S.L. Palay · V. Chan-Palay

Cerebellar Cortex

Cytology and Organization

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«... on ne peut, ni l'on ne pourra jamais parler du cervelet sans que Cajal ne vienne au devant, et quiconque l'ignorerait serait forcément obligé à coïncider avec lui sur beaucoup de points, soit dans l'interprétation, soit dans les faits qui constituent les fondaments de toutes les constructions scientifiques.»

CLEMENT ESTABLE 1923
Trab. Lab. Invest. Biol. (Madrid)
vol. XXI, p. 187.

« Malheureusement pour moi, d'autres, courant la même carrière, virent plusieurs des choses que j'avois vuës, & s'étant fait un plan moins étendu, m'enlevèrent, en publiant leurs observations, une espèce d'honneur que je croiois avoir également mérité.»

PIERRE LYONET 1762
from the preface to *Traité anatomique de la Chenille, qui ronge le Bois de Saule.*
Pierre Gosse, jr. et Daniel Pinet, La Haye.

Preface

The origins of this book go back to the first electron microscopic studies of the central nervous system. The cerebellar cortex was from the first an object of close study in the electron microscope, repeating in modern cytology and neuroanatomy the role it had in the hands of RAMÓN Y CAJAL at the end of the nineteenth century. The senior author vividly remembers a day early in 1953 when GEORGE PALADE, with whom he was then working, showed him an electron micrograph of a cerebellar glomerulus, saying "That is what the synapse should look like." It is true that the tissue was swollen and the mitochondria were exploded, but all of the essentials of synaptic structure were visible. At that time small fragments of tissue, fixed by immersion in osmium tetroxide and embedded in methacrylate, were laboriously sectioned with glass knives without any predetermined orientation and then examined in the electron microscope. After much searching, favorably preserved areas were studied at the cytological level in order to recognize the parts of neurons and characterize them. Such procedures, dependent upon random sections and uncontrollable selection by a highly erratic technique of preservation, precluded any systematic investigation of the organization of a particular nucleus or region of the central nervous system. It was difficult enough to distinguish neurons from the neuroglia. Even so, much was learned about the fine structure of the nerve cell, especially about the perikaryon, axons, and dendrites, and, most important for the purpose of this book, about the structure of the synapse.

During the past twenty years vast improvements in technique have made it possible to study all parts of the nervous system at the fine structural level. Now we are able to fix the tissue before fragmenting it, thus retaining the orientation of its components. That signal improvement has made it relatively easy to recognize types of cells and their processes with the minute clues found in thin sections, whereas before it was generally impossible. Improved fixing solutions, embedding and staining methods, as well as refinements in the electron microscope itself, have greatly increased the number and subtlety of the discriminations that can be made, so that many details formerly nonexistent in the electron micrographs were now useful in identifying structures. All of this technical advance, to which we have been privileged to contribute, has made it possible to attempt such a work as the present volume.

Concentrated labor on this book began in the autumn of 1969, when the senior author was joined in this endeavor by the junior author. With this collaboration, the pace of the investigation was greatly accelerated. Vast numbers of Golgi preparations and electron micrographs were made, permitting a fruitful interplay between traditional optical microscopy and electron microscopy.

Actually, the book was conceived a long time ago as a comprehensive demonstration presented to the annual meeting of the American Association of Anatomists in April 1964 at Denver (PALAY, 1964a). Some fifty electron micrographs of cells, fibers, and synapses in the cerebellar cortex were exhibited. During the display a well-known elder statesman of the traditional neuroanatomical school came by and, casting a

scornful glance at the micrographs, came out with "Well, what have you learned that we didn't know before?" In vain to tell him about the synapses of parallel fibers on Purkinje cell thorns, or about a new understanding of the glomerulus, or a fresh view of the pericellular basket and the pinceau, or about a thousand other points. It had all been worked out by RAMÓN Y CAJAL almost a century before. Nor were anatomists the only ones who thought that such investigation was futile. In the late 1950's a well-known neurophysiologist chided the senior author for working on the structure of the cerebellum. "Why do anatomists," he asked, "always like to study the cerebellum? Nothing interesting goes on there!" In the intervening years a great many investigators, both morphologists and physiologists, have found new and interesting things in the cerebellar cortex, so much, in fact, that the literature on the subject has burgeoned beyond the ability of anyone to cope with it. Once again the notion is prevalent among neuroanatomists that the subject is exhausted. This book is testimony to the fact that although much has been learned, a great many questions still go unanswered.

In the present volume each of the cell types and afferent fibers in the cerebellar cortex is taken up in turn and described. Both optical and electron microscopy are used and illustrated. A careful study of the cerebellar cortex with these two methods indicates that considerable reliance may be placed on the Golgi technique for the general architecture and the three-dimensional form of the cells and fibers. All of the known synapses are characterized and their function is discussed from the anatomical point of view. It would be presumptuous on our part to undertake a review of the electrophysiology of this cortex, although we have drawn freely upon the results and insights derived from that discipline. All of the drawings are original India ink tracings made with the aid of a camera lucida at high magnifications. They were prepared by the junior author especially for this book or for recent journal articles.

Finally, a word may be in order to explain our use of the laboratory rat for this study instead of the cat, which has long been the favorite of neurophysiologists. Besides believing that the cat is a most peculiar animal, we could claim a dangerous sensitivity to feline dander. But, more pertinently, the cerebellum of the rat has all of the essential machinery of the mammalian cerebellum. It is much more reliably preserved than that of the cat and there is no cytological advantage in studying the larger animal. Furthermore, our work may encourage neurophysiologists to make use of this lowly beast in which a great deal of fundamental biology has been explored.

It remains to acknowledge the support of our laboratory by research grant NS 03659 and training grant NS 05591 from the National Institute of Neurological Diseases and Stroke, Bethesda, Maryland. The composition of the manuscript was made possible by a fellowship from the John Simon Guggenheim Memorial Foundation, granted to the senior author while he was on sabbatical leave from the Harvard Medical School. We wish to express our gratitude to CAROL WILUSZ for her patient assistance in making counts and measurements, tracing fibers in Golgi preparations, and preparing the graphs; to PHOEBE FRANKLIN for her meticulous preparation of the typescript for publication and for her bibliographic searching. Finally, we should like to thank VICTORIA LI MEI PALAY for the use of Fig. 10.

Boston, September 1, 1973 SANFORD L. PALAY and VICTORIA CHAN-PALAY

Table of Contents

Chapter I

Introduction

Probably no other part of the central nervous system has been so thoroughly investigated and is so well known as the cerebellar cortex. For nearly a century all of its cell-types have been recognized, and the course and terminations of their processes have been described countless times by numerous authors. Yet unanimity on many doubtful points has not been reached. Most of our knowledge of the cerebellar cortex derives from the early work of RAMÓN Y CAJAL. It was, in fact, during the period of his first successes with the Golgi method, when RAMÓN Y CAJAL was seized with what he described in his autobiography as a *fièvre de publicité*, that the basic plan for the organization of the cerebellar cortex was worked out. Subsequent research has confirmed many of his intuitions and added only details. For a long time these observations and the plan of the cerebellar cortex that he derived from them were far in advance of the physiological understanding of this organ. The information that this cortex is divisible into three layers, each with its own distinct populations of cells, and that they are interconnected in a few simple neuronal chains was already sufficient to baffle comprehension. No one had any idea of how the cerebellar cortex should work or what operations it should perform with the impulses coming into it from diverse sources. The Sherringtonian concept that the cerebellum was somehow related to the maintenance of muscle tone, muscle coordination, equilibration, and proprioception balanced securely on a knowledge of afferent and efferent pathways that was already too encumbered with detail. The interpretation of coarse experiments with ablations and evoked surface potentials had no need for intracortical circuits (see, for example, FULTON, 1949, and DOW and MORUZZI, 1958).

1. A New Morphology

It is only in the past decade that a more precise knowledge of the anatomy of the cerebellar cortex has been required. Today we still have only glimmerings of how the cerebellar cortex operates and no clear vision of what its function is, but the situation with respect to anatomicophysiological correlations has vastly changed. Physiologists are now probing the activities of individual neurons and eavesdropping on the coordinated interchanges between the members of neuronal assemblies. A much more detailed and precise knowledge of the morphology of the cerebellar cortex is required now than hitherto in order to guide these experiments and to inform their results, as well as to contain the speculations that they induce in physiologists, cyberneticists, and morphologists alike.

This new level of morphology can be achieved by the exercise of three technical procedures—one ancient, the others relatively recent—which provide complementary views of the cerebellar cortex. The old technique is the Golgi method, which figured so strongly in the early advances in our knowledge of the cerebellar cortex, and the centenary of which should be celebrated this year. Although this method is still poorly understood, it has undergone a revival of interest and confidence during the past decade such as it has not enjoyed since the end of the nineteenth century. Its survival through this long period of neglect and antipathy is owing to a handful of adepts, whose painstaking observations kept it alive until the modern era of neurocytology reasserted its value. Even now the method has few practitioners and unnecessarily appears esoteric to the uninitiated. Important data are still to be derived from the careful study of Golgi preparations, especially when they are coordinated with the results of the more modern methods. The second method of present usefulness is the method of experimental degeneration, particularly the Nauta technique and its recent variants, for locating the terminal arborizations of axons within the neuropil. This technique provides essential data about the distribution of nerve fibers connecting one region of the nervous system with another. While these data are necessary for the location of terminals belonging to specific systems, they do not identify the actual sites of synapses. This deficit is filled by electron microscopy.

When expertly prepared, electron micrographs of thin sections display all of the nerve terminals synapsing upon any particular neuron and its processes, as well as the neuroglia. The various profiles can be classified according to their disposition, shape, and cytological content, and usually can be readily attributed to one or another part of a neuron or neuroglial cell. The problem is to identify the terminals according to their source and to recognize the neuron on which they synapse. Tracing fibers or cell processes for long distances to the cell of origin is usually impossible in the thin sections used for electron microscopy. Reconstruction of three-dimensional models from serial sections has a very limited usefulness. It is here that the complementarity of the three methods comes into play. By correlating the profiles seen in electron micrographs with the form and distribution of the neurons and their processes as learned from the application of Golgi and experimental degeneration techniques, it is possible to build up the pattern of synapses on perikarya and in the neuropil and to classify the profiles according to their sources. Thus a complete map of intercellular connections can be constructed and used in coordination with neurophysiological data to learn how the cerebellar cortex operates. In this book we have endeavored to provide such a map for an ordinary laboratory animal, the normal adult white rat.

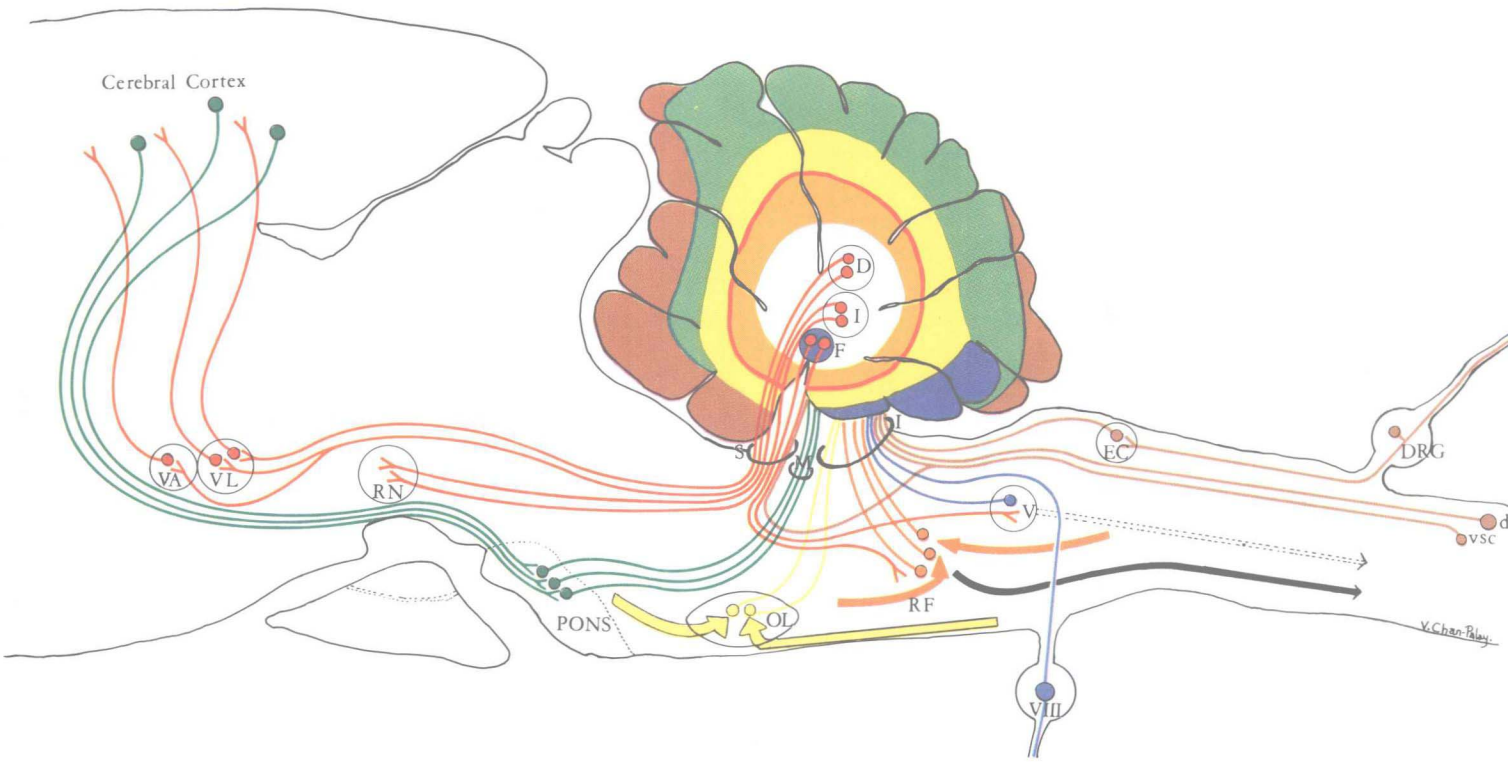

Fig. 1. Scheme of the afferent and efferent pathways of the cerebellum. This diagram summarizes the major cerebellar tracts. Although many details have been omitted for the sake of simplicity, the plan of the major cerebellar connections is presented. The afferent pathways to the cerebellum and the distribution of these fibers in the cortex of the vermis are indicated by their respective colors. Afferents from the spinal cord (brown) reach the cortex through (a) the dorsal spinocerebellar tract (*dsc*); (b) the cuneocerebellar tract; (c) the ventral spinocerebellar tract (*vsc*), a portion of which enters the cerebellum through the inferior cerebellar peduncle (*I*), and the rest through the superior cerebellar peduncle (*S*). A representative dorsal root ganglion cell (*DRG*) is shown projecting through the cervical spinal cord to the external cuneate nucleus (*EC*). Spinal afferents distribute in the cerebellar cortex in the anterior lobe and part of the posterior vermis (brown). Vestibular afferents (blue) include primary vestibular fibers from the VIIIth nerve ganglion (*VIII*) and secondary fibers from the vestibular nuclei (*V*). These fibers distribute to the fastigial nucleus (*F*) and flocculonodular lobe, nodulus, and uvula (blue). Afferents from the reticular formation (*RF*) enter the cerebellum and distribute throughout the cortex (orange). The reticular formation receives input from higher and lower centers (*orange arrows*). Fibers from the inferior olive (*OL*) (yellow) distribute to the entire cortex (yellow). Input to the olive comes from higher and lower brain centers (*yellow arrows*). All of the above inputs enter through the inferior cerebellar peduncle (*I*). Afferents to the cerebellum from the pons (green) enter through the middle cerebellar peduncle (*M*) to distribute to the entire cortex. The pons receives its input from the cerebral cortex (*green tracts*). The major efferents of the cerebellum (red) leave through the superior cerebellar peduncle (*S*). The fibers from the dentate nucleus (*D*) go to the ventrolateral nucleus (*VL*) and the ventroanterior (*VA*) nucleus of the thalamus. Fibers from the interpositus nuclei (*I*) go to the red nucleus (*RN*). Fibers from the fastigial nuclei reach the reticular formation (*RF*) and the vestibular nuclei (*V*). The reticulospinal tract (*black arrow*) and the vestibulospinal tract (*dotted arrow*) bring integrated information from the vestibular nuclei and reticular formation back down the spinal cord. (For further details, see text.)

As indicated above, the interpretation of electron micrographs requires the identification of nerve endings and other cell fragments in the random specimens provided by thin sections. Since any particular section contains only extremely small samples of thousands of fibers and cells, arranged in the most complex fashion and cut in various planes, how can they be recognized? What criteria have been developed to take advantage of the minimal clues in these sections? Of course, such discriminations proceed from established criteria for the recognition of the parts of neurons and neuroglial cells in electron micrographs. These have been reviewed in other publications (see PETERS, PALAY, and WEBSTER, 1970) and will not be repeated here. Once a profile has been recognized as a dendrite, axon, or other specific part of a cell, the next question concerns the identification of the cell type to which that part belongs. Although the chances for confusion at this point are great, the microscopist is very considerably assisted by the regular fabric of the cerebellar cortex. Our fundamental method consists of systematically cataloguing morphological features that consistently occur together until a constellation of traits has been discovered that is specific for each type of cell and its processes.

In preparations for the optical microscope, each cell type has a peculiar form, position, distribution, number, and internal structure. These distinctive characteristics must carry over to the level of electron microscopic analysis. Profiles in the thin sections must be consistent with the shapes of the cells or processes, their location, and course, as seen in Golgi preparations at the light microscope level. Thus, for example, the pattern of the Purkinje cell dendritic arborization is so distinctive in Golgi preparations that there is no difficulty whatever in recognizing its fragments in thin sections in the electron microscope. In addition, new characteristics emerge when the tissue is examined in the electron microscope—characteristics involving greater detail and differentiation of structures already known as well as new structures unsuspected because invisible or confused at the level of the light microscope. Thus the size, number, shape, and distribution of mitochondria can be important distinguishing characteristics of a particular dendrite or a perikaryon. The size, shape, and clustering pattern of synaptic vesicles, combined with the size, location, and interfacial characteristics of the synaptic junction, are critical features for the identification of the terminals of a particular type of fiber. The presence of neurofilaments or microtubules, the density or sparseness of a fibrillar cytoplasmic matrix, are other differential characteristics.

2. The Fiber Connections of the Cerebellar Cortex

Before beginning the fine structural analysis of the cerebellar cortex, it will be helpful to have an overview of its extrinsic and intrinsic connections. The fiber tracts leading to and from the cerebellar cortex connect it directly or indirectly with all of the major subdivisions of the central nervous system. These pathways are quite complicated, and many doubtful questions remain to be resolved. Even a superficial examination of these pathways could justifiably include a survey of the entire nervous system. Such a review is clearly beyond the scope of this volume, which is restricted to the fine structure of the cortex. For a detailed consideration of the pathways, the reader is referred to the chapter on the cerebellum in BRODAL's (1969) comprehensive text on neurological anatomy and to Volume III of LARSELL and JANSEN'S (1972) monumental treatise on the comparative anatomy of the cerebellum. Citations of the voluminous literature and a critical evaluation of the subject are to be found in these two works. For the present purpose, however, a few general statements are required in order to indicate the wide variety of sources from which the cerebellar cortex draws its information and to contrast that with the apparent simplicity of its architecture.

The afferent and efferent fibers of the cerebellum are drawn together into three pairs of massive fiber bundles, known as the cerebellar peduncles and named according to their relative positions in the human brain. In general, fibers leading impulses into the cerebellum enter by way of the inferior and middle peduncles, while fibers leaving the cerebellum exit by way of the superior peduncles. There are, however, exceptions, for example, certain spinocerebellar fibers that enter through the superior peduncles and certain efferent fibers from the flocculonodular lobe and fastigial nuclei that exit by way of the inferior peduncle. In general, also, the fiber paths ascending from spinal, reticular, and vestibular sources are ipsilateral, whereas those coming from the inferior olive and the pontine nuclei are contralateral. Similarly, the efferent pathways that lead to higher centers, such as the red nucleus and the thalamus, cross to the other side, whereas those descending to the vestibular nuclei and reticular formation remain ipsilateral. Here, too, there are exceptions, however, such as the uncinate fasciculus, which on leaving the fastigial nucleus crosses to the other side and distributes to the contralateral vestibular nuclei and reticular formation. Table 1 summarizes the major pathways and classifies them according to the peduncle through which they pass. Finally, although the organization of the cerebellar cortex is everywhere alike, the

Table 1. Fiber pathways of the cerebellum

Origin	Type of fiber/tract	Destination
Inferior peduncle		
Afferents:		
vestibular afferents primary (vestibular ganglion) secondary (vestibular nuclei)	mossy fibers/juxtarestiform body	cortex: flocculonodular lobe, ventral uvula, fastigial nucleus
spinal afferents dorsal nucleus of Clarke, external cuneate nucleus, intermediate dorsal gray	mossy fibers/dorsal and ventral spinocerebellar tracts	cortex: anterior lobe, vermis; part of posterior lobe, pyramis, uvula
lateral reticular nucleus (cerebral cortex, spinal cord)	mossy fibers	entire cortex
reticular formation	mossy fibers	entire cortex
inferior olive (cerebral cortex, spinal cord, caudate nucleus, globus pallidus, periaqueductal gray)	climbing fibers (crossed)	entire cortex
Efferents:		
Purkinje cells of flocculonodular lobe, lateral vermis	juxtarestiform body	vestibular nuclei
fastigial nucleus	restiform body	vestibular nuclei, reticular formation
Middle peduncle		
Afferents:		
pontine nuclei (cerebral cortex)	mossy fibers/(crossed) pontocerebellar tract	entire cortex, except flocculonodular lobe
Superior peduncle		
Afferents:		
spinal afferents intermediate dorsal gray	mossy fibers/ventral spinocerebellar tract (1/3)	cortex: anterior lobe
Efferents:		
interpositus nucleus	brachium conjunctivum (crossed)	red nucleus, thalamic nuclei VL and VA, other thalamic and midbrain nuclei
dentate nucleus	dentatorubral tract (brachium conjunctivum, crossed)	thalamic nuclei VL and VA and other thalamic and midbrain nuclei
fastigial nucleus	hooked bundle (crossed)	vestibular nuclei, reticular formation

projections of the different afferent systems follow a longitudinal plan. Each system distributes into a characteristic pattern of parallel rostrocaudal zones that cross the transverse folds of the cortex (VOOGD, 1969).

The afferent supply to the cerebellar cortex can be subdivided into four principal groups (Fig. 1): (1) vestibular (blue), (2) ascending spinal (brown), (3) descending pontine (green), and (4) olivary (yellow) and reticular (orange). These groups end in particular, sometimes overlapping parts of the cerebellar cortex, as is indicated in the color-coded diagram in Fig. 1. No attempt will be made here to detail the precise topographical distribution of these several projections onto the cerebellar cortex.

(1) The cerebellar cortex receives direct afferents from the labyrinth by way of primary vestibular root fibers, which end in the flocculonodular lobe and the ventral part of the uvula. The same parts of the cerebellar cortex also receive secondary afferents from certain regions of the medial and descending (inferior) vestibular nuclei. Since these regions of the vestibular nuclei are supplied not with primary vestibular fibers but with ascending spinal inputs, this second contingent should be included in the next large group of cerebellar afferents, the spinocerebellar fibers. Like them, all of the inputs to the cortex except for group 1 are indirect, involving one or more synaptic interruptions in their ascent or descent into the cerebellum.

(2) Impulses originating from the activity of muscle spindles, Golgi tendon organs, pressure and tactile organs in the skin and deeper tissues ascend through the spinal

cord by various spinocerebellar pathways to end in the anterior lobe and the posterior vermis. The most direct routes are by way of the dorsal and ventral spinocerebellar tracts, conveying information from the hindlimbs, and the very similar cuneocerebellar and rostral spinocerebellar tracts, concerned with the forelimbs. There is also a corresponding pathway leading from the secondary trigeminal nuclei to the same parts of the cortex.

(3) A massive descending bundle of afferents comes from the contralateral pontine nuclei, bearing information from all lobes of the cerebral cortex. These fibers are distributed to all parts of the cerebellar cortex except for the lingula and the flocculonodular lobe.

(4) The last great group of afferents consists of projections from the contralateral inferior olive to all lobules of the cerebellar cortex, and conveys influences from both ascending and descending pathways. The olive receives most of its afferents from higher levels: the cerebral cortex, especially the motor cortex, the caudate nucleus, globus pallidus, red nucleus, and the periaqueductal gray. A smaller, but important, source of afferents reaches the olive from the spinal cord, another of the indirect spinocerebellar paths. It is important to note that these various contingents of olivary afferents are not diffusely dispersed through the olivary complex but terminate in specific parts with little overlap. Since the olive has a very precise topographical projection onto the cerebellar cortex, its fibers distribute onto this cortex a sharply localized pattern of the descending and ascending influences on it. Like the olive, the lateral reticular nucleus receives descending and ascending afferents, but they are much more diffusely localized in this cell group. It also projects widely to most parts of the cerebellar cortex.

In addition to these four major groups there are numerous small bundles originating from the tegmental reticular formation and the arcuate nuclei. There is also evidence for inputs from visual, auditory, and autonomic centers, although the anatomical pathways are obscure.

The efferent projections from the cerebellar cortex are considerably easier to summarize briefly. The axons of the Purkinje cells make up all of the efferents from the cerebellar cortex, and by far the greatest number terminate in the central nuclei. This projection is organized into orderly longitudinal (rostro-caudal) zones (JANSEN and BRODAL, 1942; VOOGD, 1964, 1969). A medial zone roughly equivalent to the vermis sends its axons to the fastigial nucleus, while a more lateral, intermediate zone is connected with the intermediate (interpositus) nuclei, and the most lateral zone, roughly coincident with the hemisphere, is connected with the lateral (dentate) nucleus. In addition, there is a thin band in the lateral portions of the vermis that projects directly to the vestibular nuclei, as does the cortex of the flocculonodular lobe. The distribution of these corticovestibular fibers follows, as might be expected, a specific pattern for each part. It is to be particularly noted that the fibers from the anterior vermis end mostly in the lateral vestibular nucleus, from which a massive tract descends into the spinal cord, whereas fibers from the flocculonodular lobe end mostly in the medial, inferior, and superior vestibular nuclei.

Similarly, the zonal distribution of the corticonuclear fibers takes on added significance when the pathways leading from the central nuclei are considered. The fastigial nuclei give rise to another projection to the vestibular nuclei by both crossed and uncrossed tracts, and also send fibers diffusely into the bulbar and pontine reticular formation and to some thalamic nuclei. The intermediate (interpositus) nuclei project their fibers forward to the contralateral red nucleus in which most of them end. The lateral (dentate) nucleus distributes its fibers principally in the thalamus, especially the nucleus ventralis lateralis (VL) and to some extent farther forward in the nucleus ventralis anterior (VA). These nuclei project to the precentral gyrus of the cerebral cortex, from which again fibers descend into the pons.

Thus the efferent fibers from the cerebellar cortex lead into numerous complicated loops that have the possibility of feeding information back into the cerebellum. The existence of these loops invites the building of model circuits involving the cerebellar cortex and the central nuclei as switching stations. The authenticity of such models, however, depends upon a precise knowledge of intercellular connections, both morphological and physiological, information that is at present almost entirely nonexistent. Each nuclear group must be examined and analyzed in detail by means of single unit recording and refined anatomical methods. Such studies have only just begun in a variety of these stations. Knowledge of the cerebellar cortex is much more advanced than that of its associated clusters of neurons.

3. The Design of the Cerebellar Cortex

In contrast to the rather complex pattern of the afferent and efferent pathways briefly reviewed above, the cerebellar cortex itself displays a surprisingly uniform and simple structure. The kaleidoscopic patterns of its fiber connections are hardly reflected, if at all, in its mono-

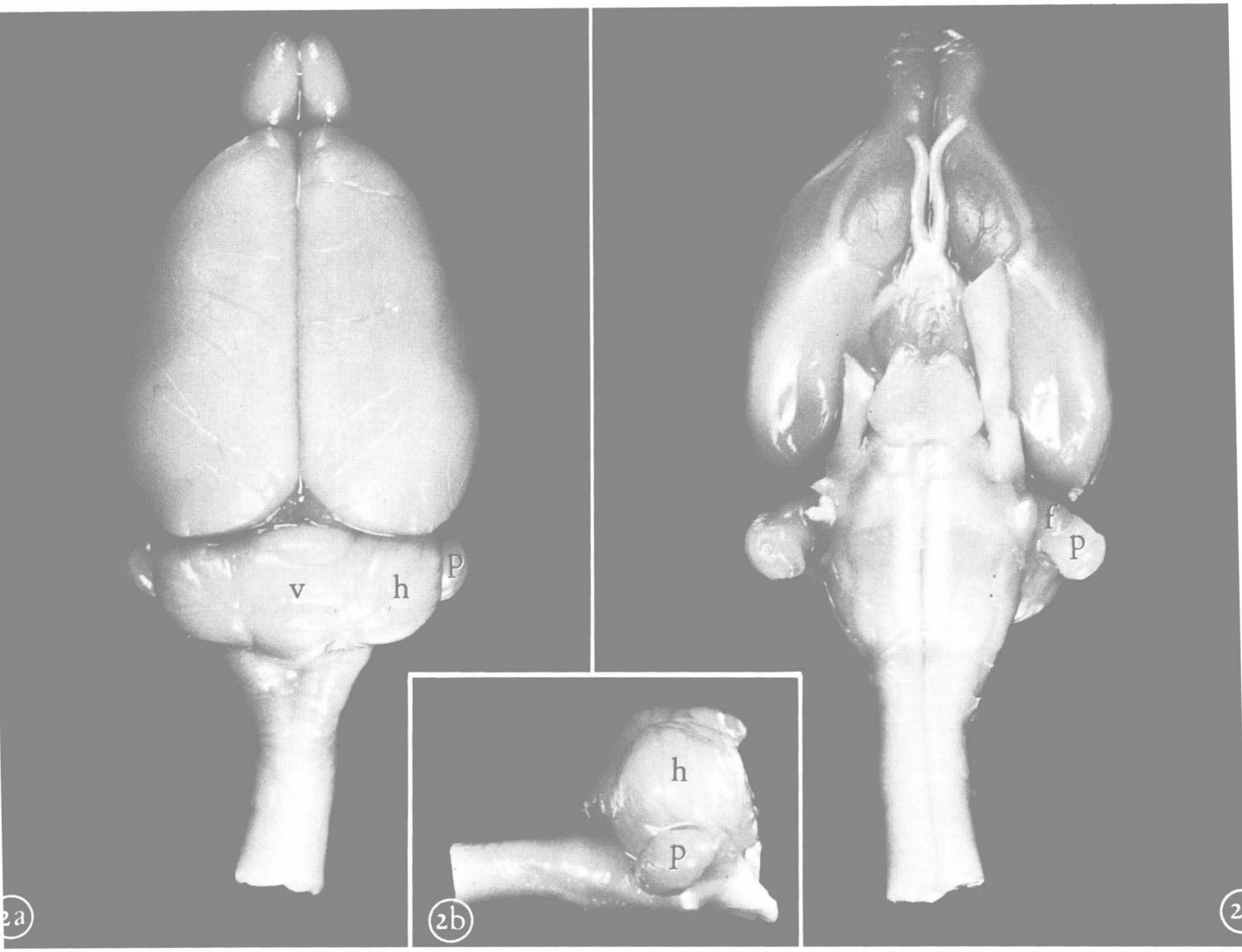

Fig. 2. a Superior aspect of the rat brain including the cerebellum. The vermis (*v*), cerebellar hemispheres (*h*), and paraflocculi (*p*) are well displayed. **b** Lateral aspect of the cerebellum and brain stem. The paraflocculus (*p*) and cerebellar hemisphere (*h*) are most prominent. **c** Inferior aspect of the rat brain. The paraflocculus (*p*) and flocculus (*f*) are well illustrated. Note that the folia of the cerebellar cortex run transversely across the cerebellum

tonous lamination. It consists simply of a highly folded sheet of cells and their processes, everywhere arranged into the same three layers (Fig. 3).[1] Furthermore, all of the folia extend in the transverse plane of the brain, from right to left, so that a parasagittal section cuts across them and a transverse section runs parallel with their longitudinal axes. The transverse folding of the cerebellar cortex is displayed in Fig. 2a–c, which shows the cerebellum of the adult rat in superior, inferior, and lateral view. At the center of each folium (Fig. 3) lies a thin lamella of white matter composed of the myelinated afferent and efferent fibers connecting the cortex with other centers. It should be noticed that the cortex, as a folded sheet covering these lamellae of white matter, has free edges and does not join up with itself to form a continuum (BRAITENBERG and ATWOOD, 1958). When unfolded, this sheet has been estimated to have an area of 50000 mm^2 in man (BRAITENBERG and ATWOOD, 1958), 2300 mm^2 in the cat (PALKOVITS *et al.*, 1971a), and only 270 mm^2 in the rat (ARMSTRONG and SCHILD, 1970).

1 There are, of course, certain exceptions to this generalization, which refers principally to mammals. In certain teleosts, e.g., mormyrids, regional variation in the form of the cerebellar cortex and its layers is carried to an extreme (KAISERMAN-ABRAMOF and PALAY, 1969; NIEUWENHUYS and NICHOLSON, 1969).

Fig. 3. Midsagittal section of the rat's cerebellum. ▶ This figure shows the three layers of the cerebellar cortex, as well as the various lobules of the cortex in the vermis. The rectangle indicates the region in lobules I and II (LARSELL, 1952) that have been enlarged in the next figure. 1 µm toluidine blue epoxy section. × 17

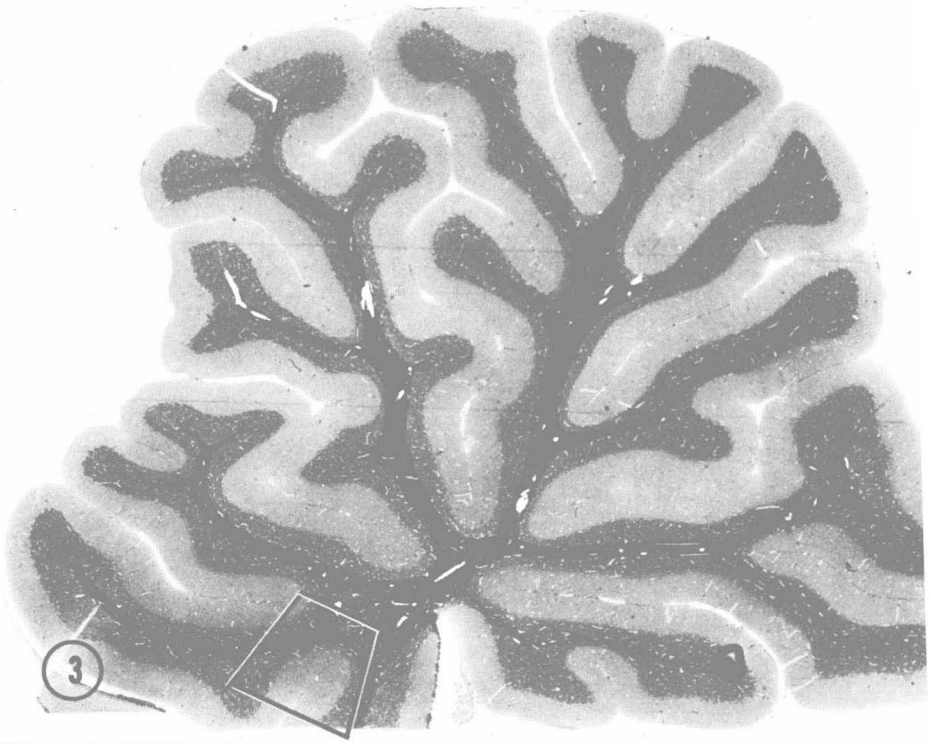

Fig. 4. Cortical layers in the cerebellum. Two lobules of the cerebellar cortex meet with their pial surfaces (*pia*) in apposition. The molecular layer (*mol*), Purkinje cell layer (*PC*), as well as the granular layer (*gr*) and white matter (*wm*) are indicated. An arrow points to the myelinated fibers of the anterior medullary lamina forming the roof of the IVth ventricle ▼