Secondary degeneration following unilateral lesions of the cerebral motor cortex / by Sutherland Simpson.

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(From the Physiological Laboratory, University of Edinburgh.)

Secondary Degeneration following Unilateral Lesions of the Cerebral Motor Cortex.

By

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(With Plates XVI, XVII and 5 Figures in the Text.)

The following paper[1]), which in a more extended form was submitted for the degree of M. D. of the University of Edinburgh last July contains a record of the results of a number of experiments, performed on cats and monkeys. The research was undertaken at the suggestion of Professor Schäfer, to whom I am much indebted for advice and assistance during its prosecution, and its primary object was to determine the path pursued by the fibres of the pyramidal tract, in their course from the cerebral motor cortex to their termination in the lower levels of the brain and spinal cord, but more particularly their mode of ending in relation to the nuclei of the cranial motor nerves in the mesencephalon, pons, and medulla oblongata. Although this — the motor path — has been more carefully investigated, and is probably better understood than any other tract or path in the central nervous system, still much remains to be discovered concerning it, more especially with regard to its terminal connections. In his book on "The Nervous System" (1900) Barker [*1*] says: — "The exact place where the fibres

[1]) An abstract of this paper was read before the Physiological Society on July 20th 1901 and published in the Journal of Physiology. Vol. XXVII. Nr. 142. p. 10.

for these nuclei" (cranial motor nuclei) "leave the main bundles" (of the pyramidal tract) "and the exact path which they follow to the nuclei have not as yet been fully determined." . . . . . "The statement that nerve fibres from these bundles do pass to these nuclei is based mainly, but not solely, upon clinical experience, physiological experiment, and analogy." That is to say, the anatomical connections of the fibres of the pyramidal tract with the cells of the anterior cornua of the spinal cord and of the cranial motor nuclei have never yet been satisfactorily established, and it was with the object of throwing some light, if possible, on this subject that the work embodied in the present paper was undertaken.

Method of Research.

In that part of the research the results of which are contained in this communication, sixteen cats and two monkeys were experimented upon, and in all these an attempt was made to divide the projection fibres arising from the left motor cortex in its whole extent. In other cases, in animals of the same species, partial cortical motor lesions were made, but all the material has not yet been examined, and of these the results will be given later when the whole research is completed. In one case Professor Schäfer was good enough to place at my disposal the brain and spinal cord of a dog in which, in the course of another investigation, he had made a lesion in the left motor cortex so that I might have an opportunity of examining the secondary degeneration resulting therefrom.

Operative Procedure. In each case the animal was fully anaesthetised with ether before the operation was begun, and was kept under the influence of the anaesthetic until it was completed and the wound closed and dressed. The hair was cut short and then shaved off the left side of the skull. A skin flap was reflected and a small trephine opening made through the bone as nearly as possible over the area of the brain which it was desired to expose; this opening was then enlarged with bone forceps, and the dura reflected so as to expose the surface of the brain.

In each of the sixteen cats used the lesion was practically the

same, so that a description of one will suffice for all. It was confined to the left cerebral hemisphere, the object being to divide all the projection fibres arising from the motor cortex in their passage through the corona radiata, and not to injure at all the basal ganglia. After all haemorrhage from the bone had been arrested, sheathed platinum electrodes were applied to the exposed cortex, and the motor area localised by stimulation with a fairly weak faradic current. Without going into details, this was found to be situated in the sigmoid gyrus (around the crucial sulcus) and the anterior portions of the first, second and third convolutions. In the earlier operations, and until some practice had been gained, a formol-hardened brain was kept at hand in order that the convolutions and fissures in the living brain might be the more easily identified. Having localised the area, a fine blunt-pointed bistoury was pushed obliquely downwards and forwards through the grey matter, to the depth of about three quarters of an inch into the white matter, close to the supero-mesial border of the hemisphere, and from one eighth to one fourth of an inch behind the posterior limit of the motor area; it was then carried outwards across the anterior portions of the 1st, 2nd and 3d convolutions almost to the lateral border of the hemisphere, and in this way a deep incision was made cutting across all projection fibres from the motor cortex of the left hemisphere (see fig. 1). The depth of the incision was always gauged on a formol hardened brain before the knife was pushed into the living brain, and care was taken to avoid injury to the large vessels at the base. After the bleeding had completely stopped, the dura was replaced, the skin wound closed with horse hair sutures, and then covered with antiseptic gauze and sealed with collodion.

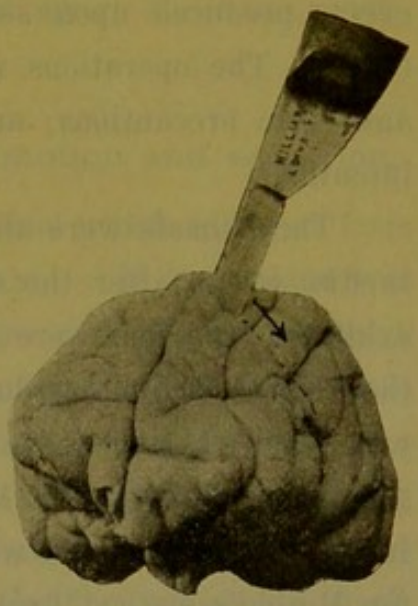

Fig. 1.
Brain of cat (natural size). — Left front view, to show how lesions were made.

In the case of the monkeys an incision was made behind the posterior limit of the motor area on the left side, as in the cats, i. e.

along the posterior border of the ascending parietal convolution from the supero-mesial border of the hemisphere down almost to the fissure of Sylvius. The knife was pushed downwards and forwards into the corona radiata in a slanting direction, and in this way the whole left motor area was "under-cut". This method of "under-cutting" the motor area, instead of completely extirpating it, was adopted in order to avoid, as far as possible, any serious functional disturbance of the hemisphere, vascular or mechanical, with a view to determine the effects produced upon sensation by a lesion limited to the Rolandic cortex. The operations were conducted with the strictest aseptic and antiseptic precautious, and in every case the wounds healed by first intention.

The animals were allowed to live for a period ranging from two to five weeks after the operation, during which time the symptoms exhibited by them were carefully observed and recorded. They were then killed by an overdose of chloroform, the brain and spinal cord was removed, and those parts which were to be examined for degeneration were put into Müller's fluid, the rest being kept in 5% formol. In the later cases the whole brain and cord was fixed in formol, but for Marchi's method fixation in formol was found to give results not altogether satisfactory.

Histological Technique. The method most frequently employed, and finally adopted as better than any other, was that of Marchi slightly modified. After partially hardening the brain or cord in Müller's fluid or a 2% potassium bichromate solution for ten days, it was cut into thin slices — not more than $^1/_{16}{}^{\text{th}}$ or $^1/_8{}^{\text{th}}$ inch thick — and placed in Marchi's fluid (Müller's fluid 2 parts, 1% osmic acid solution 1 part) for other ten days. If large excess is used (not less than twenty times the volume of the tissue) it is not necessary to change the fluid. Ground glass stoppered bottles perfectly air-tight must be employed to prevent evaporation of the osmic acid, and these should be kept in the dark to prevent its decomposition.

With a view to increase the penetrating power of the osmic acid, Orr [2] recommends as a substitute for Marchi's fluid a mixture of osmic and acetic acids, and in order to increase its rapidity of action

Vassale [3] adds to Marchi's solution a small quantity of nitric acid. Both these modifications were tried, but in my hands neither of them has been very successful. My best results have been obtained either with old fluid (i. e. fluid which has been used over and over again), to which a little fresh osmic acid was added from time to time, or by using Marchi's solution prepared from Müller's fluid in which some brain tissue had been immersed for several months previously, a method adopted by Hamilton [*31*] in staining sections. Either of these, I am convinced, will reveal fine degeneration where the freshly prepared Marchi fluid will fail to do so.

Methods of testing effects of lesion on motion and sensation.

In testing the motor and sensory symptoms which followed from the lesions, the method adopted was as follows: — If the animal was tame and quiet, it was taken out of the cage and allowed to move about the room, when its general attitude and mode of walking were observed. In the case of monkeys the manner in which they used their limbs in climbing was noted. To test voluntary power in the arms, the animal (monkey) was offered a small piece of banana or apple, or, a few currants were placed upon the floor within its reach, and its ability or inability to take or pick up these was noted. In the case of the hind limbs, the animal was lifted up, and gently swung towards the wire-netting of the cage, or dropped towards (but not on to) the floor. If the animal possesses the power of voluntarily moving its limbs, both are extended towards the cage or floor, but if voluntary power is absent in one or other of the limbs there is no such movement of that limb. With an animal suspended in this way the paralysed limb hangs pendulous while the non-paralysed limbs are usually drawn up somewhat. Voluntary power is much more easily tested in the monkey than in the cat, but when the latter is suddenly dropped towards the floor (on all fours) there may be no movement of the non-paralysed limb or limbs as a whole, but in the normal animal the toes are always extended and spread out as the foot approaches the floor, i. e. an attempt is made to catch the floor. No such movement of the toes, however, is observed in a paralysed

limb. To test the *grasping power* (in monkeys) a small stick, or preferably the observer's finger, was held out to the animal, and its power of *hanging on* to any object which it had seized, such as the wire netting of the cage, was also noted.

In testing *general sensibility* the part to be examined was touched or stroked lightly (not pricked) with a needle at the end of a long stick, while the attention of the animal was attracted by another person, so that it might not *see* that it was being touched. If tactile sensation is not impaired the animal looks round and withdraws the limb, or indicates by some gesture that it feels the touch. To test whether pain was felt it was pricked with the needle. The plan generally adopted was to test for pain first, for after an animal has been pricked once or twice, it responds more readily to a simple touch probably from apprehension of a prick. The "clip-test" introduced by Schiff, and relied on by Mott [*4*] and others, was also employed, but as pointed out by Schäfer [*5*], it is misleading, and want of response to this test indicates motor rather than sensory paralysis. If a steel clip is applied to the skin while the animal does not see what is being done, an attempt will be made instantly to remove it from a sound limb, but if the limb is paralysed no notice may be taken of it. Often it was found that an animal would respond to a simple touch, while it would take no notice of a clip.

In examining as to whether the sensations of heat and cold were affected, the animal was suspended in a sling-jacket, and when perfectly quiet, a vessel containing hot or cold water was brought up underneath it until the fingers or toes dipped into the water. If sensation was present the limb was withdrawn, or if there was voluntary paralysis of that limb the animal indicated by struggling or otherwise that it felt the hot or cold water. It was found in every case that the animal responded when hot water was applied to the foot or hand, but on the paralysed side the sensation was often delayed for a surprisingly long time, — in some cases as long at twenty seconds. The knee-jerks were tested in the usual way. The temperature of the rectum, axilla, anticubital fossa, groin and popliteal space was taken from time to time, and the condition of the pupils and of vis-

ual sensation, more especially with regard to hemiopia, was also examined. The animal was weighed at regular intervals to test the effect of the operation on its general condition. The results of each examination were recorded on a chart *at the time the observations were made;* these charts were preserved along with the notes of the case, and from them the symptoms are briefly summarised.

Results of Experiments. — Physiological and Anatomical. Cat.

Lesion — Naked-eye Appearances. When the animal was killed and the brain removed, and again after it had been partially hardened in Müller's fluid or formol, the position and extent of the lesion were noted and photographs of the brain were taken. On slicing away the anterior portion of the hemisphere, the gross effects of the lesion could be seen in most of the cases as a reddish-brown patch due to blood extravasation, and the depth to which this extended in the corona radiata could easily be made out. In every case the dura mater was found to be adherent to the surface of the cortex over the sigmoid gyrus and to a greater or less extent of the anterior extremities of the 1st, 2nd and 3rd convolutions on the left side. In one case the mesial surface of the posterior limb of the sigmoid gyrus on the right side was injured. On tracing the lesion backwards into the corona radiata it was found, in two cases, to have involved the head of the caudate nucleus to a slight extent, but in no case was any injury done to the optic thalamus, and in none of the other fourteen cases did the lesion extend as far as the caudate nucleus.

Symptoms resulting from Operation. These were found to vary considerably in the different cases, more especially with regard to the disturbances of sensation. In every case the production of the lesion was followed by motor paralysis of the right limbs. This was quickly recovered from as regards the "associated movements" of walking, running etc. The animals were not examined, as a rule, until the second day after the operation when the effects of the anaesthetic and of the shock had completely passed off, and then, when removed from the cage and allowed to walk about the room they stumbled or fell towards the right side, and when made to jump down from a table

on to the floor they always fell over on the right shoulder. This defect in walking and jumping soon disappeared and within a week, as a rule, no lameness could be detected.

Inability to perform purely voluntary, isolated or unassociated movements persisted much longer, and in several cases this power was not restored before the animals were killed, but in most of the cases where there was a powerful incentive, purely voluntary movements could be performed. If, for example, while food was presented to a cat it was prevented from getting at it with its month or left fore-paw it would stretch out and catch the food with its right (paralysed) paw. Under ordinary circumstances, however, it preferred to use the left paw.

The effects on sensation varied greatly. Tactile sensibility was absent at first in eight of the cases; it was present, but delayed, in two cases; in four cases it did not seem to be interfered with, while in one case there was slight and in another distinct hyperaesthesia on the right side, — the slightest touch of a needle was perceived more readily on the right side than on the left, although the motor paralysis was as marked in these as in any of the other cases. The sensory paralysis passed off much earlier than the motor paralysis, most frequently lasting only three or four days after the operation. In four cases, while the light touch of a needle was felt on both right limbs, the "clip-test" called forth no response on the paralysed side, so that if one had judged by this test alone, one would have come to the conclusion that these animals did not feel tactile impressions. The cold-water test was applied in thirteen cases, and in eight of these there was response at once, while in the other five ice-cold water did not appear to be felt. As is well known, cats are particularly sensitive to cold water applied to their feet. In every case there was reaction to hot water (57° C. — uncomfortably hot for the hand), but often only after a delay of several seconds, and then the animal would appear suddenly to feel it to be very painful. When either hot or cold water was applied to the feet on the left side they were instantly withdrawn, but water at 57° C. did not seem to cause pain as it did on the right side. The knee-jerk was usually

exaggerated on the right side, but in one case it was absent. In the cases in which observations were made, the temperature of the paralysed limbs was from ·5°—1° J. lower than that of the opposite side at first, but in one case it was higher. In four cases there was right homonymous hemianopsia. In two of these, this had disappeared within a week, but in Cats IV and VII it lasted as long as the animals were allowed to live, — 17 and 23 days after the operation respectively. In neither of these cases did the lesion involve the basal ganglia. A photograph of the brain of Cat IV shows the area of cortex to which the dura mater was adherent and the extension of the lesion backwards into the corona radiata (see fig. 2).

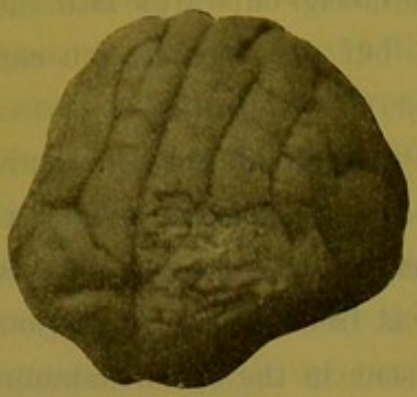

Fig. 2a.
Brain of cat (natural size) to show naked eye appearances. Left front surface view.

Secondary Degeneration. In only two cases — Cat III and Cat VI — was any part of the brain in front of the mesencephalon

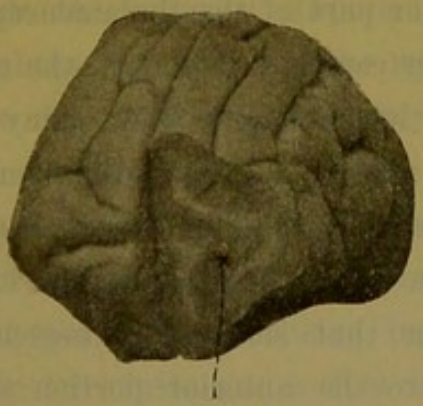

Fig. 2b.

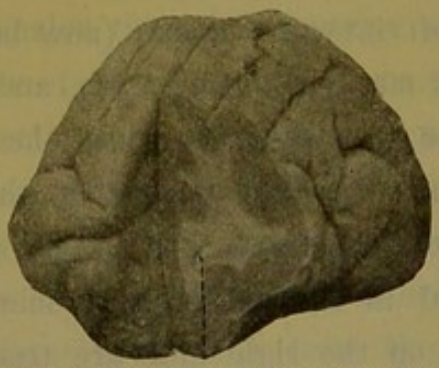

Fig. 2c.

Brain of cat (natural size) to show naked eye appearances. 2b) After anterior part of left cerebral hemisphere has been sliced away. 2c) After a second slice has been removed — the lesion does not extend to the plane of this section.

prepared by the Marchi method. In Cat III coronal sections through the thalamencephalon show degenerated fibres scattered over about the middle $^{3}/_{5}{}^{\text{th}}$ of the internal capsule on the left side; from this area a few degenerated fibres can be seen passing into the optic thalamus, and these latter are most abundant in the sections taken most

posteriorly (i. e. nearest the mesencephalon). There is a slight amount of fine degeneration in the grey matter of the thalamus, also most abundant posteriorly. Longitudinally cut degenerated fibres are seen passing through the corpus callosum and radiating outwards into the centrum semiovale of the right hemisphere, but no degeneration can be made out in the right internal capsule.

In Cat VI in coronal sections through the middle of the optic thalamus the bundles of the left internal capsule contain numerous uniformly scattered, transversely cut, degenerated fibres, except at the superior (posterior in man) extremity which is free from degeneration. A slight amount of fine degeneration is present in the optic thalamus just mesial to the internal capsule. No degenerated fibres cross in the corpus callosum at this level (sections more anteriorly were not examined), but a considerable number are visible in bundles in the inferior (anterior) part of the right internal capsule. (On examining the brain of this animal post-mortem, the mesial surface of the posterior limb of the right sigmoid gyrus was found to be damaged; this would account for the degenerated fibres in the right internal capsule). In sections through the posterior part of the thalamencephalon the left internal capsule (now becoming compacted to form the crusta) shows marked degeneration, and from its anterior portion many fibres can be seen streaming into the grey matter of the subthalamic region and corpus albicans of the same side. Similar fibres are given off from the inferior or mesial portion of the right internal capsule to end in a corresponding manner on that side. The degenerated fibres on the right side are traceable to the anterior portion of the mesencephalon, at which level they occupy a small area about the middle of the right crusta from which many fibres pass into the substantia nigra. In sections posterior to this there is no trace of any degeneration in the right crusta.

In the above two, and in all the remaining fourteen animals, the whole brain behind the thalamencephalon (including mesencephalon, pons and medulla oblongata) cut into thin slices, and segments from the cervical, dorsal, lumbar and sacral regions of the spinal cord were prepared by the Marchi method.

In transverse sections of the mid-brain through the anterior corpora quadrigemina the left crusta is found to be studded with degenerated fibres over its whole area, with the exception of a thin zone along its ventral border which is, in some cases, almost free from degeneration. At this level also the lateral extremity of the crusta is either free from or contains very few degenerated fibres. Numerous degenerated fibres pass backwards from the crusta through the substantia nigra, into and through the tegmentum towards the anterior corpus quadrigeminum of the same side, and in many cases they can be traced to the grey matter of that corpus in which they appear to end; in one or two of the cases a few are seen to curve round close to the posterior (superior) surface, and crossing in the roof of the aqueduct, to become lost in the quadrigeminal body of the opposite side see (fig. 1 pl. XVI). These fibres are present more or less numerously in all the cats experimented upon with two exceptions. In only one or two cases are any fibres seen to enter the grey matter around the Sylvian aqueduct, and these do not appear to end there but to be continued through the lateral portion of it in their course towards the anterior corpora quadrigemina. In most of the cases throughout the whole of the mesencephalon there is a varying amount of fine degeneration in the grey matter of the substantia nigra posterior to the degenerated crusta. In sections of the posterior part of the mesencephalon (through the posterior corpora quadrigemina) the left crusta is degenerated throughout its whole extent, no antero-lateral marginal zone being free as is the case at a higher level. In one or two instances a few fibres pass backwards from the outer extremity of the degenerated crusta into the tegmentum but they can not be traced to any distance, — none can be traced to the post. corp. quad.

Transverse sections at different levels in the pons Varolii show the pyramidal bundles on the left side to be filled with degenerated fibres, — coarse, medium, and fine. In some of the cases a few scattered fibres are seen in the lateral portion of the mesial fillet, behind the degenerated pyramidal bundles. There is very abundant fine degeneration scattered amongst the cells of the nuclei pontis lateral,

anterior and mesial to the pyramidal bundles. This fine degeneration stops abruptly at the middle line, none is visible on the opposite side (see fig. 2. pl. XVI). It is present in every case, and often exceedingly abundant. (Fine degeneration is usually interpreted as terminal degeneration, i. e. the degeneration of collateral or terminal fibres.) No fibres are seen to pass backwards from the pontine pyramidal bundles towards the grey matter of the floor of the 4th ventricle as had been observed from the crusta in the mid-brain, and no fine degeneration is present in that grey matter.

In the lower levels of the pons after the pontine bundles have re-united to form the anterior pyramid (in the cat the anterior pyramids are formed and come to the surface in the lower part of the pons) a few fibres begin to leave the posterior aspect of the degenerated pyramid. Most of these cross the median raphe and are lost amongst the internal arcuate fibres of the formatio reticularis of the opposite (right) side, while some disappear in that of the same side. Similar fibres continue to pass backwards from the degenerated pyramid throughout its whole extent in the bulb until the upper extremity of the true pyramidal decussation is reached. They run, not towards the grey matter in the floor of the 4th ventricle, or around the central canal in the lower or closed part of the medulla, but more lateralwards towards the base of the substantia gelatinosa of Rolando, and they cannot be traced far into the formatio reticularis. No fine degeneration is seen in the grey matter of the floor of the 4th ventricle, in any part of the medulla oblongata, although this was carefully looked for, more especially in the region of the hypoglossal nucleus. Some large pigmented cells, in one or two cases, are present in the hypoglossal nucleus on each side, but this pigmentation, which is not uncommon in the large motor cells of the cat, can easily be distinguished from degeneration by examination with the high power. In many of the cases a few degenerated fibres can be seen, cut transversely, situated in the formatio reticularis, anterior and internal to the base of the substantia gelatinosa of Rolando on the right (opposite) side. These occupy in the upper part of the medulla relatively the position of the crossed (heterolateral) pyramidal fibres in the lower

part, and of the crossed pyramidal tract in the spinal cord. When the motor decussation proper is reached, bundles of fibres are observed to come off from the postero-internal angle of the degenerated pyramid, and after crossing the middle line, to pass backwards towards the lateral portion of the grey matter around the central canal, and then to curve more outwards and become lost as they turn caudalwards in their passage towards the lateral column (crossed pyramidal tract) of the spinal cord. I have seen very few fibres passing in a similar direction from the degenerated pyramid towards the same side (homolateral) until the middle of the decussation is reached, and from this level downwards these homolateral fibres increase in number (fig. 5. pl. XVI). Redlich [*6*] says these homolateral fibres come off in greatest abundance from the middle $^{2}/_{4}^{\text{ths}}$ of the decussation. When this region of the medulla oblongata (pyramidal decussation) is cut serially, they are missed in several consecutive sections and then appear again. This is due to the fact that they come off in small bundles comparatively widely separated from each other vertically. The ratio between the decussating and non-decussating fibres vary considerably in the different animals, but the relative numbers can only be known by counting the fibres on each side in sections through the upper cervical cord, and not by comparing the two sides in any one section through the decussation. Down to the level of the pyramidal decussation a few black dots had been observed in transverse sections of the pyramidal tract of the side opposite to the lesion in several of the earlier animals, but whether these represent degenerated fibres or are merely accidental it is difficult to be certain. In material prepared later in the research when more experience had been gained in the technique, the degeneration was almost invariably wholly unilateral down to the level of the decussation.

In the cervical region of the spinal cord the degenerated crossed pyramidal tract occupies a comparatively small rounded area (relatively much smaller than in the monkey) in the posterior part of the right lateral column, close to the antero-lateral aspect of the posterior horn, and not reaching the margin of the section. From this tract, in many of the cases, a few degenerated fibres are seen to pass in to-

wards the base of the posterior horn and a varying amount of fine degeneration is present in the grey matter of this region (fig. 4. pl. XVII). A few homolateral or uncrossed degenerated fibres, varying in number in the different animals, occupy a corresponding position in the lateral column on the side of the lesion. In the dorsal, lumbar and sacral regions (figs. 5 and 6. pl. XVII), (beyond the 4th sacral segment no section was examined) fibres representing both direct and crossed lateral pyramidal tracts are present in gradually diminishing numbers. In most of the cases the direct lateral pyramidal tract (homolateral fibres) is still represented at the level of the 4th sacral segment. In sections through the lumbar enlargement a few fibres can be made out on the right side passing from the degenerated crossed pyramidal tract into the grey matter at the base of the posterior horn. In no case was there any evidence of a direct (anterior) pyramidal tract.

I had intended to count the degenerated fibres at different levels in order to find out in what regions throughout the brain and spinal cord they disappear in greatest number, but on making the attempt I found that the time and means at my disposal would not admit of this being done with any degree of accuracy.

Dog.

Lesion. A description of the lesion and the symptoms following, it in the dog examined by me, are given by Professor Schäfer in the Proceedings of the Physiological Society, Jan. 26th 1901. It is as follows: — "In the dog experimented on, a cut 5—7 mm deep was made well around the sigmoid gyrus. The result of this was to produce paralysis for voluntary motion (inability to hold a bone, awkwardness in walking) and blunted sensibility on the opposite side, and also at first homonymous hemianopsia, which however had disappeared by the 5th day. The animal was killed one month after the operation; the circumsected area gave no result on stimulation."

Secondary Degeneration. Coronal sections through the posterior part of the optic thalamus and internal capsule show the bundles of the internal capsule on the left side markedly degenerated throughout its middle three-fifths, and from these bundles fibres pass into the grey

matter of the optic thalamus in the outer or lateral half of which they appear to terminate, and there is a considerable amount of fine degeneration in this region of the thalamus. The internal capsule on the opposite side is quite free from degeneration as also is the grey matter of the optic thalamus of that side. In sections taken more posteriorly through the subthalamic region the same fine degeneration is seen in the grey matter on the left side with fibres passing into it from the internal capsule.

In the upper levels of the mesencephalon the left crusta shows extensive degeneration which does not involve its lateral and mesial extremities. Several detached bundles of degenerated fibres, cut transversely, seem to be passing downwards in the substantia nigra lying behind the left crusta, and there is a slight amount of fine degeneration scattered amongst the grey matter of the substantia nigra. No fibres can be made out passing backwards into the tegmentum, as was the case in most of the cats examined. No fine degeneration is visible in the central grey matter or in that of the anterior corpora quadrigemina.

In sections through the upper, middle, and lower levels of the pons the pyramidal bundles on the left side are extensively degenerated, and all around these, but more especially on the mesial and antero-lateral aspects, there is very abundant fine degeneration amongst the cells of the nuclei pontis. This fine degeneration is exceedingly well marked in the dog (figs. 7 and 8. pl. XVI). In the medulla oblongata above the pyramidal decussation, as in the cat, a few fibres are seen to leave the posterior aspect of the degenerated pyramid; some crossing the median raphe are soon lost amongst the internal arcuate fibres of the opposite side, while a very few disappear in the formatio reticularis of the same side. In sections through the pyramidal decussation crossed (heterolateral) and uncrossed (homolateral) bundles come off from the degenerated pyramid and curve backwards and outwards through the central grey matter towards the lateral columns of the opposite and of the same side respectively, to take up a position corresponding to that of the lateral column in the spinal cord. The homolateral fibres are only seen in small fasciculi in sections

through the lower half of the decussation; above that level they consist of isolated fibres.

In the spinal cord sections through the 1st cervical segment show the degenerated crossed pyramidal tract occupying a rounded area in the posterior part of the right lateral column, in close contact with the lateral border of the posterior horn and well removed from the periphery of the section. One or two detached bundles are seen within the grey matter at the base of the posterior horn. There is a considerable number of degenerated fibres scattered throughout an area on the left side corresponding to that of the crossed pyramidal tract on the right. Neither at this nor at any other level of the spinal cord is there any trace of a direct (anterior) pyramidal tract. In sections through the 6th cervical segment the right crossed pyramidal tract occupies a comparatively small rounded area in the posterior part of the lateral column, but it does not reach the posterior horn and there is a considerable space between it and the margin of the section free from degeneration. About a dozen degenerated fibres can be counted in the crossed pyramidal tract on the left side. In the mid-dorsal region and at the level of the 3rd lumbar segment the crossed and direct lateral pyramidal tracts are visible, the number of fibres in each gradually diminishing. In all the regions of the cord examined the crossed pyramidal tract occupies a comparatively small area but this may possibly be due to the lesion not having involved all the cortico-spinal fibres. In the lumbar region some fine degeneration is present at the base of the posterior horn on the right side.

Monkey. Case I. Macacus Rhæsus. Male. Lesion. This was produced as already described, and was found to involve the whole left Rolandic area. The animal was killed 31 days after the operation.

Symptoms during Life. There was loss of voluntary power in both right limbs; the grasping power was feeble and there was marked right sided weakness in walking and climbing. The lameness gradually disappeared after the first few days, but true voluntary power did not return. Tactile sensibility was present from the first in the right arm, but absent in the right leg, and a pin prick appeared to cause pain in both right limbs. Until the 12th day after the oper-

ation no notice was taken when cold water was applied to the right hand or foot, although when applied on the left side the limbs were withdrawn at once. Water at 57° C. was aways felt, but in the case of the right foot only after a delay of 6 seconds. There was no hemiopia.

Secondary Degeneration. Coronal sections were made through the thalamencephalon about the middle of the optic thalamus, but as these had been imperfectly penetrated by the osmic acid, the amount of degeneration in the internal capsule can not be properly estimated. There is, however, mesial to the capsule, in the lateral part of the grey matter of the thalamus very extensive fine degeneration.

In the midbrain the left crusta contains degenerated fibres studded uniformly over its middle three-fifths, the lateral and mesial fifths being practically free from degeneration. There is a slight amount of fine degeneration in the substantia nigra of the same side. No fibres are seen passing backwards from the left crusta into the tegmentum either towards the anterior corpora quadrigemina or towards the central grey matter. The cells of the 3rd nucleus are well seen on each side but no fine degeneration is visible amongst them.

Throughout the pons at the various levels, as in the cats and dog examined, there is a large amount of fine degeneration scattered around the pyramidal bundles on the left side; this is most marked on their mesial aspect and is strictly limited to the left side, none being visible across the middle line (figs. 9 and 10. pl. XVI). The bundles of the pyramidal tract on the left side contain very thickly scattered degenerated fibres, which however, are less abundant in the more laterally placed bundles than in the rest.

In the upper parts of the medulla oblongata a few fibres can be seen coming off from the degenerated left pyramid and passing into the formatio reticularis of the opposite and of the same side; these are directed not backwards towards the grey matter occupying the floor of the 4th ventricle but more lateralwards as in the cat and dog (fig. 11. pl. XVI). A few transversely cut fibres are seen on the right side near the base of the tubercle of Rolando. Sections through the upper levels of the decussation show a few bundles of degenerated

fibres coming off from the left pyramid, crossing the median raphe and then intermingling with bundles of normal fibres from the opposite pyramid; they disappear amongst the internal arcuate fibres on the right side close to the middle line. No homolateral fibres are visible at this level. About the middle of the decussation the pyramid has become much reduced in size, and large bundles of degenerate fibres cross the middle line to interlace with similar bundles from the normal (right) pyramid. Numerous large fasciculi of degenerated fibres cut transversely are situated within the grey matter between the base of the substantia gelatinosa of Rolando and the lateral nucleus on the right side. These consist of fibres which have crossed at a higher level and are now descending to reach the lateral column of the spinal cord, there to form the right crossed pyramidal tract. A very few homolateral fibres are seen passing towards the crossed pyramidal tract of the same side; these are more abundant in sections through the lower levels of the decussation (figs. 12 and 13. pl. XVII). At the level of the second cervical segment of the spinal cord the ratio of crossed to uncrossed fibres is about 100:1.

In sections through the 6th cervical segment of the spinal cord the right crossed pyramidal tract appears as a wedge-shaped area crowded with degenerated fibres, quite unlike the rounded area in the cat and dog, and absolutely, and relatively to the rest of the lateral column, much larger. The direct cerebellar tract lying between it and the margin of the section contains here and there a degenerated fibre but it is practically free from degeneration (fig. 14. pl. XVII). From the inner border of the right crossed pyramidal tract a few fibres, cut obliquely, can be seen passing towards the base of the posterior horn, and a considerable amount of fine degeneration can be made out in the grey matter at the base of the posterior horn, while none is visible in any other part of the grey matter. A few homolateral fibres are present in the lateral column of the left side. About the mid-dorsal region the right crossed pyramidal tract, now considerably reduced in size, extends nearly to the margin of the lateral column, the direct cerebellar tract having almost disappeared at this level. No fibres are seen entering the grey matter (fig. 15. pl. XVII). There are fewer

homolateral fibres than in the cervical region. At the 4th lumbar segment a few fibres can be traced from the degenerated pyramidal tract into the grey matter at the base of the posterior horn, and in this grey matter there is a small amount of fine degeneration. From ten to twenty homolateral degenerated fibres are visible on the left side (fig. 16. pl. XVII). A section passing through the 4th sacral segment (fig. 17. pl. XVII) contains 25 crossed (heterolateral) and 4 or 5 uncrossed (homolateral) pyramidal fibres. There is no evidence of a direct (anterior) pyramidal tract anywhere in the spinal cord.

Case II. Macacus Rhæsus. Male. Lesion. The whole of the left motor area was "under-cut" as in the last case and by a similar operation.

Symptoms. Following the operation there was conjugate deviation of the head and eyes to the left which disappeared after the first day. There was right-sided motor and sensory (tactile) paralysis and right homonymous hemianopsia. (I have no record as to how long these symptoms lasted.) The animal was killed 16 days after the operation.

Secondary Degeneration. In the mid-brain the left crusta is degenerated in its middle $^3/_5$ths the mesial and lateral portions being free, but no fibres can be traced into the tegmentum as in the case of most of the cats examined. There is a considerable amount of fine degeneration in the substantia nigra of the same side. In the pons there is fine degeneration in the region of the nuclei pontis around the degenerate pyramidal bundles on the left side. Sections through the different levels of bulb and spinal cord closely correspond to those already described in Monkey I. This was the first material which I had stained by the Marchi method, and in sections of all the regions below the mid-brain there was a general precipitation throughout, due to faulty technique, but this can be easily distinguished from the degeneration.

In all the cases (cats, dog and monkeys) the degenerated pyramidal tract was atrophied and appeared distinctly smaller to the naked eye than the normal tract on the opposite side. Nowhere was

the transverse section of the tract filled entirely with degenerated fibres, but there was always a varying proportion of normal fibres intermingled with those degenerated.

Summary of Results and Comparison with those of former Investigators.

1. Physiological. A complete severance of the projection fibres arising from the motor cortex of one cerebral hemisphere, with as little injury to adjacent parts as was practically possible, was found to be followed by motor paralysis of the opposite side of the body. This was recovered from almost completely in the cats, and to a large extent in the monkeys, so far as "associated movements" were concerned (walking, climbing), but the power to perform purely voluntary movements did not, as a rule, return during the time the animals were under observation. In the case of the cat, however, if the stimulus was very powerful, apparently voluntary movements were often executed with the paralysed limb; e. g. if the cat was prevented from getting at food with its left fore-paw it would use its right, although under ordinary circumstances it preferred to use the left. In the cats "associated movements" were recovered much earlier than in the monkeys.

Regarding the effects of the lesion on sensation there was not the same constancy. Frequently there was deficient or abolished tactile sensibility on the paralysed side, but in many cases this was not so, and in one or two cases there seemed to be hyperaesthesia. As a rule, sensation when absent or deficient was very quickly restored. In no case was heat sensibility absent although almost always delayed. In four cases there was hemianopsia. As a rule the temperature of the paralysed limbs was lower than that of the opposite side, but in one case it was higher. These differences in temperature between the two sides of the body soon vanished, indicating that the vasomotor disturbances which had probably caused it had passed off. The knee-jerk was almost always brisker on the paralysed than on the non-paralysed side.

The cases described emphasise the fact that there is no direct

relationship between the motor and sensory paralysis on the affected side of the body, and that therefore the motor cortex cannot be the sole seat of tactile sensation as advocated by Munk [7], Mott [8] and others, but that this must be sought for in some other part of the cortex. The transient sensory disturbances that often follow motor cortical lesions, may, as pointed out by Schäfer [5], be due to slight unavoidable injury to other parts of the hemisphere, or to altered vascular conditions produced by the operation, and when these conditions return to the normal the sensory paralysis passes off while the motor remains. They may, however, have a more far reaching cause as is shown by the fact that they are often accompanied by hemianopsia. This has been recorded by Mott [4], and by Ferrier and Turner [9], and has recently been emphasized by Hitzig [10].

2. *Anatomical.* Briefly stated, as a result of complete left motor cortical lesions in the cat, dog and monkey, in addition to degeneration of the main pyramidal tract in the internal capsule, crusta, pyramidal bundles of pons, and anterior pyramid in the medulla oblongata on the left side, and in the crossed pyramidal tract of the spinal cord on the right side, fine or terminal degeneration was present in the optic thalamus, substantia nigra, grey matter of the anterior corpus quadrigeminum and of the nuclei pontis on the left side, and in the grey matter at the base of the posterior horn in the cervical and lumbar enlargements of the spinal cord on the right side. A few fibres could be traced from the degenerated tract into the optic thalamus and substantia nigra, and numerous fibres were found to pass from the degenerated crusta to the anterior corpus quadrigeminum of the same side where they appear to end, while a few cross the middle line in the rôof of the aqueduct to the anterior corpus of the opposite side. These fibres to the ant. corp. quad. were only found in the cat. No degenerated fibres could be made out passing to any of the cranial motor nuclei and no fine degeneration was found in these nuclei or in any portion of the central grey matter around the Sylvian aqueduct, or in the floor of the 4th ventricle. In the medulla oblongata above the crossing of the pyramids a few fibres could be traced from the degenerated pyramid for a short distance

into the formatio reticularis of the opposite side and still fewer into that of the same side. In the lower levels of the decussation a few small bundles of degenerated fibres (homolateral) passed to the crossed pyramidal tract of the same (left) side, and in the spinal cord a few fibres forming a direct lateral pyramidal tract were seen which were traced as far as the 4th sacral segment. No direct anterior pyramidal tract was found in any of the animals examined.

With regard to the connection between the grey matter of the optic thalamus and the pyramidal tract Monakow [*11*] as early as 1884, employing the method of von Gudden [*12*], removed the motor area on one side in rabbits and cats, and as a result found, amongst other things, atrophy of the grey matter of the optic thalamus of the same side. Amongst recent observers Boyce [*13*] in the cat, in 1894 and Mellus [*14*] in the monkey, in the same year, both using the method of Marchi, were able to trace fibres from the pyramidal tract into the optic thalamus of the same side.

Many investigators have found either atrophy of, or fine (terminal) degeneration in the substantia nigra in relation to the degenerated crusta according to the method employed. Monakow [*11*] in 1884 in rabbits and cats, Sherrington [*15*] in 1890 in monkeys, Langley and Grünbaum [*16*] in the same year in a dog, Mellus [*14*] in 1894 in monkeys, and Dejerine and Long [*17*] in 1898 in the human subject, have recorded their observations on this point.

Fibres passing from the crusta to the anterior corpora quadrigemina have been previously observed by only two workers so far as I know, viz: — Muratoff [*18*] in 1893 and Boyce [*13*] in the following year. Boyce describes them in two cats as isolated fibres coming off from the outer extremity of the degenerated crusta and curving round to the quadrigeminal region. Muratoff figures them as passing towards the lateral border of the central grey matter. I have not found these fibres in the dog or in either of the two monkeys which I have examined, but they were present in 14 out of the 16 cats experimented upon, and in several cases they were very numerous. They do not come off from the outer extremity alone, as stated by Boyce and Muratoff, but from the whole posterior aspect of the de-

generated crusta. What particular region of the cortex they take origin from has not been determined and what their significance is I am unable to say. It may be that they are indirectly connected through the grey matter of the anterior corpora quadrigemina with the nuclei of the nerves of the eye muscles situated in this region (nuclei of 3rd and 4th nerves); that is, short neurones may be interpolated between the terminations of these fibres in the anterior corpora quadrigemina and the cells of origin of the fibres of the oculomotor and trochlear nerves. In this connection it will be interesting to determine whether they come from the "head and eyes" area of the motor cortex. Another possibility is that they end in relation to the cells of some other tract or tracts which take origin in the anterior corpora quadrigemina and pass down to lower levels. These are points still to be investigated.

No one, so far as I know, has previously called attention to the exceedingly large amount of fine degeneration which occurs amongst the cells of the nuclei pontis following motor lesions with the exception of Dejerine and Long [*17*] in an article published in 1898. This contains a record of the examination of material from five cases of cerebral hemiplegia suitable for the Marchi method. They say: — "In the grey substance of the pons the very fine and very numerous granules which we have observed in two of the cases indicate a degeneration of collateral and terminal fibres at this level, and this fact explains to us the atrophy of the grey substance of the pons which one sees in old degenerations of the crus cerebri." Sherrington [*15*] (1890) states that — "the islanded grey masses in the pons lying close to the fibre bundles of the crustal tracts among the deep transverse pontal fibres" in monkeys is one of "the regions of grey matter in which in association with pyramidal degeneration, scattered fibres may be found degenerated". This was before the Marchi method had come into general use, and these fibres probably did not represent terminal degeneration. In all the animals I have examined this fine degeneration has been present, and often exceedingly abundant; it is strictly confined to the side of the pons homolateral with the lesion. It is a well known fact that atrophy of the nuclei pontis follows degene-

ration of the crusta, and that, therefore these cells have some connection with the motor tract, but the extent and importance of this connection seems to have been overlooked by most neurologists.

With regard to the question as to whether fibres from the pyramidal tract pass directly to the cranial motor nuclei there seems to be much difference of opinion amongst investigators. Mellus [*14*] in monkeys, Romanow [*19*] in dogs, Hoche [*20*], and Barnes [*21*] in the human subject, all using the Marchi method, say that they have been able to trace fibres from the degenerated pyramid to the motor nuclei, — most crossing the middle line to the nuclei of the opposite, a few passing to those of the same side. On the other hand, Boyce [*13*], Dejerine and Long [*17*] and others expressly state that they have failed to find any fibres passing to these nuclei. In several animals I have made serial sections from the upper limit of the mesencephalon to the lower limit of the bulb, and in not one have I found degenerated fibres passing to any of the cranial motor nuclei. This is all the more surprising considering the ease with which such fibres could be traced of the anterior corpora quadrigemina. No fibres could be seen to pass backwards from the pyramidal tract, with the exception of those to the ant. corp. quad. till the lower levels of the pons were reached, and below this throughout the whole extent of the medulla oblongata, and not alone opposite any particular nucleus a very few fibres continued to be given off chiefly from the postero-mesial angle of the degenerated pyramid. Most crossed the middle line at once, disappearing in the formatio reticularis of the opposite side, comparatively few being lost in that of the same side. On comparing some of my sections with the figures given by Muratoff [*18*] and by Romanow [*19*] in their papers (on which presumably these observers base the statement that fibres from the pyramid pass to the motor nuclei in the medulla and pons) I found that there was a very close resemblance. It will be seen from these figures, three of which I here reproduce, that as in the sections I examined, the fibres in question are not directed towards the grey matter in which the cranial nuclei are situated, but seem, for the short distance to which they can be traced, to pass more lateral-wards towards the

substantia gelatinosa of Rolando. They may belong to the spinal motor decussation, being destined for the lateral columns of the spinal cord; that is to say, the pyramidal decussation may not be confined to the lower part of the medulla oblongata, but may occur to a limited extent in the upper part as well, beginning even in the lower part of the pons. In some of the cats, and in one of the monkeys a few transversely cut fibres could be made out in the formatio reticularis anterior and internal to the substantia gelatinosa of Rolando in

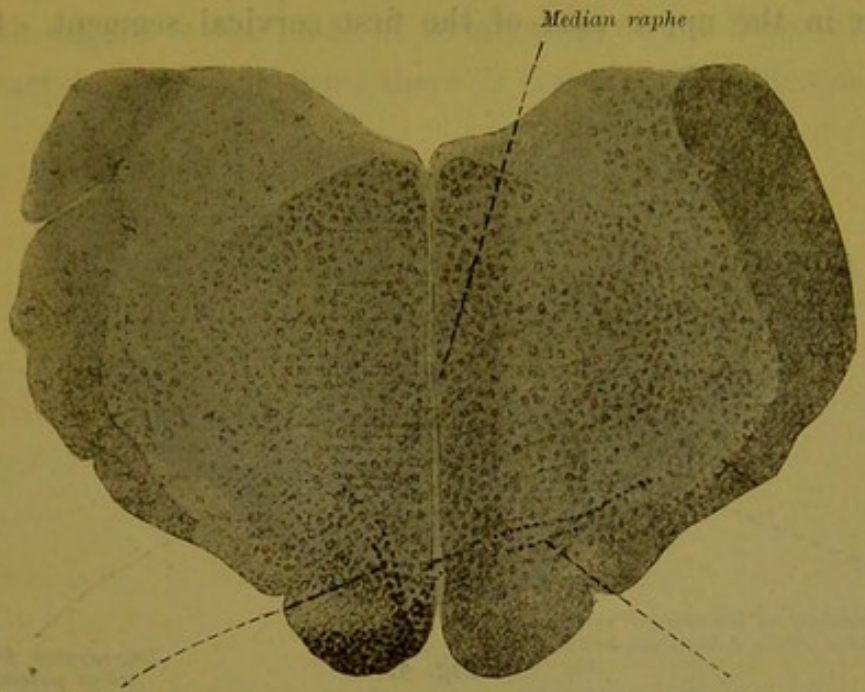

Fig. 3.

Photograph of drawing from Romanow's paper representing fibres passing from the degenerated pyramid to the facial nucleus of the opposite and of the same side.

the bulb on the side opposite to the lesion (fig. 11). These may represent fibres which have decussated at a higher level and are now passing down to join the main mass of heterolateral fibres in the lower part of the bulb. This would explain the significance of Pick's bundle, a fasciculus of fibres first described by Pick [*22*] in 1889, as ascending from the lateral column of the cord and ending in or near the nuclei of the posterior columns. Hoche [*20*] in 1898 described it as a descending tract partly of pyramidal origin and quite recently (1901) Barnes [*21*] has investigated it. He describes it in one case as follows: — "In the lower sections of the medulla are seen degenerated four small bundles of fibres closely massed together at the inner

side of the substantia gelatinosa. Traced upwards these fibres — which correspond to what is usually known as Pick's bundle — become rapidly diffused and lost in the region of the nucleus ambiguus, not a single fibre being visible in this region at the lowest pontine level, and none of them can be seen to cross the middle line. Traced downwards towards the pyramidal decussation these fibres retain their position but increase in number and compactness, lying close to the ventro-lateral aspect of the posterior horn at its junction with the substantia gelatinosa in the upper part of the first cervical segment. Here the

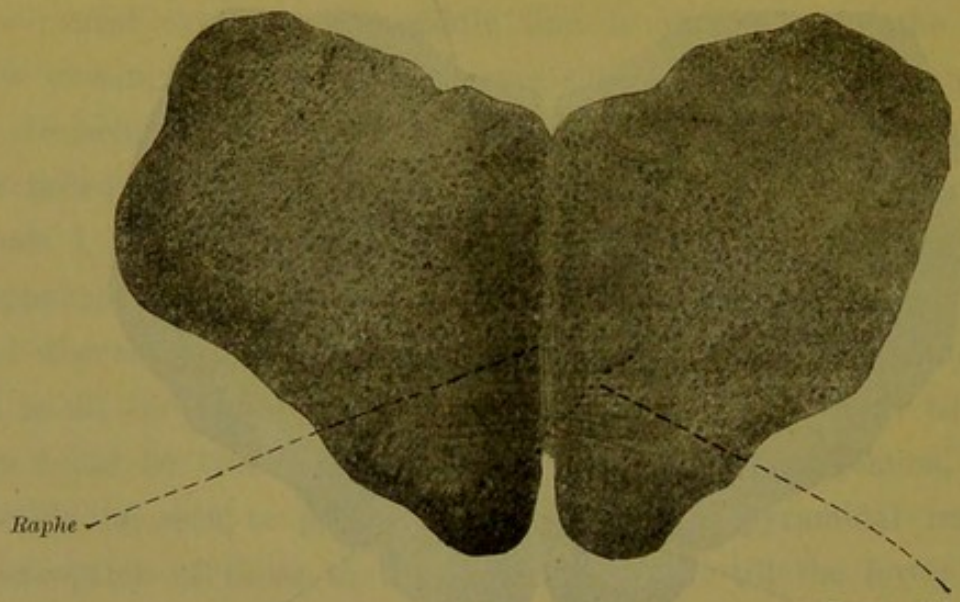

Fig. 4.

Photograph of drawing illustrating Romanow's paper.

degenerated bundle appears to gradually merge into the degenerated crossed pyramid which lies immediately adjacent to it. . . ." He comes to the conclusion that "it is probably an ascending tract which arises from the crossed pyramid at the decussation, and forms at least part of the pyramidal supply of the nucleus ambiguus; it is fairly frequently degenerated in cases of hemiplegia". So far it has only been referred to in the human subject.

Pyramidal degeneration in both lateral columns of the spinal cord, as the result of a unilateral motor cortical lesion, was first recorded by Schäfer [*23*] in a dog in 1883, and also the probable source of the homolateral fibres was first indicated by him, viz: — an incomplete crossing at the pyramidal decussation. In 1884 it was observ-

ed by Pitres [*24*] in the human subject, and in the same year by Langley and Sherrington [*25*] in the dog. Loewenthal [*26*], and again Sherrington [*27*] in 1885 recorded the same in the dog, and since that time it has been observed by almost every investigator, in man and the higher mammals. The actual passage of the homolateral fibres from the pyramidal decussation to the crossed pyramidal tract of the same side was first traced by Muratoff [*18*] in 1893, again by Risien Russel [*28*] in 1894 and by many observors since then.

With regard to the mode of termination of the fibres of the pyramidal tract in the spinal cord there is considerable difference of opin-

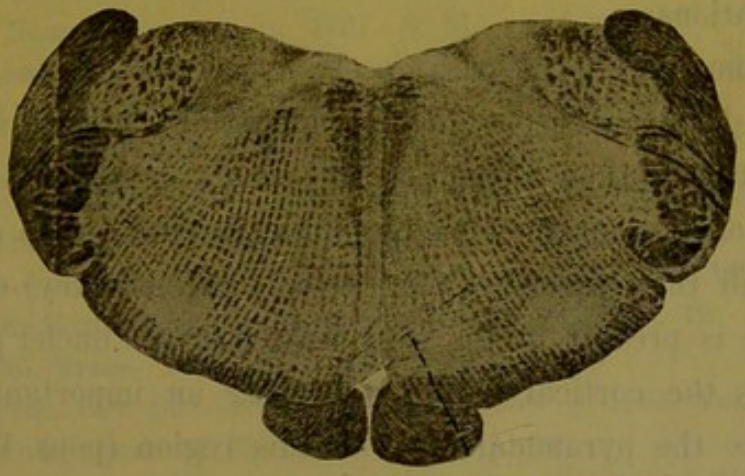

Fig. 5. *Fibres represented as passing from degenerated pyramid to facial nucleus of opposite side*

Photograph from paper by Muratoff.

ion. In 1884 von Monakow [*11*] removed the motor cortex in cats and rabbits (young animals) and as a result found atrophy of the grey matter in the region of the processus reticularis on the side of the cord opposite to the cortical lesion, whereas he could distinguish no difference between the two anterior cornua of the cord the cells and grey matter having quite a normal appearance on the two sides. From this he argued that the pyramidal fibres are directly connected with the grey matter in the lateral horn and not directly with that of the anterior horn. The conclusions he arrived at at that time have been borne out by the results of much work done subsequently, and the whole matter is fully discussed in an extensive article published by him in the Archiv für Psychiat. for 1895 [*29*]. His observations have recently been corroborated by Schäfer [*30*] who as the result of

partial section of the cord, using the Marchi method, found fibres passing from the crossed pyramidal tract into the base of the posterior horn while none could be traced to the anterior horn. The corresponding fibres which I have observed in the cervical and lumbar enlargements were most evident in the monkey but a few could be made out in the cat. They appear not to be so abundant when the lesion is a cortical one as when the cord is hemisected so that in the latter case they may come from more than one source.

In conclusion I would desire to call attention to the following which I consider to be the main points brought out in the course of my investigations: —

1. In the cat, fibres pass freely from the crusta to the grey matter of the anterior corpus quadrigeminum of the same side in which for the most part they appear to end, a few crossing the middle line in the roof of the aqueduct to terminate in that of the opposite side.

2. In all the animals examined (cat, dog, monkey) extensive fine degeneration is present in the grey matter of the nuclei pontis on the same side as the cortical lesion, indicating an important cell-station in relation to the pyramidal tract in this region (pons Varolii).

3. No fibres are seen to pass to any of the cranial motor nuclei, or to the ventral horn of the spinal cord, but a few can be traced into the grey matter of the spinal cord at the base of the posterior horn.

4. A possible explanation of the fibres seen in the upper half of the medulla oblongata leaving the degenerated pyramid and passing to the formatio reticularis of the same and of the opposite side, may be that they belong to the spinal motor decussation and are destined for the lateral columns of the cord. These fibres may correspond to what has been described as Pick's bundle in the human subject.

The drawings were done by Mr. Richard Muir of the Pathological Department of this University and I would take this opportunity of thanking him for the care and accuracy with which he has executed them.

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Description of figures of the Plates XVI, XVII.

Fig. 1. T. S. Mesencephalon of cat at level of root of 3rd nerve showing fibres passing from degenerated crusta on left side to ant. corp. quad. of same side, a few crossing to that of opposite side. × 10 diam.

Fig. 2. T. S. Pons Varolii of cat showing fine degeneration scattered around the degenerated pyramidal bundles on the left side (right in fig.). × 25 diam.

Fig. 3. T. S. Medulla oblongata of cat through lowest part of pyramidal decussation, showing homolateral and heterolateral fibres. × 10 diam.

Fig. 4. T. S. Spinal cord of cat through 6th cervical segment, showing fibres entering base of posterior horn from right crossed pyramidal tract (left side in fig.), and fine degeneration in adjacent grey matter. × 10 diam.

Fig. 5. T. S. Spinal cord of cat through mid-dorsal region shows crossed and direct lateral pyramidal tracts. × 10 diam.

Fig. 6. T. S. Spinal cord of cat through 3rd lumbar segment. Shows crossed and direct tracts with a few fibres passing into grey matter at base of posterior horn on right side. × 10 diam.

Fig. 7. T. S. Pons Varolii of dog showing fine degeneration scattered around the degenerated pyramidal bundles in the nuclei pontis. × 10 diam.

Fig. 8. The same section × 100 diam.

Fig. 9. T. S. Through upper part of pons Varolii of monkey, shows fine degeneration scattered round pyramidal bundles on side of lesion (left). × 6 diam.

Fig. 10. Same section × 60 diam.

Fig. 11. T. S. Medulla oblongata through middle of inferior olive of monkey, showing fibres passing from left degenerated pyramid to formatio reticularis of opposite and same sides. × 6 diam.

Fig. 12. T. S. Medulla oblongata of monkey through upper part of pyramidal decussation. × 10 diam.

Fig. 13. T. S. Medulla oblongata of monkey through lower part of pyramidal decussation. Observe homolateral fibres at this level. × 10 diam.

Fig. 14. T. S. Spinal cord of monkey through 6th cervical segment showing crossed and direct lateral pyramidal tracts with a few fibres passing into base of posterior horn on right side.

Fig. 15. T. S. Spinal cord of monkey — 4th dorsal segment. Shows homolateral and heterolateral pyramidal fibres.

Fig. 16. T. S. Spinal cord of monkey — 4th lumbar segment. Shows a few fibres from degenerated crossed pyramidal tract passing towards grey matter at base of posterior horn. Homolateral fibres are still seen.

Fig. 17. T. S. Spinal cord of monkey through 4th sacral segment. Shows crossed and direct pyramidal tracts still present.

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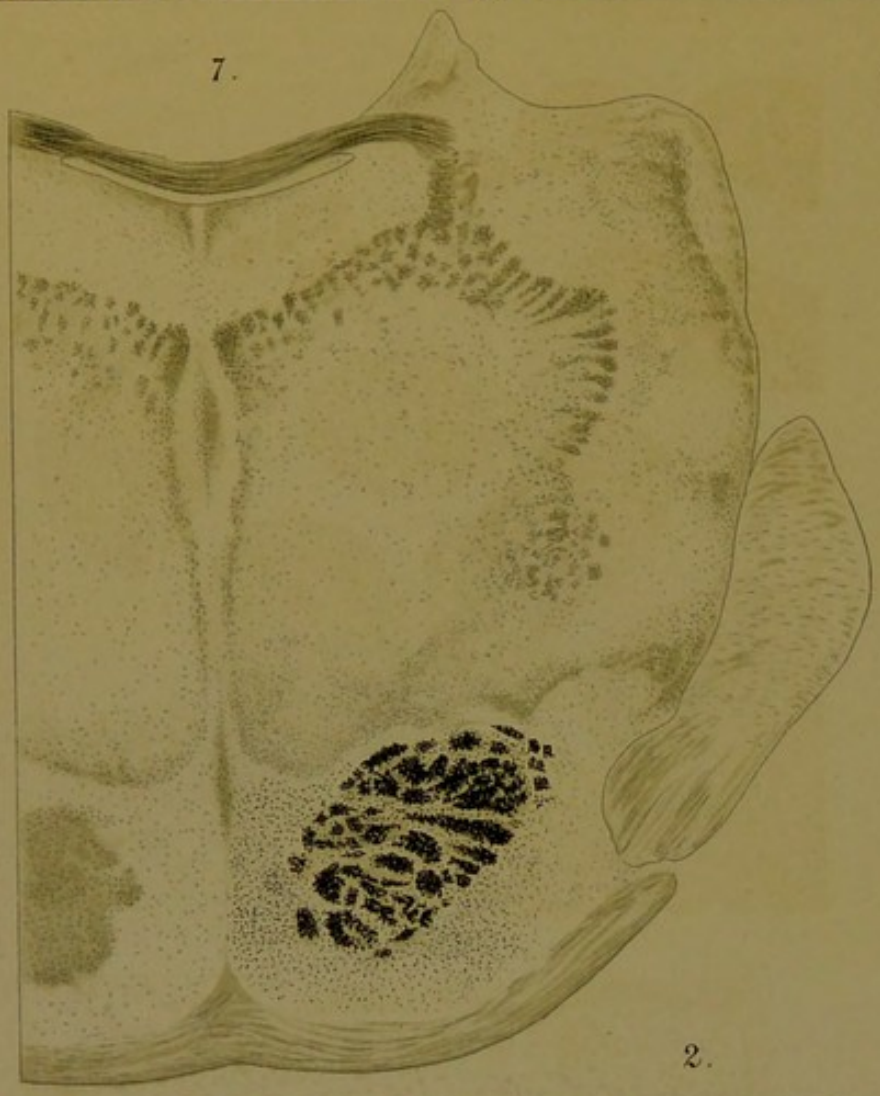

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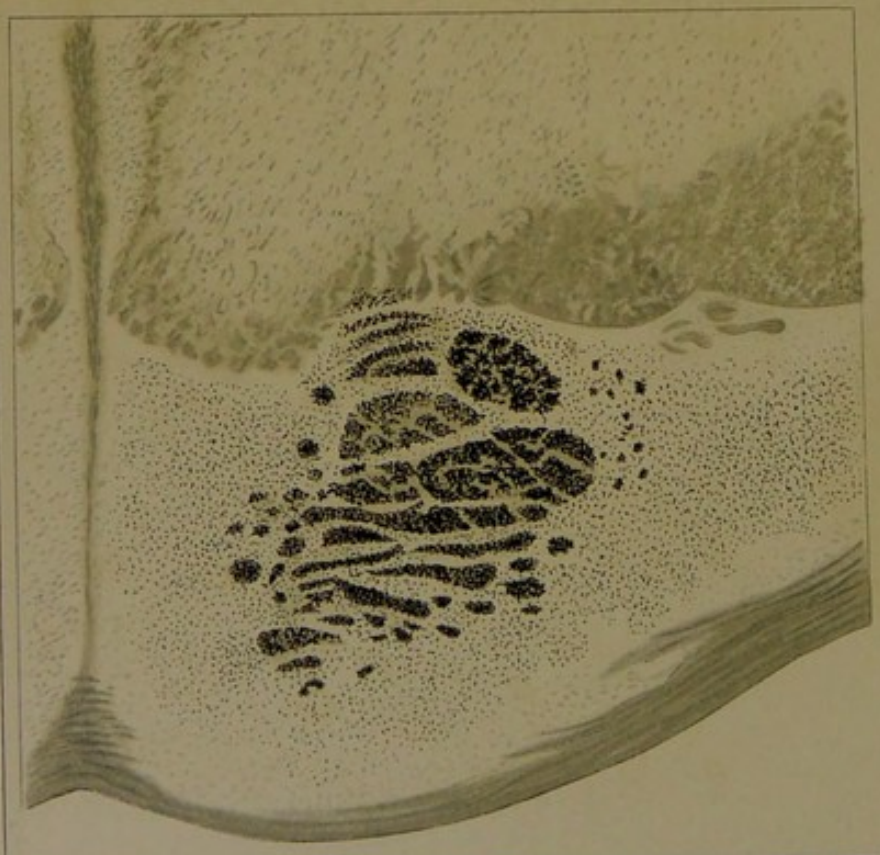

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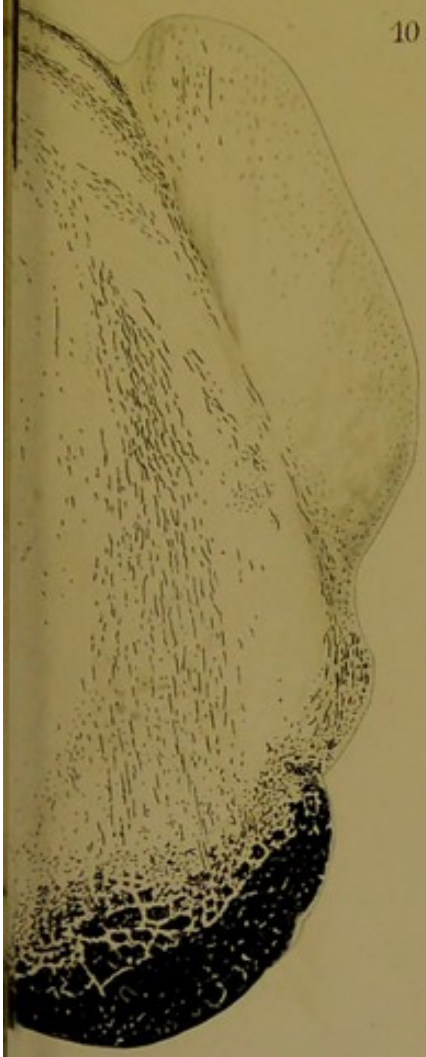

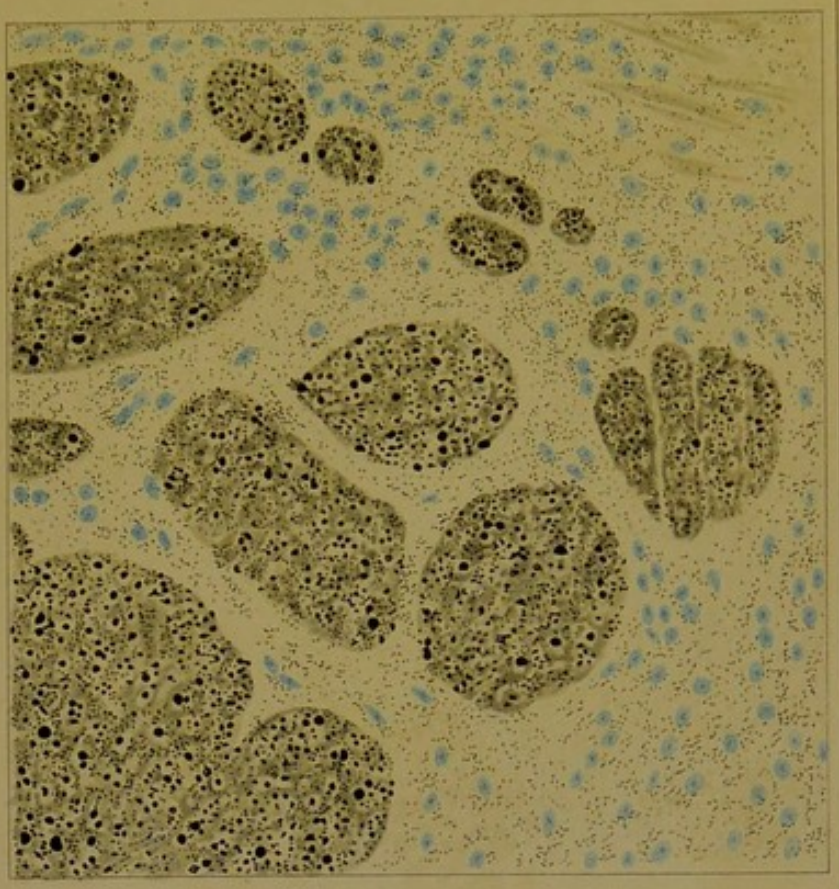

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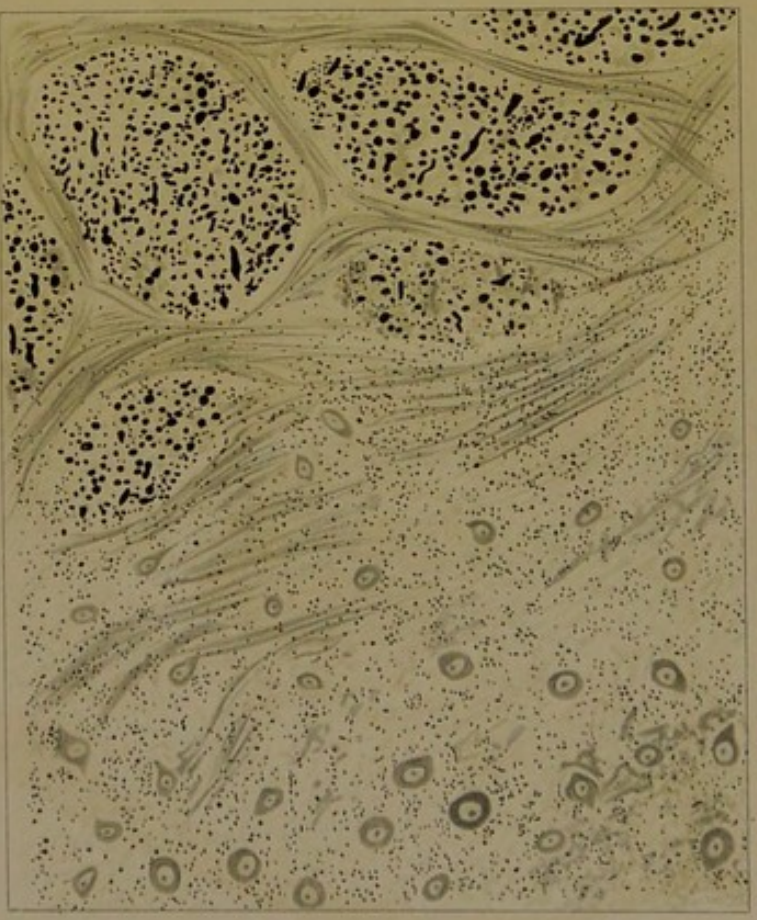
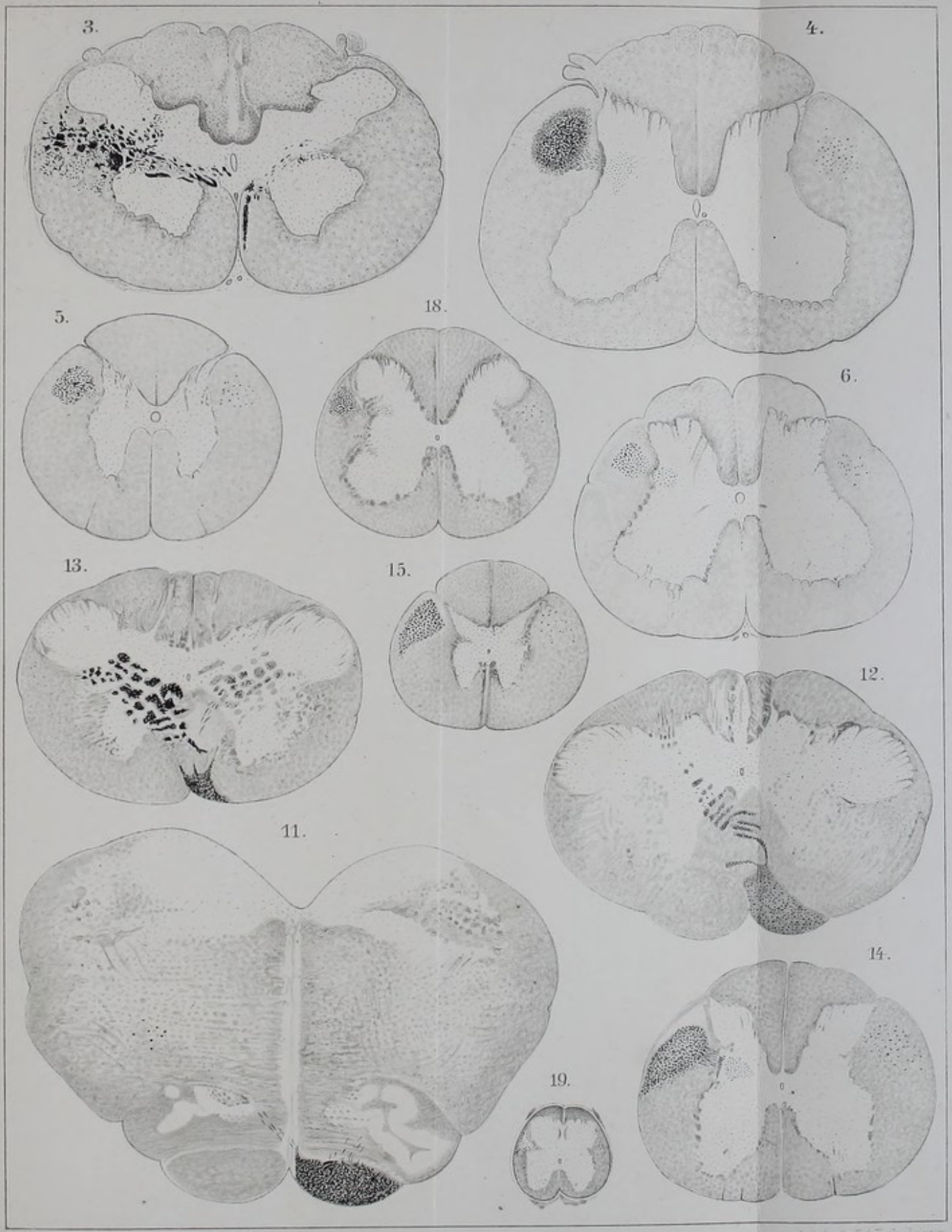


Lith. Anst. v. E. A. Funke, Leipzig.



Sutherland Simpson: Secondary Degeneration following Unilateral Lesions of the Cerebral Motor Cortex.