COMPARATIVE STUDY OF THE SENSORY AREAS OF THE HUMAN CORTEX.

BY SANTIAGO RAMÓN Y CAJAL.

In order to respond worthily to the gracious invitation with which Clark University has honored me, I ought to offer you, as was my original intention, a work of synthesis, a general summary of the present state of our knowledge of the minute anatomy of the nervous system. Unfortunately, the duties of my professorship, every day more pressing, have deprived me of the time necessary for the accomplishment of such a task, and have compelled me to moderate my ambition, and to limit it to presenting to you a modest analytical contribution to our knowledge of the microscopical structure of the sensory centres of the human cerebral cortex, a subject to which I have devoted the leisure of the past months.

This subject is so vast and so difficult that, in spite of my efforts and the time devoted to it, I have been able to clear up only a few points. Consequently, my contribution will be, to my utmost regret, a very incomplete one, treating, as it does, only the visual cortex as I have made it out in man and some of the higher mammals. I shall add, however, a few observations on the structure of other sensory regions.

This anatomical study of the sensory areas of the cortex, at the present state of our knowledge, presents points of special interest, since, as you well know, neurologists who have interested themselves in the histology of the brain are divided at present into two camps, the unicists and the pluralists.

The unicist doctrine, proclaimed by Meynert and reaffirmed quite recently by Golgi and Kölliker, supposes that all regions of the cortex possess essentially the same structure, functional diversity being due to diversity of origin of afferent or sensory nerves. This amounts to saying that cerebral specific energy of nerves is the necessary effect of the particular organization of each sense as well as of the special character of the stimuli received by the peripheral sensory surfaces, skin, retina, organ of Corti, etc.

The pluralist doctrine, upheld recently by Flechsig, without rejecting the particular influence of connections with different nerves, maintains that diversities of function result also from the particular structure of each cortical area.

It is this latter opinion, as we shall presently see, that presents a closer agreement with the observed facts. In fact, my researches tend to prove that the topographical specialization of the brain depends not only on the quality of the stimuli analyzed and gathered up by the sensory mechanisms, but also on the structural adaptations which the corresponding cerebral areas undergo; since it is very natural to suppose, even if one were to form an *a priori* judgment, that the cortical areas connected with the spacial senses sight and touch, which form exact images of the exterior world with fixed relations of space and intensity, have by accommodation to the stimuli received an organization different from that existing in cortical areas attached to the chemical senses of taste or smell, and from that which is appropriate to the chronological sense hearing, which gives only relations of succession, free from every spacial quality.

We may add that if there exist in the human cerebral cortex, as Flechsig supposes, besides the sensori-motor centres, other regions, association centres, characterized by absence of direct sensory or motor connections, it seems very natural also to associate to these important regions of the brain, with which are connected the highest activities of psychic life, a special organization corresponding to their supremacy in the hierarchy of functions.

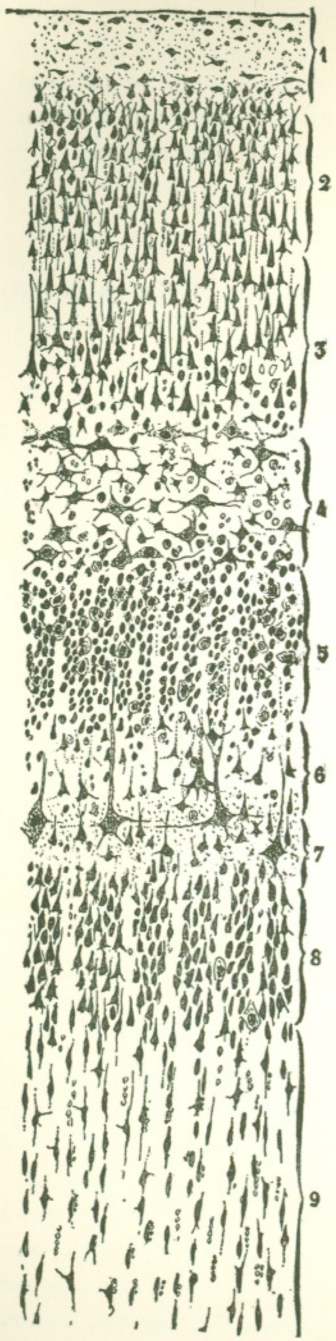
But we must not carry to an extreme the structural plurality of the brain. In fact, our researches show that while there are very remarkable differences of organization in certain cortical areas, these points of difference do not go so far as to make impossible the reduction of the cortical structure to a general plan. In reality, every convolution consists of two structural factors: one, which we may call a factor of a general order, since it is found over the whole cortex, is represented by the molecular layer and that of the small and large pyramids; the other, which we may call the special factor, particularly characteristic of the sensory areas, is represented by fibre plexuses formed by afferent nerve fibres and by the presence at the level of the so-called granular layer of certain cell types of peculiar form.

But, before proceeding to outline the general conclusions of an anatomico-physiological order, that result from all our researches taken together, permit me to present very briefly the facts of observation.

Visual Cortex.

The minute anatomy of the visual cortex (region of the calcarine fissure, sulcus cornu lobulus lingualis) has been already explored by several investigators, among whom we may make particular mention of Meynert, Vicq d'Azyr, Gennari, Krause, Hammarberg, Schlapp, Kölliker, *et al.* But their very incomplete researches have been performed by such insufficient methods as staining with carmine, the Weigert-Pall method, or that of Nissl with basic anilines — methods which, as is well known, do not suffice at all to demonstrate the total morphology of the elements and the organization of the most delicate nerve plexuses. They led, however, in spite of the difficulties which stood in the way of these first analytical attempts, toward a precise differentiation of the visual cortex from other regions of the brain. At the outset two characteristic differences attracted the attention of the first investigators into the structure of the visual cortex: first, the existence of a very thick stratum of granules, subdivided into accessory strata by laminæ of molecular appearance; and, second, the presence in the intermediate layers of the cortex of a white lamina formed of medullated fibres — which lamina may be seen with the unaided eye. This lamina, appearing in cross-section as a white line, has been named, in honor of the writers who first described it, the line of Gennari or Vicq d'Azyr.

For the sake of brevity, we shall omit a detailed description and discussion of the various layers admitted by the authorities on this region; suffice it to mention in order the eight layers described by Meynert for the human cortex: First, molecular; the second, layer of small pyramidal cells; third, layer of nuclei or granules; fourth, layer of solitary cells; fifth, layer of intermediate granules; sixth, layer similar to the fourth, containing nuclei and scattered cells; seventh, deep nuclear layer; eighth, layer of fusiform cells. We may also mention the arrangement of layers recently described by Schlapp for the occipital cortex of the monkey: (1) layer of tangential fibres; (2) layer of exter-



nal polymorphic cells; (3) layer of pyramidal cells; (4) layer of granules; (5) layer of small solitary cells; (6) second layer of granules; (7) layer poor in cells; (8) layer of internal polymorphic cells.

The investigations which I have made on the human cortex as well as on that of the dog and cat, by both the Nissl and Golgi methods, have led me to distinguish the following layers: —

1. Plexiform layer (called molecular layer by authors generally and cell-poor layer by Meynert).
2. Layer of small pyramids.
3. Layer of medium-sized pyramids.
4. Layer of large stellate cells.
5. Layer of small stellate cells (called layer of granules by the authors).
6. Second plexiform layer, or layer of small pyramidal cells with arched axon.
7. Layer of giant pyramidal cells (solitary cells of Meynert).
8. Layer of medium sized pyramidal cells with arched ascending axon.
9. Layer of fusiform and triangular cells (fusiform cell layer of Meynert).

You see that we have modified current nomenclature by introducing terms which call to mind cellular morphology. For we believe that such trite expressions as "molecular layer," "granular layer," must be

FIG. 1. — Vertical section of the visual cortex of man, calcarine sulcus, stained by Nissl's method — semischematic. 1. Plexiform layer. 2. Layer of small pyramids. 3. Layer of medium-sized pyramids. 4. Layer of large stellate cells. 5. Layer of small stellate cells. 6. Second plexiform layer, or layer of small pyramids with arched axon. 7. Layer of giant pyramids. 8. Layer of medium-sized pyramidal cells with ascending axon. 9. Layer of fusiform and triangular cells.

banished once for all from scientific language, and they must be replaced by terms which point out dominant morphological characters in the nerve structures of each layer or some interesting peculiarity relative to the course and connections of the axis cylinder processes. The number of layers could be easily increased or diminished, because they are not separated by well-marked boundaries, particularly in Nissl's preparations. Thus the number of layers which I adopt is somewhat arbitrary. By distinguishing, however, nine layers, I have followed a criterion of individualization which seems to me the most convenient and suitable for my exposition of the cortex as a mechanism composed of elements at a certain level which differ in special morphological features from those of neighboring levels. Besides, the number, extent, and size of cells in these layers vary a little in the different median occipital convolutions, as does also the degree of definite nidification, according as we study the convex or concave aspect of the gyri. Our description relates generally to the cortex of the margin of the calcarine fissure, the region where structural differentiation of the visual cortex is most pronounced.

Plexiform Layer.

The plexiform or molecular layer is one of the oldest cerebral formations in the phylogenetic series. It presents characters similar to those of the human cortex in all vertebrates except the fishes. This has been fully demonstrated by the researches of comparative histology undertaken by Oyarzun (batrachia), by myself (batrachia, reptilia, and mammalia), by my brother (batrachia, reptilia), by Eddinger (batrachia, reptilia, aves), by Cl. Sala (aves). In the visual cortex of man, the structure of this layer coincides perfectly with that which my own researches, as well as those of G. Retzius, have revealed in the motor region. The only modification which may be noted, visible even by Nissl's method, is its notable thinness in the margins of the calcarine fissure (except in the sulci, and here it appears somewhat thinned). This diminution in thickness, noted by authors generally, depends probably on the small number of medium-sized and giant pyramidal cells in the underlying layers, because it is well known that each pyramidal cell is represented in the plexiform layer by a spray of dendrites. A similar opinion has been expressed by Bevan Lewis in order to explain irregularities in thickness of this layer in different regions of the cortex of the rabbit and guinea-pig. The structure of the plexiform layer is very complex. From my own researches, confirmed largely by those of Retzius, Schäfer, Kölliker, and Bevan Lewis, it follows that it consists of an interweaving of the following elements: (*a*) the radial branches of the small, medium-sized, and giant pyramidal cells, with which we must include in addition those of the so-called polymorphic cells; (*b*) layer of terminal ramifications of the ascending axons of Martinotti; (*c*) layer formed by the arborizations of the nerve fibres, terminal or collateral, which come from the white matter; (*d*) layer of special or horizontal cells of the first layer (Cajal's cells, of Retzius); (*e*) layer of small and medium-sized stellate cells with short axons; (*f*) layer of neuroglia cells, well described by Martinotti, Retzius, and Andriesen.

a. **Terminal Arborizations of the Pyramidal Cells** (Fig. 4). — As my observations have shown in case of the mammalian cortex, and those of Retzius for the human fœtus, the radial trunk of the pyramidal cells does not end, as Golgi and Martinotti supposed, in a point entwined by neuroglia elements in connection with the blood-vessels, but in a spray of varicose dendrites covered with contact granules, spreading out sometimes over a considerable area of the plexiform layer. In my first work on the cerebral cortex, I thought that the only cells whose terminal dendrites reached up to the first layer were the medium-sized, small, and giant pyramidal cells; but my latest researches have enabled me to discover that all cells possessing a radial stem, without exception, including even those of the deeper layers, are represented in the plexiform layer by a terminal dendritic arborization. It is without doubt an important structural law whose physiological import must be very considerable. We may observe that large trunks which arise from the giant pyramids divide into a spray with very long and thick branches having their distribution in the deeper level, while the slender stems emanating from the medium and small sized pyramids form an arborization of numerous slender branches of limited extension and distributed particularly through the superficial laminæ of the plexiform layer. This distribution, which is not absolutely constant, leads us to surmise that the terminal arborizations of each kind of pyramidal cell come into contact with special neuritic terminal arborizations in traversing this first layer.

The trunk and end brush intended for the first layer appear not only in preparations made by the chromate of silver method; for I have stained them perfectly with methylene blue (method of Ehrlich-Bethe) in case of young animals, and also in adult gyrencephalous mammals, such as the dog and cat. Besides, in good preparations by Ehrlich's method, particularly when fixation has been made a short time after the impregnation, one may see very distinctly the contact granules of the dendrites, processes which I was first to describe and whose existence has been confirmed by many investigators since. With methylene blue they present the same appearance as in Golgi preparations, *i.e.* they are slender and short, stand out at a right angle, are sometimes divided, and end freely in a rounded knob. This proves, accordingly, how groundless are all the gratuitous objections which have been brought against the preëxistence of these appendages, as well as against their mode of termination. Among the entirely arbitrary conjectures which have been made as to the disposition of these appendages we include also W. Hill's opinion, who considers them the fibres of a reticulum that is incompletely stained by means of the chromate of silver. We must proclaim emphatically that at present there is no method of staining cellular processes that is capable of disproving the agreeing results of the methods of Golgi, Ehrlich, and Cox. Whoever, having as a foundation the revelations of any one of these methods, has considered it possible to demonstrate the existence of such a reticulum has only exposed to view his own lack of experience in handling these important means of analysis.

b. **Special or Horizontal Cells of the Plexiform Layer.** — These interesting elements, which I discovered in the cortices of the small mammals (rat, rabbit, guinea-pig), have been successfully investigated by Retzius in case of man, as well as by my brother in batrachians and reptiles, and by Veratti in the rabbit's embryo. They present in the visual cortex, where I have stained them very often, the same characters as in other regions of the brain. As I have already described these elements elsewhere, I shall give here only an outline, to which I may add a few remarks derived from my recent observations upon man (Fig. 2).

Following the example of Retzius, when we study the horizontal cells by Golgi's method in a human fœtus from the seventh to the ninth month, or in case of a newborn babe, we notice that they are distributed throughout the entire thickness of the plexiform layer, but are especially numerous in close proximity to the pia. Their form is very variable, sometimes fusiform or triangular, and again stellate, with the angles extending out into the long processes. But the characteristic feature of these elements is due to the fact that their processes, which are variable

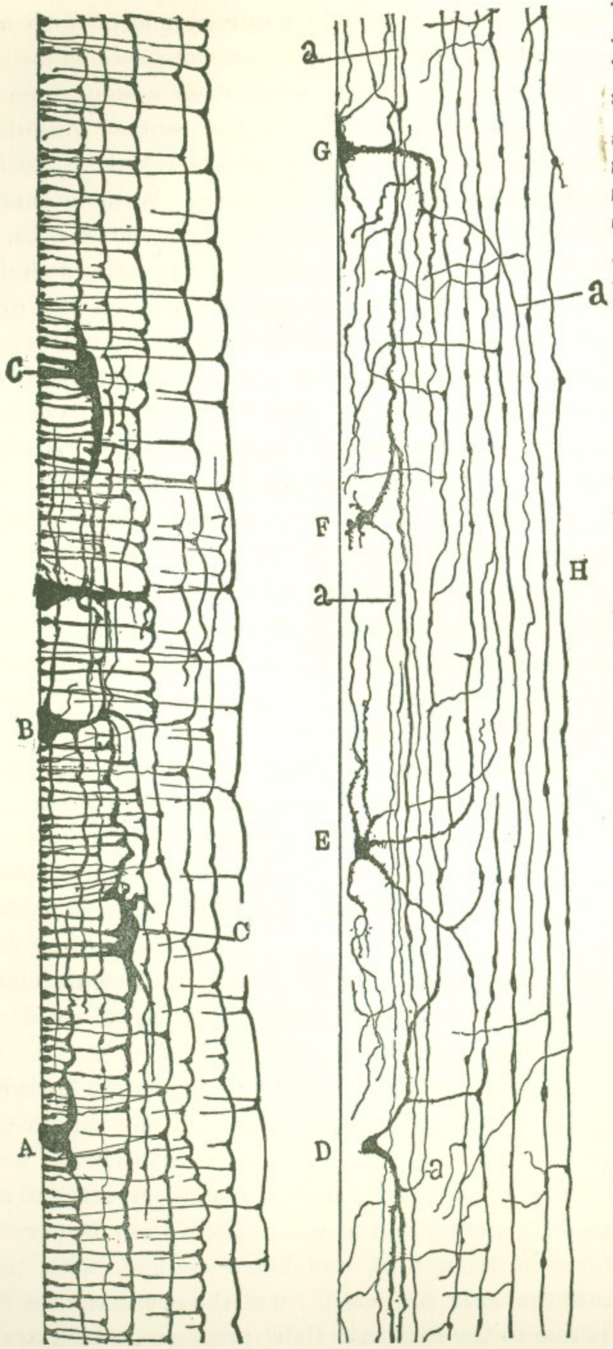


Fig. 2.—Cells of the 1st lamina of the plexiform layer. *A, B, C*, horizontal cells of the visual cortex of infant at birth; *D, E, F, G*, cells of visual cortex of infant at twenty days; *H*, horizontal fibres arising from cells of the same kind situated at a great distance within the first lamina; *a*, delicate processes having the appearance of axons.

in number and very large at their origin, give rise, after a few divisions, to an extraordinary number of varicose horizontal fibres, extremely long, from which spring at right angles numberless ascending secondary branches terminating in rounded knobs near the cerebral surface. Very often the superior surface of the cell body also gives rise to some of these ascending branches, which sometimes have a considerable thickness.

In what way do these tangential fibres terminate? Is it possible to discern among them certain processes possessing the characters of axons?

Upon careful examination of the best preparations obtained from cortices of human embryos, we discover easily that these processes, when they become very fine, have all the appearances peculiar to axons. There is no morphological distinction which would enable us to distinguish the two classes or species of cellular processes. That which most strikes one is the enormous length of their horizontal fibres (tangential fibres of Retzius). One can follow them for two or three tenths of a millimeter without being able to discover their true termination. However, in certain cases it is possible to demonstrate that the tangential fibres, after having given rise to a great number of vertical twigs, become thinner and finer, and finally subdivide into terminal branchlets, which spread out under the pia or in the superficial laminæ of the first layer.

On comparing these cells of the human brain with their homologues in the higher mammals (rabbit, cat, etc.), we discover that among the latter they give rise to a relatively small number of tangential branches, and that these extend a much shorter distance. This is the reason we consider the remarkable profusion and the extreme length of the horizontal fibres as one of the most characteristic features of the human cortex.

Retzius did not succeed in staining the horizontal cells in man except in the fœtal period. Accordingly, it was impossible to know what becomes of these elements in the adult, and whether, as Retzius is inclined to think, all the processes that we find in the embryonic period persist. My recent researches on the cortex of infants fifteen months and even fifteen and twenty days old, in which I have been successful in staining the horizontal cells, suffice to furnish a few data which, if they do not solve the problem once for all, at any rate place the question in a somewhat more favorable light.

When we examine the plexiform layer of a babe fifteen days old, we find considerable changes in the horizontal cells. First of all, we notice that they have become smaller, and that the tangential processes have diminished in diameter while they have become notably lengthened. But the peculiarity which most strikes the attention is the almost total disappearance of the ascending collateral branches. This atrophy begins in a progressive thinning of the processes and in the reabsorption of their terminal varicosities; then the whole branch disappears, so that the only structures left are the horizontal fibres, whose ensemble forms throughout the thickness of the plexiform layer a system of parallel fibres of enormous length. There are places, however, where the ascending branches persist, but very much changed as to their direction, having become oblique instead of vertical, becoming branched several times, and terminating in the plexiform layer without reaching so far up toward the pia as before. In a word, most of the vertical branches seem to me to represent an embryonic arrangement corresponding to the interstices, for the most part vertical, between the epithelial cells of the cerebral cortex of the fœtus, which proves once more, as I have demonstrated in other nerve centres, that during the period of evolution the neuron is the locus of a double series of functions: on the one side a vegetative building up of the dendrites; on the other, reabsorptions and transformations of the cells which persist.

Have the horizontal cells with which we are now concerned a true functional process? In case this is so, what is the part played by these elements in the vast system of nervous relations established in the plexiform layer?

In preparations of the human brain stained with chromate of silver, it must be confessed, it is not easy to solve this important question, since the purely morphological criterion, which is sufficient to distinguish the axon in other neurons, cannot be applied to horizontal cells, all the processes of which, on becoming finer, have the form of true axons. Thus, in spite of Veratti's affirmation, we believe that this method will shed no light upon the subject, even when applied to embryos. In order to approximate to any solution of the problem, we must use a method capable of staining nerve prolongations in a manner to differentiate them from dendrites. It was only after using Ehrlich's methylene-blue method upon the motor and visual cortex of the cat that I became convinced that the horizontal cells have in reality a very long axon, which is provided with a medullary sheath. The other processes, which we have called horizontal fibres, represent true dendrites, as is shown by two peculiarities: the great

facility with which they take methylene blue, and their pronounced varicosity after fixation with ammonium molybdate. We must repeat that this varicose alteration, which is a striking modification in the form of cellular prolongations, presents itself only in dendrites. The neurites maintain perfectly, with methylene blue, their normal contours, unless exposure to the air, necessary to obtain the selective staining, has been too long.

As to the axon, it may be sufficiently well demonstrated in horizontal sections of the plexiform layer in the form of a pale blue fibre, except the initial portion and the nodes, which present a dark blue staining. This is a property of all parts of a fibre not surrounded with a medullary sheath. At the point of certain constrictions we may succeed in discovering a few collaterals springing out at right angles, provided also with myeline sheaths. Finally, one is sometimes so fortunate as to discover in an axon of this kind true bifurcations situated at a great distance from the cell of origin, but always in the plane of the plexiform layer. Unfortunately, the methylene blue does not stain the terminal nerve arborizations. This has prevented me from learning in just what way these axons terminate and with what axons they are dynamically associated. It is possible that certain heavy horizontal fibres come into contact with the horizontal cells, since they never bend downward toward the underlying layers, as do the medium-sized and finest medullated fibres. They belong probably to the terminal arborizations of Martinotti's ascending axons and, perhaps, also to the collaterals and terminals coming in from the white matter.

c. **Cells with a Short Axon** (Fig. 3, *G*, *E*, *F*).— A few years ago, while studying the cerebral cortex of the small mammals, I discovered, besides the gigantic horizontal cells, other elements which I called polygonal cells. These are characterized by their stellate form and by their short axon, which ramifies and ends within the limits of the plexiform layer. These cells, whose existence neither Schäfer nor Lewis seem to have been able to confirm,—no doubt on account of the insufficiency of their attempts to obtain an impregnation of them,—are much more abundant than might have been supposed from my first observations. However, I must acknowledge that, they are not at all easily impregnated with chromate of silver and that, in order to find a sufficient number for study, we must make a great many attempts at staining them. On the other hand, Ehrlich's method stains them very readily in the dog and rabbit. In these animals

— and I think that it holds true also in man — the plexiform layer of the cerebrum is as richly supplied with elements with a short axon as the molecular layer of the cerebellar cortex. They occur in all levels of the layer and differ remarkably in size and shape. The majority of them are stellate and are comparable in size to other cells with short axons

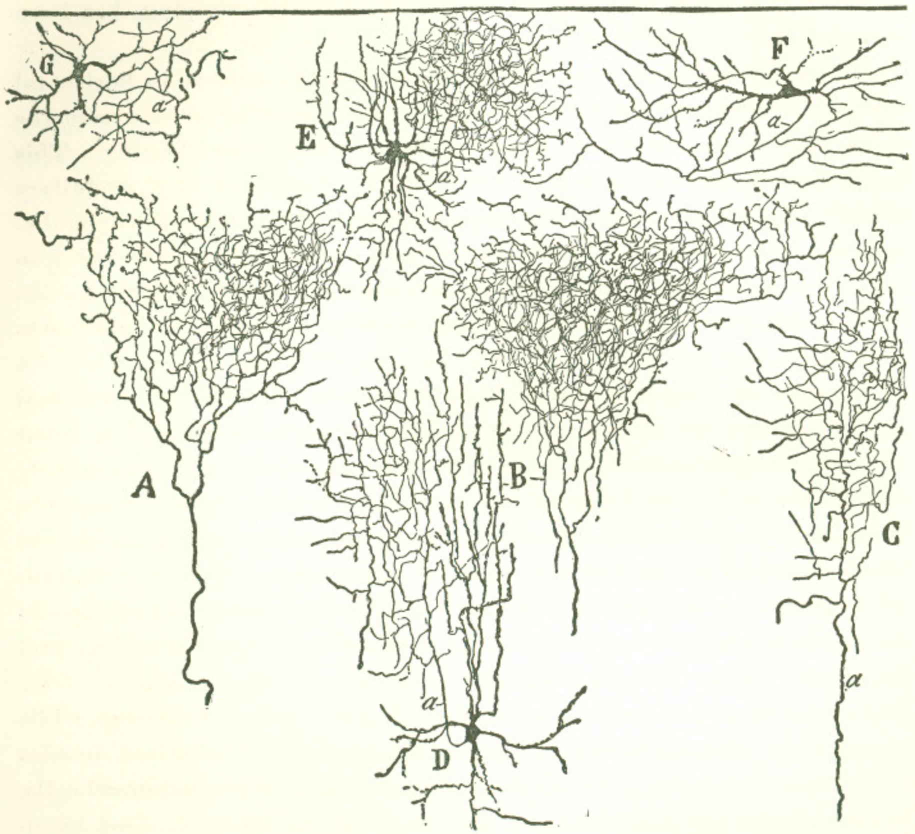


FIG. 3. — Cells and neuritic terminal arborizations in the 1st and 2d layers; visual cortex of infant 20 days old. *A* and *B*, neuritic plexus, extremely fine and dense, situated in the layer of small pyramids; *C*, an analogous arborization, but not so dense; *D*, a small cell whose ascending axon forms a similar arborization; *E*, spider-shaped stellate cell of the 1st layer; *F*, *G*, cells with short axon branching loosely in the plexiform layer; *a*, axon.

that occur in the deeper layers of the cortex. Others are smaller, resembling in their minuteness the granules of the cerebellum. But whether large or small, the morphological characters of these elements are very similar. Their dendrites are divergent, extremely branched, and distributed exclusively to the plexiform layer. Their neurites are

usually very short, subdivide in a most complicated manner in the neighborhood of the cell, but never cross the deep boundary of the first layer.

From the point of view of the direction and length of their neurites all these elements may be classified into three varieties: (1) Stellar cells with horizontal neurite which becomes resolved after a varying distance, generally very long, into a terminal arborization which has the appearance of being connected with the terminal branches of the remote pyramids. (2) Cells of generally smaller size whose neurite branches either laterally or vertically from the cell body, but always at a moderate distance (Fig. 3, *G*, *F*). (3) Very small cells (which I discovered recently in the human cerebral cortex) provided with numerous fine, divergent, and slightly branched dendrites, whose neurite, extremely slender, breaks up near its origin into a dense arborization, exceedingly fine and complicated. We shall designate these elements dwarf or spider-shaped cells. They may be found, as we shall see, in all the layers of the cortex (Fig 3, *E*).

To sum up: bearing in mind the form of cell bodies and formation and connection of axons, all the stellate cells of the plexiform layer, including the horizontal or special cells, seem to me similar to the stellate cells of the molecular layer of the cerebellum and to those which occur in the layers of the same name in the *cornu ammonis* and *fascia dentata*. Their function is probably to establish connections between terminal arborizations as yet imperfectly made out, possibly those formed by the ascending axons of Martinotti, or the association fibres coming up from the white matter with the terminal branches of the pyramidal cells. The function of the great horizontal cells would seem to be to establish connections between elements, that is to say between terminal neuritic arborizations and radial dendrites, separated by very considerable distances; while the medium-sized and small elements, with their short axons, would perform the same associative function at short or moderate distances.

d. **Martinotti's Ascending Fibres.** — There is no lack of these in the visual cortex, although it has seemed to me that they are not so numerous as in other regions of the brain. Their terminal ramifications, well known from the researches of Martinotti as well as my own, occupy really the whole plexiform layer, where they extend over wide areas, distributing themselves preferably into its deeper levels and coming in contact with cells with short axons and, possibly, also with the large horizontal cells.

Granting that the cells of origin for these fibres lie in layers of the cortex that contain sensory fibres, we might suppose that Martinotti's ascending axons represent intermediate links placed vertically between these sensory fibres and cells with short axon in the plexiform layer. And as these are connected, perhaps, with the dendrites of the pyramidal cells, the result would be that the sensory stimuli, entering the cortex in this indirect way, would be compelled to traverse two intercalated nerve cells before reaching the pyramids.

e. **Neuroglia Cells.** — These conform in the visual cortex to the well-known types of other cerebral regions. We find accordingly: (1) Cells with long radii, the marginal cells well described by Martinotti, which lie just under the pia. They emit long, smooth, descending processes radiating across the plexiform layer, ending at different levels both of this and of the layer of small pyramids; (2) Cells with short radii. These elements, long since described by Golgi, and described in detail by Retzius, by myself, Andriesen, Kölliker, and others, are characterized by their form, very often stellate or fusiform, by their location in all levels of the plexiform layer, and by the great number of their processes, short, spongy, branching, and bristling with innumerable contact granules, which penetrate into the spaces lying between the neuro-protoplasmic plexus and are well spread over the interstices of the elements which must not come into contact. It is in virtue of this intricate relation between these appendages and the cell bodies and dendrites, as well as for other reasons which we have not time to dilate upon here, that we attribute to the neuroglia elements with short processes an insulating rôle. According to my view, they prevent inopportune contacts, while their processes exercise due regard to all points of cells or fibres where contacts exist and nerve currents pass.

Layer of Small Pyramids.

This layer is well separated from the 1st, but blends by insensible gradations with the 3rd, or layer of medium-sized pyramidal cells (Fig. 4, *B*).

Examined in Nissl preparations this layer presents a great number of small pyramids, very poor in chromatic granules and separated by a plexus of fibrils much more dense than in the case of cells of the deeper layers. We find also, scattered irregularly, stellate or triangular cells

larger than the pyramids. These are the giant cells with short axon, as is shown in good chromate of silver preparations (Fig. 5, *D*, *C*). We shall now discuss the cells of this layer, beginning with the pyramids.

Pyramids. — The morphology and relations of these cells being well

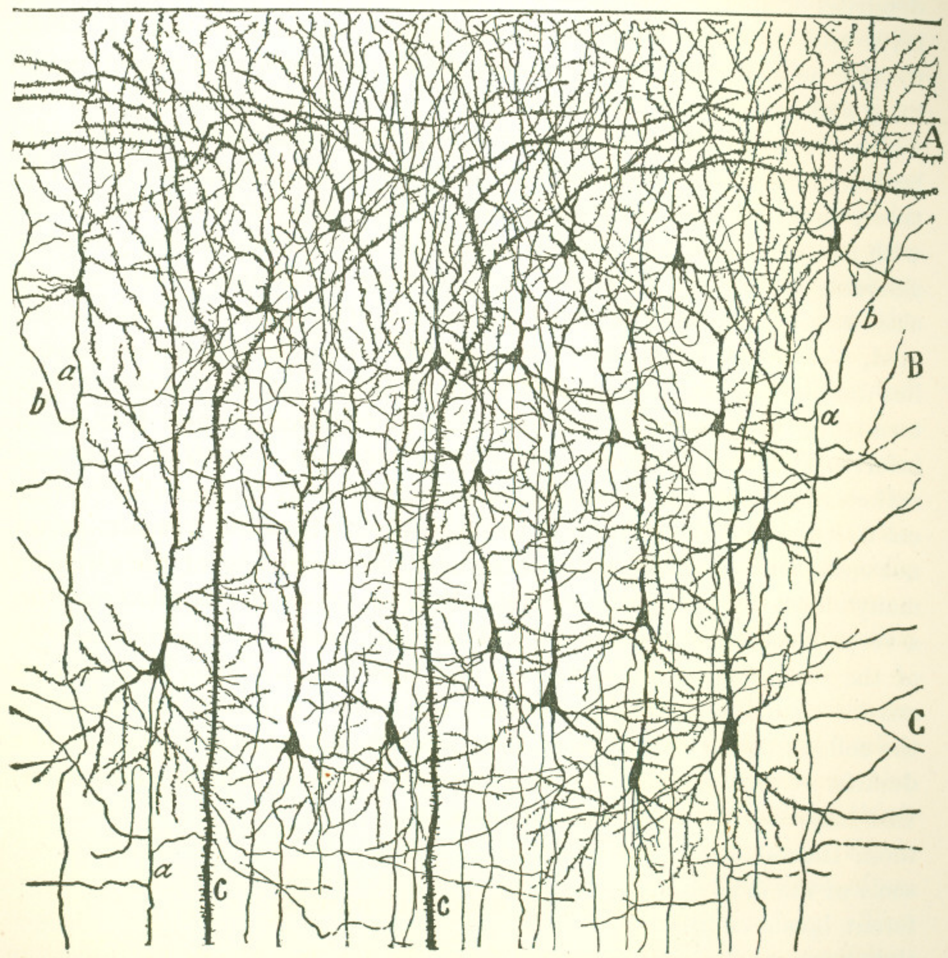


Fig. 4. — Small and medium-sized cells of the visual cortex of an infant 20 days old (calcarine sulcus). *A*, Plexiform layer; *B*, layer of small pyramids; *C*, layer of medium-sized pyramids; *a*, descending axon; *b*, recurrent collateral; *c*, dendritic trunk of giant pyramid.

known since the researches of Golgi, Retzius, and myself, I shall limit my remarks to a bare mention of a few peculiarities of their disposition in the visual cortex.

It will be noticed that these cells are generally smaller and more numerous in the visual centres than in other cortical areas. Sometimes the more superficial cells are arranged in one or two regular files and separated from those beneath by a fine dense plexus of fibres.

The small pyramids give rise to the following processes: an axial dendrite, often bifurcated near its origin, which runs to the plexiform layer and terminates in a spray of fine branches, which often ascend to the neighborhood of the pia; basilar divergent dendrites, rather long and repeatedly branched; and, finally, a fine descending axon, which, in most favorable specimens, can be followed down to the neighborhood of the white matter. From the initial portion of its course spring three, four, or a larger number of collateral processes, which traverse, with many subdivisions, in a horizontal or oblique direction, a very considerable extent of the second layer. From the small pyramids lying close to the plexiform layer, and even from some cells more deeply situated, the first two collaterals recurve, ascending sometimes, as Schäfer has discovered, up to their termination in the first layer. However, this termination in the first layer is much less frequent than might be inferred from this authority's descriptions and drawings. In our preparations of the visual and motor cortex of a child a few days old and of a cat twenty-five days old, the great majority of the recurrent collaterals do not cross the boundary of the second layer. Here, in conjunction with many neurites belonging to cells with short axons, they assist in forming a very dense plexus, which contains in its meshes the primary dendrites of the small pyramids. Generally, — and this may be considered as an answer to the authorities who strive to convert the recurrent course of the collaterals into an argument for the doctrine of the cellulipetal conduction of these fibres (v. Lenhossék, Schäfer), — I may affirm that the vast majority of the initial neuritic collaterals — and I consider such all those that arise within the gray matter — always come into contact with some of the dendrites belonging to homologous nerve cells situated at different levels of the same cortical formation. When the cells to which they correspond lie in the same or a deeper plane, the collaterals intended for them take a horizontal, descending, or oblique course; but if the cells of the same category are situated in a more superficial plane than the point of origin of the collateral, they must describe a recurrent arc in order to reach their destination.

Layer of Medium-sized Pyramids.

Being a continuation by insensible gradations of the small pyramidal layer, it contains cells of precisely similar form, differing from the cells of the second layer only in their somewhat greater size, their longer radial dendrite, and, ordinarily, by a larger number of neuritic collaterals (Fig. 4, *C*). In the deeper level of this layer may be observed — very seldom, however — large pyramidal cells, but not so large as those situated in the seventh layer.

Cells with Short Axon of the Second and Third Layers. — These elements, almost as numerous as the pyramidal cells themselves, may be seen scattered irregularly throughout the entire thickness of the two layers. They are generally more numerous near the limits of these layers, that is to say, in the superficial portion of the second and in the deeper level of the third layer.

Although in form and size these elements are very variable, and although there are transitional forms which make it often difficult to distinguish between them and to subdivide them into well-pronounced types, still, by considering the size of the cell body and the character of the axon, they may be divided into the following five classes: (*a*) cells with short ascending axon; (*b*) cells with short descending axon; (*c*) cells with horizontal or oblique axon; (*d*) dwarf or spider-shaped elements; (*e*) fusiform or bipanicled cells, whose axon breaks up into a fibrillar arborization.

a. Cells with Ascending Axon (Fig. 5, *a*, *B*). — As may be seen in Fig. 5, these cells belong to two principal varieties: (*a*) Gigantic cells, with long dendrites (Fig. 5, *A*, *C*). These are quite numerous in the visual cortex, where they occupy preferably the deep portion of the third layer. Their form is stellate, sometimes fusiform or triangular. From their angles arise several varicose, thick, and very long dendrites, often disposed as two brushes, the one ascending, the other descending. The axon takes its origin either from the cell body or from a dendrite. Sometimes it describes an arc, whose concavity is toward the surface, on its way outward to become resolved into an arborization of very few branches. The characteristic feature of this arborization is the enormous length and the horizontal or oblique direction of its terminal twigs. These traverse a very considerable portion of the second and third layers, where they make contact with numberless pyramidal cells. It

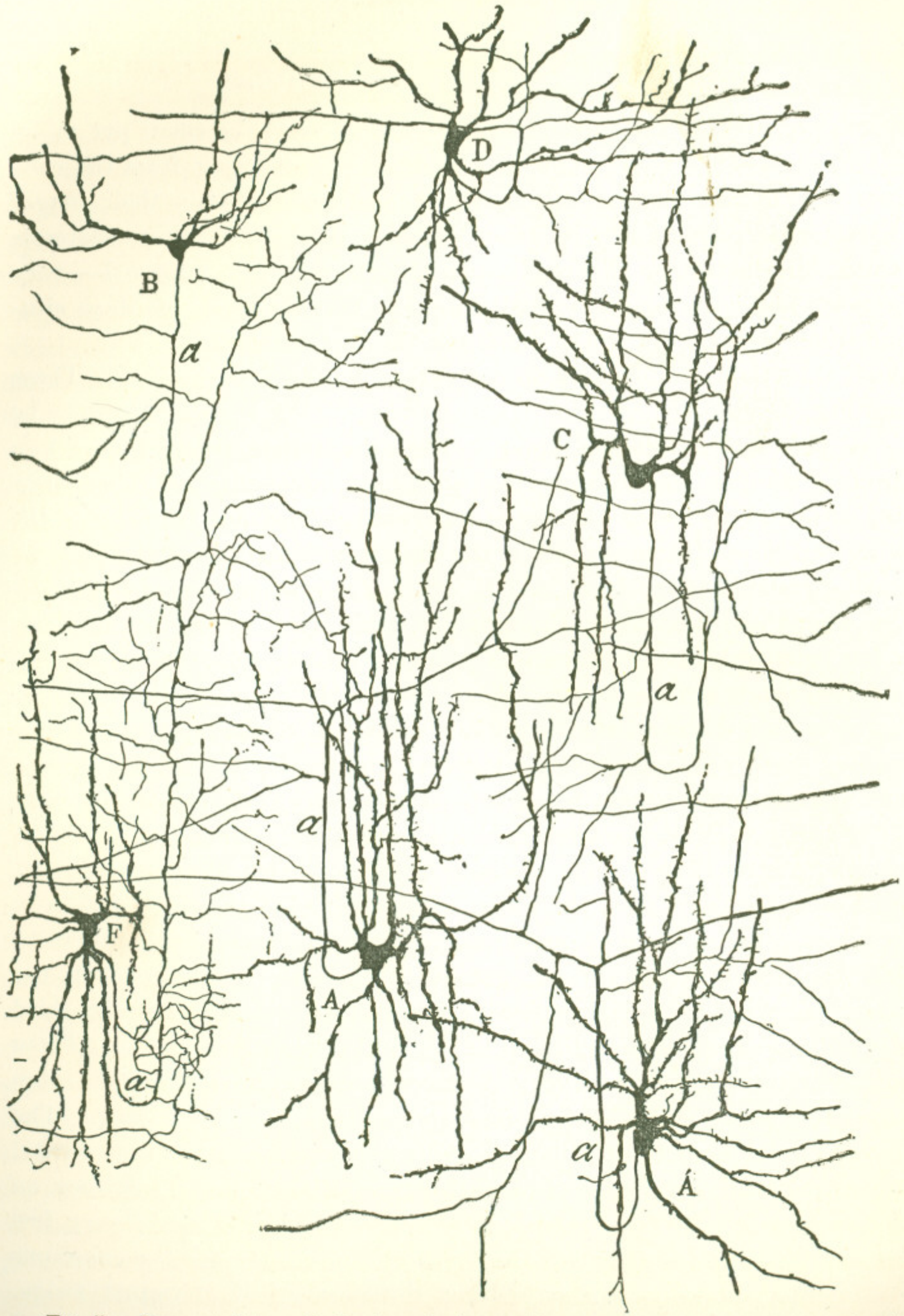


Fig. 5. —Large stellate cells having short ascending axons, 2d and 3d layers, visual cortex, infant 15 days old. *A*, elements of the 3d layer with axons divided into long horizontal branches; *B*, small cell with arched axon from the layer of small pyramids; *C*, large cell with arched axon; *D*, large cell from the boundary of the 1st layer; *F*, cell with arched ascending axon branching in a most complicated manner; *a*, *a*, *a*, axons.

may be added that these gigantic cells may be recognized even in Nissl preparations by their stellate form and considerable size. They correspond, probably, to the globular cells of Bevan Lewis and other writers. (*b*) Medium-sized type: This is a fusiform or stellate cell, whose size does not exceed that of the small or medium-sized pyramids. It is characterized above all by its axon, which is slender and ascending, and which terminates in a complicated arborization with many varicose branches and with relatively small spread at varying levels of the second and third layers. As to the dendrites, they appear varicose and diverge in all directions, but usually do not extend to the first layer (Fig. 5, *F*, and Fig. 3, *D*).

b. Cells with Descending Axons. — These are stellate, triangular, or fusiform, of medium size, and provided with many ascending and descending dendrites. They occur chiefly, as has been pointed out by Schäfer for other regions of the cortex, along the superficial boundary of the layer of small pyramids (Fig. 5, *B*, and 6, *C*). Their axons descend through the second and sometimes through the third layer, giving off to them a few collaterals, and terminate in a diffuse arborization throughout the different levels of these layers. Very frequently this axon, after descending a certain distance, emitting a few collaterals to the layer of small or medium-sized pyramids, traces an arc with concavity toward the surface and ascends to terminate in an arborization, very complicated and with exceedingly varicose branches, in the layer of small pyramids close to the plexiform layer (Fig. 5, *B*). As seen in Fig. 6, which reproduces certain cells of short axons from the visual cortex of the cat, these elements with descending axons are very numerous in other gyrencephalous mammals. We also find a variety of cell, recognized in man, pyriform, uni-polar, whose single descending process gives rise to a bouquet of varicose dendrites and an axon (Fig. 6, *a*, *b*). The collaterals and terminal arborizations of these axons form in the cat a dense plexus throughout the superficial plane of the layer of small pyramids.

The great number of cells with short axons which occur in the most superficial lamina of the layer of small pyramids has induced certain writers, such as Schäfer and Schlapp, to consider this transitional region as a special layer, which they call the layer of superficial polymorphic cells. We cannot subscribe to this innovation because, in spite of the great number of these cells, this transitional lamina contains also a large number of small pyramids, that is to say, cells which, in addition to their morphological varieties, have the same connections as ordinary pyramidal cells. Of course, if for the subdivision of the cortex into layers we take

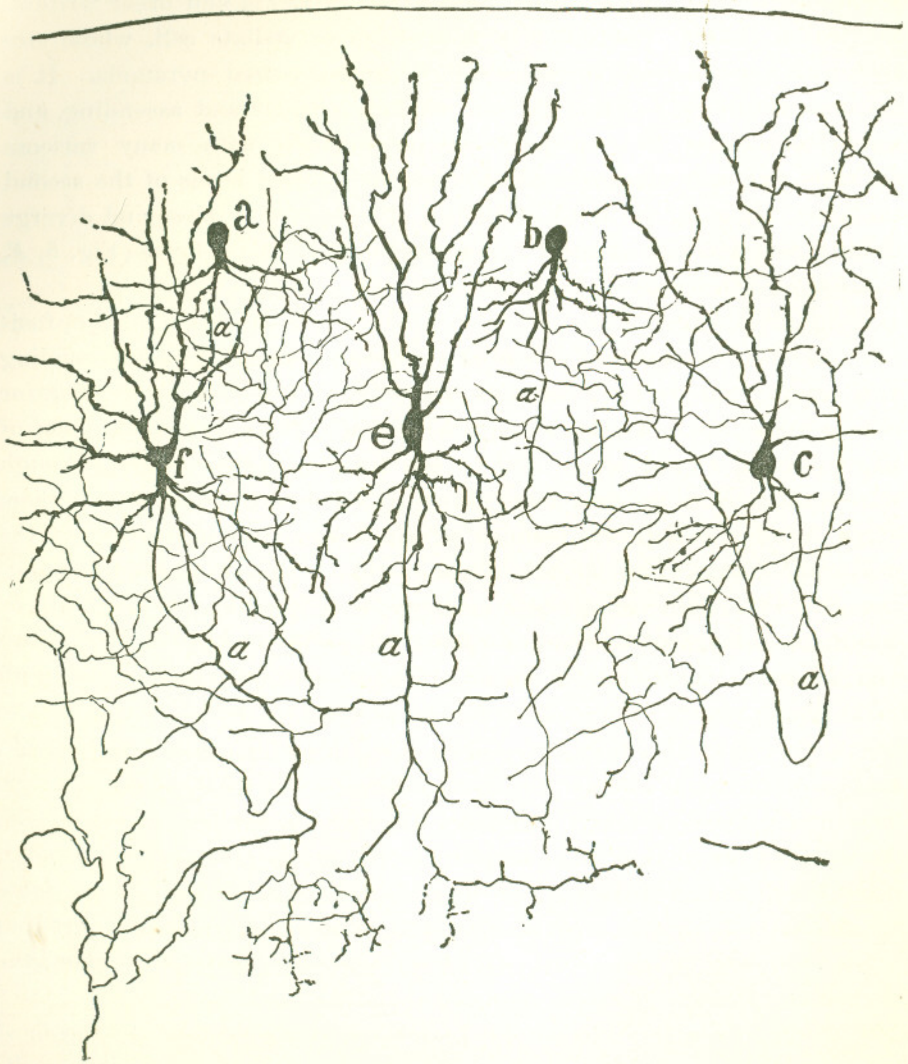


FIG. 6.—Cells with short axons from the layer of small pyramids, visual cortex of cat aged 28 days. *a, b*, small pyriform cells with short descending axons; *c*, cell with arched axon; *e, f*, cells with descending axons distributed to the medium-sized pyramids of 3d layer.

as our basis of classification the form of cell bodies, independently of other characters, we might be entitled to differentiate between the first and second layer consisting chiefly of stellate cells; because in this region, as

is well known, the small pyramids have a stellate or triangular form. But, in assigning to an element a place in his classification, one must not decide from the form alone, which in case of superficially placed pyramids is a function of their position. In fact, we find that the form of these cells varies according to their proximity to the plexiform layer. The true characteristic of a pyramidal cell consists in the presence of a long axon extending down to the white matter and of a spray of dendrites (supported or not by an intermediate trunk) spreading up into the plexiform layer. Now, in the light of such a criterion, it is easy to see that sufficient reason does not exist for making out of the most superficial pyramids a distinct category of cells to be used as a basis for the creation of a new cortical layer.

c. Cells with Horizontal or Oblique Axon (Fig. 7).—These elements, which are angular or fusiform, with their long axes more or less horizontal, possess few, but rather long, dendrites. Their axon arises generally from the lateral aspect of the cell body or from a thick polar dendrite, takes from the first a horizontal or oblique direction and, after giving off a few collaterals, terminates, sometimes after extending to a considerable distance, in an arborization widely spread but with few branches. In certain cells of this category, it is shorter and subdivides in the immediate neighborhood of the cell body (Fig. 7, *E, C*).

d. Dwarf or Spider-shaped Cells.—Brought to our attention by Cl. Sala in the corpus striatum of birds, mentioned also by my brother in the cerebral cortex of batrachians and reptiles, these strange elements are notably abundant and of very pronounced character in the cerebral cortex of man and gyrencephalous mammals. They are found irregularly scattered in all layers of the visual area. Their soma is very small, not exceeding the diameter of the nucleus by more than five or six μ. About the nucleus is a thin lamina of protoplasm which is drawn out into a great number of dendrites, delicately varicose, radiating, slightly branched and short. The appearance of these dendrites is such that one might mistake the cell, at first sight, for a neuroglia corpuscle with short processes. But, examining them with a high power, we recognize at once that their slender dendrites do not possess collateral appendages (contact granules), so characteristic of processes of neuroglia cells. Finally, attentive examination reveals the axon, a delicate fibre, which becomes resolved immediately into a very dense varicose arborization of incomparable fineness. Often this terminal plexus is so extremely fine that it appears through an ordinary objective as a yellowish or brownish spot in the neighborhood of the cell and resembling somewhat a granular precipi-

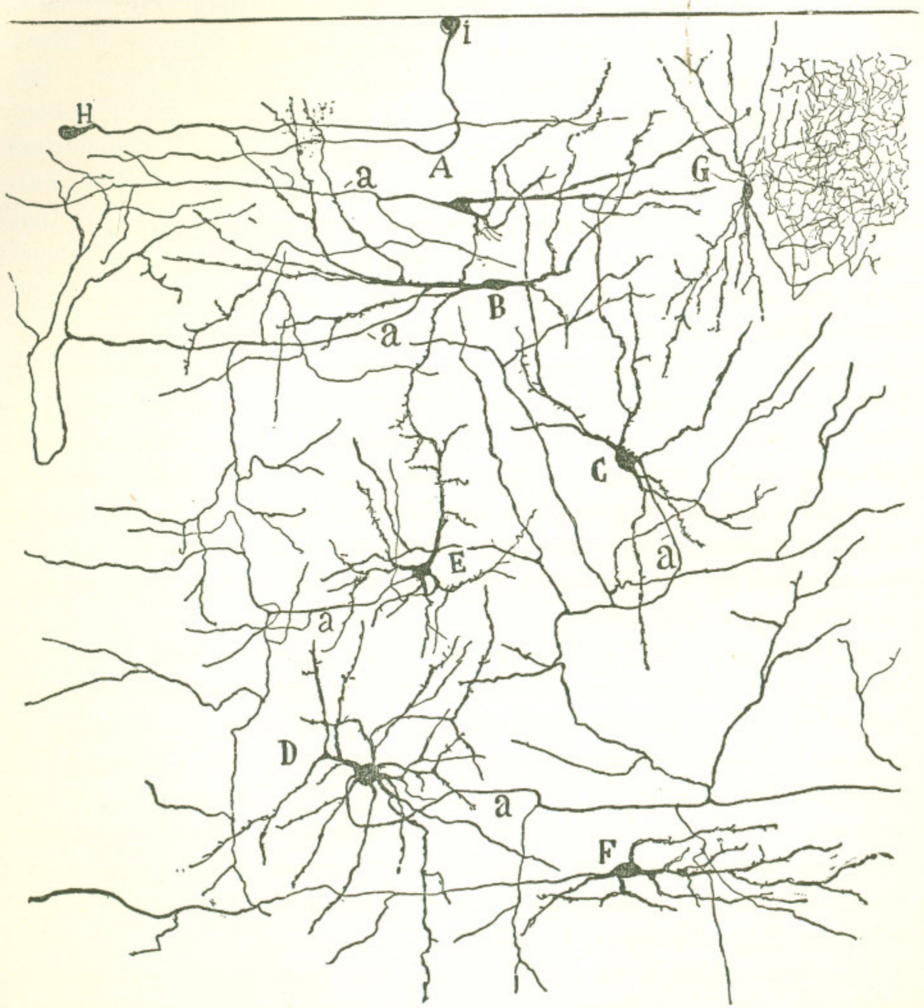


FIG. 7.—Cells with short horizontal or oblique axons situated in the 2d and 3d layers, visual cortex of infant a few days old. *A, B,* cells with axons almost horizontal from 2d layer; *C, D, E,* cells with short axon diffusely branched; *F, H, I,* pyriform cells of the 1st layer, whose significance is still uncertain; *G,* small cell with very short axon diffusely branching within the 1st layer.

tate. In some cases this arborization is coarser and can be seen with a Zeiss objective D or E. At the level of the superior boundary of the layer of small pyramids, in the visual cortex of the child and even of

other mammals, may often be seen a dense plexus of exceedingly slender branching fibrils. Their original fibre appears to come from the deeper levels of the 2d layer (Fig. 3, *A, B, C*). These terminal plexuses often take the impregnation irregularly, which gives the appearance of brownish or coffee-colored spots scattered and sometimes arranged in a row just underneath the plexiform layer. At first I was not successful in tracking satisfactorily the fibres of origin and, therefore, hesitated as to stating the significance of these interesting arborizations. Very recently, however, in two or three fortunate specimens I have been able to demonstrate the connection between this plexus and the fine ascending axons of certain small cells situated in the deeper level of the 2d or outer level of the 3d layer. I am, therefore, now inclined to consider this intermediate, or subplexiform, nerve plexus as consisting of terminal arborizations intended for the small pyramids. The fibres of origin spring from more deeply situated spider-shaped cells very hard to impregnate. I may add that these plexuses are not lacking in the cat and dog, although in these animals the fibrillæ are not so numerous nor so extremely fine as in the human brain. Permit me also to add that they occur in all regions of the cortex, although up to the present we have obtained the best impregnation of them in the visual area.

e. Small Bipanicled Cells.—In the visual region, as well as in other areas, of the human cortex we find in profusion certain small cells vertically elongated. Their axon presents the very singular feature of breaking up into long slender brushes of terminal fibrillæ. At first, I thought that these singular cells were forms characteristic of the acoustic area, for here they are remarkably developed and very numerous. Further investigation, however, has convinced me that they occur in all parts of the cortex, disposed in greatest numbers along the lower level of the 2d and 3d layers (Fig. 8 and Fig. 11, *E, F*).

As stated above, we are discussing the small spindle-shaped cells with poles radially disposed, which give rise to groups of dendrites, slender, unprovided with contact granules, very finely varicose, and often arranged in long ascending and descending brushes. In some cases these are so fine that on superficial examination they might be mistaken for delicate neuritic arborizations. But the most striking peculiarity of these cells concerns the subdivisions and course of their axons. This process is very delicate. It ascends or descends a certain distance, then generally gives off a few collaterals at right angles which soon subdivide into ascending or descending fibrillæ, and finally it breaks up into brushes of very slender filaments which run radially, extending throughout almost the entire thickness of the cortex. As a whole this arborization with its initial collaterals forms one or several parallel brushes, the fibrils of which skirt the trunks of the pyramids and adapt themselves to the cell bodies, over which they appear to creep, like the creeping fibres of the cerebellum on the branches and bodies of the Purkinje cells.

In the brain of the human infant at birth these arborizations have not attained complete development and present but few vertical branchlets. It is not until twenty or thirty days after birth that we can observe the long and complicated terminal brushes. In certain areas, the acoustic, for example, each neurite may form as many as five ascending or descending brushes. The fibrils of which they consist are so delicate that in order to see them well we must use the highest apochromatic objectives.

If now we consider all the different kinds of cells having short axons, of which we have given a somewhat fastidious description, from the point of view of their connections and their probable functions, we may characterize them as special cells of association. The form of their cell body and the disposition of the axon vary according to the number, form, and position of the cells to which they must convey nerve

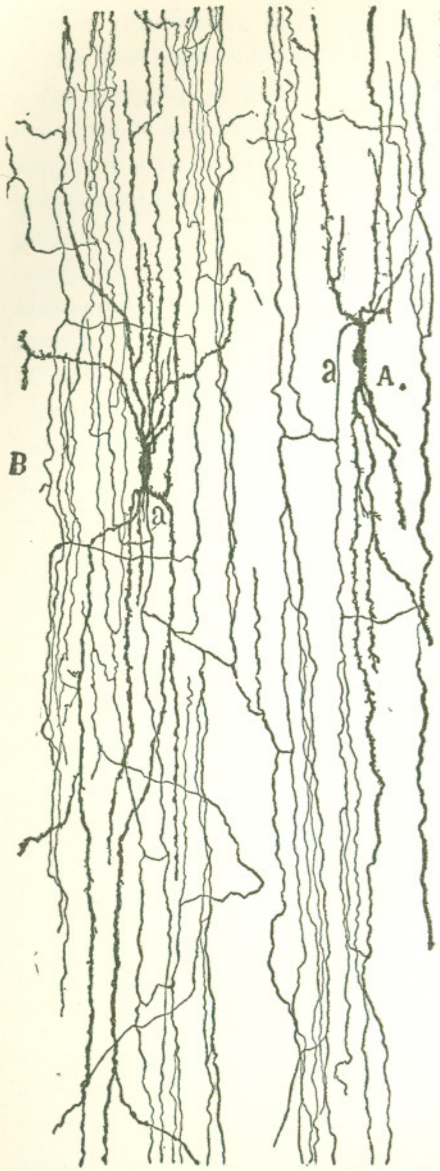


Fig. 8.—Small fusiform, bipanicled cells from auditory cortex of infant (1st temporal convolution). *A*, cell giving origin to a descending axon moderately branched; *B*, cell whose axon breaks up into a number of pencils of very long ascending and descending fibrils; *a*, axon. (Examined with Zeiss apochromatic obj. 1.30.)

stimuli. Thus cells with a horizontal axon must be intended to transmit impulses to elements, probably pyramidal cells, which occur at the same level in the cortex. Those whose axon is vertical, ascending or descending, would naturally transmit impulses to elements of different layers. Those which are bipanicled would serve to associate dynamically a great number of pyramids in vertical series. Finally, the small, spider-shaped cells may have for their function association of groups of pyramids very close together. Unfortunately for this theory, we do not know from which nerve fibres all these elements of association receive their initial stimuli. Accordingly, we must be resigned to remain in ignorance as to the path of the afferent impulses and, as well, in regard to the special influence which these elements must exercise. It seems very probable, however, that their function consists not only in facilitating the spread of incoming stimuli, but also in adding to it something new, some specific modification which cannot now be determined. We shall return to this point in our general conclusions upon this work. But we may see from the above how many paths nature has opened up to render association of nerve impulses possible in every direction and through any distance. That which proves the importance of these association cells and leads us to surmise that they play an important psychic rôle is the fact that they are extremely numerous in the human brain. They are found in the animal brain as well, but are not numerous and are usually confined to the boundary of the 1st layer.

I conclude here my exposition of the prosy topics that I chose as the theme of this lecture. And nothing remains except to thank you for the attention and good will which you have shown me in spite of the extreme dryness of the subject-matter.

LECTURE II.

Layer of the Large Stellate Cells.

My recent researches in the visual cortex of man have led to the unexpected discovery of certain large cells of stellate form possessing an axon which descends to the white matter. Figs. 9 and 10 represent very clearly the most common forms of these strange elements. They are differentiated immediately from pyramidal cells by their lack of a radial trunk. Generally speaking, the cell body is stellate, but there is no lack of semilunar, triangular, and even mitral forms. Their dendrites are thick and much branched, and extend in all directions, especially horizontally, without ever leaving the territory of the 4th layer. In man these processes are sparsely provided with contact granules, while they are very numerous in the homologous cells of the mammalia (cat and dog).

As to the axon, it is rather large, arises from the inferior surface of the cell body, descends through the 4th layer, sometimes tracing here accommodation curves, and after crossing the 5th, 6th, 7th and 8th layer, passes into the white matter and is there continued as a medullated nerve fibre. In passing through the 4th and 5th layers it gives off three, four, or a larger number of, often, very large collaterals which end in arborizations extending over a considerable area in these layers. It is not uncommon to see these collaterals taking a recurrent course to become distributed in planes above the point of origin; but in this they never trespass on the boundaries of the 4th and 5th layers. Finally, and this is a very frequent disposition in the adult cortex, this axon, after having given off its collaterals, becomes notably finer. Taking into consideration its diameter, sometimes less than that of its first collateral, we might be led to mistake it for the latter rather than a true continuation of the axon. We shall return to this peculiarity, which is presented by many cells in the visual cortex. The stellate cells present a similar character in the adult human cortex, and I reproduce in Fig. 10 their principal types impregnated (long method of Golgi) in the case of a man thirty years old. The only

difference that we remark between these cells in the adult and infant brain is the greater development of the dendrites, which extend long distances in horizontal planes in the adult. The volume of the soma also

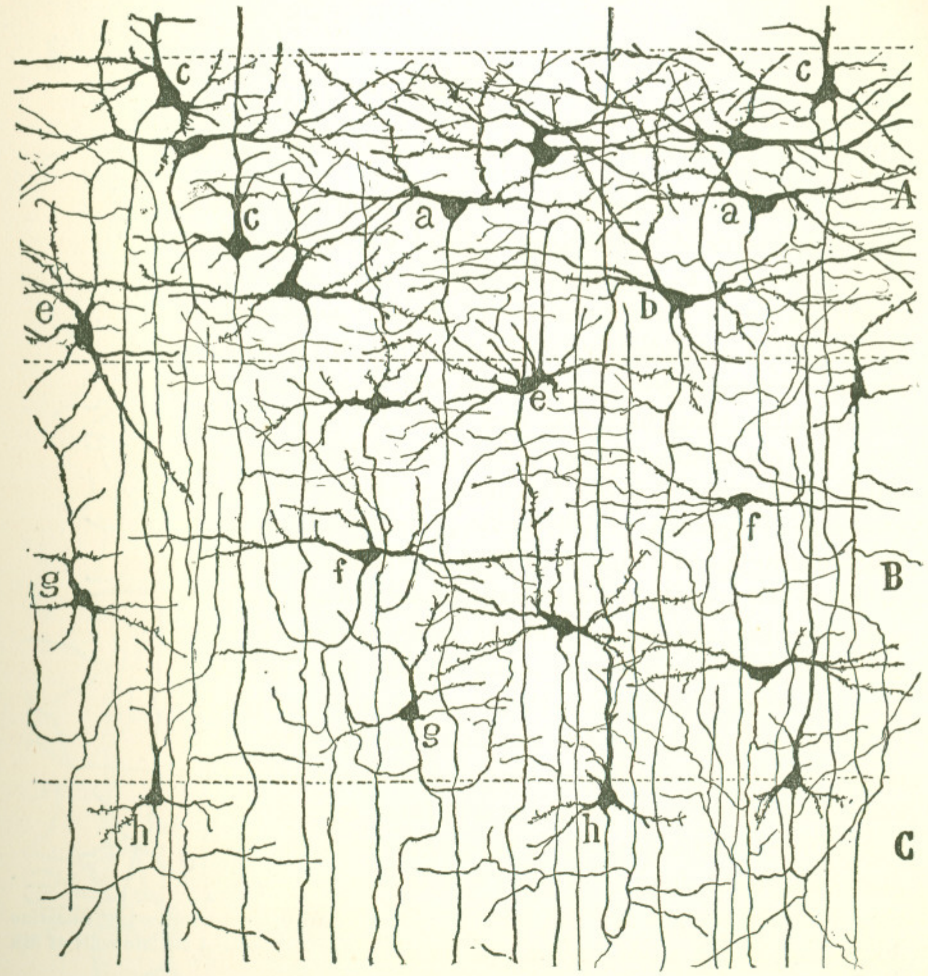


Fig. 9. — Layers 4 and 5, with portion of 6; stellate cells of the visual cortex, infant 20 days old, calcarine sulcus. *A*, layer of large stellate cells; *a*, semilunar corpuscle; *b*, fusiform horizontal cell; *c*, cell with radial trunk; *e*, cell with arched axon; *B*, layer of small stellate cells; *f*, horizontal fusiform cells; *g*, triangular cells with heavy arching collaterals; *C*, layer of small pyramids with arched axon; *h*, cells of this type.

increases with age, which shows that growth of dendrites does not depend solely on the lengthening out of the initial or primitive protoplasm of the cell, but also on an actual augmentation of cell substance.

Cells with Short Axon. — As it happens in other cortical layers, the 4th contains a large number of cells with short axon. The following three types may be distinguished: —

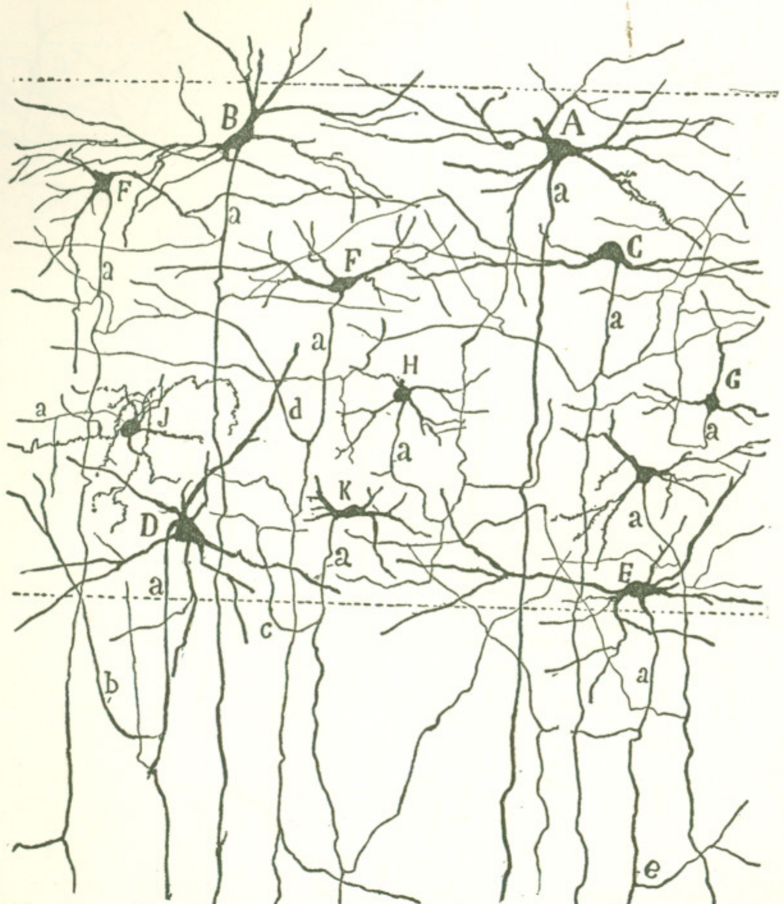


FIG. 10. — Large stellate cells of the adult brain, man 30 years old, neighborhood of calcarine sulcus. *A*, *B*, *C*, *F*, stellate cells of the 4th layer; *D*, *E*, *K*, medium-sized stellate cells of 5th layer; *G*, *H*, *J*, cells with short axon. (Golgi's slow method.)

(*a*) Cells, stellate, fusiform, or triangular, whose axon ascends to be distributed in the superficial plane of the 4th layer (Fig. 11, *A*, *C*, *D*).

(*b*) Cells of similar form and position, but whose axon distributes itself to the layer of medium-sized pyramids (Fig. 11, *B*).

(*c*) Spider-shaped cells with a notably short axon, as may be seen in Fig. 13, *E*.

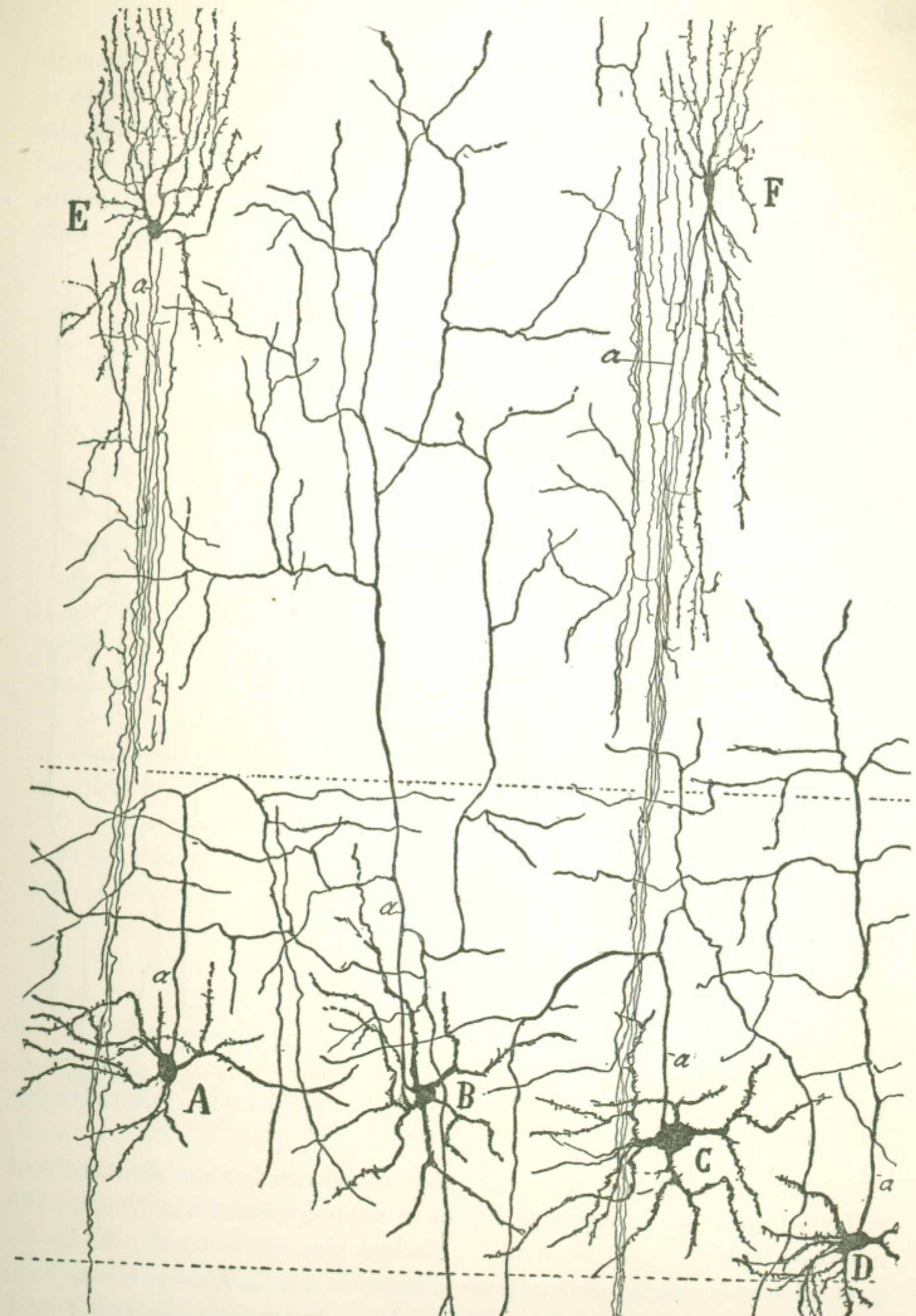


FIG. 11. — Cells of the visual cortex, infant 15 days old, 4th layer. *A*, cell sending axon to superior portion of 4th layer; *B*, cell whose axon branches to the 3d and 4th layers: *C*, another cell sending branches into the 3d, 4th, and 5th layers; *E*, *F*, very small bipanicled cells from layer of medium-sized pyramids; *a*, axon.

The cells with ascending axon are remarkable on account of the curious arched course of the latter. It has in some cases initial collaterals.

The stellate cells as well as other cells with the short axon are also found in the cortex of the cat and dog, where they form a well-defined layer of their own, corresponding, considering the character of its elements, to the 4th, 5th, and 6th in the visual cortex of the child, Fig. 12. Cells

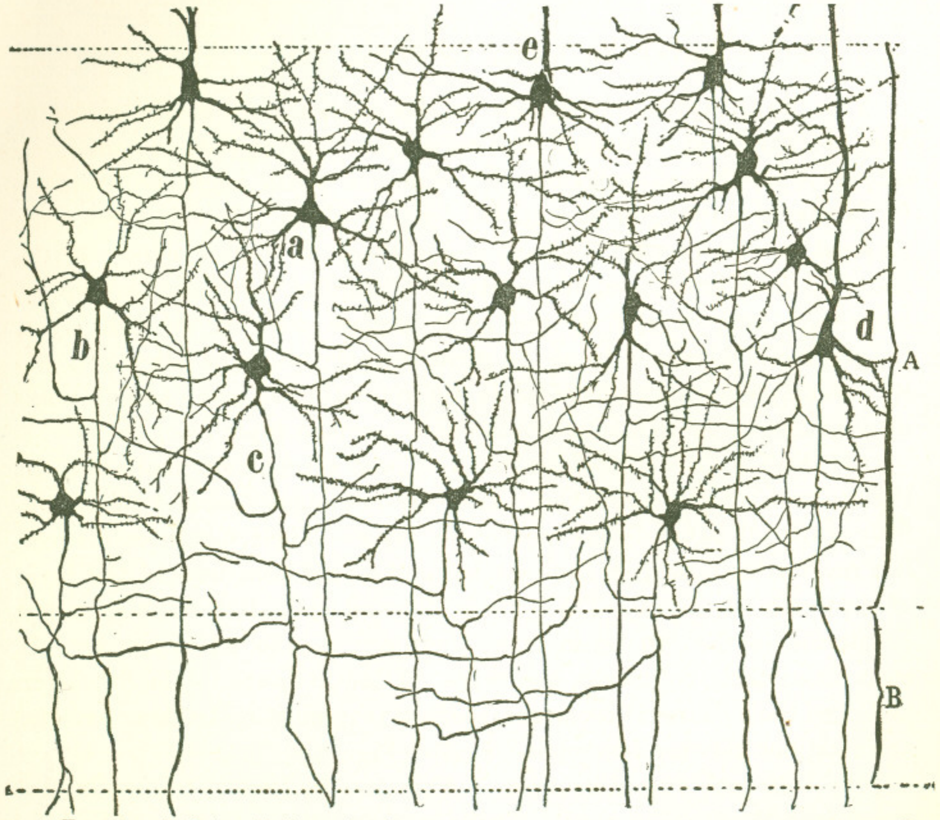


FIG. 12.—Stellate cells from visual cortex of a cat aged 28 days. *A*, layer of stellate cells corresponding to the 4th and 5th layers in man; *B*, layer of giant pyramids; *a*, *b*, *c*, stellate cells having long descending axons; *d*, *e*, medium-sized pyramids among the stellate cells.

with short ascending axon are especially numerous and are characterized by being fusiform in shape and by the contact granules which cover the cell body and principal dendrites. Besides the existence of cells in the cerebral cortex whose axons ascend, but do not make their way into the first layer as do those from Martinotti's elements, is the fact that I long since discovered while working upon the motor cortex of the small

mammals; this is, as my latest observations show, that these elements are very numerous, and that each cortical layer, or better, that each layer of a plexiform aspect, contains a special kind of this element. In addition, as we shall see in a moment, these cells form a constant factor in all the cortical layers in which nerve fibres incoming from the white matter make their terminal arborizations.

FIFTH LAYER, OR LAYER OF SMALL STELLATE CELLS.

This layer, which corresponds to the greater part of the stripe of Vicq d'Azyr, when examined in Nissl preparations appears to contain an enormous number of small rounded elements which might be mistaken for scattered nuclei not surrounded by protoplasm. But in these same preparations we may still detect, beside these corpuscles, a few others, scattered here and there, of stellate or triangular form and medium or large size, very similar to the great stellate cells of the 4th layer. Golgi's method reveals to us the great complexity of the 5th layer, and by this means we have succeeded in differentiating as many as five kinds of elements. The following are the most common types:—

(*a*) *Stellate Cells of Medium Size.*—These are exactly similar to the stellate cells of the 4th layer. They are not numerous, and lie irregularly scattered in all levels of the 5th layer. Their dendrites diverge, but run for the most part horizontally, and do not pass beyond the layer of their cells of origin. Their axons descend and, after emitting a few collaterals to the 5th layer, make their way to the white matter. In some cases their collaterals are given off lower down, in the 6th layer, and then their course is recurrent, because they must make their terminal arborizations between homonymous cells (Fig. 9, *g*, *f*).

(*b*) *Cells with Ascending Axon.*—These are fusiform or triangular, disposed with long axis vertical. Their axon is similar to that of cells of this type in the 4th layer. That is to say, after ascending a certain distance it forms a terminal arborization of arching branches distributed among the elements of the overlying layer. From its initial portion spring a few collaterals which are distributed to the 5th layer (Fig. 13, *A*, *B*, *C*).

(*c*) *Ovoid or Stellate Corpuscles* (*properly designated*, *Granules*).—These rarely exceed in diameter more than ten or twelve μ. They are the most numerous element of the 5th layer. Their soma is ovoid, spheroidal, and even polygonal in form and gives rise to three, four, or more fine, smooth dendrites, which terminate, after a short, wavy course, within the limits of the 5th layer. Their axons are very delicate and

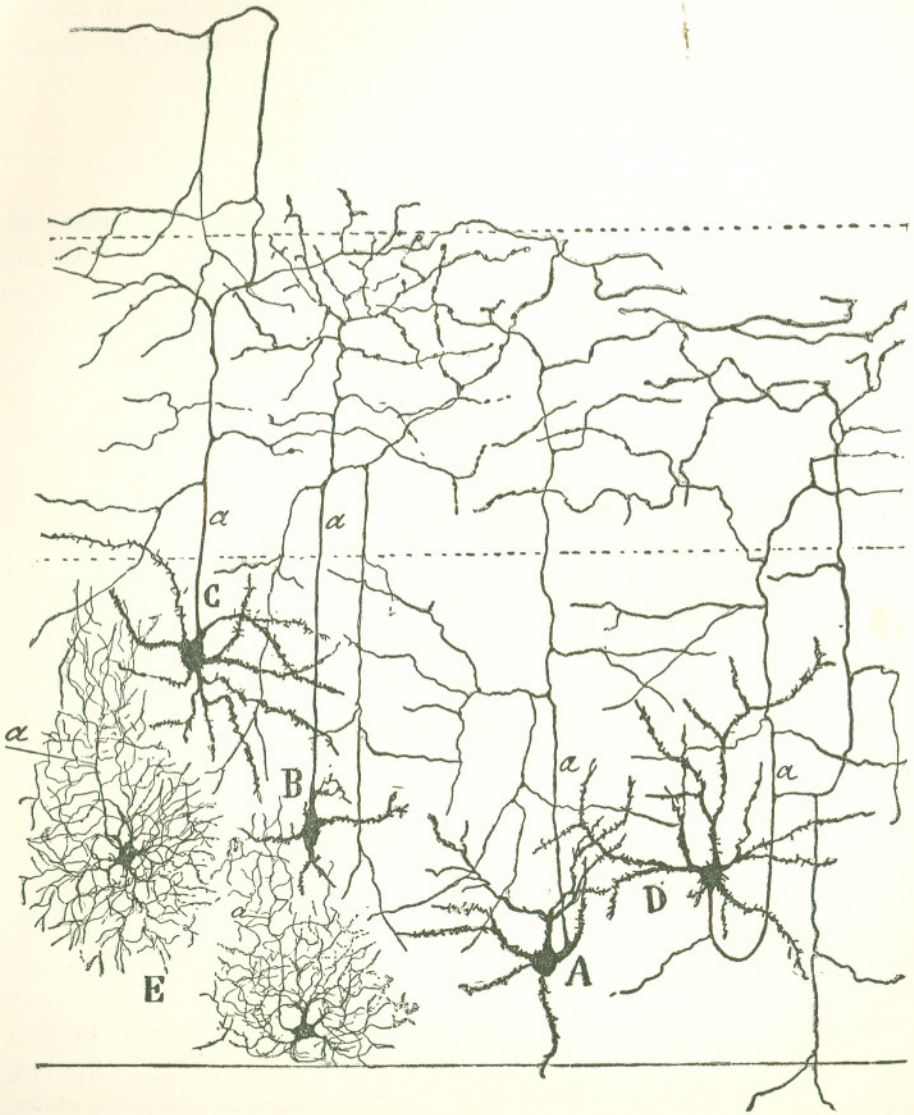


FIG. 13. — Cells in the 5th layer with ascending axon, visual cortex of infant aged 15 days. *A*, *B*, cells whose axons subdivide in the layer of large stellate cells; *C*, cells whose axons give rise to branches destined for the layer of medium-sized pyramids; *D*, cell with arched axon, the initial portion of which gives rise to branches for the 4th, 5th, and even 6th layers; *E*, very small cells, arachniform, with delicate ascending axons; *a*, axon.

take a great variety of directions, — ascending, descending, or horizontal, — and finally end in an extended arborization of few branchlets distributed exclusively to the very midst of the 5th layer (Fig. 14).

(*d*) *Dwarf or Spider-shaped Corpuscles.* — Of these there is no lack in

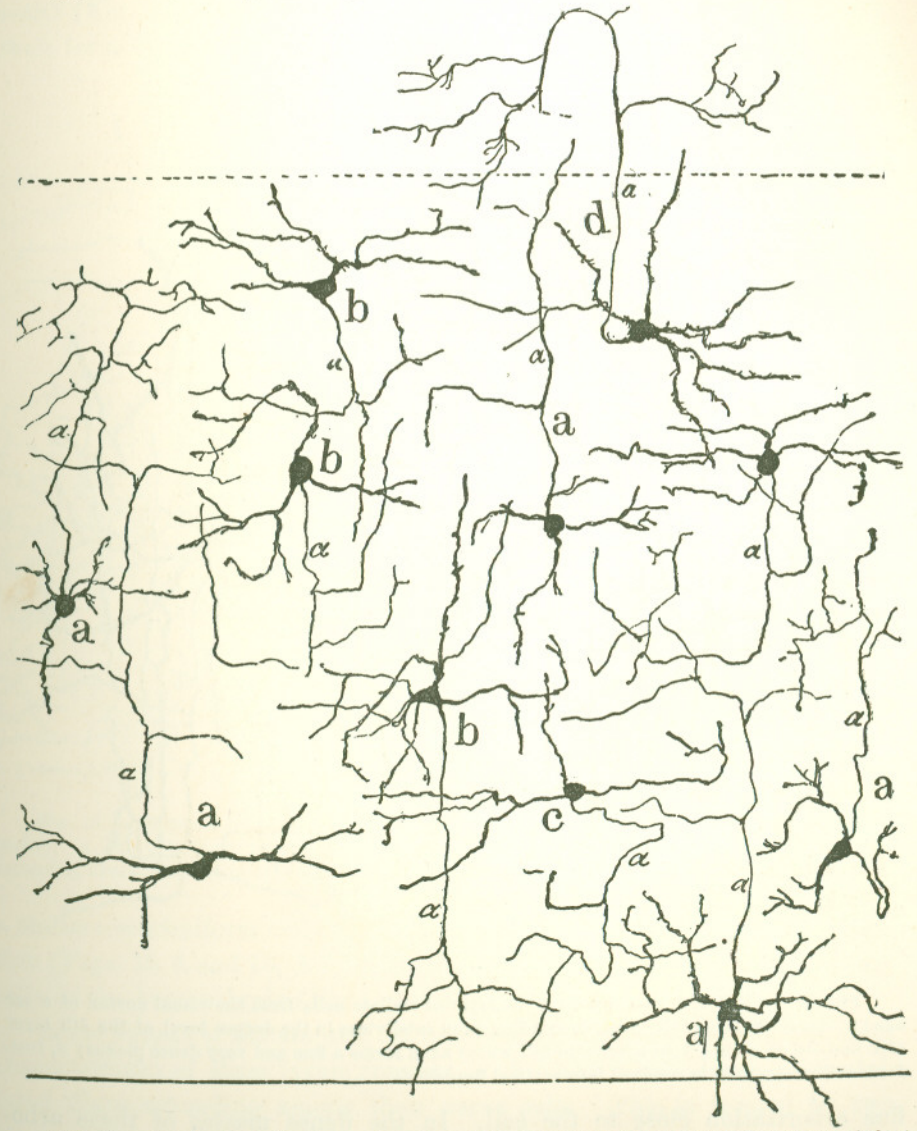


FIG. 14. — Small cells in the layer of small stellate cells, possessing short diffuse axons (infant 20 days). a, cells with delicate ascending axon; b, c, cells with descending axon; d, larger cell whose axon forms its terminal arborization in the 4th layer; *a*, axon.

this layer, whose nerve plexus they help to bewilder. Their very tiny, often ascending, axon resolves itself very soon into an extremely dense,

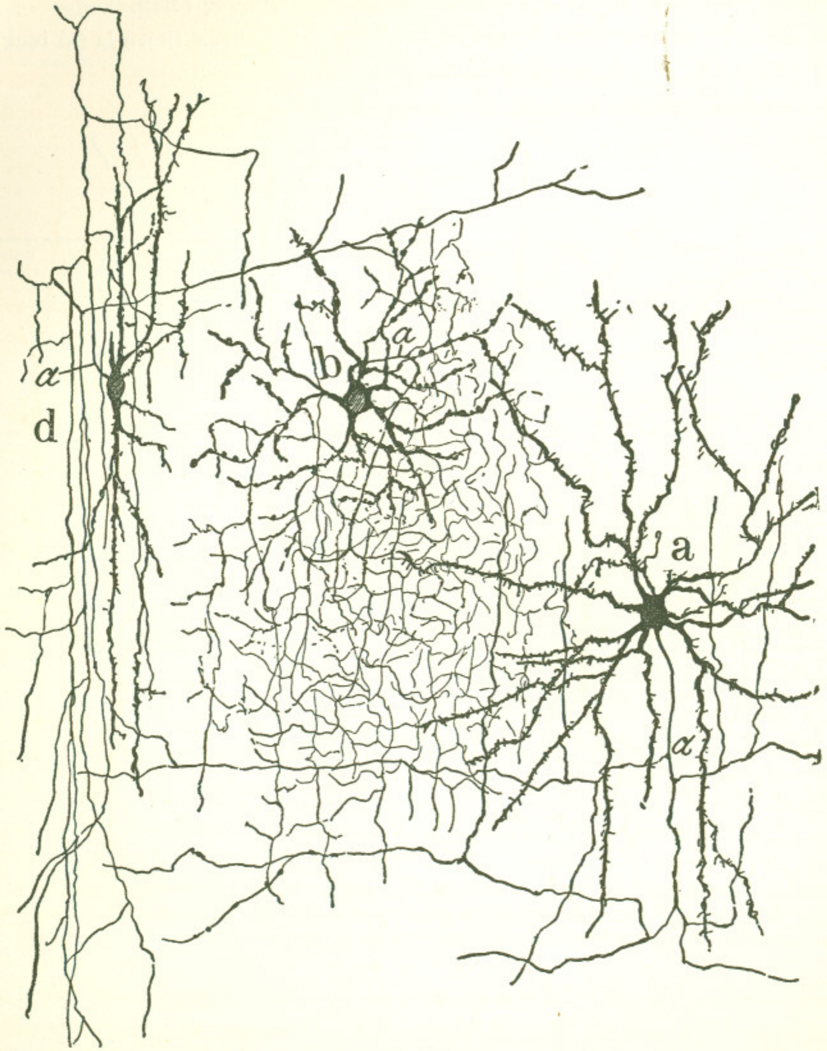


FIG. 15.—Cells with short axons of the layer of stellate cells from the visual cortex of a cat aged 28 days. *a*, large cell whose descending axon subdivides in the deeper level of the 4th layer (4th and 5th of man); *b*, arachniform cell whose axon forms a fine and very dense plexus; *d*, fusiform cell whose axon is resolved into vertical branches.

fine arborization close to the cell. In the dense masses of these arborizations we notice spaces, which probably correspond to groups of granules.

The cells with short axons are very abundant in the visual cortex of the cat, as may be observed by examining Figs. 15 and 16. Among them the more abundant types are: *a*, fusiform cells whose ascending axon is distributed to the superior levels of the layer in question (4th and 5th in man) (Fig. 16, *D*); *b*, large stellate cells with descending axon forming their terminal arborizations in the deeper levels of this layer (Fig. 15, *a*);

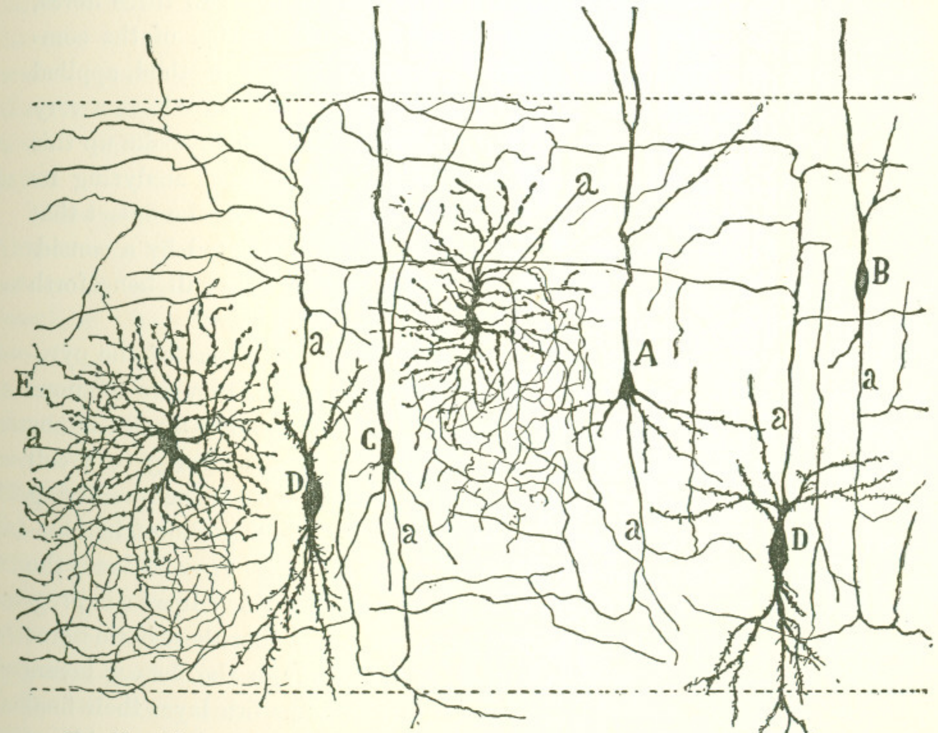


FIG. 16.—Elements from the layer of stellate cells of the visual cortex of a cat aged about one month. *A*, *B*, *C*, small pyramids with axons arched and ascending; *D*, large fusiform cells with ascending axons; *E*, arachniform cells with short axon; *a*, axon.

c, stellate-arachniform cells whose axon forms a most complicated arborization (Figs. 15, *b*, and 16, *E*); *d*, bipanicled cells larger than corresponding cells in the human brain (Fig. 15, *d*).

Nerve Plexus of the 4th and 5th layers of the Cortex. One of the chief characteristics of these layers consists in the very dense plexus of medullated fibres extending among their nerve cells. This is formed by two kinds of fibres: (1) Exogenous fibres, that is to say those coming from the white matter, probably continuations of the cerebro-optic tract. (2) Endogenous fibres, formed by the terminal arborizations of the axons which come from cells of the 4th and 5th or the underlying layers.

Exogenous Fibres. — I have already stated that Gennari's or Vicq d'Azyr's stripe corresponds chiefly to the 5th layer, but also includes part of the 4th. However, the true composition of this stripe cannot be seen in Weigert-Pal preparations, because the hematoxylin stains only the large or medium-sized fibres which possess a myeline sheath. Now these fibres, as we shall presently see, represent but a very small portion of the components of Gennari's stripes. Very fortunately Golgi's method, applied to the brain of an infant at birth or but a few days old, affords us a very clear view of the medullated and unmedullated fibres which make up this plexus. This method accordingly furnishes us a means of analyzing its origin and manner of termination. Permit me to state at the outset that the principal contingent of exogenous fibres is represented by a considerable number of fibres from the white matter, which I shall henceforth call, in virtue of their physiological significance, optic fibres.

The optic fibres are easily distinguished from the axons of the pyramids by their direction, which is oblique (in some cases they are tortuous or even stair-shaped), by their large calibre, often exceeding that of axons of the giant pyramids; finally by the fact that, instead of going to a cell as its axon, they repeatedly divide dichotomously, each branch resolving itself into a perfectly free terminal arborization spreading almost horizontally through the extent of the 4th and 5th layers. Fig. 17 reproduces the appearance of the optic plexus in a preparation in which it was impregnated almost alone. I call your attention to the fact that these optic fibres send off no collaterals, or very few, in passing through the deeper layers (9th, 8th, 7th, 6th), but immediately on reaching the 5th layer their final ramification begins. This occurs in many ways. Some fibres divide at different levels of the 5th layer into two equal or unequal branches which run horizontally to great distances, becoming resolved into a great number of collaterals which ramify throughout the entire thickness of the layer. Other fibres may be seen which, after giving off a few long collaterals during their ascent through the 5th layer, reach up to the extreme limit of the 5th layer and here become horizontal. There is no lack of fibres which ascend directly up to the limit of the layer of medium-sized pyramids and there describe arcs, and even very long wavy courses, and end by descending, dividing as they descend, through the 4th and 5th layers. Finally, from the arching portion of some of these latter fibres fine collat-

erals may be seen to spring on their way to the layer of medium-sized pyramids, where they disappear after a few divisions. To sum up, the optic fibres terminate almost exclusively within the 4th and 5th layers. In only two instances have I discovered collaterals of optic fibres which appeared to form their terminal arborizations within the 1st layer.

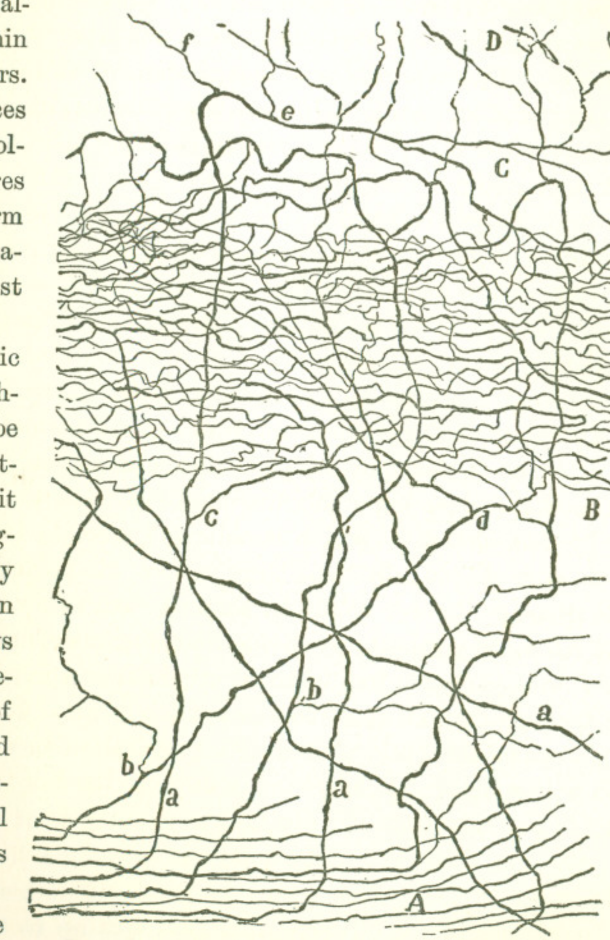


FIG. 17.—Heavy fibres coming from the white substance and subdividing in Gennari's stripe; visual cortex of infant aged three days. *A*, white substance; *B*, layer of small stellar cells; *C*, arched fibres of 4th layer; *D*, border of layer of medium-sized pyramids; *a*, trunks of the incoming fibres; *b*, collaterals for the deeper layers; *c*, ascending collaterals destined for the more superficial layers.

This plexus of optic fibres is one of the richest and densest to be found in the gray matter of the brain. If it is completely impregnated, which frequently occurs in an infant brain fifteen or twenty days old, it appears as a bewildering meshwork of wavy fibres, besprinkled with vacant spaces corresponding to the cell bodies of these layers (Fig. 18, *B*).

I may add that the appearance of this plexus diffres a little in the two layers (Fig. 18). In the 4th layer its fibres are larger and often disposed in arches or horizontal bars, its arborizations are loose and separated by ample spaces in conformity to the size of the great stellate cells; while in the 5th layer it consists of fine varicose fibrils arranged in an extremely dense lattice work with small spaces, corresponding to the small size of the medium-sized stellate cells (Fig. 18, *B*).

In the preceding brief description I have called the large exogenous fibres optic fibres. But what reasons have we to suppose that these fibres actually come in from the primary optic centres? We must acknowledge, at the outset, that the proof of their optical origin is not perfect; but there is no lack of facts which favor such a view. Some of these facts are the following: —

(*a*) In the minute brains, as, for example, that of a newborn mouse, we can follow these fibres in some cases to the radiation of Gratiolet.

(*b*) The fibres which are on their way to Gennari's plexus are very large, larger than the axons of the giant pyramids or those of cells of intercortical association.

(*c*) In the motor cortex we have found that large fibres distributed in a similar way actually come in from the corona radiata.

(*d*) In the visual cortex of a man who became blind I have discovered, by using Nissl's method, a perceptible atrophy of the stellate cells of the 4th and 5th layers. A similar case has been recently reported by Cramer; and this fact would seem to point to an intimate union between these elements and the act of visual perception, a union whose material bond is probably represented by the exogenous fibres of Gennari's plexus.

(*e*) Granted that the visual cortex must receive a great number of fibres from the radiation of Gratiolet, it is natural to refer to this source the fibres which form Gennari's plexus; since this is the distinctive plexus of this region of the brain.

From the probable fact that the plexus of Gennari's stripe is the terminus of the optic fibres, we may draw the important conclusion that the cells of the 4th and 5th layers represent histologically the principal substratum for visual sensation; because up to this point in the cortex sensory impulses heap up on the centripetal side, and here begin to become centrifugal.

Another conclusion not less interesting follows from it: for an ensemble of anatomico-physiological facts seem to show that the region of the calcarine fissure is not the locus of visual memories, but only that of sensations of luminosity, and that the residues of the latter must go (in order to become transformed into latent images) to other nerve centres. We are naturally led to consider the long axon of the 4th and 5th layers as the principal, if not the only, path joining these two kinds of centres.

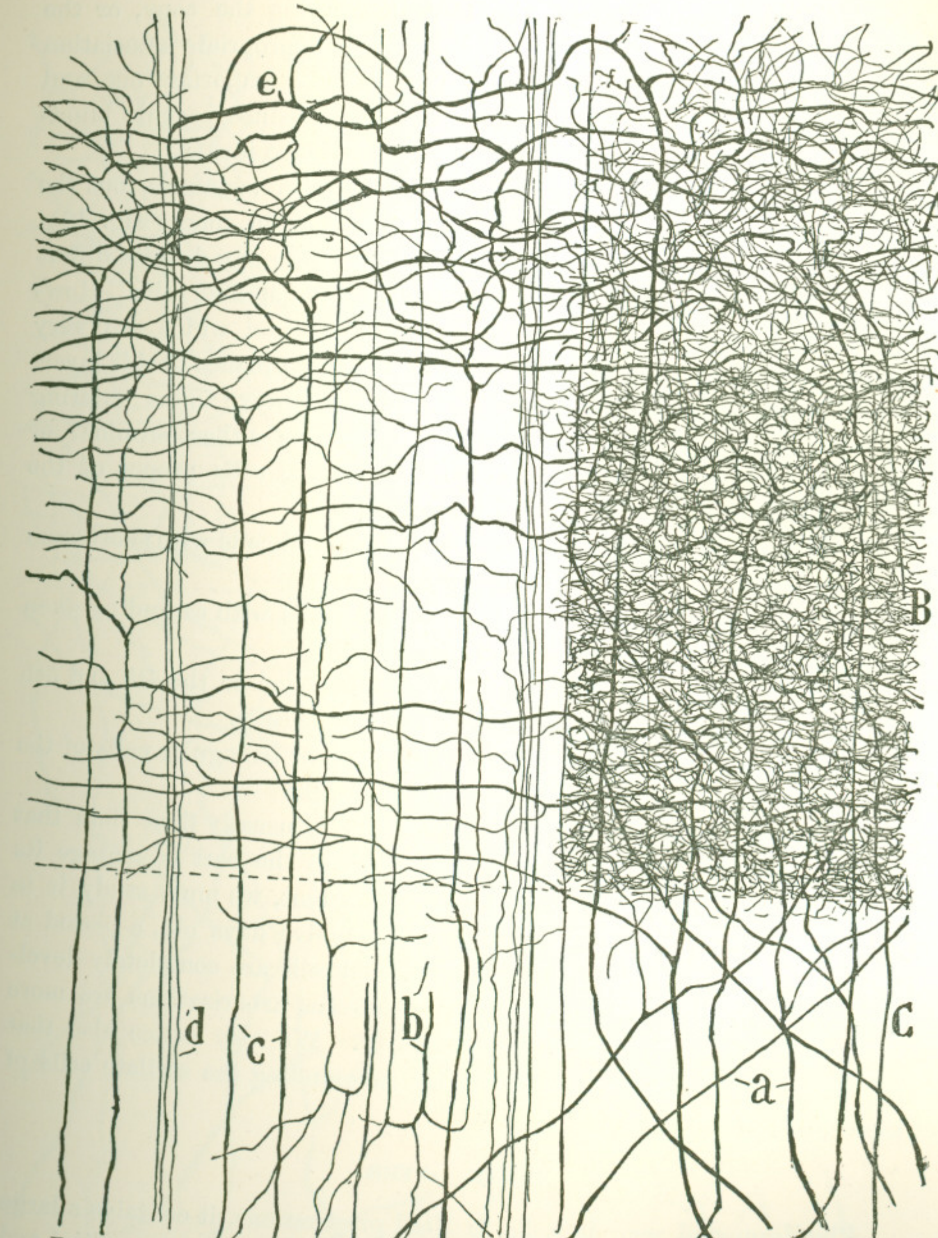


Fig. 18. — Nerve plexus of the 4th and 5th layers from the visual cortex of an infant aged 20 days. *A*, *B*, *C*, respectively, layers 4th, 5th, and 6th; *a*, trunks of optic fibres; *b*, axons of cells of the 6th layer; *c*, ascending axons of cells in the 8th layer; *d*, bundle of axons descending from the medium-sized pyramids; *e*, transverse arches of the optic fibres giving rise to ascending collaterals.

These fibres would function, accordingly, in carrying the copy, or the sensory residue, received in Gennari's plexus, to appropriate association areas of the brain. Their psychic rôle is thus a very important one, and we should suppose that their interruption would produce psychic blindness as certainly as the destruction of the occipital lobe itself.

The plexus of Gennari is well developed in other mammals, but the terminal arborizations are never as complicated as in man (Fig. 19). Further than this I have not been able to demonstrate any definite differences in arrangement at various levels of the layer of stellate cells. However, it has seemed to me that the terminal branches, which are very varicose, tend to be especially dense in the superficial planes of this layer.

Endogenous Fibres. — In addition to the large nerve fibres entering from the white matter, Gennari's plexus contains either terminal or collateral ramifications of fibres which arise in the cells proper of the visual cortex. Such are: —

(1) The very numerous branches from the small cells with short axon of the 5th layer.

(2) The terminal neuritic arborizations of cells with ascending axon lying in the 6th, 7th, and 8th layers.

(3) Arborizations of collateral branches supplied to the 4th and 5th layers by the long descending axons of the stellate cells.

(4) Terminal arborizations from the fusiform or triangular cells of the 4th and 5th layers which have ascending axons, etc.

The plexus formed by all the above fibrils is usually finer than that of the optical fibres. In order to make out to the best advantage its extreme complication throughout its whole extent, we must study it in the cortex of an infant from fifteen to twenty-five days old, a period at which the terminal arborizations of the visual cells are completely developed. It has seemed to me that the endogenous arborizations are more numerous in the 4th than in the 5th layer. We may notice also that they show a tendency to form true nests surrounding the stellate cells of these two median layers.

Sixth Layer.

Plexiform and poor in cells in Nissl preparations, it contains a large number of small pyramidal or ovoid elements with long axis vertical and provided, as may be seen in good Golgi specimens, with a radial trunk extending up to the first layer. They have also a few short basilar

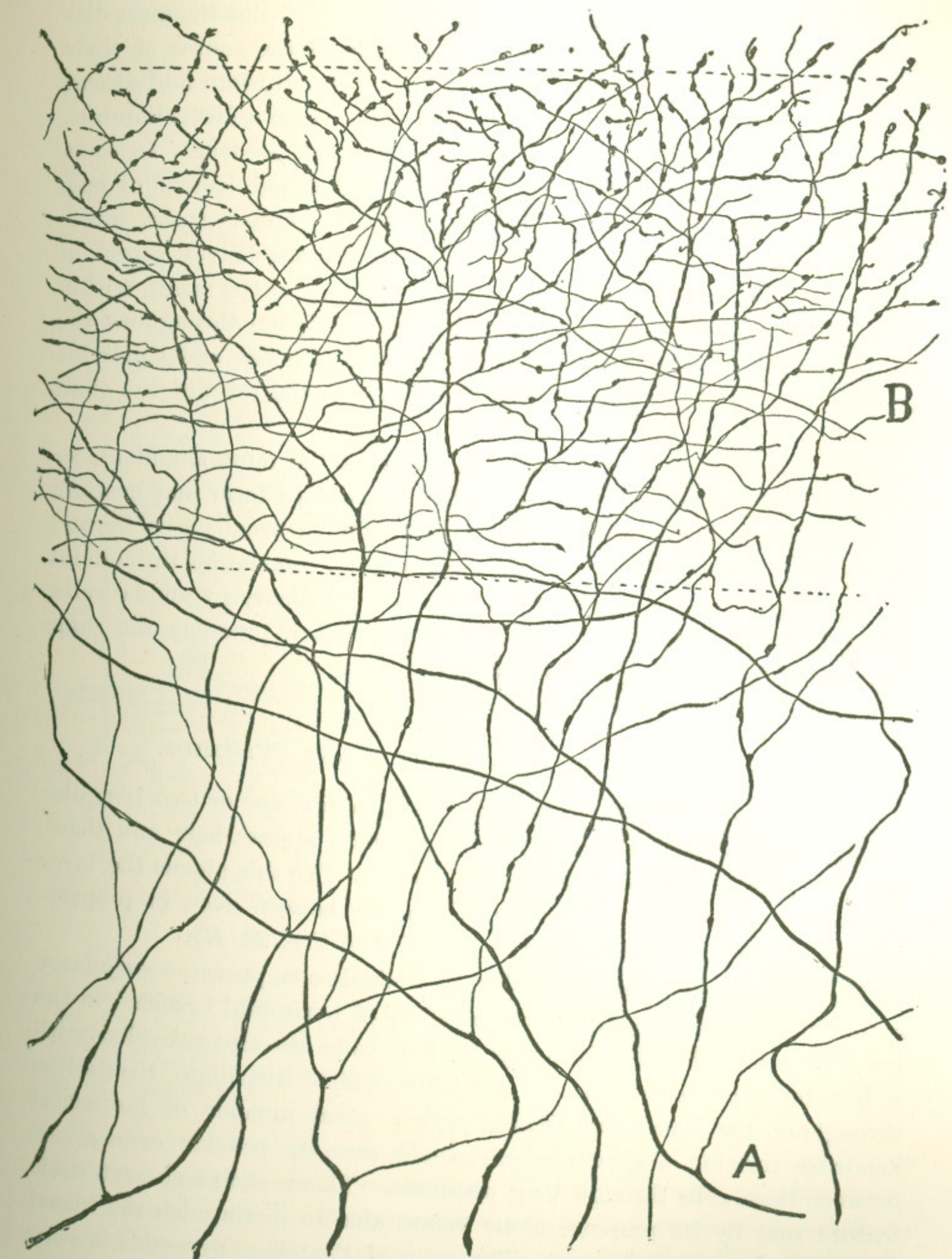


Fig. 19. — Optic fibres from visual cortex of cat 5 days old. *A*, bifurcation of fibres a short distance from the white matter; *B*, nerve plexus in layer of stellate cells (4th and 5th layers in man).

dendrites, descending or oblique and little branched. But the most distinctive character of these small elements consists in the course of their axons. These descend a short distance, then curve upward and ascend through the 6th, 5th, and 4th layers, to which they give a few collaterals, and end in a manner which I have not been able to discover. In some cases these axons have branched close to their origin and, instead of one, describe two arcs continued by ascending fibres. Other axons, moreover, make even a greater number of loops. From the convex aspect of these curves, as well as from the ascending portion of the axons, within the 6th layer spring numerous collaterals which branch throughout the entire thickness of the layer. Some descend still further and subdivide in the plexus of the 7th layer, that is to say, at the level of the giant pyramids (Fig. 20, *B*).

Besides these small cells, which are certainly the most abundant, we find two other cellular types: (*a*) Cells of stellate form and medium size. They possess radiating dendrites which do not usually pass beyond the 6th layer. Their axons ascend and form an arborization throughout the extent of the 6th, 5th, and 4th layers. (*b*) Ordinary pyramidal cells, very scarce, of medium or large size. They have precisely the same characters as the pyramids of the 7th layer.

Seventh Layer or Layer of Giant Pyramids.

Solitary Cells of Meynert.—This layer contains one or two irregular and discontinuous files of giant pyramids, which appear, here and there, lost as it were in a dense and extended plexus. To this plexus the layer owes its finely granular appearance, which may be seen even in preparations stained by Nissl's method (Fig. 20, *C*, and Fig. 22, *B*).

The cells in question, like other pyramidal cells, possess a very large radial trunk which ends in a flattened spray of horizontal branches in the lower levels of the plexiform layer. The cells are also provided with a few many-branched basilar dendrites which distribute themselves throughout the layer and, finally, with a great number of horizontal dendrites forming a plexus which would seem to provide connections between these cells through long distances. This is such a characteristic feature that by its presence alone we are able to distinguish the visual from all other cortical areas. The axon of the giant pyramids is very large, extends almost vertically through the 8th and 9th layers, and is

continued as a fibre of the white matter. Collaterals spring from its initial portion which ramify in the 7th and even the superficial levels of the 8th layer.

In addition to the giant pyramids, which in some cases are not at all

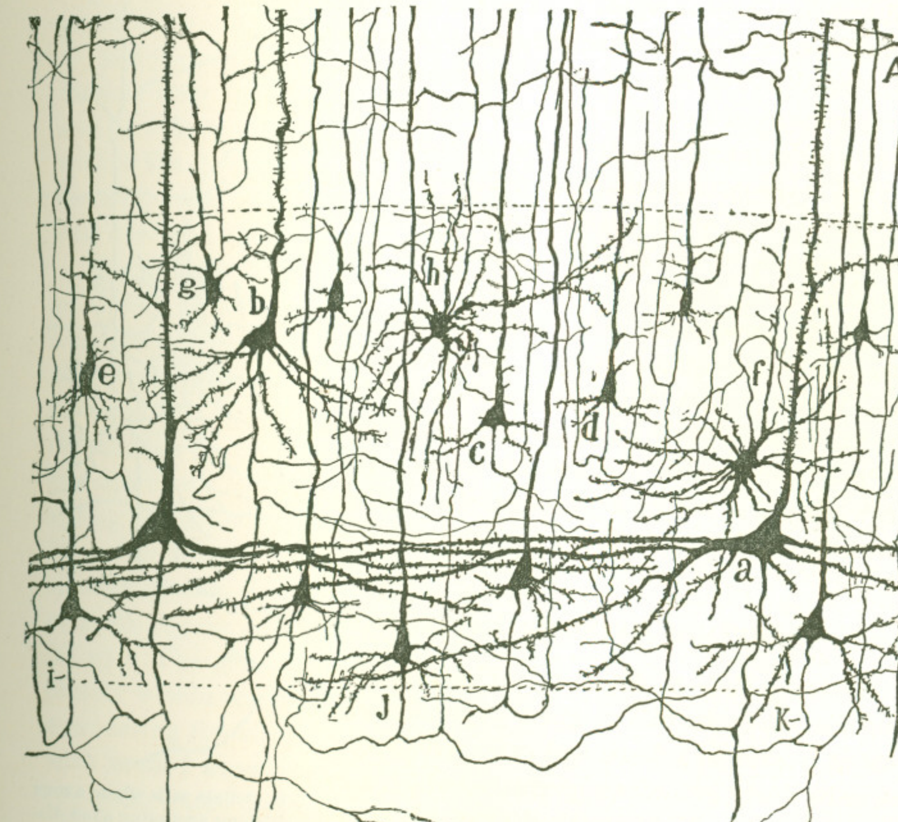


Fig. 20.—Cells of the 6th and 7th layers from the human visual cortex, infant 15 days old. *A*, 5th layer; *B*, 6th layer; *C*, 7th layer; *a*, giant pyramid; *b*, medium-sized pyramid with descending axon; *c*, small pyramid with arched ascending axon; *d*, pyramid whose axon presents two arches; *e*, pyramid whose axon gives rise to several arched fibres; *h*, *f*, *g*, stellate cells with ascending axons ramified in the 5th and 6th layers; *i*, *J*, *K*, pyramids whose axons arch and subdivide in the 7th and 8th layers.

numerous, the 7th layer contains: (*a*) a number of medium-sized pyramids possessing the same characters; (*b*) several small elements exactly similar to those of the 6th layer, the cells with the complicated forked and arched axons distributed in the manner above described (Fig. 20, *K*, *i*, *J*); (*c*) in addition may be found medium-sized stellate cells situated in the

7th and 8th layers (Fig. 21, *A*, *B*). The very remarkable feature of the latter cells consists in their terminal arborizations. Their neurites take at first an ascending or oblique course, divide into two, and then give rise to a large number of oblique or horizontal branches which occupy

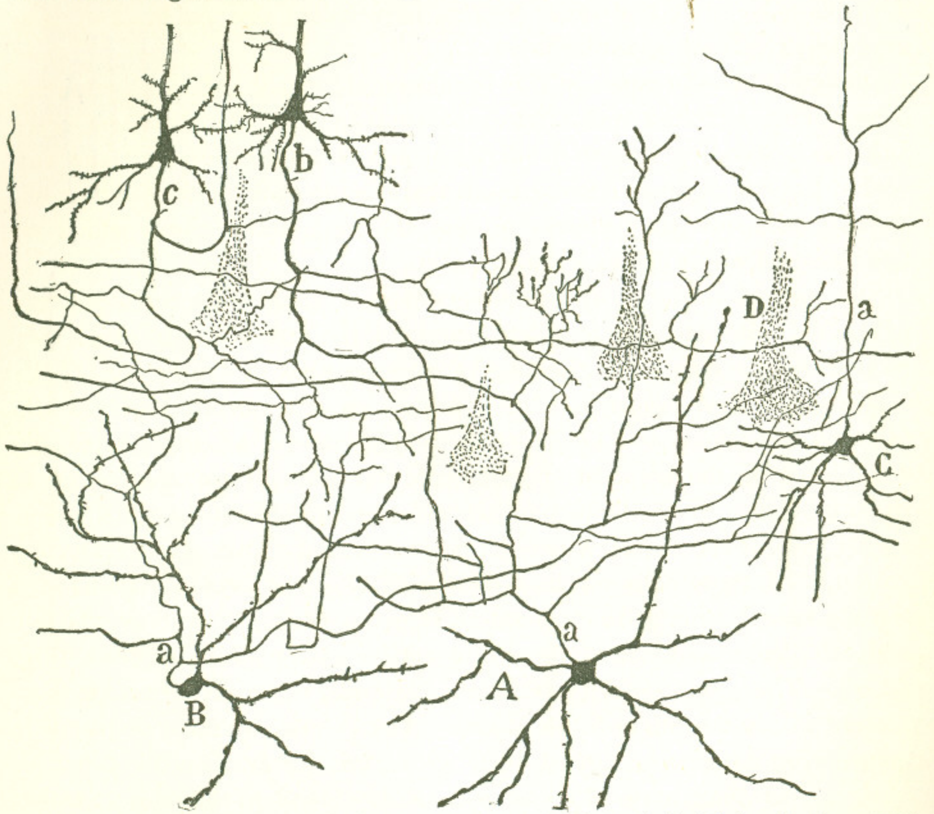


FIG. 21.—Special cells of the 7th layer, visual cortex of infant. *A*, *B*, stellate cells whose axons form terminal arborizations in the layer of giant pyramids; *C*, cell with long ascending axon distributed to the 4th and 5th layers; *D*, giant pyramid of 7th layer; *c*, *b*, axons of small pyramids of 6th layer.

a good part of the 7th layer. In the brain at birth their terminals present no special peculiarities; but in one twenty days old I have found that a number of these arborizations surround the giant pyramids, forming terminal nests. Only their arrangement is not so definite here as in the motor region, where we find it wonderfully developed. (Compare with description below.)

EIGHTH LAYER.

Examined in Nissl preparations this layer presents a mass of medium-sized pyramids and a remarkably dense formation of granules. This is the reason Meynert and other writers have called this the layer of deep granules or inferior granular layer.

Golgi's method reveals in this formation elongated cells of pyramidal form. They have the radial trunk continued, up to the plexiform layer and also descending basilar dendrites which become subdivided and end within the 8th layer. Among these there is no lack of fusiform or triangular cells, but they always present the long radial trunk which we find over the whole cortex (Fig. 22, *C*).

In general form, it will be observed that these cells resemble true pyramids. However, the peculiar behavior of their axons establishes a very clear distinction between them. As may be seen in the figure (22, i), this axon at first desçends, then describes an arc, ascends into the 7th, 6th, and 5th layers, and finally ends in a horizontal arborization chiefly distributed to the layer of stellate cells, but a few of its branches go to the 5th layer. From the loop of the axon, and in the course of its ascent, spring several collaterals, which ramify in different planes of the 8th layer. In a few of these cells we may observe that, at the bend of the axon, a slender branch, similar to a collateral, is given off, which crosses the 8th and 9th layers and enters the white matter as a medullated fibre (Fig. 22, g). The great majority of these collaterals, however, terminate completely within the 8th and 9th layers. At any rate, we must distinguish, considering the morphology of their axons, two kinds of cells: (*a*) cells with arched axon none of whose collaterals extend to the white matter; (*b*) cells whose neurite divides, at the arch, into a fine descending branch, which becomes a medullated fibre of the white matter, and into a larger ascending branch with its terminal arborization in the 4th or 5th layers.

This arched arrangement of the axon in cells of the 8th layer appears very strange. It occurs not only in the infant brain, but in the visual cortex of the adult as well. It seems, at first sight, to violate all laws that govern the length and direction of the axons in other sections of the nervous system. And, what seems still more remarkable, all these whimsical windings seem to subserve solely the purpose of shortening the stretch between the cell body and the first collaterals given off by the arch. This same phenomenon occurs in many other nerve cells. Were

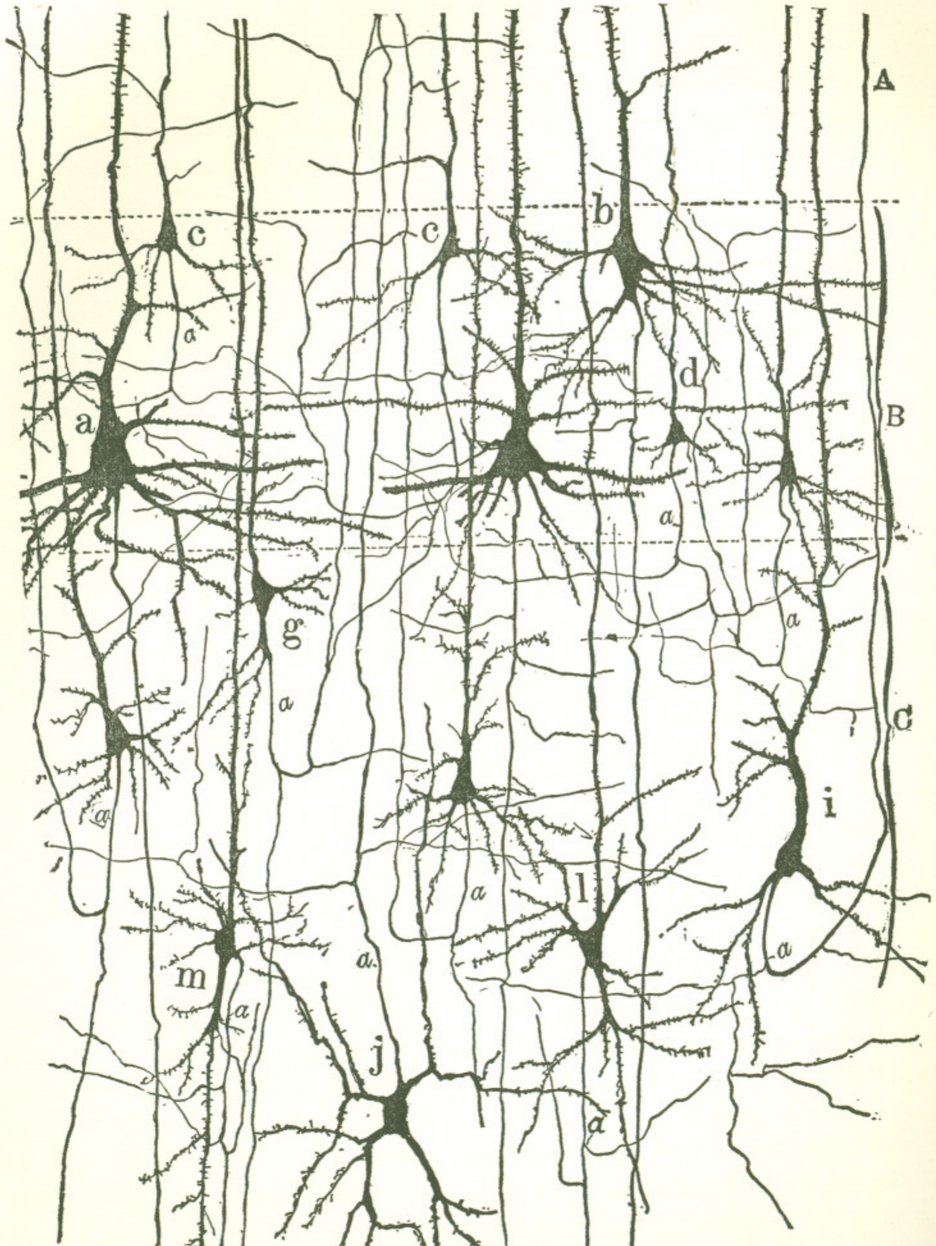


FIG. 22.—Seventh and 8th layers, visual cortex of cat, aged 20 days. *A*, deeper portion of layer of stellate cells; *B*, layer of giant pyramids; *C*, layer of medium-sized pyramids with arched axon; a, b, pyramids; c, d, small pyramids with axons distributed to 7th layer; g, triangular cell, whose axon gives rise to a large ascending collateral; i, another whose axon forms an arch and ascends; l, pyramid with axon descending to white matter; j, element from the deepest levels of the layer of medium-sized pyramids (corresponding to layer of fusiform cells in man) which gives origin to a large axon that ascends possibly to the 1st layer.

it not for a deviation from our present theme, I might adduce very convincing instances of this tendency of the axon to take the direction most favorable for the nerve impulses which arise in the cell to very quickly reach the elements connected with their initial collaterals.

Permit me also to add that the 8th layer contains giant stellate cells with ascending axon (Martinotti's cells), which runs to the plexiform layer (Fig. 22, j), and also a similar but smaller cell, whose axon gives rise to an arborization between the neighboring cells.

NINTH LAYER.

Coinciding closely with the so-called polymorphic layer of other authors, this layer contains elongated elements, fusiform, triangular, or ovoid, possessing a radial dendrite, extending up to the plexiform layer, and also one or several basal dendrites, which take a descending or oblique direction. Finally, these cells have an axon which descends in a straight line to the white matter; where, after giving off several collaterals, it continues as a medullated fibre. There are also in the 9th layer a few fusiform cells with short radial dendrites and ascending axon and a number of stellate cells with short axon of the so-called Golgi type.

In addition, the arrangement of the cells of the 9th layer varies greatly in different parts of a convolution. In the convex portion they are very numerous, fusiform, and slender, elongated and perfectly radial; while opposite the sulcus they have a quite different form, are stouter, more variable, and frequently lie with long axis parallel to the white matter, *i.e.* perpendicular to their ordinary direction. Their peripheral processes perform the most whimsical contortions in order to become radial and reach the plexiform layer. Their axon appears frequently horizontal, describing a very open curve on its way to the white matter. All these forms and many others represent adaptations of the cells to the foldings of the cortex and to its varying thickness in different parts of a convolution.

I will not impose further upon your indulgent attention with these tiresome enumerations of layers and forms of cells, in the mazes of which nature herself seems to have intended to lose the investigator and put his patience to the test. And I will close this tedious lecture with a succinct exposition of the anatomico-physiological inductions that seem to follow from my observations on the minute structure of the visual cortex of man and the mammalia.

1. The visual cortex of man and gyrencephalous mammals possesses a special structure very different from that of any other cortical area.

2. The visual region is characterized, above all, by fewness of giant pyramids and by presenting, at the level of the granular layer of other cortical areas, three distinct layers of cells of special form, to wit: the layer of large stellate cells, the layer of small stellate cells, and the layer of pyramids with arched ascending axon.

3. Gennari's or Vicq d'Azyr's stripe contains principally terminal arborizations of certain very large fibres, originating probably in the primary optic centres (external geniculate body, pulvinar, anterior corpora quadrigemina).

4. Since these optic fibres are distributed chiefly to the stellate cells of the 4th and 5th layers, it seems natural to consider these elements the substratum of visual sensation.

5. The innumerable cells with short axons in the 4th and 5th layers represent, probably, the intermediate links between the optic fibres on the one side and the stellate cells of the 4th and 5th layers and the pyramidal cells on the other.

6. As these intermediate cells are often very small and have short axons, it may be that, besides their function of diffusing the incoming impulses through the cortex, they play also the special rôle of augmenting the visual impulses by fresh discharges of nerve force, in order that they may reach, in sufficient strength, the cortical regions in which the function of commemorative recording of optical images occurs. The pathways for conveyance of visual residues from the median occipital region to the association centres in the parietal cortex are possibly represented by axons of the stellate cells of the 4th and 5th layers.

7. Granting that the giant pyramids of other cortical regions give rise to motor fibres, it would follow that in the 7th layer they possess the same function. These cells, whose dendritic trunks come into contact with the optical plexus, 4th and 5th layers, serve probably to mediate the reflexes of the eyeball and head (conjugate movements of the eyes) occasioned by elective stimulation of the visual cortex, a theory which would seem to be supported by the physiological experiments of Schäfer, Danillo, Munk, and others.

8. Granting that each giant pyramid comes into contact in the 4th and 5th layers, as well as in the first layer, with fibres that are probably associative, we may suppose that motor discharges of these cells can be effected by two kinds of impulses: by ordinary optical stimulation and by stimuli of a volitional order, possibly coming from the association centres and reaching, finally, the plexiform layer.

My own researches do not furnish grounds for further conclusions. Many points still remain to be cleared up; but their complete elucidation will be the fruit of researches more detailed and exact than those I have been able to undertake.

LECTURE III.

The Sensori-Motor Cortex.

After the study that we have just made of the visual cortex, we can be more concise in our examination of the motor area. In all cortical regions we notice general structural characters and special features which constitute the physiognomy proper of each cerebral area. Naturally, the latter will be of more interest to us, and they will form the subject of the present lecture.

I shall not stop here to give any history of researches undertaken upon the minute anatomy of the psycho-motor areas. A bibliography of the subject would be very long, tedious, and altogether superfluous, since it has already been provided in the recent studies of Retzius, Hammarberg, and Kölliker. It will suffice to name, among those to whom we are most indebted for a knowledge of the structure of the motor cortex, Meynert, Baillarger, Kölliker, Krause, Betz, Lewis, Golgi, Martinotti, Retzius, Flechsig, Kaes, Hammarberg, Nissl, etc. All these writers have selected the psycho-motor cortex for special study; and it is safe to assert that all our knowledge of the minute structure of the entire cortex has taken its character from this region, which some writers have denominated "typical." They have done this because it was thought at the time when the fundamental works of Meynert and Golgi appeared that in histological structure the whole cortex corresponded to a uniform design, presenting only unimportant variations in different regions.

Neither have I time to enumerate the layers which have been described for this cerebral region. Their number has varied under the pen of each writer with the animal and the method he has happened to employ. Thus Meynert, who made his observations on man, distinguished five layers; Stieda, Henle, Boll, and Schwalbe limited their number to four; while writers like Krause admitted as many as seven. I myself, at the time of my investigations upon the small mammals, recognized four, naming them: (1) molecular layer; (2) layer of small and medium-sized pyramids;

(3) layer of large pyramids; (4) layer of polymorphic cells. This number, derived particularly from study of the small mammals, is not valid in the more complicated human cortex. To the four classical layers of smooth-brained mammals we must add one at least, the so-called granular layer of Meynert and other writers. This layer, situated in its very midst, divides the layer of giant pyramids into two, which we may call respectively the external, or superficial, and the internal, or deep, layers of giant pyramids.

To sum up, the following are the layers which it is possible to recognize by Nissl's method in the human motor cortex (ascending frontal and ascending parietal convolutions). To conform to our scheme in the visual cortex, we have altered the terminology for this region also.

1. Plexiform layer (layer poor in cells of Meynert, molecular layer of some writers).
2. Layer of small and medium-sized pyramids.
3. External layer of giant pyramids.
4. Layer of small stellate cells (granular layer of the authors).
5. Internal, or deep, layer of giant pyramids.
6. Layer of polymorphic cells (fusiform and medium-sized pyramids of certain writers).

Fig. 23. — Section of adult human motor cortex, stained by Nissl's method (semischematic). 1, plexiform layer; 2, layer of small pyramids; 3, layer of medium-sized pyramids; 4, external layer of giant pyramids; 5, layer of small stellate cells; 6, internal layer of giant pyramids; 7, layer of polymorphic cells or deep pyramidal layer of medium-sized cells; 8, layer of fusiform cells.

These layers correspond particularly to the concave portions of the motor convolutions. Over the convexities the gray matter is thickened especially at the level of the polymorphic layer, which here appears divided into two sub-layers: an external, very rich in pyramidal and triangular cells (Fig. 23, 7); the other, internal, presenting, besides the heavy bundles of white fibres, fusiform cells disposed in parallel series (Fig. 23, 8).

1. **Plexiform Layer.** — This is similar in structure in the motor and visual areas. It contains, therefore: (1) dendritic arborizations of the pyramidal and polymorphic cells, that is to say, of all the cells of deeper layers (2, 3, 4, 5, 6) except stellate cells of the 4th layer and the cells with short axons scattered through the entire cortex; (2) terminal arborizations of the ascending axons of Martinotti; (3) the ramifications of the recurrent collaterals which come up from the axons of certain small and medium-sized pyramids; (4) the fibres, terminal and collateral, which arise from the white matter; (5) stellate cells of variable size with short axon which ramifies within the 1st layer; (6) the special, or horizontal, cells with long tangential dendrites; (7) finally, neuroglia cells of the two well-known types, with long radiating processes close underneath the pia (Martinotti, Retzius, Andriesen, Bevan Lewis, *et al.*), and type with short processes, located at all levels of the plexiform layer (Golgi, Cajal, Retzius, Martinotti).

We shall not enter upon their descriptive details, since all the structures present the same characters here as in the visual cortex. We shall merely add that in the motor cortex the plexiform layer is notably thick. It also contains a greater number of horizontal cells and terminations of the trunks of pyramidal cells (Fig. 25, *A*, *B*, *C*). Its greater thickness arises probably, as Lewis remarks, from the extraordinary number of pyramidal cells in the underlying layers.

2. **Layer of Small and Medium-sized Pyramids** (Fig. 24, 2 and 3). — We shall not stop upon these, because they are so well known. Permit me merely to call to mind the fact that their radial trunk, often forked near its origin, makes its arborization in the plexiform layer; while from the base springs a fine neurite which, in case of the small mammals, we can trace into the white matter. In the child's cortex this is made difficult by the distance, but I have been fortunate on two occasions in following this axon into the medullary substance, where it was continued as a medullated fibre. The neuritic collaterals are also very numerous

and a number of them may be seen to recur and make their arborizations in the superficial lamina of the plexiform layer.

Cells with Short Axons.—These are numerous, although it does not seem to me that they are so extremely abundant as in the visual region. In Fig. 25 I have reproduced some of these elements which habitually occur in my preparations. We remark especially: *a*, a large stellate type, whose ascending axon subdivides into horizontal or oblique branches covering a great extent of the layer of small and medium-sized pyramids (Fig. 25, *K*); *b*, a second type of similar form but whose axon forms its terminal arborization very close to the cell (Fig. 25, *E*); *c*, still another form with horizontal axon the superficial branches of which penetrate into the plexiform layer (Fig. 25, *D*); *d*, arachniform cells with axons subdivided into dense plexuses (Fig. 25, *F*, *G*); *e*, fusiform, bipanicled cells, which have been sufficiently described.

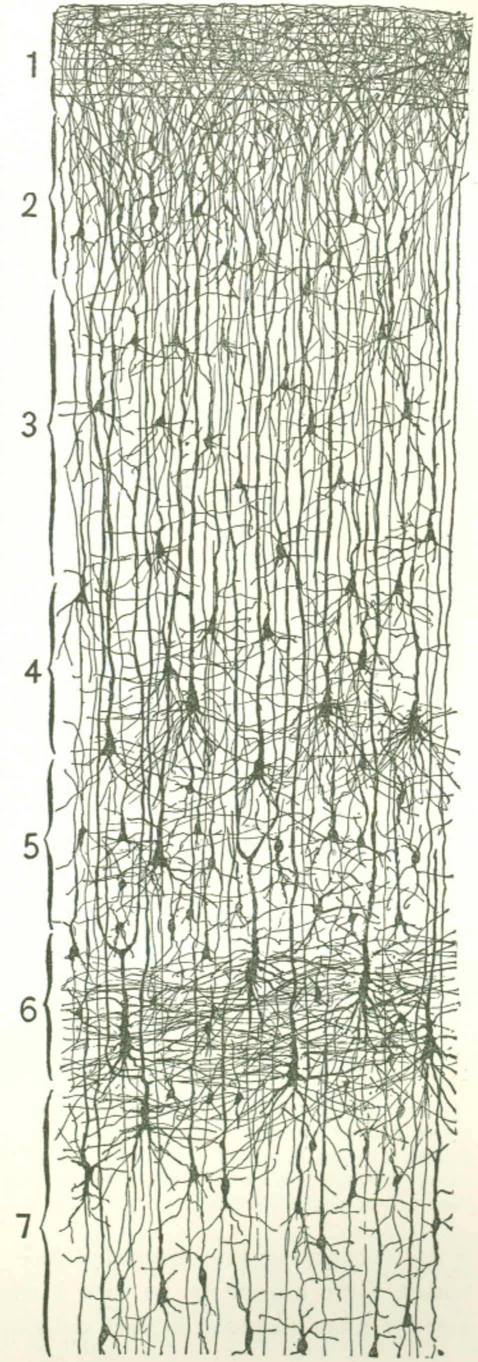


Fig. 24. — Ensemble of layers of motor cortex of infant aged one and a half months; Golgi's method (semischematic). Layers are numbered as follows: 1, plexiform; 2 and 3, small and medium-sized pyramids; 4, superficial giant pyramids; 5, granular or small stellate cells; 6, deep giant pyramids; 7, polymorphic cells, or deep medium-sized pyramids. (In this figure I have not represented the deepest portion of the 7th layer.)

Having studied all these types and many others in the visual cortex, it is unnecessary here to enter upon a more detailed description. One

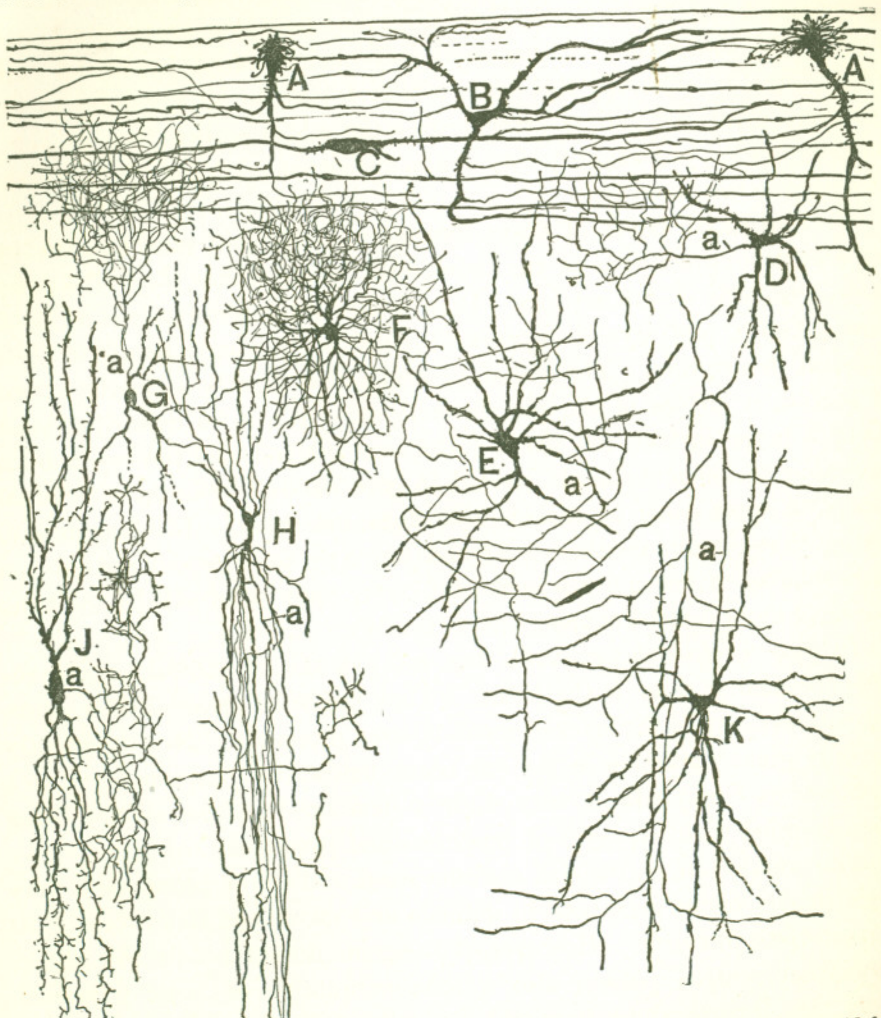


Fig. 25. — Cells with short axons of the plexiform and small and medium-sized pyramidal cell layers from motor cortex of infant aged one month and a few days. *A*, *B*, *C*, horizontal cells of the plexiform layer; *D*, cell with horizontal axon; *E*, large cell with very short diffusely subdivided axon; *F*, *G*, spider-shaped cells whose delicate axons form a dense plexus (*G*) up to the plexiform layer; *H*, *J*, bipanicled cells.

thing concerning the bipanicled cells I may add, viz., that in the motor cortex there appear to be two kinds: one, small cells provided with slender axon disposed in very delicate vertical pencils (Fig. 25, *H*); the

other consisting of relatively large cells having very long and thick dendrites and with an ascending or descending axon giving rise to terminal arborizations of extreme complexity, producing nests or terminal baskets about the bodies of the small and medium-sized pyramidal cells (Fig. 25, *J*). Possibly this type, which I take to be a variety of the common bipanicled cell, is present over the whole cortex; but as yet I have succeeded in finding it only in the motor convolutions of the infant at over one month of age.

3. **Superficial Layer of Giant Pyramids.** — Being a continuation by imperceptible gradations of the above, this layer contains the well-known large pyramids of the writers. In addition to the observations of Betz, Lewis, Golgi, and myself, however, I must add a single detail to their classical description. The radial process varies greatly as to the extent of surface it covers in the plexiform layer. When its dendrites must cover a large surface, the trunk forks near the cell, and the two trunks, deviating at an acute angle, ascend to give rise to two or more terminal sprays, in some cases at considerable distances apart. This amounts to saying that certain medium-sized and large pyramids stand related to a large number of nerve fibres in the 1st layer, while other cells of the same size have more limited connections (Fig. 24).

In gyrencephalous mammals, dog and cat, the superficial large pyramids are smaller than in the infant. They might be considered as a subordinate element in the layer of medium-sized pyramids. Most frequently the only giant pyramids in the cat occur below the granular layer, — a layer which, I may add, is very slightly developed in this animal, being often blended with the layer of medium-sized pyramids.

The number of superficial, medium-sized, and giant pyramids is very large in the motor area both in animals and man; and this is one of its characteristic features. However, the regions designated by Flechsig as association centres possess also a notable number of large pyramids. From this feature alone it would be quite difficult to distinguish the frontal and parietal from the motor convolutions.

The axon of the large and medium-sized pyramids descends, as is well known, to the white matter and is continued as one or two nerve fibres. I must call special attention to the fact that, as shown by my own researches, this fibre may fork usually into a fine branch which goes, probably, to the corpus callosum and a larger branch to the corpus striatum. This may be easily observed in the brain of a newborn mouse or in one a few days old. It may also be seen that the fibre entering the corona radiata passes beyond the corpus striatum, giving off to it a few collaterals. It is thus well established that the axon of the large pyramids is true projection fibre which takes part in forming the pyramidal tract. But we must be on our guard about accepting the view of certain writers, — v. Monakow, for example, — who ascribe this rôle, participation in the motor tract, exclusively to the giant pyramids, because I have demonstrated beyond all doubt, in the motor region of the mouse and rabbit, that a number of the axons of medium-sized pyramids and many from polymorphic cells also penetrate the corpus striatum. I therefore consider as wholly arbitrary all the opinions which tend to attribute an exclusive function to elements in each distinct cortical layer. In the cortical layers, as well as in the ventral horn of the spinal cord, there occur together elements with axons of very diverse character and connections. The motor cell takes its place beside the associational cell along with the element whose axon or collateral goes to the corpus callosum. There are, accordingly, in the cortex no "sensory layers" nor "motor layers"; because, as we shall see in a moment, the great majority of the cells are related, either by their cell bodies or by their radial trunks, to the plexus of sensory fibres. We find thus reproduced the arrangement of the spinal cord, where all the cells, or almost all, come into contact with sensory fibres of the first or second order, and all represent links in the chain of reflex connections.

4. **Layer of Small Stellate Cells** (*Granular Layer of the Authors*). — Stained by Nissl's method the layer of small stellate cells appears as a great number of nuclei surrounded with little protoplasm which contains a few fine granules of chromatin (Figs. 23, 5, and 24, 5). Most of these elements, the granules proper, are very small and globular or stellate in form. Others, I have observed, are comparable to small pyramids, being of triangular form and having a fine radial trunk. Nor is there any lack of stellate or fusiform cells of considerable size, which call to mind those of the visual cortex. All these elements appear to be mingled. However, in certain places I thought I could discover that the small globular cells are situated chiefly in the external plane of the layer, while the minute pyramids were more numerous in the deeper levels, but there are exceptions to this.

But Nissl's method does not enable us to study the fine processes of these elements. To this end we must have recourse to the chromate of silver method, and by its application — especially in case of an infant fifteen to thirty days old, a time at which the reaction is easily obtained — I have been able to demonstrate the extreme complexity of the granular layer. Good preparations show that it consists of elements with very diverse characters, which in spite of their minor differences may be classed into two groups: (1) cells with long axons which extend down to the white matter; (2) cells with short axons which end within the granular layer or in layers above it.

Cells with Long Axons. — These may be classed into two varieties, small pyramidal cells and medium-sized stellate cells.

(*a*) The small pyramid is specially numerous in the deep level of the 4th layer (Fig. 26, *A*, *B*). It has been figured by various writers, notably by Kölliker, although even he does not give us any information on the character of its axon. The cells are ovoid-pyramidal in form. They possess a radial trunk which extends up to the plexiform layer, where it ends in a few very slender varicose twigs without contact granules. It also has a few tiny descending or oblique dendrites which divide repeatedly. Finally, I have very often traced its axon to the white matter, in which it is continued as a slender medullated fibre. From its initial portion arise two, three, or four collaterals, some of which curve upward to distribute themselves through the 4th layer. In some cases the diameter of these collaterals is so large, compared with that of the axon, that they might be considered the real axons.

(*b*) Stellate Cells. Very hard to stain, and possibly quite scarce. Their dendrites arise from the angles of the cell body and run in all directions, but are distributed exclusively to the 4th layer (Fig. 26, *D*). Their axons spring from the inferior surface, descend almost in a straight line, and, after giving off a few large collaterals, very frequently arched and recurrent, are lost in the white matter. These interesting cells, exactly similar to the stellate cells of the visual cortex, are also found in the motor cortex of gyrencephalous mammals, although, to judge from my own preparations, only in small numbers. Their presence would seem to indicate distinctively sensory regions of the brain.

Elements with Short Axons. — These are also very numerous in the infant brain, representing, perhaps, the chief morphological factor of the 4th layer. Several varieties have been distinguished, of which the most common are the following: —

(*a*) Stellate or Fusiform Cells of Medium Size. Their dendrites diverge in all directions, but chiefly above and below, and end in the midst of the 4th layer. Their axon springs from the superior surface, ascends for a variable distance, and at varying levels of the layer of stel-

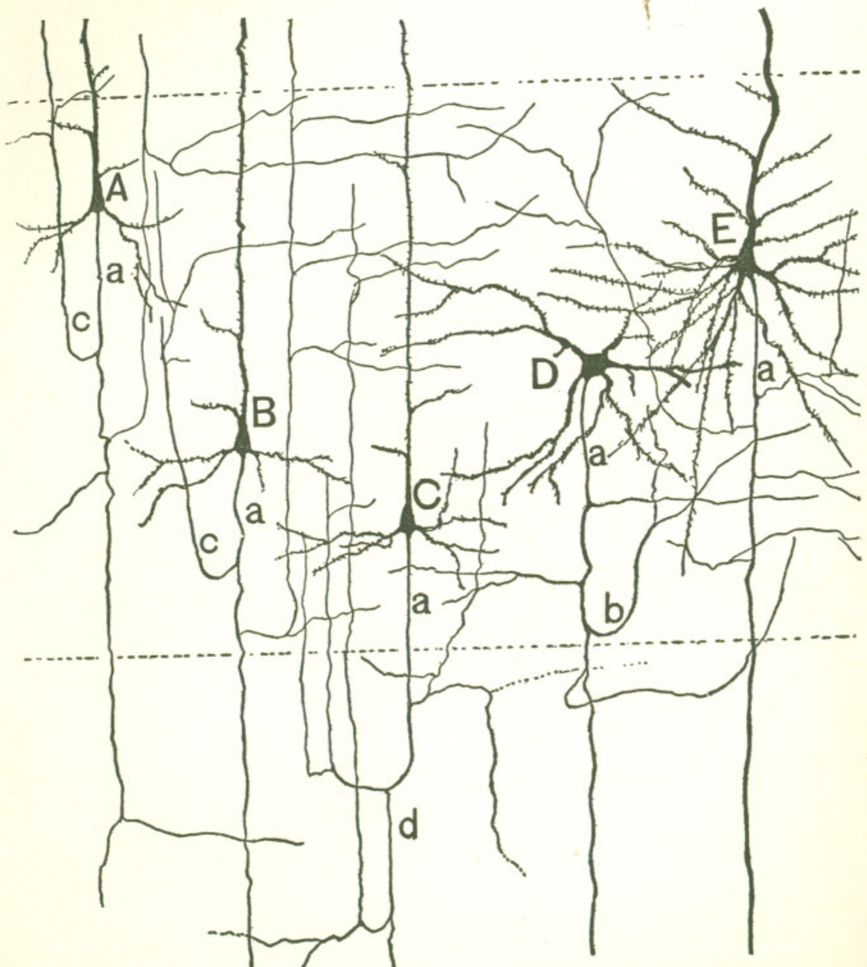


FIG. 26.—Cells with long axons from 4th layer of motor cortex of infant aged one month. *A, B, C,* small pyramidal cells; *D,* large stellate cell; *E,* medium-sized pyramid; *a,* axon; *b, c,* large descending collaterals.

late cells forms an arborization of horizontal or oblique branches of considerable length and distributed exclusively to the 4th layer. Very often the axon branches in the form of a T before proceeding to its terminal arborization, and from its initial part arise collaterals whose course

and terminations resemble those of the terminal branches. These cells, we may add, correspond in all points to the cells with ascending axons described for the 4th and 5th layers of the visual cortex (Fig. 27, *A, C, D*).

(*b*) Fusiform, Triangular, or Stellate Cells. These are somewhat

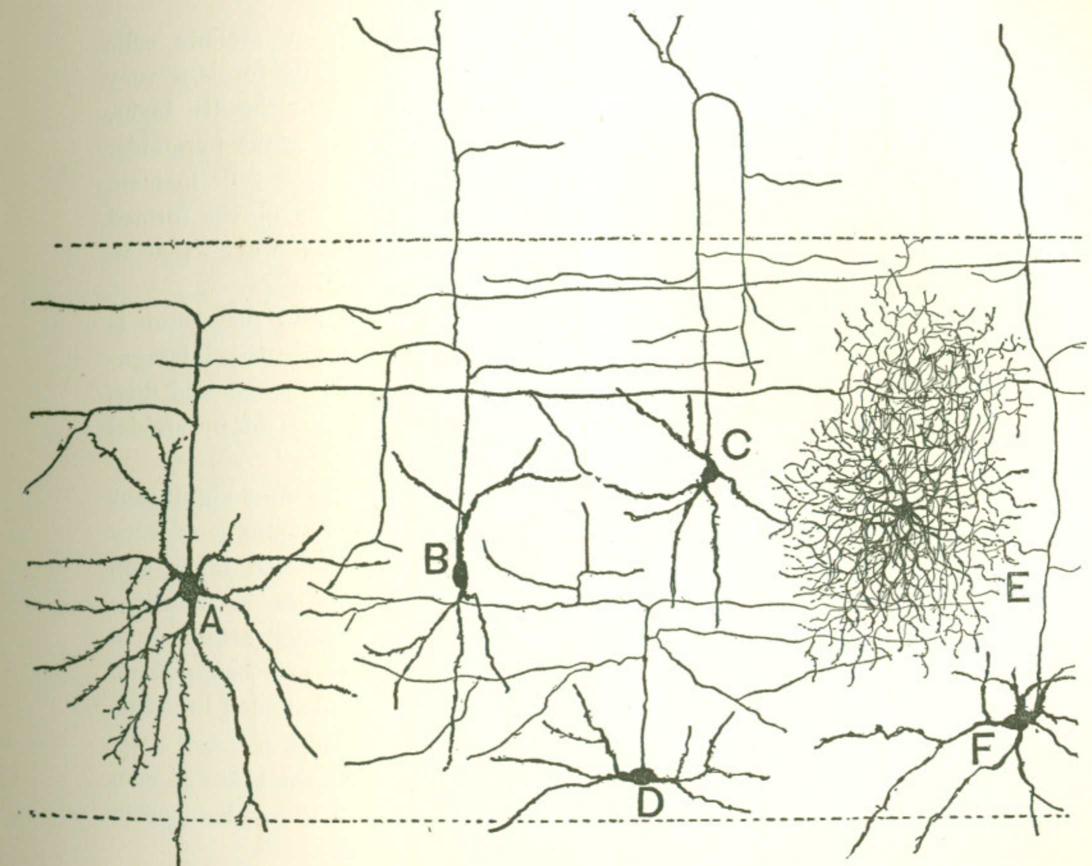


FIG. 27.—Cells with short axons from 4th layer of motor cortex of infant. *A, B, C,* cells, stellate or fusiform, with ascending axon divided into long horizontal branches; *E,* arachniform cell; *F,* cell with axon distributed to layer of medium-sized pyramids.

larger than the preceding. Their axon ascends to the plexiform layer, in which it subdivides and terminates. In its ascent it supplies a few collaterals to the 4th and 3d layers. These elements, as we see, correspond to the so-called cells of Martinotti. In a few cells of this class the axon possibly does not reach the first layer, becoming lost in the layers below (Fig. 27, *A*).

(*c*) Small Stellate or Spider-shaped Cells. These possess fine and richly subdivided dendrites and also a neurite, which forms a very rich arborization close to the cell (Fig. 27, *E*).

(*d*) Bipanicled Cells. These have the characteristics already described in our study of the visual cortex.

(*e*) Finally, in the cat and dog I have found a few stellate cells with very numerous dendrites, whose descending neurite forms a very dense and complicated arborization, for the most part in the 4th layer, but in some cases extending down to the deep layer of giant pyramids. Possibly these cells are homologous to the spider-shaped cells in man, which they resemble in the extraordinary richness of the plexus formed by the axon. It would then be necessary to suppose, however, that in the cat and dog these cells are much larger than in man.

In order to complete my description, permit me to add that there is no lack of ordinary pyramidal cells, in some cases large, scattered irregularly in the 4th layer (Fig. 26, *E*). In mammals like the cat and dog, and to a much greater degree in the rabbit, the profusion of pyramidal cells obscures our picture of the granular layer.

Sensory Nerve Plexus of the 4th Layer. — One of the most significant facts which I have discovered in the motor cortex is a plexus of very large fibres whose numerous subdivisions occupy the 4th layer and extend even into the 2d and 3d. They probably enter the cortex from the corona radiata. As early as in my first work I called attention to these fibres as being different in diameter, direction, and origin from axons of pyramidal cells, but at that time I had not succeeded in determining the region to which they are peculiar or the precise place of their termination in the cortex. My recent researches upon the brain of man and also small mammals enable me to add a few details to my description of some years ago (Fig. 28).

First of all, I have been able to determine exactly their origin and position in the brain. These are both easy to observe in the brain of a rabbit at birth and still better in that of a mouse a few days old. In the mouse it may be seen especially well that certain large fibres (called by Kölliker, who has confirmed their existence, fibres of Cajal) proceed from the corpus striatum, enter the white matter, and often extend horizontally in it for great distances. In their course they throw off long collaterals, which penetrate into the overlying gray matter. All these collaterals, as well as finally the original axon itself, ascend through the

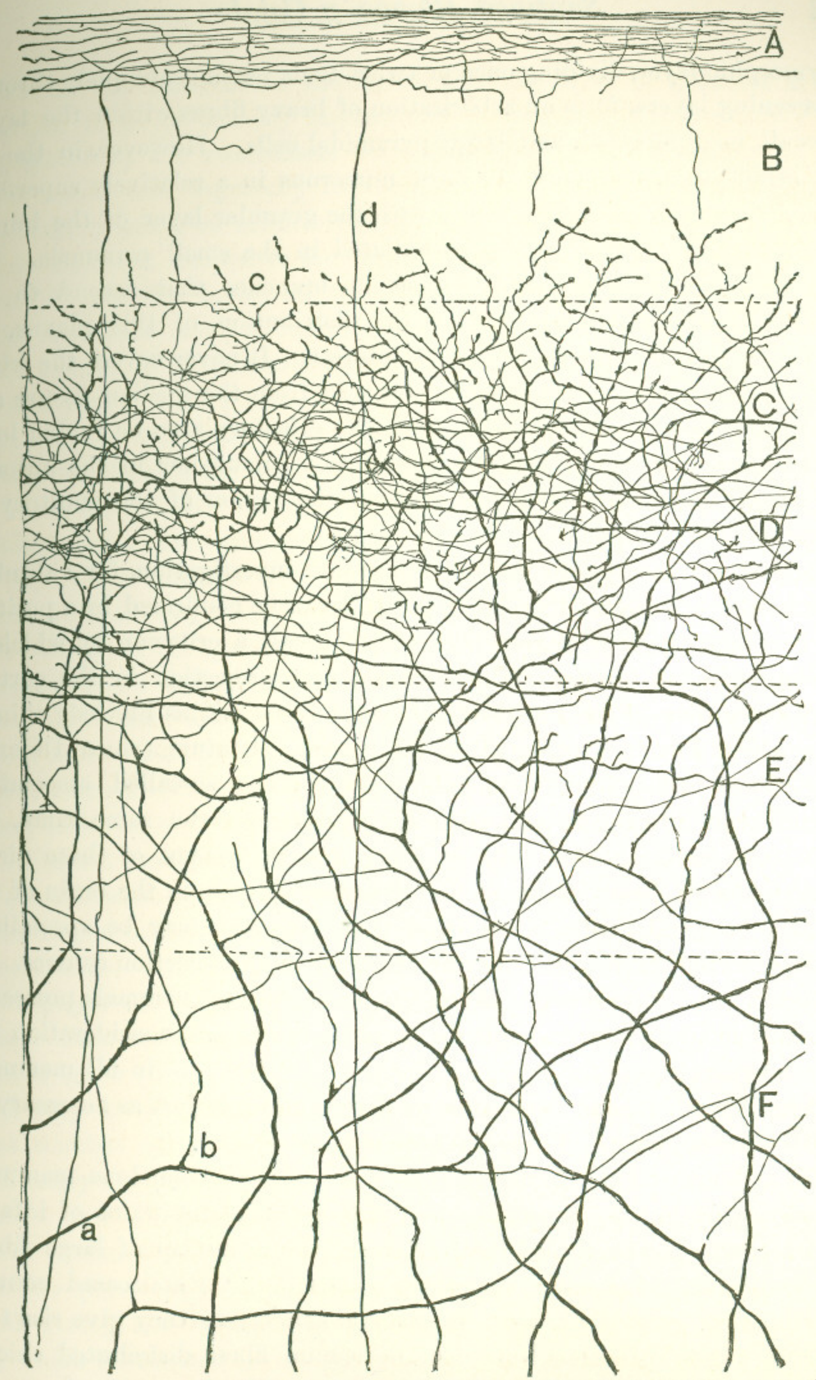


Fig. 28. — Plexus of heavy sensory fibres from motor cortex of cat 25 days old. *A*, plexiform layer; *B*, layer of small and medium-sized pyramids; *C* and *D*, layers of granules and superficial layer of giant pyramids; *E*, deep layer of giant pyramids; *F*, layer of polymorphic cells; *a*, fibre from white matter; *b*, ascending collateral; *c*, varicose terminal arborization; *d*, fibre directed to the plexiform layer, which appears to be distinct from the large fibres.

polymorphic layer, dividing once or twice, then, passing obliquely through intervening layers, form an arborization of heavy fibres within the layers of small, medium-sized, and large pyramidal cells. However, in the rat and rabbit these branches are most numerous in a relatively superficial plane, which corresponds probably with the granular layer of the human brain, — a layer that is not differentiated in the small mammals. We also find a relatively small number of branches that ascend to the plexiform layer. As to the cortical distribution of this plexus, we may also place on record a fact of interest. It never covers the whole cortex. It begins to appear some distance from the median fissure and disappears below long before reaching the olfactory area or limbic lobe. I have never observed it in the cortex of this sulcus, nor in the anterior portion of the frontal lobe, nor even in the region of the auditory or visual centres.

I shall return to this matter in a future investigation, for I think it merits most thorough study; because, if it can be confirmed in a positive manner and by other methods, we shall possess a criterion by which to distinguish between areas of association and projection in the cortex. The projection areas will probably be found to be not, as Flechsig thinks, those possessing fibres that go to the corpus striatum (since Déjerine and others have discovered these fibres in the so-called association centres) but those receiving sensory fibres. At the same time, the association centres will be characterized by the absence of these direct sensory connections. At any rate, I believe that even in the brain of the smallest mammal there are areas, of small extent it may be, specialized to store up the images or residues of the sensory projection centres. It would be most astounding if the brains of the small mammals possessed a different architecture from that of man, taking into consideration the fact that all the senses have the same essential structure in all mammals and that memory — visual, tactile, muscular, etc. — is just as necessary to their lives as to our own.

The sensory plexus is highly developed in gyrencephalous mammals and in man. I have found it well impregnated in the brains of infants at birth and a few days old. Here it appears made up of large fibres having an oblique direction and a flexuous or even staircased course. After dividing several times in the 6th and 5th layers they give rise to a singularly extended arborization of horizontal fibres distributed chiefly to the layer of granules or small stellate cells. We thus see in the motor cortex, as was the case in the visual, that the layer of granules is the principal focus of sensory impressions. From this terminus they are propagated by the numberless cells with short ascending axons to the layers above and especially to the medium-sized and giant pyramids. However, it must be acknowledged that the sensory plexus is not so narrow and well defined as the optic. For, although its greatest density occurs in the 4th layer, its terminal branches divide in their ascent to the superficial layer of medium-sized and giant pyramids. The fibres which extend up to the small pyramids in man are not numerous. It is for this reason that I cannot agree with Bevan Lewis in ascribing to them sensory functions. I do not wish to be understood to deny the sensory function of the small and medium-sized pryamids. According to my view, all the cells of the motor cortex are sensory because they all, possibly, come into contact either directly (cells of the 3d, 4th, and 5th layers) or indirectly, through the intervention of cells with short axons, with sensory terminal arborizations. But, since some cells send their axons to the pyramidal tracts, we are able to distinguish them as *sensori-motor cells of the first order.* The others, which send their neurites to other motor areas of the brain, possibly effect contact with sensori-motor cells of the first order located elsewhere. These cells of indirect sensori-motor communication we may be warranted in calling *sensori-motor cells of the second order.* It goes without saying that this distinction is purely hypothetical; for no method enables us to determine the precise point within the brain where the axons of the pyramidal tracts of the corpus callosum or of bands of association fibres form their terminal arborizations.

5. **Layer of the Giant and Medium-sized Pyramids.**— In the adult human brain stained by Nissl's method, a section of the motor cortex reveals, below the granular layer, a layer of plexiform or granular aspect filled very thickly, but in no particular order, with a few giant and a great number of medium-sized pyramids (Fig. 29).

Usually the giant pyramids are located near the 4th layer, forming there a few irregular ranks. Impregnated by Golgi's method, they appear similar to the same cells in other regions of the cortex, but differ in a few particulars. The body is generally conical, very much elongated, giving rise at the apex to a large trunk, often dividing near the cell, which terminates in the 1st layer in the usual manner. A group of long complicated dendrites diverges from its base, and from the sides spring several very long horizontal processes which subdivide into terminal brushes, and these, intertwining with similar structures from neighboring cells of the same level, form a dense and very characteristic

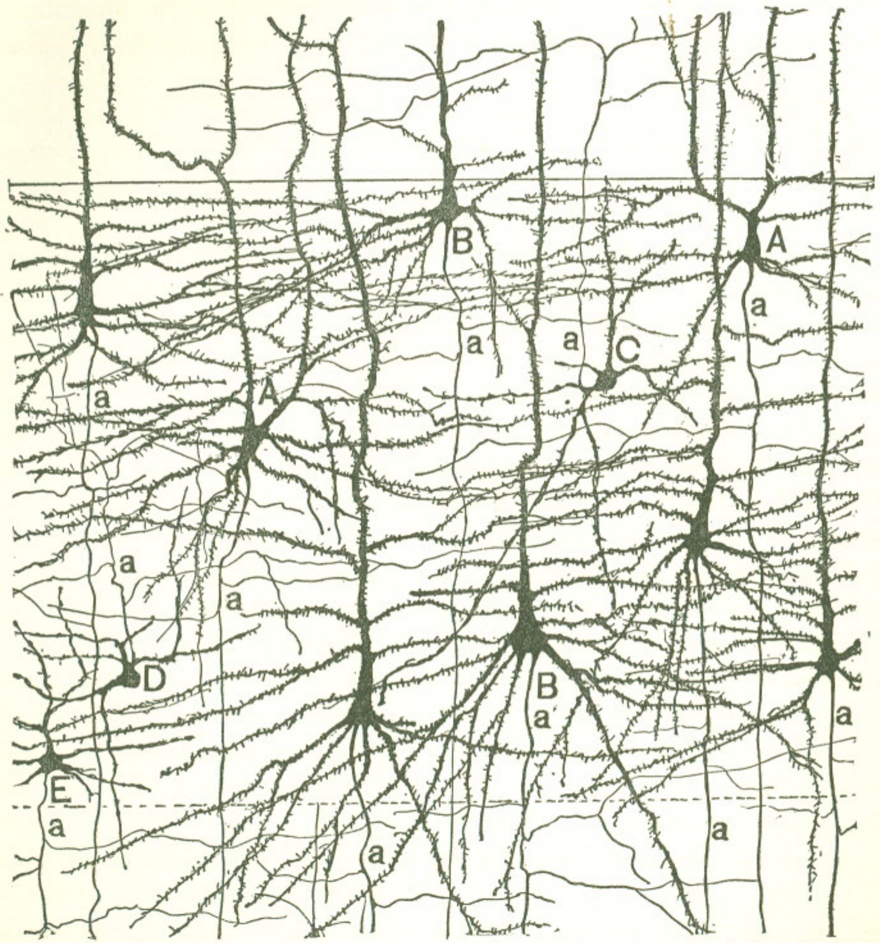


Fig. 29. — Deep layer of giant pyramidal cells from motor cortex of infant aged 20 days. *A*, *B*, pyramidal cells; *D*, *C*, elements with short axons.

protoplasmic plexus. It is the same arrangement we already know so well in the visual cortex, except that, instead of one plexus, there are many. The axon is large and, after giving off very long collaterals to the 5th and 6th layers, it passes on to become a medullated fibre of the white matter.

The medium-sized pyramids are very numerous, much scattered, and

occur in greatest profusion in the lower levels of the layer. They do not differ in character from the giant pyramids, except as to the lateral somatic dendrites, which are few and not characteristic.

Besides the pyramidal cells the 5th layer contains a few other kinds of elements. From the point of view of their morphology the following are the more striking types.

(*a*) *Cells which form Terminal Nests.* — These cells, very similar to those which give rise to the basket fibres of the cerebellum, are most numerous in the 5th layer between or below the giant pyramids. I have found them also in the layer of granules or small stellate cells.

Their volume is small, similar to that of a small pyramid, and in form they appear stellate or triangular with very long and much-branched varicose dendrites. The neurite, however, presents the most distinctive feature. It ascends, forking close to its origin, and breaks up into a ramification of very many branches, ascending, oblique, or horizontal. After a few subdivisions, all these branches make their way to the giant and medium-sized pyramids to form very complicated varicose arborizations close around their cell bodies and principal processes, after the manner of the terminal baskets of the cerebellum or the nests found in Deiter's nucleus. Each nest contains arborizations from several cells, and each basket cell helps to form a large number of nests (Fig. 30, *d*).

(*b*) *Cells with a Diffusely Branched Ascending Axon.* — This is a fusiform or stellate cell located at different levels of the 5th layer, to which it sends its dendrites. The axon ascends to the superior limits of the layer where it forks, and its terminal branches form a loose horizontal arborization of an enormous extent and connected probably with the deep giant pyramids (Fig. 29, *C*, *D*).

(*c*) *Small Pyramids with Arched Axons.* — This cell, which I have studied particularly in the motor cortex of the cat, is entirely similar to the element which we found in the 6th and 7th layers of the visual cortex. The cells possess a fine dendrite which ascends to the first layer, where it ends in a very modest and delicate arborization. Their axon descends and, after giving off a few relatively long recurrent collaterals, appears to fork and end in the midst of the 5th layer. The branches which spring from the bend of the arch descend in some cases, but I have not been able to trace them down to the white matter.

(*d*) *Cells with Long Ascending Axon.* — These are fusiform or triangular cells with long polar dendrites which never reach the first layer.

Their axon arises from the superior surface of the cell, and, after giving off a few branches to the 5th and 4th layers, it continues its ascent to the plexiform layer and there makes its terminal arborization.

6. **Layer of Polymorphic Cells.** — This layer contains the same elements as the layer of the same name (9th) in the visual cortex (Fig. 31), that

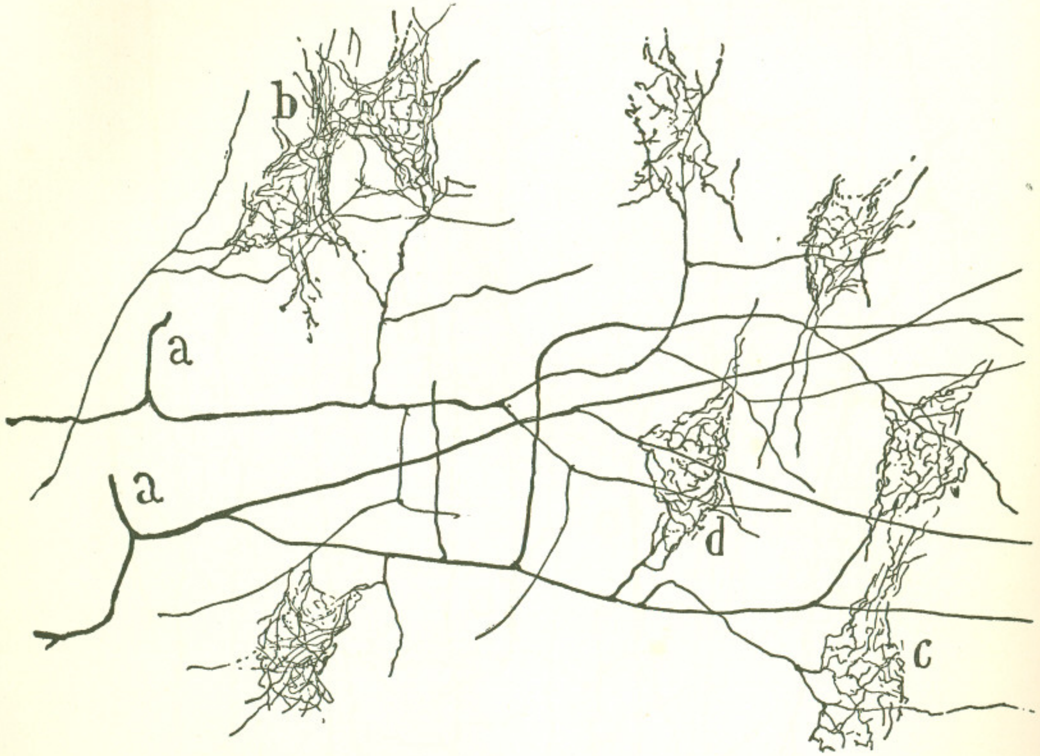


FIG. 30.—Pericellular terminal arborizations from the deep layer of giant pyramids, motor cortex (ascending frontal convolution) of infant aged 25 days. *a*, axons giving rise to oblique and horizontal branches; *b*, *c*, *d*, terminal nests.

is to say, fusiform cells with two long polar dendrites, triangular cells, and true pyramids. Their axons all go to the white matter. Their ascending trunks, which are never lacking, become very attenuated on account of the branches given off while passing through the 4th layer and reach the 1st layer as an exceedingly delicate fibril, which ends in a fine, slightly extended, notably varicose dendritic spray.

In Fig. 31, I have reproduced the principal types of cells found in the polymorphic layer. Besides the medium-sized pyramidal and triangular types having long descending axons (Fig. 31, *A*, *B*), there occur other

forms in great numbers. These are fusiform or triangular cells whose axons penetrate into the superposed layers, furnishing to them a great

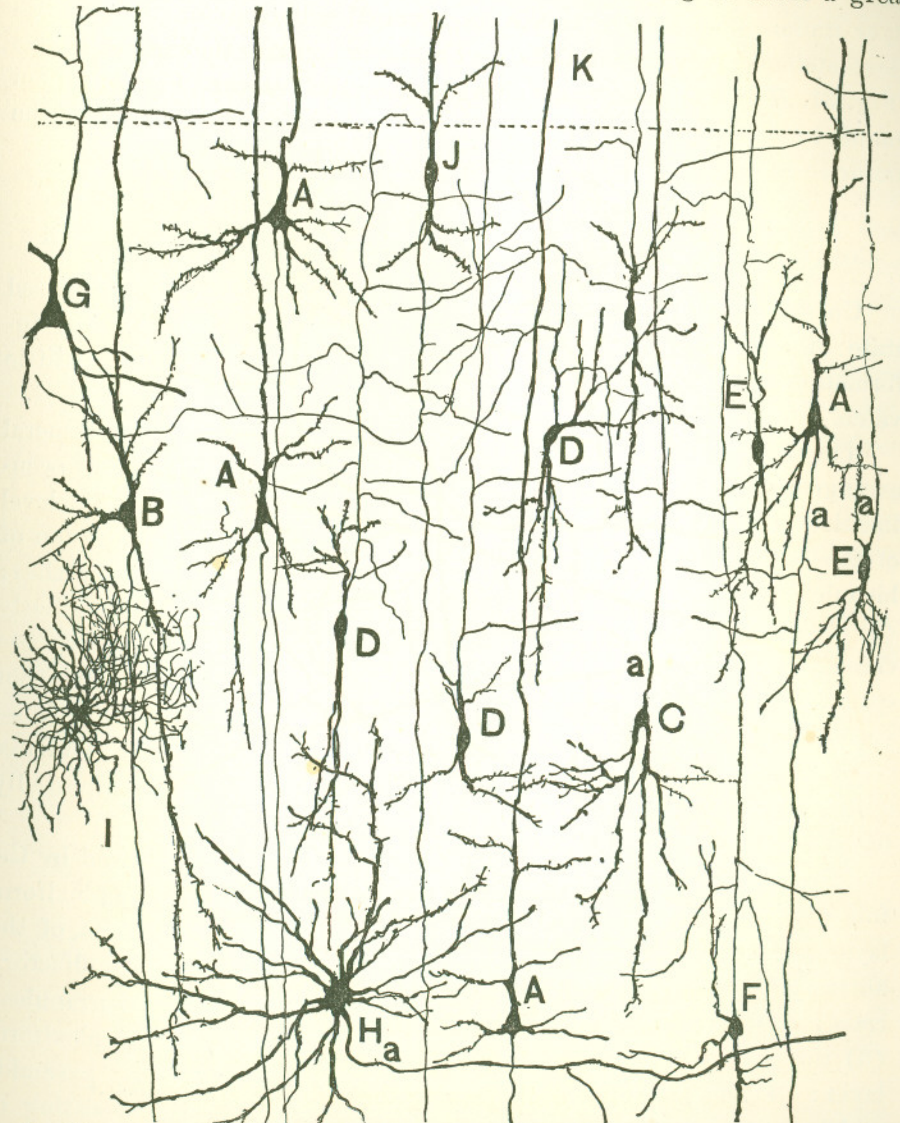


FIG. 31.—Principal types of polymorphic cells from motor cortex of infant aged 20 days. *A*, *B*, cells with long axons extending to white matter; *C*, *D*, *E*, fusiform cells with ascending axon; *H*, giant stellate cell.

number of branches. Some of these axons seem to end in the deep layer of giant pyramids, but others appear to pass beyond this. Finally, there is no lack of arachniform cells (Fig. 31, *I*), cells with short axon of the sensory type of Golgi, whose axons form terminal arborizations in the layer under consideration. I may add that I have found in two cases giant stellate cells with heavy horizontal axon which gives off collaterals (Fig. 31, *H*). I do not know the ultimate fate of this process and am unable to say whether these scattering cells form a constant feature of the motor cortex.

CORTEX OF ACOUSTIC, OLFACTORY, AND ASSOCIATIONAL AREAS.

Unfortunately, my own researches are not as yet in a very advanced state in regard to these important cortical centres. So that any information that I can give must necessarily be fragmentary and of little value.

The acoustic resembles exactly the motor cortex as to general arrangement of cells and layers, but differs from it in a few peculiarities: (1) by the fineness of the fibres forming the plexus at the level of the layer of granules or small stellate cells; (2) in the profusion of bipanicled cells with their very delicate and complicated neuritic brushes; (3) above all, by the presence of certain special cells scattered irregularly through the entire thickness of the cortex. The very large axon of these special cells extends in a horizontal or oblique direction, but I have not yet been able to determine exactly its manner of termination. These large cells are fusiform and lie horizontally. From their polar dendrites spring a number of fine ascending branches, which subdivide repeatedly but do not extend up as far as the plexiform layer.

The olfactory cortex, that of the limbic lobe, is characterized by the following peculiarities: (1) the enormous development of the plexiform layer and the presence in it, in addition to its usual structures, of the antero-posterior fibres that come from the external root of the olfactory tract; (2) the absence of the layers of small pyramids and granules; (3) the presence of certain large horizontal cells below the plexiform layer; (4) the peculiar form of the medium- and large-sized pyramids which emit from the deep end of the cell body a brush consisting of numerous much subdivided dendrites; (5) above all, the fact that the sensory plexus, *i.e.* the fibres which come from the olfactory bulb, makes its terminal arborization exclusively in the plexiform layer and in the most superficial portion of that layer, corresponding to that of the small

pyramids. This significant fact, brought to light by the studies of Calleja, shows us that the sensory fibres do not end in the same level of the cortex in all regions. Hence, the layer specialized to serve as substratum for the phenomena of sensation may change its position in different sensory areas.

Our task is now drawing to its close. My work upon the topographical structure of the cortex has been fragmentary and leaves much to be desired. Many things, in fact, are still undiscovered. But, despite the very incomplete state of my researches and the narrow limits of the field they cover, I may draw a few anatomico-physiological conclusions, of which the chief are the following: —

And first, as to the hierarchy of centres in the cortex of the human brain, comparing it with the mammalian brain, we may call to mind that, while it does not contain wholly new elements, it presents very distinctive characteristics, to wit: —

1. The enormous development of the horizontal cells of the plexiform layer and the considerable length of their so-called tangential fibres.

2. The great abundance of cells with short axons scattered throughout the whole cortex, cells which form special varieties by reason of differences in their forms and the directions of their axons.

3. The presence of cells with short axons, very slender (bipanicled spider cells), with terminal arborizations whose delicacy is not approached by anything found in any animal.

4. The considerable development of basilar dendrites of the pyramidal cells.

5. The presence among the mid-layers of the cortex of a formation of so-called granular cells, a kind of focus occupied by enormous numbers of pyramids with short axons descending, arched, and ascending. This granular formation is present in gyrencephalous mammals, but in them it is very poor in cells with short axons and in small pyramids. In the smooth-brained animals it is almost wholly lacking.

The human cortex has evolved, accordingly, along three different lines: by multiplying cells with long axons and, above all, those with short axons; by decreasing the volume of cells and the diameter of certain fibres in order to make possible within the limits of space a delicate and greatly improved organization; finally, by varying and infinitely complicating the external morphology of the nerve elements, undoubtedly with the purpose of multiplying, in correspondence with their complexity, functional associations of all kinds.

As to differences and analogies in regional structure, the following propositions may be regarded as established: —

1. The sensory as well as the so-called associational areas are made up by a combination of two orders of structural factors. The first order consists of common factors, which show very little modification. They are represented by the plexiform layers and the layers of pyramidal and polymorphic cells. The second order comprises special factors, structures peculiar to each cortical area. Their chief anatomical feature resides especially in the granular layer and is related mainly to the presence of particular centripetal fibres and of special types of cells with long axons (stellate cells of different kinds).

2. It seems probable that the common factors perform functions of a general order concerned, possibly, with ideas of representations of all kinds of movements related to the special sensations of which the cortical region is the seat. It seems also probable that the special anatomical factors of the sensory areas perform the function of elaborating specific sensations (sensation of seeing, hearing, etc.) and also of conveying sensory residues to the so-called association centres, where they may be transformed into latent images.

3. Each sensory cortical centre receives a special category of nerve fibres (fibres of central sensory tracts). Their cells of origin, as has been shown by the researches of v. Monakow, Flechsig, v. Bechterew, and many others, reside in the particular nuclei of the medulla, corpora quadrigemina, and optic thalami. It is precisely the presence of these sensory fibres of the second order that constitutes the prime anatomical characteristic of the centres of sensation or projection.

4. The absence of these sensory fibres, which come from the corona radiata, may be used in all mammals to distinguish the so-called association centres. These centres, which exist even in the mouse, also have a nerve fibre plexus distributed among their median layers (layer of granules in the association areas in man). The fibres, however, which constitute them are very fine and appear to come from sensory centres of the brain. Possibly the cells about which these sensorio-ideational fibres terminate represent the substratum or, at any rate, the first link in the chain of nerve elements whose function is the representation of ideas.

5. Since we have seen that each afferent fibre in the sensory cortex comes into contact with an extraordinary number of nerve cells apparently scattered without any order, we must suspect that these relations conform to the preconceived design of a well-determined and constant organization.

As, at present, it seems to be impossible to discover these relations, we may surmise that each sensory fibre comes into contact, directly or through other cells, solely with those pyramids whose stimulation is necessary in order to effect, after the manner of the reflex arc, movements coördinated and intentional. We may also surmise (supposing that the stellate cells of the tactile and visual cortex form the link between the sensory and ideational centres) that each sensory afferent fibre, bringing a unit of sensation (the impression received by a cone of the retina or by the terminal arborization of any peripheral nerve fibre), enters into relation exclusively with the group of nerve cells entrusted with the function of conveying this impression to a particular point in the associational cortex.

Many other hypotheses are possible, but I must conclude for fear of tiring your kind and sympathetic attention and exhausting your patience. I fear that I have already made too free use of hypotheses and have pretended to fill the gaps of possible observations with arbitrary suppositions.

It is a rule of wisdom, and of nice scientific prudence as well, not to theorize before completing the observation of facts. But who is so master of himself as to be able to wait calmly in the midst of darkness until the break of dawn? Who can tarry prudently until the epoch of the perfection of truth (unhappily as yet very far off) shall come? Such impatience may find its justification in the shortness of human life and also in the supreme necessity of dominating, as soon as possible, the phenomena of the external and internal worlds. But reality is infinite and our intelligence finite. Nature and especially the phenomena of life show us everywhere complications, which we pretend to remove by the false mirage of our simple formulæ, heedless of the fact that the simplicity is not in nature but in ourselves.

It is this limitation of our faculties that impels us continually to forge simple hypotheses made to fit, by mutilating it, the infinite universe into the narrow mould of the human skull, — and this, despite the warnings of experience, which daily calls to our minds the weakness, the childishness, and the extreme mutability of our theories. But this is a matter of fate, unavoidable because the brain is only a savings-bank machine for picking and choosing among external realities. It cannot preserve impressions of the external world except by continually simplifying them, by interrupting their serial and continuous flow, and by ignoring all those whose intensities are too great or too small.

I cannot conclude this, my third and last lecture, without a word of tribute to this great people of North America,—the home of freedom and tolerance,—this daring race whose positive and practical intelligence, entirely freed from the heavy burdens of tradition and the prejudices of the schools, which weigh still so heavily on the minds of Europe, seems to be wonderfully endowed to triumph in the arena of scientific research, as it has many times triumphed in the great struggles of industrial and commercial competition.