An Address ON LOCALISATION IN THE "MOTOR" CEREBRAL CORTEX.

*Delivered to the Pathological Society of London,
December 17th, 1901.*

BY

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THE subject of cerebral localisation is one of obviously great extent. We should be lacking in all sense of proportion did we suppose ourselves expected to attempt before such a meeting as this to deal with it except in regard to some portions with which as experimentalists we are acquainted at first hand.

We may recall, however, how very different is the point of view from which the cerebral cortex is to-day regarded from that taken prior to the observations of Hughlings Jackson and the experiments of Hitzig and of Ferrier. Up to that epoch, experimentalists had failed to get evidence of localisation of function in the cortex of the hemispheres, though in microscopic structure the great sheet of grey matter presented such similarity to nervous formations, regarded elsewhere as nerve centres. Progress of knowledge in regard to the nervous system has been always indissolubly linked with determination of localisation of function in it. This has been so from the time of the Bell-Magendie discovery of the differentiation of function in the two spinal roots; and another instance is Flourens's delimitation of the respiratory centre in the bulb. The discovery of localisation of function in parts of the cortex laid the foundation for an advance of knowledge regarding it, which has led to the supply to the student of charts of its functional topography very similar to the geographical maps of continents which are supplied to the school-boy. And just as the schoolboy, looking over the political map of a continent, is liable to forget the complexity of the populations and States which it so simply represents, so that we, looking at the brain chart of the textbook, are liable sometimes to forget the unspeakable complexity of the reactions thus rudely symbolised and spatially located.

If we may be allowed an *a priori* consideration it is this,—that though it is not surprising that such territorial subdivision of function should exist in the cerebral cortex, it is surprising that by our relatively imperfect artifices for stimulation we should be able to obtain clear evidence of the localisation which does exist. The nerve-cell chains that together build up the nervous system are in the architecture of that system so arranged that the longest of them all tend to pass through the cerebral cortex. Every increase in the number of links composing a nerve-cell chain seems to increase greatly the uncertainty of its reactions under artificial excitation. With increase in number of links goes increase in numbers of side-branches and connections. The difficulty of getting long cell-chains to react in a regular way under artificial stimulation seems greatly enhanced by the multiplication of the side connections, because the momentary condition of any cell-chain is in part a function of the condition at the moment of all the other cell-chains with which it is connected. The cortex cerebri might therefore well have been expected to yield under artificial stimulation only extraordinarily irregular results. We owe to Hitzig and to Ferrier the pregnant demonstration that as regards the motor region this expectation is not well founded. It is mainly of the reactions of the Rolandic area of the cortex that I shall venture to speak, and Ferrier showed that the application of faradic currents to that cortex excites with great regularity movements which vary in distribution as the electrodes are moved from place to place in the region, but that the reactions remain very regularly similar under repeated application of the stimulus to any one and the same spot. Ferrier's mode of indicating the topo-

graphical arrangement of the reactions he obtained is seen in his well-known diagrams of the cortex. His motor centres, as he termed them, were marked in his figures by circular areas. "The areas have no exact line of demarcation from each other, and where they adjoin stimulation is apt to produce conjoint the effect peculiar to each." He showed these motor centres to extend forward over the frontal lobe, including these reactions of the eyeballs. Regarding their extension round the upper edge of the hemisphere and down upon the mesial surface he noted them in the marginal convolution. "This convolution in the parieto-frontal region gave rise to movements of the head and limbs apparently similar to those already obtained by stimulation of the corresponding regions on the external surface."²

This ever-memorable original research by Ferrier ranks among the classics of experimental neurology and physiology. It has been followed by a number of kindred contributions from workers largely of our own country—names familiar to us all—Schäfer, Horsley, Beevor, Mott, Ballance, and others. These have led to the detailed knowledge we possess of the localisation of functions in the cerebral cortex of the common ape, the macaque. These are concisely given in the well-known figures of the textbooks. It was an interesting step further when Dr. Beevor and Professor Horsley published eleven years ago their observations on the localisation of the "motor" functions in the Rolandic cortex of an orang-outang. Their experiment has remained the single one for which an anthropoid species of ape has been laid under contribution. It has exercised a notable influence on the scheme of "motor" localisation adopted as probably obtaining in the brain of man. An experiment upon the brain of an anthropoid ape presents special interest from the two points of view—(1) the cortical organ in these species is, except for man, at its highest development; and (2) it undoubtedly presents that type of development which culminates in man.

Of the three or four species of anthropoid apes that are known, most authorities agree that the gorilla is that which possesses the most highly developed cerebrum; next to it probably comes that of the chimpanzee, and last, but not far below that of the chimpanzee, comes that of *Simia satyrus*, the orang-outang. But there are great individual differences, and the simpler examples of chimpanzee brains seem inferior in development to well-developed examples of the brain of the orang.

We have recently had the opportunity of making physiological experiments on all the known species of anthropoid apes. As it is upon the chimpanzee that we have obtained the larger number of our observations, we will mention first our results upon that type. We have used besides the ordinary chimpanzee (*Troglodytes niger*), the rare variety of which the celebrated "Sally" of the Zoo was a specimen, *Troglodytes calvus*—by some considered a separate species.

In the chimpanzee the scheme of topography which we find existent is illustrated. We ask your attention to the extent of the so-called "motor" area presented by it. The extent and arrangement differs considerably from that found by other observers in the lower apes and from that found in the orang by Dr. Beevor and Professor Horsley.

The so-called motor area occupies unbrokenly the whole length of the precentral convolution, and in most places the greater part or the whole of its width. It extends into the depth of the Rolandic fissure, occupying the anterior wall, and in some places the floor, and in some extending even into the deeper part of the posterior wall of the fissure. We have examined 19 hemispheres, but have never found the motor area extend to the free face of the postcentral convolution. At the upper mesial edge of the hemisphere the motor area extends round and down upon the mesial face of the hemisphere; but we have not found it reach the callosal-marginal fissure. The anterior limit of the motor region is, for the most part, not coincident with any fissure. The front portion of the region usually dips into and across the upper part of the superior precentral fissure, and lower down it not infrequently dips into the inferior precentral fissure. Occasionally the front edge of the region dips into almost the whole length of the superior precentral sulcus. It is not the extent of the motor area which appears to be variable;

the variant is the sulcus itself. The great variety of individual pattern exhibited by the convolutions and sulci in these richly convoluted brains gives opportunity for studying critically the claim of value of these fissures as landmarks to the topography of the functional centres of the cortex. From this point of view their use for strict localisation is almost *nil*. Not only are the extremes of pattern exhibited by the convolutions extraordinarily different one from another, but the frequency of the individual variation is so great that hardly a pair can be found in which the existent convolutions are when compared with the same minuteness as we apply to the functional centres really closely alike. Professor Schäfer, in his important contribution to the physiology of the motor cortex in 1887, pointed out that the fissures of the cortex do not mark in any sense the boundaries of the functional areas of the organ. Our examination of the considerable number of anthropoid brains we have now worked through convinces us that not only do the fissures of the frontal region not mark physiological boundaries, but that they are not even reliable landmarks to the functional topography, since their relation is too inconstant and variable. The degree of subjection of these fissures to individual variation and the frequency of their asymmetry in the two hemispheres is in striking contrast to the far greater constancy from individual to individual and far greater symmetry of bilateral situation, which we have found hold good for the arrangement of functional centres of the motor region as examined by physiological methods. A practical outcome of this is that we have found it essential for accurately detailed localisation when we have desired the opening through the skull to be kept to a small size, not to trust to the anatomical details of the exposed cerebral surface, but to obtain orientation as to the topography by application of the electrodes and observation of the movement, if any, which was excited. In our early experiments we thought to obtain much help by having at hand an individual brain already experimented upon; and we thought to save time in recording the results of the fresh experiment upon chart outlines prepared from the specimen already worked upon. But the variation of the convolutions from individual to individual has been too great to allow of these expedients being employed. Defeated in this way the only recourse must be to the electrodes. Two landmarks of real value are the genua of the Rolandic fissure.

A matter of some surprise to us has been the ease with which faradism elicits movements from this so-called motor region of the cortex of the anthropoid. It is general belief that for excitation of the cortex in man the intensity of the faradic currents has to be much greater than that effective for the cortex of the monkey. Our predecessors with the orang-utang state that the cortex of that animal required much more intense electric stimuli than the cortex of the bonnet monkey. Their impression was, however, based on no direct comparison. We have actually compared the excitability of the cortex of the anthropoid with that of the bonnet monkey by employing exactly the same current in each case. We find that the excitability as measured by the least intensity of current required to evoke motor reaction is practically the same in the anthropoid and in the lower ape. The motor cortex of the anthropoid, though undoubtedly far more complex in many ways than that of the lower ape, remains as readily amenable to electric stimulation. If, therefore, it is really necessary to employ intense faradisation for the human motor region that is a difference between the human motor region and that, not only of the lower ape, but of the anthropoid.

A further point cognate to the above on which our experience differs from that of our predecessors regards epileptiform discharge from the cortex. It will be remembered that Dr. Beevor and Professor Horsley never observed epilepsy to follow excitation in the brain of their orang, although their electrodes were occasionally kept in contact for five seconds. Though we also find that in some individual anthropoids the tendency for the discharge from the cortex to take an epileptiform character is very slight, yet in other individuals the tendency under apparently the same external conditions is strong. In the majority of the individuals upon which

we have experimented, cortical epilepsy has been easily provoked.

Turning to the localisation in the cortex, the sequence of representation starting from below upward follows closely that already known for the lower apes. Broadly speaking, the sequence runs tongue, mouth, nose, ear, eyelids, neck, hand, wrist, elbow, shoulder, chest, abdomen, hip, knee, ankle, toes, perineal muscles, anus, and vagina. It is noticeable that movements of the eyeballs do not appear in this list. As did Beevor and Horsley in the orang, we in the chimpanzee find a frontal area extending into the middle and inferior frontal convolutions, excitation of which gives conjugate deviation of the eyeballs to the opposite side. We find this area separated from the area yielding the other movements by an intervening space of so-called "inexcitable" cortex, as our predecessors found in the orang. We find this intervening space broken, however, by a small area whence movements of the eyeballs can be elicited, which partially bridges between it and the upper facial region on the precentral convolution.

The sequence of representation of movement which we note follows a plan more in accordance with the order of the spinal series of segments than that hitherto obtained, because we find between the representation of shoulder and hip an area which, next to the shoulder, yields unilateral movement of the chest muscles, and, next to the hip, yields unilateral movement of the abdominal muscles.

A noteworthy discrepancy between our results and those of our predecessors is regarding the extension of the excitable "motor" region to the free surface of the postcentral convolution. We have seen nothing to lead us to include that surface or any part of it in the "motor" area of any of the anthropoids we have used. In our experience the electrodes, carrying even very strong currents, when placed upon the surface of the postcentral convolution, fail to evoke any obvious effect, though when placed, using a weaker current, upon the precentral they evoke extremely widespread movement. I may add also that though small lesions in the precentral convolution cause marked paralyses and descending spinal degenerations, similar and larger lesions in the postcentral produce not even temporary paralysis and no unequivocal degeneration.

With regard to the degenerations, it is noteworthy that from a hand-area lesion the spinal pyramidal degeneration shows in the chimpanzee the feature of a ventral direct pyramidal tract not obviously inferior in size to that of man. On the other hand, a lesion somewhat smaller situate in the region for the ankle and foot produced a pyramidal degeneration in which a direct ventral tract is not obvious. The hand-area lesion gave a heavy degeneration of the homolateral pyramidal tract in the lateral column on the same side as the cerebral lesion.

As regards the symptoms resulting from the cortical lesions, the extirpation of a great part, if not of the whole, of the hand area from the right hemisphere caused an immediate severe crossed brachiolegia without the slightest sign of paresis in either face or leg. The paresis affected most the fingers, which were kept helplessly semi-extended, the wrist being dropped. The elbow seemed little, if at all, affected, but the shoulder was distinctly paretic, there being great difficulty in raising or abducting the upper arm at the shoulder. The paresis diminished quite rapidly, and in six weeks time the animal had largely recovered the normal usefulness of the limb.

A lesion in the leg area similarly caused temporary paresis of the opposite leg, especially in the toes and at the ankle joint. The lesion was smaller and the recovery more rapid than with the arm-area lesion. It is perhaps noteworthy that the knee-jerk, which showed no alteration under the arm-area lesion, here showed exaltation immediately, that is, a quarter of an hour after the leg-area lesion, and that when the paresis to inspection had passed off the knee-jerk still nevertheless exhibited great briskness on the crossed side.

Although we have used a more minutely localised method of excitation than our predecessors, we have not found in any of our anthropoids those remarkable inexcitable intervals noted by them between the main regional divisions of the area—that is, between the upper and lower facial areas, between the facial and the arm, between the arm and leg.

On the other hand, we have seen often confirmed what our

predecessors with the orang have well pointed out, namely, the greater integration of localised representation of movements in the anthropoid as compared with the lower ape. Thus there is not one of the fingers that we have not seen move separately and alone under excitation of certain points of the cortex: again isolated movement of the pinna of the ear, of the tip of the tongue, rare in the lower monkeys are easily obtainable in the anthropoid.

Finally, one word with regard to the extent of the so-called motor area. From our observations we think it probable that perhaps as much of that area lies hidden from the surface in the sulci as actually lies at the free surface on the convolutions. Nevertheless, we endorse the opinion expressed by Beever and Horsley that the so-called motor area in the anthropoid brain forms altogether a smaller fraction of the total surface than is found in the lower types of monkey. If it has grown in extent—as undoubtedly it seems to have done—other regions belonging to that so-called inexcitable field whence electric stimulation excites no obvious response have increased still more. It is especially with the exploration of that great inexcitable field that the progress of research has to deal. We cannot help thinking that this progress will have to look for means to the patient combination of clinical and microscopical research rather than to the excitation experiments of the laboratory.

We would call your attention to the fact that the results on the gorilla confirm perfectly those we have obtained on the chimpanzee and orang. This is a matter of interest because many considerations go to show that the gorilla's brain is the highest form of brain excepting only that of man himself.

We have ventured to put before you only the broadest features of the results at present accumulated by us. The detailed collation of our observations may bring out points of interest of a more detailed kind, but the process of collation will be a matter occupying a good deal of time.

REFERENCES.

- ¹ *Functions of the Brain*. London, 1876. ² *Ibid.* ³ *Festschrift zu Karl Ludwig*. 1887. Leipzig.

ON THE QUANTITATIVE ESTIMATION OF CHLOROFORM IN ANIMAL TISSUES.

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Prefatory Note.—I have summarised in the following brief account the results of the quantitative estimations of chloroform carried on by Dr. Dodgson in the physiological laboratory of St. Mary's Hospital Medical School during the years 1898 and 1899 at my suggestion and by aid of a grant from the British Medical Association. Dr. Dodgson's work and the preparation of his report were interrupted by his appointment to investigate the results of antityphoid inoculation in South Africa. His absence having become unexpectedly prolonged, and the work begun by him having passed into other hands by reason of the appointment in July last of a special Chloroform Committee by the Council of the British Medical Association, I have at Dr. Dodgson's desire prepared the following summary of his laboratory notes. The credit for work done is Dr. Dodgson's. The responsibility for the summary is mine, and I trust that any defect of this summary will at some future time be made good by a fuller account of the subject from Dr. Dodgson's pen.

SUMMARY OF DR. DODGSON'S OBSERVATIONS.

The methods of quantitative estimation hitherto employed are in chronological order:

1. That of Lallemand, Perrin, and Duroy, 1850.
2. That of Schmiedeberg, 1867 (modified under his direction by Pohl, 1891).
3. That of Gréhan and Quinquaut, 1883.
4. That of Chancel and Farmentier, 1885.

In principle the method of the French observers consists in the decomposition of chloroform by a strong solution of

potash and subsequent volumetric estimation of chlorine the resultant potassium chloride.

This procedure is directly applicable to an aqueous solution of chloroform, and can be applied to a mixture of chloroform and air, the gas being first brought into aqueous solution by shaking with a sufficient volume of chloride-free water. In the case of blood and tissues, the chloroform present is first distilled off *in vacuo* and a chloride estimation made as before in the distillate. Gréhan estimated chloroform in the distillate by the reducing power upon Fehling's solution.

In the German method of estimation the chloroform present in a fluid or tissue is distilled off and slowly aspirated through a combustion tube filled with calcium or preferably magnesium oxide, and the resultant chloride estimated as before by AgNO_3 . This method is also applicable to the quantitative estimation of chloroform in air, a known volume of the gaseous mixture being slowly driven through the combustion tube by mercury displacement.

After trial of all these various methods with known weights of chloroform in water, in blood, and in small animals, the following procedure was adopted as giving the most trustworthy results as regards the quantitation of chloroform in small animals and organs of large animals.

[The results of preliminary trials by the potash method need not be given in detail. These results were less promising of accuracy than the preliminary results of combustion, which therefore was adopted as the standard method. It is possible, however, that on further trial the method by digestion with strong KOH may prove to be an available one. The experiments reported by Dr. Edmunds in the *Lancet* point in this direction.]

In the early trials of this method made by Dr. Dodgson the deficit per 100 in 5 successive experiments was with the distillate 13, 12, 20, 23, 15, and in 2 experiments with the original solution (1 c.cm. of CHCl_3 in 999 c.cm. of water)—20 and 21. The only remarkable point in these results is that the error was about the same (20 per cent.) for 100 c.cm. of the original fluid, as for the distillate of 100 c.cm.—that is, that as much CHCl_3 is recoverable from the distillate of an aqueous solution as from the original solution.]

APPARATUS AND METHOD (SEE FIG. 1, p. 1860).

A.—Distillation and Combustion.

A is a glass vessel with two-way Drechsel stopper to contain the distilland (water, blood, organ, or small animal) and placed in a water bath. The inlet and outlet tubes are connected respectively with W B (a wash bottle) and F C (a froth chamber). The volatile products of distillation are slowly drawn through a combustion tube (B B) by means of the aspirator (C). The combustion tube (B B), 80 cm. long and 14 mm. in diameter, is filled with granulated MgO (previously washed until chloride free), and kept at red heat in an ordinary gas furnace. Two wash bottles containing respectively KOH and AgNO_3 , placed between combustion tube and aspirator, serve to stop and to indicate any possible escape of HCl through the combustion tube. No such escape occurred, however; the rate of aspiration was maintained at about 60 bubbles per minute.

Estimations were also made without heat in the cases of chloroform in water and chloroform in blood—in the latter case for the sake of avoiding coagulation of proteids—air being slowly aspirated through the solution at ordinary temperature. In this case a longer duration of experiment was necessary than when heat was employed. The two ends of the combustion tube were bent at a right angle, and connected with the other parts of apparatus by mercury joints M. M. at the two ends.

The duration of a distillation was generally four to six hours (*vide tables*), at the end of which time the chloride present in the combustion tube was titrated, and from this result the amount of CHCl_3 in the distilland calculated.

B.—The Estimation of Chloride.

This was conducted as follows:—The combustion tube when cooled was turned up and filled with 30 per cent. HNO_3 . The solution when complete is transferred to a beaker; the tube is washed out with a known volume of distilled water. The titration of chloride is carried out with AgNO_3 and AmSCN with iron alum as the indicator (Volhard's process).