MOLECULAR PHYSIOLOGY

Nervous System

M. N. Subash
Professor of Neurochemistry and HOD
Neurochemistry Department
NIMHANS
Bangalore

6-Mar-2006 (Revised 3-Aug-2006)

CONTENTS

Keywords

Central nervous system; Nerve cells; Nerve fibers; Nerve impulse; Neurotransmission; Synapse; Neurotransmitters; Action potential; Reflex action; Reflex arc.

Introduction

The nervous system is composed of all nerve tissues in the body. The functions of nerve tissues are to receive stimuli, transmit stimuli to nervous centres, and to initiate response. The central nervous system consists of the brain and spinal cord and serves as the collection point of nerve impulses. The peripheral nervous system includes all nerves not in the brain or spinal cord and connects all parts of the body to the central nervous system. The peripheral (sensory) nervous system receives stimuli, the central nervous system interprets them, and then the peripheral (motor) nervous system initiates responses. The somatic nervous system controls functions that are under conscious voluntary control such as skeletal muscles and sensory neurons of the skin.

The autonomic nervous system, mostly motor nerves, controls functions of involuntary smooth muscles, cardiac muscles, and glands. The autonomic nervous system provides almost every organ with a double set of nerves - the sympathetic and parasympathetic. These systems generally but not always work in opposition to each other.

The sympathetic system activates and prepares the body for vigorous muscular activity, stress, and emergencies. While the parasympathetic system lowers activity, operates during normal situations, permits digestion, and conservation of energy. The two systems generally act in opposition to each other. For example, stimulation by the sympathetic system on the heart would increase contractions, while stimulation by the parasympathetic system would decrease heart contractions. Where dual control of an organ exists, both systems operate simultaneously although one may be operating at a higher level of activity than the other.

Organization of the central nervous system

The CNS consists of the brain and the spinal cord. The brain is an extremely complex organ that can be said to give us appreciation of sensory input; serves as the originator and coordinator of motor activity, and acts as the repository for experience, intelligence, moral and social behaviour.

The largest portion of the fore brain is the cerebrum, accounting for more than four fifths of the total brain weight. The cerebellum is the next largest part, and the brain stem, consisting of the pons, medulla and mid brain is the smallest. The diencephalon is more or less a separate functional region that is usually described with the cerebrum. Hind brain constitutes pons and medulla, latter extend to spinal cord. Part of the Central Nervous System (CNS) containing large population of nerve cells is gray matter, while the rest of the portion containing axonal and dendrite arborization is called white matter. It appears white due to presence of myelin.

The Cerebrum

The cerebrum is in the form of two halves (left and right), or hemispheres, each of which bears many folds, or convolutions. Up folds are termed Gyri, and shallow down folds are called Sulci. Deep infoldings, called fissures are found in several areas of each hemisphere and subdivide the hemisphere into lobes. The outer surface of the cerebrum is covered with a 2.5 to 4.0 mm thick layer of neurons containing grey matter, termed the cerebral cortex. The rest of the hemisphere consists of myelinated fibre tracts, the white matter or medullary body.

The cortex, which contains the greatest number of neurons, acts as the region giving appreciation of sensations, serves as the source of motor activity, and contains areas responsible for moral and social values.

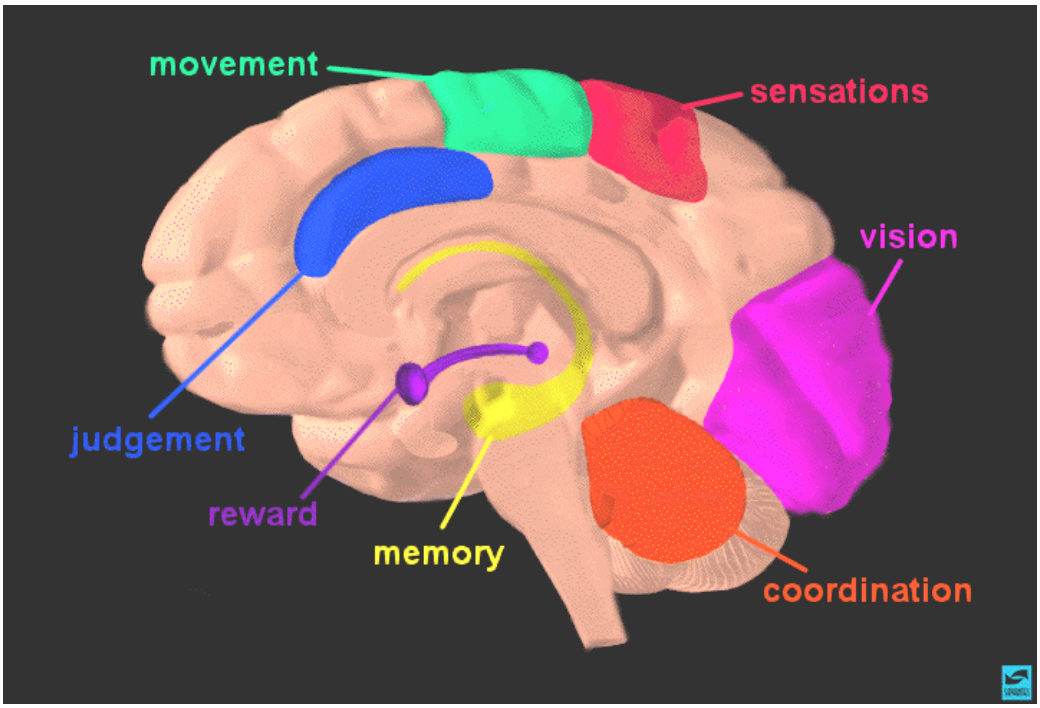

Fig.1: Human brain

The Basal ganglia

This includes the caudate nucleus, the putamen, the globus pallidus, the claustrum, the subthalamic nucleus, and the substantia nigra. The major connections that the ganglia make are with cerebral cortex and thalamus. An internal circuit is formed from cerebrum to ganglia to thalamus and back to cerebral motor areas. The ganglia are thus postulated to influence the motor cortex. In general, it would seem that the ganglia are concerned with suppression of certain types of motor function that would destroy the purposeful nature of motor activity.

Thalamus

The paired thalami constitute about 80% of the diencephalons and the two thalami are connected across the midline by an intermediate mass. The thalamus consists of groupings of neurons called nuclei and appears to function mainly as a relay station to the cerebrum for all varieties of sensory input except olfaction. It may also give crude awareness of pain.

The Hypothalamus

It weighs about 4 g and is considered to be composed of a variety of nuclei organized into three major areas:

- The Supraoptic area above the optic chiasm.
- The Tuberal area above the pituitary gland.
- The Mammillary area above the mammillary body.

All parts of the hypothalamus appear to be connected to one another. Output passes via nerves or chemicals to the pituitary gland, by nerves to the limbic system and midbrain, and from there to body's viscera. The major functions of the hypothalamus are concerned with regulation of those homeostatic functions related to organism survival.

The Brain stem

The superior colliculi receive impulses from the occipital (visual) cortex of the cerebrum for reflex movements of the eyes, such as objects that are moving across the visual field. The inferior colliculi are part of the auditory pathway to the cerebrum. Some fibres pass to the superior colliculus, producing eye movements in response to sound, such as when turning the eyes toward the source of a sound. The cell bodies giving rise to the third (Oculomotor) and fourth (Trochlear) cranial nerves lie in the midbrain. Lesions in the midbrain typically affect auditory and visual reflexes and, if the peduncles are involved, produce deficits in voluntary movement.

The Midbrain

The Midbrain is the uppermost (1.5 cm or so) of the brainstem. Its anterior portion consists mainly of two large bundles of s called the cerebral peduncles. The peduncles carry motor projection fibres from the cerebrum to the spinal cord and to the cerebellum. Just posterior to the peduncles lies the substantia nigra, mentioned previously in connection with the basal ganglia. The posterior portions of the midbrain contain the red nucleus, a group of neuron cell bodies that give rise to a motor pathway (Rubro spinal tract) conveying impulses concerned with muscle tone to the skeletal muscles, and the colliculi.

The Pons

The pons is about 2.5 cm in length and is easily recognized by a large mass of s forming a conspicuous bulge in its anterior aspect. The bulge is termed the basal pons and consists of s descending to the spinal cord (Cortico spinal s) and fibers passing from its synapses in the pons to the cerebellum (Ponto cerebellar s).

The latter pathway notifies the cerebellum of what the cerebrum intends during voluntary activity and is a part of a system that the cerebellum employs to coordinate and refine muscular activity. The posterior portion of the pons, called the tegmentum, contains large bundles of sensory fibers ascending to the thalamus and the nuclei of cranial nerves 5 (Trigeminal), 6 (Abducent), 7 (Facial), and 8 (Vestibulo cochlear). A respiratory centre known as the pneumotaxic centre lies within the pons. It is a part of the control mechanism that permits outflow of air (Expiration) from the lungs.

The Medulla Oblongata

It is the inferior (3 cm or so) of the brain stem. It is continuous through the foramen magnum of the skull with the spinal cord. Prominent in the anterior portion of the pons are the cortico spinal fibres that mostly cross over in the medulla and continue down the cord as the cortico spinal tracts involved in voluntary movement. Several obvious nuclei (gracile, cuneate) are present in the posterior part of the medulla. They are areas for synapses of ascending

pathways carrying sensory information. The nuclei of cranial nerves 9 (Glosso pharyngeal), 10 (Vagus), 11 (Accessory) and 12 (Hypoglossal) lie in the medulla. The cerebellum lies on the posterior aspect of the brain stem, attached to it by three pairs of cerebellar peduncles that contain both afferent and efferent nerve fibres. A centrally placed vermis supports the two laterally placed cerebellar hemispheres. Small folds abound in all parts of the cerebellum are known as folia. These folia let the convolutions of the cerebellum provide a vastly increased surface area for placement of neurons. An outer covering of grey matter, the cerebellar cortex, overlies the medullary body of white matter. Deep nuclei lie more or less centrally within the organ.

The Cerebellum

The Cerebellum is composed of three portions:

- The vestibule cerebellum is the phylogenetically oldest part of the organ and anatomically corresponds to the flocculus and nodule. This portion is present in all vertebrates. As the name vestibulo suggests, this portion of the cerebellum has afferent and efferent connections mainly with the vestibular apparatus of the inner ear (semicircular canals and maculae). The information conveyed is related to changes in head position, acceleration, deceleration and angular movements. Recently, fibres from the retina and from the parts of the brain concerned with eye movements have been shown to terminate in the vestibule cerebellum.
- The spino cerebellum corresponds anatomically to the vermis and receives general Sensory (touch, pressure, thermal) and proprioceptive impulses chiefly from the ascending pathways of the spinal cord. These types of impulses give information concerning the rate, force, and direction of movements as detected by skin, muscle, and tendon receptors. This aspect of movement is sometimes called performance.
- The pontocerebellum corresponds anatomically to most of the anterior and posterior lobes of the organ and is the largest part of the cerebellum in animals capable of skilled or complex types of movement. The major input to this part of the cerebellum is via pontocerebellar fibres originating from nuclei in the pons that, in turn, have received impulses from the motor regions of the cerebral cortex. This part of the system conveys cortical intent.

Cerebral hemisphere

Each cerebral hemisphere is divided into following four lobes by three fissures.

Frontal lobes

Lying in the pre-central gyrus is area 4, designated as the primary motor area. It is an area conferring voluntary control over movement in humans. It is somatotopically oriented; that is, different cortical regions project ultimately to specific muscles in a particular body area. It may be noted that the body is represented in an upside down fashion, and that the areas where complex movements are required (ex. hands and face) have larger areas of representation; hence the disproportionality of the body as represented by the Homunculus. Supplementary motor area occupies areas 24 and 31 on the medial aspect of each hemisphere. Body representation is more crude here, stimulation bringing contraction of larger groups of muscles.

The axons from cells in these motor areas constitute 40 to 45% of the fibres giving voluntary control over muscular activity. Efferent fibres control muscles primarily on the opposite side of the body, since they cross in the brain stem. Area 6 is designated as the pre-motor area and provides input to area 4. Stimulation in area 6 causes contraction of muscles only if area 4 is intact. It is particularly concerned with movements of the head, neck, and trunk. Some degree of learned motor activity may lie in area 6, because lesions here interfere with performance even though no voluntary paralysis results. Area 8 is called the frontal eye field, and if stimulated, it causes eye movements of a scanning nature. The motor areas described form a part of what is called electrically excitable cortex, because stimulation results in obvious movement. The remaining portion of the frontal lobes gives no obvious movement or sensation if stimulated.

The areas, 9 through 12, are designated as the frontal association areas. In animals, damage in these areas causes hyperactivity and excessive emotional display, suggesting an inhibitory function of the region. In humans, there is great diversity in symptoms displayed as a result of lesions in areas 9 through 12. Changes are most often seen in personality, emotional reactions, and ability to accept life's responsibilities, moral and social.

The Parietal lobes

The somesthetic or general sensory areas include areas 3, 1, and 2 located in the post central gyrus. The area contains some motor function and this is evidenced by the fact that stimulation gives generalized and non-skilled movements. The area represents the termination of those pathways dealing with general sensation, the sensation of touch, pressure, pain, heat, cold and joint and limb position. As in area 4, there is a somatotopic representation, with the body upside down and areas of greater density of receptors receiving larger representation. The areas provide localization of a stimulus but do not apparently discern much about the quality of the stimulus. Areas 5 and 7 are termed the parietal association areas and do provide information concerning stimulus quality. Connections between areas 5 and 7 and the visual and auditory portions of the brain also exist.

The Occipital lobes (visual area)

Area 17 occupies a large part of the occipital lobe, especially along the borders of the calcarine fissure. Input to the area is provided by fibres ultimately originating in the retina. Both eyes are represented in both lobes, with central vision posteriorly and peripheral vision anteriorly. Anterior to area 17, on the lateral side of a hemisphere and above and below it medially, are areas 18 and 19, called the visual association areas. Relating past to present visual experience, binocular vision, and depth perception are some of the vision related functions handled by these areas.

The Temporal lobes

The auditory area includes regions 41 and 42. The cochleas of both ears are represented in one temporal lobe. Areas 22 and 21 are in general, association areas and are probably the major regions of memory storage.

Other functional areas

The taste area corresponds to Brodmann's area 43. The area is located in association with the general sensory cortex serving the tongue and pharynx. A vestibular area (anterior 40, lower 3, 1, and 2) has been placed in the temporal lobe anterior to the auditory area. Most of the fibres of the vestibular system project to the cerebellum.

There is evidence to support the contention that all functions are not equally represented in both hemispheres. The speech area is being a left sided region. This creates what is called a left cerebral dominance for language function. The right hemisphere appears to be superior in non-language functions such as spatial perceptions and creative functions associated with art and music.

The Medullary body

The term medullary body refers to all of the myelinated fibres (white matter) of the cerebrum. The basal ganglia are large masses of grey matter buried within the medullary body.
Three types of fibres compose the medullary body.

Commissural fibres
These fibres form the only means of connecting the two cerebral hemispheres to permit transfer of information between them. The corpus callosum is the major bundle of commissural fibres, estimated to contain 300 million fibres. The anterior, posterior, and habenular commissures are much smaller bundles.

Projection fibres
These are bundles of fibres that enter the cerebrum from outside or originate within the cerebrum and leave it. Examples are the incoming auditory and visual projection fibres and the outgoing motor pathways to skeletal muscle.

Association fibres
These fibres connect different parts of the same hemisphere. These types of fibres enable one type of information to affect an entirely different part of the cerebrum such as in motor responses to visual or thermal stimuli.

Functions

Following the designation of cortical areas as devised by Brodmann, particular types of functions can be located in each hemisphere. Much evidence about function is provided by direct brain stimulation during surgical procedures or by associating symptoms of pathology with lesions of the brain. Brains, like faces, contain basic regions but also like faces, they are not identical to one another.

Functions of the Cerebellum

In general terms, the function of the cerebellum is: to compare intent and performance with regard to muscular activity and movement; to ensure that the movement is accurate and coordinated and moves with appropriate force and direction. It operates entirely at a subconscious level.

Error control

By comparing intent and performance, the cerebellum ensures that a movement goes where it is supposed to go, at a proper rate and with a force appropriate to the resistance being overcome. Such an action usually involves initial strong contraction of one set of muscles and subsequent contraction of antagonist muscles to control the movement. The purkinje cells exert a waxing and waning inhibitory effect on the deep nuclei that have been excited by cerebral cortical and peripheral information and in this manner, they refine and control the movement.

Damping

Most body movements are pendular in nature, with a movement in one direction opposed by a force applied in the opposite direction. There is thus a tendency for a back and forth motion to occur, called tremor. The cerebellum cancels or damps this tendency, for smooth movements.

Prediction

By comparing information received from eyes, body parts and cerebrum, the cerebellum calculates when a motion should be slowed and ultimately stopped.

Cerebellar cortex cells

The cerebellar cortex contains the cells and circuitry that enables the organ to carry out its functions, and the structure is the same in all parts of the organ. The inner or deepest layer of the cortex, called the granule layer, consists of many closely packed granule cells and cells called Golgi cells. The middle layer of the cortex consists of a single row of large purkinje cells associated with basket cells. The purkinje dendrites ramify in the outer molecular layer and are associated with stellate cells. Input to these cells is provided by mossy and climbing fibres. Mossy fibres synapse with Golgi or granule cells (and also send branches to the deep nuclei), while climbing fibres reach all five basic cell types (granule, golgi, purkinje, basket, and stellate) and the deep nuclei. This input is all excitatory. The deep nuclei receive impulses from the mossy and climbing fibres and from the purkinje cells. The deep nuclei generate the output of the cerebellum to all aspects of motor activity and the impulses are apparently all excitatory to the cells affected. The purkinje cells, on the other hand, are invariably inhibitory to the nuclei they affect.

The net effect of this circuitry is summarized as:

- All nuclear output is excitatory.
- Cortical input to the nuclei is inhibitory.
- All input to the cortex is excitatory.

Cells of the nervous system

The functional and structural units of the nervous system are its neurons. They arise from ectodermally derived cells - neuroblasts. Spongioblast cells, also derived from ectoderm, give rise to glial cells that have supportive and nutritive functions. One variety of glial cells is of mesodermal origin.

Neurons

Neurons have a variety of shapes and sizes in different parts of the nervous system. They may be generally divided by function into - motor, sensory, and internunical neurons.

For understanding the basic structure of neurons in general, a multipolar motor and a unipolar sensory neuron will be described. A cell body is surrounded by a typical plasma membrane. The membrane encloses the neuroplasma or perikaryon, the cytoplasm of the cell. The neuroplasm contains the usual cellular organelles (Golgi bodies, mitochondria, ER, etc.) but appears, several years after birth, to lose or develop a non-functioning cell centre. This implies that, after a period of time, the cells lose their capacity to divide mitotically and replace lost cells. The neuroplasm has its ER in the form of irregular masses of ribosome-studded vesicles called Nissl bodies. Hollow microtubules called neurotubules run through the cytoplasm and into the processes of the neuron, probably helping to maintain the form of the process. The nucleus of the cell is surrounded by a membrane that encloses the karyoplasm of the nucleus. Chromatin and large nucleoli reside in the nuclear fluid.

The cell body gives rise to one or more elongated processes. In a multipolar type of neuron, there are clearly two morphologically distinct types of processes:

1. Multiple, highly branched, short, irregular diameter, afferent (towards cell body) conducting processes are known as dendrites.
2. The axon is a long sparsely branched, regular diameter, efferent (away from cell body) conducting process that commonly bears one or more sheaths - a lamellated interrupted fatty covering called the myelin sheath.

The breaks in the sheath are nodes of Ranvier, and the segments between nodes are designated as Internodes. Each internode appears to be the product of a glial cell (oligodendrocyte) in the central nervous system.

Basic neuronal properties

Neuronal membranes have a membrane potential value to which the membrane must be depolarized to initiate an action potential. A stimulus, to be effective, must posses certain strength. The term threshold applies to both quantities. Thresholds of neuronal membranes vary according to the chemical and physical environment of the neuron and thus are not always constant. Once initiated, an action potential is conducted in decrement less fashion along a normal nerve fibre. That is, there is no decrease in strength of the impulse. Since propagation of the impulse is caused by biological processes, it should not lose strength unless something interferes with those processes.

If a stimulus can cause depolarization of the neuron's membrane, the response is all or none. It is like pulling the trigger of a gun. The gun will fire if the pull is strong enough; if not, nothing happens. The nerve fibres possess a refractory period, the time during which it is in the depolarized state. The length of the refractory period is about 1 m sec. The fibre is ready to conduct another impulse very quickly. Many nerve fibres show accommodation, evidenced by a rise in the threshold of the fibre. The fiber becomes hyperpolarized when a threshold voltage is applied to it, the more slowly the stimulus depolarizes the fibre, the greater the strength of the stimulus required to initiate an action potential. This phenomenon may enable the fibre to ignore stimuli that persist once the CNS has been notified of the presence of the stimulus.

Under proper circumstances, two or more stimuli that are only sub-threshold can add together to initiate an action potential. This is called summation. Temporal summation occurs when two stimuli are applied in close succession to a single fibre. There is a local partial depolarization from one stimulus that is furthered by the second stimulus. Spatial summation occurs when two sub-hreshold stimuli are applied simultaneously but at different points on a neuron. They combine to cause depolarization and development of an action potential.

Basic neuron description

A neuron, also known as a nerve cell, is the information processing and transmission device of the nervous system. They come in a variety of shapes, sizes, and types. In the human body, certain neurons reach up to three feet long. While differences exist between particular neurons given their specialization, most neurons are comprised of four primary structures: the soma, dendrite, axon and terminal buttons.

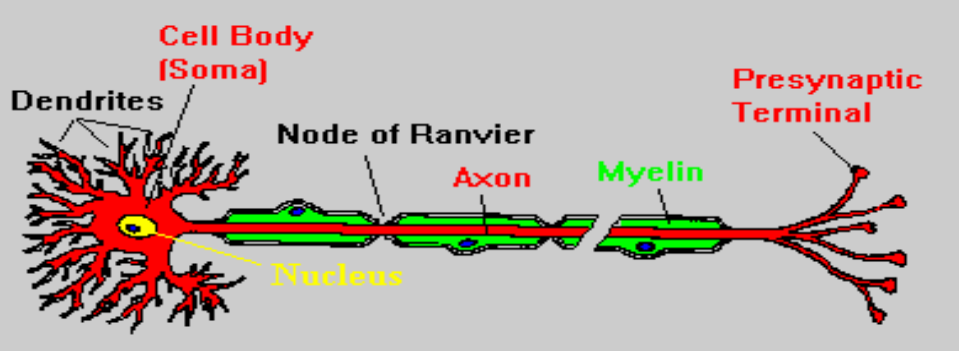

Fig. 2: Neuron

Soma: The soma is the cell body of the neuron. It houses the nucleus and the majority of cell components which sustain the life processes of the cell. The shape of the cell body varies greatly between the different types of neurons.

Dendrites: The dendrites branch out from the soma resembling branches of a tree (dendron is a Greek word for tree). With the exception of sensory neurons, the dendrites are the mechanism through which a neuron receives communication, incoming information, from other neurons. Sensory neurons transmit information where the incoming signal is generated by specialized receptors in the skin. Messages between two neurons are transmitted across the *synapse*, a junction between the receiving dendrites of one neuron and the information sending *terminal buttons* of another. Communication between neurons is a one-way affair. Signals are sent out by one neuron through the terminal buttons and received by the cell membranes of the receiving neuron.

Axon: The axon is a long, slender cytoplasmic extension that carries information away from the soma to the terminal buttons. Axons are usually covered by a myelinated sheath. The axon carries a basic message called an *action potential*. The action potential is a brief electrical/chemical event which starts at the end of the axon near the soma and travels downward to the terminal buttons. The action potential is consistent. It remains the same in size and duration even through axonal branches. Each branch of an axon receives a full charge.

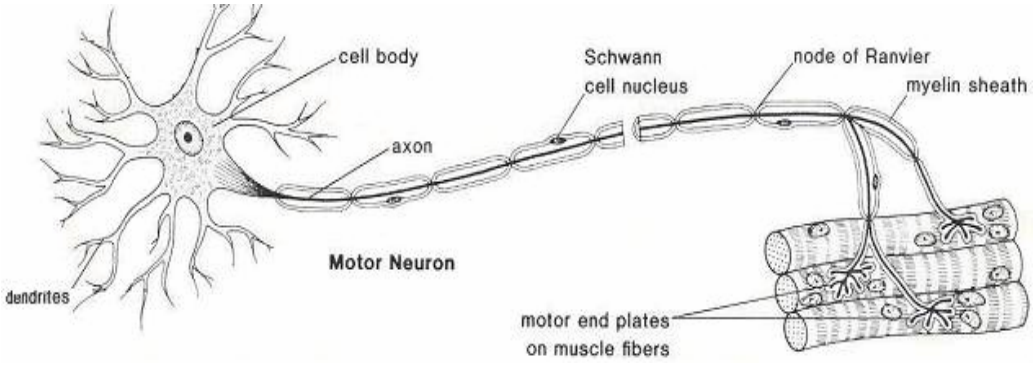

Fig. 3: Motor neuron

As with the dendrites, axons come in different shapes. Furthermore, the three principal types of neurons are classified by the manner in which their axons and dendrites leave the soma. The most common type of neuron is the *multipolar* neuron which has one axon and many branches of dendrites. *Bipolar neurons* are depicted by having one axon and one dendritic tree, each located at opposite ends of the cell body. Bipolar neurons are typically sensory. They have a dendrite which receives information from a receptor which gets sent onto the central nervous system informing it of external events. *Unipolar neurons*, as found in the somatosensory system, consists of one stalk containing terminal buttons at one end and a dendritic tree at the other.

Terminal buttons: Most axons divide and split many times. At the ends of the branches, there are small knobs which are called *terminal buttons*. The terminal buttons secrete *neurotransmitters* which affects the receiving cell. Neurotransmitters can be either excitatory or inhibitory. The nature of the neurotransmitter determines whether the receiving cell will send a message down its axon and communicate with the one, connected to its terminal buttons. A single neuron can receive information from hundreds of other neurons thus creating an intricate neural network. Additionally, the terminal buttons of a neuron can form synapses at the dendrites and/or cell body membranes of adjacent neurons.

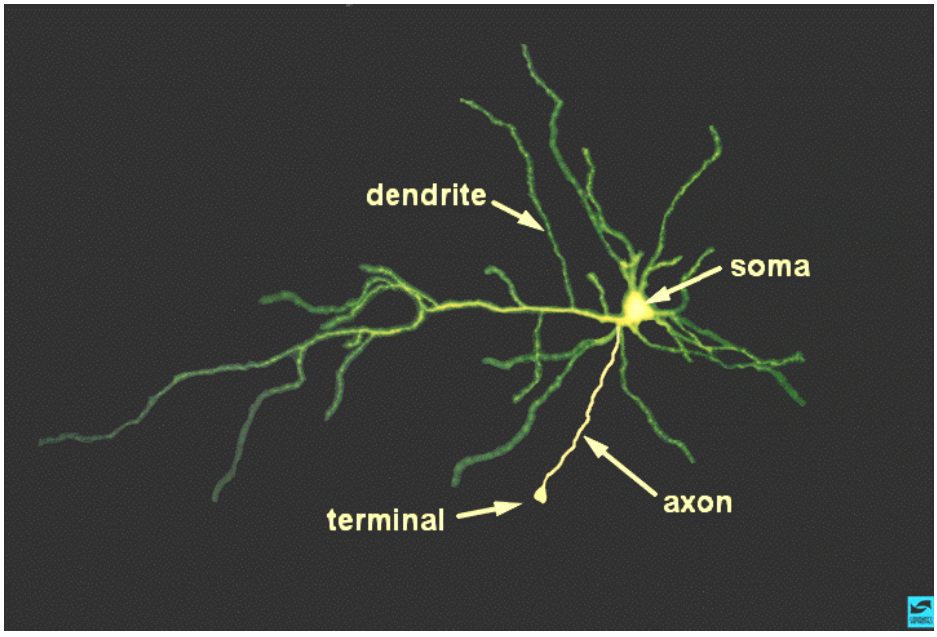

Fig. 4: Neuron

Internal structure: The boundary of the nerve cell is defined by the cell membrane. Within the membrane are protein molecules which serve special functions for the cell. Some of the proteins detect substances outside the cell, such as the presence of hormones, and pass the information onto the interior of the cell. Other proteins serve as the cell's gatekeeper, allowing some substances to pass into the cell while barring others. Some proteins functions as transporters carrying certain molecules into and out of the cell.

At the centre of the neuron is the *nucleus*, which is round or oval and covered by a nuclear membrane. Inside are the *nucleolus* and *chromosomes*. The nucleolus manufactures small structures that are involved with protein synthesis, called *ribosome.* Genetic information is contained on long strands of *deoxyribonucleic acid* (DNA), which make up the chromosomes. When portions of the chromosomes (genes) are active, they cause the production of messenger *ribonucleic acid* (mRNA). Messenger RNA exits the nuclear membrane and attaches itself to ribosomes where the production of a specific protein takes place. Proteins provide structure and serve as *enzymes,* directing the chemical processes of a cell by controlling chemical reactions *Cytoplasm* makes up the bulk of the cell. It is a jellylike, semi-liquid substance that fills the space within the membrane. Cytoplasm streams and flows, it is not static. Small, specialized structures essential for the cell are contained within it to perform its duties. The small structures include the following:

Mitochondria: This structure takes food and breaks it down into energy, which the cell can use to carry out its job. Because it has its own DNA, mitochondria are believed to have been their own organism which later merged inside the larger cells, a process and phenomenon known as symbiogenesis.

Endoplasmic reticulum is a structure that serves as a storage reservoir and channel for transporting chemicals through the cytoplasm. Lipid molecules are also produced here.

The *Golgi apparatus* assembles some complex molecules made up of simpler, individual molecules. It makes new synaptic vesicles out of the membranes of old vesicles which have served their purpose. In this sense, the apparatus functions as the cell's recycling centre. The Golgi apparatus also operates as a packaging facility. It prepares and wraps proteins destined for export.

Lysosomes are produced by Golgi apparatus. They are small sacs which contain enzymes used to break down substances no longer needed by the cell. Lysosomes can cause cell death or suicide.

The *microtubule* is the scaffolding of the cell. It is the skeleton of the cell and is involved with the transportation of substances from one place in a cell to another. Unlike most other types of cells found inside the body, neurons cannot be replaced when they die. All the neurons a person will have, are present at birth. Once a neuron is destroyed, it can never be replaced. In addition, neurons possess a very high rate of metabolism requiring a constant supply of nutrients and oxygen. The needs of the neuron must be met by support cells in order for the neuron to survive.

Axon Hillock

Larger neurons have a markedly expanded region at the initial end of the axon. This axon hillock is the site of summation for incoming information. At any given moment, the collective influence of all neurons that conduct impulses to a given neuron will determine whether or not an action potential will be initiated at the axon hillock and propagated along the axon.

How the neuron works (electrically)

Neurons have a negative electrical charge inside their cell membrane which makes them polarized. Polarization is caused by the free movement of positively charged potassium ions through the cell membrane, *and* the retention of large, negatively charged molecules within the cell. An active process keeps positively charged sodium ions outside the cell. Every cell has this difference in electrical charge, but when a stimulating current is applied to neuron, a unique event takes place. Stimulation of the neuron causes potassium ions to flow into the cell which reduces the negative charge. This process is called depolarization. At a certain moment, the membrane changes and the cell become permeable to sodium which quickly enters the cell causing a positive charge to occur within the neuron. This event is called the *action potential*.

Once the action potential is reached at one area of the neuron, it moves down the axon via ion exchange at specific points called nodes of Ranvier. The size of the action potential is self-limiting. A high internal concentration of sodium results in the pumping out of potassium followed by sodium ions. This restores the negative charge within the cell membrane causing the neuron to be repolarized.

The entire process takes under 1/1000 of a second. The process can be repeated after the refractory period. The attainment of action potential results in the release of neurotransmitters at the terminal buttons. Thus, the electrical processes of a neuron constitute inner-cellular communication.

How the neuron works (chemically)

When the internal electrical signal of the neuron reaches the tip of an axon, small pre-synaptic vesicles that contain neurotransmitters within the cell are stimulated. The neurotransmitters are then released into the synaptic cleft, a submicroscopic space between two neurons. The released neurotransmitters attach to specialized sites, *receptors*, on the surface of the adjacent neuron.

Once a neurotransmitter is received by the receptors of a neuron, the cell depolarizes and generates its own action potential. The stimulus of a neurotransmitter has a limited duration. The duration of a stimulus from a neurotransmitter is limited by two factors: the breakdown of chemicals in the synaptic cleft, and the reuptake by the neuron which sent the neurotransmitters. Neurons are now known to produce more than one type of neurotransmitter.

Synapse

The term Synapse refers to the anatomically specialized junction between two neurons. The end branches of a pre-synaptic neuron's axons make contact with the dendrites, cell body, or axon of a postsynaptic neuron. There is no anatomical continuity between the two neurons.

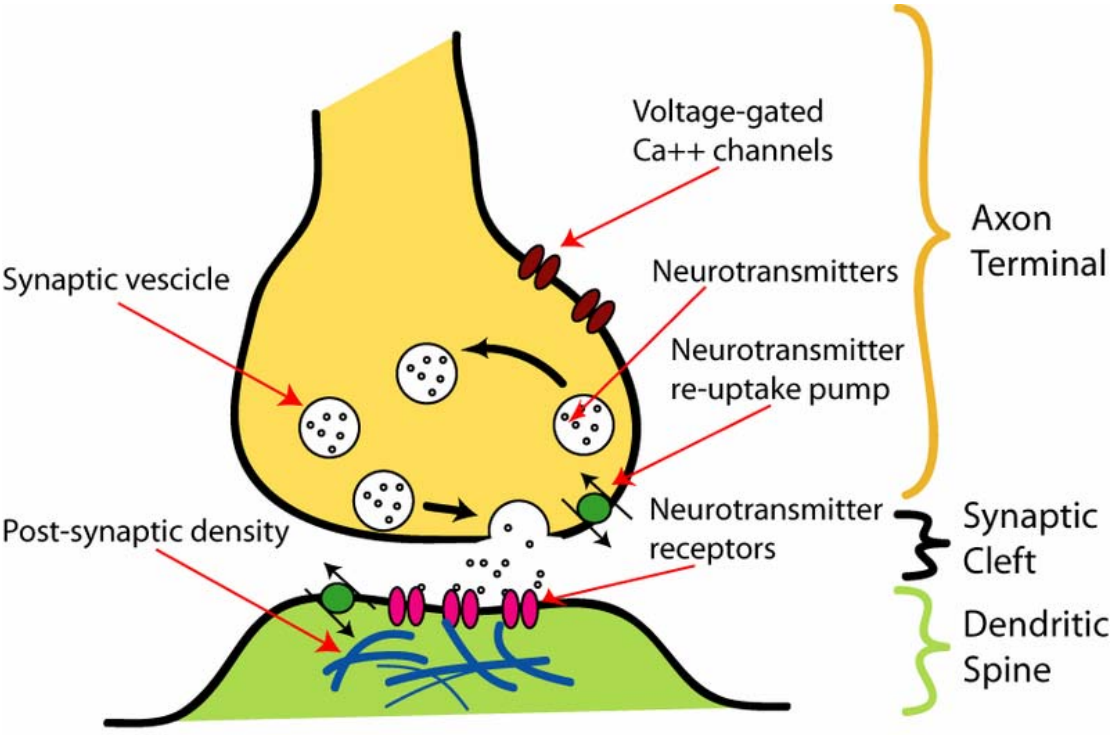

Fig. 5: Synapse

Synapses are of two types: chemical and electrical
The chemical type predominates in mammalian nervous systems.

How the synapse operates (inhibitory/excitatory)

Neurons communicate to each other by means of synapses; they release neurotransmitter, which diffuse across the synapse. Synapses are formed where neurotransmitters diffuse across the gap between the terminal buttons of one neuron and the membranes of adjacent neurons. The transmitter substance can produce brief depolarization or hyperpolarization, which are termed as postsynaptic potentials. Postsynaptic potentials may either increase or decrease the firing of the axon in the postsynaptic neuron. The gap (synaptic cleft) between the terminal buttons of one neuron and the membrane of another is very small, normally measuring a mere 200 angstroms wide. The gap is filled with extra cellular fluid through which the neurotransmitter diffuses.

Synaptic vesicles are located in the cytoplasm of the terminal button, along with mitochondria and a golgi apparatus. The vesicles are small rounded objects which generally come in two sizes - small and large. Small synaptic vesicles are found in all terminal buttons and contain molecules of the transmitter substance. They are produced in the terminal buttons by the golgi apparatus. The golgi apparatus operates as a recycling center. It makes new synaptic vesicles out of the membranes of old vesicles which have since released their substance into the synaptic cleft. Large synaptic vesicles are produced in the soma where they are

subsequently transported down to the terminal buttons. The large vesicles contain one of a number of different neuropeptides.

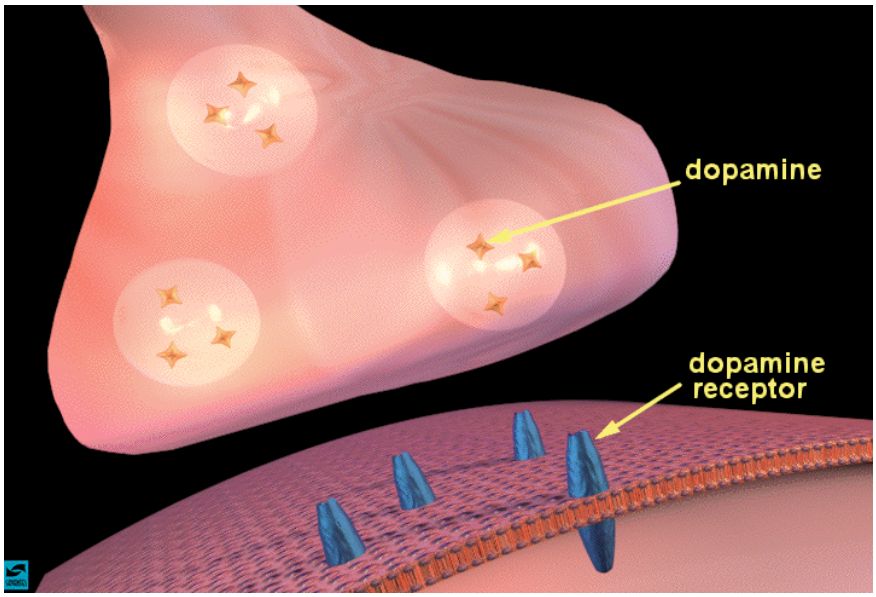

Fig. 6: Synapse for dopaminergic neuron

When an action potential reaches the terminal buttons, small synaptic vesicles located just inside the postsynaptic membrane attach themselves to the membrane and then break open. Their contents are expelled into the synaptic cleft. The event takes only a few milliseconds. The way in which an action potential causes synaptic vesicles to release their transmitter substance is as follows: some of the synaptic vesicles are docked against the pre-synaptic membrane where they are ready to release their contents into the synaptic cleft. Voltage-dependent calcium channels are located at the release zone of the pre-synaptic membrane. Depolarization by an action potential causes the calcium channels to open. At this moment, calcium ions flow into the cell propelled by electrostatic pressure and the force of diffusion. The entering calcium causes the fusion pore to open. While this is occurring, the membrane of the synaptic vesicle fuses with the pre-synaptic membrane. This causes the vesicle to be "pulled apart" causing the release of the vesicle's neurotransmitter into the synaptic cleft.

After the synaptic vesicle has released its payload, the terminal button gains the vesicle's membranes that have fused with it causing the terminal to become larger. In order for the terminal button membrane to maintain its optimum size and cease its expansion, the newly acquired vesicle membrane is received by the golgi apparatus where it is recycled in the production of new synaptic vesicles. The new vesicles are packaged with molecules of transmitter substance and transported to the pre-synaptic membrane.

The neurotransmitters released by the synaptic vesicles diffuse across the synaptic cleft and attach to the "lock and key" binding sites of special protein molecules attached to the postsynaptic membrane. When binding takes place, the postsynaptic receptors open up one or more *neurotransmitter-dependent ion channels* that permit the passage of specific ions into or out of the cell. Presence of transmitter substance in the synaptic cleft allows certain ions to pass through the membrane which is the local membrane potential. The opening of ion channels by neurotransmitters can take place in one of the two ways: direct or indirect. The

direct method involves the presence of the appropriate transmitter molecule in the synaptic cleft, and a neurotransmitter-dependent ion channel equipped with its own binding site on the postsynaptic membrane. The postsynaptic receptor/ion channel is called an *ionotropic receptor*. When a molecule of neurotransmitter attaches to the binding site, it causes the ion channel to open allowing sodium ions to enter the cell.

The indirect method of opening ion channels is more common and involves a series of chemical events. Receptors involved with the indirect method are called *metabotropic receptors* for they require the cell to expend energy in opening the channels. One way in which ion channels are opened via the indirect method involves the binding of the transmitter substance with the receptor, which then activates a G protein located nearby. The inactive G protein contains three subunits. When activated, the alpha subunit breaks away from the other subunits and attaches to a special binding site of an ion channel. This causes the ion channel to open, permitting ions to pass through the channel causing a postsynaptic potential.

The second method mimics the first indirect method in the first two steps, but instead of the alpha subunit binding directly with an ion channel, it attaches to and activates an enzyme located in the membrane. The enzyme then causes the production of one of several different chemicals in the cytoplasm of the cell. The newly produced chemicals, called *second messengers*, initiate another series of chemical steps that causes the ion channel to open resulting in a postsynaptic potential.

Postsynaptic potentials can be either depolarizing, *excitatory*, or hyperpolarizing, *inhibitory*. Therefore, alterations in membrane permeability must be caused by the movement of particular types of ions. Within the postsynaptic membrane, there are four types of neurotransmitter-dependent ion channels: sodium (Na^+), potassium (K^+), chloride (Cl^-), and calcium (Ca^{2+}).

The most important source of excitatory (depolarizing) postsynaptic potentials is the neurotransmitter-dependent sodium channel. Sodium is kept outside the cell by sodium-potassium transporters which wait for the forces of diffusion and electrostatic pressure to push it in. When sodium channels are opened, depolarization occurs and an excitatory postsynaptic potential takes place. The sodium-potassium transporters also maintain a small surplus of potassium ions within the cell. When potassium channels are opened, some of these cations will leave the cell. The efflux of positively charged potassium ions hyperpolarizes the membrane generating an inhibitory postsynaptic potential.

Inhibitory transmitter substances open chloride channels at many synapses rather than, or in addition to, potassium channels. The effect of opening chloride channels is dependent upon the membrane potential of the neuron. If in rest, nothing will happen because the forces of diffusion and electrostatic pressure are perfectly balanced for the chloride ion. But, if the membrane potential has already been depolarized by the activity of nearby excitatory synapses, the opening of chloride channels will permit chloride to leave the cell bringing the membrane potential back to rest. Opening of chloride channels operate in neutralizing excitatory postsynaptic potentials.

Calcium ions are positively charged ions located in high concentrations outside the cell. When calcium channels are opened, the membrane is depolarized causing an excitatory postsynaptic potential. Certain enzymes are activated by the release of the calcium. They have a variety of effects, such as the production of biochemical and structural changes in the postsynaptic neuron.

Neurotransmitters

Release of neurotransmitter: Transmission of nerve impulses is accomplished when a nerve impulse causes the rupture of vesicles containing the chemical transmitter from the nerve ending.

Interaction with receptor: The neurotransmitter crosses the synapse and interacts with receptors located on the membrane of the next neuron. This interaction may produce membrane permeability changes, which result in an excitatory response.

Degradation of neurotransmitter: After each impulse, it is necessary to inactivate or terminate the neurotransmitter's action. This may be accomplished by degradation as in the hydrolysis of acetylcholine.

Diffusion from the receptor: The NT may simply diffuse from the receptor site after a short period of time.

Resynthesize or restore NT: The neurotransmitter may be retaken back into the storage site or new NT is synthesized.

The neurotransmitters may be excitatory or inhibitory in nature like acetylcholine, and monoamines like Norepinephrine and Serotonin and others are the examples of certain classes of neurotransmitters, which are largely involved in the brain functions.

Nerves that release acetylcholine are called cholinergic nerves. Cholinergic nerves are part of the parasympathetic system, somatic motor nerves, preganglionic sympathetic nerves and central nervous system.

The major neurotransmitters (mode of action/s)

Although neurotransmitters have two types of effects, depolarization or hyperpolarization, many of them are not hard-wired. Many transmitters do not always have the same effect. The nature of the ion channels that are controlled by the postsynaptic can determine the effects of some transmitters. Transmitter substances are generally categorized into four groups: *acetylcholine, monoamines, amino acids,* and *peptides*.

Acetylcholine (ACh)

ACh is released at synapses on skeletal muscles and can also be found in the ganglia of the autonomic nervous system, as well as the target organs of the parasympathetic nervous system. Because the substance is located in "convenient" places outside the central nervous system, it has been extensively studied by neuroscientists. On the membrane of skeletal muscle fibres, ACh has an excitatory effect. It exhibits an inhibitory effect upon the membrane muscle fibres in the heart. This means that effect that a transmitter substance has is not determined by the chemical itself, but by the nature of the postsynaptic receptors it stimulates.

Acetylcholine is found in the brain as well. There, it is involved with learning and recall, as well as in controlling the stage of sleep during which dreams occur. The substance is composed of *choline* and *acetate*; two substances which require internal bioengineering for

use as ACh. ACh is deactivated by the enzyme acetyl cholinesterase (AChE). This enzyme is present in the postsynaptic membrane and cytoplasm of the terminal buttons.

Two types of ACh receptors exist, ionotropic and metabotropic. ACh ionotropic receptors are stimulated by nicotine and are referred to as *nicotinic receptors*. Such receptors are exclusively found in muscle fibres; smaller amounts of this receptor are found in the central nervous system. Metabotropic ACh receptors are stimulated by muscarine, a poison found in mushrooms, and are hence referred to as *muscarinic receptors*. These receptors are primarily found in the central nervous system.

The reason that several types of receptors exist for the same neurotransmitter substance has to do with the receptor's coupling to different kinds of ion channels, and to different G proteins which have different physiological effects. Ionotropic receptors produce rapid postsynaptic potentials; metabotropic receptors produce slower and longer potentials, and can also produce physiological processes within the cell to occur. Additionally, some receptors are sensitive to neuromodulators causing a single neurotransmitter to have a variety of effects in different locations of the nervous system.

Monoamines

The monoamines include the four chemicals: *epinephrine*, *norepinephrine*, *dopamine*, and *serotonin*. The molecular structures of these chemicals are similar to each other causing some drugs to affect the activity of all of them at the same time. Epinephrine, norepinephrine, and dopamine belong to the subclass of monoamines called catecholamines. Serotonin belongs to the monoamines subclass called indolamines.

Monoamines are produced by several systems of neurons within the brain. The majority of these systems consist of a small number of cell bodies located in the back of the brain. The axons of these cells branch repeatedly give rise to an enormous number of terminal buttons widely distributed throughout the brain. Monoaminergic neurons serve to modulate the function of widespread regions throughout the brain. They serve as volume controls that increase or decrease the activities of particular brain functions.

Dopamine (DA)

Dopamine produces both excitatory and inhibitory postsynaptic potentials depending upon the receptor site. Dopamine has been discovered to perform various important functions associated with movement, attention, and learning. *Tyrosine* is the precursor molecule for both dopamine and norepinephrine. When tyrosine receives OH, it becomes L-DOPA. The enzyme DOPA decarboxylase causes the L-DOPA to lose a carboxyl group causing it to become dopamine. When the enzyme β-hydroxylase attaches a hydroxyl group to dopamine, it creates norepinephrine. The enzyme *monoamine oxidase* (MAO) regulates the production of the catecholamines. MAO is found in the blood where it deactivates amines, which could potentially cause dangerous increases in blood pressure.

Parkinson's disease is caused by the degeneration of dopaminergic neurons, which serve to connect two parts of the brain's motor system. This disease is characterized by tremors, rigidity of the limbs, poor balance, and difficulty in initiating movements. The cell bodies of these neurons are located in the brain's *substantia nigra*. Those with Parkinson's disease are

given L-DOPA, which serves to stimulate the production of dopamine. Consequently, a patient's symptoms can be alleviated.

Dopamine may also prove to have a connection with the mental disorder namely schizophrenia. The disorder involves hallucinations, delusions, and the disruption of normal, logical thought processes. Drugs, which block activity of dopaminergic neurons reduce these symptoms causing researchers to speculate that schizophrenia is caused by over activity of these neurons. Furthermore, patients with Parkinson's disease being treated with L-DOPA occasionally display schizophrenic symptoms.

There are at least five types of dopamine receptors, all of which are metabotropic. The two most important ones are the *D_1* and *D_2 dopamine receptors*. The D_1 receptors appear to be exclusively postsynaptic. Stimulation of these receptors increases the production of the second messenger cyclic AMP. D_2 receptors are found both pre-synaptically and postsynaptically in the brain; stimulation of the D_2 receptors causes a decrease in cAMP.

Most of the neurons that release catecholamines do so through axonal varicosities, beadlike swellings of the axonal branches. The varicosities give the axonal branches the appearance of beaded chains. They form synapses with the base of the dendritic spines or the dendritic shaft.

Epinephrine / Norepinephrine (NE)
Like ACh, norepinephrine is also found in the autonomic nervous system and has been subjected to extensive research. The chemicals are also referred to as adrenalin and noradrenalin. Epinephrine is a hormone that is produced by the adrenal medulla. It has also been discovered that epinephrine serves as a transmitter substance in the brain; yet it is not as important as NE. The transmitter substance is referred to as NE, whereas it's adjectival form is noradrenergic.

Noradrenergic neurons within the brain are involved with the control of alertness and wakefulness. Their synapses in the central nervous system produce inhibitory postsynaptic potentials. At the target organs of the sympathetic nervous system, they typically have an excitatory effect. The transmitter is produced from dopamine with its final step of synthesis occurring *inside* synaptic vesicles. Once the vesicles are filled with dopamine, the dopamine is converted to NE through the action of dopamine β-hydroxylase. Monoamine oxidase destroys excessive amounts of NE in the terminal buttons.

Several types of noradrenergic receptors exist. The receptors are usually called adrenergic receptors for they are sensitive to epinephrine and NE. Neurons in the central nervous system contain both *α-1* and *α-2 adrenergic receptors* and *β-1* and *β-2 adrenergic receptors*. These four types of receptors are also found in various organs where they are responsible for the effects of the catecholamines when they function as hormones. All four receptors are also coupled to G proteins that generate cAMP.

Serotonin (5-HT)
Serotonin produces inhibitory postsynaptic potentials at most synapses. Most of its behavioural effects are also inhibitory. 5-HT is known to play a role in the regulation of mood, the control of eating, the control of sleep and arousal, and in the regulation of pain. The serotonergic neurons are involved with the control of dreaming. LSD hallucinations appear to be caused by the drug interfering with the activity of serotonergic synapses, which

causes the user to dream while he/she is awake. The amino acid *tryptophan* is the precursor for serotonin. The enzyme tryptophan hydroxylase adds a hydroxyl group, which produces 5-HTP. The enzyme 5-HTP decarboxylase removes a carboxyl group from 5-HTP resulting in 5-HT, serotonin. Seven types of serotonin receptors have been discovered. Of the seven (5-HT_1 to 5-HT_7), 5-HT_2 receptors are found exclusively in postsynaptic membranes. The other six have been found both pre-synaptically and post synaptically. With the exception of the 5-HT_3 receptors, all serotonin receptors are metabotropic.

Amino Acids

Glutamic Acid (glutamate)

Glutamic acid and GABA produce postsynaptic potentials by activating postsynaptic receptors. Glutamic acid has direct excitatory effects on axons. GABA has inhibitory effects. The two substances serve to raise and lower the threshold of excitation, which affects the rate at which action potentials occur. Glutamate is found throughout the brain where it appears to be the principal excitatory transmitter substance. MSG, as found in some oriental food, contains the sodium salt of glutamic acid that can cause the mild neurological symptoms of dizziness and numbness in some people. Five types of glutamic receptors have been found. Three are ionotropic, the other two metabotropic. The NMDA receptor has been linked to produce some of the synaptic changes responsible for learning.

Gamma-amino butyric Acid (GABA)

GABA is produced from glutamic acid through action of the enzyme GAD which removes a carboxyl group. GABA is an inhibitory transmitter substance with widespread distribution throughout the brain and spinal cord. The $GABA_A$ receptor is ionotropic and controls a chloride channel. The $GABA_B$ receptor is metabotropic and controls a potassium channel. GABA-secreting neurons normally produce an inhibitory influence and are present in large numbers throughout the brain. Some research suggests that epilepsy is caused by an abnormality in the biochemistry of GABA-secreting neurons.

$GABA_A$ receptors contain binding sites for at least three transmitter substances and neuromodulators. The main site is for GAGA, whereas a second site binds with a class of tranquilizing drugs known as the *benzodiazepines*, which includes Valium and Librium. These drugs reduce anxiety, promote sleep, reduce seizure activity, and produce muscle relaxation. The third site binds to barbiturates and alcohol. Because GABA is an inhibitory neurotransmitter, the effects of benzodiazepines, barbiturates, and alcohol are the increase of neural inhibition. It is believed that the presence of these receptor sites implies that the brain produces neuromodulators that cause a stress reaction by either blocking or activating these receptors.

Glycine

This amino acid is thought to be the inhibitory neurotransmitter in the spinal cord and lower portions of the brain. Although more research is needed to better understand glycine, it is known that the bacteria which causes tetanus, releases a chemical that blocks the activity of glycine synapses. The removal of the inhibitory effect of these synapses causes the muscles to contract continuously.

In addition to neurotransmitters, two other types of transmitter substances are released by the terminal buttons of a neuron: *neuromodulators* and *hormones*. Neuromodulators are more dispersed and travel farther than neurotransmitters. They are released in larger amounts,

which allow them to diffuse over a greater area of the brain, thus stimulating more neurons than do neurotransmitters. Hormones are released into the extra cellular fluid and travel about the body through the bloodstream. Hormones can affect a neuron by stimulating receptors on either the surface of the cell membrane or deep inside their nuclei. Neurons containing the appropriate receptors are affected by the presence of the hormones. Affected neurons can alter behaviour.

Neurotransmitters, neuromodulators, and hormones affect nerve cells by attaching to a specific region of the receptor molecule called the *binding site*. This is the site at which neurosubstances and the receptors of nerve cells match one another, much like a lock and key. Whereas the neurosubstance functions as the key, the receptors act as a lock- their duty is to allow only the "right" kind of neurosubstance into the cell. Chemical that attach to a binding site are called *ligands.* In their natural form, ligands are the neurotransmitters, neuromodulators, and hormones. However, other chemicals found outside the body can function the same way as the natural ligands. Artificial ligands include the substances of some plants and the venom of animals. Such ligands can also be manufactured in a laboratory.

Pheromones can also function as artificial ligands. They are chemicals, which enter the environment through sweat, urine, or the secretion of specialized glands. Their odour can be detected by receptors in the noses of other animals. When pheromones contact such receptors, they typically affect the reproductive behaviour of other members of the same species. Pheromones are known to attract potential mates, cause sexual arousal, inhibit aggression, and alter the activity of the endocrine system.

Membrane potentials

All living cell membranes may be demonstrated to have electrical potentials across them. Measurements may be made by placing a fine electrode inside a cell and in the fluid around the cell and connecting the two through a voltmeter. An electrical difference or potential can be recorded, which is usually referred to as a resting potential (one that exists when the membrane is not stimulated or active in transmitting a depolarization wave). In its resting state, the membrane may also be said to be polarized. The value of the resting potential varies in different cells, from 5 to 100 mV, and the inside of the cell is electrically negative to its environment. What follows, applies to all cells and in particular to nerve and muscle cells.

Origin of the resting potential

Animal tissues and fluids have no significant supply of free electrons, electrical charges being carried by ions of dissolved dissociable substances. It makes sense, then, to suggest that an unequal distribution of charges and development of an electrical difference on the two sides of a cell membrane is the result of an unequal distribution of ions on the two sides of the membrane. If one looks at the distribution of major ions in the fluids outside the cell and inside the cell, the necessary concentrations are present. Comparison of the species of ions between ECF and ICF shows a marked difference and show that in compartments, anions (negatively charged) and cations (positively charged) balance.

There is also an obvious diffusion gradient for ions that have large differences in ECF and ICF. Movement is largely prevented by the electrical attraction of positive and negative ions, inspite of diffusion tendencies. Thus, the diffusion gradient is balanced by a voltage gradient.

Measured potentials are about 90 mV to the exterior. The match between calculated potential and actual value suggests that chloride$^-$ (Cl^-) is passively distributed and needs no other mechanism than diffusion and voltage gradients to explain its distribution. The close agreement between calculated and actual values for K^+ suggest that it may be responsible for the resting potential and is largely if not wholly, distributed by electrochemical processes only. The wide discrepancy between calculated and actual potential for Na^+ discourages any attempt to explain its distribution by diffusion or voltage. The variance has to suggest that the anomalous distribution of Na^+ is the result of an active process, since both voltage and diffusion must tend to move Na^+ into the cell. Low intracellular sodium is maintained by a Na^+ positive pump, utilizing metabolic energy derived from ATP, to remove sodium actively from the cell against gradients. The small difference in K^+ potential may be explained by assuming K^+ pumping into the cell. It would seem that the same pump that removes Na^+ from the cell also brings K^+ into the cell; that is, there is a coupled pump operating.

In summary, the establishment of a resting potential of the observed magnitude is the result of active transport of Na^+ and K^+, with the membrane more permeable to K^+ than to Na.

Development of an action potential

The second question to be answered is, how the all or nothing action potential is generated, given the origin of the resting potential described above. In short, how does the membrane of an excitable cell become depolarized? During an action potential, the membrane potential nearly reverses itself. This suggests that there has been an increase in membrane permeability to Na^+ and that it moves into the cell to create a positive internal charge. An effective stimulus produces a 500 fold increase in membrane permeability to Na^+, perhaps by shutting down the Na/K pump. About a 40 fold increase in permeability to K^+ also occurs but does not contribute much to the potential change. The relationship of ion flow to electrical changes is presented in removal of the stimulus, the pump resumes, and the original state is restored (Repolarization).

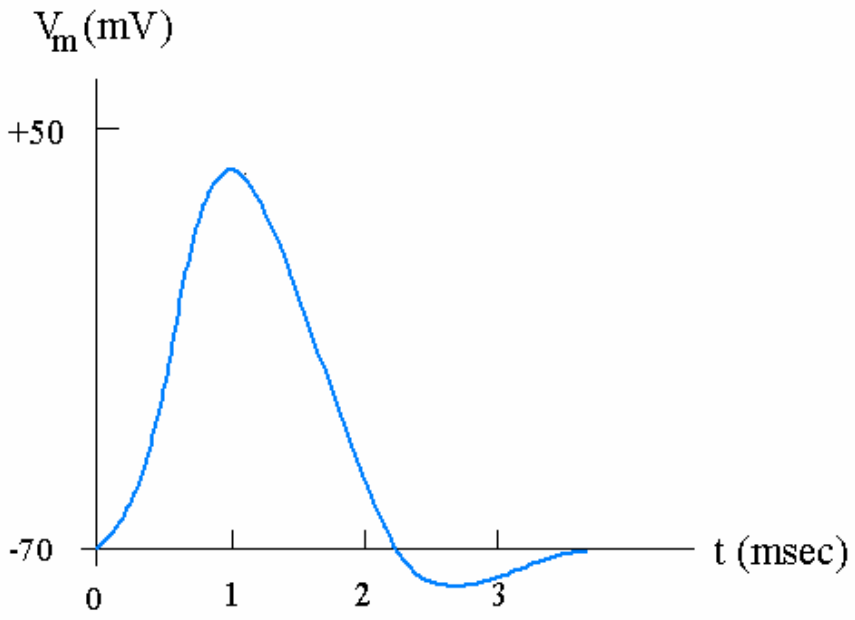

Fig. 7: Membrane potential generated

Transmission of an action potential

It is a statement of fact that once formed, an action potential is relentlessly conducted along a membrane until it reaches some terminus. In nerve cell axons that do not have insulating myelin sheaths, the process occurs as follows: An area of depolarization lies next to a still polarized area. Utilizing the ion-laden extracellular fluid (ECF) and intracellular fluid (ICF), a local current flow develops from positive to negative areas. It is as if, two tiny batteries had been connected by ionic flow; indeed, this phenomenon is sometimes called the battery effect. The current flow is of sufficient strength to depolarize the next segment, which develops an action potential that causes depolarization, current flow, depolarization of the next segment, and so on. Nerve cells are normally stimulated at one end, so that the impulses are conducted in one direction. Repolarization occurs as the impulse moves along the fibre membrane. In nerve fibres with myelin sheaths, the current flow can occur only where there are breaks in the sheaths - that is, at nodes of Ranvier. This results in the action potential being developed at the nodes that lie 2 to 3 mm apart. The impulse will then cover a given distance in jumps rather than steps, speeding its rate of passage along the fibre. This type of conduction is called salutatory conduction.

Reflex action

Reflex action is a stereotyped (involuntary) motor response elicited by a defined stimulus. A reflex action is mediated via the reflex arc. A reflex action or reflex is a biological control system linking stimulus to response and mediated by a reflex arc. Reflexes can be *built-in* or *learned*. It occurs very quickly before thinking. Before the message is sent to the brain, the spine picks it up and sends it back to the muscle causing spasm.

Simple reflex

A simple reflex is entirely automatic and involves no learning. An example is the escape reflex (e.g., the sudden withdrawal of a hand in response to a pain stimulus), or the patellar reflex (the jerking of a leg when the kneecap is tapped). Sensory cells (receptors) in the stimulated body part send signals to the spinal cord along a sensory nerve cell. Within the spine, a reflex arc switches the signals straight back to the muscles of the body (in this case, the arm or the leg) (effectors) via an intermediate nerve cell and then a motor nerve cell; contraction of the leg occurs, and the muscle contracts (the arm or leg jerks upwards). Only three nerve cells are involved, and the brain is only aware of the response after it has taken place. Such reflex arcs are particularly common in animals, and have a high survival value, enabling organisms to take rapid action to avoid potential danger.

Conditioned reflex

A conditioned reflex involves the modification of a reflex action in response to experience (learning). A stimulus that produces a simple reflex response becomes linked with another, possibly unrelated, stimulus. For example, a dog may salivate (a reflex action) when it sees its owner remove a tin-opener from a drawer because it has learned to associate that stimulus with the stimulus of being fed.

Reaction time

For a reflex, reaction time or latency is the time from the onset of a stimulus until the organism responds.

Human reflexes

Reflex actions seen in adult humans include accommodation reflex; achilles reflex; anocutaneous reflex; babinski reflex; biceps stretch reflex; brachioradialis reflex; crossed extensor reflex; mammalian diving reflex; gag reflex; gastroc-soleus reflex; H-reflex; patellar reflex (knee-jerk reflex); photic sneeze reflex; pupillary reflex; quadriceps reflex; salivation; scratch reflex; sneeze; tendon reflex; triceps stretch reflex; vestibulo-ocular reflex and withdrawal reflex

Processes such as breathing, digestion and the maintenance of the heartbeat can also be regarded as reflex actions, according to some definitions of the term. Newborn babies have a number of other reflexes which are not seen in adults including suckling; hand-to-mouth reflex; moro reflex, also known as the startle reflex; grasp reflex; asymmetrical tonic neck reflex (ATNR); symmetrical tonic neck reflex (STNR); tonic labyrinthine reflex (TLR).

Reflex arc

A reflex arc is the neural pathway that mediates a reflex. It generally does not involve the brain. In higher animals, it is composed of a spinal "reflex integration center" composed of interneurons to connect affector (sensory stimulation) and effector (response) signals. While the reflex generation may be initiated by nociceptive input, extensive processing takes place within the spinal cord. The neural connection from the primary sensory neurons to the motor neurons is a poly-synaptic pathway.

In lower animals, reflex interneurons not necessarily inolve the spinal cord, A reflex to a stimulus is almost simultaneous, as the reflex arc doesn't involve the brain at all.

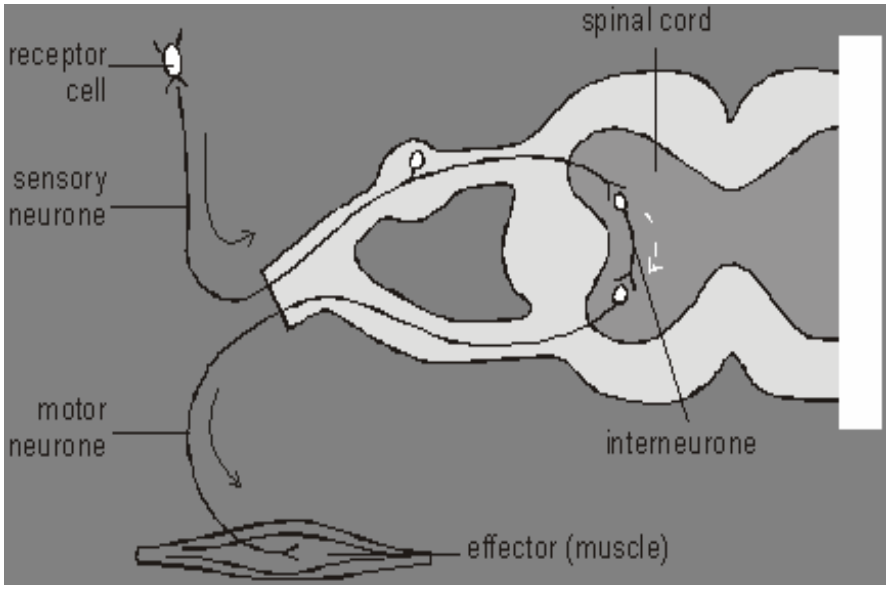

Fig. 8: Reflex arc

For a reflex, reaction time is the time from the onset of a stimulus until the organism responds.

Types

Simple reaction time is the latency between a fixed stimulus and a fixed response. Complex reaction time is the latency between a variable stimulus and a respectively variable response. Go/No Go reaction time task in which participants respond to one particular event but ignore other events. Choice reaction time task in which participants respond differentially to two stimuli by pressing one key for event A and a separate key for event B.

Factors

The major factors affecting reaction time are: recognition; choice; number of stimuli; type of stimulus; stimulus intensity. There are many other factors that can also affect reaction time: practice and error; fatigue; sex; age; race; distraction and vision.

Suggested Reading

1. "Autonomic Nervous System," Microsoft (R) Encarta.. 1994 Funk & Wagnall's Corporation.
2. "Brain," Microsoft (R) Encarta. 1994 Funk & Wagnall's Corporation.
3. Carlson, N. (1977). Physiology of Behavior, 5th Ed. Boston, MA: Allyn and Bacon.
4. Hooper, J. & Teresi, D. The 3-Pound Universe. New York: G.P. Putnam's Sons.
5. Joseph, R., Dr. The Right Brain and the Unconscious: Discovering the Stranger Within. New York: Plenum Press.
6. "Nervous System," Microsoft (R) Encarta. 1994 Funk & Wagnall's Corporation.
7. "Neurophysiology," Microsoft (R) Encarta. 1994 Funk & Wagnall's Corporation.