ARCHITECTONICS AND STRUCTURE OF THE CEREBRAL CORTEX

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XV

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Historical note

Evidence of structural organization in the cerebral cortex was first noted by Francesco Gennari, an Italian medical student who, on February 2, 1776, found within the cortical substance of the human brain a white line most obvious in the occipital lobe.[484] The " line of Gennari " is a reliable landmark of the primary visual cortex, the area striata. Vicq d'Azyr (1784)[1262] and Soemmering (1788) also observed Gennari's line,[1206] but it was not until 1840 that the French psychiatrist Baillarger demonstrated that the white band appears to be composed of two bands separated by a thinner dark one.[451] These bands can be traced throughout the large portions of the cortex and have been called by modern authors " external and internal bands of Baillarger." The term " Gennari's line," which corresponds to the external band of Baillarger, has been reserved for the visual cortex. In recent years Elliot Smith[1197] has been able to divide the human brain into some fifty zones characterized by differences in Baillarger's dark and white bands. However, the modern era of research on the structure of the cerebral cortex may be said to begin with the Viennese alienist Meynert,[912] who in 1867 systematically studied the cortical cells and established the fact that throughout the brain these cells are arranged in five horizontal layers. He considered two major divisions of the brain, which roughly correspond to what Kölliker called " rhinencephalon " and " pallium " and Vogt calls " allocortex " and " isocortex." The terms " archipallium " and " neopallium " have also been suggested, but as they are based on an ill-defined philosophical concept, they should be avoided. The allocortex has a white outer lamina and the isocortex a grey one. In 1874 the Russian histologist Betz[104] discovered in the fifth layer of Meynert (human precentral cortex) the giant pyramidal cells which still bear his name. Several years later the English neurologist Bevan Lewis[105, 106] established the general existence of large pyramids in Meynert's fifth layer and suggested a division of the cortex into six cellular layers. Bevan Lewis' diagram was later adopted by Vogt and Brodmann, and has come into general use, although the designations of the layers have repeatedly been changed.

A great advance was made in 1891 by the Spanish histologist, S. Ramón y Cajal.[1047] Golgi, the Italian neurohistologist, had in 1886 described the exact morphology of the pyramids and discovered that cells with short axons ramified within the cortex, *i.e.,* Golgi's type II cells. His pupil Martinotti (see Cajal) had noted cells with axons reaching the plexiform layer. Cajal added the description of cells with horizontal axons in the first cortical layer, and in addition he discovered the afferent fibres of the cortex. All the essential elements of the cortex had then become known. Ramón y Cajal's observations were confirmed and substantially extended by the Swedish anatomist, Retzius who called the horizontal cells "Cajal's cells," and by the German anatomist, Kölliker who designated the afferent fibres "Ramón's fibres." Kölliker's account of the structure of the human cortex (1896) is one of the masterpieces of neuroanatomy,[709a] and it marks the end of an historical period of research on the cerebral cortex. Between 1899 and 1902 Cajal[1047] made a thorough study of the finer structure of several regions of the human cortex, to which extensive reference will be made later. This study led to the recognition of the structural differences between the pre- and postcentral convolutions of the human cortex.

At the beginning of the present century a new branch of neuroanatomy was created, *i.e.,* "architectonics." Its foundations were laid, to be sure, by Meynert, Hammarberg,[526] a young Swedish histologist working in S. E. Henschen's clinic, and by Cajal and others; but it is correct to state that architectonics began with the independent work of Campbell[199] in England and Vogt[1270] and Brodmann[151] in Germany, all making their first communications in 1903. Architectonics, let it be said in advance, is concerned, not so much with the structure of the cortex as with subdivision of the brain into regions of specific structure. Campbell's communications, presented by Sherrington to the Royal Society of London in 1903, were published in book form in

1905. He demonstrated that the human brain, as well as the brain of other primates, carnivora and ungulata, contains several regions of specific structure. In the human brain Campbell recognized some twenty regions and described the cellular — cytoarchitectonic — and fibrillar — myeloarchitectonic — structure of each brain (fig. 62A, B).

The German school of architectonics at first did not lay great emphasis upon the plan of stratification. As indicated by the Vogts (1919, p. 300),[1269] Vogt and Brodmann, after careful study of the literature, selected a cytoarchitectonic diagram, which happened to be that of Bevan-Lewis (cf. Brodmann, 1909, p. 15), to which the Vogts gave a myeloarchitectonic equivalent (see their fig. 19).[1269] These diagrams were for several years a tool by means of which, first Vogt and Brodmann, and then their numerous associates, carried out extensive parcellations of the brain of man and of a large number of other mammals.[154] Each one of the cytoarchitectonic layers or myeloarchitectonic zones was for these workers a place in which to look for structural variations. In 1909 the six-layer diagram of stratification acquired a new signification. Brodmann then stated that the diagram, up to that time a purely morphological concept, was based on an embryological moment. In the human embryo up to the sixth foetal month the cortex is unstratified, but soon stratification appears in the form of six alternately light and dark layers which are the same throughout the brain and, therefore, represent the fundamental type of stratification. Later on, differentiations take place in the various architectonic regions, either because some of the embryological layers decrease or disappear, or because one or more of them increases and becomes subdivided into sublayers. But no matter how deep the change may be, every adult stratum is derived from one of the embryological layers. Only in the allocortex was the six-layer plan never demonstrable, and according to Brodmann the allocortex was heterogenetic. This theory has been elaborated by the Vogts[1269] and others[392] (see Lorente de Nó[818]). Out of Brodmann's sweeping theoretical concept grew an ever increasing series of papers by numerous authors who tried to penetrate more deeply into the significance of the six layers. Studies of comparative anatomy made by Ariens Kappers and his associates[664] led to a complementary concept, namely, that the six-layer type was due to phylogenetic evolution of a primitive three-layer type, each layer having a primordial function. The enthusiasm evoked by Brodmann's concept overshadowed the factual information collected by a number of most reliable authors up to the time of publication of the books by Campbell[199]

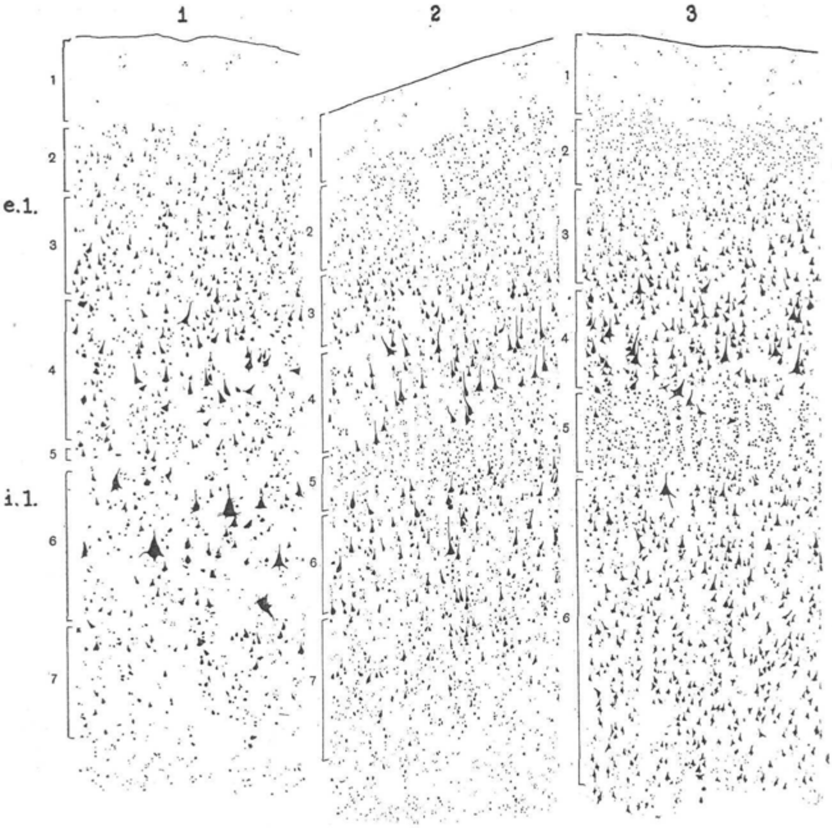

FIGURE 62A

Cytoarchitectonic pictures of representative areas of the human brain after Campbell.[199] Only the bodies of the cells are stained.

1. *Motor cortex* (area 4 of Brodmann). The stratification (Arabic numerals at the left) suggested by Campbell does not agree with later established facts and is probably incorrect. The approximate widths of the external (e. l) and internal (i. l) laminae have been indicated. This area is often called gigantopyramidalis because it is characterized by the presence of Betz pyramids. Its architectonic limits are, therefore, easily determined. (Remainder of legend on bottom of opposite page)

and Cajal.[1049] No more attention was paid to the fine structure of the cortex; studies on intracortical connections became irrelevant, and everything was explained in terms of the six- or of the three-layer diagram. Slowly but unfailingly these theoretical concepts dominated every line of research on the cerebral cortex and even experimental physiology has been deeply influenced by them. Thus it has come about that in one of the latest books on anatomy of the nervous system[665] the intimate structure of the cortex is described in but a few words, although many pages are devoted to embryological and phylogenetic establishment of the six-layer diagram; but Brodmann's concept has proved to be based on faulty evidence.[818] At the foetal stages at which Brodmann reported the absence of stratification, the cortex, when properly stained by the Golgi method, appears to contain the various specific types of nerve cells found in the adult brain. The cells of each type — pyramids, stars, spindles, cells with short axons or with ascending axons — are recognizable by their processes and by the position they occupy in relation to other cells. It is evident that at these embryonic stages the stratification is already definitively established and consequently that Brodmann studied only the final phases of differentiation. Therefore his observations have no direct bearing on the problem of elementary cortical organization. Moreover, the embryonic " light " layers correspond to zones of the cortex where the plexuses of dendrites and axons, which are not stainable by the Nissl method, are relatively better developed, so that the " dark " and " light " layers of the embryonic cortex do not coincide with the cell layers of the adult brain.

As forcibly stated by Cajal,[1047] the elementary pattern of cortical organization must be determined by means of intensive study of regions of specific structure, and this study should be carried out with the help of methods capable of yielding complete pic-

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2. *Postcentral cortex*, near to the wall of the central sulcus (area 3 of Brodmann). The stratification suggested by Campbell is probably correct, although with only architectonic information, the limits given between layers are largely hypothetical. Comparison of 1 and 2 reveals that without knowledge of the structure of the cortex, the existence of two different areas can be ascertained. In fact, the division was made despite a wrong concept of the structure of the precentral cortex.

3. *Temporal transverse cortex* (auditosensory of Campbell, probably 41 or 42 of Brodmann). There are striking similarities and differences between the postcentral and the temporal transverse areas. For example, while the stratification appears to be the same in both cases, nevertheless, the thickness of the layers, their densities, the sizes and forms of the cells, etc., are very different. No difficulty is experienced in distinguishing architectonic areas as different as are these two. It is to be noted that Campbell did not find sufficient reason to distinguish between layers *6* and *7*.

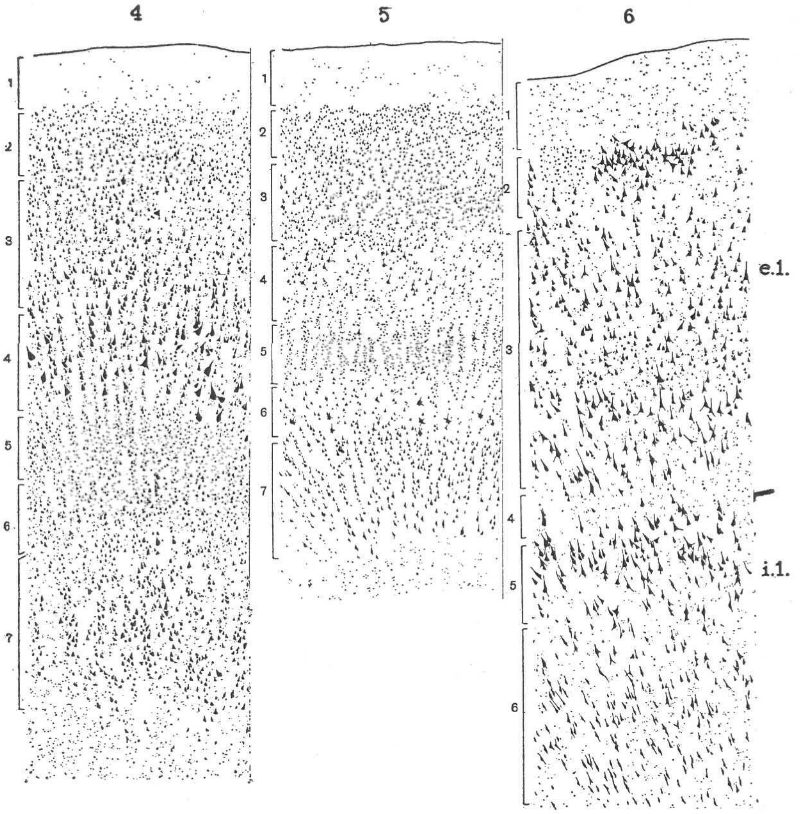

FIGURE 62B

4. *Occipital cortex* (visuopsychic of Campbell, 19 of Brodmann). Campbell did not distinguish between layers *6* and 7, but the approximate limit has been indicated here. Note the large size of the pyramids in layer 4 (IVa), and the small size of the pyramids of layer 6 (V). To distinguish between this area and the temporal transverse or postcentral areas also offers no difficulty. (Remainder of legend on bottom of opposite page).

tures of the cortical cell and fibres. Examination of the architectonic Nissl picture is only a first step in the analysis. The layers of cells found in the cytoarchitectonic pictures have been interpreted and labelled in many different ways. Even the authors of the cytoarchitectonic school have published most inconsistent descriptions, for although the layers have always been labelled according to the six-layer diagram, it often happens that equal denominations in two different photographs refer to entirely different systems of cells, in fact as different as a layer of nerve cells in one photograph and a layer of glia cells in another photograph.[818]

At the present state of knowledge any plan of stratification suggested for the frontal and prefrontal isocortex is entirely hypothetical: but for the parietal, temporal and occipital isocortex it is already possible to indicate a plan of stratification that is in agreement with the elementary pattern of cortical organization (figs. 63, 64, 65).

Stratification of the parieto-temporo-occipital isocortex

External lamina	I (*1*).	Plexiform layer,
	II (*2*).	Layer of small pyramids,
	III (*3*).	Layer of medium sized pyramids,
	IVa (*4*).	Layer of star pyramids,
	IVb (*5*).	Layer of star cells.
Internal lamina	V (*6*).	Layer of large deep pyramids,
	VI (*7*).	Layer of spindles.

The arabic numerals were used by Cajal and Campbell (fig. 62), who differentiated a layer, their layer 4 of external large pyramids, which in this report is called a layer of star

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5. *Area striata* (visual of Campbell, 17 of Brodmann). This area is immediately recognized by the small size of the cells and the appearance of an apparently empty (light) stria at the middle of the vertical section. This has often been interpreted as a result of duplication of the layer of granules (IV). As a matter of fact, however, layer 4 (IVa) is comparable to 4 of the rest of the occipital cortex. It must be noted that the stratification at the left of the drawing is not the same as at the centre, because at the centre the star pyramids are found at higher levels than at the right.

6. *Cortex of the lobus pyriformis* (28 or entorhinalis of Brodmann). The numbers of the layers have a significance entirely different from that in drawings 2 to 5. For example, 4 is a layer of glia cells because at that level (cf. fig. 67, IIIa) there are no bodies of nerve cells but only a dense plexus of dendrites and axons and glia cells. Layer 2 corresponds to II in figure 67, 3 to III, 4 to IIIa, 5 to IV, and 6 to V and VI. Even if the exact stratification of this area is unknown or misinterpreted, the determination of its architectonic boundaries can be accurately made.

pyramids and must be incorporated into Bevan Lewis' diagram.[105] However, since the latter has come into general use, the additional layer is designated IVa. It must be emphasized that the boundaries between layers, with the exception of the boundary between IVb and V, are never sharp, and that if they are ascertained with the help of only the architectonic picture are entirely hypothetical. Figure 62 shows several drawings of the architectonic picture of representative areas of the human brain taken from Campbell's book. Although not as perfect as the photographs published by the German school, they clearly demonstrate the differences in cell size, density of the layers, layer thickness, etc., upon which the architectonic subdivision of the brain has been based.

GENERAL PLAN OF STRUCTURE OF THE CEREBRAL CORTEX

Several structural features which repeat themselves throughout the entire cerebral cortex are likewise found in subcortical centres of higher complication, such as the quadrigeminal bodies, tuberculum acusticum, etc.: but many, if not all, cortical regions are characterized by specific structural traits that make it impossible to describe an elementary structural pattern which is valid for the whole cortex, unless after important simplifications the cortex is considered as a chain of neurons built on the plan of reflex arcs. How this can be done is shown in figure 66 and will be discussed in the following pages, but it is necessary first to investigate the actual structural plan of representative cortical regions. The study can be carried out in any cortical region of any mammal, but it is facilitated by investigating the same region in various types of mammals and determining the structural traits that are common to all.

A number of cortical areas, although not many, can easily be recognized in all the mammals studied, *i.e.*, in mouse, rat, cat, monkey, and man. They are, for example, the primary visual cortex — area striata — which receives the optic radiation from the geniculate body: the area entorhinalis[818] which sends to Ammon's horn the powerful tracts described by Cajal; and the somatic sensory area which receives the thalamocortical projections from specific zones of the ventral nuclei. When any of these areas is intensively studied in different mammals, it is found that some of the structural details remain constant despite the variations in cell number, cell form and size, and the disappearance in the lower mammals of many types of cells found in the brains of the monkey and above all of man. *What remains constant is the arrangement of the plexuses of dendritic and axonal branches, i.e., of the synaptic articulations through which nerve impulses are transmitted.* This constancy is fortunate, because if it were otherwise studies made of the comparative anatomy and physiology of the cortex would have but a limited value. The semidiagrammatic drawings shown in figures 63, 64, and 65, which include representative types of cortical cells and fibres, are based on Golgi stains of the somatic sensory cortex of the mouse; but changes in the proportions of the drawings would make the diagram valid for the corresponding cortical regions of any other mammal, including man.*

Examination of the dendritic apparatus of the cells reproduced in the middle part of the drawing reveals how incomplete is the information upon which cytoarchitectonic research has based its far-reaching conclusions. The Nissl picture reproduced at the left in figure 63 gives approximate information about the form of the bodies of the cells, but leaves undescribed the distribution of the dendrites, which as a rule constitute by far the larger part of the synaptic surface of the neuron. On the basis of the architectonic picture, it is impossible to determine, for example, whether cells *14* and *15* (fig. 63) establish

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* It is scarcely necessary to emphasize that in the following description only the general features of cortical structure are considered. For example, the long pyramids (figs. 63, *7*, *8*, *9*) will be viewed as a unitary type of neuron, while in fact, according to the distribution of the branches of their axons, they must be classified into several categories.[816] Likewise the specific afferents (fig. 63, *a*, *b*) are described as fibres of a single class, while they have been shown to include fibres with somewhat different distributions in the layers of the external lamina.[816, 818] These simplifications are permissible when the problem is that of ascertaining the elementary cortical pattern; but they should be avoided in study of the physiology of specific cortical areas. Exhaustive descriptions of cortical cells and axons have been published by Cajal[1047] (see complete bibliography by Cajal;[1049] Lorente de Nó;[816, 818, 819] O'Leary[972] and O'Leary and Bishop, 1938 unpublished).

the majority of their synaptic contacts outside the layer in which their bodies are located, nor is it possible to differentiate between cells as radically different as *8* in figure 63, and *24* or *25,* in figure 65. Cortical fibres are reproduced in figures 63, 64 and 65. While segments of them are myelinated, those segments which establish synaptic connections with dendrites or cell bodies are unmyelinated and consequently not stainable by the Weigert method. The myeloarchitectonic picture indicates the location of the myelinated segments of the cortical fibres, but does not give the slightest information about the zones of the cortex where the axons actually end.

The cortex has four main types of cells:

1) Cells with descending axons often reaching the white substance, to be continued by a fibre of projection or of association (figs. 64, *1* to *10,* and 66).

2) Cells with short axons ramified in the proximity of the cell body, often within a homogeneous zone of the dendritic plexus (fig. 65, *21* to *25*).

3) Cells with ascending axons ramified in one or several cortical layers (fig. 65, *18* to *20*).

4) Cells with horizontal axons (fig. 65, *22*).

The cortical neurons have synaptic connections with fibres of various kinds: afferent fibres, which are the axons of neurons coming from the thalamus (fig. 63, *a, b, c, d*); association fibres, which arise in other cortical areas (fig. 63, *e, f*); and intracortical fibres (figs. 64 and 65). In order to multiply the synaptic contacts, both dendrites and axons branch out repeatedly and form plexuses, the composition of which is indicated in figures 63, 64 and 65. Even a cursory examination of the distribution of the dendrites of the cells with descending axons (fig. 63) reveals the existence of a most remarkable arrangement, partly described by Cajal[1047] and first systematically analyzed by Lorente de Nó.[816, 818]

From the body of the cells arise several relatively short dendrites which may be called " basilar dendrites " and a long dendrite, the " shaft," directed toward the surface of the cortex. The length of the shaft is peculiar to each type of neuron. During its ascending course the shaft gives off collateral branches at levels characteristic for each type of neuron. Since the basilar dendrites are short and the collateral branches of the shaft are oriented chiefly in a horizontal direction, the result of the branching of the processes of the cortical cells is to fractionate the vertical section of the cortex into several strata of more or less horizontal dendrites crossed by vertical shafts. It is a remarkable fact: (i) that no two successive strata are articulated with the same fibres, and (ii) that each stratum contains dendrites from several architectonic layers. The cortical fibres of exogenous or endogenous origin run chiefly in a vertical direction, and by means of side branches establish synaptic contacts with dendrites or cell bodies of some of the zones of the dendritic plexus through which they cross (figs. 63, 66). The vertical fibres and their collateral branches form a plexus having as many strata as the dendritic plexus; each stratum has its specific composition. In some strata of the fibrillar plexus the collateral branches have a predominantly horizontal course and form the horizontal dark bands found in the myeloarchitectonic picture.

As indicated in figure 63, the cortex has been divided into six horizontal zones, each corresponding to a major group of strata of the dendritic plexus. These zones will be called "layers," and parts "sublayers" or "strata." The cell bodies represent but a small fraction of the dendritic plexus, and for this reason the cytoarchitectonic layers often have no immediate relation to the actual zones of dendritic and axonal plexuses.[818]

Layer I, the plexiform layer of Cajal, contains, besides horizontal cells (fig. 65, *22*) and a few cells with short axons, the terminal bushels of pyramids and spindles of all the lower strata.

Layer II, in addition to segments of the shafts going to layer I, contains the basilar and collateral dendrites of the small pyramids (fig. 63, *1*).

Layer III possesses pyramids (fig. 63, *2, 3*) similar to those of layer II. Often, almost regularly, their shafts give off branches in layer II, so that no definite limit exists between the two layers. However, a division is advisable because branches of the specific afferents (fig. 63, *a, b*) are in contact with dendrites, at least the basilar den-

FIGURE 63 — For legend see bottom of opposite page.

drites, of pyramids of layer III; but there are few, if any, pyramids of layer II that have basilar dendrites long enough to reach the zone of distribution of the specific afferents.

Layer IV has two strata in which two main types of neurons are found, star cells (fig. 63, *5*) with dendrites distributed entirely within layer IV, and star pyramids (fig. 63, *4*, *6*) which have shafts reaching the plexiform layer.* The star pyramids are distinguished (fig. 63,

* The division of the cells with descending axons of layer IV into star pyramids and star cells is of first importance. When this division was first made,[816] it was not realized that the large star pyramids form a distinct stratum in the upper zone of layer IV (sublayer IVa). This stratum has later been identified in the whole temporo-parieto-occipital isocortex, and it is important that it is present in the optic cortex of all the mammals studied, including the mouse, rat, cat, monkey and man. Since Cajal did not identify it, he described the optic cortex as having a specific structure. The sublayer of star pyramids is present in the area striata as well as in the area peristriata. The sublayer of large star pyramids is called by the German architectonic school IVa and IVb in the area striata, but III in the area peristriata. Both cortical areas when studied in Golgi stains show the same elementary pattern and stratification, the architectonic differences being due to the fact that in the optic cortex the plexuses contain many more horizontal branches

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Figure 63 — At the left side a diagrammatic Nissl picture of the parietal cortex of the adult mouse stained after Nissl. The cell layers are marked with Roman numerals. Except between IVb and Va there is no sharp boundary between layers. At the centre, bodies and dendrites of representative types of cells with descending axons; to avoid complication of the drawing the axons have not been included (see fig. 64). At the right the main types of cortical afferent fibres.

1. Pyramids of layer II; *2* and *3*, pyramids of layer III; *4*, large star pyramids; *5*, star cells; *6*, small star pyramids; *7*, *8*, *9*, long deep pyramids; *10*, short pyramids; *11*, medium pyramids; *12*, *13*, short pyramids of layer VIa; *14*, long spindles; *15*, medium spindles; *16*, short spindles; *17*, deep star cells; *a*, *b*, specific thalamic afferents; *c*, *d*, unspecific or pluriareal afferents; *e*, *f*, association fibres. The cells have been reproduced from two consecutive sections through the brain of an adult mouse, stained after Golgi-Cox, and the fibres from section through brains of 11-day old mice stained after Golgi. In examining this drawing it must be considered that the cells of each type appear at the same level at more or less regular intervals, so that the dendrites of all the cells form a very dense plexus, articulated with fibrillar plexuses such as that formed in layer IV and the lower part of III by the afferent fibres *a* and *b*. It must be noted that the dendrites of the cells of each type are distributed only through especial zones of the cortex. For example, cells *5* have dendrites only in layer IV, cells *10* only in layer V and cells *17* only in layer VI, while other cells like *14* have dendrites in all the layers. The cells with dendrites in several layers as a rule have a number of dendrites concentrated in one layer, for example, the side branches of the shaft and the basilar dendrites of cells *4* are located in layer IV, those of cells *7*, *8* and *9* in layer V, etc.

4) from the ordinary pyramids by their shafts which have numerous horizontal collateral branches within layer IV, but none in layers II and III. After having given off its collateral branches the shaft usually becomes thinner and ascends to layer I, to end without branching or with a poorly developed bushel. The basilar dendrites of the star pyramids also run chiefly in a horizontal direction, in some cortical areas even exclusively so; but in other areas many of them descend toward the lower levels of layer IV, although without in general reaching the limit of layer V. The *lower stratum* of the fourth layer (IVb) contains both star cells with dendrites exclusively in layer IV and small star pyramids with thin shafts which reach layer I (fig. 63, *6*). Layer IV is also characterized by a dense fibrillar plexus formed by arborizations of the specific afferents. The boundary between layers III and IV is not sharp, because some of the basilar dendrites of the pyramids of layer III descend into layer IV; and especially in the cat, the shafts of some of the upper star pyramids may have one or two branches in the lower stratum of III. The limit between layers IV and V is usually sharp, for at that level both the protoplasmic and the fibrillar plexuses suffer a radical change (fig. 63).

Layer V in addition to the bodies of the classical pyramids (fig. 63, *7, 8, 9*) contains the bodies of two other types of cells recently described,[816] for which the designations of " medium " and " short " pyramids may be used. It is characteristic of the classical pyramids (*7* to *9*) to have a shaft which reaches the molecular layer, where it often ends by means of a complicated brush of branches, but at times remains undivided. It is also characteristic of these pyramids that not only the basilar dendrites, but also the collaterals of the shaft are distributed exclusively within layer V.[1047] When the cell body is located near the upper limit of layer V (fig. 63, *7*), the shaft has no collateral branches; but if situated at lower levels (*8, 9*), the shaft has a number of collateral dendrites, none, however, passing beyond the upper limit of layer V.

The medium pyramids (fig. 63, *11*) form an interesting type of cell. They have several dendritic branches in layer IV where their shafts end and therefore they have numerous synapses with the fibrils of the afferent plexus, almost as many as are found in the case of some star cells. The shaft of the short pyramids (fig. 63, *10*) ends within

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than in the area peristriata. It is noteworthy that among the numerous plans of stratification described in the literature that suggested by Campbell (Plate XI, figs. 1 and 2)[199] and reproduced here in figure 62B, *5* is the only one that is strictly correct. Dr. Campbell died at Sydney, Australia, 4 Nov. 1937.

layer V. Short pyramids are also seen in the upper part of layer VI (fig. 63, *12, 13*). In fact, the limit between layers V and VI is not at all sharp. It is important to mention that layer V has three definite strata, the largest pyramids being found in the middle one (Vb). It is not possible here to enter into the details justifying this division which, as will be seen later, may prove to be of high significance.

In *layer VI* are found three types of cells similar to the three types of pyramids mentioned above. The long spindles (*14*) have a shaft which gives off collateral dendrites in layer VI and then ascends undivided and without collaterals to reach layer I. The shaft of the medium spindles (fig. 63, *15*) ends in layer IV within the plexus of specific afferents. Finally the short spindles have a shaft ending in layer V (fig. 63, *16*). In layer VI there are also a number of cells (fig. 63, *17*) with dendrites distributed exclusively within the limits of their own dendritic stratum; these may be called deep star cells. A division of layer VI into two sublayers (VIa, VIb) is from many points of view necessary, but for the purpose of the present report it may be disregarded.

Cortical afferents

The main types of the afferent fibres of the cortex have been represented on the right side of figure 63. A number of branches have been omitted in order not to complicate the diagram excessively. Some of the fibres (*a, b, c, d*) come from the thalamus (thalamocortical projections), and others (*e, f*) from cortical regions (intracortical association fibres). Fibres *a* and *b* represent the specific afferents: for example, the fibres coming from the external geniculate body to the visual cortex, those from the internal geniculate body to the acoustic cortex, the fibres from the thalamic relay nuclei to the somatosensory area, etc. They ascend myelinated and undivided through layers VI and V, and having once arrived at layer IV, divide repeatedly into numerous branches, forming a plexus located chiefly in layer IV. Some branches ascend still further to layer III where they form a much less dense plexus.

It is evident that although the cells of layer IV have the greatest number of *synapses* with specific afferents, many cells of other layers also have such synapses — for instance, the long pyramids (fig. 63, *7, 8, 9*), the long spindles (fig. 63, *14*) in their shafts, and the medium pyramids and medium spindles (fig. 63, *15*) in the terminal bushel of their shafts. But the short pyramids (fig. 63, *10, 12, 13*), the short spindles (fig. 63, *16*), and the deep star cells (fig. 63, *17*) have no synaptic contacts with the specific afferents. There is no doubt that the latter categories of neurons are stimulated by impulses resulting from cortical activity, through impulses carried by the unspecific afferents (fig. 63, *c, d*), or by association fibres (fig. 63, *e, f*).

A second type of afferent is represented in figure 63 by fibres *c* and *d,* which are of thalamic origin and innervate at least two adjacent cortical fields. Whether this type of afferent is present in all cortical areas is still unknown; in the mouse, these afferents have been found in several specific areas, but their existence has not been verified in higher mammals. Their ultimate destination is unknown, but it has been established[813] that during their course in the white matter they give off collaterals ascending into the cortex and reaching as far as layer I. During their ascending trajectory the collaterals give off branches at all levels of the cortex, but chiefly in layer VI.

A third type of afferent is found in the association fibres (*e, f*) which come from other cortical areas, from either the same or the opposite hemisphere; in the latter case they are called callosal fibres. The association fibres give off collaterals in the deep layers, especially VI; but their main territory of distribution is in layers I to IV, and especially II and III. As will be seen presently, the interareal association fibres (*e, f*) have a distribution similar to many of the collaterals of the descending axons (fig. 63); this indicates that when a cortical cell discharges impulses into its axon it must modify the activity of the cells in the area in which it is located in a way similar to that in which the activity of the cells of other cortical areas or even of subcortical centres is modified.

Cortical efferents

Representative types of cortical descending axons have been reproduced in figure 64. It may be seen in the semi-diagrammatic but otherwise accurate drawing that the cortical axons, without exception, even when they leave the grey matter to form fibres of projection (fig. 64, *8*) or of association (fig. 64, *4, 7, 10, 17*) have an extensive intracortical arborization.

FIGURE 64

Intracortical distribution of the branches of representative types of descending axons. In order not to complicate the drawing, branches have been omitted and others have been drawn shorter than they really are. The numbers on the cells are the same as in figure 63. Note that the collateral branches are concentrated in layers I–III and V–VI. The axons of cells *1* and *5* are entirely distributed within the cortex although in higher mammals, especially in man, they may reach the white substance. The axons of cells *4*, *7*, *10* and *17* are fibres of association, and the axon of cell *8* is a fibre of protection.

Since the impulse conducted by a fibre necessarily passes into its collaterals and branches of the descending axons are distributed in the same territories as the cortical afferents, there can be no doubt that the effect of the impulses entering the cortex depends largely upon the impulses at that moment circulating through the descending axons as a result of the existing cortical activity. The intracortical distribution of the axonal branches is as systematic as that of the dendrites; again there is a sharp difference between layers I to IV and layers V and VI.

The axons of the pyramids and star cells of *layers I to IV* (fig. 64, *a* of neurons *1, 4, 5*) have their ramifications chiefly within the grey matter, although a number of axons of pyramids, especially of the large star pyramids, reach the white substance and form association and callosal fibres. During their descending traject they give off a number of collaterals; the initial branches are poorly ramified recurrent fibres distributed among the fellow pyramids, chiefly among those located at higher levels. It is a remarkable fact that layer IV receives but few collaterals from the axons of the pyramids of layers II and III, although the axons of the cells of layer IV have collaterals in that layer. Once arrived at layer V, all the pyramidal axons give off a great number of more or less horizontal branches, distributed throughout layers V and VI, but especially in the upper part of V.

The axons of the pyramids of *layer V* are as a rule continued by efferent projection (fig. 64, *8*) or association (fig. 64, *7*) fibres. It is noteworthy that the short pyramids located (fig. 64, *10*) in layer Vc and in the upper stratum of layer VIa form one of the main sources of the callosal tracts. The axons of the spindles of layer VI also often reach the white substance to form a fibre of association. Likewise the deep star cells (fig. 63, *17*) of layer VI give rise to association fibres, chiefly those which after a short course through the white matter again penetrate the cortex, *i.e.,* the U fibres.

All the axons of layers V and VI without exception have several repeatedly branched collaterals, a number of which remain in layers V and VI where they constitute a rather dense plexus of chiefly horizontal fibres; but in addition, many of these axons have one or more recurrent collaterals which, usually myelinated, cross through layers V and IV to reach layers III and II where they branch out and end among the pyramids of those layers, or even ascend to layer I.* It is significant, as first es-

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* In the lower mammals the collaterals of the descending axons have but short horizontal trajects in the strata of the external lamina, but in the higher mam-

tablished by Cajal, that in some cortical fields the recurrent collaterals of the small pyramids of layers Va and Vc (fig. 63, *7, 9*) and of the spindles of layer VI (fig. 63, *14, 15, 16*) are the most important parts of the axonal apparatus, for the reason that they are thick and the axon does not reach the white substance (cf. Lorente de Nó,[818] fig. 5). A glance at figures 63 and 64 reveals *the great importance of the system of collaterals of cells with descending axons.* The fibrillar plexus of layers V and VI is chiefly composed of their branches and, what from a theoretical point of view is even more important, the fibrillar plexus of layers II and III receives the great bulk of recurrent collaterals from the axons of the cells of layers V and VI. Layer IV has but few collaterals coming from descending axons other than the axons of its own stars and star pyramids, and even those collaterals usually ascend to layers III, II, and I where they end. Although the system for intracortical conduction of impulses formed by the branches of the afferent fibres and of the descending axons is a powerful one, it is almost overshadowed in wealth and complexity by the plexus of ramifications of the short and ascending axons.

Neurons with short axons

There are many types of cells with short or ascending axons, in fact they constitute a considerable part of the cell population of the cortex — the larger the number, the higher is the brain in the series. As already stated, these cells may be classified into three main groups: *

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mals, especially in man, the horizontal trajects are long and form powerful horizontal striae of myelinated fibres which have received various designations in myeloarchitectonic descriptions. They help to fractionate the external lamina into substrata which in cytoarchitectonic descriptions are termed IIa, IIb, IIIax, IIIb, etc. Since these substrata vary from field to field the designations have a different signification each time, and their value is therefore only "geographic."

* In the following paragraphs an attempt is made to systematize the description of the cells with short axons. It has been customary (cf. footnote on p. 299) to divide these cells into types according to the layers in which the bodies are located. This procedure, justifiable from a certain point of view, leads to the differentiation of an excessive number of cell types, because sometimes similar cells distributed through several layers are described as belonging to several different types. However, it must be noted that within the three main classes considered in the text, several specific types distributed through one or several layers can be differentiated.

a) Cells of the classical type II of Golgi with rather short dendrites which often extend through only one zone of the dendritic plexus (fig. 65, *23* to *26*). The axonal arborization is distributed approximately in the same territory that is covered by the dendrites. Cells of this type are found in every cortical layer or, better said, in every stratum of the cortical plexus. Thus, cell *23* lies within the plexus of layers II and III, cell *24* in layer IV, cell *25* in layer V although chiefly in Va, and cell *26* in layer VI. It is an important fact that these axons (fig. 65, *24, 25*) may form baskets enveloping the bodies of the pyramids and other cells with descending axons, so that the discharge of the cell with a short axon results in powerful, practically simultaneous stimulation of a large number of other cells.

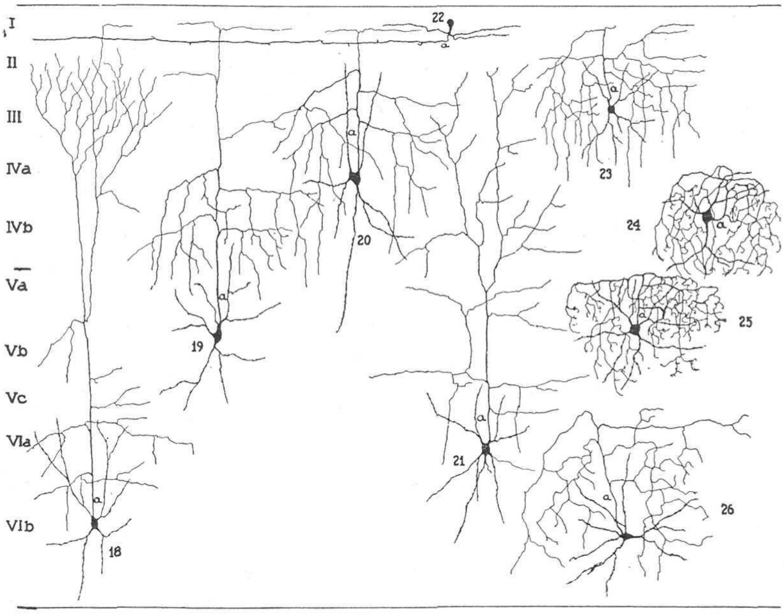

FIGURE 65

The three main types of cells with intracortical axons: *18, 19, 20, 21,* cells with ascending axons; *22,* cells with horizontal axon; *23, 24, 25, 26,* cells with short axons.

b) Cells with ascending axons (fig. 65, *18* to *20*) are also found in every cortical layer; their dendrites are sometimes distributed within one layer (fig. 65, *18, 21*) but frequently they cross several layers (fig. 65, *19, 20*). These axons in some cases form dense arborizations similar to those of the short axons (fig. 65, *18, 19, 20*), but in other cases their arborization is lax (fig. 65, *21*). There are ascending axons distributed through many layers, and axons with the arborization concentrated in one layer. Thus the axon of cell *21* is distributed in layers II to VI, and that of cell *18* gives branches to layers I, II, III, V and VI, but does not establish contacts within layer IV. The axon of cell *19* has a dense arborization in layer IV and gives but few branches to the upper layers. Finally the axon of cell *20* is rather uniformly distributed through layers I to IV. It is an immediate consequence of the existence of cells with ascending axons that when the cells of the upper layer with descending axons stimulate the cells of the deep layers, volleys of impulses are sent back to the upper layers. For example, when a discharge of the star cells causes the pyramids of layer V to respond, cells such as *19* will send impulses back to the layer of star cells; similarly cells such as *18* will send impulses to layers II and III.

c) The cortex also has cells with horizontal axons, the most conspicuous type being the horizontal cells of layer I (fig. 65, *22*); their axons run for long distances, establishing contacts with the shafts of the pyramids and spindles of layers II to VI. In the same class belong cells with short axons which have their axonal arborization in the same layer where the body is located but at some distance from it, so that the impulses carried by their axons are delivered to cells with descending axons not reached by the same fibres which stimulate the short axon cell (fig. 67, *5*).

Interaction between neurons

It is possible now to reach a comprehensive view of the organization of the cortex. The small strip reproduced on the left of figure 63 is the vertical section of a cylinder having a specific afferent fibre like *a* as axis. All the elements of the cortex are represented in it, and therefore it may be called an *elementary unit,* in which, theoretically, the whole process of the transmission of impulses from the afferent fibre to the efferent axon may be accomplished. Within the elementary unit there are cells which establish synaptic connections with the afferent fibre and cells which make no such connections; the latter cells, of course, will be stimulated only as a result of cortical activity. Save for layers I and II, all cortical layers contain cells having synaptic contacts with the specific afferents, so that it would be improper to call any one layer " receptor." On the other hand, every layer except I has axons reaching the white matter, and therefore no layer may be called the " effector." It is true that in some cortical fields, such as the motor cortex, a powerful efferent tract arises from pyramids in layer V; but in other fields, such as the entorhinal cortex and the occipital fields, the main efferent tracts arise from the upper layers. In every case the function of the cortex consists in stimulating distant centres, and this " effect " is sometimes accomplished by " association tracts " ending in other cortical fields, and again by " projection tracts " ending in the subcortical centres. Moreover, layers V and VI are the source of powerful " association " tracts.

In these circumstances it is obvious that there is no basis for considering the cortex as composed of several layers with specific primordial functions: reception, association, and projection. From the functional point of view it is a unitary system composed of vertical chains of neurons, among which anatomically the most important are those starting at the articulation of the specific afferents and the cells of the external lamina. The neurons with descending axons of this lamina send their impulses to layers V and VI, from which impulses are sent back chiefly to layers II and III. The association fibres have their endings in layers II, III and VI, which are strategic places where the impulses that they conduct may modify the circulation of impulses through the cortical chains. The architectonic layers contain the bodies, *i.e.,* only a small part of the dendritic apparatus of these cells, which form similar links in the vertical chains. This arrangement must be related to the existence of cells with short axons, such as cells *24* and *25* (fig. 65). The synaptic terminals of these axons are located on the bodies of the cells with descending axons, so that when the short axon cell discharges, powerful stimuli are delivered simultaneously to a large number of neurons. Hence the assumption lies at hand that the impulses circulating through the vertical chains are synchronized at the level of the architectonic layers and sublayers. The abundance of cells with short axons and their systematic distribution suggest that at certain phases of cortical

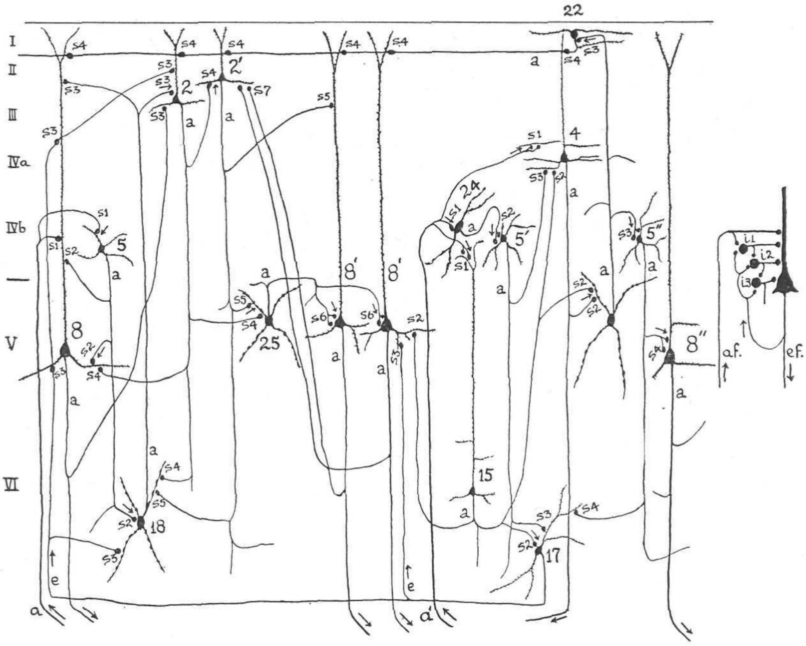

FIGURE 66

Diagram of some of the intracortical chains of neurons. The number on the cells and the letters *a* and *e* on the fibres the same as in figures 63, 64 and 65. The axons of the cortical cells are marked with a. Note that only a few dendrites and axonal branches have been included in the diagram. The synaptic junctions are indicated with the letter *s* (*s1*, *s2*, etc.) and with a thickening of the axon. It is assumed that the synapses marked with an arrow are passed by the impulses.

The small diagram at the right is a simplification of the diagram at the left. The afferent fibre *af.* activates the large pyramid which is the origin of an efferent fibre *ef.* and also a system of cortical internuncial cells (*i1*, *i2*, *i3*); the recurrent collateral of *ef* delivers impulses again to the internuncial system. This diagram summarizes the plan upon which the central nervous system is built.

activity the cells of the various layers fire off in more or less synchronous volleys of impulses.

Since for physiology the important data are those referring to the arrangement of the neurons in synaptic chains, through which nerve impulses may be transmitted, it is of interest to consider in some detail the neuron chains present in the cortex. Some of these chains, including a large pyramid (origin of projection fibre) have been represented in the diagram of figure 66, *8;* similar chains, however, may be drawn for any other type of cell. The diagram needs little explanation. The assumption is that impulses enter the cortex through the specific afferents *a* and *a′,* and the synapses marked by an arrow are crossed by the impulses. It is at present believed that many of the impulses arriving at the synapses of a cell fail to cross the synapse because they do not reach threshold; but there is no evidence to prevent the assumption that any synapse is passable, provided that the conditions necessary for summation are fulfilled. For the sake of illustration, arrows have been placed on those synapses in which the convergence of the fibres of homogeneous origin favours transmission, but arrows might have been placed on any of the others. At any rate, the fact must be borne in mind that since synaptic stimulation demands simultaneous activation of several synapses, the transmission of impulses through the cortex requires the activity of many more cells than can be included in a diagram.

When, following the arrows, the successive synapses are crossed, it will be seen that impulses are delivered again and again to the same cells (fig. 66, *8*), the letters s_1, s_2, etc. indicating the order of the corresponding synapse. The impulses carried by fibres *a* and *a′* arrive at synapses of the first order, those of cell *5* at synapses of the second order, those of cell *5′* at synapses of the third order, those of cell *5″* at synapses of the fourth order, etc.* Since the passage over a synapse means a delay of the impulse by roughly 0.6 msec., (ch. IV) the order

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* The fact that cells of the same anatomical type, for example neuron 5, figures 63, 64 and 65, may deliver to the effector neurons (fig. 66) impulses of the second, third, etc. order indicates that during cortical activity the composition of the chains of neurons must certainly vary. The impulses entering the cortex find many paths through which they might circulate. Some of the paths are passable, because conditions for summation such as instantaneous convergence of impulses are given. Other paths are impassable, but may become passable later when cortical activity creates impulses capable of summating with the afferent impulses. At the same time some ordinarily open paths will be closed, for example, when cortical activity raises the threshold of strategic links in the chains of neurons.

of the synapse indicates the time at which the impulses arrive at cells *8* after the first impulse has entered through fibres *a*. It is evident that each *a* impulse causes the cortical cells to be bombarded by a succession of impulses, thus creating in them a constant state of *facilitation,* and eventually stimulating them to discharge into their axons (ch. IV).

Two important features of the neuron chains must be emphasized: (i) All the chains, including one or several synapses, are superimposed upon the simplest chain, including only the articulation of fibre *a* and cell *8* (two-neuron arc) shown at the extreme left; (ii) The chains include closed loops, as for example, *8–2, 18–8,* or *8′–2′, 25–8′* (fig. 66). These two features are graphically illustrated in the simplified diagram at the right of figure 66, *which indicates that the cortical chains are in no way different from the chains of internuncial neurons in any part of the central nervous system.* Fibre *a* carries the afferent impulses, cells *8, 8′* and *8″* are the effector neurons, all the other neurons are internuncials. With this definition in mind, the analysis of the transmission of the impulses through subcortical centres may be directly applied to the cortex. A discussion of this problem will be found in other publications.[817, 818, 819]

When the chains of neurons in figure 66 are examined closely it will be observed that they are of two types. Some of the chains include short links with cells of a single layer, as for example links *25–8′* in layer V, and links *24–5′* in layer IV. Other links are long and include cells of different layers, as for instance, links *18–2, 15–4, 8′–2′,* etc. The long links vary but little in different mammals, but the short links increase progressively in number from the mouse to man. Thus, in the cortex of the mouse, the cells with ascending axons are relatively numerous, while those with short axons are relatively rare. In the human cortex there is an increase in the number of cells with ascending axons, but the increase in the cells having short axons is much more pronounced, so much so that in some cortical regions they outnumber the cells with descending axons. Furthermore, the increase in the short axon cells is not restricted to any one layer, but takes place in all of them, although in different cortical regions the increase is more pronounced in certain layers, for example, in the area striata in layer IV and the motor area in layer V. *Cajal assumed that the large number of cells with short axons was the anatomical expression of the delicacy of function of the brain of man.* At present that assumption is almost a statement of fact, for it is known that synaptic transmission demands the summation of impulses under strict conditions, and it is evident that the more heterogeneous is the origin of the synapses on the cells with descending axons, the more rigid become the conditions for threshold stimulation, and the more accurate the selection of the paths through which the impulses may be conducted.* The reduction of the number of cells with short axons, without essential modification of the long links in the chains of cortical neurons, makes the cortex of the mouse the " skeleton " for the human cortex, and no objection can be raised against the use of the diagrams given in figures 63, 64, 65, and 66 as a first approximation and interpretation of experimental results obtained in the higher mammals. These diagrams reproduce the elementary cortical pattern.

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* The elaboration of the elementary pattern takes place not only by the increase of the number of cells with short axons, but also by fractionation of the dendritic and axonal plexuses. For example, in the mouse the fractionation of the plexus of layers II and III is poor, but in the higher mammals, especially in man, an exquisite fractionation takes place in some cortical areas or, better said, at some places of each cortical area. The shafts of the pyramids of III do not give off side branches in II, and even within layer III two, three or even more sublayers appear, because the shafts of some pyramids in the main have side branches only near the cell body, and because next to the pyramids of average size small pyramidal cells appear with dendrites only within one substratum. The side branches of the vertical fibres also become grouped in substrata (cf. footnote, p. 308). The result is the fractionation of the plexuses into small strata containing synapses of but few types. It is remarkable that within each architectonic field characterized by receiving one set of specific afferents, for example the optic radiation, there are many zones of widely different structure recognizable in the ordinary Nissl picture by their position in relation to the sulci, even to the smallest indentations of the surface. Thus it comes about that the area striata is composed of an enormous number of vertical parallelopipedons with the longer horizontal axis parallel to the main system of fibres in the stria of Gennari and related to the numerous shallow sulci detectable in the surface of the calcarine cortex. In each parallelopipedon, which has microscopic size, the thickness of the layers and even the relative number of cells of each type varies between considerable limits. The drawing of Campbell (fig. 62) happens to include different parts of two adjacent parallelopipedons.

Besides elaboration by the addition of cells with short axons in various mammalian brains, the elementary cortical pattern, by losing some of the cell types, for example the star cells of layer IVb or some of the long chains, undergoes simplification within the brain of each animal type. The elementary pattern in figures 63, 64, and 65, with unessential modifications, is found to be valid for the cortex of the following regions: postcentralis, parietalis, occipitalis, and temporalis. But when studying the temporal lobe, in passing over the fissura rhinalis, it is found in the area entorhinalis (fig. 62B, *6*) that the afferent fibres fill the entire external lamina, so that their plexus is located immediately beneath and even within the plexiform layer. There are no cells comparable to those of layers II and III of the temporo-parieto-occipital isocortex. The layer of deep large pyramids (V) becomes very thin and seems to have lost its sublayers Va and Vc. The structure of the entorhinal area is illustrated in figure 67 in which, it will be observed, all the pyramids of the external lamina have the same relations to the afferent fibres as the star pyramids have in the isocortex. From certain points of view it would be permissible to compare the whole external lamina of the entorhinal cortex to layer IV of the isocortex, but the comparison would have small value and would mask the fact that in the area entorhinalis the impulses conducted by the recurrent fibres of the internal lamina meet the afferent impulses on the same cells of the external lamina, while in the isocortex the afferent and the recurrent cortical impulses are in part delivered to different cells (layers IV and II–III).

Since the cortical chains in the isocortex differ from those of the allocortex, no common pattern is valid for both, unless an important simplification is made and the temporo-parieto-occipital pattern is considered to be an elaboration of the entorhinal pattern. Then, viewing the external and internal laminae as more or less unitary systems, it may be said that the whole cortex, from the central sulcus, over the Sylvian sulcus to the occipital pole and back to the retrosplenial and callosomarginal sulci, is composed of two laminae. The upper lamina receives the specific afferents; the lower does not. The upper lamina has cells with efferent axons which reach only, or at least almost exclusively, other cortical regions (association fibres); while the lower lamina in addition has fibres of projection. Both laminae are interrelated by numerous vertical chains. In the isocortex the chains have greater complication because the number of links in each chain is larger.

No other cortical area has a simpler structure than that of the

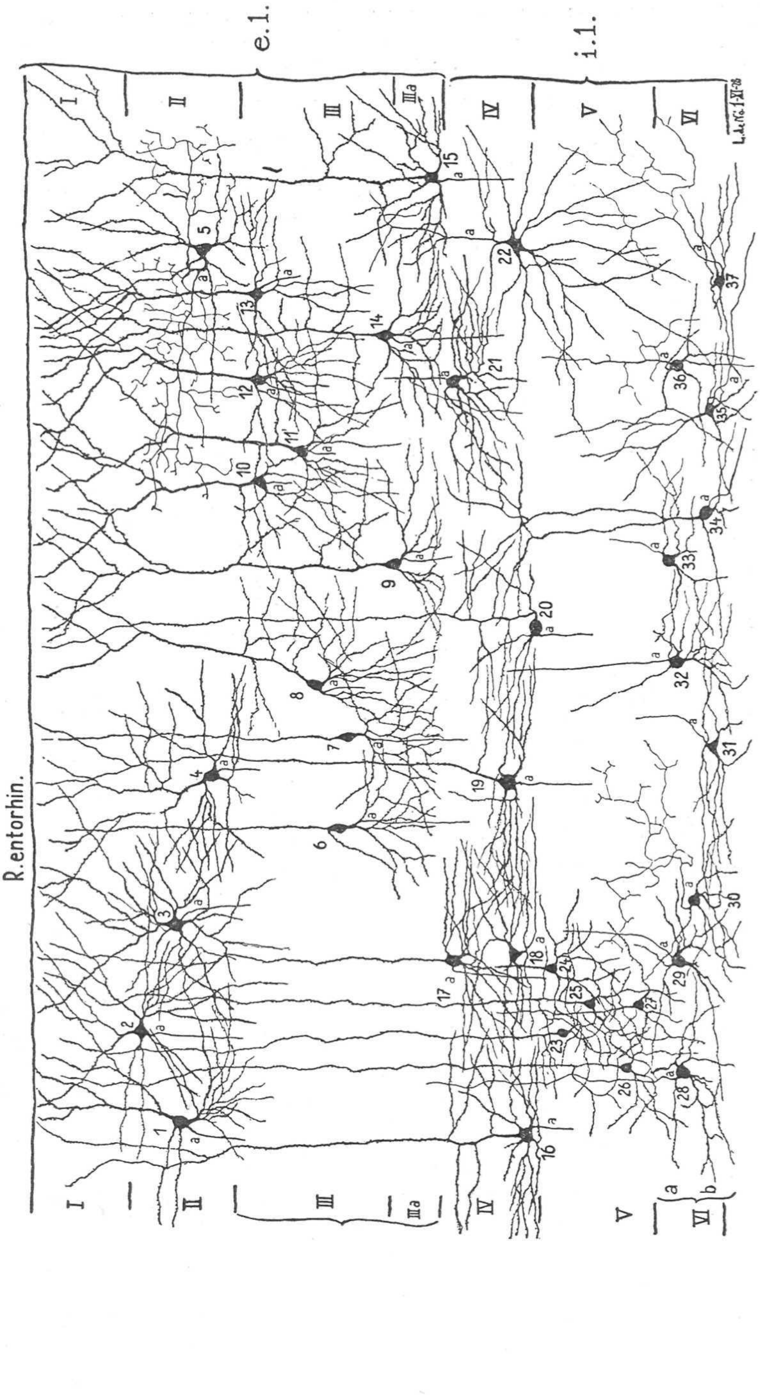

FIGURE 67 — For legend see bottom of opposite page.

entorhinal region, because the primary olfactory cortex[1047, 972] is in fact a subcortical centre comparable to the geniculate bodies, etc. The diagrams of figures 63 and 67 cannot as yet be said to be directly valid for the entire cortex, for the elementary pattern of the regio precentralis, frontalis, limbica, retrosplenialis, prefrontalis, and insularis is unknown.

Considerable information is available about the precentral cortex,[1047] but it is in part conflicting and decidedly incomplete. Cajal's data about the insular region are fragmentary, and the findings of the present author on that and the other unknown regions are still insufficient for definite statement. Hypothetical plans of stratification of these regions have been suggested by the cytoarchitectonic schools.

How the problem of the *motor* cortex stands at the present time may be stated in a few paragraphs. In 1900 Cajal made the remarkable observation that in the human precentral cortex, although the cell layers may be compared with those of the postcentral cortex, the specific afferents end in different layers; but this fundamental observation was unfortunately made by him too late. Having first discovered the afferent plexus in the precentral cortex, he examined the structure of the postcentral cortex with the idea that the said plexus should be found in the same place as in the precentral convolution. Much to his surprise this proved not to be true. However, Cajal did not fully realize that the suggested comparison of the cell layers and dendritic plexuses in the precentral and the postcentral cortices could not be maintained. The situation was the more puzzling

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Figure 67 — Diagram of the dendritic plexus in the entorhinal area (from Lorente de Nó, 1934). The numbers of the layers in this area do not correspond with the numbers of the layers in the isocortex (fig. 63). The architectonic picture of the human entorhinal area is reproduced in figure 62B, *6; e.l.* and *i.l.*, the two main laminae.

1 to *4*, pyramids of layer II; *6* to *15*, pyramids of layer III. Note the distribution of basilar dendrites and of collaterals of the ascending shafts within the external lamina. In IIIa there is a dense plexus with but few cell bodies. *16*, *17* and *19*, *20* large deep pyramids with side branches only within the layer; *23* to *27*, long spindles; *34*, medium spindle; *35*, deep star cell; *5*, cell with short horizontal axon in layer II; *18*, *21*, *22*, *28*, *29*, *31*, *32*, *33*, *36*, cells with ascending axons; *30*, *37*, cells with short axons of layers V–VI. The axons have been marked with a. In this area the specific afferent fibres are distributed in layers II, III, and IIIa and lower part of layer I.

since Cajal found that both regions have a layer of " granules "; but while in the precentral cortex the granules are found *below* the plexus of the afferent fibres, in the postcentral cortex they are *within* the plexus of the afferent fibres. Cajal's description of the afferent plexuses is so categorical that it must be taken as a statement of fact devoid of theoretical interpretation.

The present author has not been able to study the human precentral area as completely as is necessary for a definitive solution of the problem, but fragmentary observations added to more complete studies on the motor cortex of the cat, rat, and mouse suggest that the architectonic layers of granules in the precentral area are not comparable to the granular cells of the postcentral region. The superficial stratum of granular cells of Cajal (1900, his fig. 17A) which is mixed with medium sized pyramids is perhaps comparable to the fourth layer of the parietal isocortex. But the deep layer of granules of the motor cortex can be compared only to layer Va of the parietal isocortex. Hence the division of the motor cortex into two lamina suggested in figure 62A, *1* (*e.l.* and *i.l.*). Emphasis, however, must be placed upon the fact that the appearance of " granules " and of numerous short pyramids in the upper zone of layer V marks the beginning of a new structural pattern characteristic of the frontal isocortex.

In the case of the mouse, where the cells with short axons are not so numerous as in the cat or man, it may be found that the division of the cortex into two laminae is still possible, but also that the enormous widening of layer V, the appearance of large numbers of short pyramids in Va, and the great increase in the number of deep star cells in layer V cause the appearance of vertical chains subordinated to the unspecific afferents (fig. 63, *c, d*) and association fibres (fig. 63, *e, f*) which are not present or poorly developed in the parieto-temporo-occipital isocortex.

When the changes in structure of the cortex in the regions medial to the motor cortex are studied, it is seen that while advancing toward the limbic region, layers II and III of the outer lamina become progressively thinner and the afferent plexus approaches the plexiform layer. Finally in the so-called granular limbic and granular retrosplenial regions, as originally demonstrated by Cajal, the afferent plexus lies immediately below that layer. The outer cortical lamina is, therefore, greatly reduced, while the inner cortical lamina suffers a relatively smaller reduction. This suggests that the limbic and retrosplenial structural patterns in relation to the precentral pattern are in the same situation as is the entorhinal pattern compared to the postcentral pattern.

No attempt will be made here to suggest a diagram of stratification of the frontal isocortex, for in this account all anatomical hypotheses have been avoided. Since no information on certain fundamental points is available, any stratification made would be based only on assumptions. The elementary pattern of the frontal cortex is unknown and this lack of knowledge must be frankly admitted. The architectonic schools have assumed that the so-called " granular " frontal cortex is comparable in its stratification to the postcentral cortex. This comparison of the layers of " granules " may be correct, but it also may be erroneous. Until the afferent fibres of these fields are studied in suitable material, the question can not be definitely settled.

THE ARCHITECTONIC CHARTS

If use is made of the concept of the elementary unit introduced previously, it may be said that the cortex is composed of an enormous number of elementary units, not simply juxtaposed but also overlapping. Each elementary unit has a series of axonal and dendritic plexuses, where the synapses between intracortical elements and afferent fibres with cortical cells are established. The bodies of the cells which form similar links in the intracortical chains are grouped in horizontal layers. Therefore any change in the constitution of the intracortical chains must produce a variation also in the density of the plexuses, *i.e.,* in the Nissl pattern, in the size of the empty intercellular spaces, and likewise in the number of cells in each layer. As the Nissl method stains only the cells, but leaves the plexuses unstained, it does not yield absolute data regarding the structure of the cortex. It does, however, reveal its relative changes. The detection of structural modifications is made easier by the fact, forcibly demonstrated by O. and C. Vogt[1269] and later by M. Vogt,[1268a] that the changes take place simultaneously in several layers and often in all the layers. This was indeed to be expected, for the cortical neurons are arranged in chains that include cells from several layers, and a change in one layer must bring about changes in the others. The Vogts also have demonstrated that the changes take place not through transition zones, as assumed by Brodmann[154] and later by von Economo and Koskinas[360] but suddenly.

The ability of architectonics to detect changes in structure on the basis of the cytoarchitectonic Nissl picture or of the Weigert myeloarchitectonic stain cannot be questioned, not only because these studies have a sound theoretical foundation, but also because when they are complemented by selective methods, such as the Golgi or Golgi-Cox, the architectonic changes are found to be sharp and accompanied by alterations of the plexuses (Lorente de Nó,[818] p. 433). A difficulty arises when it is desired to set a limit to the parcelling. Campbell described 20 different fields in the human brain, Elliot Smith increased the number to 50, Brodmann also mentioned about 50, but in 1919 the Vogts announced the existence of over 200 fields. And even this number seems now to be too small, because the careful parcellations of some areas of the human brain and that of primates made by Rose[1098] and E. Beck[83] have revealed that the cytoarchitectonic divisions may be carried much farther than was previously thought desirable. A study of the excellent photographs published by Vogt, Rose, and Beck leaves no doubt that the architectonic differences really exist, and also that the divisions can be carried even farther. The recent parcellations made by E. Beck[83a] of the areas of the occipital lobe afford conclusive proof in this respect.

Architectonics is, therefore, an analytical tool which if used intensively will lead to an elaborate parcellation of the brain; theoretically, it should be possible by its use to go down almost to the elementary unit. However, the number of architectonic fields cannot be definitely stated, as it depends on the degree of change in the architectonic picture which the observer selects as standard. It is no secret that the classical architectonic charts were not made with uniform standards. Many architectonic fields were differentiated at the level of the central sulcus, because that region was intensively studied; later a comparable number of fields in the temporal lobe was described by Vogt and Beck and in the occipital lobe by Beck. In striking contrast to these parts of the architectonic charts, the parietal lobe is described as having only a few fields, but no author has published a parcellation made on the basis of a rigorous criterion.

It is an immediate consequence of the histological methods used in architectonic research that the nature of the changes at the boundary of fields remains unknown. For that reason any architectonic criterion which aims to divide the field boundaries into categories and to group the fields into larger divisions must be faulty. Only one example need be mentioned. In Ammon's horn, an area most suitable for architectonic studies, limits as important as those due to the ending of certain afferent tracts were ignored by the cytoarchitectonic school, and instead there were suggested limits for which no significant change in intercellular connections could be detected.[819] In these circumstances there can be no doubt that architectonics requires the help of other lines of research, anatomical and physiological, to group the individual fields into larger regions. The present grouping into regions, which is in fact made according to the macroscopic anatomy of the human brain, is clearly untenable. It is related to the projection of the thalamus into the cortex, but only along general lines. There can be no question that some of the areas, for instance the frontal region, contain heterogeneous fields offering differences more marked than those existing between, for example, the granular and the agranular limbic regions.

The recent development of cytoarchitectonics for which the Vogts, Rose and E. Beck are to be credited has demonstrated forcibly the shortcomings of the classic comparative cytoarchitectonics. Brodmann published charts of a number of different mammalian brains which it was believed were comparable. The individual fields were numerated in the same manner in the various mammals, and it was indicated that fields with the same numbers were homologous; it was further assumed that some fields were phylogenetically young, and specific human fields were described. Brodmann's concept has proved to be erroneous. It is not difficult for experts in cytoarchitectonic research to ascertain the way in which Brodmann established the "homology" between the fields of different mammals. Parcellations of the individual brains were made and a few fields were homologized on the basis of reliable data. These fields included the areas gigantopyramidalis, limbica, retrosplenialis, insularis, striata, and perhaps one or two more. The other fields were numbered hypothetically, not on the basis of specific structure, but on their gross anatomical relations to the known fields. This procedure, it must be stated, was not entirely unjustified, but it demanded parcellation of the individual brains with comparable criteria. In some of the larger brains, Brodmann differentiated many more fields than in the smaller brains for which he used a less rigorous architectonic criterion, and therefore a phylogenetic increase was assumed. However, when later Beck[83] parcelled the temporal lobe of the chimpanzee, he found that it contained many more fields than had previously been suspected, that it had in fact the same main fields as has the temporal lobe of man. Parcellation of the occipital lobe of the macaque (Beck, 1934) also revealed the existence of numerous subdivisions heretofore unsuspected.

It may be found that some of the new field boundaries used are artificial and irrelevant, but anatomically they are of the same order as the boundaries in the central convolutions, for the value of which experimental physiology has afforded conclusive proof. What the division of the brain into fields means is not a problem of architectonics, but rather one of experimental physiology and clinical neurology. Physiological research will no doubt group the small fields into larger units, but it must also analyze the role played by even the smallest anatomical subdivision. How many fields the individual mammals have is unknown. There is no doubt but that all mammals must have nearly the same major divisions of the cortex, because the thalamic nuclei do not differ in a radical manner from mammal to mammal; as a matter of fact, however, noth-

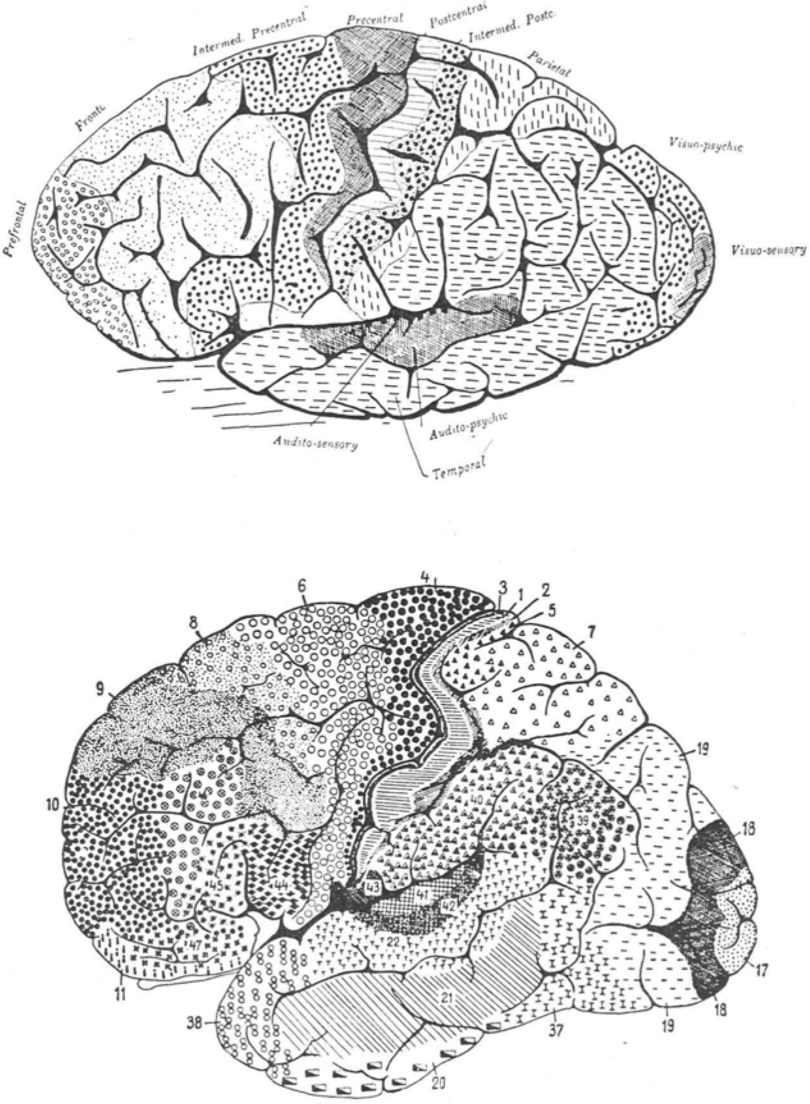

FIGURE 68

Cytoarchitectural maps of the human cortex. A. Campbell's map,[199] the prototype of all subsequent cytoarchitectural charts of the human brain. B. Brodmann's map[154] giving his numerical designation of the principal areas.

ing is known about the smaller subdivisions. The evolution of the structure of the cortex in the mammalian series reveals itself chiefly in an increase in the relative number of cells with short axons without essential alteration of the elementary pattern. Possibly future research will lead to the establishment of an elementary " field pattern," including the thalamic nuclei, and then it may be hoped that the comparative anatomy of the brain will be successfully studied. For one set of fields, those of the Ammonic system, an elementary pattern has already been established and it is found that this remains constant for every mammal, from the mouse to man;[818] but whether conclusions drawn from the study of a system may properly be applied to the rest of the cortex is an open question.

A complete chart of the human brain or of the brain of primates is not yet available. The published charts of Vogt, Rose, and Beck include only segments of the brain. A general orientation, however, can be obtained by a study of the old charts of Campbell[199] (fig. 68A) and the similar ones of Brodmann[154] (fig. 68B); also of the chart of von Economo and Koskinas[360] which, in fact, is Brodmann's chart with unsystematic elaborations.

SUMMARY

Modern research on the cortex has proceeded along two different lines: the study of the intimate structure of the cortex and of intracortical connections, and the subdivision of the brain into regions of specific architecture. Architectonic studies made on the basis of stains of the bodies of the cells (cytoarchitectonics) or of stains of myelinated fibres (myeloarchitectonics) have revealed that the human brain contains several hundred areas, differently built, which may be grouped into a few regions corresponding roughly to the lobes and other major divisions of the old anatomists. A first division in allocortex and isocortex is made on the basis of the existence of a superficial layer of myelinated fibres, which layer is white in the fresh brain; it is considerably more prominent in the allocortex. This division corresponds roughly to that in the rhinencephalon and the pallium of old anatomists. The main re-

83. Beck, E. Das Hörzentrum des Schimpansen in seinem myeloarchitektonischen Aufbau. *J. Psychol. Neurol., Lpz.*, 1928, **36,** 325–349, 11 fig.

83a. Beck, E. Die myeloarchitektonische Felderung des in der Sylvischen Furche gelegenen Teiles des menschlichen Schläfenlappens. *J. Psychol. Neurol., Lpz.*, 1929, **36,** 1–21.

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Der Occipitallappen des Affen (Macacus rhesus) und des Menschen in seiner cytoarchitektonischen Struktur. I. Macacus rhesus. *J. Psychol. Neurol., Lpz.*, 1934, **46,** 193–323.

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151. Brodmann, K. Beiträge zur histologischen Lokalisation der Grosshirnrinde. I. Die Regio Rolandica. *J. Psychol. Neurol.*, 1903, **2,** 79–107; II. Der Calcarinatypus, *Ibid.*, 133–159.

154. Brodmann, K. *Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues.* Leipzig, J. A. Barth, 1909; reprinted, 1925, xii, 324 pp.

199. Campbell, A. W. *Histological studies on the localisation of cerebral function.* Cambridge, University Press, 1905, xx, 360 pp. (see p. 242).

360. Economo, C. von, and Koskinas, G. N. *Die Cytoarchitektonik der Hirnrinde des erwachsenen Menschen.* Vienna, J. Springer, 1925, 810 pp., atlas with 112 pl. Abbreviated English text: *The cytoarchitectonics of the human cerebral cortex.* Trans. by S. Parker. London, Oxford University Press, 1929, xii, 186 pp.

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gions of the isocortex are prefrontalis, frontalis, intermediate precentralis, precentralis, postcentralis, parietalis, occipitalis, temporalis and insularis, and those of the allocortex are limbica, retrosplenialis, entorhinalis and Ammon's horn formation. A *complete* chart of the brain of man or of any mammal is not as yet available. Brodmann's numerical designations of the principal fields have been adopted for descriptive purposes.

Studies on the fine structure of the cortex have revealed that, although in architectonic pictures the horizontal stratification seems to be the most important factor in cortical organization, the intracortical connections are established chiefly in vertical directions so that the whole vertical section of the cortex must be considered as a unitary system. The cortical cells are arranged in vertical chains and the architectonic layers indicate only where the bodies of cells, which are similar links in the chains, are located. But those cells, by means of long dendrites, establish connections in other layers. The elementary pattern of the postcentral-parieto-temporo-occipital isocortex is described and compared with the simpler pattern of the entorhinal cortex. It is emphasized that the pattern of the precentral, frontal, retrosplenial and limbic cortices is still unknown.

The white lines separating certain of the cortical laminae are due to strata of medullated fibres. The best known is the line of Gennari, in the area striata of the occipital lobe (visible to the naked eye). The same line is present, although less thick, elsewhere in the cortex, and there is known as the external line of Baillarger. The Gennari-Baillarger lines form the outer part of the fourth cortical lamina. The internal stria of Baillarger corresponds with the inner half of the fifth lamina (internal pyramidal layer). The line of Kaes and Bechterew is found on the outer margin of the third cortical lamina (external pyramidal layer).

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