Answers to such questions cannot be found in the neurobiology of simple brains.

Methods for directly visualizing living processes in real time in experimental animals using video-enhanced microscopy and voltage sensitive dyes are being utilized to answer some of these questions. Phenomenal advances have already been made in imaging technologies which enable one to study higher mental functions in conscious, performing human beings utilizing PET or functional MRI scans. Areas of the brain participating in functions like reading simple alphabets or random words or sentences or nonsense script have been identified. Similarly, the region of the cortex involved in intention to move or actually voluntarily moving a part of the body are being delineated. Studies are underway on more complex intellectual functions. No doubt future technological advances would permit study of more complex behaviours. Optimists believe that the 20th century which has witnessed the unravelling of the atom and the gene may also see the mystery of mind resolved. Whether this dream is realized or not, it is true that the journey towards that end will be expedited by sharing of the expertise of diverse groups of scientists like those participating in this symposium.

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Neuromorphology

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Information is processed, focused and disseminated in the nervous system by neurons connected in serial and parallel pattern. These connections are either discrete or diffuse. Most of these neurons and their connections can be traced physically by various techniques using dyes, antibodies against neuronal chemicals radioisotopes and scanning. This has helped in reconstruction of the neural network and also to create computer programs of brain network for discrete functions and intelligence.

BRAIN is the most complex of all the organs. To comprehend how the brain controls thinking, feeling, learning, memory and other functions, one has to understand the anatomy of the brain, or more scientifically termed, the central nervous system.

Each function of the brain can be broken down into an enormous variety of activities. Each activity has different components and each component requires integration of a number of cells or neurons. This forms a unit or a module. Each module has a characteristic connection pattern consisting of the input, the output and the interconnecting neurons. Neuron forms the functional unit of the nervous system. It has a trophic centre, which is the cell body, with the nucleus and processes which extend short or long distances from the cell body. Processes make contact with other neurons or organs or tissues in the body for integrating and controlling functions.

According to Brodal[1] structural organization of the central nervous system exists in an orderly manner. Groups of neurons subserving a single function are organized at different hierarchical levels. Though each group subserves a special function in the broad sense, each neuron of the group has primarily a particular role. This is easily understood from the location in relation to other neurons in the same functional group and also in other related functional groups, connections and the chemicals synthesized for transmission of impulses.

Divisions of the central nervous system

The central nervous system (CNS) consists of the spinal cord, medulla, pons, midbrain, diencephalon, basal ganglia, cerebral cortex and cerebellum (Figure 1).

Spinal cord

Spinal cord is the lowest part of the CNS housed in the vertebral canal and is tubular in shape. When traced upwards it merges with the medulla, which forms the lowest part of the brain located inside the skull. Spinal cord receives and transmits all the information to and fro between the body and the higher centres of the CNS. Information is passed along discretely arranged processes of the neurons, which form fibre tracts. Spinal cord contains the neurons which command the motor activities of the limbs and the trunk and also neurons which give rise to processes for transmitting most of the sensory modalities to the higher centres.

Medulla, pons and midbrain

These three regions of the CNS are collectively termed as the *brain stem*. This area too has similar functions as the spinal cord and caters to the head, face and neck regions. In addition, there are other neuronal groups and fibre tracts which contribute and integrate other functions.

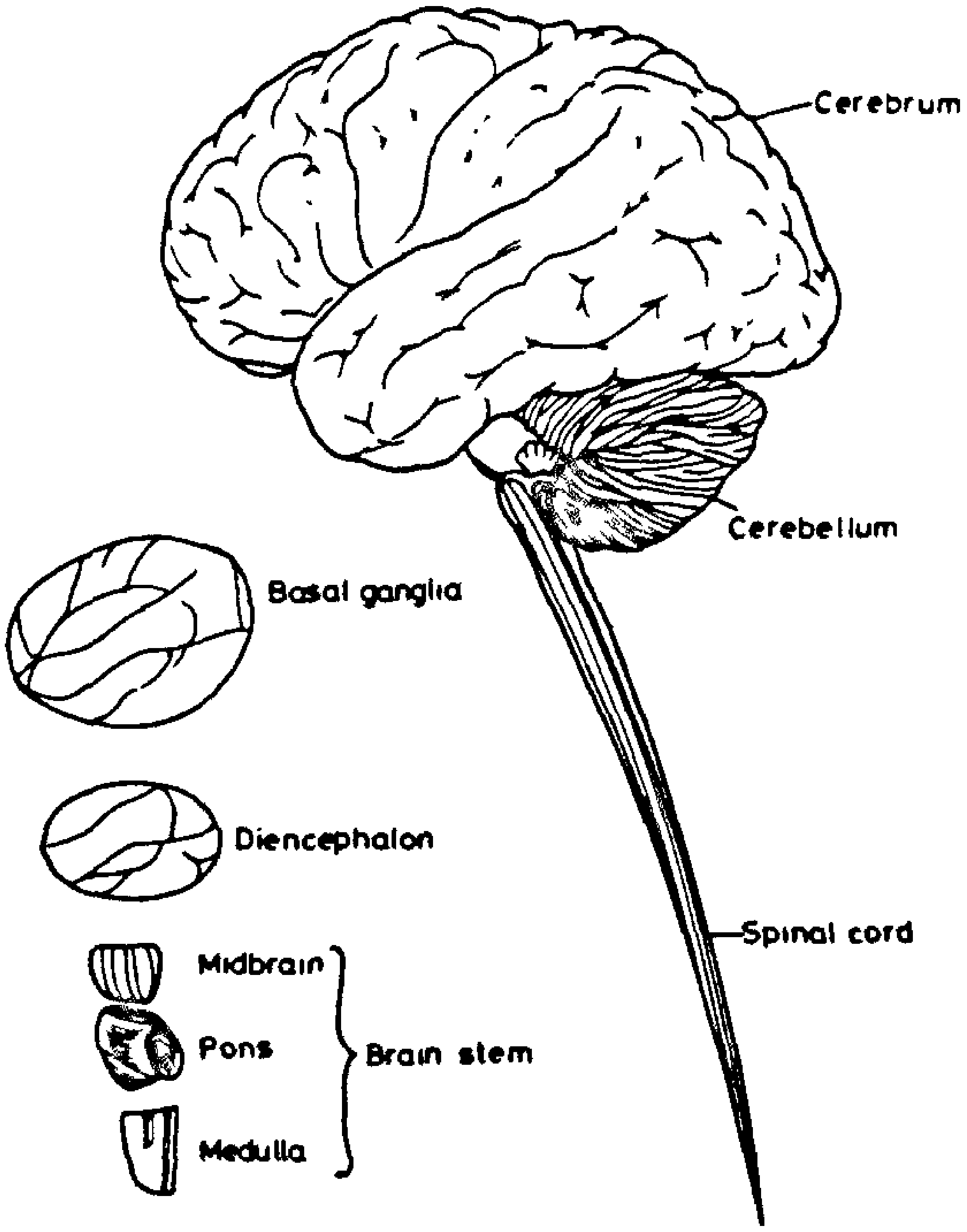


Figure 1. Different parts of the central nervous system.

Brain stem is occupied by a significantly large central core occupied by a reticulum of neuronal processes and cell bodies. Because of the structure, it is named reticular formation. Structurally, it is difficult to pinpoint functional regions in the reticular formation unlike other parts of the brain. However, there is a definite orderliness in the input from the fibre tracts passing through the brain stem. The reticular formation has connections with the higher centres, conveying all the information at a slower pace from the lower centres.

Diencephalon

This part can be divided into thalamus and hypothalamus. Thalamus functions as a relay station for sensory input from the lower centres to the cerebral cortex and also for special senses like sight, hearing and taste. Further, thalamus acts as a nodal point for transmission of information from subcortical motor centres to the motor cortex.

Hypothalamus integrates the activities of all the organs in the body which are not under voluntary control through descending connections. Hypothalamus also controls hormonal secretions of the various endocrine glands.

Basal ganglia

These are a group of nuclei (each nucleus is made up of a large number of neurons with similar functions) which are concerned with body movements. These nuclei have to-and-fro connections with the cerebral cortex.

Cerebral cortex

This part of the CNS is maximally developed in the human. It is concerned with perceptual, cognitive and motor functions. Functional areas are demarcated by certain landmarks. Structurally, cortex is divided into lobes by well-defined grooves or sulci. Thus, we have frontal, parietal, occipital and temporal lobes. Frontal lobes control motor activity of the whole body, including that of the eyes and speech. Prefrontal cortex is a large area of the frontal lobe, the function of most of which is still under speculation. This is considered to be the decision-making area in the brain and receives input from all the other parts. Parietal lobe is concerned with sensory perception and association functions of general sensations. Occipital lobe is mainly concerned with perception of vision. Temporal lobe is for hearing and memory. Adjacent areas of temporal, occipital and parietal lobes function as association area for vision, hearing and speech. Emotional or visceral brain is contributed by parts of the cerebral cortex, hypothalamus and also some other nuclear groups.

Cerebellum

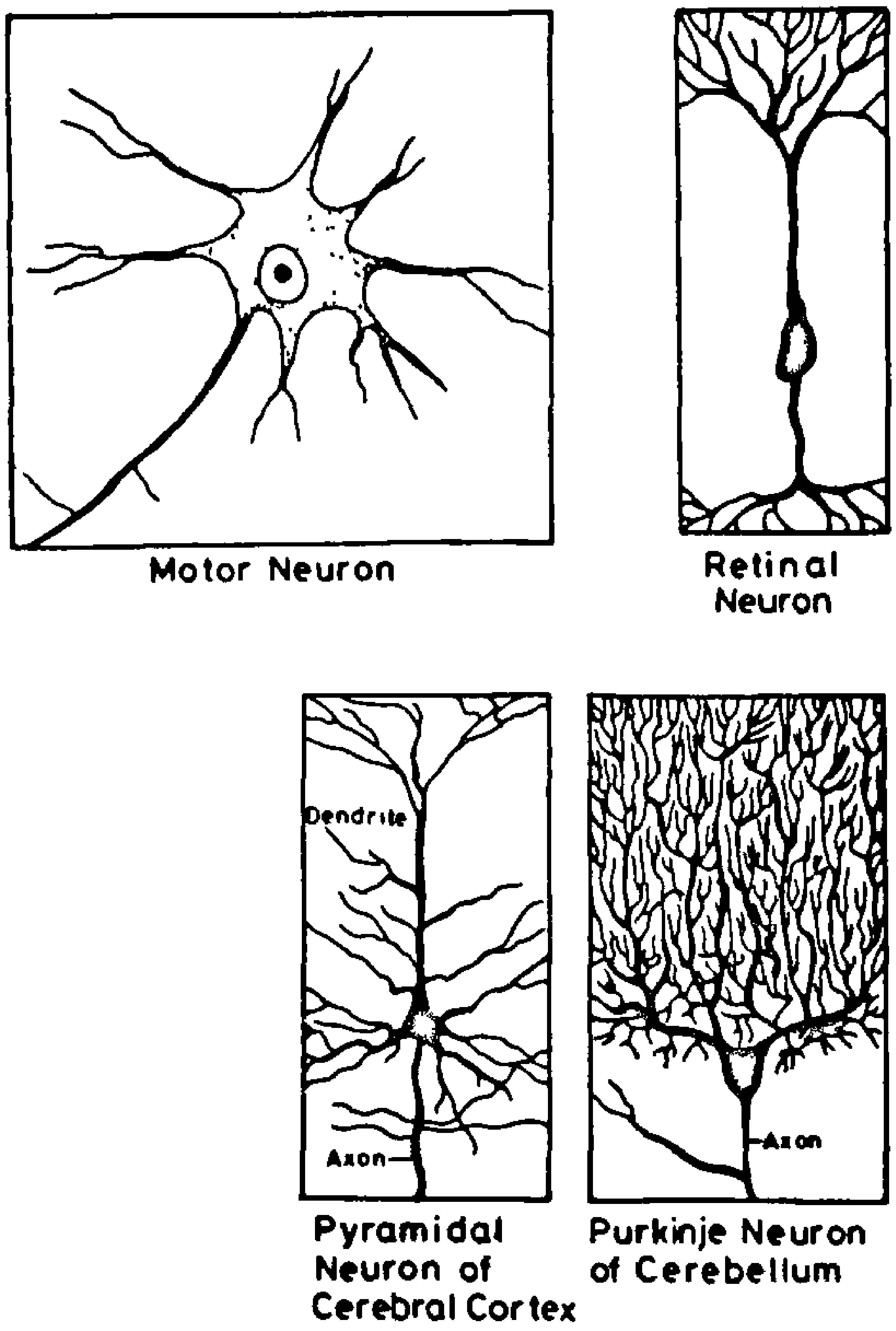
This is also known as the small brain. In short, it means that all the information received by the lower and higher centres is also reaching the cerebellum. It is primarily concerned with regulation of posture, balance and coordination and velocity of movements. Cerebellum is considered to have a control on initiation of motor movements by the motor cortex. Special senses are also represented in the cerebellum.

Special senses

Special senses like vision, hearing, taste and smell have well-organized individual pathway from the peripheral receptor region to the cerebral cortex for their conscious perception. For example, visual pathway is responsible for identifying objects in space and tracking movements of objects in motion. Retinal neurons are individually programmed for shape, movement in space and basic colours. Neurons have serial and parallel connections to perform the functions effectively. Spatial representation of the visual field perceived by each eye is apparent throughout the visual pathway. There is a partial crossover of the fibres at one point to facilitate binocular vision. The lateral geniculate body, a part of the diencephalon, forms an important relay station for the visual impulses. Fibres from the lateral geniculate body reach the occipital cortex, where the visual functions are processed. Each fibre ends on neurons in a specific region of the cortex. These neurons set up connections with adjacent neurons located in a vertical strip of the cortex. This segment of the cortex forms a column responsible for a particular function from a specific part of the retina. Thus, the cortex is divided into many such vertical strips. Coordinated activity of such columns in the visual cortex is responsible for the stereoptic and binocular vision.

Neuron

Neuron is the *structural and functional* unit of the nervous system. Each neuron, besides the cell body, has processes. One of the processes is the axon, which is slender and has uniform diameter. It also branches at right angles. Other processes, the dendrites, may be single or multiple. These branch at acute or obtuse angles and taper towards the terminal part. Many of them have tiny projections, termed *spines*, which appear as thorns on the rose bush. Axon conveys information from one neuron to the other. The dendrites, on the other hand, receive information brought by the axons. There are multitudes of such axonal endings on a single neuron. Spines increase the surface area of a neuron and form contact points in addition to the somal and nonspinous surface of the dendrites. Neurons are of different sizes and shapes and the processes spread in predetermined directions designed for specific functions (Figure 2).



Motor Neuron

Retinal Neuron

Pyramidal Neuron of Cerebral Cortex

Purkinje Neuron of Cerebellum

Figure 2. Different neurons are drawn from Golgi-stained preparations.

The points of communication among neurons are specialized junctions and are termed as *synapses*. Here the cells are not in contact but are separated by a cleft. When message arrives at the axonal end of the synapse, there are intense molecular activities which help in releasing a neurotransmitter into the cleft between the releasing and the receiving ends. This ligand–receptor complex sparks off a volley of reactions to generate and propagate a fresh impulse to the next station (refer to the diagram in P. N. Tandon's article).

Connections

In the CNS, interneuronal connections are serial or parallel. Information transmitted from the lower to the higher centres through serial connections. Transmission of pain sensation from the body to the cortex can be taken as an example. Free nerve endings in the periphery transduce the pain sensation to electrical impulses. Fibres which carry pain sensation relay on certain neurons in the spinal cord or medulla through synapses, where chemical transmission takes place. These relay neurons get an input from the midbrain, which has a modulatory effect on pain. Fibres from these neurons cross over to the opposite side and form a discrete tract. This tract gives branches to the diffuse reticular formation in the brain stem. The reticular formation in turn sets up a slow alternate route for pain transmission to the cerebral cortex. The direct tract relays in the thalamus and thereafter reaches the sensory cortex, which is responsible for perceiving pain. The sensory cortex represents different parts of the body. Thus, the body representation for sensation is in a strip of the cortex in the parietal lobe (refer to the diagram showing body representation in the cortex in the article by P. N. Tandon). Each segment representing a part of the body is made up of small vertical columns of neurons, which receives the input from a tiny area of the periphery. Thus, one vertical column gets more or less one fibre carrying pain sensation. Such columns in the cerebral cortex are integrated together for perception of pain, its quality and nature and the location in the body[2].

Alternate pathway for pain through the reticular formation forms a parallel connection to the main pathway. This is concerned with behavioural modulations caused by pain.

Thus, there are serial and parallel connections in the central nervous system. Each has a number of relay stations, at which modulation of the functional modality takes place. This modulatory process gets increasingly refined towards the final destination. For example, the quality of the pain and the precise site at which the pain is felt is perceived only at the cortical level.

Sensations received from the body and from the outside world need to be stored for future reference and necessary action. Temporal lobe of the cerebral cortex is the memory area. From the temporal lobe past experiences are retrieved to integrate with recent ones to understand the implications and formulate future action. This function is reportedly undertaken by the prefrontal area of the frontal lobe. There is precise wiring between temporal cortex and prefrontal area to help in memory and decision-making functions.

For execution of a motor function or movement, motor cortex needs input with information regarding the state of the muscle, position of the joints on which the muscles act and the status of the immediate environment. Sensory cortex, which receives and perceives the necessary information, conveys it to motor cortex. Basal ganglia, which have a major role in the gross movements of the body, and the cerebellum, which regulates the balance of the body and head, velocity of movements and coordination of the muscular activities, have also connections with the motor cortex. Motor cortex in turn controls the neurons in the lower centres which are directly involved with innervating the muscles and thus initiating the movements (Figure 3).

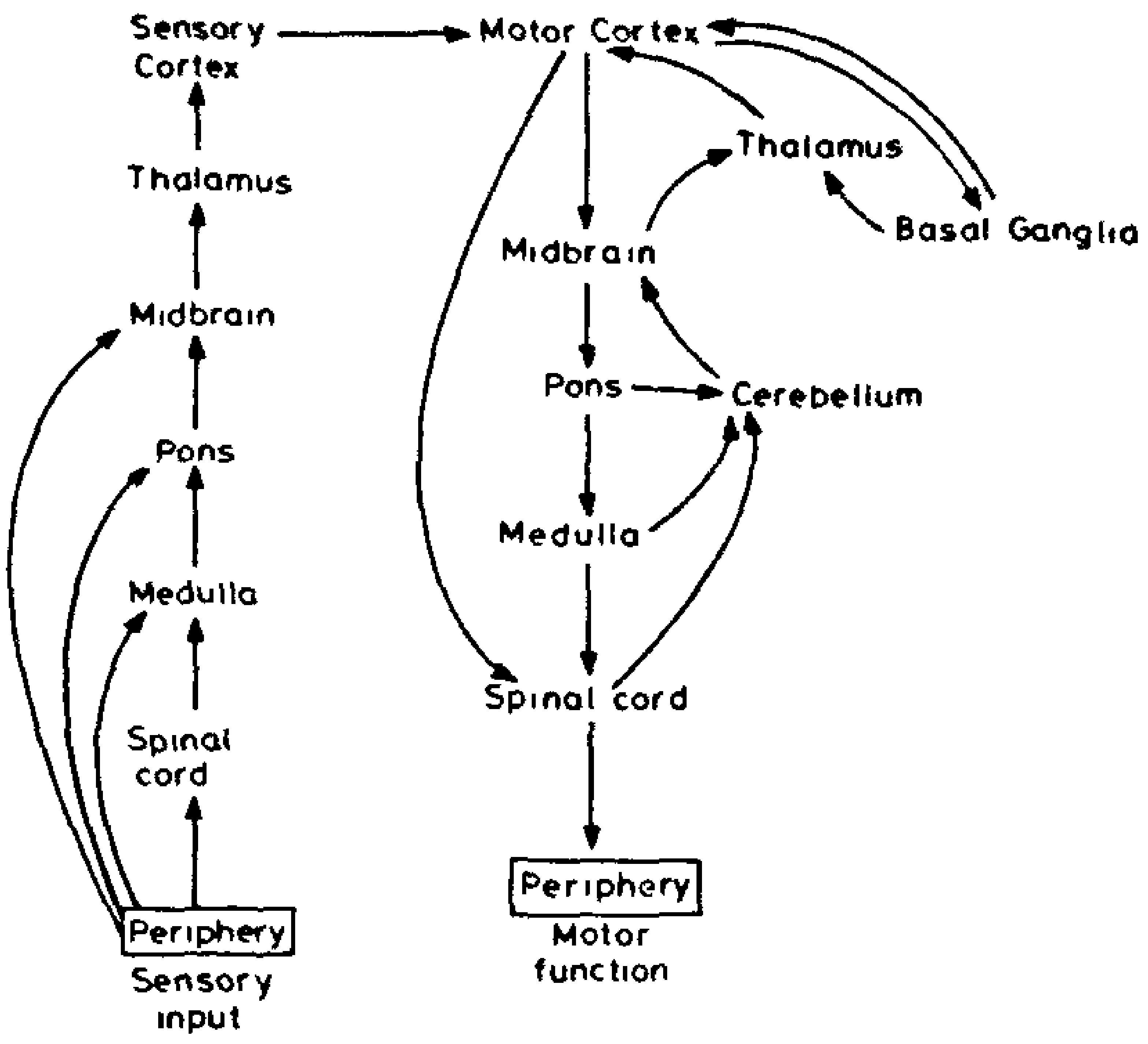


Figure 3. Diagram to show connections for motor activity

Over and above the circuitry described so far between higher centres and lower centres, there are local circuits set up for reflex activity. Like other circuitry, there are input and output neurons and neurons interposed between them. This type of connections are seen at all levels.

On gross examination brain appears bilaterally symmetrical. However, one half of the brain is dominant for specific functions. The left half of the cerebral cortex is dominant in right-handed persons and is also considered to be controlling the motor speech irrespective of left- or right-handedness. In spite of the dominance, information is shared by both halves through fibre connections.

Study of the structure of the nervous system

It is not easy to perceive the structure of the brain by conventional methods. Naked-eye observation gives only the gross structure of the brain and not the complicated connections. Even with the sophisticated methods now available, it is difficult to demonstrate the entire structural pattern. Figure 4 represents a reconstruction of the structure of the CNS.

With conventional staining techniques we can only perceive the cell bodies of the neurons and the supporting glial cells. Among the cell bodies are the

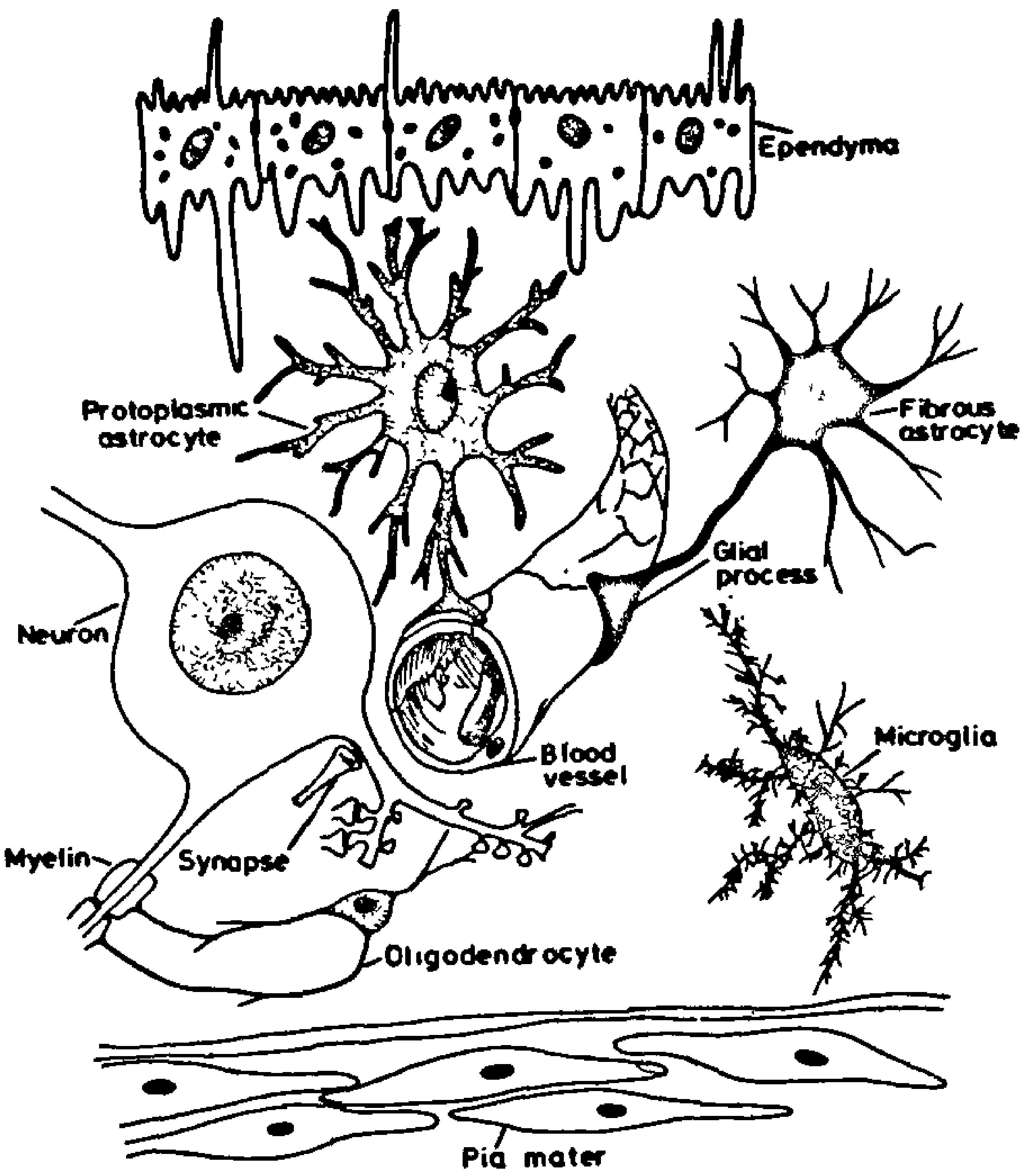


Figure 4. Structural elements of the central nervous system.

blood channels supplying nutrition needed for the continuous activity of the neurons. On using specialized staining techniques with silver salts, neurons can be fully impregnated so that the cell bodies along with the processes are fully visible. Golgi established this technique in the 19th century, which is still in vogue to demonstrate a neuron in its entirety. The size, shape and the dendritic tree and its branching pattern differ from neuron to neuron. Dendritic spread and the axonal trajectory determine the extent and type of connection of each neuron.

During the early days connections in the nervous system were studied by transecting the fibres and localizing the neurons and their target by tracing the degenerative changes. This was not an easy task as it was time-consuming and the degenerative process was normally limited at the first synaptic junction. Visual system is the only exception. Thus, this method has only a limited application in studying connections in the nervous system.

Now there are tracing techniques which demonstrate the precise wiring pattern of the neurons. Substances can be introduced into the target organ or in the fibres. These substances could be a protein or a fluorescent dye or a radiolabelled material which is normally utilized by the cell for its metabolic activities. These can be localized by different methods in the cells and processes and at a few sites across the synapses, thus delineating the complete pathway. Electrophysiological recordings from identified neurons have helped in delineating the function of the neuron. Thus, pattern-driven neurons and movement-driven modules in the visual system have been established. It has been easier to study the visual system because of its accessibility at the periphery and comparatively simpler connections.

Recently, neuronal connections and pathways have been studied in fomalin-fixed human brains obtained at autopsy with dyes which spread in the lipid moiety of the membranes. This has opened up the possibility to confirm and trace the tracts in human brain which so far have been extrapolated from experiments in lower mammals.

Another way of studying neurons and their connectivity is by their chemical nature. Each neuron has its own specific neurotransmitter. More than one neurotransmitter can be encountered in one neuron. Often, some of these are peptides. These can function as transmitters at the synapses or as modulators for synaptic activity. Specific antibodies against these chemical components can be used to trace the cell bodies and processes. With different chromogens or fluorescent dyes, double labelling of a single neuron can be done to locate different connections.

Detailed information on each of the identified components can be studied by electron microscope. Labelling with electron-dense substances like gold, silver or other chemicals can be used to study ultrastructure and chemical nature and thus the function of each component.

All the above studies refer to observations in two dimensions. Previously, reconstruction of two-dimensional observations was laboriously done for spatial spread and connections of the neurons. This process is made easy now by sophisticated programmes and computer facility. Dedicated programmes process serial images and store and reconstruct them, and provide accurate spread and connections of the neurons in three dimensions. New confocal microscope can scan and photograph very thick sections at different depths so that spatial orientation of the neurons and their processes is more accurately recorded than with the conventional method of collecting information from serial sections[4].

In conclusion, brain is an organ with complicated and intricate wiring pattern. All the activities in the body are integrated and controlled by the brain through information input and command output. Structure of the brain can be unravelled to some extent by conventional and modern techniques.

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