ON THE MOTOR CORTEX.

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The doctrine of cerebral localization from its most shadowy beginnings is perhaps a century and a quarter old, although in its present form as a demonstrated postulate of science it numbers but the years of a single generation. Throughout the nineteenth century, philosophers, clinicians, and brain physiologists have followed one another in the occupation of this most fascinating question, and have contributed each their part to its final resolution, a consummation still far distant. It has been approached from five main view-points, in order of their antiquity, as follows:

- (1) Speculative,
- (2) Clinico-pathologic,
- (3) Physiologic,
- (4) Anatomic,
- (5) Embryologic.

As mythology precedes history so phrenology came before rational cerebral physiology. The founders and chief exponents of this system were Gall and his disciple, Spurzheim, whose work embraces the closing years of the eighteenth century and the beginning of the nineteenth. Although based in the main upon the observation of accidents and coincidences, and built out by a tendency to *reading in*, the labors of these philosophers have also considerable clinical value and may be said to have opened the field in which was to be explored the modern question of brain centers. Two tenets of Gall's teaching have largely influenced the course of subsequent investigation and express in general present accepted belief, namely, (1) the intimate union between psychology and brain physiology, and (2) the essential principle—that specific functions reside in determinate areas in which they are *innate*. Two dozen or more such centers Gall

described—each presiding over a separate quality or operation of the mind.¹ It is noteworthy that a hundred years later, at the beginning of the twentieth century, a new defender² of phrenology should arise, whose deductions are in many respects more remarkable than those of the master.

Broca and Hughlings Jackson stand at the beginning of the clinical method. The first observations were in connection with speech disturbances, and even before Broca, Gall and others had noted that defects in articulation were associated with circumscribed lesions of the brain, particularly of the frontal region. It remained, however, for Broca (1863) to show that in right-handed individuals the part of the brain directly connected with motor speech is the base of the third left frontal convolution (Broca's center). This was the first step. Six years later Jackson contributed his classical work on Cortical Epilepsy. His statements are the more remarkable from the fact to which Hitzig³ refers in his Hughlings Jackson lecture, that the observers of his time still entertained the misconception derived from the teaching of Flourens that the motor centers were situated exclusively in the corpus striatum. Jackson started with the postulate that the grey matter and it alone has the power of initiating movements. In his *study of convulsions* he describes the onset and course of the partial unilateral seizures which characterize the condition since called "Jacksonian Epilepsy." "When a fit begins in the hand," he wrote, "it goes *up* the arm and *down* the leg. Now patients who have fits beginning in the foot tell me that the spasm goes *up* the leg and *down* the arm." Here are the first definite suggestions of separate cortical areas representing various muscle groups, the successive involvement of which by contiguity determines the march of symptoms in the Jacksonian fit, and whose existence was soon so amply confirmed by physiological research.

In 1870 appeared the pioneer work of Hitzig and Fritsch. These observers by means of galvanic stimulation of the dog's

¹ Gall: *Sur les Fonctions du Cerveau et sur celles de chaque de ses Parties*, 1825.

² Hollander: *The Mental Functions of the Brain*, 1901.

³ *Hughlings Jackson and the Cortical Centers in the Light of Physiological Research*. Brain, Winter, 1900.

cortex, confirmed the conclusions of Jackson and established beyond dispute the existence of *motor centers* in the brain. "Apart from a few empirical generalizations and brilliant hypotheses," Ferrier⁴ remarks, "the doctrine of cerebral localization first entered on the stage of demonstration and prediction with the experimental researches begun by Fritsch and Hitzig in 1870." The motor area as defined by Hitzig was embraced in rather wide limits. In 1874 he wrote, "A considerable portion of the cerebral hemispheres, one may say, nearly a half, is directly related to muscular movements, while the remainder evidently has no connection with them—at least not directly." He believed that the Rolandic area was a pure motor zone, in the sense that here arose the actual impulses which found direct expression in muscular movements, at the same time agreeing with Jackson that it was not a pure motor zone in the sense that here were represented in close juxtaposition centers for incoming sensory and outgoing motor impulses. According to his recent statement, this area is the seat of *muscle consciousness*, the place of the "apperceptive working up" of sensory impressions into motor images. The central elements for the innervation of a given muscle group, are in general, he believes, distributed over the whole motor cortex, being more closely collected in only a few points—the areas of maximum representation. With the precentral convolution he associates the origin of voluntary movements pre-eminently.⁵

Following Hitzig, many observers have attacked the question of localization from the standpoint of animal experiment—Ferrier (1873), Munk, Schiff, Horsley and Beevor, Goltz, Bastian, Bianchi, Sherrington and Grünbaum (1901), and others. Their deductions have by no means all harmonized, being indeed often antagonistic on essential points. They have, however, stimulated investigation along more conservative lines, serving as checks upon speculation, and the original premise of Hitzig has been abundantly established, namely, that certain parts of the cortex are intimately associated with motor phenomena, while

⁴ *Cortical Localisation in its Practical Relations.* Brain, July, 1889.

⁵ Hughlings Jackson Lecture, cit. supra; v. also Neurol. Centralb., 16 Nov., 1901, and Centralb. f. Nervenheilk. u. Psychiatrie, Dec., 1901.

the remaining parts have no such direct relation. Moreover, these areas have been defined within fairly accurate limits, including the representation for the various muscles and muscle groups.

No other worker in this field has excited so much controversy, often such violent opposition, or has achieved more brilliant results than Flechsig. From observations on the time of myelinization of the various tracts in the central nervous system, Flechsig¹ divides cortical areas into two great groups, (1) sensory (projection) centers, and (2) association centers.

Under the term "Körperfühlsphäre" (Munk used this term to indicate the Rolandic zone), he includes all those regions in which terminate sensory tracts carrying impulses from skin, muscles, joints and organs (the special sensory areas, cuneus, first temporal and uncinate gyrus being excluded). This extended region of general sensibility comprises the central convolutions, base of the first frontal, the paracentral lobule, and the entire limbic lobe (callosal gyrus and hippocampus), all of which show advanced myelinization at birth. It is further expanded by another system, including the pole of the first frontal and the bases of the second and third frontal, in which myeline appears during the first months of independent existence. The fibres which make up this wide distribution represent the upward continuations of the posterior column fibres of the cord, interrupted in the lateral nucleus of the optic thalamus, and all approximated in the *carrefour sensitif* of Charcot, where myelinization can be seen at a period when all the remainder of the internal capsule in front, which is to be occupied by the pyramidal tract, remains unstained. By the term "Tastsphäre," Flechsig distinguishes that part of the territory of general sensibility which is comprised in the Rolandic zone. It represents the earliest of his myelogenetic systems and constitutes the center *par excellence* for tactile, kinæsthetic and stereognostic sensibility. The postcentral convolution, he maintains, is predominantly sensory, receiving the terminations of the posterior

¹ Flechsig, Neurol. Centralbl., No. 19, 1894. *Gehirn und Seele*, 1896. *Die Localisation d. geistigen Vorgänge insbesondere d. Sinnesempfindungen des Menschen*, 1896.

column fibres, while the precentral is predominantly motor, containing the cells of origin of the pyramidal tracts.⁷ To this point there will be occasion to refer hereafter. Roughly, one-third of the cortical surface Flechsig showed to be thus directly connected with the periphery by means of projection fibres, and representing the primordial myelogenetic areas. These are distributed among four primary centers in order of development as follows: (1) Tastsphäre (somæsthetic area, motor zone), embracing the central convolutions; (2) olfactory area (possibly also including taste), hippocampus and uncus; (3) visual area, occipital lobe, calcarine fissure; (4) auditory area, first temporal convolution, especially that part which is concealed in the fossa of Sylvius.

The remaining two-thirds of the cortex show no myelinization at birth and remain relatively poor in projection fibres. They make up the association centers, the seat of the intelligence according to Flechsig, which by their marked development in the human species, differentiate man from the lower animals. Three such centers are described: (1) Anterior, including a large portion of the prefrontal lobe, the seat of the "superior psychism" of the Italians; (2) middle or insular association area, the converging center for the motor and sensory tracts concerned in language; (3) posterior, the largest of the three, extending over parts of the parietal, occipital and temporal lobes, and constituting the center for visual and auditory word memories.

To discuss the theory of Flechsig or consider the criticisms of his work, would leave no time for other matters.⁸ His original conception of projection and association centers gave a distinctly new view of cerebral physiology, and in general terms has been accepted by the majority of observers, although few are able to follow him in his ultimate deductions. Munk⁹ rejects entirely the theory of sensory and association or thought

⁷ *Developmental (myelogenetic) Localisation of the Cerebral Cortex in the Human Subject*. Lancet, Oct. 19, 1901.

⁸ V. Centralbl. f. Nervenheilk. u. Psychiatrie, Oct., 1896. Also a series of polemics between Hitzig and Flechsig, *Nevraxe*, 1900, I, 3; II, 1; 1901, I, 2.

⁹ Ref. Neurol. Centralbl., März 1, 1902.

centers. Vogt,¹⁰ a former pupil of Flechsig, was one of the first to raise his voice in opposition. "En construisant sa théorie," he declares, "Flechsig n'a pas suffisamment étudié ses coupes." It is doubtless true that Flechsig has overestimated the value of the myelinization method in the delimitation of cortical centers; and one can imagine of what the distinguished professor at Halle was thinking when he observed that the two requisite qualifications in scientific work were "keenness of observation and curbing the imagination." Flechsig's brain maps are undergoing frequent alteration and one must always be under the fear that one has not the latest edition.

It remains to speak of the histologic method and the service it has rendered in the differentiation of functionally separate cortical areas. Meynert¹¹ was the first to describe the minute anatomy of the cortex, dividing it into a series of layers, each possessing individual characteristics. He did not, however, recognize the structural differences which various convolutions present, and his description may be regarded as applicable in general to the association zones. According to Meynert, the cortex may be separated into five distinct laminæ: (1) A narrow subpial layer containing few small cells; (2) layer of numerous small cells closely crowded together; (3) layer of large pyramidal cells; (4) layer of small irregular cells (granular zone of the authors); (5) layer of spindle cells.

Betz,¹² in 1881, first pointed out the essential characteristic which distinguishes motor from sensory regions, namely, the presence of extremely large pyramidal cells in the neighborhood of Meynert's fourth layer. These cells reach their most colossal dimensions in the paracentral lobule, and were named by Betz *Riesenpyramiden* or giant cells. In recognizing a sensory and a motor cortex, Betz drew an analogy from the functional arrangement in the cord and argued that the same arrangement held for the brain, there being an anterior or motor pole and a posterior or sensory pole.

Hammarberg,¹³ in 1895, gave a detailed description of the

¹⁰ Jour. d. Physiol. et d. Path. Gén., juillet, 1900.

¹¹ Stricker's Handbuch d. Gewebelehre, 1871.

¹² Ueber die feinere Structur der menschlichen Gehirnrinde. Centralbl. f. d. med. Wissensch., 1881, Nr. 11-13.

¹³ Untersuchungen über d. norm. Anat. der Hirnrinde, 1895.

motor and sensory types of cortex and called attention to the presence of Betz's cells in the former, and especially to the fact that here also the cells of the granular zone (Meynert's fourth layer) are conspicuously few or absent. Hammarberg describes six layers in the grey matter: (1) Molecular layer, (2) small pyramidal cells, (3) medium and large pyramidal cells, (4) granular layer, (5) Betz's cells and medium pyramidal cells, (6) spindle cells.

The most significant work in cortical histology is that which has been done by S. Ramón y Cajal since 1890. In that year from observations on the cortices of small mammals this author¹⁴ described four essential laminæ: (1) Molecular, (2) small pyramidal cells, (3) large pyramidal cells, (4) polymorphous cells. In his monograph on the motor cortex in man (1900) Cajal¹⁵ enumerates eight layers: (1) Plexiform or molecular layer, (2) small pyramidal cells, (3) medium pyramidal cells, (4) external zone of large pyramidal cells, (5) granular zone (Meynert's fourth layer) containing small irregular and stellate cells and small pyramidal cells, (6) Betz's cells—ganglionic cells of Bevan Lewis, (7) polymorphous, triangular, and medium pyramidal cells, (8) spindle cells.

Cajal agrees with Flechsig in distinguishing sensory from association centers; he does not, however, insist upon the absence of projection fibres from the latter as their characteristic point of difference. On the other hand, he describes in the sensory areas a specific terminal plexus of centripetal fibres ending, in the Rolandic area, in the neighborhood of the medium pyramidal cells.

It has been mentioned that Flechsig recognized a real difference in function between the precentral and postcentral convolutions, pointing out as well structural unlikeness. Hammarberg was of the opinion that in the upper part of the motor zone, the convolutions separated by the fissure of Rolando were histologically similar. Cajal has demonstrated that on the contrary the postcentral gyrus is of practically uniform structure

¹⁴ *Textura de las circunvoluciones cerebrales en los maníferos inferiores*. Barcelona, 1890.

¹⁵ *Studien über die Hirnrinde des Menschen,—Die Bewegungsrinde*, übersetzt von Dr. J. Bressler, Leipzig, 1900.

throughout, which is essentially different from that of its neighbor in front. The specific sensory end plexus which Cajal describes is found in the precentral but not in the postcentral convolution, which also in other respects resembles the association areas. The differential characters of these two convolutions mentioned by Cajal will be discussed later in connection with our own observations. Thus far Cajal has considered minutely three cortical centers, the occipital, Rolandic, and temporal convolutions, discovering in each peculiarities of structure which seem specifically adapted to their individual function, and by which they can be recognized and distinguished microscopically."

Such in brief are the epochs in the history of cortical localization and the methods by which it is being worked out. Flechsig is perhaps its extreme advocate. He does not allow the possibility of functional substitution but holds to the doctrine of specific localization of function, the inevitable expression of inherent regional differences in structure. From the first this teaching has had its opponents among both physiologists and anatomists. The deductions of Gall and his predecessors suffered severely from the position taken by Flourens," who taught that the theory of functional localities in the brain was untenable and that all parts of the cortex had precisely the same significance. The views of Flourens found acceptance with many observers and cast a cloud of skepticism over the findings of regional brain physiology which endured for many years. The chief opponent of the work of Hitzig and Ferrier was Goltz. This investigator declared as a result of extirpation experiments on the dog's cortex that the effect of a lesion depends upon the *amount* of cerebral substance which is involved rather than its *location*. Goltz removed brain areas by means of the "flushing out" method devised by himself, and which Hitzig holds to be of little value as a means of determining the functional value of definite localities, inasmuch as it cannot be said to produce strictly local lesions. Goltz' work showed the phenomena of consciousness were the result of functioning of the entire cerebral cortex, without however invalidating the fundamental conception of anatomic localization.

¹⁰ *Die Sehrinde*, 1899; *Die Bewegungsrinde*, 1900; *Die Hörrinde*, 1902; übersetzt von Bressler.

¹¹ *Examen de la Phrenologie*, 1842.

Loeb¹⁸ strongly supports the views of Goltz, and lifts up his voice against the standpoints of Hitzig on the motor centers, of Munk on the visual centers, and of Flechsig on the association centers. He is inclined to admit an anatomical localization in the cortex "to a certain extent," and yet he asserts that "the only specific function of the brain, or certain parts of it, which we have been able to find is the activity of associative memory."

Psychic localization is explicitly denied. Regarding the belief of many observers that the higher intellectual faculties have their seat primarily in the frontal lobes, Loeb remarks, "I have repeatedly removed both frontal lobes in dogs. It was impossible to notice the slightest difference in the mental functions of the dog. There is perhaps no operation which is so harmless for a dog as the removal of the frontal lobes."¹⁹ In the same chapter the author says, "A dog that has lost the anterior halves of both cerebral hemispheres has a tendency to run with its head bent down. A dog which has lost the posterior halves of both hemispheres shows the opposite tendency. It moves very little and its head is carried high in the air; while dogs after the loss of the anterior halves of the cerebral hemisphere often become irritable and ugly; dogs which lose the occipital halves of both hemispheres invariably become good-natured and harmless."²⁰ To one not acquainted with the author's technique these statements are at least confusing. Moreover it is difficult to understand why psychic localization in man should be unconditionally denied as a result of experiments upon dogs. Bianchi from extirpation of the frontal lobes in *monkeys* comes to an opposite conclusion from that of Loeb with regard to the seat of intellectual activity. The results of the enormous work of Flechsig on the development of the *human* cortex Loeb dismisses with the remark, "I have removed the cortex of Flechsig's 'centers of association' in dogs without having noticed anything that justifies Flechsig's hypothesis." What Flechsig's hypothesis is concerning centers of association *in dogs* is not clear.

The view-point of histologic differences Loeb holds to be of little value in the differentiation of brain functions. Kölliker

¹⁸ *Physiology of the Brain*, 1902.

¹⁹ Loeb, loc. cit., p. 257.

²⁰ Loc. cit., p. 264.

also regards the structural dissimilarities of various cortical areas to be of little significance.

It has been said that Flourens located the motor centers exclusively in the corpora striata. This erroneous view has been championed by Luciani and Tamburini.

The cortical areas which are now recognized to be definitely connected with voluntary movements occupy the region of the fissure of Rolando but have no fixed or constant boundaries. In the lower vertebrates they cover a relatively wider extent of brain surface than in the primates and man.²¹ The sulci do not mark the boundaries of functional zones as Schäfer²² pointed out.

Charcot and Pitres²³ from clinical observation of a hundred and eighty-five patients with various forms of paralysis, together with post-mortem section, concluded that the motor zone comprised the *ascending frontal, ascending parietal and paracentral gyri*, the orbital, prefrontal, occipital, superior and inferior parietal and temporo-sphenoidal lobes being non-motor.

According to Barker²⁴ the motor area is made up of the *anterior and posterior central, the bases of the first, second and third frontal, and the paracentral*, corresponding to the Körperfühlsphäre of Munk and the Tastsphäre of Flechsig.

Obersteiner²⁵ reckons the *anterior and posterior central, paracentral, base of the third frontal and the anterior portion of the superior parietal* as belonging to the motor area. Text-books in general figure both central convolutions as representing the centers for voluntary movements.

In 1887 Beevor and Horsley²⁶ suggested that the precentral convolution was much more definitely concerned in motor phenomena than the postcentral. This view has found increasing favor. Tschermak²⁷ experimenting upon anthropoid apes finds

²¹ Cf. the original statement of Hitzig regarding the dimensions of the motor cortex. Also the findings of Beevor and Horsley and Sherrington and Grünbaum in apes and monkeys.

²² Festschrift zu Karl Ludwig, Leipzig, 1887.

²³ From Rev. de Méd., 1883. Ref. Brain, VII, p. 270.

²⁴ The Nervous System, 1899.

²⁵ Nervöse Centralorgane, 1901.

²⁶ Phil. Trans. Royal Society, CLXXVIII.

²⁷ Congress of Physiologists, Turin, 1901.

that only the precentral convolution gives unquestionable motor responses. Especially important is the work of Sherrington and Grünbaum.²⁸ These investigators experimented upon all known species of anthropoid apes, using the galvanic current for stimulating the cortex. Most of their observations were made upon the chimpanzee. As a result of their experiments they draw the following conclusions regarding the motor cortex.

The motor area includes the entire length of the precentral convolution and usually the whole of its width. It extends to the bottom of the fissure of Rolando occupying its anterior wall and in some places its floor, occasionally even reaching to the deeper part of its posterior wall. It never reaches the free surface of the postcentral gyrus. Anteriorly there is no fixed limit. It dips into the precentral sulcus to a varying extent or may exceed it. Superiorly the motor zone extends on to the mesial surface of the hemisphere but does not reach the calloso-marginal fissure. Confirmatory results were obtained by these experimenters with the orang, and also with the gorilla which stands nearest to man in the order of primates. They found further that destructive lesions in the precentral convolution were invariably followed by paralysis and descending degeneration, while similar or even larger lesions in the postcentral were followed by no such results.

Probst's²⁹ findings in the pathology of amyotrophic lateral sclerosis furnish additional evidence in favor of precentral localization. This is a disease of motor-conducting paths and can sometimes be traced from cortex to muscle. Probst noted severe involvement of the anterior central, the base of the first frontal and the lip of the second frontal convolutions while the postcentral remained nearly intact.

Cajal's³⁰ conclusions based upon histologic studies tally well with those of recent clinical, pathological and experimental work. The true motor area according to Cajal embraces the precentral convolution including its upper termination and part of the paracentral lobule, together with the bases of the first and

²⁸ *Localisation in the "Motor" Cerebral Cortex*. Brit. Med. Jour., Dec. 28, 1901.

²⁹ Arch. f. Psych., XXX.

³⁰ *Die Bewegungsrinde*, cit. supra.

second frontal convolutions. His belief that the fissure of Rolando separates "two motor areas of different structure if not of specific histology" recalls the hypothesis of Flechsig, before mentioned, of the functional diversity of these two regions.

THE MOTOR CORTEX.²¹—If a section be taken through both central convolutions at right angles to and including the fissure of Rolando several macroscopic peculiarities are noticed. The precentral considerably exceeds the postcentral in the area of its cross section and differs from it in contour, being roughly wedge-shaped with the base of the wedge inward, while the postcentral is wedge-shaped with the base of the wedge toward the surface. This difference is accounted for by the fact that the central sulcus does not sink perpendicularly into the medullary substance but dips backward in the depths, its bottom lying nearer the occipital pole than its mouth. Thus is formed an anterior convolution whose base is broadened at the expense of the posterior for the accommodation of the large number of coarse pyramidal fibres running through its white matter from the giant cells which are distributed along its summit and sides. Measurements across the summits of the two convolutions from the center of the central sulcus to the centers of the pre- and postcentral sulci do not show exaggerated differences in width; the precentral gyrus, however, in places where the two can be compared by reason of definite limiting sulci, usually exceeds the postcentral by one to three or four millimeters. Measurements deep in the fissure show more pronounced differences and when the bottom is reached the precentral convolution averages twice the breadth of the postcentral. In a formaline brain the average width of the precentral, from superior to inferior termination of the fissure of Rolando and including measurements across the width and base of the cross section, was found to be 15 mm., while the average width of the postcentral was 11 mm.

Corresponding with the inequality in width of the two convolutions is an equally marked dissimilarity in the thickness of the

²¹ The material used in these observations was obtained from a number of brains of which two were taken from patients who were the subjects of alienation. The pathological findings in these two cases are reported in the articles by Drs. Paton and Rusk and the one by Dr. Dunton. In neither case was any apparent diminution in number of cells or fibres observed.

grey cortex. This is less noticeable on the surface, although almost invariably the anterior cortex shows an appreciable excess in thickness, but as one follows the sulcus toward the white matter the difference becomes very conspicuous, reaching a maximum at about the mid-depth of the fissure. In this location the precentral cortex may present a thickness two or even three times that of the postcentral. As one turns around the bottom of the fissure to ascend the posterior wall the narrowing of the cortex is quite abrupt. The average width of the precentral cortex from measurements taken at mid-summit, mouth of the fissure, mid-depth, and bottom, from the fossa of Sylvius to the median fissure, was found to be 3.8 mm., the average width of the postcentral cortex being 2.8.

Even more striking than the naked-eye differences are those in the minute anatomy of the two convolutions at corresponding levels, and to these reference will be made after the type of motor cortex has been presented as a basis for comparison.

The motor zone extends from the Sylvian sulcus to the callosomarginal fissure. The cortex is widest in that part of this area which extends on to the mesial surface of the hemisphere in front of the termination of the Rolandic fissure. Here also the deep ganglion cells reach their greatest size—*Riesenpyramiden* of Betz. This region, which constitutes the anterior portion of the paracentral lobule, may therefore be taken as a type of pure motor cortex, and its description will apply with slight modifications to the entire zone, serving to differentiate it from specific sensory and association areas.

In a section from the anterior paracentral, hardened in alcohol and stained with Unna's polychrome methylene blue, the unaided eye recognizes in the cortex a series of darker and lighter streaks of varying width. Most superficial is the wide molecular layer showing a slightly darker and sharply defined edge owing to the presence here of the dense subpial glia network. Below the molecular layer which stains lightly on account of the few cellular elements which it contains is seen a narrow dark streak fairly well outlined, representing the closely packed zone of small pyramidal cells. Next succeeds a wide lighter area which gradually becomes darker as one approaches the interior, until about the mid-depth of the cortex is reached.

Here a moderately circumscribed dark zone is observed, the external layer of large pyramidal cells. The inner border of this zone is well marked, while externally it blends with the broad field of medium pyramidal cells, except here and there where a definite row of large pyramidal cells is found. Immediately below this level is a narrow band of relative clearing well marked off from the structures on either side, and which can be traced quite around the convolution. It represents the granular zone of the authors (Meynert's fourth layer), which in the motor areas is sparsely occupied, and becomes the more conspicuous from the fact that it is bounded above and below by well developed layers of large ganglion cells. The lowermost of these layers is the most characteristic feature of the paracentral cortex. It contains the giant cells of Betz which can be seen as a line of deeply stained points following the contour of the convolution, continuing uninterrupted over the superior border of the hemisphere into the precentral and first frontal gyri, and disappearing below in the calloso-marginal sulcus. The individual cells are plainly visible and their number can be approximated macroscopically. Below the line of Betz's cells a fine light streak can usually be discerned. It is explained by the relative scarcity of small elements in the immediate vicinity of the giant pyramidal cells. Finally, the undermost layers of the cortex appear as an evenly shaded zone blending somewhat with the slightly stained white substance on the summits of the convolutions, but better differentiated from it in the depths of the fissures where the cortex as a whole is considerably narrower and its composing elements more condensed.

Weigert preparations show the characteristic fibre picture of the motor zone. In these also the chief structural peculiarities are recognized with the naked eye. Just under the pia a dark line indicates the site of the tangential fibres which are particularly numerous in the paracentral lobule. Nearly the upper half of the cortex is occupied by a zone which takes up but little stain—supraradiary zone of Edinger—containing the specific end-plexus of exogenous fibres—*Schalt-plexus* of Cajal. This zone is limited below by a dark narrow band composed of horizontal fibres—Baillarger's outer stripe—below which the tissue takes a much deeper stain owing to the increasing number of

radial bundles of nerve fibres between which lies the interradiary network of Edinger. A little more than midway from Baillarger's outer stripe to the medullary substance a similar but less distinct concentric marking is visible, occupying the neighborhood of the giant pyramidal cells. This is Baillarger's inner stripe or the outer association band. The cortex is thus roughly divided into two nearly equal laminae, an outer faintly staining layer external to the superficial large pyramidal cells and an inner darker zone, the two being separated by the outer stripe of Baillarger.

The following description is based on the examination of sections stained with hematoxylin and eosin, Nissl's methylene blue, Unna's polychrome methylene blue, and by the Weigert-Pal method. For a more detailed histology, particularly with reference to dendritic branchings and the fate of the axis cylinder as revealed by the Golgi method, reference must be made to Cajal.

CELL DISTRIBUTION OF THE PARACENTRAL LOBULE.

Cellular elements are found in the cortex from the outermost to the innermost border, lying immediately beneath the pia-arachnoid and occurring between fibre bundles where cortex and medulla blend. In these extreme positions only neuroglia nuclei are seen, although the ganglion cells occupy nearly as wide a territory.

MOLECULAR LAYER.—This zone is characterized by the paucity of contained cells, particularly ganglion cells. Underlying the pia is seen a very narrow band staining a little more deeply than the remainder of the molecular layer and made up of glia network. It contains no nervous elements but numerous neuroglia nuclei, some of which lie on the free surface adjacent to the pia. Below this level ganglion cells are irregularly distributed. They vary greatly in size, the smallest being but slightly larger than the small neuroglia nuclei, while the largest types may be four or five times as large. Of the smallest forms no more can be seen than a vesicular nucleus with eccentric nucleolus, and partial or complete perinuclear chromatin ring, with a narrow wisp of protoplasm at one or more points. No processes can be followed and no Nissl bodies are to be seen.

Occasionally a fold in the nuclear membrane presents. Some of these minute forms with almost no visible protoplasm are with difficulty distinguished from neuroglia nuclei, which also vary somewhat in size and in depth of staining, the smaller being darker. Cajal mentions as differential points the larger size of the nucleus in the ganglion cell, the presence of the chromatin ring which he considers intranuclear, and the occurrence of a well-formed nucleolus. The glia nuclei, however, also contain nucleoli, sometimes a single large one, and they frequently present a dark contour. Morphologically it may be all but impossible to determine whether certain forms are glia or nerve cells. In a successful polychrome preparation the two varieties can usually be recognized by their staining reaction, the ganglion cells staining deep blue with a distinct purple tinge, while the neuroglia nuclei present a faint greenish cast; although this criterion does not serve in every instance, the difference is often striking when a nerve cell is closely surrounded by several glia nuclei, a relation which all types of nerve cell present at all levels in the cortex.

As the nerve cells of the molecular layer increase in size they decrease in numbers. The large forms are conspicuous but rare. They lie indifferently high or low in the layer, and one may now and then be seen in contact with the submeningeal glia zone. They possess a considerable cell body of irregular triangular, stellate, spindle, or rarely pyramidal form, whose branching processes can occasionally be followed two or three cell-diameters. The nucleus usually occupies the greater portion of the cell but not always, and chromophilic particles in the surrounding protoplasm are plainly visible. Among the larger elements a spindle-shaped cell here and there occurs, sometimes with its long axis parallel with the surface of the convolution and again at a right or oblique angle with it. Some of these forms evidently correspond with the autochthonous horizontal cells of Cajal.

True pyramidal cells are not found in the molecular zone, and although an occasional large cell assumes this form, the characteristic descending axis-cylinder of the pyramidal cell with its achromatic cone of origin cannot be demonstrated. Lipochrome is not observed in the cells of this layer.

Sections stained after the Weigert-Pal method show a rich tangential system whose fibres present considerable variation in size. The finer strands run horizontally or obliquely, forming a loose network but tend more and more to assume a course parallel with the surface as the higher levels are reached. The calibre of these fibres varies somewhat, those representing the terminal branches of pyramidal cells in proportion to the distance of their underlying cells of origin.

The most conspicuous elements in the tangential system are the coarse varicose fibres which stretch across the field and can in some instances be followed for several millimeters without appreciable reduction in thickness. Their size is usually out of all proportion to that of the various branches of exogenous fibres, and they belong, according to Cajal, to the specific horizontal cells of the plexiform layer, first described by him in small mammals and by Retzius in man. Occasionally a thick ascending fibre is seen turning into the molecular layer which suggests the interpretation of Kölliker and others that the coarse horizontal fibres have their origin in the lower levels of the cortex or in the white matter. Cajal believes that they represent a system of superficial association fibres, "*nicht nur zwischen getrennten Zonen einer, sondern auch benachbarter Windungen,*" and their unusual length seems to justify this view. Besides the autochthonous fibres and the terminal ramifications of the underlying pyramidal cells, the plexiform layer contains the end processes of cells with short axis cylinders from the upper layers of the cortex, the axone terminations of Martinotti's cells and fibres rising from the medullary substance.

SECOND LAYER—SMALL PYRAMIDAL CELLS.—This well circumscribed zone contrasts strongly with the one just described. The cells are numerous and closely packed, and the separating line between the two layers can be sharply drawn. On the medullary side the line of demarkation is much less distinct, the pyramidal cells increasing in size and the smaller cells decreasing in number as the third layer is entered. In thickness the second layer nearly corresponds with the first, averaging about 0.2 mm.

In comparing the cell elements of the two laminæ one finds that the smallest forms in the second approximate in size the largest of the first, and that whereas in the molecular layer the large

types are very rare, the small cells of the second layer which somewhat resemble them are extremely numerous, especially in the upper part where the two layers meet. There is, moreover, the added type of neurone, the typical small pyramidal cell which characterizes the zone and which occurs most frequently in its lower levels. The second layer may therefore be divided into two, an upper characterized by an excess of small cells with insignificant cell body, and a lower in which larger forms predominate, particularly the pyramidal cell.

The small cells present a nucleus slightly larger than that of the glia cell, staining less deeply and showing the differential color reaction above mentioned. They possess a nuclear membrane which may contain a fold, with partial or complete chromophilic ring, a distinct nucleolus, and suggestions of a protoplasmic cell body with processes which however cannot be followed. Rarely a bipolar form with somewhat elongated nucleus is seen, lying with its long axis vertical or occasionally horizontal or oblique. The larger cells assume a variety of forms, although no more perhaps than are seen among the large cells of the fourth or sixth layer. Triangular, polygonal and irregularly rounded forms occur, and all stages of approach to the true pyramidal cell are met with.

The latter, scattered throughout the zone, are more numerous in the lower two-thirds and present all the essential characters which distinguish the giant cells of a lower level. They possess a roughly triangular cell-body containing a number of chromophilic particles, often a well-defined nuclear cap (Kernkappe), or a lateral clump of chromophilic elements (Schlüsselchen); a round or oval central or eccentric nucleus with membrane sometimes folded (Längsfalte), and nucleolus; a capital process, basal dendrites and descending axone with achromatic cone of origin. As compared with the giant cells, the nucleus is disproportionately large in the small pyramidal cells. Not infrequently the pyramidal cells are tilted at various angles even to 90 degrees, so that the cell appears to be lying on its side; very rarely an element appears with apical process descending and base uppermost. Now and then a small pyramidal cell seated in the upper margin of the second layer gives off a capital process which can be traced for some distance into the

molecular zone. The typical cell with protoplasm, rich in chromophilic particles, is relatively rare in comparison with the great number of triangular or polygonal cells of smaller or equal size in which but a few fine particles or an occasional chromatine clump can be demonstrated.

Fat pigment is now and then found in the small pyramidal cells.

THIRD LAYER—MEDIUM-SIZED PYRAMIDAL CELLS.—A noticeable thinning out of the cell elements marks the transition from the second to the third layer, coincidently with a progressive increase in size of the pyramidal forms which occur in the latter almost to the exclusion of the other types, although a few small irregular vertical fusiform cells are still met with. The width of this layer in the paracentral and motor area generally is its characteristic feature. It is the widest zone in the cortex, and the one whose greater development in the precentral convolution accounts chiefly for the marked difference in the depth of the grey matter between the two central gyri. The average width of the third layer in the paracentral is about a millimeter. As the lower levels of the zone are approached the pyramidal cells become larger and more widely separated from each other, the processes become more conspicuous both in number and size, and assume more and more the characteristic distribution. The apical dendrite can sometimes be followed five or six cell-diameters in good polychrome specimens. One or more neuroglia nuclei are frequently found in the pericellular space. It is among the middle-sized pyramidal cells, according to Cajal, that end the specific centripetal fibres of the sensori-motor area, forming a plexus which he suggests may form the substratum of touch, pain and temperature sensibility.

FOURTH LAYER—SUPERFICIAL LARGE PYRAMIDAL CELLS.—In those parts of the paracentral which exhibit a well developed sixth zone rich in giant cells, the fourth layer has an inconstant value, the two layers being in general in inverse proportion to each other in extent, cell content, and size of the individual elements. The stratum of superficial large pyramidal cells occupies a level somewhat above the mid-depth of the cortex. In places a definite row of large cells is visible contrasting well with the smaller forms of the layer above, while elsewhere they

gradually increase in size through the third and fourth zones and no line of separation can be drawn. The clear spaces are always larger in this region than higher in the cortex, owing to the greater extent of dendritic ramifications characteristic of the larger cells. Lipochrome is more commonly observed as the cells become larger. In appearance the fourth layer type closely resembles the Betz' cell of the sixth except that it is much smaller; indeed a superficial large cell of any considerable size is never seen in the same vertical section with Betz' cells. A common observation in the smaller pyramidal cells of all levels is to find the chromophilic substance clumped at one place, around the nucleus or at some point in the periphery of the cell, most often along the base especially in the vicinity of the axis-cylinder cone and the lateral basal dendrites. A considerable nuclear cap is frequently apparent.

FIFTH LAYER—GRANULAR ZONE.—In the anterior paracentral and precentral gyri this layer is poorly defined. On going through the cortex from the periphery toward the white substance one notices on reaching the fourth layer an irregularly distributed increase in the number of small cells which become more numerous as the level of this zone is passed. Between the superficial and deep pyramidal cells a considerable interval presents 0.2 mm. to 0.5 mm. or even more, in which several cell types occur, including occasional medium and large pyramidal cells. No sharp separating lines can be drawn, however; the boundaries of the fourth, fifth and sixth layers are indeterminate and overlap. Scattered widely therefore between the third and sixth layers, but more concentrated below the fourth, occur the so-called *granules* of the authors. They consist of minute pyramidal and spindle forms, but more characteristically of small irregularly rounded, oval or polygonal cells with insignificant cell body and poor in chromophilic substance, possessing usually only a perinuclear ring which may be incomplete or absent. The small pyramidal and granule cells of this layer correspond in appearance with those of the second. Cajal has shown that the granule cells possess short ascending axis cylinders, ending at various levels, some reaching the plexiform layer (Martinotti's cells), and others stopping at the second, third or fourth zone. He believes that they have a specific associative function and

concludes that the fifth or granule layer "ein intermediärer Bestandtheil der Hirnrinde ist, in welchem sich die Zellen mit kurzem Axencylinder d. h. die intracorticalen Associationszellen concentriren."²²

SIXTH LAYER—GIANT PYRAMIDAL CELLS.—The pyramidal cell is the predominating type throughout the grey substance. It attains its greatest size and complexity of structure in the sixth layer of the motor cortex. A more careful consideration has therefore been reserved for this specific element, the Betz cell of the paracentral lobule.

Our knowledge of the internal morphology of neurones has largely accumulated since the publication of Nissl's method of staining in 1885. This method distinguishes the chromophilic elements (Nissl bodies) from the achromatic fibrillar constituents of the cell, and until the appearance of the work of Apáthy on the conducting elements in 1897, formed the only basis for the determination of the finer ganglion cell pathology.

CHROMOPHILIC ELEMENTS.—During the developmental stage Nissl bodies are first seen as a few scattered deeply-staining clumps at the periphery of the cell, the body of which stains a lighter even blue (soluble chromophilic substance). Van Biervliet,²³ who has studied the evolution of the chromophilic substance in the anterior horn cells, states that the first definite Nissl bodies appear at the third month of intrauterine life. Their development is centripetal and at the fourth or fifth month the cell presents an appearance closely resembling that of the adult cell during well-marked axonal reaction, and which van Gehuchten therefore termed *physiologic chromolysis*.²⁴ The nucleus occu-

²² Cajal, loc. cit., p. 61.

²³ *La substance chromophile pendant le cours du développement de la cellule nerveuse*. Nevraxe, I, 1, 1900.

²⁴ The normal adult cells of Clarke's column show a characteristic central chromolysis suggesting that of the embryonic horn cell of the fourth month. That this is a normal condition in Clarke's cells was pointed out by Marinesco (Revue Neurol., Octobre 30, 1899). The fact that these cells are of later development than the anterior horn cells, appearing first at the fourth month (Obersteiner), when the latter exhibit the typical peripheral ring of chromophilic particles (Randschollenkranzbild), suggests the possibility that the cells of Clarke's column may afford an example of the persistence of an embryonic type in the adult. If the observation of

pies an excentric position and there is a central clear zone of soluble chromophilic substance in which Nissl bodies have not yet been laid down. At term the nucleus is central and Nissl bodies fill the cell, the faint blue background, which shows between them, indicating that the soluble substance has not been completely used up. In the normal cell of adults the ground substance can be nearly or entirely bleached, showing that the soluble chromophilic substance which is present during the entire embryologic stage disappears with the maturity of the cell. From these and other observations, notably the pathological changes occurring in the *distance-reaction*, Nissl, v. Gehuchten, Lugaro, Marinesco and the majority of authors have concluded that the chromophilic particles represent the reserve nutrient constituents of the cell. They are probably composed of nucleo-albumen.

Nissl resolves the chromophilic particles into masses of very fine granules and describes delicate filaments radiating from them. The masses are ragged in outline and in form and arrangement conform to the limiting conditions of the cell periphery or nucleus to which they may be adjacent. Thus along the borders of the cell they are elongated and disposed in more or less parallel rows, while toward the center the clumps become more rounded and compact and are distributed concentrically about the nucleus, the innermost forming the perinuclear ring which is separated from the nuclear membrane by a very slight but appreciable interval, the perinuclear space. A considerable aggregation of chromophilic elements is usually observed at some point of the nuclear periphery, most commonly perhaps at the top, forming a crescentic cap (*Kernkappe*). It may also occur at the base or one side, sometimes giving the nucleus an indented or reniform aspect. In the capital process and basal dendrites the stainable substance appears as elongated bands which can be followed as far as the processes are visible, becoming narrower and longer in proportion to the distance from the cell. A roughly triangular clump marks the place where a

Schacherl (*Obersteiner's Arbeiten*, VIII, 1902), that in embryos the bodies of Clarke's cells are completely occupied by Nissl bodies is correct, we have here a curious instance of the reverse order of development of two types of cell of different function.

process is given off from the cell body or where a bifurcation of a dendrite takes place (Verzweigungskegel, cone de remplissage of Benda, bifurcation cone of Nissl). The axis-cylinder and its cone of origin contain no chromophilic particles.

LIPOCHROME.—In the cortical cells, this is present as the light yellow variety in contradistinction to the dark brown pigment of the locus cæruleus and substantia nigra. It is a normal constituent of all types of nerve cell which have undergone a certain degree of functional activity, representing an end product of cell metabolism and derived, according to Marinesco, from broken-down Nissl bodies. Fat pigment is absent in the new born, appears in the spinal ganglion cells at the sixth year (Pilcz²²), in the anterior horn cells at the eighth year, and in the cortex somewhat later, increasing during the life of the individual. Marinesco states that the pyramidal cells do not show pigmentary degeneration before the twentieth year. That it occurs much earlier there can be no doubt, as can often be demonstrated in osmic acid preparations at about the beginning of the second decade (Obersteiner). Rosin²³ dates the first appearance of pigment at about puberty. We have observed it in the cortex of a negro girl of eleven who died following operation for Jacksonian epilepsy. Fatty metamorphosis is always associated with a local disappearance of the Nissl bodies. In sections stained with methylene-blue it shows first as a faint yellow sheen between the chromophilic particles which present perhaps but the slightest traces of disintegration. Soon, however, fragmentation takes place and a circumscribed clump of fat-pigment granules may be seen, lying in any part of the cell, preferably near the base and at a distance from the nucleus. In other instances a considerable degree of chromolysis may be present without the appearance of lipochrome, or it may develop late in a chromolytic area. There is doubtless a difference in the significance of these two processes. The first, which may be called primary pigmentation, represents possibly the normal local involution of the nutritive elements; the pigment appears early in the regressive change and does not show a tendency to marked

²² *Beitrag zur Lehre von der Pigmententwicklung in den Nervenzellen.* Obersteiner's Arbeiten, III, 1895.

²³ Virchow's Archives, 162; v. Neurol. Centralbl., Aug. 1, 1901, S. 712.

and rapid diffusion. In the other case, secondary pigmentation, the process is later and attacks the chromophile substance during functional activity, but when it has reached a stage where separation is no longer possible. Secondary pigmentation is then likely to be rapid and diffuse. Pigment is never seen in the nucleus, and this structure migrates to that portion of the cell where the Nissl bodies are best preserved and farthest from the breaking-down area, between which and the nucleus a dense compensatory clump of chromophilic elements is frequently seen skirting the nuclear membrane and apparently walling off the trophic center of the cell from the advancing destructive process.⁷⁷

ACHROMATIC SUBSTANCE.—This includes that portion of the cell-body which does not stain by Nissl's method. It contains at least two essential structures, (1) the conducting elements of Apáthy, primitive fibrils of Bethe, and (2) the unorganized supporting substance, trophoplasm of Marinesco.

The fibrillar structure of the ganglion cell, first recognized by Max Schultze in 1868, has become an almost universally accepted fact. By the methods of Apáthy, Donaggio, Bethe, the chromophilic substance of Nissl is left unstained while the achromatic substance takes up the color and its structure is more or less perfectly revealed. That fibrils may enter the cell by one of the processes and course independently through it without branching or anastomosis, to leave by another process or the axis-cylinder, is amply shown in Bethe's preparations. This author has also observed a centripetal fibril of a basal dendrite turn sharply around the point of bifurcation of the latter to become at once a centrifugal fibril without entering the cell-body at all. This occurrence has also been described by Vogt.⁷⁸ Nissl supports the view of Bethe that the primitive fibrils are anatomically independent of the ganglion cells, and run uninterrupted through them. On the other hand, Apáthy describes an intricate intracellular anastomosis of the entering fibrils which

⁷⁷ It is generally stated that pigment is observed in the various large types of nerve cells except the cells of Purkinje, in which it has not been found. Rusk (*Amer. Jour. Insanity*, July, 1902) has recently described traces of pigment seen by him in Purkinje's cells from a case of Huntington's chorea.

⁷⁸ *Centralbl. f. Nervenheilk. u. Psych.*, Dec., 1901.

suggests that conduction must in some way be altered or influenced as the fibrils pass through the cell-body. This view is shared by Marinesco, van Gehuchten, v. Lenhossék, Lugaro, Cajal, Donaggio and others. Donaggio²⁹ has recently given an account of a system of secondary fibrils shorter and finer than the primitive fibrils of Bethe and occurring between the meshes of the intracellular reticulum.

The methods of fibril staining are all very tedious and complicated and cannot be said as yet to have yielded constant results. The origin, intimate disposition, mutual relations and ultimate fate of the primary fibrils of the nervous system are still unsettled questions. It is thus an unfortunate fact that most of our information on the histology and pathology of the nerve-cell concerns itself with what is presumably the lesser important of the two prime constituents; the majority of our descriptions are based upon findings by the Nissl method or some similar process by which the nutritive elements are revealed, while those which have to do *par excellence* with nervous function, the conducting elements, remain entirely undiscerned.

Levi (1896) discovered a constituent of the trophoplasm which shows this substance to be the seat of marked chemical activity during function. By means of an acid fuchsin and methylene-green stain he found that during fatigue there was an excess of granules in the cell which took up the fuchsin, while during recuperation these granules decreased in number and were replaced by granules having an affinity for the methylene-green, the latter being greatly in excess during repose.

No limiting membrane has been demonstrated for the nerve-cell. The marginal portion, however, differs from the rest of the cell in its chemical reaction, is more resistant to maceration, according to Martinotti, and the Nissl bodies in this location Marinesco believes to have a greater endurance. The three cell-zones, peripheral, central, and perinuclear, undoubtedly possess peculiar characteristics, both chemical and histologic, and perhaps functional. They present peculiarities of structure as regards both Nissl bodies and fibrillar elements.

CANALICULAR SYSTEM.—Adamkiewicz was the first to de-

²⁹ Rivista Sper. di Fren., 1901, 27.

scribe intracellular spaces or canals. These he observed in the spinal ganglion cells and considered to be lymph spaces. Holmgren confirmed the views of Adamkiewicz and described the connections between the endocellular canals and the pericellular lymph space. Holmgren also observed processes of stellate glia cells entering the peripheral canals. Donaggio⁴ has lately studied the intracellular canaliculi. He describes a fine network of canals, taking often a wavy course, and maintaining a connection with the perinuclear lymph space into which he has seen two or three delicate canaliculi opening. Fragnito's⁵ view of the pluricellular origin of the ganglion cells accounts for the canals of Holmgren, as the spaces left between the approximated neuroblasts which go to make up the neurone.

THE PROCESSES of the giant pyramidal cells are particularly large and richly branched. They represent gradually narrowed off portions of cell protoplasm in contradistinction to the axis-cylinder which springs abruptly from its cone of origin situated at some point of the cell-base or occasionally on one of the large dendrites near the cell, and maintains a uniform calibre throughout, while the dendrites become progressively smaller from frequent subdivision. His (1889) taught that the neuraxon was the first process to develop in the neuroblast. Bechterew (1899), Paton⁶ (1900), Hatai⁷ (1902), showed that the dendrites and not the axis-cylinder process are the first to appear. The capital process constantly develops much earlier than the basal dendrites, and keeps its integrity for a considerably greater distance from the cell, the lateral processes usually dividing dichotomously. The constant difference in the time of development and in the mode of distribution of the two characteristic cell-processes, apical and basal, suggests an inequality in importance and dignity of function. The apical process appears early and is a more integral part of the cell. Its terminal ramifications are destined exclusively for the plexiform layer. The basal processes appear late and send their branches into the same layer in which the cell lies or to lower levels.

⁴ Riv. Sper. d. Fren., 1900, 26, p. 188.

⁵ Annal. di Nevrologia, 1900, XVIII, 6, p. 433.

⁶ *The Histogenesis of the Cellular Elements of the Cerebral Cortex.* Baltimore, 1900.

⁷ Jour. Comp. Neurol., June, 1902.

THE NUCLEUS of the large cells is regularly round or oval and centrally situated as distinguished from the eccentric nucleus of many of the smaller types. It possesses an enclosing membrane, a reticulo-granular structure and a central deeply-staining nucleolus, around which a narrow clear space can be demonstrated, the *perinucleolar* space. From this can usually be traced five or six light radiating lines, suggesting the *perinuclear* space and canaliculi of Donaggio. Chemically the periphery of the nucleolus differs from its interior, having an affinity for basic stains, while the central portion is acidophile (Levy). Within the nucleolus may be seen several darker points (endonucleoli of v. Lenhossék). Almost constantly the nucleolus exhibits one or several light areas (Obersteiner's nucleololi). There may be one central nucleololus or two or three irregularly disposed, usually rounded in outline. Occasionally one is observed on the limb of the nucleolus. In this location the nucleololus may be seen to exceed the limits of the nucleolus, lying partly within and partly without and bounded externally by an extremely fine dark line—the nucleololus thus presenting the appearance of a minute vesicle. The smaller pyramidal cells frequently show a conspicuous fold in the nuclear membrane (Längsfalte). This cannot be demonstrated in the giant cells. Nissl "calls attention to the constant appearance of the membrane fold in certain types of cells and its absence from others in the normal condition. "Auch unter pathologischen Verhältnissen wird man es niemals in solchen Zellen, die es in der Norm nicht zeigen, antreffen."

The giant pyramidal cells tend to arrange themselves in pairs, threes or small groups, the groups being separated by radial fibre bundles. Two or three cells are frequently disposed *en échelon* or superimposed one above the other. In external morphology they show considerable variation, the most constant difference being seen if one compares cells from the summits of the convolutions with those in the depths of the sulci. In the former situation the typical pyramidal form predominates, and the vertical axis constantly exceeds the horizontal, while in the sulci broad polygonal and polymorphous types are characteristic.

⁴⁴ Centralbl. f. Nervenheilk. u. Psych., 15 April, 1902, p. 255.

The other forms described, small and medium-sized pyramidal cells, granule cells and fusiform cells are also met with in the sixth layer.

SEVENTH LAYER—POLYMORPHOUS CELLS.—Below the level of the giant cells a narrow zone can often be seen in which there are relatively few stained elements, the space being occupied by dendritic ramifications. Below the clear area occur numerous smaller forms of the pyramidal cell, together with oval, triangular and polygonal varieties. In all of these, as in the smaller types universally, the nucleus usually occupies the greater part of the cell-body. Granules are occasionally seen. Especially numerous in this layer are the fusiform cells with ascending and descending protoplasmic processes. They vary considerably in size, the largest lying higher. The nucleus is often elongated, the nuclear membrane showing a fold parallel with the long axis of the cell. The course of the processes is sometimes oblique. Cajal has observed in this zone occasional large stellate cells with horizontal processes, which he concludes are to mediate long-distance association. Fat pigment is found in the cells of the seventh layer.

EIGHTH LAYER—SPINDLE CELLS.—The radial arrangement of cells which can in many places be traced through the cortex into the layer of small pyramidal cells becomes more conspicuous in the lower zones and is best shown in the spindle cell layer. While no sharp dividing line can be drawn between the seventh and eighth zones, in the former the cells are larger and more numerous and the triangular and polygonal forms predominate, while in the eighth layer the cells become progressively fewer as the white matter is approached, the intercellular spaces are wider, the cells are smaller, and spindle forms exceed all other types. Small triangular and stellate cells may still occasionally be seen. For a variable but considerable distance between the fibre bundles of the medullary substance, long narrow fusiform cells can be traced. The nucleus is elongated, the cell-body slight and without formed Nissl bodies.

In Weigert preparations, as one traces the fibres from below, it can be seen as soon as they are distinguishable above the densely-staining medullary zone that they assume three general directions, vertical, horizontal and oblique. The great mass of

coarse fibres from the centrum semi-ovale is collected into loose radial bundles which assume a straight course through the cortex and can be followed to the lower levels of the third layer, where they lose their myeline and are no longer visible. Between the radial bundles, and sometimes running with them, are finer strands which take different courses, oblique or horizontal, but which cannot be followed beyond the lower cortical levels. Coarse oblique fibres can also be seen emerging from the depths and running with unchanging course as far as the eighth or seventh zone. Horizontal fibres are present at all levels of the cortex, but are more thickly collected in two, occasionally three, transverse bands—the tangential system—and the outer (and inner) stripes of Baillarger. The tangential fibres of the molecular layer have already been referred to. They are especially numerous in the paracentral and precentral convolutions, owing to the large number of end branches from the underlying large pyramidal cells which penetrate the molecular zone and there take a horizontal direction, thus giving the zone an unusual width in these regions.

Obersteiner states that the outer stripe of Baillarger (Genari's band), lies in the lower portion of Meynert's third layer and that it is chiefly composed of collaterals from the axis-cylinder processes of the pyramidal cells. According to Cajal, the horizontal fibre plexus in the zone of medium-sized pyramidal cells corresponds with the upper part of the specific end plexus of exogenous fibres described by him as characteristic of the sensori-motor cortex, which in all mammals may therefore be recognized in "dass sie ein dichtes Geflecht von sehr dicken exogenen Fasern hat, welches in Niveau der mittelgrossen Pyramiden, d.h. oberhalb der äusseren grossen Pyramiden liegt."⁴ This plexus Cajal found in the precentral and bases of the first and second frontal but not in the postcentral convolution. It is best seen in the foetus of seven or eight months before myelinated fibres have obscured the field. He describes it as composed of three zones—lower, middle and superficial. In the first, which includes the meeting place of cortex and medullary substance, the fibres take a vertical or diagonal course,

⁴ Die Bewegungsrinde, p. 81.

crossing the radial bundles at various angles; in the middle zone they assume a horizontal direction; in the uppermost they are broken up into a fine plexus which occupies the whole of the third layer of the cortex, even extending into the lower portion of the layer of small pyramidal cells. Most of the finer branches possess no myeline sheath, hence the relative clearing in the third layer in Weigert preparations. The coarser fibres in the lower part of the superficial zone of Cajal's plexus are myelinated, however, and "dieser markhaltige Plexus ist nicht Anderes als der von den Autoren sogenannte Gennari'sche Streif, die Lamina medullaris externa (Kölliker, etc.)."⁴⁶ Sometimes a second ill-defined transverse band can be made out in the lower cortical levels, made up of the horizontal processes of Cajal's deep association cells.

The above histologic characters apply to a section of the anterior paracentral, including the upper termination of the precentral and base of the first frontal gyrus.

Between the anterior and posterior central convolutions, constant differences in structure exist by which they can be differentiated either macroscopically or microscopically. The gross differences have already been mentioned. They are best seen by comparing the cortex on the anterior and posterior walls of the fissure of Rolando. In such a comparison the postcentral convolution is recognized by four peculiarities: (1) Its narrowness, the precentral exceeding it in width by a third or a half. (2) Its staining more deeply in the upper half than the corresponding part of the precentral, on account of the denser occupation by small and middle-sized pyramidal cells which in the postcentral are confined within much narrower limits. (3) A narrow, lightly staining zone marking the position of the sixth layer, which in the postcentral contains no giant cells and therefore stains less deeply. (4) A sharper separating line between cortex and medulla. The broad precentral cortex stains more evenly, is less well differentiated from the white substance, and in the upper half of the Rolandic zone shows macroscopically a row of dark points in the deep portion corresponding to the light band in the postcentral and representing the giant cells

⁴⁶ Loc. cit., p. 86.

of the sixth layer. With a very low magnification the individual characters of the two convolutions are even more marked, and each of the cortical layers presents distinguishing features. The first and second are noticeably wider in the precentral, the small cell layer being less densely packed. The most marked excess in width is observed in the medium-sized pyramidal cell layer of the precentral, with a corresponding diminution in density of the cell contents. The fourth layer is therefore situated considerably nearer the surface in the postcentral gyrus and its cells are larger and more numerous, particularly on the summit of the convolution. Thus the postcentral resembles the association zones in that its largest cells are situated in the fourth layer, while in the motor precentral the largest cells occur in the sixth layer. All the layers below the fourth are much better defined in the postcentral than in the precentral gyrus. The fifth layer (granule zone) is broad and contains many more small elements, suggesting also in this respect the cortex of the association zones. The sixth layer in the postcentral shows a notable dearth of cell elements, the giant pyramidal cells being entirely absent. A better differentiation is seen between the seventh and eighth layers of the postcentral than in the precentral.

Weigert preparations show peculiarities in the fibre pictures quite as noticeable as those above mentioned for the cells. The radial bundles are thicker and denser and have a longer course above the medulla in the precentral cortex. In the anterior wall of the Rolandic sulcus there are numerous radial fibres, while they are conspicuously few in the posterior wall. The anterior cortex also shows a much richer system of deep horizontal fibres (association fibres by Cajal), the difference being especially marked in the sulcus, where these fibres are extremely few in the posterior central. Baillarger's zone is also better marked and the deep oblique fibres are more numerous in the anterior central. The line in the midcortex where the radial bundles stop is much plainer in the postcentral, owing to the scanty development of a fibre plexus in the third layer, while in the precentral this thick plexus partially obscures the line of termination of the radial fibres. Finally, the tangential layer in the precentral is broader and its constituent fibres are much

more numerous, as would be expected from the fact that these fibres largely represent the upward prolongation of the apical processes of the large pyramidal cells. The extremely coarse strands described in connection with Cajal's autochthonous cells are not observed in the plexiform layer of the postcentral convolution.

In following the fissure of Rolando from its lower to its upper termination one meets with considerable changes in the structure of the central convolutions, all of which, however, are very gradually effected. At the lowermost level of the Rolandic zone, no such striking differences are seen between the pre- and postcentral gyri as obtain higher up. The inequalities in width and differentiation already noted are present but in much less exaggerated degree. No giant cells are found in either convolution. In the precentral an occasional large cell occurs in the sixth layer but the majority are distributed over the fourth and fifth, there being no definite granular zone. In the postcentral, on the other hand, the large pyramidal cells are almost entirely confined to the fourth layer, below which a well-marked granular zone is apparent. The chief point of difference therefore in the cortex of the two convolutions at this level is the better definition of the fourth and fifth layers in the posterior central.

The facial area which is innervated by neurones with relatively short axis cylinders contains no giant cells. These first appear as one ascends the central sulcus at a variable point about a fourth or fifth of the distance from the sylvian to the median fissure, which probably marks the beginning of the arm area. At this level only a few giant cells can be seen. They are situated deep in the fissure near its bottom, in the sixth layer of its anterior wall. No giant cells are present in the anterior cortex on the summit of the convolution. In the postcentral on the contrary the layer of superficial large pyramidal cells becomes much better developed as it emerges from the sulcus to reach the free surface and occasionally on the summit of the convolution or in the anterior wall of the postcentral fissure a very large cell occurs. These cells do not occupy the sixth layer but are always found above the granule zone and do not moreover reach the size of the sixth layer cells of the anterior convolution of the same level. While in general it

may be said that the pyramidal cells of the largest type are limited to the strictly motor cortex (precentral convolution and its antero-superior adnexa), one may nevertheless now and then be found outside of this region, as has been pointed out by Bevan Lewis. In the arm area the precentral cortex assumes an appreciable increase in thickness, due to the progressive development of the layer of middle-sized pyramidal cells. In this area there are, therefore, besides the two differential postcentral characters of the facial area, two additional precentral features, a wide third zone and the presence of giant cells in the sixth layer. Corresponding with the appearance of the latter a rich tangential system develops in the anterior wall of the sulcus, while in the posterior wall it remains very rudimentary, and is also poorly developed on the summits of both convolutions.

Continuing upward through the motor area the cortex becomes progressively broader, the sixth layer cells increase both in size and number, and the place of greatest density both of the giant cells and the overlying tangential fibres is gradually shifted rising out of the sulcus to the free margin of the convolution. In the middle third of the Rolandic region corresponding roughly with the limits of the arm area, the giant cells occupy the entire anterior wall of the fissure, being densest in the upper portion of the area opposite the origin of the superior frontal sulcus. Above this level they gradually spread over the free border of the convolution occupying both summit and fissure. In the latter position they become steadily fewer and in a section including the upper extremity of the central sulcus giant cells are usually found only along the summit of the precentral convolution. Throughout the leg and trunk areas they show a marked increase in size.

The tangential fibres of the precentral cortex always correspond in density with the underlying giant cells, being best developed in the sulcus in the middle third, and on the summit of the convolution at the upper extremity of the motor zone.

As has been mentioned, the structure of the precentral and base of the first frontal continues essentially unchanged into the paracentral lobule. In a vertical section through the middle of the precentral and including the paracentral and callosal gyri, Betz's cells are seen to continue uninterruptedly as far as the mouth of the calloso-marginal fissure, beyond which giant cells

of slightly smaller size can be followed for a variable distance along the superior wall of the sulcus or even to its floor. They are not present in the lower wall or in the gyrus cinguli. If an oblique section be taken from the paracentral so as to include the termination of the fissure of Rolando, Betz cells can be followed to the mouth of the fissure or for a variable distance down its anterior wall but do not occur in the posterior wall.

The anterior paracentral is of practically uniform structure throughout. In the lower portion adjacent to the callosal gyrus the cortex is a little narrower owing to a thinning of the zone of medium-sized pyramidal cells, and the granular layer is slightly more conspicuous. This narrowing of the third layer increases as one passes around the bottom of the sulcus into the cingulum, where the granular zone occupies a relatively high position.

A considerable change in structure is noted between the anterior and posterior segments at the paracentral, and an imaginary vertical continuation of the central fissure over the face of the lobule roughly divides the two segments. Betz cells are confined to the anterior segment and are limited fairly constantly by the imaginary line, on passing which posteriorly the cortex gradually assumes the postcentral type. The third layer becomes narrower, the fifth more conspicuous and higher in the cortex. Fairly large cells are still found in the sixth layer until the lip of the ascending ramus of the sulcus cinguli separating the paracentral from the precuneus is reached. Beyond this point as a rule no large cells are found in the sixth zone while the cells of the fourth assume an increased size. On reaching the surface of the precuneus the cortex is still narrower, the fourth and sixth layer cells smaller and the granular zone much better developed.

The *pli de passage* therefore partakes of the characters both of the precentral and postcentral cortex and the two types are differentiated just as certainly as on the convexity of the hemispheres where they are separated by the Rolandic sulcus. In that part of the paracentral lying below the termination of the sulcus the characteristic postcentral feature, a prominent granular layer, and the characteristic precentral feature, a sixth zone of giant cells, are seen existing together.

All changes in cortical types are effected very gradually, and this is equally the case whether they are separated from each

other by the conditions of the surface configuration or not." The giant pyramidal cells embrace the hemisphere from the callosomarginal sulcus to a point near the lower end of the sylvian fissure, with an approximately vertical zone which is widest in its upper portion. This is the specific motor zone, and behind it exists another zone of different structure and doubtless different function. The central sulcus separates these two zones nearly but not absolutely, while the neighboring fissures are of no significance as functional or histological landmarks. The chief object of the fissures is evidently to furnish increased room in the cortex for expanding incoming fibres and the development of intracortical and association and projection neurones. Fissure formation is earliest stimulated where functional activity is greatest, and this is admittedly in the projection centers. Hence we have three primary fissures, the Sylvian, Rolandic and calcarine, each associated with a specific early function, though not necessarily marking an absolute bound to its area of representation.

The experimental findings of Sherrington and Grünbaum may be referred to again in connection with the question of cell distribution. These observers differ in one noteworthy particular from most of their predecessors, namely, "the extension of the excitable 'motor' region to the free surface of the postcentral convolution. We have seen nothing to lead us to include that surface or any part of it in the 'motor' area of any of the anthropoids we have used." They find the excitable area to include the length of the precentral "and in most places the greater part or the whole of its width. It extends into the depth of the Rolandic fissure, occupying the anterior wall, and in some places the floor, and in some extending even into the deeper part of the posterior wall of the fissure."

On the histological side the general postulate that difference in structure indicates difference in function is applicable to the cortical areas. "Es führt also schon die anatomische Betrachtung allein zu der Anschauung, dass die verschiedenen Rindengebiete des Grosshirns functionell nicht gleichwertig sein können" (Obersteiner). It may be assumed that the true motor area includes

"Bevan Lewis showed that in the lower animals the passage from one cortical type to another is abrupt, thus contrasting with the manner of transition in man.

only those portions of the cortex which present the specific elements of the sixth layer. "Dass die grössten pyramiden Zellen an gewissen Stellen bei den motorischen Leistungen eine Rolle spielen, ist sicher" (Obersteiner). These elements increase in size from below upward in direct proportion to the length of their axis cylinder processes. The facial neurones with short axis cylinders are small, the arm neurones are larger, the neurones of the paracentral whose axis cylinders are destined for the lumbar cord are gigantic. Sherrington and Grünbaum do not say where in the precentral gyrus the motor area was found not to occupy the whole of its width. Of the four highest species of primates, the orang-outang, chimpanzee, gorilla and man, they examined the brains of the first three and obtained uniform results in all. It is not unreasonable to suppose, therefore, that the final step in the series would not have broken the chain of evidence. If, accordingly, the cell distribution in man and in the gorilla are comparable, we should expect it to be in the face and arm, particularly the forearm cortex, that the excitable area does not include the entire width of the precentral convolution, for in the lower half of the Rolandic zone the motor cells are nearly confined to the anterior wall of the sulcus, in the lowest levels not even reaching the free surface of the convolution. It is also not stated in what places the excitable area extended to the deeper parts of the posterior wall. This we should expect to be most often the case in the upper mid-portion of the motor zone, for here most frequently can giant cells be followed around the bottom of the sulcus and into its posterior wall, in some instances an isolated cell being found a third or even a half of the way up, in the sixth layer, but never reaching the free surface of the postcentral gyrus, the summit of which is always entirely free from giant cells. It is in this portion of the motor cortex that giant cells show their widest distribution, exceeding the limits of the precentral fissure and extending for a variable distance along the superior frontal gyrus. Two or three may also sometimes be seen in the depths of the postcentral fissure in its anterior wall. It is preeminently in the sulci that motor impulses arise. The giant cells in the fissures far outnumber those on the surface of the brain. Sherrington and Grünbaum found the excitable area to extend on to the mesial face of the hemisphere, without, however, reaching the calloso-marginal

fissure. This latter result we should anticipate in the posterior segment of the paracentral, for in this location no Betz cells are found. In the anterior segment, on the other hand, Betz cells can often be followed through the whole vertical diameter of the lobule, one of the largest forms being sometimes situated not far from the lip of the calloso-marginal fissure, while giant cells of but slightly smaller size continue into its depths. In this portion of the paracentral therefore we should expect to find motor excitability extend from its upper to its lower boundary.

The occurrence occasionally of giant cells outside of the motor cortex has been mentioned. Such cells are denominated the ganglionic cells of Bevan Lewis. Their presence shows that centralization has not yet become complete. The characteristic abundance of giant cells in the gyrus hippocampus indicates not only the close association between sensory and motor function, but gives evidence as well of the associated development and early intimate union between the phenomena of olfaction and movement, so important in the lower animals.

RÉSUMÉ.—The motor cortex occupies the middle region of the hemispheres, intermediate between the general and special sensory areas on the one side and the specific association or psychic center on the other. This zone is the earliest to functionate and the central sulcus forms to give increased room for its developing elements. It has been defined by the brilliant experimental work begun by Hitzig and Ferrier, by the clinical and pathological findings of Broca, Hughlings Jackson, and a legion of subsequent observers, by the intricate myelogenetic method of Flechsig, and by the histologic studies of Betz, Hammarberg and Cajal. Beginning with the observation of Hitzig that the motor area embraced nearly a half of the brain surface, its confines have gradually become narrowed. It has long been assumed roughly to include both central convolutions and the paracentral. Beevor and Horsley cast a suspicion upon the motor function of the postcentral gyrus. Flechsig discovered embryologic differences which he believed justified him in considering the postcentral the seat of general incoming sensory impulses, and the adjoining precentral the seat of outgoing motor impulses. Finally, Cajal described a specific fibre distribution in the precentral convolution which he believes serves to differentiate it as the motor type of cortex.

That a motor type of cortex exists is abundantly proved. It is characterized by its unusual width dependent upon the marked development of the medium-sized pyramidal cell layer containing the specific plexus of Cajal, by the absence of a clearly defined granular zone, and by the presence of giant cells in the sixth layer with thicker and denser radial bundles and a richer development of the overlying tangential fibres which are of maximum density in those portions of the convolution which contain the greatest number of giant cells, both being more conspicuous in the fissure in the lower half of the Rolandic zone, and on the summit of the convolution in the upper part of the motor region. Passing beyond the limits of the motor area, superiorly, inferiorly, anteriorly, or posteriorly, one observes a gradual change in the cortical type, the third layer becoming narrower, the fifth wider, and the specific elements of the sixth disappearing. This change is typically illustrated in a cross section through anterior and posterior central convolutions. The paracentral presents both types of cortex, the transition taking place below the extremity of the fissure of Rolando although no surface marking determines the boundary.

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