

MICROGYRIA AND ITS EFFECTS ON OTHER PARTS OF THE CENTRAL NERVOUS SYSTEM.

BY THE LATE W. PAGE MAY, M.D., D.Sc., F.R.C.P.

Fellow and Lecturer of University College, London.

(From the Pathological Laboratory, London County Asylums, and from the Physiological Laboratory, University College, London.)

MICROGYRIA, which has hitherto been usually known under the name of hemiatrophy of the brain or arrested development of the nervous system, has been comparatively rarely described, and merits further study.

The following case came ultimately into the hands of Dr. Mott, to whom I would here cordially express my thanks for kindly allowing me to investigate the material and for many valuable suggestions during the course of the work.

SUMMARY OF THE CASE.

Vascular lesion of the right cerebral hemisphere involving chiefly the right centro-parietal region of the cortex with portions of the frontal and temporal lobes and portions of the right basal ganglia. Atrophy and arrested development of the right pyramidal tract, right mesial filet and associated structures in the mid-brain, pons, medulla and spinal cord. Atrophy of the opposite (left) side of the cerebellum with some of its various nuclei and peduncles. Atrophy of the left side of the spinal white and grey matter. Diminution in number of motor cells chiefly in the cervical and lumbar enlargements.

CLINICAL HISTORY.

Since earliest life the patient had suffered from left hemiplegia and mental hebetude. The mental deficiency steadily increased and became early associated with unilateral and epileptiform convulsions of the ordinary type. Sight and hearing were normal but the above symptoms progressed and terminated fatally in his thirty-sixth year.

Brain.—In the brain the coarse deviations from normal are best seen by a reference to the accompanying photographs. There is a remarkable difference in the size of the two hemispheres, the right being about two-thirds as large

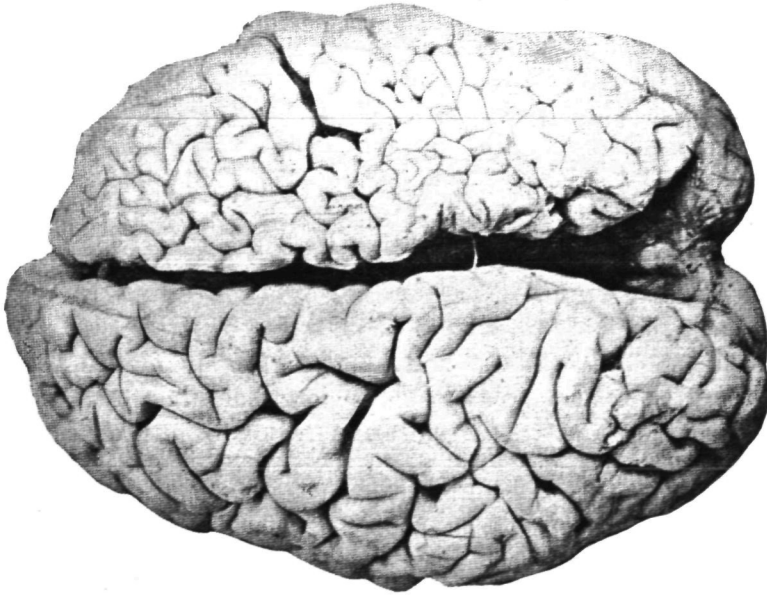


FIG. 1.



FIG. 2.

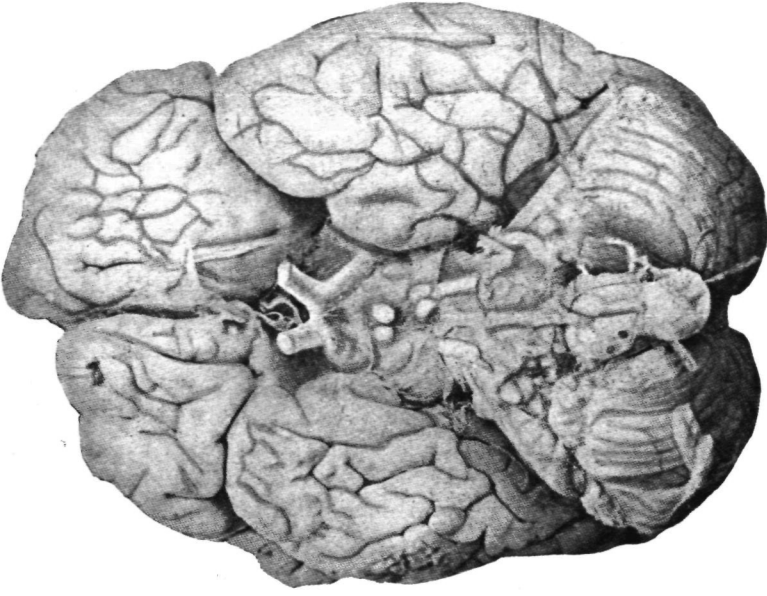


FIG. 3.

as the left, which is normal. The stress of the disease has fallen chiefly on the centro-parietal region of the right side, less on the frontal and temporal and least on the occipital lobe. The convolutions in the affected areas are shrunk in all three dimensions, i.e., they are shorter, narrower and less deep than normal and wanting both in grey and white matter. The corpus callosum is thinner than in health, but the olfactory lobes, optic tracts and cranial nerves are unaffected.

The mode of investigation adopted was to remove pieces of certain selected areas of the cerebral cortex, cerebellum and spinal cord and to stain them by various methods for minute microscopic examination of the cells and fibres. The remainder of the brain and portions of the spinal cord were cut in serial section and stained by the Weigert-Pal process, certain of these sections being again counterstained by alum, cochineal or other suitable colouring matter.

Microscopic examination of the cerebral hemisphere showed that everywhere in the affected region the cortex is thinner than normal and this most of all in the right ascending frontal convolution. All the cortical layers are wasted, but especially the pyramidal and fourth layer.¹ In the leg and body areas the very large, so-called Betz cells are not only much diminished in number and in size but have fewer processes than in health and all of them present some degenerative change. In several sections of this region, only one group of moderately good Betz cells could be found. These were situated on the flat external surface of the right ascending frontal convolution (not in the depth of the Rolandic fissure), and even they were stunted and had fewer processes than natural and showed other signs of degeneration. The right arm area presented much the same appearance as above but the pyramidal layer was not quite so much affected. In the corresponding regions of the left cerebral cortex the histological appearances were normal. The pyramidal and Betz cells were abundant and of healthy structure and no signs of hypertrophy or compensatory overgrowth was traceable. In the right facial area all layers are thin and there are very few large cells in layer '4, whereas the left facial area seems normal. In the right ascending parietal convolution all layers are much wasted except the granular layer, which looks healthy. The right first frontal gyrus has less than half its normal depth and the pyramidal layer is especially poor, whereas the left first frontal is normal. The temporal convolutions are histologically fairly normal, but the pyramidal layer is distinctly better seen in those of the left side than of the right. The visuo-sensory area in the calcarine region of the occipital lobe

¹ The classification of the layers of the cerebral cortex here adopted is that given by Mott [1], at a meeting of the Ophthalmological Society of London, Nov., 1904.

presents no definite abnormal change on either side but in the right visuo-psychic area the pyramidal layer is distinctly poorly developed.

With regard to the changes in the nerve fibres of the cerebrum, it is noteworthy that the incidence of the disease is chiefly on the efferent

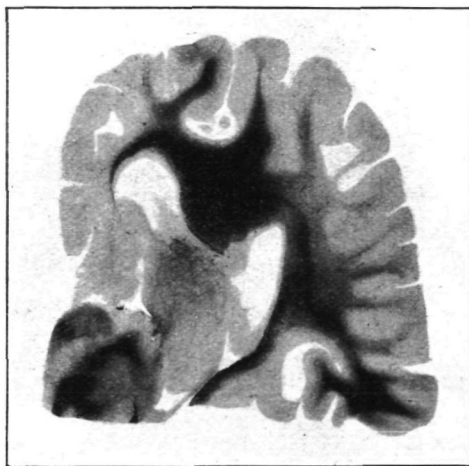


FIG. 4.

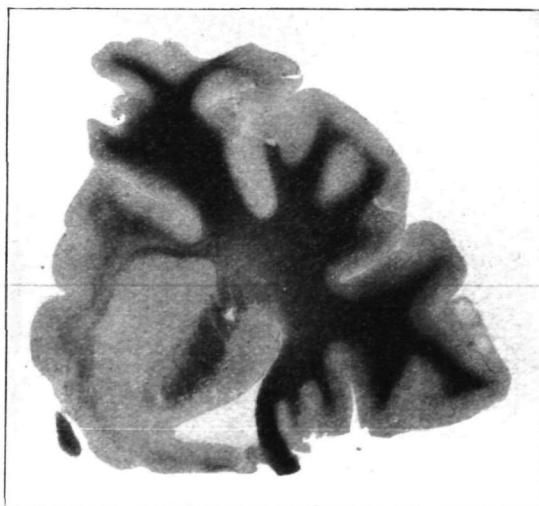


FIG. 5.

projection fibres of the affected side, which are much diminished in number, and present signs of wasting and sclerosis. The tangential fibres of the cortex and the fine network in the inner line of Baillarger

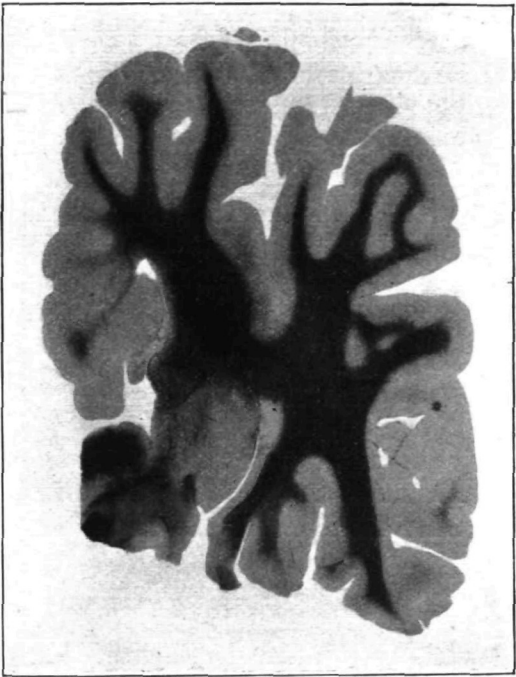


FIG. 6.

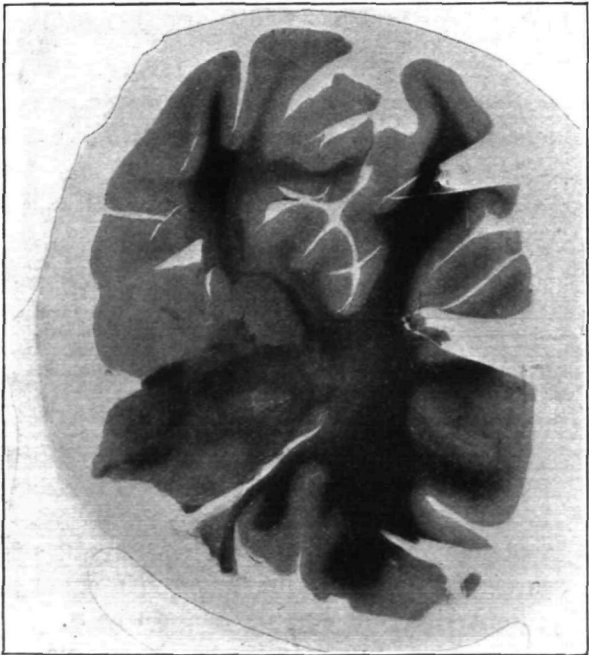


FIG. 7.

are also slightly though definitely affected in the same way. On the other hand, the fibres forming the associational bundles are not at all, or, if at all, scarcely to an appreciable extent.

In the opposite (left) cerebral hemisphere, as already remarked, no compensatory increase of cells could be found, and the nerve fibres seemed in every way normal in number and appearance. The corona radiata on the right side is much smaller than on the left (roughly about half). The right internal capsule is not only much reduced in size in its fronto-caudal plane, but also laterally where its posterior limb (the limb chiefly affected) measures from $2\frac{1}{2}$ to 3 mm., as compared with 5 to $5\frac{1}{2}$ mm. for the healthy side. In its vertical dimensions the right internal capsule is only very slightly reduced. It contains few medullated nerve fibres, and shows all the ordinary signs of atrophy and sclerosis.

The corpus striatum presents only very slight deviation from normal. The nucleus caudatus seems healthy throughout, but the lenticular nucleus, and especially the globus pallidus, are slightly wasted and not quite so rich in fibres as on the normal (left) side. On the affected side the optic thalamus is smaller both antero-posteriorly (i.e., fronto-caudally) and laterally than should be the case, and owing to a marked diminution in the number of its nerve fibres its nuclei are all less distinct than normal. The paucity of fibres is especially striking in the lateral nucleus of the right as compared with that of the left optic thalamus. Moreover, though the right arcuate nucleus is fairly well delineated the "centre-median" of Luys is scarcely traceable, and the red nucleus is less than half the size of that of the right side, and extremely poorly provided with fibres. On the left side the optic thalamus is healthy, and all its nuclei are well seen, notably the dorsal, lateral and median nuclei, the centre of Luys, nucleus arcuatus, and red nucleus and corpus subthalamicum, all of which are well seen and differentiated.

The island of Reil on the right side is smaller than normal, and its convolutions imperfectly developed. The claustrum, together with its capsula externa on its inner side, and its capsula extrema on its outer side, are well marked but slightly thinner than on the normal side. Moreover, the two capsules diminish in thickness from above down (i.e., dorso-ventrally), so that in their lower halves they are scarcely represented, and their junction below at the base of the island of Reil with the inferior longitudinal bundle and the medullary fibres around the anterior commissure is not traceable.

In the right temporal lobe the medullary fibres are generally less numerous than on the normal side, though the auditory radiations

extending as a large bundle of well stained fibres from the lateral margin of the middle geniculate body to the first temporal convolution are well marked. Similarly the general wealth of fibres in the occipital lobe is less than on the normal side, yet the optic radiations extending from the lateral geniculate body around the posterior-descending horn of the lateral ventricle to the visuo-sensory area of the calcarine region are also well marked. Moreover, standing out in marked contrast to the remainder of the fibres of the temporo-occipital lobe, is the inferior longitudinal bundle which has abundant well stained fibres forming in these transverse (frontal) sections a well defined sickle-shaped mass which has its broader end above at the base of the island of Reil, and curves externally around the descending horn of the lateral ventricle, tapering away to a fine point of fibres in the region of the nucleus amygdala.

It will be seen on reference to the accompanying photographs that the third ventricle and the lateral ventricles, with their cella media, are moderately distended. This porencephalic condition still further reduces the space, which in the left hemisphere is occupied by healthy brain tissue.

Midbrain.—On the right side there is marked atrophy of the pyramidal, and less so of the middle fillet fibres. The red nucleus, as previously mentioned, is smaller than normal, and the perpendicular fibres of the crus, especially those lateral to the corpus subthalamicum, are distinctly less numerous than in the healthy hemisphere. The lateral fillet, the middle and lateral geniculate body, the anterior and posterior corpora quadrigemina on the affected side present no deviations from normal.

Pons.—The tegmentum on the right side is smaller than on the left and the middle fillet fibres are here contrasting with the middle fillet in the medulla much wasted and form a band about half as deep and not quite so broad as that of the opposite side. Also the longitudinal fibres in the mesial portion of the middle fillet are notably very much diminished in numbers, so that the nucleus reticularis tegmenti seems not only to occupy the position which should be chiefly filled by them, but actually to extend laterally, forming a thin band of grey matter with middle fillet fibres dorsally and ventrally to it. The central tegmental tract and the posterior longitudinal bundle seem slightly smaller on this side than on the left, whereas the fibræ paramedianæ are slightly less marked and the superior cerebellar peduncle distinctly less marked on the left side than on the right. The lateral fillets and

lateral pontine bundles are equal on the two sides, and with the above exceptions all the remaining structures and longitudinal systems seem normal in the tegmentum of both sides.

In striking contrast with the wasted (or lesser developed) tegmentum of the affected side is the larger development of the crural portion on that side. This is obviously due to the fact that in contra-distinction to the cerebral hemispheres the right half of the cerebellum is healthy whilst its left half is wasted. For, as is well known on physiological and anatomical grounds, one half of the cerebrum is in closest relationship functionally with the opposite half of the cerebellum. Hence in this case the large mass of transverse pontine fibres which chiefly form the middle cerebellar peduncle on the right side, and is in connexion with the larger right half of the cerebellum, is distinctly bigger than its fellow and displaces the anterior median groove of the pons to the left. It is interesting to note too that in relationship with the changes in the frontal and temporal lobes the temporo-pontine bundles situated in the dorso-lateral angle of the pons are somewhat wasted, and the fronto-pontine fibres situated mesio-ventrally are also wasted, but less so, in keeping therefore with the lesser affection of the main mass of the associated area of the frontal lobe. The right pyramidal bundles are much wasted and to a considerable extent broken up, more so than on the left side, by the transverse fibres of the pons.

Medulla.—Corresponding abnormalities obtain in the right half of the medulla where the pyramidal fibres are greatly diminished in number and some in size. The middle fillet is also smaller than its fellow, though the difference in bulk is not nearly so great as between the middle fillets higher up in the brain stem and notably in the mid-brain. Also, there is a distinct relative smallness on this side (right) of the nucleus lateralis, and of the inferior olive. The internal arcuate fibres are less numerous and also the *fibræ comitantes quinti*, though the spinal roots of the fifth nerve seem equally well developed. It is to be expected that the inferior olive, which is known to give origin to the system of afferent fibres (olivo-cerebellar) which cross the middle line and terminate chiefly in the opposite half of the cerebellum, should in this case be smaller on the right side because it is thus in connexion with the smaller half of the cerebellum (the left), but it is curious that the internal arcuate fibres should be more numerous on the left side of the medulla than on the right, because after decussating in the middle line they bend forwards (frontally), and to a great extent form the right middle fillet which is smaller than its fellow. It could not be

proved that the left posterior column nuclei from which the left internal arcuate fibres almost entirely take origin were larger (or smaller) than the right, yet the fact that the internal arcuate fibres were more numerous on the left side was not only apparent in the medulla, but similarly their homologues throughout the pons were also more numerous and better stained than those on the right. The bundle of Schütz, a network of fine fibres extending from the medulla to the cerebral peduncles and lying just dorsal to the twelfth and similar nuclei, is less evident on the right side than on the left. But, as would



FIG. 8.

be anticipated, the right inferior cerebellar peduncle, formed chiefly by the junction of the right direct cerebellar tract with fibres coming from the larger left inferior olive and passing to the (larger) right half of the cerebellum, is larger on the right side than on the left. The remaining structures in the medulla seemed normal, and call for no comment.

Cerebellum.—The gross changes in the cerebellum are best realized

by a reference to the accompanying figure. The left half (i.e., the side opposite to the affected cerebrum) is much atrophied. On microscopic examination it is found that in the wasted area the cells of Purkinje are small in number and in size and their processes are much stunted, though here and there a few comparatively healthy cells may be seen. The granular layer, and slightly also the molecular layer, is thinner than in health and seem to be equally affected throughout their depth. An outer layer of round cells, two or three deep, immediately beneath the Purkinje cells, as found by Mott and Tredgold in a similar case, are not in this instance visible. The so-called cells of Golgi seem also distinctly diminished in number in the diseased area. The left nucleus dentatus is smaller and thinner in all dimensions than the right, and evidently associated with this is the fact that the left superior cerebellar peduncle which takes origin from it is smaller than its fellow. The nuclei globosus and emboliformis are slightly smaller and less rich in fibres than on the opposite side, and the left nucleus fastigii (*vel* tecti) is very distinctly smaller, and owing to a paucity of fibres and internuclear fibrillar network is paler and less well marked than on the right side.

The spinal cord.—The spinal cord is profoundly asymmetrical, and though both sides are affected, the left is much smaller than the right—the atrophy of the left side of the cord being in keeping with the arrested development of the right cerebrum and the left side of the cerebellum. The right half of the spinal cord presents no obvious diminution in size except in its anterior column. On microscopic examination it is seen that the right direct pyramidal tract and the left crossed pyramidal tract are much smaller than normal, the number of their fibres is much diminished, and, in addition, many of the fibres present show the ordinary signs of secondary degeneration and sclerosis. Moreover, these processes have not been limited to the above mentioned tracts, but involve also, though to a slighter extent, the deep; and more particularly the marginal, fibres of the left antero-lateral column. Similar slight changes are noticeable in the right crossed pyramidal tract and right antero-lateral column due to affection of some of the homolateral fibres. The posterior columns present no definite abnormalities, but the white fibres of the anterior commissure are in most sections decidedly more abundant on the *left* side than on the *right*. The left anterior column, which, by contrast with the atrophied right, seems almost larger than normal, is very well developed, and has displaced the median longitudinal fissure to the right. The

grey matter of the spinal cord is affected on the two sides, and that somewhat irregularly at different levels. The central canal, though not unduly dilated, is here and there multiple, so that two or three small canals lie in contact, each surrounded by the ordinary (healthy) columnar epithelium. The stress of change in the grey matter has naturally fallen on the anterior horns, and on the whole the left anterior horn is smaller, narrower, and more stunted than the right. This is especially seen in the cervical and lumbar enlargements. In a somewhat similar case as this, published by Mott and Tredgold, and previously quoted, the cells chiefly wasted were in the lateral and postero-external groups, but here, though these are to a large extent affected, and in some places practically absent, it is noteworthy that at certain levels the mesial groups, both anterior and posterior, as well as the central group of cells, are almost absent in the left anterior horn. The cells, mostly of smallish size and fusiform, of the lateral process to which Bruce has recently called attention, are well preserved at most levels, and better on the right than left. The columns of Clarke are little affected, but in the lower dorsal region their cells are larger and slightly more numerous on the right side. In all cases, however, these cells show a marginal accumulation of granules, with a peripherally displaced nucleus, that is to say, the ordinary structure of the Clarke-Stilling cells.

REMARKS.

Such cases as described above have usually been known under the name of hemiatrophy of the brain or arrested development of the nervous system. All of them are probably due originally to a vascular lesion, either arterial or venous, occurring in foetal or early life. The chief organic changes result from arrested development of certain parts of the central nervous system, whilst others continue to grow more or less as in health; hence the title of atrophy or hemiatrophy seems ill-chosen. On the other hand, as a result of arrested development and function in certain structures, others often far distant from the original lesion undergo secondary and tertiary atrophy, and these atrophies may give rise to the most striking organic changes or symptoms in a case, and therefore the term of arrested development of the nervous system or hemiagenesis suggests a distorted idea of the case. On the whole, it seems to the writer that the term microgyria, which involves no causal theory of the disease, and yet at once indicates the grossest change visible to the naked eye in such a case, is better than either of the other two in common usage.

Mott and Tredgold [2] state that these cases readily group themselves into two classes: (1) Cortical, in which the lesion is confined to the cortex or underlying white matter. (2) Basal, in which the original lesion is situated in the structures at the base of the brain; and they describe three cases as illustrating this. Though undoubtedly most of these cases can be thus conveniently grouped, there are occasionally others in which the original lesions may be both in the cortex and in the basal structures of the brain. Judging from the relative amount of disease in the cortical efferent systems and in the structures originating or terminating in the basal ganglia, the writer is of opinion that the case described above falls into an intermediate group of cases, partly cortical, partly basal.

Mott and Tredgold [3] state that "it has been conjectured that a descending thalamo-spinal path exists in man." By reference to two cases, including one of microgyria, and by a lucid deduction from facts, they proved the existence of such a path, and gave photographs of it. It may be of interest in this connexion that the writer, at a meeting of the Physiological Society at Cambridge in August, 1904, demonstrated specimens of the brains and cords of twelve monkeys in which he had caused degeneration in such a descending thalamo-spinal path by production of a localized lesion in the optic thalamus. This atrophy, or degeneration of the thalamo-spinal path, in the case described in this paper, is not (unlike that in the case described by Mott) obtrusive, because, firstly, the relative amount of disease in the thalamus is smaller; and, secondly, the amount of disease in the surrounding structures in the record is relatively greater.

It is not within the scope of this paper to enter into further detail, which, with organic changes in nearly every part of the central nervous system, would take one too far afield. The main fact that the right half of the brain is structurally and functionally chiefly associated with the left half of the cerebellum, and with both sides of the spinal cord, but chiefly the left, finds striking illustration in the present case, and further detail is given in the body of the paper.

REFERENCES.

- [1] MOTT, F. W. "The Progressive Evolution of the Structure and Functions of the Visual Cortex in Mammalia"—The Bowman Lecture, *Trans. Ophth. Soc.*, January, 1905, vol. 25, p. liii.
- [2] MOTT, F. W., and TREDGOLD, A. F. *Brain*, 1900, vol. xxiii, p. 239.
- [3] *Ibid.*, p. 248.