Principles of Neuroanatomy

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Preface

This book is written to provide an outlook on neuroanatomy for medical students, advanced undergraduates, and any others who desire some basic explanations of the fundamental principles of organization and plans of circuitry of the nervous system. A concise and convenient compilation of such generalizations should provide a useful supplement to the student's conventional neuroanatomy texts, a guidebook for anyone seeking a simple, integrated sampling of a complex subject, and even (we hope) a new view or a review for experts.

In neuroanatomy, basic principles are all too easily lost. Our goal is to distill from the seemingly endless detail the central facts, concepts, and principles of neural organization that make neuroanatomy the fundamental and enjoyable science of brain function that it is. Most, but certainly not all, of these principles have been known for many years, and are satisfying philosophically for their beauty of natural order. When brought out from the undergrowth of facts, they make neuroanatomy a meaningful topic where before it was mostly memory and mystery. The straightforward features reflected in the overall design of the nervous system give the student encouragement and a sense of purpose in learning the plethora of names and welter of pathways, from which at some point we know there can be no escape.

In our presentation, frequent analogies and comparisons are made with everyday matters. We try to carry over into our text certain informal qualities that come out when we are lecturing to medical and biology students. At these times, such rough-and-ready explanations of neural function are often the best ways to get the message across. Its informality notwithstanding, this book is as accurate as we can make it, contains what we believe are the most important concepts, and reflects our impressions of the latest outlooks of neuroscience.

A special effort has been made to provide an overview of the organization of neurotransmitter subsystems in the nervous system. This extremely important information is now an integral part of neuroanatomy. Our respective backgrounds in neuroanatomy and neurochemistry have encouraged us to combine our views of this exciting horizon on the brain.

This work grew out of a previous effort in which we collaborated on sections of an introductory psychobiology text, *Behavioral Neuroscience* (Academic Press, Inc., 1980). In presenting neuroanatomy at an elementary level for that text, we felt that an easy style provided an attractive view of neuroanatomy, one that encouraged the student to like the subject. Thus, we decided to undertake this book, striving for an overview, a light, clear style, and good illustrations. In places, we have retained sentences or expressions from Chapters 2 and 18 of the earlier book, because we found that we could not say certain things better or express ourselves more clearly.

We hope this book can be used for many years—as an adjunct to standard texts, as a checklist of basics for students and teachers, and as a primer for students and scientists from other fields. Last but not least, we think of all those people who ask so many questions about the brain. If they can find answers in this volume, or at least a new perspective that makes them glad they asked, we shall feel well repaid.

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Tucson, Arizona J.B.A.
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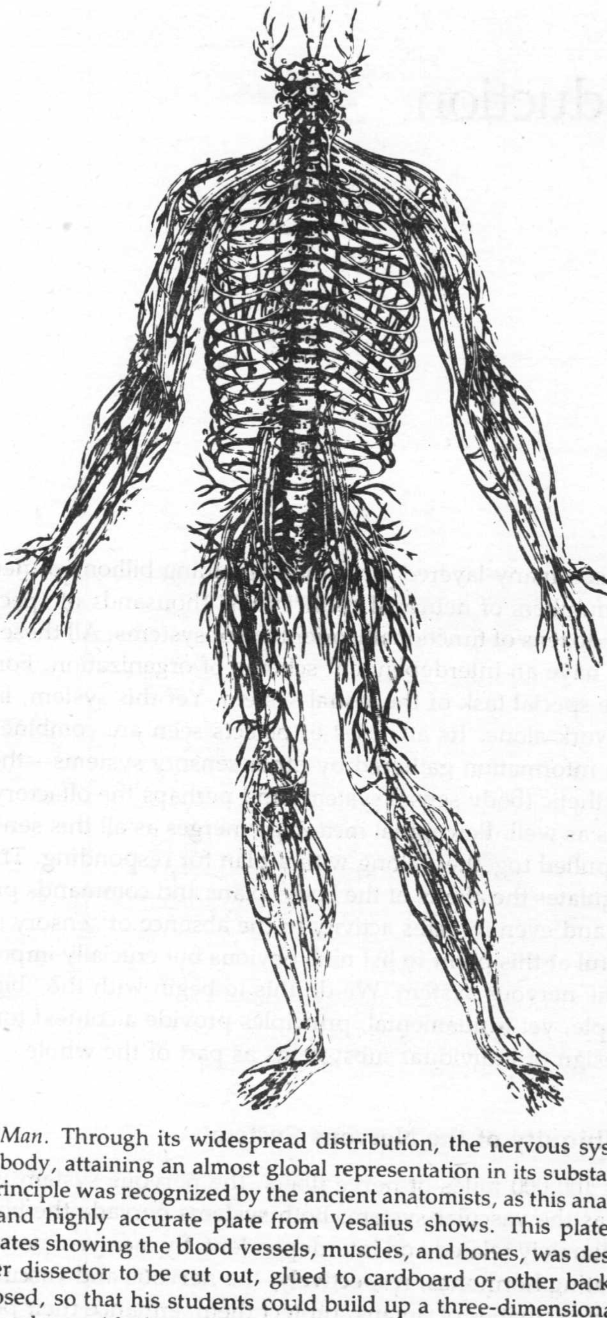
Introduction

The brain is a many-layered structure containing billions of neurons and countless numbers of neuronal connections, thousands of specialized regions, and dozens of functionally oriented subsystems. All these elements, moreover, have an interdependent scheme of organization. For example, sight is the special task of the visual system. Yet this system, like others, does not work alone. Its analyses of objects seen are combined at some point with information gathered by other sensory systems—the auditory and somesthetic (body sense) systems and perhaps the olfactory and gustatory ones as well. Perceptual meaning emerges as all this sensory information is pulled together, along with a plan for responding. The nervous system regulates the affairs of the body, plans and commands programs of response, and even initiates activity in the absence of sensory stimuli.

It is useful at this point to list nine obvious but crucially important attributes of the nervous system. We do this to begin with the "big picture." These simple, yet fundamental, principles provide a context for considering the design of individual subsystems as part of the whole.

1. The Ubiquity of the Nervous System

With over 100,000 miles of nerve fibers, the nervous system is nearly as extensive as the vascular system. Both systems pervade the body, and in fact are intimately related and interdependent. By means of nerve impulses and circulating hormones, respectively, the nervous and vascular systems integrate the activities of organs, protect them, enhance their performance



The Nerve Man. Through its widespread distribution, the nervous system pervades the body, attaining an almost global representation in its substance. This cardinal principle was recognized by the ancient anatomists, as this anatomically beautiful and highly accurate plate from Vesalius shows. This plate, as well as other plates showing the blood vessels, muscles, and bones, was designed by that master dissector to be cut out, glued to cardboard or other backing, and superimposed, so that his students could build up a three-dimensional picture of the body along with the intricate details of anatomy.

to meet stress or exercise demands, promote their growth, and maintain their healthy tone and vigor.

The central masses and myriad outreaching threads of the nervous system trace not only the external form of the body, but nearly every structure and feature in it (see accompanying figure). However, the density of nerve supply varies from place to place according to local tissue requirements. The degree of innervation in a body region signifies how large a role that region has in sending or receiving neural messages. In places liberally supplied with nerve endings (such as the cornea, lip, or bed of a nail), stimuli are almost always felt, and can be especially painful. In places not well supplied by nerve fibers (such as the thigh or buttocks), stimuli are less well discriminated, and when they lead to pain are often more easily tolerated. Similarly, muscles vary in the numbers of nerve fibers relative to muscle fibers; the higher this ratio, the more delicate the control of the muscle and the movements in which it is employed.

2. The Unity of the Nervous System

All parts of the nervous system are linked so that each part (at least potentially) can be in touch with every other. Some connections are quite direct, while others involve many intervening neurons. But although its circuitry is complex, the nervous system has total connectivity, thus offering body-wide communication.

A message from any body part enters the peripheral nervous system (PNS) and travels centrally over its network of branches until it reaches the brain or spinal cord, depending on where the message came from. Once inside the central nervous system (CNS), the message is analyzed there. How? By a process called integration, whereby central neurons combine and compare messages from many sources. In this process, some messages go to nearby points through local circuits, others to remote locations over long-distance lines. Ultimately, instructions are sent back to muscles and glands. Thus, though the transactions are often complex and unpredictable, activity in one part of the body can affect, through the agency of the nervous system, the activity of the other parts. Out of all these neural transactions comes a unified body, its parts working in harmony.

3. Centralization of the Nervous System

The term central nervous system is no coincidence. Indeed, the basic design plan of the nervous system is centralization. In delivering appropriate and all-encompassing responses, the nervous system generally does not allow for local transactions between body parts without involvement of the CNS. The system does not provide direct peripheral "hookups" over which, let us say, the index finger and thumb could hold a private conversation. Except for the passage of nerve impulses from one point along a nerve to another, incoming signals from one part of the body seldom reach another part directly, no matter how close that other part may be. Exceptions to this principle relate to local responses to painful stimuli. The swelling, reddening, and itching/burning feeling following irritation of the skin are associated with inward conduction of nerve impulses for short distances along a nerve fiber, and then outward conduction over a branch of that same fiber—along with release of substances related to tissue damage. This cutaneous "triple response" is either primitive or quite advanced.

But mainly, the signals that go out to body parts are not the same as the sensory messages that entered the CNS beforehand. On the contrary, such outgoing signals convey instructions drawn up by a multitude of central neurons in various brain regions. Some of these neurons not only monitor the incoming signals, but also keep track of others received simultaneously, earlier, or later from other parts of the body. And these multimodal neurons may be under directives from still other parts of the CNS itself, as to plans in the making. The result is a comprehensive analysis derived from a well-centralized organization.

4. Structural Specialization of the Nervous System

From the single neuron to the entire system, the nervous system displays structural and functional specialization. Sensory stimuli are processed by specialized subsystems (the visual system, auditory system, etc.). Less obvious are the special circuits for particular types of activities—eye movements, respiration, pain modulation, and affect, to cite just a few contrasting examples.

Structural specialization includes adaptations for speed of processing (as in a reflex), dependability (as in parallel processing and cellular redundancy), and peripheral feedback (as in closed-loop circuits). The neurons that carry out these functions are as structurally specialized as the subsystems themselves. In fact, neurons and their myriad connections are the foundation of specialization.

5. The Purposefulness of Neural Components

Each specialized component of the nervous system has a definite function, though we do not yet appreciate the task of each and every part. While the essential structural relationships—neurons, neuronal processes, synapses, and so forth—have been known for years, much of neuroanatomy is yet unknown. New information continues to emerge rapidly, particularly regarding the relationship of function to structure. Often, the maze of detail seems meaningless, and even bothersome at the time it is learned. Nevertheless, it has always turned out that each part of the nervous system has an important role, and thus understanding each part contributes to the understanding of the whole. Each neural component, therefore, is both necessary and functional.

6. Precision of the Nervous System

The vertebrate nervous system is accurately and reproducibly assembled. In animals of the same species and genetic background, the nervous system is virtually identical. There are marked variations between species, but the general properties and overall organization are sufficiently similar to develop generalizations, albeit careful and well considered ones. In man, there may be much more individual variation in brain structure, but still the common themes far exceed the differences.

Much of our knowledge of human neuroanatomy is derived from analysis of pathways and structures in other mammals and extrapolation of these findings to man. One of the great frontiers in modern science is to identify and understand in more detail the unique features of the human brain.

7. Plasticity of the Nervous System

Though reliable, the circuitry of the nervous system displays an inherent modifiability or plasticity. Abnormal visual experience early in development, for example, can produce remarkable changes in the synaptic organization of the visual cortex (Chap. 5). Such inherent plasticity probably permits the repair or fine tuning of circuits for certain changing functions—for example, depth perception must be recalibrated as the head grows and interpupillary distance changes. Neuroanatomy is just beginning to identify the adaptive modifications of the nervous system which occur with maturation and aging. Moreover, following injury, nerve fibers (probably more than we realize) can sprout new connections and rearrange old ones, not only in the periphery but in the CNS itself.

8. Chemical Coding of Neural Circuitry

Function is determined not only by a neuron's structure, integrative properties, and connections, but by the transmitter it delivers. This chemical messenger may exert brief, focused effects or long-lasting, generalized influences on the target nerve cell. All neural circuitry is chemically coded (Chap. 14), and the new neuroanatomy is being written in terms of connections *and* transmitters.

9. Metabolic Demands of the Nervous System

An important aspect of neuroanatomy is the vasculature of the nervous system, the set of vessels providing delivery of nutrients and removal of waste products. As we might expect, the metabolic requirements of the nervous system, in terms of substances needed and energy consumed, are high relative to those of the total body. About a fifth of the oxygen that we extract from each breath and a fifth of the calories (in the form of glucose) that we ingest as food each day are the prodigious expenses we pay for the ceaseless activity and readiness (with no need for warmup) of the system. This constant and almost unvarying need for oxygen and glucose by the nervous system (whether we are asleep or awake, relaxed or busy solving problems) is met by a rich blood supply (see Chap. 15). In keeping with these figures, the circulatory system brings about a fifth of the blood pumped from the left ventricle directly to the brain, and it supplys additional amounts of blood to the spinal cord and all the craniospinal nerve branches as well.

This list of organizing principles is by no means complete, but it does call attention to some remarkable attributes of the system. In this text, we shall refer back to these basic principles, and point out others. All are worth keeping in mind: they afford perspective and make the subject meaningful.

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Basic Principles and Elements

Neurons

The design of the brain is in large measure the design of its constituent neurons (Fig. 1-1), although its supportive neuroglial cells probably have greater importance than we know. Neurons, truly remarkable cells, are the fundamental genetic, anatomical, functional, and trophic (nutritive or sustaining) units of the nervous system. These characteristics are the four tenets of the neuron doctrine, a once-controversial restatement of the cell theory applied to nervous tissue around the turn of the century.

One truth emerges more than any other: the variety of cell structure in the nervous tissue, central or peripheral, is far more complex than that seen in any other tissue. Whereas cells in other tissues, such as red blood cells, are highly redundant, nerve cells are highly individualized. In certain neural regions, they approach, or even attain, "zero redundancy." There are many specialized populations of neurons, and within a population single cells express their own individuality, both by their position in some circuit(s) and by their form. It is, above all, this neuronal specialization that gives the system its speed, fidelity, and flexibility as well as its integrative capacity.

In order to understand such complex cells as neurons, it helps to have some means of categorization. There are many classifications, and each has its limitations. Nonetheless, it is useful to distinguish two major classes: *projection neurons* with axons coursing between one region of the CNS and another, and *local-circuit neurons* with axons extending to other cells in the immediate vicinity.

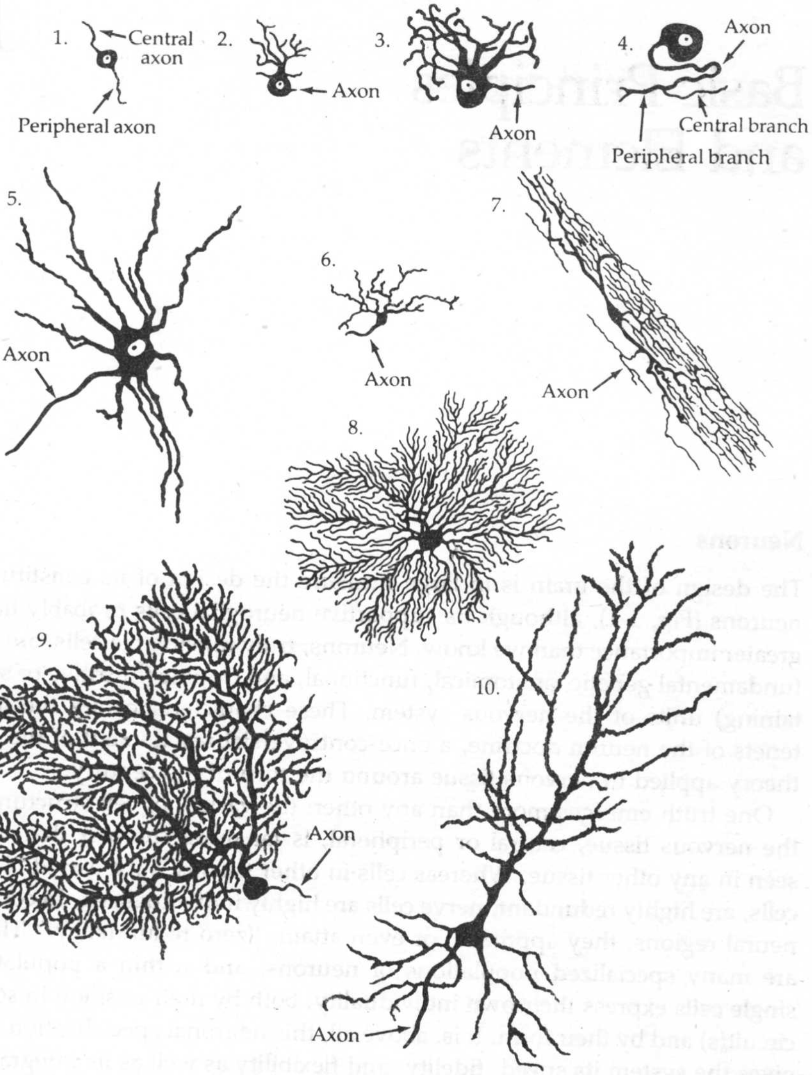

FIG. 1–1. *Neurons and neuronal variety.* Scaled drawings of neurons to illustrate their great diversity. (1) Bipolar neuron in nodose ganglion of vagus nerve. (2) Parasympathetic neuron. (3) Sympathetic neuron. (4) Pseudounipolar neuron of trigeminal ganglion. (5) Spinal motor neuron. (6) Small neuron in substantia gelatinosa of spinal trigeminal nucleus. (7) Spindle-shaped neuron from nucleus of tractus solitarius. (8) Cortical projection neuron in thalamus. (9) Purkinje cell from cerebellum. (10) Pyramidal cell from cerebral cortex. (Cells redrawn from S. Ramón y Cajal and also from C. Fox, Wayne State University)

Projection neurons and local-circuit neurons are not classified on the basis of cell size, length of axon or type of contact; it is only their role in either long-distance or local communication that separates them. A projection neuron is often large, with a long axon, and a local-circuit neuron is frequently small, with a short axon; but these features do not necessarily go together.

This scheme is different from, but not inconsistent with, the traditional one of sensory neurons, motor neurons, and interneurons (see below). It can be traced back to the concepts of early neuroanatomists. Faced with the astonishing richness of neuronal types in the CNS, the Italian histologist Camillo Golgi suggested late in the 19th century that nerve cells be classified according to the length of their processes. At about the same time in Spain, Ramón y Cajal similarly grouped all neurons into long-axon and short-axon cells. While the discoveries and thoughts of these scientists, and others of their time, are outside the scope of this book, many of their ideas are still with us today.

Projection Neurons and the Parts of Neurons

Most large neurons are projection neurons, and such big cells fit into the "classic" mold of a neuron: they have a long axon, a cell body, and dendrites emanating from that cell body. These cells are thus multipolar, have many synaptic endings on their dendritic tree, and send impulses to one or more places over their axon. Motor neurons, pyramidal cells in the cerebral cortex, and Purkinje cells in the cerebellar cortex are familiar examples.

The several major parts of a typical projection neuron are readily identifiable. The cell body is developmentally the earliest part of the neuron to arise, and it is the trophic part that maintains the life of the neuron and its often far-flung processes.

The dendrites form treelike arborizations, which are often marvelously elaborate; they are the primary receptive processes of the neuron. They afford contact points (synapses; see below) for the terminals of incoming nerve fibers (axons), and for other fibers passing by the dendrites to different destinations. They act as minicomputing centers to receive and integrate all the different inputs. In CNS neurons, dendrites originate from the cell body as one or more primary branches, which in turn branch and become finer and finer. Most nerve fibers arriving at dendrites terminate on spines — minute thorns of the dendrite's surface that serve as highly specialized ports of entry for afferent signals. As one might expect, the