and not enjoying things.
- Drugs used to treat depression are known as selective serotonin reuptake inhibitors(SSRIs).

**Effect of drugs on synaptic transmission**

**L-dopa**

- Symptoms of Parkinson's disease are treated by **L-dopa**. It is a structural analog of dopamine.
- When this drug is given, it gets converted to dopamine by **enzyme dopa-carboxylase** in the brain.
- This means that a high level of dopamine is available to bind the receptors, which results in more action potential across synapses and give patients more controlled movements.

**MDMA**

- **MDMA** is used to treat the symptoms of depression.
- It increases the level of serotonin in brain by inhibiting the reuptake of serotonin by presynaptic neurons as it blocks the reuptake proteins.
- This means serotonin level remain high in synapse, which results in more action potential across synapses that control mood.

**Human genome project**

- HGP was started in 1990 and completed in 2003. It has identified all genes of the human genome and stored all information in databases that can be used to identify genes which are involved in disease.
- Common genetic variations are also known by this project that helped in developing drugs that suit people according to particular variations in them. These drugs are called **personalised medicines**.
- Doctors can also use genetic information to personalise patient treatment but it raises some social, ethical and moral issues.
- Drugs will be **more expensive** if they are developed for specific variation.
- These drugs may be less effective for some people due to different variations. So they will refuse it.

**Use of genetically modified organisms (GMOs) for producing drugs**

- GMOs are those organisms whose DNA is modified to produce the desired protein, which can be used as a drug.
- **Genetically modified microorganisms** are engineered by insertion of plasmid containing desired the gene. Modified microorganisms are then grown in large containers to produce desired protein in large amounts, which can be purified and used as drug.E.g. **Human insulin**.
- **Genetically modified plants** are engineered by insertion of desired gene into their DNA via bacteria that infects them. Modified plant cell produces desired protein that can be purified and used as drug. E.g. **Cholera vaccine.**
- **Genetically modified animals** are engineered by insertion of fertilised egg containing desired gene (inserted in nucleus). Modified animal produces protein, which is purified from milk of animal and can be used as drug. E.g. **Human antithrombin.**

**Benefits of GMOs**

- **Modified crops** are more nutritious and high yield.
- Large amount of enzymes for industrial purpose can be produced.This reduces cost.
- Modified plant vaccines can be available everywhere (refrigeration not required).
- Many disorders can be treated by genetically engineered proteins.
- Drugs developed from modified animals and plants are cheap and affordable to large numbers of people.

**Risks of GMOs**

- Some people think it is not right to modify animals and they are also worried of long term impacts of GMOs.

**Role of nature and nurture in brain development**

Development of brain occur differently due to two things: Nature (genes) and nurture (environment). Following are the methods to study the effect of nature and nurture on brain development.

**Animal experiments**

- Scientists experimented on genetically similar and genetically dissimilar animals with different environmental conditions to study the development of the brain.
- **Case -1** They experimented on genetically similar rats providing them different environmental conditions (nurture) to find the effect of nurture on brain development.
- Scientist found that rats raised in **stimulating environment** develop large brain size and better scores on problem solving skills as compared to rats raised in boring environments.
- **Conclusion:** Nurture affects brain development.

- **Case -2** Scientists experimented on genetically dissimilar mice. One mouse is genetically engineered, lacking a specific gene (Lgl1 gene), and another mouse normal.
- Engineered mice develop enlarged fluid-filled brain and other mice have normal brain development.
- **Conclusion:** Nature (gene) also affects the development of the brain.

**Twin studies**

- To study the effect of nature or nurture on development of the brain, scientist did following the experiments:
- **Case -1** Identical twins are genetically similar, they are raised in different environments and found that similarities between them are due to nature (genes) and dissimilarities are due to different environment (nurture).
- Example: **Nature** plays an important role in stuttering of identical twins even if they are raised in different environments.
- **Case -2** Identical twins are raised with non identical twins in a similar environment. Any difference in brain development will be only due to nurture.
- Example: **Nurture** plays an important role in similarity in reading ability of identical twins and non-identical twins.

**Cross-cultural studies**

- Scientists studied the brain development of large groups of children of the same age brought up in different cultures.They found that there are large differences in brain development and they are as a result of nurture not nature and any similarity between them is due to nature.

**Newborn studies**

- Scientists study the brain development of newborn babies whose brain is not affected by the environment. They found that what they are born with is due to nature not nurture.
- Example: New born babies have many abilities like they can cry and can feed. These abilities are a result of nature not nurture. On the other hand, they also lack lots of abilities like speech, they will learn it later. Gaining of a speaking ability is the result of nurture not nature.

**Brain damage studies**

- Scientists study the brain development of chosen function in a child **with and without brain damage** because the child's brain is still developing.
- They found that brain development is result of **nurture** if the brain damaged child still develops the chosen characteristic, but it is result of nature if the brain damaged child doesn't develop the chosen characteristic.