ON THE STRUCTURAL ALTERATIONS OBSERVED IN NERVE CELLS.

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I. Of the anterior horns of the spinal cord after section of the posterior roots.
II. After the division of the Axons belonging to them.

THE object of this investigation is an enquiry into the nature of certain structural changes which occur in nerve cells whose functional state has been altered either by a cutting off, of the afferent impulses which normally impinge upon them, or by the loss of continuity in their axons.

Method of Preparation of the Tissue.

Throughout my method of preparation of the tissue for examination was as follows:—Immediately after death pieces of brain or spinal cord were taken about 3 cm. in thickness and fixed in a saturated solution of perchloride of mercury for 12 to 24 hours, washed in running water for 24 to 48 hours, hardened in gradually ascending grades of alcohol for 24 hours each, and then for from three to six hours in absolute alcohol. The blocks of tissue were then cleared in xylol and after saturation for several hours in xylol paraffin and paraffin, embedded and sections cut, usually 7 μ in thickness, occasionally 3 μ. Ribbons of sections were floated from warm water on to a clean slide and heated in an oven at 37° C. for several hours.

The method of staining used was that described by Held [1], viz. a double stain of erythrosin and methylene blue according to the following formula: erythrosin 1 grm., glacial acetic acid 3 drops, water 150 cm.

Stain for about five seconds; wash in water, then stain and warm in a solution of the following composition: methylene blue 3·75 grms. sapo Venet. 1·75 grms., water 1000 cm. This is diluted with an equal volume of 5 % solution of acetone. I have however omitted the addition of Venetian soap and acetone without impairing the effect.

After washing, the sections are treated with absolute alcohol for a few seconds, which differentiates the colours as well as dehydrating, and shortens the process, cleared in xylol and mounted in Canada balsam.

The Normal Cell (see Plate).

Prepared in this way a normal cell of the central nervous system has the following characteristics:

1. The axis cylinder stains red and can be seen to arise from a crescentic shaped elevation of the cell body. It is quite free from the Nissl bodies.

2. The nucleus has a clearly defined membrane and consists of a clear portion in which is the red stained chromatin network. The nucleolus is large and stained deeply blue.

3. The body of the cell is stained red and throughout is densely covered with the blue stained Nissl bodies. In thinner sections the contrast between the differently coloured parts of the cells is more marked. In an ordinary cell from the anterior horn of the spinal cord the stichochrome arrangement of the Nissl bodies gives to the cell a distinctly streaked appearance, which is spoken of by Von Lenhossek as "tigroid." Held (*loc. cit.*) has studied especially the intimate nature and origin of the Nissl bodies and has shown that anatomically they consist of the finest granules and that between these lie vacuoles. To see this condition it is necessary to cut sections from 1—2 μ in thickness. Vacuolation of this character was rarely seen in any of my preparations in sections about 7 μ thick.

4. The dendrons also stain red and along their course are the Nissl bodies.

In connection with the normal cell I may mention that pigment was never found in the cell of the cat or rabbit but plentifully in man and the monkey. The histochemical tests of Macallum show that the pigment does not contain iron in either organic or inorganic combination.

I.

On the condition of the spinal cord observed after section of several posterior roots.

Method of operation. Laminectomy was performed under strict antiseptic precautions. Only sterilised warm normal saline was used for sponging purposes after the muscles had been cut through. The dura mater was freely opened and the roots cut in the region of the cauda equina about $\frac{1}{3}$ of an inch from their entrance into the spinal cord.

In all cases quoted the wound healed without suppuration. The segmental number of the roots cut was ascertained in each case by post-mortem dissection, counting from the last ribs. The number of ribs was thirteen on both sides in all cases.

Naked eye appearance of the cord. There was an entire absence of meningitis. A small amount of soft tissue was often found loosely adhering to the dorsal aspect of the cord, it was easily removed and the underlying surface of the cord appeared in most cases quite normal, in some slightly discoloured.

Examination of the cord. A very large number, 1—3 hundreds of sections, were cut from each of the several spinal segments and stained in the manner described. On examination a large number of markedly altered cells were found showing the changes detailed below.

Characteristics of the affected cells. These present different appearances.

1. The most striking and perhaps the commonest form is that shown in the figure. As seen under an apochromatic lens mm. 3·0, aperture 1·40, compensating Oc. 12, it presents the following features; the nucleus is markedly eccentric, it has a clearly defined membrane and well-marked chromatin network.

The nucleolus is well defined. The chromatic masses have completely disappeared from the greater part of the cell, and are localised round the nucleus. It is noteworthy that the Nissl bodies retain their form as discrete masses, the part of the cell which stains red has a distinctly striated character. In cells generally similar the processes may be present or absent (see plate).

2. Other cells have a similar appearance except that the blue masses are broken down into the form of a fine powder (Fig. 2).

3. Similar to above but nucleus absent (Fig. 3).

4. Cell increased in volume without a vestige of the colouring matter, it has a rather hyaline appearance and the nucleus is absent (Fig. 4).

5. Lastly, there are a number of cells possibly indicating the initial change. At one point in the periphery there is a chromatolysis

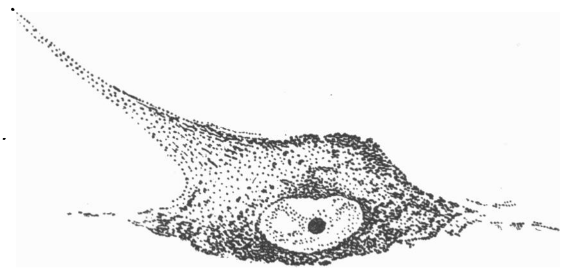


Fig. 1.

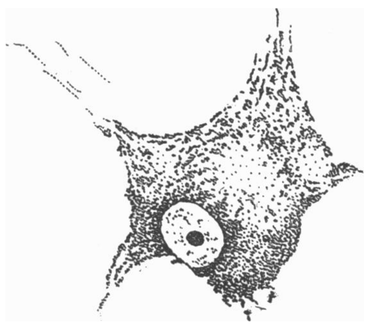


Fig. 2.

Fig. 3.

Fig. 4.

resulting in the appearance of a reddish zone; the nucleus is a trifle eccentric and the rest of the cell shows the ordinary Nissl bodies. It could not be definitely settled whether the place at which this process commenced was the origin of the axis cylinder, but certainly a good many cells were found which strongly suggested this (Fig. 1).

The number of altered cells and their positions in the spinal cord.

Owing to the same cells being seen in several consecutive sections it was difficult to find a reliable method of enumeration. The numbers in the tables given were obtained as follows:—no normal cell was counted unless the nucleolus was clearly visible and the same altered cell was of course not counted twice when it could be recognised as such. Another difficulty was that the affected cells are not uniformly distributed over the segment, for example thirty consecutive sections may show only normal cells, the next thirty a considerable number of affected ones. Hence for examination series of alternate tens of sections were taken.

1. *Cat.* Killed on the 10th day. Section of VIth VIIth VIIIth IXth post-thoracic roots.

	Condition of postero-external group		Condition of remaining cell groups	
Segment	Total no. of nucleoli counted	No. of altered cells	Total no. of altered cells in Anterior group	Median group
VI		0		
VII	247	55	2	3
VIII	126	30	7	

2. *Cat.* Killed on 12th day. Section of VIth VIIth VIIIth IXth post-thoracic roots.

VI		0		
VII	187	44	5	
VIII	116	28	4	

3. *Cat.* Killed on 17th day. Section of VIth VIIth VIIIth IXth roots.

VI	146	0	3	
VII	347	47	20	13
VIII	86	28		
IX	112	9	4	

4. *Cat.* Killed on 23rd day. Section of Vth VIth VIIth roots.

V & VI		0		
VII	73	33		

5. *Cat.* Killed on 21st day. Section of VIth VIIth VIIIth roots.

VI	164	17	3	4
VII	173	49	3	0
VIII	70	9	10	2

6. *Cat.* Killed on 24th day. Section of VIIth VIIIth IXth roots.

VII	167	23	21	10
VIII	119	8	4	2

7. *Monkey.* Killed on 28th day. Section of Vth VIth VIIth VIIIth roots.

V, VI & VIII		a few		
VII Upper portion	55	27	14	2

8. *Cat.* Killed on 17th day. Section of Vth VIth VIIth VIIIth roots.

V & VI		0		
VII	112	13		14
VIII		a few		

9. *Cat.* Killed on 12th day. VIth VIIth VIIIth cervical and Ist dorsal root.

Practically no altered cells found.

In addition to the cells of the anterior horn, the small cells present in the posterior horn showed in some instances a similar alteration.

The condition of the opposite side is important; in two cases it was entirely free from any altered cells, in four others a few cells, the total number being under ten, were found which showed the characteristic chromatolysis. In the three other cases a larger number were found; in two instances these were in the VIth segment, in the anterior or median groups—they were present in greatest number in the VIIth segment, and here again at least half were found in the anterior cell group; segments VIII and IX were practically free.

Summary of the result of these experiments.

After section of several posterior roots from the Vth to the IXth post-thoracic inclusive a considerable percentage of obviously altered cells are found, their distribution in the case of the cat is practically limited to the VIIth and VIIIth segments, and especially to the postero-lateral group of cells in those segments.

In the monkey the upper part of the VIIth segment is picked out. The effect is to a very slight extent a crossed one and presents the remarkable feature that more affected cells were found in the VIth segment of the crossed side than on the side of the lesion.

In the cervical region, in one case similar but slight changes were found limited to the VIIth segment; in the other case the spinal cord was practically normal.

Significance of these results.

An examination of a large number of sections from normal spinal cords failed to show cells in any way comparable to those just described and the question of artefaction can, I think, be dismissed.

Neither is the escape of the cerebro-spinal fluid capable of producing any such alteration. Sections cut above the seat of lesion but from a piece of the cord over which the dura mater had been opened always showed the typical normal structure.

With regard to inflammation and disturbance of the blood supply the great number of sections were entirely free from any sign of inflammation or connective tissue change, and except for the presence of the altered cells the side of lesion could not be recognized. I do not think that the connective tissue change is attended by any comparable alteration in the cornual cells. In some sections in which there was proliferation of the tissue of the posterior horn extending inwards in the grey matter, no alteration whatever was observed in the cells. If it produces any change, it is most likely one which causes shrinkage and disappearance of the cells and not an alteration such as that described. That the nerve cells undergo profound alteration in consequence of a disturbance in the vascular system is well known from the work of Munzer and Wiener(2), Marinesco(3), Lamy(4) and Ballet(5).

But certain appearances of the cells noted in my observations are not generally found as the result of a primary vascular disturbance: viz. the eccentric position of the nucleus; the persistence in some cells of the normal arrangement of the chromatic bodies, though these are much reduced in number and driven up to the periphery, the entire absence of vacuolation (see figures by Marinesco and others) and in many instances the maintained integrity of the cell processes.

It may also be pointed out that the only artery divided in the operation is the posterior radicular, a small branch distributed to the caput and posterior root, it does not extend much laterally and is in no relation with the large cornual cells which are almost exclusively supplied by ramifications of the anterior spinal artery.

The view I wish to maintain is that the changes are the result of the withdrawal of the afferent impulses which normally impinge upon the cornual cells. After sections of the posterior roots connected with a limb, the loss of muscular tone is pronounced, the limb is almost flail-like, and in addition to an ataxia, Dr Mott and Professor Sherrington [6] have shown that there is a marked impairment of movement, especially of the hand or foot. Hence the anterior cornual cells must be in a highly altered functional state.

The peculiar distribution of the altered cells affords further support in this view.

First, as regards their marked limitation to the postero-external group.

(1) Histological evidence shows that this group is most richly innervated by the collaterals from the posterior roots.

In the cases of tabes dorsalis presenting muscular wasting, an affection of this group of cells has in several cases been found, and Charcot [7] attributed this to its intimate relation with the reflex collaterals. Schaffer [8] has also adopted this view and has described a case of tabes with atrophy of the peroneal muscles, in which certain cells of the anterior horn showed a chromatolysis.

(2) The cells of the group also are connected with the muscles of the palm and sole, which are concerned in grasping movements of the hand and foot and opposition of the pollex; movements which as shown by Mott and Sherrington cannot be performed by an animal after the section of certain posterior roots.

(3) The observations of the condition of the spinal cord in a large number of cases of old standing amputations uniformly show that the maximum in intensity of atrophy in the anterior cornual cells falls on the posterior external group. This fact led Friedlander and Krause [9] to regard the group as sensory in nature and comparable with Clarke's column.

Homén [10] in a detailed analysis of the condition of the spinal cord in the case of a dog in which he had amputated the thigh 27 months previously shows that the postero-external column was much more affected than any of the other remaining cell groups, and he also found a similar condition in amputation at the shoulder-joint. In such cases any alteration resulting in the cells from destruction of their axons must affect the several groups equally, and I shall show in the second part of this paper that division of an anterior root is followed by changes in practically all the cells on that side of the corresponding segment, and that these changes are not more advanced in any one group. Hayem[11] and Mayser[12] working with the older histological methods showed that a similar localisation of the atrophied cells occurred in the spinal cord, as a result of section of the sciatic nerve; and Dutil using the Nissl method of staining, again found that in a guinea-pig after section of the same nerve, the characteristic changes were chiefly found in the lateral group though more anteriorly.

These observations afford evidence that the postero-lateral group is especially dependent for the maintenance of its functional activity on the integrity of the afferent impulses.

Secondly, the limitation to VIIth and VIIIth post-thoracic segments.

I find again the explanation in the observations of Mott and Sherrington. These observers have shown, in the monkey, that when the Vth, VIth and VIIth post-thoracic roots are divided the sole of the foot is anæsthetic and the defect in movement is extreme, and conversely that, "if the sensory roots of the whole series of the spinal nerves, belonging to a limb be severed, with the single exception of, in the lower limb the VIth post-thoracic (distributed to the whole extent of the foot), a certain degree of impairment of movement of the limb results, which appears rather a weakness than clumsiness, but the degree of impairment is altogether quite slight."

In the cat the corresponding roots are the VIth, VIIth and VIIIth. Further, the VIIth and VIIIth anterior roots are distributed to the muscles which move the foot and digits, the movements of which as just noticed are practically abolished after severance of the afferent roots.

These observations show that the motor cells of the VIIth and VIIIth segments especially depend on the reflex impulses as an incitement to an efficient discharge.

The escape of the sixth segment is interesting, its motor fibres are distributed in considerable part to the extensor muscles of the knee and it is known that extension as a primary reflex movement is most difficult to obtain.

Turning again to the records of the condition of the spinal cord after amputation, though exact statements as to the segments in which the atrophy of the anterior cornual cells occurs are not in most of the cases given, it can be seen that it is especially the lower part of the lumbar enlargement which is involved.

Thus, without attempting any detailed analysis of these cases, I may instance Vulpian's[13] case of amputation just above the left ankle, in which the atrophy of the grey matter was found in the second and first sacral segments.

In two cases of Campbell's[14] of amputation just below the knee the diminution of cells was found in IInd and Ist sacral and Vth lumbar segments. In cases of amputation of the thigh recorded by L. Clarke[15], Dejerine and Mayor[16] the diminution of cells was noted to be limited to the lower part of the lumbar enlargements, in those recorded by Dreschfeld[17] and Reynolds[18] to the lower and middle part of the lumbar region, and in a similar case recorded by Marinesco[19], it is stated that no diminution was noted in the number of the cells higher than the level of the IVth lumbar segment. So also in experimental amputations at the thigh and shoulder-joints in young dogs Homén (*loc. cit.*) notes that the diminution in the number of cells on the side of the lesion was limited to VIIIth, VIIth and VIth post-thoracic segments in the lower limb, to the first dorsal and VIIIth and VIIth cervical in the case of the upper limb.

These cases of amputation show the final results in the several spinal segments which follow interference with a motor nerve cell (*a*) by destruction of its axon, (*b*) by cutting off the afferent impulses, and they show that the atrophy is not uniformly proportional to the extent of the lesion.

At this point it is necessary to refer again to some observations to be described in the second part of this paper, viz. that after division of an anterior root, changes are found in all the cells within a very short time.

At present I have no personal knowledge of the ultimate fate of these cells, assuming that, after amputation of a thigh, for example, and consequent cutting of all the axons of the cells of the various spinal segments connected with the muscles of the limb, an initial structural alteration occurs in these cells, we have to explain why the final result should be practically limited (as far as mere diminution in number) to the postero-external group and to certain segments. The explanation why certain cells are more vulnerable, is to be found I think in their special dependence on the integrity of the afferent impulses, and I wish to emphasise, that the changes described as occurring after section of the posterior roots are of a very different type to those which follow division of an anterior root. They are much more intense, the process of chromatolysis has advanced further and in many cases to such a degree, that all trace of the chromatic bodies is absent and the nucleus has disappeared. Such cells will probably ultimately atrophy and become incapable of recognition.

II.

On the changes that occur in a nerve cell after division of its axon.

That a relation exists between the structure of a nerve cell and the integrity of its axon is shown by evidence of three kinds.

(i) In newly-born animals Gudden long ago showed that section of a nerve trunk gives rise to complete disappearance or perhaps an arrest of development of the cells of origin.

(ii) In adult animals a somewhat similar condition has been noticed if a long time has elapsed since the occurrence of the lesion.

Forel[20] in 1887 cut the facial nerve in two guinea-pigs at the stylomastoid foramen and allowed the animals to live 262 days and 141 days respectively; in both cases he found marked diminution in the number and size of the cells in the side of the lesion.

Darkschewitsch[21] in 1892 also divided the facial and hypoglossal nerves and after six weeks found changes in the nuclei of origin, the cells being diminished in number, atrophied and shrunken. The changes found in the cord after amputations have already been alluded to and evidence adduced to show that one factor concerned in their production is the cutting off of the afferent impulses which normally innervate the anterior cornual cells by means of the reflex collaterals of the posterior roots.

(iii) Nissl[22] in 1892 introduced his method of staining nerve cells by methylene blue, and stated that in so short a period as 24 hours after division of the trunk of the facial nerve an alteration in structure could be found in the corresponding nucleus. The changes described by Nissl may be thus summarised:—After 24 hours the blue bodies may be seen to undergo an alteration at one point in the cell which consists in a loss of their distinctive shape and arrangement and a dispersion over the body of the cell. In from 2 to 3 days this change spreads all over the cell. The Nissl bodies become paler and ultimately take the appearance of minute specks of colouring matter. On the fourth day the whole cell is swollen and more globular and the processes are homogeneous. On the sixth day the cells appear as if uniformly covered over with the finest coloured particles and the processes have disappeared. The nucleus passes towards the periphery and finally disappears. The change takes place with greater rapidity in some cells than others, but at the 18th day all the cells in the nucleus are thus broken up.

Nissl speaks of these changes as produced by a "Methode der primaren Reizung" and regards his observation as having established the fact that the cutting off of a nerve cell from its end organ calls forth regressive changes in the cell in fully grown animals.

A number of observers have confirmed and extended this observation. Van Gehuchten[23] describes and figures changes in the oculomotorius nucleus produced three days after section of the third nerve in the orbit. Bach[24], Flatau[25], Bernheimer[26], and Schawbe[27] have utilised the method as a guide to the localisation of the different groups of cells which compose the oculomotorius nucleus. Marinesco[28] also and Fleming[29] have obtained similar results, and Lugaro[30] has figured changes in the spinal ganglion cells as a result of section of the sciatic nerve. Llewellys Barker[31] in a recent paper refers to this subject and figures markedly altered cells obtained by Erlanger in the case of the facial nucleus after section of its nerve trunk. My own observations have been made in the condition of the spinal cord after section of an anterior root, of the oculomotorius nucleus after intracranial division of the third nerve, and of the facial nucleus after division of that nerve at the stylomastoid foramen.

Section of an anterior root. The cauda equina of a cat was freely exposed by opening up the dura mater, a posterior root pushed aside and the corresponding anterior root severed near the spinal ganglion*. The same precautions as mentioned in the cases of division of the posterior roots were taken. A post-mortem dissection showed that in each of three instances the seventh post-thoracic root had been divided and the completeness of the section was confirmed by the presence of the Wallerian degeneration in all the fibres of the distal pieces of the root. Aseptic healing took place in all the instances quoted.

Exp. 1. Animal killed on the tenth day. Examination of the VIIth segment of the spinal cord. Very few apparently normal cells were met with and these were chiefly small ones. The slightest change noticed and which was also that which occurred most frequently consisted in a loss of any definite arrangement of the blue coloured Nissl bodies. Fine blue granules were uniformly disseminated throughout the cell bodies and hence the cells presented the appearance

* Onufrowitz (*Journal of Nervous and Mental Diseases*, 1895) has also studied the condition of the spinal cord in the lower dorsal region after division of an anterior root. He used vesuvin for staining and found changes somewhat similar to those now described by myself.

of being less deeply stained than normal. In cells of this type the nucleus remains practically normal.

In other cells the alteration was more pronounced; the nucleus was smaller than normal; it had lost its well-defined margin and became wavy in outline and was surrounded by a reddish zone from which chromaphitic bodies were absent. This is a stage of chromatolysis. In a few cells the nucleus had lost its central position and become eccentric.

In rare cases there was an invasion of a disintegrating process of chromatolysis from the periphery.

Exp. 2. Animal killed on the 14th day: the cord presented the same general appearance as in the former case, the change however being a little more advanced. A typically altered cell had the following appearance. The nucleus which was central had lost its definite outline, and its membrane was not visible, the nuclear chromatin had not the ordinary net-like appearance but had the appearance of an irregular homogeneous star-like body. A nucleolus was invisible but several darkly blue stained particles might represent it. Round the nucleus was a space which contained fewer chromatic masses than the periphery; hence it looked reddish but was dotted with a fine dusty blue substance.

The peripheral blue had entirely lost its characteristic striated arrangement and was represented by a diffuse blue mass on which many darker points appeared (see plate).

A small minority of cells showed the process of chromatolysis beginning at the periphery, and in a few the nucleus assumed a distinct eccentric position.

Exp. 3. Animal killed on the 14th day. The changes found were similar in all respects to those detailed above.

Examination of the oculomotorius and facialis nuclei after division of the corresponding nerve trunk.

A detailed account of the results obtained is given below. I wish to emphasize that so far as my own observations are concerned, the resulting changes are much less marked than those described as occurring after section of a spinal anterior root. This is especially so in the case of the IIIrd nerve where the changes are altogether very slight.

At an earlier period of this investigation, in the Report to the British Association, 1897, I stated that I was unable to find in these cells changes corresponding to the descriptions of other observers.

I am still of this opinion as regards the degree of change met with, but further experience, especially that of changes in the spinal cord, leads me to believe that some difference, notably in the manner of distribution and form of the Nissl chromatic bodies, can be made out in the cranial nuclei.

Individual variation no doubt plays a part in the production of these cell changes, but that there may be much difficulty in recognizing them is, I think, shown by the divergent results obtained by Schawbe and Bernheimer in the case of the IIIrd nerve (*loc. cit.*).

Division of the facial nerve at the stylomastoid foramen.

Exp. 1. Facial trunk exposed at its exit from the stylomastoid foramen, and torn out, complete paralysis of the ear, face and lid muscles resulted. Animal killed on the 20th day. An examination of the nucleus of origin showed that in about ⅓ of the cells no change could be detected.

Among the remaining cells several varieties of alteration noted.

(i) The most common is that in which the chromophitic masses, losing their stichochrome arrangement, become dispersed as minute blue particles over the body of cell, the nucleus being situated centrally and normal in appearance.

(ii) A condition almost exactly similar to that described as found in the spinal cord—Exp. 2—with similar alteration in the contour of the nucleus, and the appearance outside it of a reddish zone, indicating commencing chromatolysis.

(iii) Very rarely cells were found exhibiting the eccentric nucleus and disintegration of the protoplasm from the periphery.

Exp. 2. Operation similarly performed, but animal killed on the 14th day. The appearances are almost exactly similar to those detailed above and there is the same proportion of normal cells.

Exp. 3. In this case the facial nerve was divided so that the auricular branch was left intact, the same class of changes found, but almost half of total number of cells appeared normal. An examination of the nucleus of origin on the intact side showed the presence of a few cells whose structure was similar to that of certain of the altered cells in the opposite nucleus.

Division of the IIIrd nerve intracranially.

Professor Sherrington kindly gave me the corpora quadrigemina of a cat and a monkey in which this operation had been done and a third specimen of the oculomotorius nucleus in a cat was prepared by myself.

The corpora quadrigemina of a man in whom the eyeball had been enucleated six months previously, were also examined.

Exp. 1. *Cat.* Killed on the 8th day. The changes are very slight and are just sufficient to enable one to distinguish the side of lesion by examining with a high objective. The characteristic change is again that the blue chromophitic masses lose their striated arrangement and become disseminated throughout the protoplasm as minute bluish particles. In some the nucleus is diminished in size and has a wavy outline, and a few show the type with the eccentric nucleus or with a clear, reddish zone round the nucleus. Among the normal cells of the oculomotorius nucleus the majority show a striated (stichochrome) arrangement of the chromophitic Nissl bodies, but in some these are arranged in the form of a network (arkyochrome), and in the case of cells belonging to this type I find it extremely difficult to say whether there is a distinct alteration in structure of the chromophitic masses.

Exp. 2. *Cat.* Killed on the 16th day. Examination of the nucleus showed an appearance similar to that detailed above, if anything the alteration is less evident.

Exp. 3. *Monkey.* Killed on the 28th day. The changes found in this case are of an entirely different nature and consist of a distinct diminution in number of the cells, throughout the whole length of the nucleus. I am unable to distinguish in any cells changes of a similar character to those described above. In transverse section the oculomotorius nucleus consists of a central and two lateral portions. The diminution in the number of the cells was found to affect the whole of one side with the exception of the upper dorsal group of cells. The central cells were symmetrical.

In this case a proliferation of the connective tissue occurred which was limited to the most anterior part of the nucleus examined, it existed in 40 sections of 7μ each, and in that region almost entirely obliterated the lower part of the dorsal group of cells.

Exp. 4. *Man.* Died 6 months after enucleation of one eyeball. The cells of the nucleus of the IIIrd nerve appear throughout symmetrically arranged and no difference in structure could be noticed on either side of the nucleus. The cells in the middle of the nucleus, which are here larger and more numerous than in the extremities, stain deeply and show a well-defined distribution of the chromatic masses:—towards the limits of the nucleus in either direction the cells are smaller and many of them on both sides possess an eccentric nucleus, while the Nissl bodies are very scanty, the cells in fact presenting appearances similar to those occurring in pathological conditions.

The appearance does not however I think indicate any morbid state, possibly it is a post-mortem change, but the smaller cells of various parts of the nervous system often show similar features even when the tissue is quite fresh. Individual variation has also to be considered. In the case of the monkey mentioned above, two distinct types of cells equally distributed were seen in the oculomotorius nucleus, one more spherical and lightly stained, the other polygonal and deeply stained, but the cells of this nucleus in a second monkey were uniformly of the same type.

REMARKS.

These results agree sufficiently with those of other observers to enable me to accept as a general law that in a cell loss of continuity of its axon is followed by definite structural changes.

Marinesco (*l.c.*) divides the process into two stages.

Reaction:—characterised by a breaking up of the chromatic substance, the nucleus retaining its central position and the cell its normal contour.

Degeneration:—characterised by the occurrence of a *chromatolysis* which begins according to Marinesco and Nissl in the neighbourhood of the origin of the axis cylinder and spreads towards the dendrons. In this stage the nucleus assumes an eccentric position.

In most instances the changes in my preparations have not advanced beyond the first stage. Owing to the large size of the cells, this is specially well seen in preparations of the spinal cord from the first series of experiments. The stage of commencing chromatolysis was reached in a few.

In the case of the facial nucleus again the changes noticed belong chiefly to the stage of reaction, the more extreme changes of the nature of degeneration which from the descriptions and figures of other writers, would appear to be very common, were only rarely represented in my preparations. The same is also true with regard to the oculomotorius nucleus—cells showing signs of the stage of degeneration were practically absent, thus contrasting markedly with the figures published by Flatau, who also divided the IIIrd nerve intercranially.

The condition of the nucleus in the monkey is remarkable. At the end of 28 days there was no trace of any of the changes just enumerated but a distinct diminution in the number of the cells in the side of the lesion.

In the upper part of the nucleus the marked connective tissue reaction which is present would account for this disappearance of cells, but the rest of the nucleus is free from any such invasion.

Is this alteration comparable to that described by Forel and Darkschewitsch (*l.c.*) in the case of the facial and hypoglossal nerves? If so it has certainly occurred at a very early date; Ballet has however as early as 37 days after section of the sciatic nerve found a marked diminution in number of the cells of the anterior horns in the corresponding spinal segment, the remainder showing the normal structure.

The view adopted by this observer was that the atrophy and disappearance represented the final result of the process of chromatolysis.

It is difficult in transverse sections to recognise the various groups which compose the oculomotorius nuclei, but the sections show clearly that the most dorsal (superior) group of cells was least affected and it is probably this region which gives origin to fibres of both IIIrd nerve (Gudden) and hence might *a priori* be expected to suffer least.

In contrast to the results of this experiment is the observation on the condition of the same nucleus in the Human subject. The perfectly normal appearance in this case supports the view put forward by v. Gehuchten at the recent Congress in Moscow, that atrophy of the nucleus of origin after division of the nerve trunk is not yet an established fact.

In conclusion I beg to express my obligation and thanks to Professor Sherrington for his kindness and help, and especially for valuable suggestions in connection with the former part of this paper. My best thanks are also due to Professor Boyce, who has throughout aided me by advice and criticism.

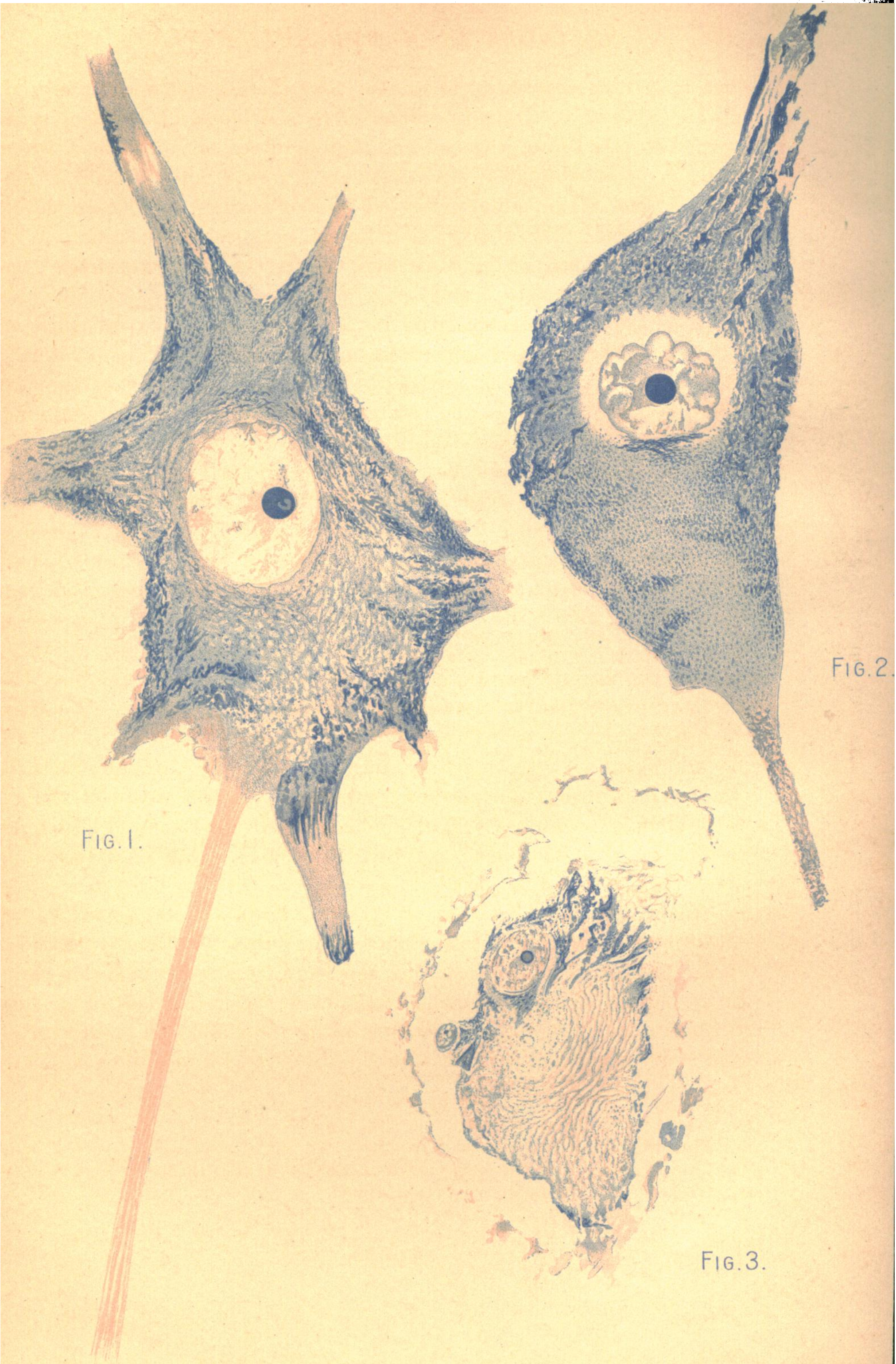
SUMMARY. PART II.

1. Distinct and easily recognisable changes in nearly all the cells of a segment of the spinal cord are found on the side of the lesion after section of an anterior root.

2. Similar but less marked changes follow division of the facial nerve, and still less distinct alteration after division of the oculomotorius nerve.

3. The fate of such altered cells and the ultimate condition of the nucleus of origin are not yet definitely ascertained.

4. The age and nature of the animal experimented on, is a factor in determining the rapidity and degree of alteration met with in the nerve cells.



Edwin Wilson, Cambridge.

PLATE I.

(Drawings made with the camera lucida. Magnification—apochromatic system 3·0 mm. Apert. 1·40. Compensating Oc. 12.)

Fig. 1. A normal anterior cornual cell.

Fig. 2. Anterior cornual cell 14 days after section of the corresponding anterior root.

Fig. 3. A cell from the postero-lateral group of the anterior horn 23 days after section of several posterior roots of the cauda equina.

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