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Part I.—Original Articles.

Some New Features in the Intimate Structure of the Human Cerebral Cortex.

By JOHN TURNER, M.B., County Asylum, Brentwood, Essex.

THE new features are—(1) a beaded network which envelops the pyramidal cells of the cortex cerebri, and which has not hitherto been observed in human brains, but only around the nerve-cells of some of the lower animals (guinea-pigs and rabbits) when subjected to the influence of methylene blue injected into the tissues during life; and (2) an intercellular plexus of extremely fine fibrils which has, I believe, never before been actually demonstrated in any brains, human or otherwise.

The method by which I am able to show these structures was originally described in part xci, autumn, 1900, of *Brain* (pp. 524—529). This was only a short preliminary notice, and was followed by a fuller account in the summer number, 1901, of the same journal. But, previous to the appearance of this paper, I gave a microscopical demonstration at a meeting of the Neurological Society in May, 1901.

The method consists in staining pieces of cortex as they are

taken from the cadaver in a mixture of methylene blue (1 *per cent.*) and peroxide of hydrogen (10 *per cent.*)—four parts of the former to one part of the latter. They are kept in this mixture from seven to ten days, and then fixed in 10 *per cent.* of molybdate of ammonium, thoroughly washed, dehydrated, soaked in xylol, embedded in paraffin, and cut.

In the second of the papers to *Brain* I laid great stress upon the influence of light on the success of the stain, chiefly because all, or nearly all, my successes occurred during the summer-time. I now believe, however, that this idea is quite erroneous, and that light has no influence at all on the reaction. I have obtained a successful result in tissue kept in a dark cupboard all the time it was in the staining fluid. The successes were probably due to some slight decomposition changes in the tissue, which would be facilitated by warm weather.

It must not be supposed from this term that I use material which presents any gross alteration of a decomposition nature, or which can in any way be characterised as decayed. I am referring to a supposititious delicate chemical change manifested in *some* cases during the process of decomposition, which allows the tissue to react in this characteristic way to the stain, and which sometimes occurs shortly (7 hours) after death, and perhaps sometimes (in septicæmic cases) even before death. The delicacy of this change is shown by the fact that whilst one part of a small piece of material will take on the stain beautifully, contiguous parts often fail to react at all.

In the successful sections we meet with no obvious alterations in the contour of the nerve-cells, and in most cases the fixation is so perfect that absolutely no trace of a pericellular or perivascular space exists.

I have carried out a number of trials with tissues put into the staining fluid at different intervals after death, and these, although not decisive, on the whole bear out this contention; but not all material will give the reaction, however long after death it is kept, before being put into the stain. Some of my best results were obtained with the brains from cases of recent and acute insanity, in which, in all probability, no demonstrable structural alteration of the nervous matter had occurred.

I have made many trials with the brains of dogs, cats, kittens, guinea-pigs, doves, etc., but have so far only succeeded

in getting slight indications of the reaction in a cat's brain, and in a two-months-old pup, kept forty-six hours after death before staining; in the latter the thorny processes of the Purkinje cells showed faintly, but unmistakably.

The great delicacy of the reaction is indicated by the fact already mentioned of the selection of the stain for individual parts of the piece of tissue; and further, while sometimes one part of a cell stains faintly, the remainder colours quite darkly. Apparently with certain chemical changes in the tissue the pyramidal cells, which usually stain very lightly, tend to take on a dark colour, and in these cases their dendrites can be followed for considerable distances, and the picture has a resemblance to a Golgi preparation. To some extent my method is the complement to Golgi's, for whereas this picks out *par excellence* the pyramidal system of cells, mine, as a rule, almost entirely neglects these, and especially selects other cells, which I have termed "dark cells," on account of their affinity for the stain.

In this paper I shall deal almost entirely with the cerebrum; only a passing reference will be made to certain points in the intimate structure of the cerebellum, where these serve to confirm results obtained in the former.

The following are the points I shall treat of in the order named:

1. The pericellular network.
2. The differentiation of cells into pale and dark varieties.
3. The origin of the network from dendrites of the dark cells.
4. The junction also of collaterals with the network.
5. The intercellular plexus.

The Pericellular Network.

This structure has been seen around the nerve-cells of some of the lower animals by means of Ehrlich's "intra-vitam" method of staining, but I was the first to show it in the human brain. Ehrlich's method, however, does not bring out so much detail as mine, and does not, I believe, reveal the network and its appendages in their entirety, so that the accounts drawn from tissues stained by the "intra-vitam" method are wanting, in accuracy at least, when applied to the structure seen about human nerve-cells.

Drs. W. Aldren Turner and W. Hunter (1) give a careful description of it, as observed about the cells of rabbits, guinea-pigs, etc.

From their account, and the stress they lay on *the* fibril passing to join the network, which they term the cellulipetal fibre, it is evident that they look upon the network as a closed sac drawn over the cell body, as it were, and resulting from the ramification of a solitary nerve-fibril; but such a conception, at least in the human brain, is very far from representing the facts of the case.

The network in man consists of fine dark fibrils, on which, at varying distances, are small dark beads, or sometimes rings, which, as a rule, are the nodal points of the meshes. The beads vary considerably in size, the average being about 1 μ. The size of the mesh and the coarseness of its fibrils also differ, so that, while sometimes one meets with a big-meshed net, having consequently relatively few beads, and with very delicate fibrils, at others the beads are larger, very closely clustered together, or even partially coalescing, and the fibrils much coarser.

It extends not only over the cell body, but over the apex and dendrites, and in one case I have been able to trace it for over two hundred micro-millimetres along the dendrite of a Betz cell. It does not appear to invest the axon at all.

Now in contradistinction to the description of it drawn from the lower animals, it is emphatically not a closed sac having its origin from a single fibril. Multitudes of delicate branches, like free tags, can be seen on all sides passing to the beads of the network, not only over the cell body, but to that part of the structure which envelops the apex and the dendrites. These fine fibrils can often be traced back to thicker ones, which in many cases must come from manifestly different sources. This is an important fact, because it shows that the network is in continuity with more than one cell of origin.

Another point to be noted is that practically the same network often extends over two adjacent cells.

This structure is obviously a pericellular one, and I do not think it will be necessary to enter into a discussion as to its possible neuroglial origin in face of the facts which I shall bring forward, viz., that I can demonstrate its direct origin from the dendrites of the dark cells, and there can be no question that

these are nervous, as their axis-cylinders can be identified ; and secondly, I can also demonstrate that collaterals blend with the network.

It has been previously assumed that it is an offshoot from axis-cylinders of the pyramidal cells ; that, in fact, it represents the arborisation of a collateral from one pyramidal cell breaking up around the body of another. This idea is not altogether correct, for although collaterals do certainly make union with the network, there is no evidence to show that they are directly concerned in the formation of this structure ; while on the other hand I can show, in several instances, its direct origin from the ultimate splitting up of the *dendrites* from the dark cells. Even before the actual demonstration was arrived at, the remarkable similarity between the beaded fibrillæ of the network and those obviously proceeding from the dark cells rendered this assumption almost a certainty. Axis-cylinders and collaterals, as I shall point out later on, in as far as they are represented by my method, do not show beads or varicosities on them.

So far as I am able to determine at present this network is only met with over cells of the pale variety, *i. e.* the pyramidal cells. It can be seen over these in all the layers where they are met with except the second layer, and probably the innermost, or layer of spindle-cells, and I think that in all probability it envelops these also, but unfortunately they lie in parts which do not take on the reaction to the same extent as the middle layers ; at the most one sees here and there a dark cell picked out in the lower part of the second layer.

Taking for granted, then, that the network is a nerve structure, its presence all along the dendrites is evidence that these parts are concerned in the conduction of nervous impulses, and are not merely, as Golgi and others think, roots having only a nutritional value to the cell. On this point I think that the demonstration of the dendritic origin of the network will be sufficient of itself to dispose of this idea.

Thorns.—Before leaving these pale network-enveloped pyramidal cells I wish to make a few observations on the occurrence of the so-called "thorns" or "gemmules" with which their apex and dendrites are studded when prepared by Golgi's method.

Dr. Alexander Hill (2) believes that these structures are

formed by the overflowing from the cell-plasm of a softer staining substance along the course of fibrils which the method of Golgi does not reveal. And as his remarks on the appearances sometimes shown by the thorns are highly suggestive, from my point of view, of the part which the beaded network plays in their production, I shall quote them :—"Sometimes the thorns appear as rods with knobs at their ends (gemmules). Sometimes one dot or several dots are seen unconnected with the dendrite, but so placed as to indicate that they have been led into position by an invisible fibril. Occasionally the thorn is replaced by a filament of considerable length."

There has always been a strong feeling with some that these little bodies were artificial, and probably produced by deposits of silver along the protoplasmic processes. When, however, Ramon y Cajal (3) announced in 1896 that he had been able to demonstrate them by methylene blue on cerebral cells, the view of their natural origin was strongly reinforced, and they received notice in the text-books.

With all due deference to the opinion of such a distinguished observer, I suspect, in view of the facts which my method shows, that these thorns are, strictly speaking, of artificial production in the case of the pyramidal cells of the cerebrum. I am inclined to believe that they are not intrinsic parts of the cell at all, but belong to the network, and represent deposits of silver about the beads and numerous fibrils, which, as I have stated, pass off from all parts of the network in great numbers.

It may be considered that this is a somewhat presumptuous statement to make, as I have already said that my method practically neglects the staining of the pyramidal cells. This is so as a rule, but with some conditions, the nature of which we do not understand, and which are accompanied by alterations in their chemical structure, these pyramidal cells here and there stain deeply, and so also do the antler cells of the cerebellum. And when this state of affairs is present the latter show most beautifully numbers of little lateral projections along their dendrites, whereas the pyramidal cells never do ; their dendrites certainly do on these occasions show an irregular and somewhat shaggy aspect, but I think that this appearance can be much more satisfactorily explained as due to the beads and fibrils *surrounding* the dendrites than as representing an integral portion of the dendrite itself, and they unquestionably show no

resemblance to the crowds of little projections seen regularly arranged alongside the branches of the antler cells.

I am well aware of the risks one runs in arguing from *negative* appearances, as it were, in cerebral microscopical anatomy, but I think that when a method under certain conditions shows structures plainly in one part of the nervous system, one is at least justified in being sceptical about the existence of these structures in other parts when they do not appear.

Ramon y Cajal does not appear to have demonstrated thorns on the Purkinje cell branches with methylene blue—at least I can find no reference to such an observation,—and they are not alluded to in the last edition of Quain's *Anatomy* as occurring here, just in the place where, as I can show, they almost unquestionably exist as intrinsic parts of the cell structure.

The Dark Cells.

The second feature to be noticed is the differentiation by this method of the cortical cells into two classes, *viz.*, those which stain of a very pale blue colour, often almost colourless, and those which stain very deeply, nearly black.

The pyramidal cells and the giant cells of Betz belong to the first class or pale variety, and the other consists of cells scattered irregularly throughout the cortex. It is quite remarkable the sharp distinction which the same staining fluid draws between these two classes of cells. This marking off of the cells is maintained in the molecular layer of the cerebellum; in that organ the antler cells are the pale ones, whilst the basket and small cortical cells are the dark.

In both cerebral and cerebellar cortex, however, occasionally the pale variety tends in places to stain deeply, but it is seldom that they approach the dark colour of the other variety. Sometimes this alteration affects only a part of the cell, so that, whilst the apex and dendrites may be dark, the body may be pale, or sometimes one portion of the body will be dark and the remainder light. This alteration, as already mentioned, seems to depend on some delicate chemical change, often, but not of necessity, accompanying pathological conditions.

Besides the difference in staining affinity, there are other points of distinction between the two kinds of cells.

a. The pale or pyramidal cells are definitely orientated. The dark are not; they lie in any direction, and sometimes, as will be referred to later on, their axis cylinder arises from the surface aspect and sometimes from the lower border. This lack of orientation is particularly well shown among the dark cells of the cerebellum.

b. Size and shape.—Generally speaking, they are smaller than the pale, and many of them are quite minute and easily overlooked under low powers (quarter inch). Some, however, reach a relatively large size, almost as big as a medium-sized pyramidal cell. They are of diverse shapes—round, oval, polygonal, and triangular—and in the frontal cortex I have met with a number which are very long and slender, spindle shape.

c. Position.—They occur with certainty from the lower part of the second layer inclusive down to the commencement of the innermost layer of the cortex. I am not able to speak of the other layers, as the reaction does not take place in these.

d. The largest number of them are seen, roughly speaking, at the junction of the outer and middle third of the cortex. In a comparison between frontal, ascending frontal, and occipital cortex, which are the three regions I have chiefly examined, they seem to be least numerous in ascending frontal. Both frontal and occipital contain many more, but I am not certain in which of these two they are most numerous.

In the frontal besides the spindle variety we meet with large numbers of small, often angular, cells, and in the occipital chiefly with small rounded or pentagonal ones, and here they seem to be most thickly clustered about the layer of small granule cells, either just above it, within it, or just below it.

e. Nucleus.—This stains even darker than the cytoplasm, and appears as a homogeneous body, and not granular like the nucleus of the pale variety.

f. Axis cylinder.—This is easily recognised, and the description given of it applies also to the axis cylinder of the pale cells. It has a perfectly smooth contour, and is generally at its origin disposed in somewhat sharp twists reminding one of a corkscrew. At its commencement it stains deeply, but at a little distance from the cell it gradually loses its colour and appears as a very pale blue or grey fibril. When it can be followed for any distance it shows here and there dark areas

of several μ in length. At these sites it is sometimes slightly swollen, at others shrunken; very often from these parts branches are given off—generally, but not always, at right angles to the parent stem. In some preparations these axis cylinders and collaterals can be seen in large numbers and traced for very long distances (*e.g.*, 600 μ), but they never, so far as I have observed, show any beads along their course.

I take it that the pale fibre is myelinated, and that the dark areas referred to represent the sites of nodes of Ranvier. Although the above description applies to myelinated fibres, yet a study of the axis cylinders of the basket cells of the cerebellum, which are not myelinated, and which stain deeply throughout their course, confirms the observation that axis cylinders and collaterals by my method do not show beads or varicosities.

g. Dendrites.—The main protoplasmic branches have generally a shaggy aspect, and are usually given off from the body of the cell abruptly, not passing off, as it were, by insensible degrees like the apical process of a pyramidal cell. They divide at somewhat infrequent intervals, and the branches can often be followed a very long distance without any sensible diminution in calibre, which is a point in marked contrast to the axis cylinder, which very rapidly dwindles to a small fibril. The finer (ultimate) branches of the dendrites are always beaded. Although I have just stated that the branches divide at infrequent intervals, yet apparently, all along their course, quite fine threads pass off nearly at right angles from the bigger branches along which they are closely set; these, together with the terminal fine-beaded fibrils just alluded to, form a dense inter-cellular plexus which pervades the entire matrix of the grey matter wherever the staining is successful.

The Origin of the Network from Dendrites of the Dark Cells.

I have been able in several instances to trace the actual passage of one of the finer branches of a protoplasmic process of a dark cell into a network, of which it evidently forms an integral part.

In one case a stout dendrite, proceeding from a dark cell, terminated in a triangular-shaped mass, from the base of which two delicate branches proceeded; one of these again widened

out into a triangular shape, and gave off from its base two more threads which terminated in beads, the whole structure manifestly forming part of a network over a pale cell. This is very clearly shown in the figure, page 13. The dark cell, from which the dendrite passing to the network proceeds, is not in the picture. From the base of its terminal triangular mass two delicate fibres proceed. One is out of the plane of the photograph; the other is shown, passing down to end in another triangle, from which two fibres ending in beads pass off. The body of the pale cell is scarcely shown, but its dark prominent nucleus and the beaded fibrils around indicate its position.

Sometimes a comparatively stout dendrite blends directly with a network; sometimes a stout fibre courses up alongside a pyramidal cell, and gives off at intervals extremely fine fibrils to supply the network.

The Junction of Collaterals with the Network.

This is another feature which can be clearly shown. The appearances by which myelinated axis cylinders can be recognised have been previously mentioned, and in some sections very large numbers of extremely fine axis cylinders and collaterals can be seen, but they require very careful looking for, as they are by no means conspicuous objects, owing both to their small size and to the fact that except at the nodes they stain very faintly.

Fig. 2 shows a collateral blending with a network. The axis cylinder passes across the upper part of the picture, and at the dark nodal area near its centre gives off a short collateral, which fuses on to the darkly-stained network around a pyramidal cell, whose outline is roughly indicated by beaded fibrils.

As this collateral remains pale till its junction with the dark fibril, it probably retains its myelin sheath up to this point. In another case the axis cylinder or collateral could be followed for some considerable distance before its junction with the network; its origin was not in the field of section, and there were no beads on it. From what cells do these axis cylinders come? It seems most probable from the pyramidal, because, as already shown, it is from the dendrites of the dark cells that the network arises, and union of their axons also with this structure would result in short circuiting.

If, then, they come from the pyramidal cells, and the unions are not exceptional cases, the unavoidable implication is that these cells also, by a round-about route, are in organic continuity with each other.

Inter-cellular Plexus.

I shall now proceed to give a somewhat fuller account of the inter-cellular plexus, which has already been briefly referred to. It seems probable that Golgi's method does not show it at all; at any rate, if it does it gives no means of discriminating it from the mass of other details shown.

Again, as the method in question fails to show the network, and as the inter-cellular plexus is essentially a part of this structure, this seems another reason why it should not be revealed by this process.

Golgi's cells of Type 2 have particularly shaggy dendrites. It is from these cells, among others, that the plexus arises, and I imagine that it is at these shaggy points that the chief number of the fine fibrils forming the plexus are given off, and just here, apparently, the silver stain fails, for it shows no further indication of a fibre.

Long ago Gerlach (4) postulated the existence of a diffuse net or felt-work in the grey matter which resulted from the ultimate dendritic branchings of the nerve-cells, and from which originated nerve fibres, which became medullated and (speaking of the spinal cord) formed the dorsal nerve roots. Gerlach's view, therefore, quoting Barker (5), was that "the axis cylinders of motor nerves represent nervous processes coming off directly from nerve cells, while the sensory fibres of the dorsal roots are to be looked upon as nerve fibres arising from nerve cells only indirectly, through the intervention of a diffuse network made up of their protoplasmic processes."

More recently Golgi (6) has supposed the existence of a delicate and intricate inter-cellular network, differing, however, widely from Gerlach's conception. This observer denies to the cell body any participation in the passage of nerve currents; he believes that the functions of the nerve-cells and their dendrites are purely nutritive. The nerve currents, according to him, pass solely along axis cylinders and their collaterals. He describes two types of nerve-cells, of which Type 1 is motor and Type 2 sensory in function. Now, the axis cylinders of

Type 2 divide and branch in the most profuse manner, and he believes that a dense network results in the grey matter from these diffuse branchings and from the collaterals of cells of Type 1.

Nissl (7) has, within the last few years, also brought forward, on purely circumstantial evidence, the view that there is a dense extra-cellular fibrillary structure, which indeed constitutes, in his opinion, the essential difference between grey and white matter. His view, based largely upon the work of Apáthy and Bethe, is that this felt-work comes directly from the nerve-cells.

Apparently, so far as I can gather, the fibrils of this extra-cellular plexus are assumed to be continuous with the fibrillæ, of which some observers consider the axis cylinder to be formed, and these fibrillæ, running uninterruptedly through the nerve-cell in the unstainable substance, leave it by way of the protoplasmic branches to form the extra-cellular plexus. Nissl admits that at present this supposed structure is quite undemonstrable.

The idea, therefore, of a plexus of nerve fibrils pervading the grey matter has been very generally in the minds of neurologists for many years past, but they have hitherto not been able satisfactorily to demonstrate it.

Now, my method very clearly reveals an extremely dense plexus of delicate, beaded nerve fibrils; indeed, so dense is it, and so fine the individual fibrils, that in successful preparations it gives to the grey matter, when viewed with a low power, an indistinct or slightly blurred appearance.

The fibrils of which it is composed are so extremely delicate that they are barely visible with a magnification of 800 diameters, and although they intersect each other in all directions there are certain appearances which indicate that they do not form a network but only a felt-work, by which I mean that although the fibrils overlap each other they are not joined together at the overlapping points. It is possible, as a rule, when two fibrils intersect, to bring one quite clearly into focus, and thereby fling the other out. Again, it is not at all an uncommon thing to be able to follow an individual fibril for a very long distance—several hundred μ—and these throughout their course give no indication of being connected with any others.

Although this plexus is so exceedingly fine, it is capable of being fairly satisfactorily photographed, but of course such a

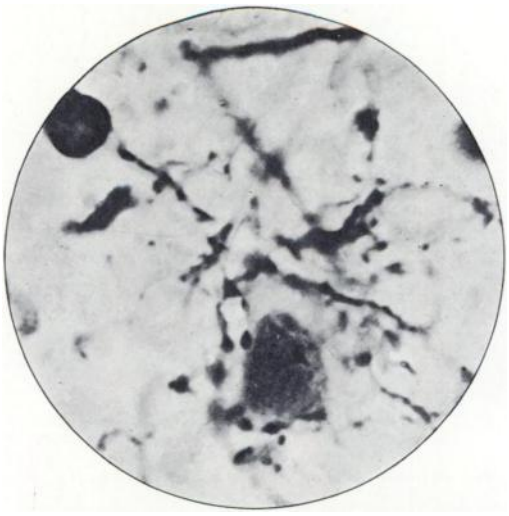

FIG. 1. —Shows a dendrite dividing terminally to form part of network over a pale cell. (× 1,360.)

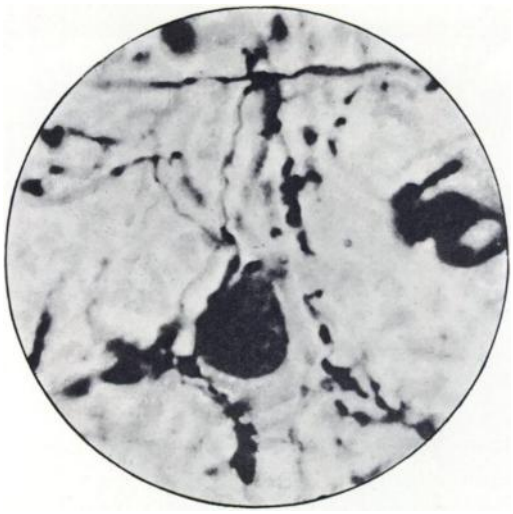

FIG. 2.—Shows collateral making union with network over a pale cell. (× 1,380.)

To illustrate Dr. JOHN TURNER'S paper.

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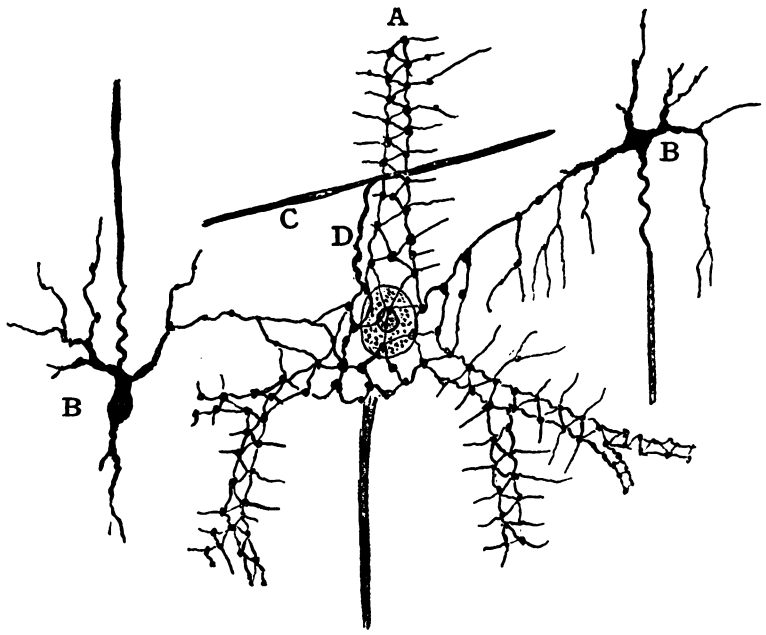
procedure will give us but a poor idea of the wealth of fibrils concerned, as it necessarily includes those only in one plane.

The fibrils can frequently be traced directly into the network over the pale cells, and where they join there is a bead or thickening, so that there can be no doubt that the inter-cellular plexus and the network form parts of one continuous structure. But the fibrils of the plexus can also, without doubt, be traced to the dark cells, of which they form the ultimate extensions of their dendrites.

No doubt among the myriads of fibrils met with are also many fine collaterals, which one may have a difficulty in distinguishing from the others, especially if not myelinated; but I think that unquestionably the great bulk of the plexus is formed in the manner above described.

Thus it is apparent that the inter-cellular plexus I can demonstrate differs essentially from either that conceived by Gerlach, Golgi, or Nissl, inasmuch as it is not a derivative of the



pyramidal cells at all, but results from the dendritic branchings of an entirely distinct system, *viz.*, the dark-cell system.

The accompanying diagram shows clearly the points that

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can be demonstrated by my method and which are directly opposed to the current idea of the relationship which the nerve-cells are supposed to bear to one another. The pyramidal cell (A) (representing my pale-cell system) is invested by a beaded network which extends over its processes as well. The network is practically an extension of the dendrites of the dark cells (B B). One of these latter cells is shown with an axon passing upwards, the other with an axon passing downwards, and both give off collaterals. It will be observed that the dark cells are organically united to each other by means of the network.

Many other fibrils are represented springing from the network, and these, of course, represent the termination of dendrites from other dark cells not shown in the diagram.

A short collateral (D) passing off from the axis cylinder (C) also makes union with the network. The cell to which (C) belongs is not shown in the figure, because I have not yet succeeded in tracing one of the collaterals or axis cylinders which join the network to their cell of origin, but in all probability they are given off by pyramidal cells.

CONCLUSIONS.

Showing some of the bearings of these observations on the current ideas of nerve structure.

The bare facts which I can demonstrate must, whatever interpretation we may put upon them, lead to considerable modification in our views of the structure of the brain cortex. For, in the first place, they show that there is a distinct system of cortical cells which, by means of the ultimate branchings of their dendrites, are in organic continuity with each other through the medium of a peri-cellular network enveloping the pyramidal cells.

And secondly, they show that collaterals also blend with the network, so that if these collaterals arise from the axis cylinders of pyramidal cells, which in all probability they do, and this union is not an exceptional occurrence, this implies that in a round-about fashion the whole pyramidal system of cells is also joined together, and that therefore practically all the cortical cells are in continuity with one another.

Time will not permit of more than a passing reference to the views of other investigators which tend to a similar conclusion, but I shall mention Dr. Alex. Hill's (8) observations on the fusion of the axis cylinders of the granule cell of the cerebellum with one another, and also Held's (9) observations on the blending of axis cylinders with the bodies of other cells, which he has described as occurring in the nucleus of the trapezoid body—a fusion which he terms "a zone of concrescence."

Such observations all tend to show that the rigid conception of each nerve-cell and its processes as a separate entity having no direct connection with other cells (the neuron theory) must be abandoned or greatly modified. I am speaking now of the doctrine of the neuron as formulated by Waldeyer, and which insists on an anatomical independence of cell units. I see that Dr. Mott, in a paper recently read to the Medico-Psychological Association ("Importance of Stimulus in Repair and Decay of the Nervous System," *Journal of Mental Science*, October, 1902), does not now insist on an anatomical independence, but on a trophic or nutritional, and yet, curiously enough, in another part of the same paper he quotes with approval the experiments of Dr. Warrington, which, if confirmed, show that cells have no such trophic independence. For Warrington shows that if you cut off one system of cells which is in physiological and functional connection with another, the latter is affected and its cells die.

With regard to the interpretation to be placed upon such of my observations as admit of discussion, I would suggest that the difference in staining properties, shape, etc., points to a difference in function, and as we have very good grounds for associating motor functions with the pale or pyramidal system, that the probabilities are that the dark cells are concerned with sensory functions; in other words, that they are the bearers of afferent stimuli.

If this be allowed, then it follows that we can by this method very distinctly show the ultimate termini of the afferent stimuli—the site where ingoing currents end and where outgoing currents are initiated—and this, of course, will be at the network and its contained cell.

In my second paper to *Brain* I pointed out that whilst in the cerebral cortex the pale cells far exceed in number the

dark, in the cerebellar cortex an opposite condition exists, and I mentioned how well this fact harmonised with Herbert Spencer's conception of the cerebrum as the great organ for the co-ordination of movements in sequence, and of the cerebellum as the organ for the co-ordination of movements in simultaneity. But if we may assume that the dark cells are conductors of afferent stimuli, it follows also that nerve currents do not invariably flow in one direction, *viz.*, from the dendrites towards the cell body and thence outward by its axis cylinder, a view which is very generally held. The current must flow to the dark cells by way of their axis cylinders, and from thence to the network by way of the dendrites, whilst in the pyramidal system, of course, it will pass in a reverse direction. But inasmuch as it can be shown without doubt that certain of the dark cells of the cerebellar cortex envelope the bodies of the antler cells with a basket arrangement formed by the splitting up of their axis cylinders or collaterals, then, if these cells also form part of the afferent system, in them the current flows in a reverse direction to what it does in the rest of the cells of this system.

Such conclusions may not seem satisfactory, but we must remember that the upholders of the one-way doctrine have equally awkward facts to face, *viz.*, in the case of the cells of the posterior spinal ganglia. These, as is well known, are unipolar cells, and the single process divides by a T-shaped junction not far from the cell. Now this process has all the characters of an axis cylinder; above all, it is myelinated. And yet, to meet the requirements of the advocates of this theory, we are asked to believe that one half of the T-shaped process is not an axis cylinder at all, but a dendrite, which, in this solitary instance, has taken on all the anatomical peculiarities of an axis cylinder.

These suggestions are, however, only tentatively offered, for inasmuch as my method fails to display any of the complicated structures which we have good reasons for supposing are concerned in the formation of the pyramidal cells, and in the face of the important results obtained by Apáthy (10) and others in leeches, which show a most complicated system of fibrils pervading the whole nervous system and apparently passing uninterruptedly through the nerve-cells, it will be well for the present to keep an open mind on many points concerning the

intimate relationship of the cells to one another. But, however much we may feel induced to apply conclusions drawn from such lowly organisms to those so much higher in the scale, we must, of course, give the chief place in our consideration to observations actually made on human brains, and however perplexing and difficult it may at present appear, yet these conclusions from invertebrates must be made to harmonise with details of structure demonstrable in man before they can be accepted as applying to human cerebral anatomy.

In the discussion which followed the demonstration of my specimens at the British Association meeting, Professor Schäfer said he was satisfied as to the general accuracy of my facts, but dissented from some of the interpretations put upon them, *e.g.*, in reference to conduction both ways along cell processes, he did not agree that there was sufficient justification for looking on the dark cells of the cerebrum and the cerebellum as similar in function. He referred to the fibres coming from the thalamus, which Golgi's method shows with free endings in the cortex in proximity to the processes of the pyramidal cells, and suggested that stimuli from these fibrils might excite not only the pyramidal cell, but at the same time the dark cells by means of the network; and he suggested that the dark cells represented a system conveying stimuli in the same direction as the pyramidal system, *viz.*, from the dendrites to the axons, and about the functions of which we knew nothing whatever.

Many objections can be urged against this view. Apart from the inadvisability of introducing a system of cells into our conception of the structure of the cortex, about the functions of which we are ignorant, it is difficult to conceive of the efficacy of a stimulation so vague and dispersed as would result from the excitation of this system in the manner which Professor Schäfer suggests. Admitting, as he does, that the dark cells are joined together through the medium of the network, an excitation applied to this structure in the above manner would only result in a diffuse stimulation extending in all directions along the fibres of the inter-cellular plexus, over an area proportional to the strength of the stimulus, and could not affect any one particular cell or group of cells.

The very accurate adjustment of the network to the pyramidal cell and its dendrites points strongly, I consider, to this structure being concerned in the excitation of its enclosed cell.

The meaning of such a disposition of the network is, according to Professor Schäfer's view, difficult to perceive.

Although in its scope my method at present falls far short of the Golgi method, yet in the particular regions where it succeeds it reveals far greater detail and delicacy of structure.

I believe that wherever Golgi's method shows us collaterals or axons ending in proximity to dendrites of pyramidal cells, we must go a step further and presuppose the existence of an actual junction with a network, neither the connecting fibril nor the network being shown by Golgi's method.

The assumption that stimuli pass only in one direction along cells and their branches, rests, so far as I know, on purely anatomical considerations. Such physiological evidence as we have, although perhaps not conclusive, appears to show that stimuli pass both ways. Thus long ago Kühne's experiment with the gracilis of the frog demonstrated the passing of stimuli both ways, and more recently Budgett and Green (*American Journal of Physiology*, 1899, iii, p. 115) have succeeded, after section of the left vagus above its ganglion, in joining it to the peripheral cut end of the hypoglossal. When such a preparation, two or three months after the operation, is excised, together with the tongue, excitation of the peripheral end of the vagus causes the tongue muscles to contract, showing that stimuli can pass up the vagus to take effect on the tongue muscles.

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