NEUROPHYSIOLOGY:

The Fundamentals

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Preface and Acknowledgments

The student of medicine, biomedical science, or allied health is asked to master an enormous amount of material. Presented as textbooks, lectures, handouts, and examinations, the material may appear bewildering in variety and overwhelming in quantity. In an attempt to deal with it, the student may passively remember bits and pieces but never master the essential concepts of the subject matter. This is especially true in neurophysiology, which has a terminology of its own and combines elements of anatomy, physics, chemistry, psychology, neurobiology, and neurology, as well as physiology. Textbook treatments are often wordy and replete with poorly defined abstractions.

This book is designed to assist the beginning student in several ways. Each chapter contains a concise, concrete, and well-illustrated discussion of a particular topic in neurophysiology. The aim is to be clear about essentials rather than encyclopedic in scope. The chapters can stand by themselves as an introduction to neurophysiology, especially for those in allied health courses and readers who do not need more detail, or can be followed by more detailed sources. Examples from everyday life, medicine, and laboratory research contribute to the meaningfulness of the material. Each chapter ends with a set of review exercises—items to describe, explain, list, draw, and so on. The best way to learn is to do something with the subject matter, whether by experiments, clinical practice, or, as with the exercises, by describing the material to yourself and others. The exercises can serve as a guide to study in which you participate actively, as well as a basis for review before examinations. If you can satisfy the objectives of these exercises, you will have a mastery of a basic core of neurophysiology.

It is a pleasure to acknowledge a number of people who contributed to the production of this book. Barbara Lavine provided encouragement and moral support, as well as practical assistance with several figures and the index. Richard A. Kenney, Ph.D., encouraged me to begin and carry through the enterprise and provided illuminating discussions of the material. Reading and helpful criticisms of all or part of the manuscript were provided by Dr. Kenney and by Rebecca Anderson, Ph.D., Marie M. Cassidy, Ph.D., Paul Mazel, Ph.D., Lawrence Rothblat, Ph.D., Paul F. Teychenne, M.D., and Penelope S. Myers, M.A. These colleagues were aware of the limitations imposed on each topic by the introductory nature of the book, and the author takes responsibility for the accuracy of the outcome. Sharon Reutter assisted with library research and editing. Medical, graduate, and allied health students provided a responsive audience for which this material was developed.

Special thanks are due to Virginia L. Schoonover and Judith Guenther for their expert rendering of most of the figures in the book; to Debra Fink, Selma Klein, and Lisa Landau for their skilled typing of the manuscript; and to Sarah Boardman and her editorial colleagues at The Collamore Press for their advice and support in carrying the book to completion.

Contents

1. Structure and Function

How the nervous system is designed to communicate information and control activity

The Cellular Structure of the Nervous System

Neurons

The building blocks of the nervous system are the nerve cells or neurons. Neurons are specialized to generate and carry information by means of electrical and chemical signals. A typical neuron, as shown in figure 1–1, consists of an enlarged area called the *cell body* (or soma), which contains the nucleus and much of the metabolic machinery of the cell; the *dendrites,* several short, thin extensions that divide into branches like a tree and receive information from other neurons; and the *axon,* a specialized thin extension that transmits neural signals for a relatively long distance, after which it divides into several branches that end on other cells. The axon shown in figure 1–1 is covered by segments of an insulating lipid material, the *myelin sheath,* and arises from the cell body at the *axon hillock,* a cone-shaped region, followed by the *initial segment,* a short length of bare axon before the myelin-covered length of axon begins.

Variations on this basic scheme can be found. For example, the axon may lack a myelin sheath; the axon may be short; or the cell body (in spinal sensory neurons) may be placed to one side of the axon.

Synapses

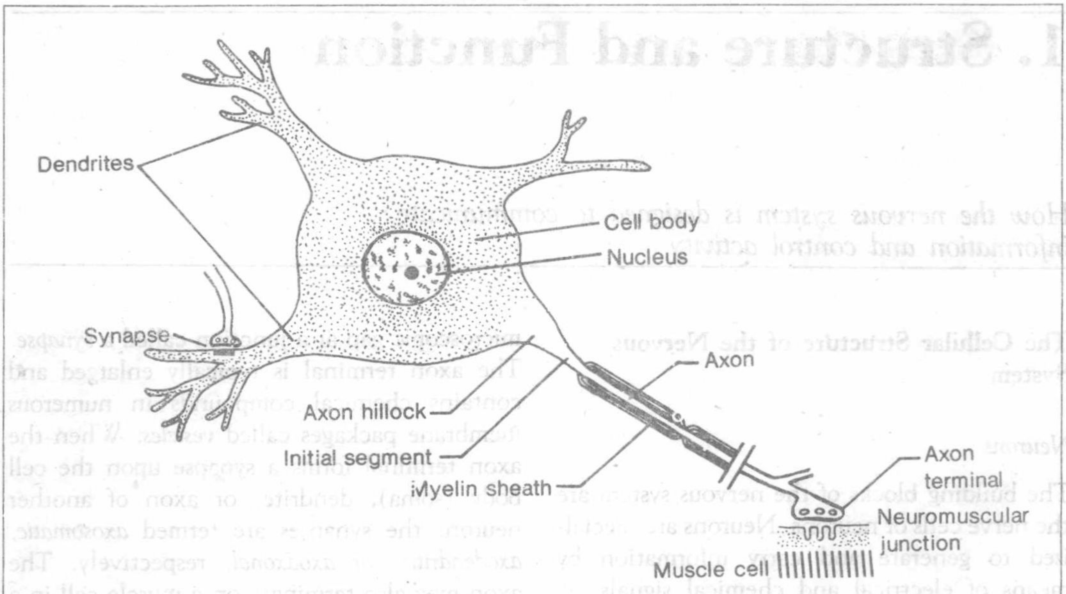
The axon of one neuron (or its branch) communicates with another neuron across a microscopic gap at a junction called a *synapse.* The axon terminal is typically enlarged and contains chemical compounds in numerous membrane packages called *vesicles.* When the axon terminal forms a synapse upon the cell body (soma), dendrite, or axon of another neuron, the synapses are termed *axosomatic, axodendritic,* or *axoaxonal,* respectively. The axon may also terminate on a muscle cell in a synapse called a *neuromuscular junction,* or on a gland cell.

Receptors

Sensory receptors are structures that convey information about the outside world and the interior of the body to the spinal cord and brain (figure 1–2). Anatomically, they include a wide variety of types: free nerve endings; nerve endings associated with capsules, hair follicles, muscle fibers, or other cells; and highly modified nerve cells, such as the rods and cones of the retina. Each sensory receptor is specialized to receive a particular type of stimulus (touch, light, sound, chemicals, or others) and translate it into an electrical signal. After modification, these signals are carried into the spinal cord and brain by sensory nerve axons associated with the receptors. Thus, receptor activity is the initial input stage of the nervous system.

Effectors

Moving, talking, and facial expression are controlled by *muscle fibers,* one form of effector



A

Figure 1–1. (A) *Diagram of a typical neuron, showing cell body, dendrites, synapse, axon with myelin sheath and axon terminal, and a neuromuscular junction.* (B) *Photomicrograph of an alpha motoneuron in ventral horn of cat spinal cord. Four dendrites emanate from the cell body. Arrow points to the axon, at the junction of the initial segment with the myelinated portion.* (C) *Photomicrograph of a bundle (or fascicle) of myelinated axons, forming a small peripheral nerve, shown in cross-section. Dark borders around each axon are myelin sheath. White circle in center of bundle is a blood vessel. The nerve shown is cranial nerve IV (trochlear) of the rat, which supplies eye muscle fibers; it contains an average of 270 axons, the largest of which are 10 μ in diameter. Courtesy of Dr. James M. Kerns.*

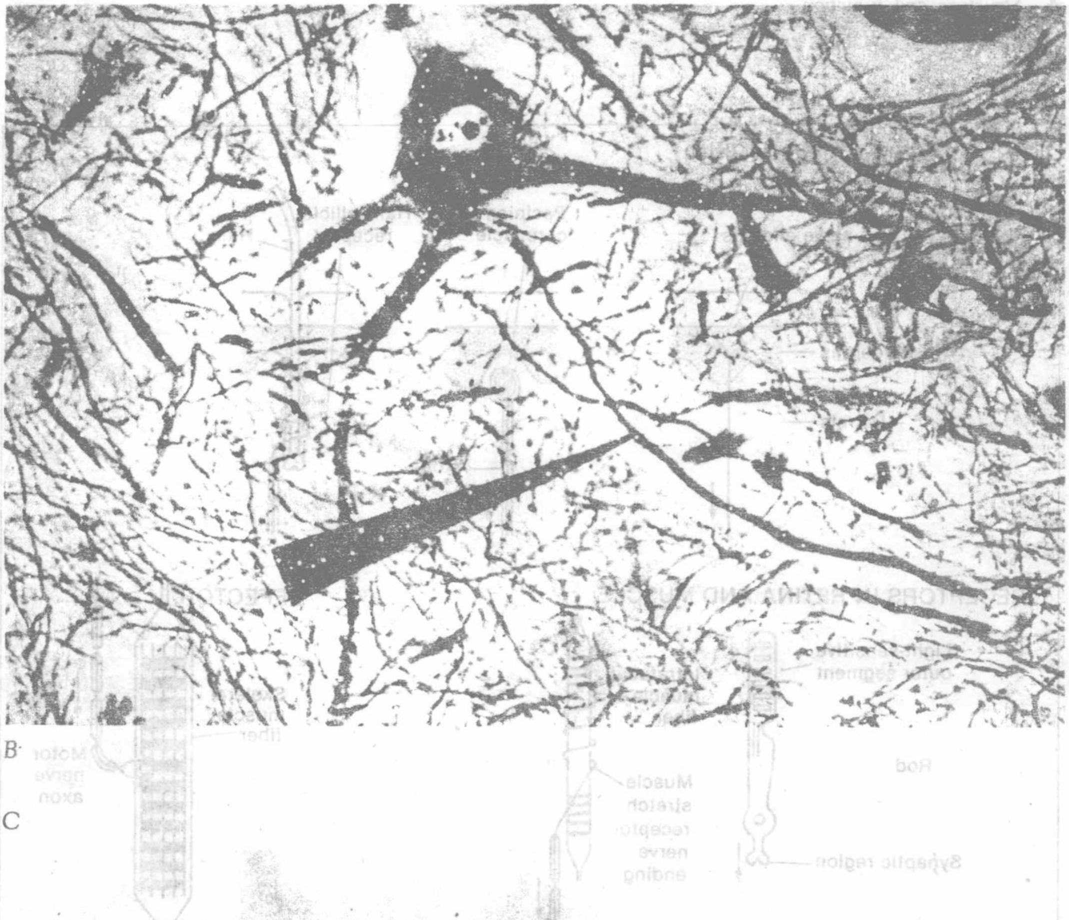
(figure 1–2). In addition, the internal environment of the body, including blood pressure, metabolic rate, and body temperature, is controlled not only by muscle fibers but also by the secretions of *glands*, another form of effector. The effectors are the means by which the nervous system exerts an effect on both the outside and inside environments. Their activity represents the final output of the nervous system.

General Plan of the Nervous System

The two main divisions of the nervous system are the *peripheral nervous system* (PNS) and the *central nervous system* (CNS) (figure 1–3).

The Peripheral Nervous System

The peripheral nervous system (PNS) consists of the *peripheral nerves,* bundles of axons (nerve fibers) that function to carry signals back and forth between peripheral organs (receptors and effectors) and the central nervous system. These nerve fibers are subdivided according to the peripheral organs on which they end: *somatic* nerve fibers supply skin, skeletal muscles, tendons, and joints, and visceral nerve fibers supply the gut and other *visceral* organs. Classified according to function, *afferent* nerve fibers carry sensory information to the central nervous system (input), while *efferent* nerve fibers carry motor-command signals from the central nervous system to the effectors (out-



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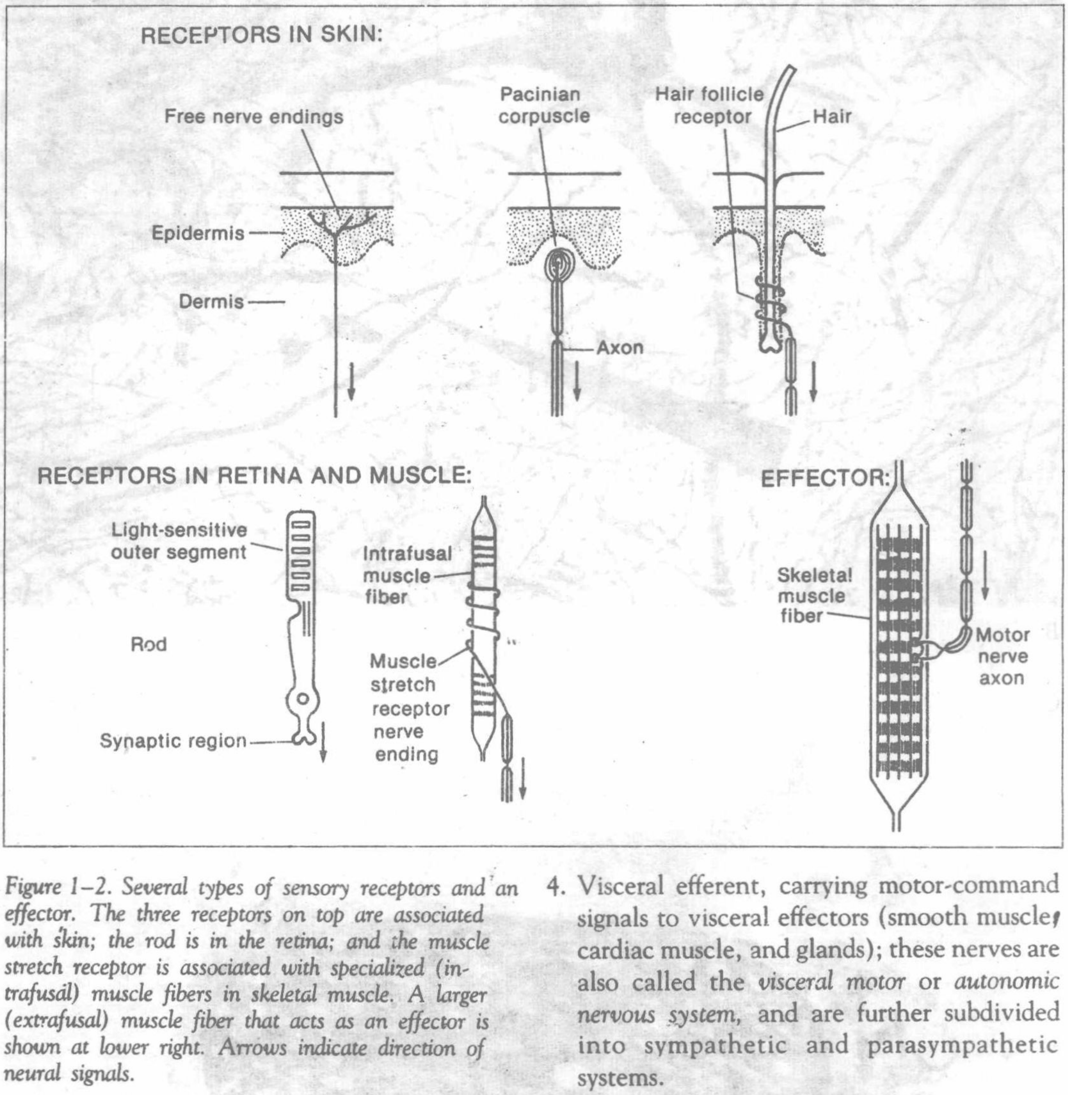
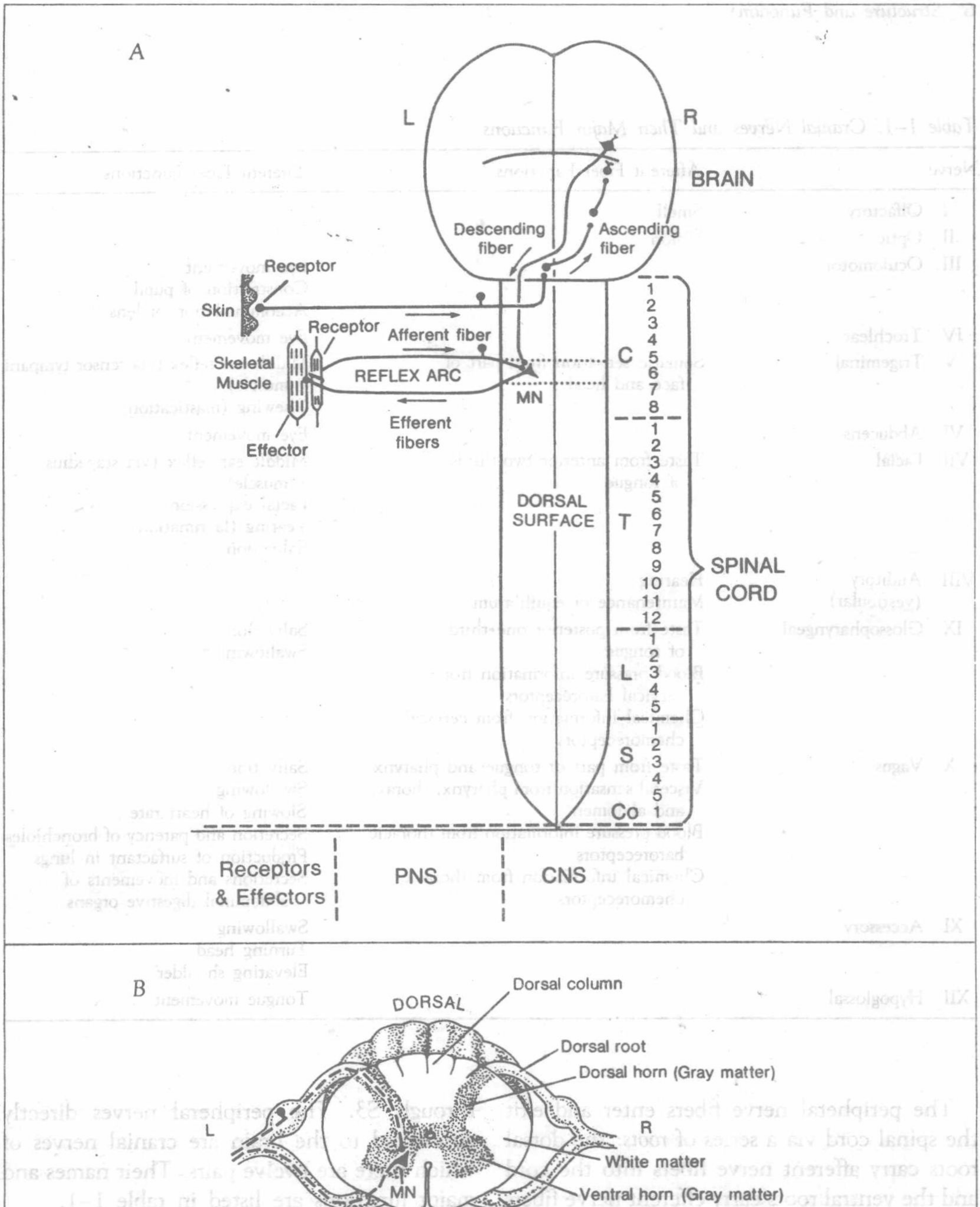


Figure 1–2. Several types of sensory receptors and an effector. The three receptors on top are associated with skin; the rod is in the retina; and the muscle stretch receptor is associated with specialized (intrafusal) muscle fibers in skeletal muscle. A larger (extrafusal) muscle fiber that acts as an effector is shown at lower right. Arrows indicate direction of neural signals.

put). There are then four types of peripheral spinal nerve fiber:

1. Somatic afferent, carrying sensory information from skin, skeletal muscles, tendons, and joints
2. Somatic efferent, carrying motor-command signals to skeletal muscles
3. Visceral afferent, carrying sensory information from the visceral organs
4. Visceral efferent, carrying motor-command signals to visceral effectors (smooth muscle, cardiac muscle, and glands); these nerves are also called the *visceral motor* or *autonomic nervous system*, and are further subdivided into sympathetic and parasympathetic systems.

Figure 1–3. (A) *Diagram of nervous system as seen from dorsal surface (not to scale), divided into peripheral nervous system (PNS) and central nervous system (CNS), consisting of spinal cord and brain. Spinal segments are* **C** = *cervical,* **T** = *thoracic,* **L** = *lumbar,* **S** = *sacral, and* **Co** = *coccygeal. Only somatic afferent and efferent fibers are shown.* **MN**, *motoneuron (alpha motoneuron controlling muscle fibers in arm). Ascending fibers shown carry sensory information from spinal cord to somatic sen-*



sory cortex of brain; descending fiber shown carries motor information from motor cortex of brain to spinal motoneuron. (B) A segment of spinal cord, corresponding to section within dotted lines in A. White matter contains axons, gray matter contains cell bodies, dendrites, and synapses. Within gray matter, dorsal and ventral horns are shown; within white matter, dorsal column is shown. Dorsal root contains afferent fibers, and ventral root contains efferent fibers originating in motoneurons; dashed lines indicate individual fibers corresponding to those shown in the reflex arc in A. Enlarged area (ganglion) of dorsal root contains cell bodies of afferent fibers. Dorsal and ventral roots join to form peripheral nerves.

Table 1–1. Cranial Nerves and Their Major Functions

Nerve	Afferent Fiber Functions	Efferent Fiber Functions
I Olfactory	Smell	
II Optic	Vision	
III Oculomotor		Eye movement Constriction of pupil Accommodation of lens
IV Trochlear		Eye movement
V Trigeminal	Somatic sensation from part of face and head	Middle-ear reflex (via tensor tympani muscle) Chewing (mastication)
VI Abducens		Eye movement
VII Facial	Taste from anterior two-thirds of tongue	Middle-ear reflex (via stapedius muscle) Facial expression Tearing (lacrimation) Salivation
VIII Auditory (vestibular)	Hearing Maintenance of equilibrium	
IX Glossopharyngeal	Taste from posterior one-third of tongue Blood pressure information from cervical baroreceptors Chemical information from cervical chemoreceptors	Salivation Swallowing
X Vagus	Taste from part of tongue and pharynx Visceral sensation from pharynx, thorax, and abdomen Blood pressure information from thoracic baroreceptors Chemical information from thoracic chemoreceptors	Salivation Swallowing Slowing of heart rate Secretion and patency of bronchioles Production of surfactant in lungs Secretions and movements of abdominal digestive organs
XI Accessory		Swallowing Turning head Elevating shoulder
XII Hypoglossal		Tongue movement

The peripheral nerve fibers enter and exit the spinal cord via a series of *roots:* the dorsal roots carry afferent nerve fibers into the cord and the ventral roots carry efferent nerve fibers from the cord. The roots are labeled according to associated segments of the vertebral column: cervical (C), thoracic (T), lumbar (L), sacral (S), and coccygeal (Co). They are numbered within each segment (C1 through 8; T1 through 12, L1 through 5, S1 through 5, and Co-1). The arm is innervated by spinal nerves C4 through T1 and the leg by nerves L2 through S3. The peripheral nerves directly connected to the brain are cranial nerves of which there are twelve pairs. Their names and major functions are listed in table 1–1.

The Central Nervous System

The central nervous system (CNS) consists of the brain and spinal cord (figure 1–3A), each of which is enclosed in a bony covering, the brain within the skull and the spinal cord within the vertebral column. Both are divided at the midline into a left and right half and have surfaces labeled *dorsal* (toward the back) and *ventral* (toward the front).

Within the CNS are *white* and *gray areas*. The white areas contain bundles of nerve axons (also called *nerve fibers*); their color is imparted by the myelin sheath around the nerve fibers. There are several anatomical terms for specific bundles of nerve fibers within the CNS, such as *tract, column, fasciculus, lemniscus,* and *radiation.* The gray areas contain the cell bodies of neurons, their dendrites, and associated synapses.

In cross-section, the gray areas in the spinal cord form a butterfly-shaped area in the center of the cord, surrounded by a ring of white matter (figure 1–3B). The white matter contains bundles of axons passing up and down through the cord connecting areas of the cord with each other and with the brain, while the central gray area contains numerous synaptic regions. Thus, a sensory signal may enter the cord through a dorsal-root nerve axon that (1) travels up to the brain in an ascending column or tract or (2) enters the gray area to synapse on other nerve cells. Within the brain, gray areas consist of cell bodies and synapses organized into *nuclei* (clusters) and *layers* (in the surface of the cerebrum and cerebellum).

The brain is the highest level of the CNS. It is the organ ultimately responsible for movement, perception, and thought. The brain has four major divisions (figure 1–4):

1. The *brainstem* partially resembles an extension of the spinal cord upward into the head. It is composed of the medulla, pons, and midbrain. Like the spinal cord, the brainstem contains white bundles of nerve fibers (called lemnisci, tracts, and so on) carrying signals both up and down, gray nuclei containing cell bodies and synapses, and the roots of peripheral nerves—the cranial nerves—arranged in a more complex fashion than the spinal nerves and carrying information from the eyes and ears as well as other sources. Within the core of the brainstem a network of nerve cells called the *reticular formation* is essential in regulating wakefulness and sleep, respiration, and cardiovascular function.
2. The *cerebellum* is a globular structure connected to the dorsal surface of the brainstem by bundles of nerve fibers. Its surface is covered with folds, so that it partly resembles a ball of twine. A major function of this organ is to correct errors so that movement proceeds in a smooth and controlled manner—so that the hand, for example, can reach for and pick up a cup without spilling the contents.
3. The *thalamus* and *hypothalamus*, together called the *diencephalon*, are gray areas containing nuclei (clusters of cells) located above the brainstem and near the center of the brain, surrounding the walls of the third ventricle. The thalamus is a major relay

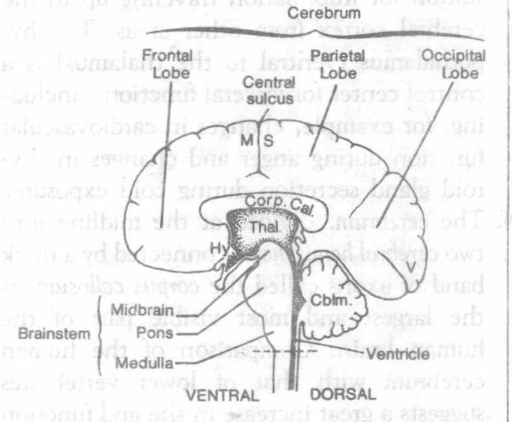


Figure 1–4. The right half of the brain in diagrammatic form, as seen from the left (a midsaggital section). Abbreviations: **Cblm.** *= cerebellum,* **Thal.** *= thalamus,* **Hy.** *= hypothalamus,* **Corp. Cal.** *= corpus callosum,* **M** *= motor cortex,* **S.** *= somatic sensory cortex,* **V.** *= visual cortex. Temporal lobe not shown. The ventricles contain cerebrospinal fluid. Dashed line shows juncture of spinal cord and brain.*

station for information traveling up to the cerebral cortex from other areas. The hypothalamus (ventral to the thalamus) is a control center for visceral functions, including, for example, changes in cardiovascular function during anger and changes in thyroid gland secretion during cold exposure.

4. The *cerebrum,* divided at the midline into two *cerebral hemispheres* connected by a thick band of axons called the *corpus callosum,* is the largest and most visible part of the human brain. Comparison of the human cerebrum with that of lower vertebrates suggests a great increase in size and function in the course of evolution. The outer surface or cerebral *cortex* is known as the gray matter because of its layers of nerve cells. The surface area of the cortex is increased by its numerous folds (gyri), separated by grooves (sulci and fissures). Beneath the cortex is the white matter, consisting of nerve fibers traveling to and from the cells in various parts of the cortex. Each cerebral hemisphere is divided into four lobes (figure 1–5): the *occipital* (at the back of the head), the *parietal* (top), the *temporal* (sides), and the *frontal* (at the front of the head, behind the forehead). The cortex contains motor areas that govern voluntary movement and keep reflex movements under control, sensory areas that register incoming information from sensory receptors (with separate areas for vision, hearing, body sensation, and so on), and association areas that associate information from several sources and carry out such higher functions as the understanding of speech and the recognition of objects. Within the white matter are gray areas that contain clusters of cells and synapses and are divided into nuclei. Between the sides of the thalamus and the cerebral cortex are the *basal ganglia,* containing several nuclear structures that help to regulate posture and movement. Below the surface of the tip of the temporal lobe is the *amygdala,* containing nuclei that can influence such behaviors as fighting and eating; the amygdala is part of the limbic system, a group of primitive structures within the cerebrum.

Neural Signals

The nervous system uses signals to transmit information. Information is transmitted from the outside world into the nervous system (by means of sensory processes), from one part of the nervous system to another, and from the nervous system back to the outside world (by means of motor processes). The signals are carried by the nerve cells, including their extensions, the dendrites and axons. In everyday life, signals include traffic lights, Morse code, and the electronic pulses within computers. In the nervous system, signals can be divided into action potentials, graded receptor potentials, graded synaptic potentials, and chemical transmitter release.

Action Potentials

Like one of the voltaic cells in a battery, the nerve cell at rest is electrically charged across its membrane. The charge gives rise to an electrical potential difference, a *membrane potential,* measured in *millivolts* (thousandths of a volt, abbreviated mV). The magnitude of this potential difference ranges from 55 mV to 90 mV, with the inside of the cell negative compared with the outside. This membrane potential is altered by the *action potential,* a brief reversal of polarity that sweeps along the nerve axon (figure 1–6).

The action potential is triggered by electrical or other stimuli above a certain strength. When neural signals need to be transmitted over long distances, such as from one end of an axon to another, the signals used are action potentials.

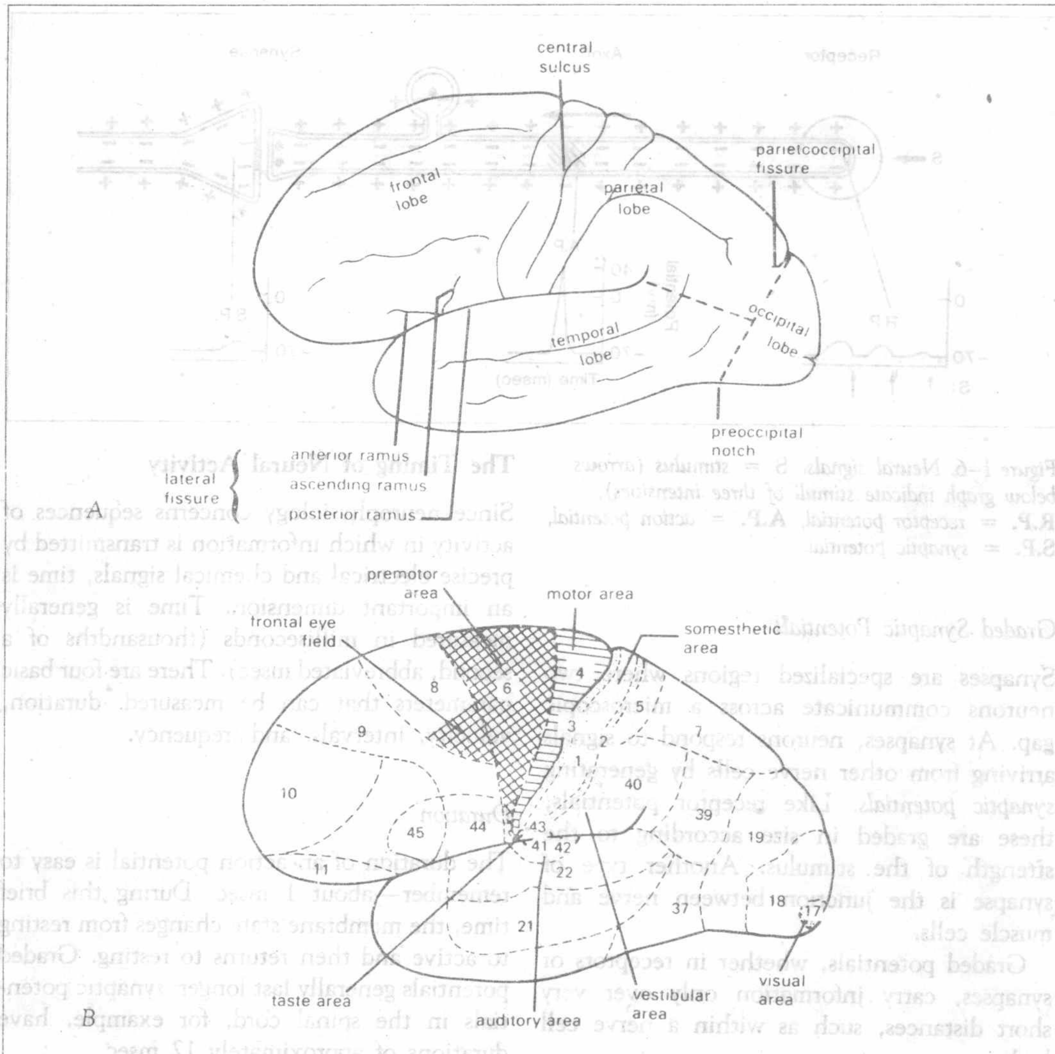


Figure 1–5. Lateral views of the left cerebral hemisphere. (A) Division into lobes; sulcus and fissure are terms for grooves in the cortex; the lateral fissure has three rami or branches. (B) Subdivision into areas based on function (auditory, visual, and so on) and on the structure of cell layers, or cytoarchitecture, with numbers given by Brodmann. From Barr, M.L. The Human Nervous System: An Anatomic Viewpoint (3rd ed.). Hagerstown, Md.: Harper & Row Publishers, Inc., 1979. Reprinted with permission.

Graded Receptor Potentials

In neurons specialized to receive sensory stimuli (receptors), stimuli can produce a change in membrane potential called a *receptor potential.* The change is graded in size, depending on the stimulus. For example, in receptors sensitive to pressure on the skin, the greater the pressure the greater the potential change (figure 1–6).

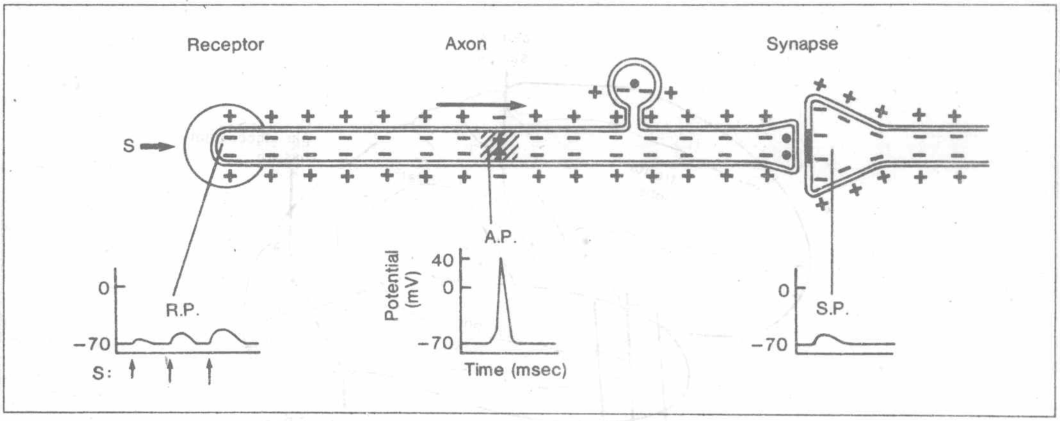


Figure 1–6. Neural signals. S = *stimulus (arrows below graph indicate stimuli of three intensities),* **R.P.** = *receptor potential,* **A.P.** = *action potential,* **S.P.** = *synaptic potential.*

Graded Synaptic Potentials

Synapses are specialized regions where two neurons communicate across a microscopic gap. At synapses, neurons respond to signals arriving from other nerve cells by generating *synaptic potentials.* Like receptor potentials, these are graded in size according to the strength of the stimulus. Another type of synapse is the junction between nerve and muscle cells.

Graded potentials, whether in receptors or synapses, carry information only over very short distances, such as within a nerve cell body.

Chemical Transmitter Release

The synaptic gap between neurons is generally crossed by chemical transmitters (for example, acetylcholine or norepinephrine). When an action potential reaches the end of a nerve axon, it causes the release of a chemical transmitter stored in the axon ending, which diffuses across the synaptic gap to the next nerve cell. Chemical transmitters, therefore, carry information from cell to cell.

The Timing of Neural Activity

Since neurophysiology concerns sequences of activity in which information is transmitted by precise electrical and chemical signals, time is an important dimension. Time is generally measured in milliseconds (thousandths of a second, abbreviated msec). There are four basic parameters that can be measured: duration, velocity, intervals, and frequency.

Duration

The duration of an action potential is easy to remember—about 1 msec. During this brief time, the membrane state changes from resting to active and then returns to resting. Graded potentials generally last longer; synaptic potentials in the spinal cord, for example, have durations of approximately 12 msec.

Velocity

The action potential is conducted along axons at velocities ranging from about 1 to 100 m/sec, depending on the structure and function of the axon. For example, among different fibers in peripheral nerves, those conducting at a velocity of about 100 m/sec may carry muscle-length information; those conducting at about 50 m/sec may carry touch and pressure information; and those conducting at about 1 m/sec

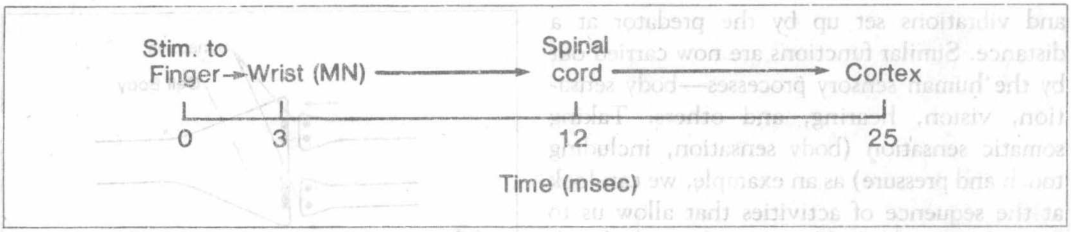


Figure 1–7. The time sequence of neural responses along a sensory pathway. MN = *median nerve. (Neural responses at cervical spinal cord and somatic sensory cortex are averaged evoked potentials, obtained by computer processing of electrical signals recorded with disc electrodes on the skin).*

may carry pain and temperature information. These velocities are slowed down in certain diseases and therefore can be useful in clinical diagnosis.

Intervals

Time intervals in neural transmission can be precisely measured, even from outside the body. For example, recording electrodes on the skin can be used to measure the intervals between an electrical pulse applied to the fingertip and the action potentials at several stages of the sensory pathway. The action potential is first conducted from the digital nerves in the finger to the median nerve, from which it can be recorded at the wrist after an interval of about 3 msec (figure 1–7). After about 25 msec, a neural response can be recorded over the appropriate area of the cerebral cortex. When the time interval and the distance between two points along the peripheral nerve are determined, distance can be divided by time to calculate the conduction velocity. For the pathway to the cerebral cortex, the time interval includes synaptic delays as well as nerve-conduction time.

In a single nerve cell, the time intervals between action potentials depend on two factors: the properties of the nerve cell and the strength of the stimulus affecting it. A stronger stimulus generally causes a shorter interval between action potentials.

Frequency

Frequency can be defined as the number of events per second. In the case of action potentials in a single nerve cell, the frequency is the number of action potentials per second and is the inverse of the mean interval between action potentials; the frequency is high when the intervals are short. Thus, a stronger stimulus generally causes a higher frequency of action potentials. Another way of approaching this is to say that the frequency of action potentials generally acts as a code, transmitting information about the strength of a stimulus. (Inhibition and other factors modify this code in ways that will be discussed in later chapters.)

In the case of electrical waves recorded from the brain as part of the electroencephalogram (EEG), the frequency is the number of waves or cycles per second (c/s). A well-known type of EEG pattern consists of alpha waves, occurring at about 10 c/s. Different levels of sleep or wakefulness are associated with higher or lower EEG frequencies.

The components described thus far can be further organized according to three overall processes: sensory, motor, and higher.

Sensory Processes

A primitive animal creeping along the ocean floor has a reasonable chance of survival if it can escape when brushed by a larger predator, and a greater chance if it can sense the shadows