An Introduction to Neurophysiology

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Preface

This book arose out of disappointment with most existing accounts of neurophysiology. Over ten years of tutoring and lecturing to medical and psychology students, neurologists, psychiatrists and even anaesthetists in training, I have come across very few texts which have managed in the least to convey the fascination and excitement of neurophysiology. Most fail rather dismally to overcome a central problem which neurophysiology faces: its techniques generate a wealth of results yet these often contribute rather little to our understanding of how the brain actually works. Indeed there are many who believe that the subject is regressing because it is incapable of interpreting its own data. This schism between results and their explanation is a particular problem of multi-authored books in which individual specialists cautiously under-interpret their contributions and carefully eschew speculation, presumably because they feel that textbooks should always stick to 'established facts'—as if there were such things. The result is that they succeed in producing rather dry and fact-filled texts which fail to capture the excitement of the subject.

Immodestly, therefore, I have tried to cover the whole of neurophysiology, adopting the same style and approach throughout. I have attempted to include only results which help to explain how particular neurophysiological mechanisms work, and have avoided those that do not contribute to such understanding. I fear the reader will find that this impudent aim has far exceeded the modest capacities of the author. It has certainly led to far more speculation than one would normally expect to find in a textbook. This is particularly true of the second half of the book, which deals with motor systems, because these are so much more difficult to study or understand. I am confident that most of these speculations, and I fear that also many of the 'facts' presented, will turn out to be wrong. But I crave the reader's indulgence and bid him remember the words of Lord Bacon: 'Truth is more likely to come out of error if this is clear and definite, than out of confusion.'

I am very much indebted to Geoffrey Walsh's *Physiology of the Nervous System* (Longman, London), which is a shining example of how neurophysiology can be made interesting and exciting. Naturally, I am also indebted to current texts in neurophysiology, such as those written by V. Mountcastle, T. Ruch & H.D. Patton, S.W. Kuffler & J.G. Nichols and B. Katz, whose ideas for presenting material have, of course, influenced my own. I am grateful to my colleagues in the University Laboratory of Physiology, Oxford, many of whom, unwittingly or not, have helped with the writing of this book. I am grateful also to Blackwell Scientific Publications for their editorial help, and to Clare Little of Oxford Illustrators for converting my appalling scrawls into the delightful illustrations you see before you. I thank my wife, Clare, for putting up with the long gestation of this book, but above all I appreciated the company of my daughter, Lucy, each morning. Watching her 'doin' some drawin'' generated more ideas about how sensory and motor systems work than I would ever have believed possible.

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Chapter 1
Basic Structure of the CNS—Neuroanatomy and Neuroanatomical Methods

The foundation of neurophysiology is neuroanatomy. Without a thorough knowledge of the 'wiring diagram' of the brain we would be quite powerless to understand it. Without details of the microscopic structure of nerve cells and particularly of their contacts with each other we would be equally lost.

CELLS IN THE NERVOUS SYSTEM

The nervous system of most animals consists of separate nerve cells or *neurones*. These communicate with each other at specialized contact areas called *synapses* (a term coined by Sir Charles Sherrington from the Greek word for 'to clasp'). In the human nervous system there are perhaps 10^{15} neurones, and even these are outnumbered by their supporting cells, known as *glia* (Fig. 1.1), which include: *oligodendrocytes* which supply the myelin sheaths for central nervous fibres; *Schwann cells* which do the same for peripheral nerves; *astrocytes* which surround blood vessels, filling the role of fibrous tissue in other tissues; *microglia* which are the central-nervous scavengers, analogous to the macrophages found in the rest of the body; and *ependymal* cells which line the spinal canal and cerebral ventricles.

A 'typical' neurone consists, like most other cells, of a nucleus surrounded by cytoplasm which contains organelles such as mitochondria, ribosomes, vesicles, microtubules, etc., and is bounded by a cell membrane. It is bathed by a small amount of extracellular fluid (e.c.f.) which is doubly protected from the vagaries of the blood itself by the *blood–brain barrier*.

Nerve fibres

What distinguish nerve cells from other cells morphologically are their extended processes—branched *dendrites* often bearing thousands of 'spines', upon which other neurones synapse. These dendrites lead signals towards the cell body or soma, and usually a single *axon* leads away from the cell (Fig. 1.2). In some sensory neurones, e.g. those carrying cutaneous signals from the foot, the dendrites and axon together may be as long as 2 m. By contrast, small *interneurones* within the central nervous system may possess axons which are only a few microns in length. Many axons are ensheathed, by oligodendrocytes within the CNS or by Schwann cells peripherally; these provide a layer of thick insulating material, *myelin*, for the larger, rapidly conducting axons.

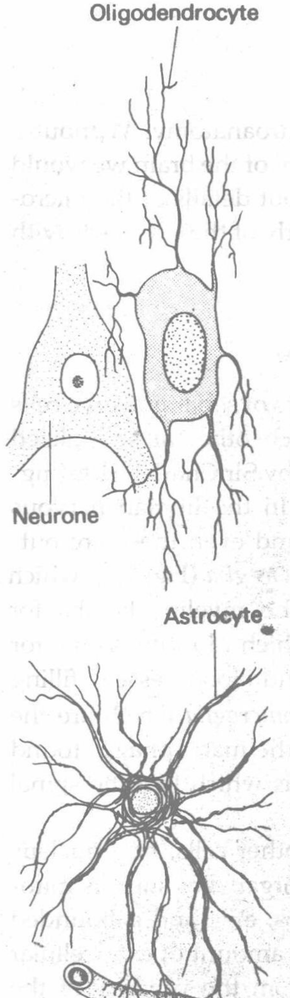

Fig. 1.1. Glial cells.

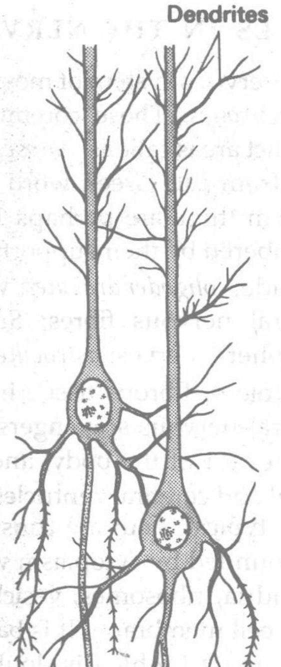

Fig. 1.2. Pyramidal neurones in cerebral cortex.

Reflex arc

The basic organization of the CNS is surprisingly simple (Fig. 1.3). Receptors in the periphery (skin, eyes, ears, etc.) connect with sensory nerve fibres. These are the long processes of nerve cells whose cell bodies lie close to, or within, the CNS. In the case of spinal sensory nerve fibres, the cell bodies are found in the *dorsal* *root ganglia* which lie near the dorsolateral surface of the spinal cord. The central processes of these neurones pass into the spinal cord via the *dorsal roots* and either (1) pass immediately upwards towards the head; or (2) make contact in the *dorsal horn* of *grey matter* of the spinal cord with second-order, relay neurones which then pass information upwards towards the brain; or (3) make contact with *interneurones* (none of whose processes extends further than a few millimetres locally); or (4) make contact directly with *motoneurones* situated within the ventral part of the grey matter, the *ventral horn*. The axons of ventral horn cells (which constitute the *motor nerves*) are directed back via the *ventral roots* to the motor apparatus of the body, the skeletal muscles. Thus the basic organizational unit of the

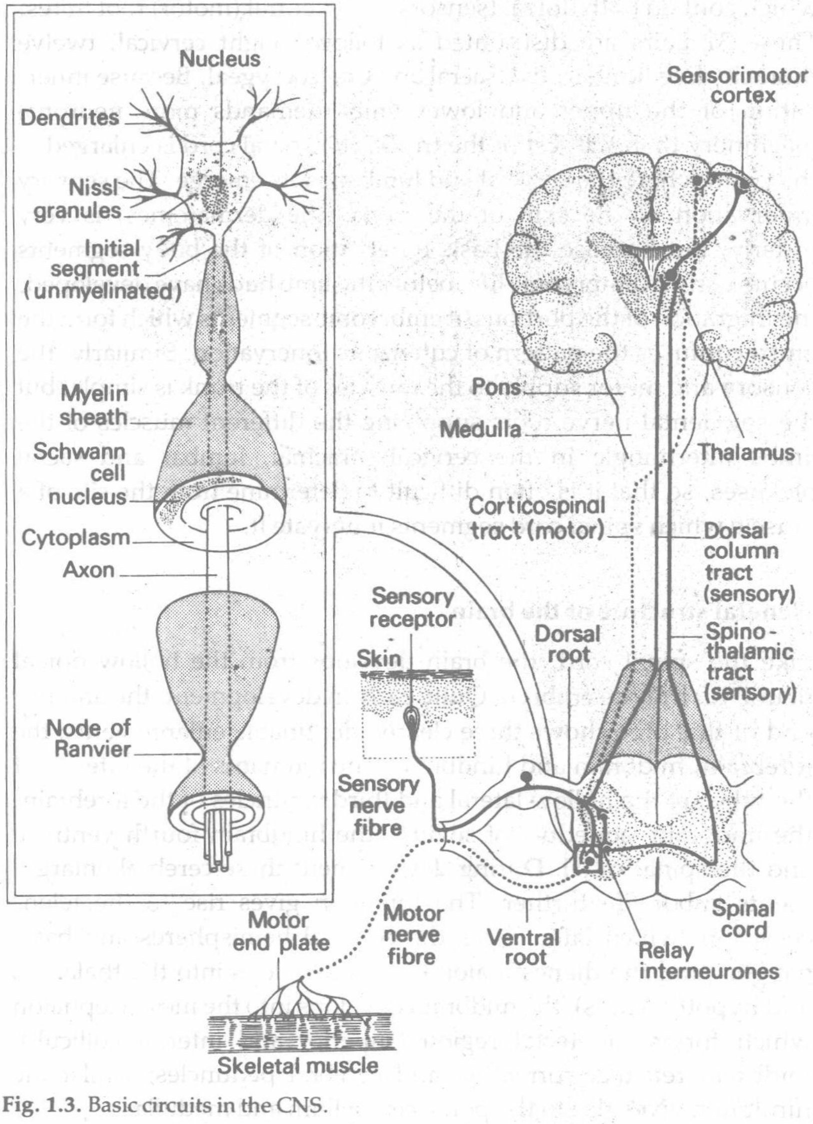

Fig. 1.3. Basic circuits in the CNS.

spinal cord (a *reflex* arc) consists of sensory nerve fibres passing via dorsal roots to the dorsal horn to connect with mononeurones in the ventral horn whose axons leave for the muscles via the ventral roots. The unidirectional flow of signals into the spinal cord via the dorsal roots and out of it via the ventral roots is known as the Bell–Magendie 'law'; unfortunately it is now known to be an oversimplification, and therefore cannot be considered a law.

Spinal segments

The spinal cord derives many of its features from the segmental organization of the lower animals from which we have evolved. It consists of 31 segments, each giving rise to a pair of spinal nerves which contain both dorsal (sensory) and ventral (motor) root fibres. These 31 pairs are distributed as follows: eight cervical, twelve thoracic, five lumbar, five sacral and one coccygeal. Because innervation of the upper and lower limbs demands more neuronal machinery than the rest of the trunk, the spinal cord is enlarged at the point where the cervical and lumbar roots emerge. The sensory innervation of the skin of the trunk (the dermatomes) is very orderly, but because the basic innervation of the body segments occurs early in embryonic life, before the limb buds have developed, the migration of the portions of embryonic segments which form the limbs confuses the pattern of cutaneous innervation. Similarly, the sensory and motor supply to the muscles of the trunk is simple, but the segmental nerve roots supplying the different muscles of the limbs intermingle in the cervical, brachial, lumbar and sacral plexuses, so that it is often difficult to determine from the site of a muscle which spinal cord segments innervate it.

General structure of the brain

Like the spinal cord, the brain develops from the hollow dorsal neural tube of the embryo. Quite early in development, the anterior end of this tube shows three clearly identifiable enlargements: the forebrain, midbrain and hindbrain. The remnants of the interior of the tube are the hollow lateral and third ventricles of the forebrain, the midbrain 'aqueduct of silvius', the hindbrain fourth ventricle and the spinal canal. During development these cerebral enlargements subdivide further. The forebrain gives rise to the telencephalon (which later forms the cerebral hemispheres and basal ganglia) and the diencephalon (which develops into the thalamus and hypothalamus); the midbrain develops into the mesencephalon which forms the tectal region (superior and inferior colliculi), midbrain reticular formation and cerebral peduncles; whilst the hindbrain gives rise to the pons, cerebellum and medulla.

The meninges

The entire brain is contained in, and suspended and protected by, three membranes, the meninges, known as the dura mater, arachnoid mater and pia mater. The innermost, the pia mater, envelops neural elements themselves. The arachnoid mater lies outside the pia, enclosing the subarachnoid space which contains cerebrospinal fluid (c.s.f.). This fluid, whose composition is controlled more closely than that of blood as a result of the blood–brain barrier, is secreted by *choroid plexuses* in the ventricular system of the brain, flows from there into the subarachnoid space surrounding the brain and spinal cord, and is reabsorbed into the venous sinuses by the arachnoid villi. The blood–brain barrier (Fig. 1.4) is not a single anatomical entity but refers to the protection afforded by the combined effect of the cerebrospinal fluid (c.s.f.) and extra layers of arachnoid and pial membrane interposed between the blood capillaries and nerve cells in the brain. Thus the brain floats in c.s.f. and is chemically and mechanically protected by it. Furthermore, wherever blood vessels enter the brain, continuations of the pial and arachnoid membranes accompany them, forming an important part of the blood–brain barrier. The outer meninx is the dura mater, which lies immediately underneath the cranium and spinal canal. Within the layers of dura are formed the venous sinuses, which drain blood from the brain and reabsorb c.s.f. through the arachnoid villi.

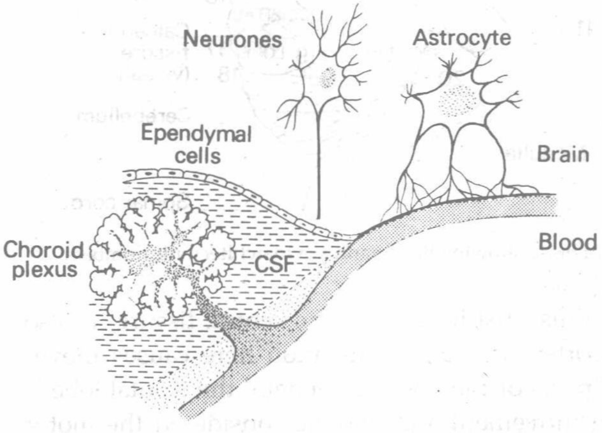

Fig. 1.4. The blood–brain barrier. Neurones are separated from blood by c.s.f., ependymal cells and astrocyte processes surrounding blood vessels.

The cerebral hemispheres (Fig. 1.5)

The left and right cerebral hemispheres are the most conspicuous structures in the human nervous system. It is their complexity and size which provides us with consciousness and our superior ability to adapt and react to changing circumstances, and to profit from the previous experiences not only of ourselves, but also of others with whom we can communicate complex ideas by speech and writing.

The hemispheres are separated from each other by the longitudinal (or sagittal) fissure. This deep cleft is crossed by the corpus callosum, which is a large band of fibres connecting the two hemispheres. Within the hemispheres lie the lateral and third ventricles and the basal ganglia, thalamus and hypothalamus. The cerebral cortex is greatly increased in area by folding into convolutions (gyri), which are separated by fissures (sulci). The lateral sulcus (Sylvian fissure) is the most prominent of these and separates the temporal lobe from the frontal, parietal and occipital lobes above it. The second largest is the central or Rolandic fissure which passes downwards, laterally and slightly forwards from a point about a third of the way between the frontal and occipital poles. It delineates the frontal lobe from the parietal lobe posterior to it. The parietal lobe is separated from the occipital lobe behind it by the parieto-occipital sulcus.

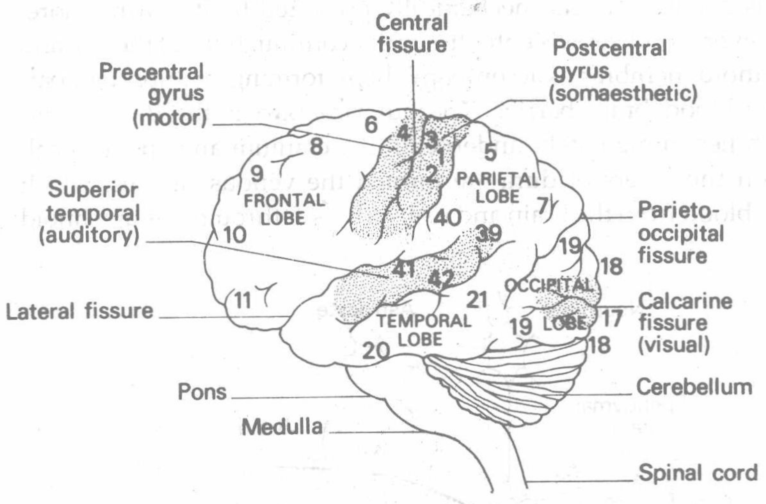

Fig. 1.5. External view of brain showing Brodmann's cytoarchitectonic numbers.

The precentral gyrus, just in front of the central fissure, is also called the motor cortex, because stimulation here causes movements of different parts of the body. In general the frontal lobe is most active during movement and may be considered the motor part of the cerebral cortex. Behind the central sulcus in the postcentral gyrus, lies the primary somaesthetic sensory area; in the superior temporal gyrus lies the primary auditory receiving area; whilst at the very back of the occipital lobe, surrounding the calcarine fissure, lies the primary visual cortex. Between these specialized sensory regions lie large areas of 'association' cortex. Thus areas behind the central sulcus are mostly devoted to sensation rather than movement.

Basal ganglia (Fig. 1.6)

The basal ganglia or deep cerebral nuclei (cf. deep cerebellar nuclei) are paired masses of grey matter lying within the cerebral hemispheres. The most prominent of these is the corpus striatum which consists of the caudate nucleus and putamen, separated from each other by the internal capsule. These project to the globus pallidus which lies medial to them, and this in turn mainly projects medially to the thalamus.

Thalamus (Fig. 1.6)

The thalamus is a large, oval structure lying above the hypothalamus and medial to the basal ganglia, beside the lateral and third ventricles. It develops from the diencephalic division of the forebrain, and almost all fibres passing to the cerebral hemispheres relay in one of its many nuclei (as shown in Fig. 8.8). These include nuclei relaying specific sensory information [the lateral geniculate (vision), the medial geniculate (hearing), the ventroposterolateral (somaesthesia)]; motor afferent nuclei (the ventrolateral and ventroanterior); nuclei supplying association cortex (the pulvinar, dorsomedial and anterior); and non-specific nuclei which project to other thalamic nuclei and to the basal ganglia (the intralaminar and reticular).

Hypothalamus (Fig. 1.6)

The hypothalamus is a small portion of the diencephalon forming the floor and lower part of the wall of the third ventricle. Like the thalamus, it consists of many small nuclei. These are responsible for many of the homeostatic functions of the body by regulating the autonomic nervous system and the hormone orchestra, and by influencing drives and emotions, such as eating, drinking, defence, sexual behaviour and sleep.

Midbrain (Fig. 1.7)

The midbrain or mesencephalon extends from the upper pons to the lower border of the hypothalamus. The most conspicuous features of its ventral part are two huge fibre bundles, the cerebral peduncles, which carry motor fibres away from the cerebral cortex and sensory fibres towards the thalamus. On the dorsal surface of the midbrain (also called the tectum or tegmentum) lie the superior (visual) and inferior (auditory) colliculi, together called the corpora quadrigemina. Within the substance of the midbrain lie two motor nuclei, the red nucleus and substantia nigra (black nucleus), and the

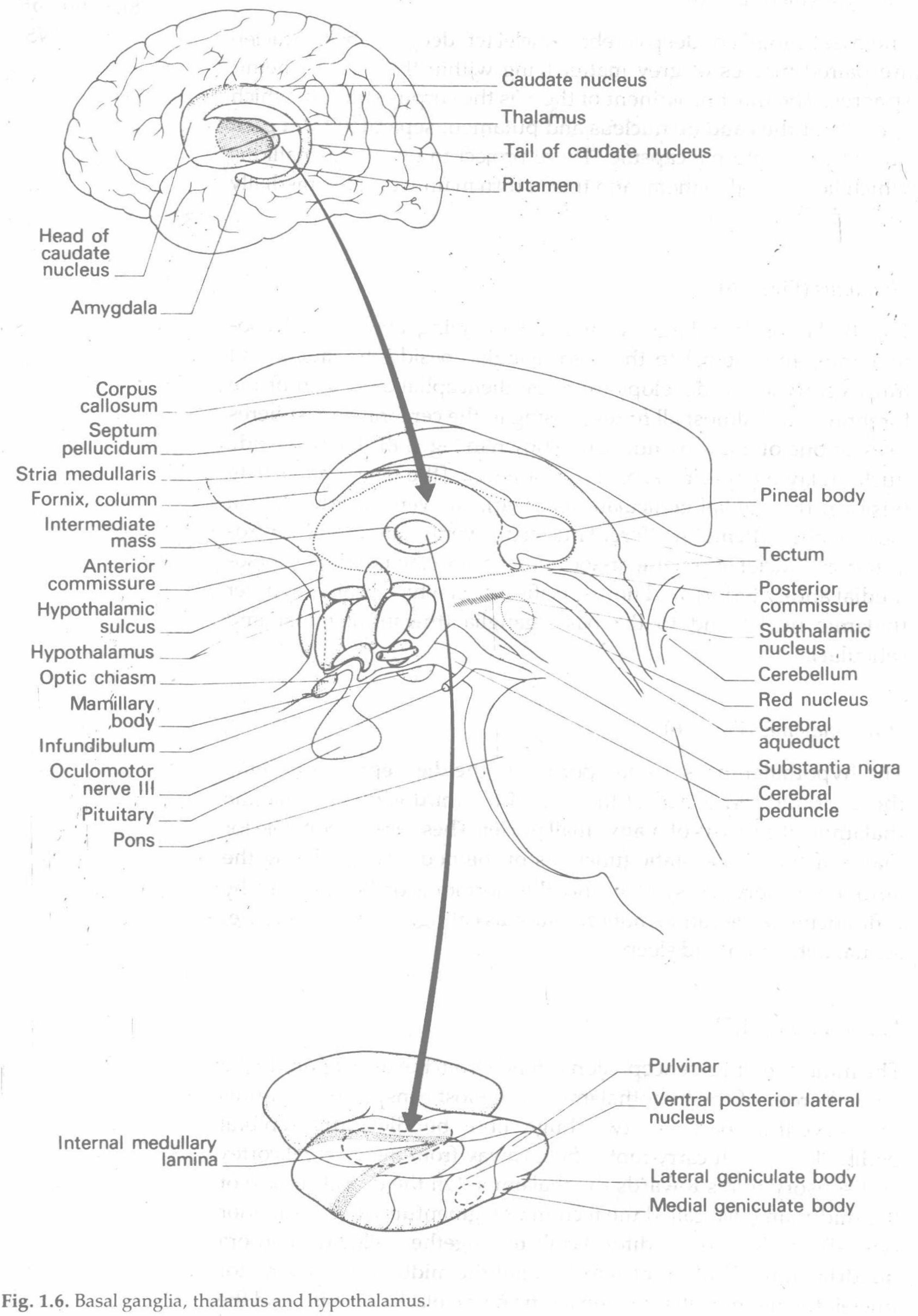

Fig. 1.6. Basal ganglia, thalamus and hypothalamus.

nuclei of the third and fourth cranial nerves, which supply extrinsic and intrinsic muscles of the eyes.

Pons varioli (Fig. 1.7)

The pons appears to form a bridge between the two halves of the cerebellum, hence its name. Its most obvious feature is the band of fibres on the ventral surface connecting the pontine nuclei within it to the cerebellar hemispheres via the middle cerebellar peduncles. The pontine nuclei receive signals from the cerebral cortex destined for the cerebellum. Through the pons pass the motor and sensory fibres which form the cerebral peduncles in the midbrain. It also contains nuclei of the Vth, VIth, VIIth and VIIIth cranial nerves and motor nuclei in the pontine reticular formation which participate in postural, cardiovascular and respiratory control.

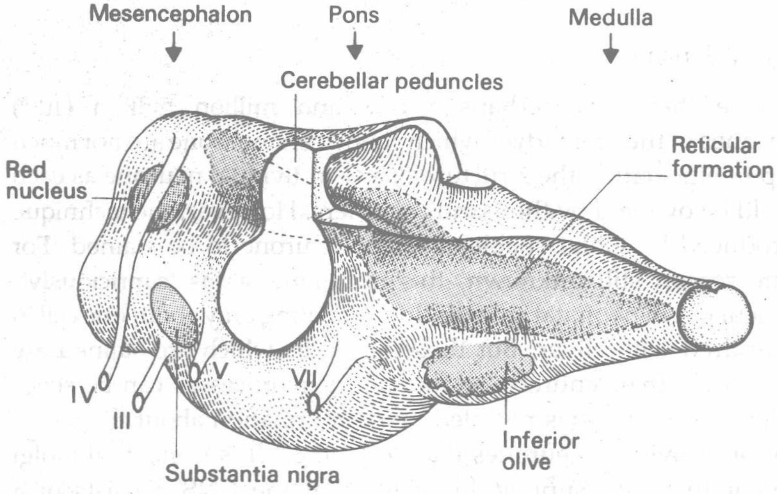

Fig. 1.7. The brainstem.

Medulla oblongata (Fig. 1.7)

The medulla is continuous with the pons above and the spinal cord below and therefore carries all the ascending and descending tracts which communicate between the spinal cord and brain. On its ventral surface lie two roughly pyramid-shaped structures, the 'medullary pyramids', which are the 10% of corticofugal fibres remaining after the rest of those passing through the cerebral peduncles have left the pons to supply the cerebellum and other brainstem motor structures. Just above the junction of the medulla with the spinal cord, at the pyramidal decussation, most of the left-hand-side pyramidal tract fibres cross over to the right and vice versa. They then form the lateral corticospinal tract in the lateral column of the spinal cord. Above this decussation, somaesthetic fibres relaying in the dorsal column nuclei also decussate to form the medial lemniscus, which passes upwards towards the thalamus. Thus these sensory fibres come to lie on top of the medullary pyramids.

In addition, the medulla contains nuclei of the Vth, IXth, Xth, XIth and XIIth cranial nerves, another large relay of signals destined for the cerebellum (the inferior olive) and further dispersed collections of cell bodies separated by a network of fibres, which participate in respiratory, cardiovascular and postural control (the medullary reticular formation).

NEUROANATOMICAL METHODS

Study of the intact or coarsely sliced brain has now revealed most of what it can. However, examination of the brain's intimate structure by light and electron microscopy remains extremely fruitful.

Golgi technique

Because there are perhaps a thousand million million (10^{15}) neurones in the brain, dyes which stain every neurone are not much help in elucidating the structure of any individual neurone as each would be overlaid by thousands of others. However, the technique introduced by Golgi enables a single neurone to be stained. For some reason still unknown, this technique stains 'capriciously', particularly in neonatal animals, impregnating only about one cell in a hundred with silver. But those few cells which are stained are outlined in their entirety, so that all their processes can be seen. Golgi's technique has revealed more information about the structure of individual neurones than any other. It is ironic that Golgi used it to try to support his belief that the CNS consists of a continuous network of fibres with a continuous cytoplasm (a 'syncytium'), rather than many thousands of discrete but contiguous neurones as suggested by Schwann's *cell theory*.

Neurone doctrine

Ramon y Cajal, who laid the foundations of much of our knowledge of the structure of the nervous system, exploited Golgi's technique to demolish the nerve net theory and to substantiate in its place the 'neurone doctrine'—the cell theory applied to the nervous system. He realized that the Golgi method stained whole individual neurones but not their neighbours, and therefore that all neurones must be separate from one another. He was able to demonstrate that each neurone receives signals from others via its dendrites, transfers them to its cell body or *soma* and dispatches the signals onwards, sometimes great distances, via its axon (Fig. 1.3) which then makes