The Savill Memorial Oration ON LOCALIZATION OF FUNCTION IN THE NERVOUS SYSTEM.

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BY

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I HAVE chosen the subject of localization of function in the nervous system because I have thought for some years that the information obtainable by our students from the current textbooks of medicine and of neurology is very much behind the times, when compared with the results of modern biological and physiological research, and that this information does not convey a satisfactory working hypothesis to the medical man. The subject is, moreover, very much in the air at this moment, for in the few months since I accepted this oration and decided upon this subject two exhaustive reviews have appeared, the one in America by Marion Hines, and the other in France by R. Brugia, under a preface by Pierre Marie. In comparison with these detailed and lengthy works, anything that I can put before you in the short space of an hour must be but a brief outline of present opinion, supported and modified perhaps a little by my personal clinical observations. There was another excellent review upon "cortical localization" thirteen years ago, from the physiological and experimental aspects, by the distinguished physiologist Professor Graham Brown.

I may well introduce my subject by putting before you a quotation from the conclusions from each of these reviews, beginning with that of Professor Graham Brown, who wrote:

"The experimental evidence gives no grounds for the supposition of the localization of the function of voluntary movement in the 'motor area' as distinguished from any other part of the cortex."

Graham Brown sought to find proof that the "motor area" was more than a mere spot upon the outgoing path for voluntary movement, and by his experiments showing "primary facilitation," in which careful unipolar stimulation of a cortical point in the "motor area" raised the excitability of that cortical point, and those showing "secondary facilitation," in which similar stimulation of the same area caused the neighbouring region of the inexcitable post-central cortex to become excitable, he claimed to advance a proof that the "motor area" was something a little more than a mere receiver and transmitter upon the chief outgoing path for voluntary movements, and that change and modification can take place at this station:

Dr. Marion Hines, who writes rather as a reviewer than as a pioneer upon this subject, concludes in the following way:

"The diagrams of local representation of function in the cerebral cortex so prevalent in the last part of the nineteenth century have gradually become dimmer until finally point localization has disappeared even from the motor cortex under the careful experimental analyses of Leyton, Sherrington, and Graham Brown. Only the projection of the retina upon the calcarine now remains. And yet in the light of our present knowledge to consider the cerebral cortex as equipotential is hardly justified, nor to hold the opinion that the kind is immaterial, providing the bulk is sufficient."

Dr. Hines might, with a little thought, have rid her mind of the calcarine cortex, for the succinct projection of the retina upon the calcarine is admittedly a precise patterning of the impingement of visual afferents upon the cortex. The calcarine cortex is an important station upon the sole path by which visual impressions reach the cortex in man, at any rate, and holds a similar position with regard to the visual path as does the motor cortex to the chief outgoing path, in that lesions of these two regions block these paths respectively. Dr. Hines has rejected a succinct localization of function of former days for a much

more vague, indefinite conception of localization of function. You may remember that this was also the position taken by Sir Henry Head in his later writings. But this conception of vague localization has one thing in common with the old conception of succinct localization, and that is that both are centred around the regions where great incoming paths impinge, and where great outgoing paths emerge from the cortex, interference with which is readily manifest in disturbance of function, and that blocking of such paths cannot be excluded as causing a large part of the functional loss resulting from ablation of these regions. I do not wish to infer that the conception of vague localization of function is wrong or untenable, but it requires careful criticism. Surely it is impossible to think otherwise than that a part of the cortex—the latest and highest development in evolution—which receives the visual impressions will be especially important in connexion with the visual function otherwise than as a receiving and transmitting station, and similarly in the case of the motor emergent and other sensory receptive regions. But such thought does not altogether entail a conception of local function.

Dr. Brugia will have nothing of localization of function in the nervous system. He refers to this conception as the "seduction of all seductions," to which so many have gone under. At the end of his book of nearly two hundred pages he claims to have put forward adequate and convincing proofs that in the nervous system there are no centres of local function, neither for the reception of impressions, nor for exteriorization, nor for co-ordination, nor for volition. He commences by pointing out that the nerve cell is a structure appended as it were to the outside of the true fibrillar conducting nerve substance which passes through it to end elsewhere, and that the proved function of the nerve cell is only nutritional, and that it cannot be a centre of function. He refers to the primary metameric nerve unit, and says with truth that from the peripheral receptor, through the afferent and nerve cells, to the efferent and the muscle, no part can be called the centre of reflex activity; no part can be deemed dominant over the others; every part is equally important in the occurrence of the reflex action. Reflex activity is the function of the metameric nervous unit as a whole. Brugia builds up the nervous system physiologically, as it is built up morphologically by interconnexion and fusion between the primary metameric units, and when this interconnexion begins there is convergence of paths and modification of the result of activity in any one segment—there is co-ordination. This is, of course, Sherrington's "principle of convergence." The forward metameres become highly developed and dominant from specialization, and the brain appears. But the whole nervous system acts as did the primary metameric nervous unit, not in terms of separate function in its several parts, but as a whole and entirely reflexly. He calls the metameric units "neuromyomes." Though he denounces a little loudly the earlier pioneers upon this subject, his summary is worthy of consideration, and especially does it bring into prominence the great importance of bearing clearly in mind the high part played by the peripheral nervous system, both receptors and effectors, in the activity of the higher parts of the nervous system, and the profound derangement of function which accompanies the severance of communication between these parts.

In my quotations from these three reviewers I have said enough to prove that a change of thought has been taking place with regard to the nature of activity of the various parts of the nervous system, and I must proceed to give very briefly some of the reasons for this change. I will first refer to the cerebral cortex.

The cerebral cortex, described by Sherrington as the principal ganglion of the distance receptors—namely, the receptors of smell, sound, and visual impressions—was in the earlier stages of its development the principal ganglion of the receptors of smell only, and its connexions with the functions of sight and hearing are secondary connexions. It is developed as an appendage to the olfactory paths, the primary connexion of which was with the thalamus. It begins as an outgrowth between the two primary masses of grey matter in which the olfactory tract terminates on either side, the inner of these remaining as

the hippocampal region and the outer as the pyriform lobe or uncinate region, and develops into the dominant part of the nervous system, perhaps because of the immense importance of the function of smell in finding food and in scenting danger. In some animals whose activity depends very largely upon the sense of smell, the severance of the olfactory tracts causes a complete destruction of the function of the brain. A shark, for example, with the olfactory tracts cut resembles in every way a shark with its forebrain removed. It is apathetic, motionless, and it will not feed. Appetite and activity are lost. I will now compare the shark with another fish, which does not rely entirely upon smell, but chiefly upon sight in getting its food and avoiding its enemies. If we remove from this second fish the forebrain, which is not much connected with visual function, it does not make great difference to him. He remains lively, he feeds well, and will select his food and distinguish between red worms and white worms. If we blind him we shall reduce him almost to the level of the decerebrate shark. I am stressing this point to impress you with the very great reduction of function which occurs in the higher regions of the nervous system from de-afferentation, whether this deprivation of afferents occurs in the peripheral nervous system or, and this is even more important to my subject, in the central nervous system—for example, in the immediate subcortex. I may here repeat the story of the decerebrate frog and the flies, which has been often quoted as suggesting how much the forebrain adds to the capacity of the nervous system of this lowly animal. Such a frog does not compete well in the struggle for existence when in a comfortable aquarium with other frogs. But if we take this frog without forebrain and place him with a normal frog in a covered glass bowl and set free a dozen flies within that bowl, the decerebrate frog will get all the flies and the normal frog will get none. The reason for this is that the normal frog is aware that his surroundings are unusual and is uncomfortable; he spends his time in fear and attempts to escape, and before he has got over his embarrassment the decerebrate frog, who is not so aware and not so discomforted, but attends only to the grosser matters of appetite, has caught all the flies.

It is remarkable that the olfactory function, with which the development of the cerebral hemispheres is so intimately connected, seems not to be interfered with by any local lesion of the convolutions, whether unilateral or bilateral, provided the olfactory tracts are intact. Chatelin examined 5,000 cases of wounds of the brain, unilateral and bilateral, and found no loss of the sense of smell or taste. Our only knowledge of the connexion of these functions with any individual part of the brain rests upon the developmental and anatomical facts, and upon the occurrence of hallucinations of taste and smell in the epilepsy which may result from tumours in the uncinate region. Possibly the afferent paths of smell and taste have a very general impingement, as opposed to a local impingement, upon the cortex, and in great measure escape in local lesions of the convolutions. There are two clinical facts which seem to support the proposition. The one is that only in epilepsy commencing with an olfactory or gustatory aura does one meet with a highly organized hallucination comparable to an experience of actual life, and this hallucination may be one of hearing, of vision, of idea, or a combination of these. All other hallucinations in epilepsy and with local lesions of the hemisphere in other regions than the uncinate gyrus are crude sensations and not comparable with those of common experience. The other fact is the well-known high potentiality of a sensation of smell to rouse cerebral activity to a high pitch in the form of vivid memory. Such high hallucinations and such sudden arousing of vivid memory are compatible with the direct association of the olfactory path with many regions of the cortex and with the origin of the neopallium as part of the olfactory apparatus.

The so-called "motor area" of the cortex, the discovery of the electrical excitability of which by Hitzig and Fritsch in 1870 revived the old theory of the phrenologists and, supported by the clinical observations of

Broca and Hughlings Jackson, seemed to place the hypothesis of local function in the several regions of the cortex upon a sound basis, has been the region in which recent experimental research has first and most disproved the tenability of this hypothesis, in its highly developed form certainly, and perhaps in any form at all. It must be borne in mind that there are three regions in each hemisphere from which movements can be elicited by unipolar electrical stimulation. One is at the posterior pole of the hemisphere and another is on the outer surface of the prefrontal lobe, both of these giving movements of head and eyes to the opposite side. The third comprises the whole of the ascending frontal gyrus, and from it, and it alone, the cortico-spinal tract or pyramidal tract arises. This ascending frontal convolution is mapped out in cortical points set in ladder-like fashion, stimulation of which produces movements of lower extremities, trunk, upper extremities, and face region from above downwards. Physiologists do not believe that the other regions of the cortex are not excitable, but that they are so much more lowly excitable as only to be aroused by such strengths of electrical stimulation as at once spread widely to other regions and render analysis impossible. One of these regions—the post-central gyrus—can be raised into a motor area by Graham Brown's method of secondary facilitation to which I have already referred.

Now in a chimpanzee Sherrington and Leyton removed the whole of the cortex from both ascending frontal gyri in two stages, separated by a considerable interval of time—the right first and the left subsequently. After each of these operations there was a temporary paralysis of the opposite side, which recovered perfectly. The left post-central cortex was then removed, but this produced no further disability. Later they examined this animal and found that no movements of face, body, or limbs could be elicited by stimulation of any part of the cortex, so that no other part of the cortex had taken on the role of electrical excitability of the removed cortex. The experimenters had removed the "cortical centres for movement," and had shown that no excitable area was left, and that none had been redeveloped. They had utterly destroyed the pyramidal system, for this had degenerated throughout. They had destroyed the post-central cortex on one side and had excluded the possibility of that potentially excitable region having taken over the motor function. They had left the chimpanzee with enough of his nervous system to recover and get along quite ably.

Now the interpretations which may be made of this sequence of events are, first, that we may believe that the cortical centres for movement were really ablated, but that the function of movement reverted to an ancestral home in the lower regions of the nervous system. This explanation, as Graham Brown points out, is possible, but most highly improbable. Secondly, we may think that the function of voluntary movement is concerned with the cerebral cortex in general, and that the ascending frontal convolution and its pyramidal tract are the chief, but not the only, outgoing path for movement, and that the ablations caused the temporary paralysis (1) because the usual way out was blocked and the alternative path took time to acquire function; (2) because the mechanism of motility was maimed as a whole by the loss of one of its elements and transcortical connexions, and time was required for compensation; (3) because some of the cortex which must be concerned especially with the receipt of impressions arousing motor activity was lost. The latter explanation is the highly probable one.

Graham Brown subsequently performed a very similar experiment, again upon a chimpanzee. He removed the whole of the cortex of the post-central gyrus, first upon the one side and subsequently upon the other. Clinical lesions of the post-central gyrus in man of this magnitude would have produced the most profound disability of the limbs and ataxy on both sides from loss of sense of position and astereognosis, for in man this post-central region has been held to be the centre for the more discriminating functions of sensibility. But this chimpanzee did not show any signs of disability at all, for within a few days of the completion of these ablations he learned to get open the cupboard in which his food was kept. The

cupboard was locked and latched and the door was tight-fitting, so that this monkey had to turn the key with one hand and the handle with the other, and had at the same time to put his foot against the impost and pull the door open. Watchful lest his crime should be detected, he even learned to do this complicated act with his back to the door—that is, without the guidance of his sight. He seemed not to have lost any of his function of sensibility at all. Graham Brown thereafter removed the left motor area of this animal, and the usual temporary hemiplegia ensued. But before a fortnight had elapsed, after repeated efforts to get the cupboard open meanwhile, he succeeded in doing so, and soon acquired his customary facility.

In considering the bearing of this experiment we must keep carefully in mind that the function of movement and the function of sensibility are not two separate functions, but that they are so intricately blended as to be inseparable. We have no consciousness of movement in ourselves except from the sensations which result in its accomplishment. We learn every skilled act by gradually laying down, by repetition, the pattern of the sensations which are produced by its correct performance. We reproduce them from the memory of these sensory patterns. We become clumsy with our skilled acts when cut of practice because the memory of the finer details of the sensory pattern tends to fade, and we reinforce these again by further repetition. It was for these reasons that Bastian rejected the idea of a motor centre in the cortex, and insisted that it must be a sensorimotor centre.

In Graham Brown's chimpanzee it is certain that the post-central cortex was not the chief, nor apparently even an important, higher sensory centre, for its removal produced no disability. It was not a region in which this animal stored his memories of spatial relations and highly skilled movements, for he developed these subsequent to its complete removal; and, adding the left motor area to the extensive regions of the cortex which the animal had already lost, there was sufficient cortex left for the recovery of good function. This experiment supports further the argument that the cerebral cortex, with its afferents, efferents, and transcortical connexions, acts as a whole.

There is one other experimental fact which has a profound significance and to which I would especially draw your attention. The "motor area" for the face, jaw, tongue, and larynx, to which I may refer as the face-excitabile cortex, is well marked in all animals from marsupials upwards, and it is a large area in the higher animals. Ablation of this face-excitabile cortex, either unilateral or bilateral, has never produced even the least transitory paralysis of face, jaw, tongue, or larynx. Sherrington removed the whole of the face-excitabile cortex in a young chimpanzee, with the result that the animal became at once more grimacing, more teeth-chattering, and much more noisy than before. One must conclude, therefore, for these animals that there is no localized centre of motor function for these important regions in the cortex, but yet that there is always an excitable path to these regions emerging locally from the cortex which does not seem to be the usual or even the important path of emergence for movements of face, jaw, tongue, and larynx, since complete ablation produces no disturbance of function.

When one compares the results of these experiments of cortical ablation in so high an animal as the chimpanzee with the results of pathological lesions of the same regions in man (which usually, but not invariably, obtain), there is difficulty in correlating the two. While it is allowable to use comparison between a lower and a higher animal in general, it is particularly unsafe to do so in connexion with the nervous system of man, the function of which is so far removed above that of the highest animal, and of which so much of the structural as well as functional development occurs after birth and during the course of training; and individualities of structure are without doubt sometimes determined by that training, so that the brains of men are not all fashioned alike, and may not behave alike when troubled with local injury. The chief

difference between the brain of the chimpanzee and the brain of man is striking—not that the latter has more grey matter, but that he has much more white matter, weight for weight. The supremacy of the brain of man is associated structurally with a much richer association and more direct connexion between its several parts, and is therefore a better organ functionally; on the other hand, it seems to have become more dependent upon solitary afferent and efferent paths than is the case in lower animals, and therefore its function is more disturbed by local lesions. From birth to adult age this dependence upon solitary paths seems to increase.

Clinically one does not meet with lesions comparable to the accurate cortical removals of experimental physiologists. There is one case commonly cited in which Horsley removed the arm-excitabile cortex of a boy on the right side. This patient is said to have recovered sufficiently to play tennis, though never so well as before the operation, and so may be said to show to some degree the recovery which occurs in apes. Pathological lesions are rarely confined to the cortex, and when there is evidence that a lesion is chiefly one of the cortex and not progressive, recovery of function occurs which may be complete, as in the experiments on animals, if the lesion is of the motor area, but little or no recovery seems to occur when the lesion is one of the visual area or of the post-central convolution. The absence of recovery in lesions of the visual cortex seems to me to be reasonably explained by the regularly patterned impingement thereon of the solitary afferent visual path, which is blocked out by the lesion at its termination, with no alternative path possible. Similarly, I would seek to explain both the disability with spatial relations and stereognostic sense which occur in lesions of the post-central gyrus in man as contrasted with the chimpanzee, and the absence of recovery after such lesions, by assuming a direct impingement and patterning upon the post-central gyrus of the afferents subserving that division of sensibility which Head has termed epicritic sensibility by a solitary path newly developed and peculiar to man.

Graham Brown, in his careful description of the movements which result from cortical stimulation in the limbs of the chimpanzee, takes great pains to emphasize that these movements are entirely different from any movements seen in the natural life of the animal. They have not the complexity of pattern, nor the purposefulness of natural movements. They are simple movements, well-nigh the same as those resulting from the stimulation of a peripheral nerve, whereas he says simple movements are never seen in the natural life of the chimpanzee. He evidently means, though he does not say so, that stimulation of the motor cortex is stimulation of a path passing through the cortex, and that it is not stimulation of a function in a centre in which that function is localized.

In man the cortex of the brain has been experimentally stimulated in many cases where the brain has been exposed by a wound in conscious patients, with the result from the ascending frontal gyrus that crude and simple movements followed as in the ape. The patients experienced a sensation of forced drawing of the limb, which they described as exactly the same as that produced by faradization of a peripheral nerve, and in no way resembling any sensation produced by voluntary movement. Similarly, stimulations of the post-central gyrus produced crude unnatural sensations of tingling, again resembling those resulting from faradization of a sensory nerve, and nothing more than these. One case, however, has been recorded in which the occipital pole was exposed, and the observer states that when the electrodes were applied to the region of the cuneus, crude sensations of light were experienced by the patient, and when the electrodes were passed over on to the outer surface of the lobe, the visual sensations assumed a higher character. This single observation is, however, so out of keeping with the clinical experience of visual hallucinations in connexion with lesions of the outer surface of the occipital lobe, which are invariably crude and unorganized, as to be unacceptable without further experiment.

I submit, therefore, that the evidence brought forward up to this tends to show that the loss of function produced

by local cortical ablation results almost entirely from the blocking of a nervous path which is entering or emerging from that part of the cortex, and that the positive results of cortical stimulation are due to stimulation of this path. Local cortical ablation will produce no loss of function if there is a facile alternative path to or from the rest of the cortex. It will give rise to temporary loss of function if a secondary path is available, and permanent loss of function only when no other path is available.

Lashley has recently made a very interesting series of observations upon the cerebral cortex of rats. From very numerous ablations of the cortex he has found no signs of localization of function, but he has proved that the capacity to form motor habits in these animals is reduced in direct proportion to the amount of cortex removed, and by equal amounts of ablation in any of the different cyto-architectural fields. He concludes that the capacity to learn such habits depends upon the available amount of the cortex as a whole, and not at all upon which region remains after ablation, and that the mechanism of integration is to be sought in the dynamic relations among the parts of the central nervous system and not in details of structural differentiation.

I may here, in passing, refer to Dusser de Barrenne's experiments upon strychnine sensitization of the cortex in the cat and in the macaque. In these animals, of course, removal of the cortex corresponding with the post-central cortex of man produces no loss of sensibility, yet he sought to connect these regions with sensibility notwithstanding, and he found that after painting this region with strychnine solution there was hyperaesthesia of the whole body, but much more marked on the opposite side and towards the periphery of the limbs, that there were signs of increased proprioceptive sensibility only on the opposite side, and that these results were absent when strychnine was applied to any other region of the cortex. It would seem, therefore, that in spite of the negative results of ablations, a sensory path does impinge upon this region of the cortex in the cat and in the ape as it does in man.

I will describe another class of experiments which are of much interest and have a profound bearing upon this subject. They were first performed by Robert Kennedy in 1900. Two dogs were taken and all the nerves of the left forelimb were divided above the elbow. In the one dog the nerves were at once rejoined in proper order. In the other the central end of the musculo-spiral was dissected into four strands and joined to the peripheral ends of median, ulnar, musculo-cutaneous, and musculo-spiral respectively. The central ends of median, ulnar, and musculo-cutaneous were cut off as short as possible and left dead-ended. Both dogs recovered the use of the forelimb perfectly and both recovered in exactly the same time. You will bear in mind that in the second dog all the flexor afferents and efferents had been changed on to an extensor path. On stimulating the motor cortex of this second dog it was found that the well-known region for flexion of the paw was no longer excitable, while stimulation of the extensor region now produced contraction of the flexors and of the extensors with equal facility.

Kennedy thought that he had shown that a given area of the motor cortex could be made to change its function, or rather, that it could be made to take on a fresh additional function by switching on to this area a fresh afferent and efferent peripheral path. His conclusions were much criticized on the grounds that the flexion and extension regions of the dog's cortex are not far enough separated from one another to allow of such absolute statements, and further that Kennedy had not taken sufficient precautions against peripheral regeneration from the stumps he considered dead-ended.

A few years later Osborne and Kilvington repeated these experiments in such a way as to avoid the possibility of these errors. They found it possible to divide the left middle cord of the brachial plexus in the dog, and, cutting the proximal end very long, to pass it under the trachea and unite it to the peripheral end of the right middle cord, also cut very long. The central end of the right middle cord was enclosed in a blind rubber tube to prevent sprout-

ing. This dog recovered well; it could walk and run naturally and could use either forepaw to hold down a bone. A very long time was allowed to elapse after recovery before this dog was examined. It will be observed that the extensor afferents and efferents of the right forelimb had been thrown into the left middle cord and therefore on to the right motor cortex. Stimulation of the right motor cortex now gave movements in both forelimbs. In the left there was extension of paw and flexion of elbow, in the right contraction of the triceps and extension of the paw. Stimulation of the left cortex produced movement in the right limb only, entirely excluding any movement in the triceps or paw extensors. To put it shortly, the cortical points for extension of the right forelimb of this dog had been removed from his left hemisphere and had been implanted in his right hemisphere. The left middle cord was then divided high up and its distal end stimulated, when exactly the same movements occurred as had resulted from stimulation of the right cortex. Experiments were carried out on other dogs in which the left middle cord was sutured to the upper part of the right brachial plexus. Good recovery of function occurred, and the subsequent results of cortical stimulation were in every way parallel to those of the first experiment. Kennedy's results were in every way confirmed.

From these experiments, which Sir William Bayliss considered fundamental in connexion with the function of the cortex, have arisen certain rules. First, if a peripheral mixed nerve is cut the corresponding motor cortex loses its electrical excitability. (This, I submit, is only another way of saying that if you block an efferent path near its periphery there can be no result from stimulating that same isolated path as it leaves the cortex, and I infer from this that the results of stimulation in the motor area are those of stimulation simply of an outgoing path and not stimulation of a centre of function.) Secondly, it does not matter to which area of the motor cortex nor to which hemisphere you transfer your peripheral innervation; complete recovery of function occurs—motion, co-ordination, and sensibility—provided that the path in and the path out are fully restored. (From which I infer that the path is much more important than the whereabouts in the cortex.) Lastly, in this recovery of function the afferents must be all-important. Their functional recovery after the disorientations produced by the experiments I have just described must precede the regaining of co-ordinated and ultimately perfect movement, which can take place only by proprioceptive guidance. We have already seen that the only consciousness of movement performed comes from the periphery via the afferents. The unusual patterns from the latter, when a false or ineffective movement is performed and when a fresh act is being trained in, will apparently guide any part of the cortex to complete functional restitution. There is in the function of movement a running analysis from the proprioceptive system, and sometimes in addition from the visual and auditory systems, which is absolutely essential to this function, and from this fact it is probable that movements and sensibility are not separately represented in the cortex, though the afferent and efferent paths may connect on with the cortex in regions widely apart.

I have already referred to the visual region of the cortex as simply the place of reception of the visual path in very regular order. A very great part of this visual cortex may be destroyed in man with little lowering of the visual faculty. A bullet passing through both occipital lobes and causing thrombosis of both calcarine arteries and great destruction of the cortex of the cuneus may leave the impingement of the macular fibres upon the posterior limits of the calcarine fissure and on the posterior pole intact. Central vision remains perfect and the visual faculty is really not impaired at all. There is simply the loss of the peripheral fields. Both in the South African war and in the great war I have seen examples of this occurrence. If the bullet passes farther back and crosses the calcarine ending and posterior pole, there is destruction of much less of the cortex, but there is much more disturbance of the visual faculty, though again only because the more important macular afferents are destroyed. Destruction of

one occipital lobe, again, produces no breaking up of visual function. A case illustrating this fact was for many years under my observation. A large tumour with many lobes like a dahlia root was dug out from the patient's left occipital lobe. Arising from the tentorium, it had grown across the occipital lobe and had become superficial in the region of the cuneus. Yet this man had no difficulty in returning to work at a skilled mechanic's bench, at which he has carried on for more than twenty years. He tells me that directly he had learned to dodge his absolute right hemianopia, his filing was just as true and his visual judgement was just as good as before his illness and operation.

Destruction of both occipital lobes causes profound disturbance of the visual faculty even in animals, and in man extensive lesions of the white centres of both these lobes, such as occurs in Schilder's disease, has a similar effect, which increases rapidly as the degeneration extends forwards, though there is no involvement of the cortex—as if the occipital lobes were indeed more closely associated with the visual faculty, afferents apart. I have seen no clinical evidence to connect the outer cortex of the occipital lobes with any higher visual function, nor the cortex of the left angular gyrus with the acceptance of written language or with visual disorientation. Visual disorientation has always, in my experience, resulted from a bilateral lesion of the white matter severing the transcortical path running forward from the occipital lobes. One such case resulted from a bullet traversing the brain from one angular gyrus to the other. There was right hemianopia, but vision was not otherwise impaired. He could see and name every object, but he could never avoid running into the tables and chairs in the ward, and when a handful of money was thrown on the ground and he was placed beside it, though he could name and count the coins and make a correct addition of them, he was unable to find them to pick them up. This patient lived many months in this condition, perishing ultimately from ventricular abscess from a scrap of cloth which the bullet had taken into the brain. The nature of the lesion was verified by necropsy. This patient could not connect his visual impressions with his outgoing executive path because the connecting path in the white centre was cut.

The faculty of hearing is only disturbed in man by a lesion of a very small area of the cortex of the temporal region, and then only when the lesion is bilateral. No case has been recorded in which this narrow bilateral lesion has not seriously impaired hearing. This region, known as Heschl's gyrus, is an architecturally distinct region of the cortex, and it is known to receive the radiation from the mesial geniculate body which presumably constitutes the central auditory path. It is an astonishingly tiny area were it a centre of function for so great a faculty as that of hearing. Heschl's gyrus on the left side is of high importance as subserving the faculty of speech. I submit that the cortex of this gyrus is of high importance in connexion with hearing and speech because it is the sole recipient of the central auditory path, and that it is not a centre of function.

The modern conception of the relations of the brain with the function of language began when Dejerine proved that loss of acceptance of written language on the one hand, and loss of exteriorization of speech on the other, could result from purely subcortical lesions, or rather transcortical lesions, which severed the connexions of the left temporal region with the visual receptive area and with the outgoing path respectively. Subsequent pathological evidence, of which I have seen a great deal, seems clearly to prove that loss of acceptance of spoken language, or "word-deafness," is most commonly due to a lesion of the white matter, undercutting the left temporal region, and so dividing the afferents in the central auditory path, and that it is sometimes due to a lesion of Heschl's gyrus, upon which these same afferents impinge. Inasmuch, therefore, as "word-blindness," "word-deafness," and aphasia result relatively or absolutely as permanent events from local lesions of the brain, they are caused by destruction of afferents and efferents, and not by destruction of centres. I was taken to task by Sir Henry Head some years ago for formulating this proposition, on the ground that in mentioning subcortical lesions I was dealing with

matters outside speech in its relation to the cortex. I would explain that I consider that the faculty of speech is not the pouring out, as it were, of water from well-stored cisterns in the cortex; it is a high, delicate, and easily upset faculty, which depends very greatly for its functional stability upon a running analysis of correct execution which we receive with our ears and with the proprioceptors of the articulatory mechanism when we speak, and with our eyes and the proprioceptors of our hands when we write. If the two afferent paths by which this running analysis of spoken speech is carried out are cut across, the pattern of speech rapidly deteriorates; though at first it may be voluble, later it degenerates into a jargon bearing no resemblance to the language originally spoken, and, finally, speech tends to be completely lost. As both these afferent paths seem to enter the cortex in the region of Heschl's convolution, they are frequently involved by lesions of the white matter undercutting the left temporal cortex. This is the only lesion known to cause jargon aphasia, and it is a common lesion causing word-deafness. I have seen this proved at many necropsies. One that occurred in my practice only a month ago may be of interest. This was a woman with a tumour involving the left insular cortex, who had suffered for many months with symptoms of increased intracranial pressure without localizing signs. During the last week of her life, and then only, she developed word-deafness and jargon aphasia, word-blindness and right hemianopia, and became totally aphasic. The brain showed a yellow softening oedema extending backwards from the tumour of the insula throughout the white matter underlying the left temporal and the angular cortex. The whole cortex of the outer surface of the hemisphere was normal.

But apart from lesions involving these afferent and efferent paths, which, I contend, cause such profound disturbance of the speech faculty, there is another matter of profound importance, which, together with the lesions of the paths I have just mentioned, will account for all disturbances of the speech faculty, without reference to local centres of function in the cortex. This is the functional breaking up of the speech faculty when the level of its physiological activity is lowered from any cause whatever, including local lesions involving the anatomical substratum. The more difficult functions, the less deeply impressed functions, the functions acquired late, are lost first and most. The foreign language drops out while the mother tongue remains perfect. Solitary nominal recall set in no pattern to swing it up the hill fails, while the patterns of speech still remain facile. Voluntary speech fails sooner than reflex speech, and the patient, unable to exteriorize any spontaneous speech, may easily repeat any word he hears or copy any writing that he is shown. Visual speech fails early in most subjects, for it is the latest of the speech functions to be acquired. The comprehension of spoken language is the last of all to go, for this is the most deeply impressed and the first speech function to be acquired, and from it all other speech functions are trained in. This breaking up of a faculty with the loss of its elements in order of their depth of impression is known as "diaschisis." This term was introduced by von Monakow years ago to explain the occurrence of temporary "word-blindness," which so often accompanies the aphasia resulting from lesions of Broca's region. The word actually means breaking of the connexions, and I cannot help thinking that von Monakow, in using this term, had in his mind the disruption of the afferent, efferent, and transcortical paths, which I am contending are so important in the production of local loss of nervous function.

The association of the speech faculty with the left hemisphere of the brain does not compel the assumption that centres for that function are situated in that hemisphere in right-handed persons. But the alternative must be that the primary paths—afferent, efferent, and transcortical—must be developed in relation with the left hemisphere alone. The facile and invariable recovery of speech after lesions of the left hemisphere in children at an age when neuroblastic development is active and the laying down of fresh paths is possible favours this alternative. The choice of the left hemisphere is to be connected with that supremacy of the left hemisphere long present in

the human race in its expression of right-handedness. This seemed to be the view of Hughlings Jackson in his oft-repeated remark that he "considered that the right hemisphere was equally important, or even more important, than the left hemisphere, in connexion with the speech function in the right-handed person." Why it should be more important does not seem clear, but for Hughlings Jackson doubtless the right hemisphere would be further removed from the impingement of the tract subserving speech upon the left cortex, and therefore would constitute a realm of more complicated and higher function.

The connexion of the prefrontal lobes with mentality does not seem to rest upon the surest of facts. Mentality should be a function of the nervous system as a whole. Very widely spread destruction or isolation of the cortex anywhere and in either hemisphere will, for a time at least, result in grave depression of this function. What has struck me forcibly in my clinical experience is that lesions of the prefrontal region involving the cortex are so much less potent in this respect than destructive lesions of the prefrontal white centre, extending as these often do backwards to catch the forward fibres of the corpus callosum and part of the radiation from the temporal isthmus, and the obvious inference is that by such lesions of the white matter so much more of the cortex is functionally isolated, so many more of the transcortical paths are severed, and the possibility of compensation by other regions of the cortex is thereby defeated. I have seen the gravest disturbances of mentality from cortical and from subcortical lesions in every part of the brain, but more from subcortical lesions; of all lesions producing mental reduction those of the corpus callosum, however, have been the most striking and constant, and especially when the splenium is destroyed. One can well realize why the great anatomist Willis was convinced that the seat of the soul was in the corpus callosum. He had doubtless seen, as I have seen several times, a lesion of this structure associated with such loss of memory from moment to moment, such disorientations of association in consciousness, the more striking for the complete absence of hebetude, as to convince one for all time of the high potency of transcortical lesions in breaking up higher nervous functions. It is to such transcortical lesions rather than to any cortical lesions that the phenomena of apraxia, agnosia, and disorientation are attributable. Huge lesions of the brain, both of cortex and subcortex, even in the positive regions, are sometimes seen with little disturbance of nervous function. Most of such lesions have occurred in early life, and while neuroblastic development is still active. For example, a man of 24 years of age perished of tuberculous meningitis in my ward at St. George's Hospital. We found a porencephaly involving almost the whole area supplied by the left middle cerebral artery. Yet he was right-handed, and was a skilled artisan, and had shown no signs of a defective nervous system.

In a child under the age of 6 years a lesion involving Heschl's gyrus on the left side produces no permanent aphasia, but complete restoration of speech occurs provided sufficient intelligence remains. Nor does a lesion of the parietal region produce the very permanent defects of sensibility which are seen in the adult. This is another way of saying that, provided sufficient healthy cortex is available, and provided neuroblastic development be active, the paths which subserve these late developing functions will be redeveloped in connexion with other regions of the cortex. For in the brain the later developing structures are so much determined by the development of function, and for this reason it is indeed probable that human brains are not all structurally the same as regards details of anatomy subserving the higher and later developed functions.

It may be argued with justice that the different structure of the several parts of the cerebral cortex suggests an especial function for each region. But there are more than forty such areas which have been mapped out as architecturally distinct, the fascinating study of which has not yet thrown any light upon the part which each area may take in the make-up of nervous activity as a whole.

The cortex of the cerebellum shows no more localization of function than that determined by the bilateral symmetry

of the body. The limbs of the same sides are more affected by lesions of the lateral lobe; the head, neck, and trunk more by lesions of the vermis. The lability and the compensatory possibilities of this cortex are most remarkable, for it may be said of the symptoms resulting from an acute and terminable lesion affecting chiefly the cortex, severe though these always are, that they invariably recover. It is of especial interest that irritative lesions of one of the chief afferents to the lateral lobe—namely, the vestibular nerve—produce exactly the same symptoms as does an acute lesion of the lateral lobe. For example, acute vestibulitis is only distinguishable from an acute vascular or inflammatory lesion of the lateral lobe by the deafness due to a simultaneous involvement of the cochlea, when this is present. When, however, the white connexions are destroyed, even locally and by small lesions, permanent symptoms result, and these are sometimes of local distribution. Thus, one may see the eyes, or speech, or the trunk, or the upper limb, but very rarely the lower limb, exclusively or predominantly affected. Any localization of function that there is in the cerebellum seems to be in the white matter and to result from destruction of the afferent and efferent paths of local direction.

The oculomotor nucleus has been resolved by anatomists into a very definite series of paired and unpaired subnuclei, and an attempt has been made to invest these subnuclei with local function. The results have not proved of clinical value, and even hypothetical "supranuclei," which are supposed to rearrange the cerebral incitations for the oculomotor nucleus, have been called upon to help the matter out. Such localization seems unnecessary and untenable on physiological grounds; for the oculomotor nucleus is nothing more than one region in the path subserving the movements of the eyes where a resorting of nerve fibrils occurs from the terms in which we use our eyes into terms of the peripheral nerves. There is, in addition, the path of the metameric light reflex thrown in.

Now we know well that the outgoing incitations from the brain to the oculomotor nucleus arrive at that nucleus in terms of conjugate upward movement, downward movement, and lateral movements and convergence; for all ablations and excitation of the brain prove this. Moreover, lesions just in front of the posterior commissure which do not touch any part of the oculomotor nucleus will cause paralysis in each or all of these terms, according to the position and extent of the lesion, and in these terms only. The path as it descends lies lateral to the nucleus and its elements turn in to the nucleus in known order: first those for upward movements, then those for downward movements, then those for convergence, and, lastly, those for lateral movements. It is this turning of the several elements of this path at different levels which determines local loss of function in terms of vision when there is a local lesion of the oculomotor nucleus, and not because a function is located in the grey matter thereof. Actually a lesion of the oculomotor nucleus, or of any other nucleus or mass of grey matter, potentially creates three lesions: the first in the incoming path, for this does not end abruptly; the second in the convergence, and this will produce irregularity, loss of balance, and inco-ordination in the result; the third in the outgoing path, for this does not gather abruptly.

CONCLUSIONS.

1. In the consideration of a faculty of the nervous system it is just to locate the function in the whole of the anatomical substratum connected with it, and not in any one part of it. The substratum is a path commencing in the periphery, entering the central nervous system and converging with other paths which modify its function at each convergence; entering the cortex of the brain and spreading widely with infinite convergences and modifications of function and gathering again thence to return to the periphery. In so far as this path is compact and single it is vulnerable to local destructions. Inasmuch as it is diffuse or duplicated in another place, it is not vulnerable. In the cortex of the brain the paths soon become diffused. Keep away from those regions of the cortex through which the compact single paths to and from the periphery are known to pass and ablations will produce no loss of function, for the path is here too widely spread and the

function too widely distributed to be influenced by small local loss; nor will such terms as "annexes," "association areas," or the word "psycho" prefixed to any word that you may wish satisfy us, in the absence of any definite evidence, as to the functions of the highest product of evolution—the cerebral cortex.

2. The chief difference between the brain of a bird, in which no ablation produces local loss of function, and that of a mammal, in which ablations in certain definite regions produce temporary loss of function, and again between these two and the brain of man, in which certain ablations produce permanent loss, seems to lie in the progressive development as one ascends the animal scale of direct and compact paths to and fro between the cerebral cortex and the periphery, and these paths tend to become exclusive as regards a definite function in the highest animal; whereas in the less high animal the indirect and ancestral path is still utilizable when the direct path is damaged. The brain of all the higher animals must be built up structurally and functionally more or less upon the same plan.

3. The experimental physiologists of to-day have laid down that the motor cortex is only so-called by them because it is more excitable than the rest of the cortex, and that even in this region lability of function, facilitation, and deviation of response are much more characteristic features than is localization; and that there must be other mechanisms than this precentral cortex which act directly upon the lower motor mechanism by means of direct descending fibres; and that normal motor activation takes place through descending fibres from many parts of the cortex; and that in complex motor activity the cerebral cortex acts as a whole, though the activity of some parts of it may be accentuated and of other parts depressed; and that the activity of any one part of the cortex is conditioned by the balance of innumerable activities which proceed

from other parts of the cortex. (I have here used the words of Graham Brown.) The physiologists have abandoned the localization of function within the cerebral cortex, and this position is in accord with the clinical evidence in man.

4. The past century has seen the question of localization of function in the higher parts of the nervous system introduced by Gall and the phrenologists in 1810; denied by Flourens in 1824 from his ablation experiments upon the bird's brain, for he contended that the brain represented the living animal as a whole, and not in terms of separate parts or functions; reintroduced by Hitzig and Broca in 1860, and carried to a high degree of theoretical detail by the later Victorian authorities, amongst whom, however, Hughlings Jackson stood conspicuously apart, for his theory of the nervous system essentially denied separation of function in its highest parts; again gradually changing in the early part of the twentieth century for a vague and indefinite localization or for a localization of function in the conducting paths only, as adopted by Sir Henry Head in 1924; and finally rejected so far as the cerebral cortex is concerned by both physiologists and clinicians at the present time.

5. It is obvious that each region of the cerebral cortex must be of equal functional importance in the make-up of the perfect animal, yet it is difficult to give up the belief that those regions of the cortex which immediately border upon the junctions of the cortex with the sensory path, the visual path, the auditory path, and the pyramidal path, are more especially connected with the functions these paths subserve. But it must be carefully borne in mind that the evidence in favour of this belief, upon the experimental side, is solely the facilitation experiments of Graham Brown, while upon the clinical side there is no certain evidence whatsoever.

CONTROL OF OCULAR DISEASE OF VENEREAL ORIGIN.

A SURVEY OF THE METHODS EMPLOYED IN SCOTLAND.*

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THE disastrous consequences to humanity which have resulted from venereal disease are well known and universally deplored. Laudable efforts have been made by the medical profession to counteract this evil. An International Ophthalmological Congress appears to be a suitable occasion on which to present a survey of what has been done in recent years in Scotland for the control, by preventive measures as well as by actual treatment, of the ocular disturbances which are associated with venereal disease.

I.—THE CONTROL OF PURULENT OPHTHALMIA.

In 1879, by the discovery of the gonococcus which bears his name, Neisser laid the scientific basis for the treatment of this purulent inflammation.

In 1880 Credé of Leipzig introduced the prophylactic method of dropping a nitrate of silver solution (2 per cent.) into the conjunctival sac of newborn infants, and thereby at once reduced the incidence of ophthalmia neonatorum in a remarkable degree. His method was largely adopted throughout the civilized world, with immense benefit.

In 1901 I had the honour to be appointed, in succession to my revered master the late Dr. Argyll Robertson, to undertake the duties of ophthalmic surgeon to the Royal Blind Asylum in Edinburgh, and in my first annual report, submitted to the managers on December 1st, 1902, I passed in review the causes of blindness in 12 inmates—25 males and 67 females. I drew attention to the fact that nearly one-third—31.8 per cent.—of all the cases admitted owed their blindness to purulent conjunctivitis, which had been permitted to occur in newborn children, generally for want of proper precautions which should have been taken at

birth. The directors sent a copy of this report to all the dispensaries and local medical institutions in Edinburgh. Representations made by ophthalmic and gynaecological colleagues in other parts of Scotland lent their aid towards disseminating fuller knowledge, but ophthalmia neonatorum still remained of frequent occurrence.

In 1907 the British Medical Association appointed a committee to investigate and report upon the prevalence and prevention of ophthalmia neonatorum in the United Kingdom. The report was actually prepared by the late Mr. Sydney Stevenson of London, who was chairman of the committee, and was issued in 1909. It revealed the fact that in the various blind asylums and schools the proportion of patients whose blindness was due to ophthalmia neonatorum formed an average of about 35 per cent., and that there had been no certain diminution of the disease during recent years. Attention was also drawn to the fact that numerous cases had been known to occur among patients attended by medical practitioners, as well as in those attended by midwives only.

In 1911 the Local Government Board (now the Department of Health for Scotland) instructed Dr. T. F. Dewar, one of their medical officers, to investigate the position in Scotland. In the report which he submitted in 1912 Dr. Dewar estimated that approximately 500 cases of ophthalmia neonatorum occurred in Scotland annually. Of these, from 30 to 40 suffered some impairment of vision, and from 5 to 10 became economically blind. He found that medical opinion as to making ophthalmia neonatorum a notifiable disease was not unanimous, partly for sentimental reasons, but to some extent owing to a prevalent belief that under the existing conditions the disease was already becoming less frequent in Scotland. He pointed out the need for midwives being instructed to play their part more efficiently in the prophylactic treatment. Following the example of England, some local authorities in Scotland had already adopted compulsory notification, and after the circulation of Dr. Dewar's report the number of authorities which voluntarily adopted the action rose from 26 in 1912 to 40 in 1916.

In 1915 a Midwives Act for Scotland was passed, and under the rules drawn up by the Central Midwives Board for Scotland it became incumbent upon every midwife to call in to her assistance a registered medical practitioner

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