THE PRODROMES TO CORTICAL LOCALIZATION*

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This lecture is dedicated to the memory of a man who excelled as greatly in qualities of character, in probity and dignity, as in mind. University College and its hospital has had a major share of great men and we do well to honour them. It would not become me to try afresh a description of Rickman Godlee since entirely admirable accounts have been given by those better equipped with personal knowledge than I. I can do no more than add my respects.

A suitable exercise for this occasion would be the making of a journey back into the past. Its object would be to discover what sort of knowledge Rickman Godlee must have possessed at the time of his famous operation on young Henderson, an event so perfectly described by Wilfred Trotter (1934) that it would be rash to venture it again.

We know that Godlee was a well informed anatomist since he had taught the subject for long in his earlier years. That fact, together with the intimate knowledge of antiseptic principles learned from his famous uncle, fitted him as few men could have been for the bold surgical adventures that he undertook in skull and chest. But though we can be sure that Godlee knew the anatomy of the brain very well, what of its physiology? What could he have been taught or have learned about that? More particularly, by what steps had that knowledge been built up during the nineteenth century? There is much to examine. There is no tract in the cord or brain-stem, no nucleus, no aggregation of cells, no sulcus, no convolution but has a history of its own, a history in all cases still uncompleted. In the present conspectus it will be difficult to make more than a regrettably cursory survey of much fascinating material, of discoveries by men famous in their day and famous still. We shall find confirmation of Frederic Bartlett's (1950) statement that an element of doubt is present in all beliefs, that no man believes what he believes all the time. We shall see doubt increasingly invading neurophysiological

thought in the middle of the nineteenth century up to the final revolution that occurred in Godlee's lifetime.

Early View on Brain Function

The history of brain function can be arranged in an overlapping pattern, in which anatomy and comparative anatomy, dissection and experiment, fused by degrees with clinical medicine and gross pathology. Many of the experimenters were clinicians and one finds them often in a dilemma in which the facts of bedside observation were at war with deductions drawn from experiment, but as usual the latter were taken as the sounder evidence. They were compelled therefore to propose or adopt theories for neurological events which must have strained their credulity. I shall quote examples later.

It is remarkable that the anatomists were able to form as good a picture as they did of nervous activity by a judicious mixture of common sense with observation and by comparisons between the nervous structure of different animals. The matching of structure with potentialities of behaviour had obvious merits but it was a more difficult task than then appeared and is far from done with yet. The fact that creatures could move, eat, reproduce themselves, fight, and survive with little more than a double thread of nervous tissue and ganglia of various sizes and shapes would suggest strongly that the cerebral hemisphere of the higher species had mental rather than motor properties. There seemed to Herbert Mayo in 1827 to be a "principle of improvement" in the nervous system plain to the eye, and this gave a particular point to the researches in comparative anatomy of Cuvier, Vicq D'Azyr, Arnold, Tiedemann, Newport, Robert Owen, and Carpenter. At the same time dissections of the brain by those men and by Rolando, Charles Bell, Reil, Gall and Spurzheim, Serres, Mayo, and a host of others, led to a useful working plan of the relationship of the hemispheres to the brain-stem and spinal cord. It came to be generally conceded

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FIG. 1.—Dissection of pyramid running supposedly to the corpus striatum (Herbert Mayo, 1827).

that in the carnivores and in man the posterior columns of the cord were sensory and the anterior motor, leaving the lateral columns indeterminate. The posterior columns were traced to the thalami and the anterior to the corpora striata. This conclusion was not arrived at without pain for in contemporary engravings the artists failed to make the pyramid end in the corpus striatum as can clearly be seen in Solly's diagram and in Mayo's beautiful dissections (so much admired by Elliot Smith). Bell too speaks of the pyramids as streaming either through or past the striate bodies towards the cortex. To some the apparent continuity of the posterior columns with the cerebellum suggested a sensory function there, but this view was not held by many. Alexander Walker (1834) wrote a long and quarrelsome book in which he contended that the posterior columns were motor and the anterior columns sensory but on the whole at that date the best opinion agreed that the striata and anterior columns were motor, the thalami and posterior columns

sensory. As late as 1869 the curious reader will find in Carpenter's *Physiology* (7th edition) a designation of the corpus striatum as the motor ganglion, the optic thalamus as the sensory. Of discrete limb localization there was nothing. It is true that Saucerotte (1778) in his essay presented for the prize offered by the Academie Royale de Chirurgie on contrecoup, concluded that the striata were motor to the hind-limb, the thalami to the fore-limb. This view found experimental confirmation from Serres and Loutan (1826) and clinico-pathological endorsement by Foville and Serres independently. The proposal met with little support in England, but the existence of a theory for the independent cerebral representation of arm and leg indicates clearly the need felt by clinicians for an explanation of the monoplegias. Bouillaud (1830) voiced their unrest.

After Saucerotte's abortive attempt to find a separate localization for limb movements nothing very positive happened for the best part of 100 years. In the meantime the physiologists by experi-

ment crystallized all knowledge into a formula that confirmed anatomical results and was accepted for decades. It was based on the fact that experimental excitation of the brain-stem from the quadrigeminal tubercles downwards as far as and including the spinal cord led to movements, frequently convulsive. The cortex itself was inexcitable and indeed movement was the more easily caused the further the experimenter descended from it along the neuraxis. From Haller (1755) and Lorry (1760) to Legallois, onwards to the best observer of them all, Flourens, and on again to Magendie and everyone else, all were agreed upon this—the brain was unresponsive except at the lower and lowest levels. The hemispheres were the seat of the “will”; they excited movement by playing on these motor mechanisms. But how they did so no one knew and no nice man would ask! So we find even as late as 1886 Hughlings Jackson writing, “When I first began the investigation of nervous disease I supposed, as most other physicians then did, as perhaps most still do, the seat of epilepsy to be in the medulla oblongata”. The impressive words here are “as most still do”—so deep was the imprint of the physiological teachings of the past on his contemporaries’ minds. Their reluctance to accept evidence that swerved abruptly away from tradition would have amused, and I fear delighted, Wilfred Trotter. Flourens had shown that creatures lacking their hemispheres could still move, swallow, fly, swim, but had lost the will to do so. They lived in a sleep but were denied the privilege of dreaming (so Flourens said). Very soon Bouillaud showed that very similar states resulted from excision of the frontal lobes only: his animals became, he said, “profound idiots”. Many years were to pass before Munk, Goltz, and Ferrier would return to this subject better equipped to analyse it. Imperfect though the earlier experiments were they none the less led to important conclusions such as that loss of the vision in the contralateral eye resulted from hemispherectomy, a disability soon proved to follow injury to the geniculate bodies. Again, Flourens’ experiments on the cerebellum settled once and for all its coordinating function. Rolando had been wrong about this, for seeing how extremely weak and clumsy his animals were after wide damage to the cerebellum, weak yet not paralysed, he concluded that the cerebellum’s function was “sthenic”. Up to a point this is true but Rolando spoiled it because of his seduction by the sirens’ song of the new science of electricity; he saw the cerebellum as a living voltaic pile energizing the whole brain. Rolando, though a trifle off his course in this, was at least nearer the truth

than Magendie who proved to his own entire satisfaction that injury to the cerebellum made the animal run backwards, whereas injuries to both corpora striata made it run forwards as if propelled by an irresistible force.

Looking back over this period, one in which a surprisingly large number of important books on neurophysiology and neurology were written, we see that the experimenters, frustrated by the failure of their crude cerebral stimulations, turned more and more to ablations. We shall see later why their stimulations failed. In the meanwhile we must be content with the general inference that the corpus striatum was first choice as a motor organ. A few writers recorded movement following its stimulation, but as many denied it. One thing was certain, that hemiplegia followed its destruction in man, or so they held.

The Phrenologists

Before proceeding further we must pause for a glance at the phrenologists. Their work from the time of the Napoleonic wars onwards played a most important part in all scientific thinking. The proposition of Dr. Gall, supported by Dr. Spurzheim, that the hemispheres were not functionally univalent but were a mosaic of special properties, mental or emotional, that they were in fact a “plurality of organs”, made an immediate appeal to European thought. The special point to which attention should be drawn today is the excellence by the standards of their time of their huge “*Anatomie du Cerveau*”. They were the first to show that the trigeminal nerve was not lightly implanted in the pons but that its root fibres could be dissected down as far as the inferior olive. Gall in particular was a serious anatomist. He was on the side of the angels in insisting that the study of the brain by horizontal slices, the common dissecting room method then and one too much used by pathologists today, was no way to study that organ intelligently. All dissection must be from the medulla and base upwards. Only thus could any relation between structure and function be discerned. It was an admirable practice. It has its lessons for us today for we have concentrated on the cortex too long. Only in such a way can we see the brain as an integrated organ for the synthesis of experience, as the afferent system that Sherrington from his earliest days insisted that it was.

We can look back on phrenology now with a more tolerant eye. We see it most obviously as the first attempt, though a wrong one, at the functional parcellation of the cortex. But if we read the literature of that time we quickly see that the more

intelligent adherents to the cause, such as the members of the Edinburgh Phrenological Society, made the first important enquiries into applied psychology, especially criminal psychology and into the natural history of delinquency. Their work in those directions has not been properly appreciated. There was so much that was ridiculous, especially their decision that the cerebellum was the seat of sexual urges. But even there they were the fore-runners of Freud in making sex a subject proper for discussion. "Why", wrote Gall, "make use of circumlocution in treating of the most indispensable and powerful of all the instincts?" Their localization of sex in the cerebellum, though it must have led to as many piquant drawing-room discussions as did Freud's doctrines, proved a major mistake and contributed much to the ultimate discredit of all

their theories. Yet years later we may discover Marrant Baker in the 1867 edition of Kirke's "Handbook of Physiology" casting a wistful look back and saying that "even if the system of phrenology might be false, the theory might be true". However pure the intentions of Gall and Spurzheim when they began, it is manifest that they quickly allowed themselves to be seduced by the curious, the fashionable, and the wealthy, and became little better than charlatans. Their 33 areas with singular properties became objects of scorn.

There is another reason for speaking of phrenology. It is because of its eventual influence on Broca's localization of speech. Bouillaud had become an adherent, if a critical one, to phrenology. He accepted the phrenological localization of language and memory of words in the under surface of the frontal lobes, though, as he said, "Dr. Gall had announced rather than demonstrated" the fact. Bouillaud was the first to express surprise that no neurologist had enquired before 1827 into the location of the pathological lesions present in patients with those verbal difficulties that Trousseau later christened aphasic. "I do not know" he said "why no one has occupied himself with a subject not less interesting in its physiological relation than in its medical". He was quite right: no one had. The lesions would be found, Bouillaud said, always in the frontal lobes and offered a prize to anyone who could bring contrary evidence. It was never won, or, more accurately, never paid. But so it came about that when Paul Broca published his first specimen from an aphasic subject in 1861, his famous "Tan, Tan", he hit upon the posterior end of the third frontal convolution, not because it alone was diseased, far from it, but because it was nearest to the phrenologist's subfrontal orbital surface speech areas. The whole story, and a fascinating one it is, has been exquisitely told by Souques (1928). He gives full credit to the prior observations of Marc Dax who, before anyone else, observed that it was the left hemisphere that was usually found damaged in aphasics, a fact that did not dawn on Broca until he had seen Dax's posthumous but unpublished thesis.

Further Experiments

It is time that we returned from these bye-ways to the main road. Although new experiments being made apace they were doing little to disturb the accepted teachings, yet we can discover growing unrest at the discrepancies between theoretical and applied neuropsychology. Let us turn for instance to Longet whose book of 1842 is the most important in the first half of the nineteenth century. He

FIG. 2.—Phrenology's plurality of organs. Area 29 (in orbit) is the centre for language, 23 for colour perception, 32 is wit (Spurzheim).

FIG. 3.—Cortical layers in different animals according to Baillarger (1840). The large central section is pig's cortex, with fibres entering grey matter.

reviewed the experimental proofs of himself and others. Of his own he says this :

"On dogs, rabbits and on some kids we have irritated with a knife the white substance of the cerebral lobes, we have cauterised them with potash, nitric acid etc.; we have run galvanic currents through them in all directions without succeeding in evoking involuntary muscular contractions ; the same negative results were found in directing these agents to either grey or white matter."

Longet goes on to sound a warning note against the too rigid interpretation of these laboratory results. He said :

"However, the pathologist would fall into a grave error of generalising on what experiment reveals if he deduced that, in partial affections of the cerebral lobes of men, all must follow as in these experiences. Indeed every day in acute and chronic affections of these organs one sees, on the contrary, epileptiform phenomena supervene, partial contractions of the face, of the mouth. . . . To explain the invasion of convulsive phenomena experimental induction leads us to suppose that in men disease can stir in the bosom of the brain irritations such as artificial and immediate stimulation cannot provoke."

Longet's general inference was completely true. Local disease of the brain induced in some way a sort of undefined selective effect on the executive lower levels. Local palsies, for example, caused by fibrous tumours of the meninges, had to be explained by attributing them to counter-pressure on the striate bodies or lower down still, and if the same sorts of lesions caused fits, why, they were due to counter-irritation of the mid-brain or spinal cord. Longet had many important experimental results to record. One of these was that in his own experience he had found the corpora quadrigemina themselves inexcitable but that movements occurred only when one penetrated deeply towards the white matter of the mid-brain. The anterior were stations on the visual pathway.

Mention must now be made of some long forgotten experiments by the King's College neurologist, R. Bentley Todd, whose name lives coupled to the post-epileptic hemi- and mono-plegias that he was the first to describe in detail though they had been studied by Bravais. Todd's work was described in the Lumleian lectures for 1849 on convulsive diseases. He very rightly asked how a spinal or medullary theory of epilepsy could account for those many fits in which loss of consciousness was the only sign. It might have been accounted for on a mesencephalic basis if the opinion of Gerdy (1840) was adopted that this structure was the seat of consciousness. Over 100 years later that theory was to be reborn. But Todd's ideas were not quite those of Gerdy. He proceeded to describe his own experiments on rabbits. He had wished, he said,

to ascertain whether galvanic stimulation of the brain (by a "magneto-electric rotation machine") gave rise to anything similar to the tetanic effects seen by excitation of the spinal cord. Similar but still tetanic contractions were obtainable, he found, from the medulla. His next objectives were the corpora quadrigemina and the mid-brain but in process of exploration he made an observation that has been forgotten, perhaps because Hitzig was unaware of it and Ferrier overlooked it.

"Having passed fine bradawls into the cranium in such a direction as I had previously satisfied myself would lead to this organ, [the mid-brain] I subjected it to the influence of that machine ; general convulsions were produced of a character essentially different from those which resulted from stimulating the spinal cord and the medulla oblongata. They were combined movements of alternate contraction and relaxation, flexion and extension, affecting the muscles of all the limbs, of the trunk, and of the eyes which rolled about just as in epilepsy. On inserting the awls into the hemispheric lobes still different effects were produced by the application of the machine. I could observe nothing like convulsions but slight convulsive movements of the muscles of the face took place which were no more than what would be caused by the stimulus of galvanism acting upon the nerves of the face.

These experiments, which I repeated several times, and each time with like results, seem to denote that convulsions are modified according to the part of the cerebro-spinal axis which is primarily excited."

Todd goes on to say that stimulation or disease of the spinal cord or medulla would cause tetanus-like or opisthotonic attacks ; of the corpora quadrigemina or the mesencephale they would be epileptic. How modern all this is, though it has been eclipsed by much that was discovered later. Todd refers to experiments by Weber confirmatory of his own. Todd was unable to see anything surprisingly new in these small movements that could be caused by stimulating the hemispheres. His words suggest either that he regarded them as artefacts or more likely that they were not epileptic enough for his purpose. This was a pity since he so clearly had hold of something vitally interesting. The specific mention of electricity by Longet and Todd will only surprise us into the reflection that this method of stimulation had been so little used and then without revelation during the decades since the days of Galvani's (1791) and Volta's (1800) publications.

Nerve Cells and the Cerebral Cortex

So far no mention has been made of the cellular structure of the brain. There was a good reason. None of the neurologists so far considered could see any utilizable linkage between structure and action, except in the broad way that nervous energy very

likely originated in the grey matter, as Willis had believed. It is clear enough to our eyes that had they given more weight, or even their serious attention, to the discoveries that the improved art of microscopy was making they might have found some of the missing clues. Excellent anatomist though Reil was, he had held that the grey matter was only laid on the white without any real continuity. Several authorities were of the same opinion. That the fibres of the white matter could be seen entering the grey was shown conclusively by Baillarger (1840). It is interesting that his monograph, the first devoted to the cortex alone, should have enabled him to have described at once the six-layered cortex that we know today. A white line had already been reported "in the cortex of the posterior convolutions" by Vicq D'Azyr (1786) and by Gennari (1782). Meckel (1817) observed a white lamination in the cornu Ammonis but nowhere else. Only Baillarger saw the six layers as a widespread cortical arrangement. He says nothing about cells; he saw the cortex, as Willis had done, as a motivator. He recollected Rolando's explanation of the laminated arrangement of the cerebellar folia which had reminded Rolando so strongly of a voltaic pile that he assumed that the cerebellum's function was to energize the brain and to be to that extent motor. Baillarger thought that it was rather the cerebral layers that had this function. He traced white fibres into the cortex and found many running horizontally. We still remember Baillarger and the inner and outer white fibre bands that he was the first to delineate.

Nerve cells themselves had been seen originally in the large ganglia of the mollusc by the French naturalist, Dutrochet (1824), in 1839 by Valentin, by Purkinje (1837), by Ehrenberg (1836), and in increasing detail by Remak, Hannover, Bidder, Stilling, Clarke, Wagner, Todd and Bowman and many others famous in the annals of micro-anatomy. In 1851 both the crossed and the direct pyramidal tracts were accurately located in the cord by Türck of Vienna. Türck's obser-

vations were of uncommon merit and can be read with profit to this day. He could not be sure of the precise origin of the pyramidal fibres superiorly. They seemed to come from high up in the brain, maybe from the lenticular nuclei and from the cortex. His experimental cord incisions and clinical deductions made him as sure as he could be that they were motor in function. Nine years later he proved that the sensory pathways ran through the posterior part of the internal capsule.

As for the cerebral convolutions, they had been figured by anatomists for centuries with increasing precision. Names were attached to them only by degrees. For our immediate purpose the most important was the fissure of Rolando. It was actually named by the French anatomist, Leuret (1839), who in his plates of the brain paid more attention than anyone has yet done to the sulci. He had, he said, found a furrow about midway along the brain's convexity and found it very constant in both monkey and man and said, "I have called it the furrow of Rolando". Rolando had described it eight years before. However, it should have been named after Vicq D'Azyr who had priority over Rolando, but the edition of Vicq

FIG. 4.—Luys' (1865) centres for face, trunk, and leg in the corpus striatum.

D'Azyr's anatomy that Leuret used lacked some of the plates through some fault of editorship (see Broca on this subject, 1878). The fissure was renamed the central sulcus by Huschke in 1854.

It was in front of this furrow that W. Betz, Professor of Anatomy in Kiev, described briefly in 1874 the great pyramidal cells of the fourth cortical layer. Unfortunately he did not illustrate his short paper, the results of which were amply confirmed with excellent figures by Bevan Lewis in 1879. Betz merely gave the average sizes and positions of the cells and described them as having large axis cylinders and large vertically directed dendrites. "Ich möchte sie Reisenpyramidalenzellen nennen" he said. He added that he found them in dogs in just that part of the brain that Fritsch and Hitzig had found excitable four years before. Betz said that they doubtless have motor functions, and that terse statement marks an epoch in neurology. The rest of Betz's paper is given up to the naming of the continuation of the motor area over onto the medial surface of the brain. He proposed the name "lobulus paracentralis" for this, a name that has survived. Betz believed that it, rather than the precentral convolution, was the homologue of the excitable cortex of the dog.

This cursory survey of so much of the greatest importance has not perfectly synchronized with the neurological story of the cortex. It has led us on too far. We must go back to the publication of Luys' researches in 1865, for he had something to say about motor cells that might be overlooked. Luys believed that the corpora striata were the effective motor organs, but he was as badly in need of separate mechanisms for head, arm, and leg as his predecessors. Rather fancifully he assigned them to the different arcades of the corpus striatum and made hard mechanical diagrams to show this functional arrangement. But though he did this he was impressed by the cortical cells. Comparatively large cells he saw in histological sections lying deep in the cortex. They were, he stated, incontestably motor in function. He drew that conclusion from comparison with the anterior horn cells of the spinal cord, which were so much larger than the sensory cells of the posterior horns. On the same grounds he correctly assumed the substantia nigra to be involved somehow in movement. He added that those cells "which seem more particularly devoted to act as the substratum to manifestations of voluntary movement are localised in the deepest layers of the cortical cells". Does this appear to be a contradiction—motor cells in the cortex, discrete motor centres in the striatum? Not by any means. Luys proceeded to say that

there exists in the cortex distinct localizations whence the corpus striatum draws its exciting principle, but he could not define them topographically. He may well have had in mind the precentral gyrus because he described its local atrophy in patients with old-standing amputations.

The difference, then, between what was believed before and after 1870 is a matter of where the localization of discrete function lay, whether in basal ganglia or in the cortex. We can see already in Luys' work that invocation of the cortex that was the hall-mark of Hughlings Jackson's work. And we shall do well to recollect that even after Ferrier had fully established the existence of motor centres in the cortex for all manner of small movements, there were many who thought that the motor paths ended in the corpus striatum. For instance, in Dodd's vast review in 1878 of the whole subject up to date, there is a diagram showing the efferents from the excitable cortex ending in the corpus striatum. It may be objected that others surely thought that the cortical efferents ran down into the cord. Certainly, they did. But no great number of observers or research workers ever believe exactly the same things. It would be dull if they did and progress would be slower. As for Luys, it was in the same interesting volume that he described the nucleus that has since borne his name.

Jackson, Hitzig, and Ferrier

The stage is now set for the entrance of the last three figures—Hughlings Jackson, Eduard Hitzig, David Ferrier—who lead us to Sir Rickman Godlee. Jackson's superb contribution was based on induction from the experimental material provided by people with epilepsy. Between 1861 and 1870 he had concentrated his attention on local fits, convinced as he was that the simpler the epilepsy the more profitably it might be studied. He once wrote:

"I am fully aware that there are admirable accounts of the worst fits as types, but some of the accounts are descriptions more of dramas of great human interest than calm and coldly scientific observations in an orderly sequel of the outward phenomena of an inwardly suffering nervous system."

He brought his views to a focus in his famous papers, "A Study of Convulsions" (1870), followed by two more of equal importance in 1873 and 1875. His observations and his conclusions are so well known and have been commented upon and expanded with such masterly penetration by F. M. R. Walshe that I need refer only to those most relevant to our immediate purpose. Jackson from the beginning was convinced that there was a "dis-

charging lesion" in local fits, and that they were caused by damaged nerve cells. The alteration that made them liable to explosive discharge was, he thought, of a chemical character.

As for the part of the brain involved, Hughlings Jackson originally believed that it was the "region of the corpus striatum" or the convolutions near to it. He says "The loose term 'region of the corpus striatum' is used" and a few lines later he adds:

"As the convolutions are rich in grey matter I suppose them to be to blame, in severe convulsions at all events; but as the corpus striatum also contains much grey matter I cannot deny that it may be sometimes the part to blame in slighter convulsions. Indeed, if the discharge does begin in the convolutions, no doubt the grey matter and lower motor centres, even if these centres be healthy, will be discharged secondarily by the violent impulse received from the primary discharge."

This of course is true. It would not be unfair to say that Hughlings Jackson had arrived at the cortex as able to produce movements, if convulsive ones, before the physiologists and that only respect for their laboratory findings caused him to express himself in such guarded language. Years later when the excitability of the cortex had been fully established he made no secret of his original attribution of local fits to the corpus striatum and the neighbouring convolutions. Addison had said that fits without loss of consciousness usually meant that a gross cerebral lesion, such as a tumour, was present. This was a wise clinical generalization and Jackson agreed with it but in his acceptance he showed the particular quality of his genius. He was not so much interested in the tumour as in the evidence that such examples presented of local instability in the neighbouring damaged nerve cells. That this was an enormous advance in neurology is very clear.

In Hughlings Jackson's day the most powerfully explosive substances were nitrogenous, e.g., nitroglycerine; he suggested that the nitrogenous substances in nerve cells might become altered if they were diseased into unstable compounds and assume "explosive" qualities in a physiological sense.

FIG. 5.—The large pyramidal cells in deeper layers of cortex that Luys (1865) thought were motor.

Just so today Russell Myers (1951), for instance, uses a modern physical description when he refers to this explosive instability in a different way saying that "epileptogenic focus" may be envisaged as a cortical site of biophysical and biochemical alterations of cell-membrane permeability and cellular respiration leading to depolarization of the neurons. The two statements so many years apart are expressions of probability in the light of existing physical knowledge. Neurology had travelled far since the days when Bravais (with whose name Jackson's is usually somewhat indiscriminately coupled by the French) had written his monograph on unilateral epilepsy (1827) without seeing in it the disclosures that Jackson found. I have discussed the subject of Bravais on a previous occasion (1935). Local fits, as we have seen, could not in any way be regarded as something newly observed in medicine. It was the new interpretations by Jackson that were everything. It would be only too easy to diverge into a lengthy discussion on Hughlings Jackson who deserves so much. From this time onwards epilepsy could not be, as he put it, "a proper name" but a state in which each example must be regarded as demonstrating some or other of the physiological properties of the brain.

Fritsch and Hitzig

We come now to the paper that revolutionized cortical neurophysiology. It appeared in Reichert and Du Bois-Reymond's *Archiv für Anatomie, Physiologie und wissenschaftliche Medizin* and was the work of two 32-year-old *privatdozenten* in Berlin. It was dated April 28, 1870. Eduard Hitzig wrote several more papers on neurological matters during his life but did not collaborate again with Fritsch. He became professor at the Nervenklinik in Halle, and reviewed the controversies aroused by the doctrines of localization in the second Hughlings Jackson Lecture (1900). The differences in the qualities of Hitzig's and Jackson's minds are very apparent in this address. Fritsch was a zoologist who wrote on electrical fish, amongst other things. In Hitzig's important book "Untersuchungen ueber das Gehirn" (1874) the 1870 paper is reprinted in full with minor alterations. The idea of testing the excitability of the cortex once again in spite of all the failures that had gone before was Hitzig's. He had run galvanic currents through the heads of human beings and seen movements of the eyes. This had encouraged him to try the animal cortex anew. The success of the attempt is known to all the world. The authors attribute the failure of their predecessors to several causes. The loss of excitability which they observed when there had been heavy blood loss in the operative approach would be one important reason. Another and fundamental reason was that the excitable part of the carnivore's brain lay so far forward that it might easily have been missed and no doubt often had been. They suggest that operators had paid too much attention to the posterior parts of the brain because the shape of the skull made that part more inviting for the trephine. In their own early

experiments they took away half the skull, but finding the excitable region so circumscribed, they were able later to expose it through a trephine opening. They summed up their own success by saying, "The method is everything". Their conclusions may be summarized as follows, largely in their own words :

- (1) "One part of the convexity of the hemisphere of the dog is motor, another part is not motor."
- (2) "The motor part lies, generally expressed, more forwards, the non-motor lies more posteriorly. By means of electrical stimulation of the motor part one gets combined muscle contractions of the opposite half of the body."
- (3) "These muscle contractions allow themselves to be localised by the use of quite weak currents to defined, circumscribed muscle groups."
- (4) "The regions responsive to stimulation were very constant in dogs as verified by the greatest response from the weakest currents."
- (5) "The fact is securely founded that a considerable part of the nerve masses of the hemisphere, one can say about a half, stands in relationship to muscle movement."

This is surely an over-estimate. The other, posterior part, was probably the birthplace of the will to move. Their conclusions on the motor function of the anterior half of the brain confirmed the predictions of Meynert (1867) based on dissection and histology.

In their once frequently reprinted figure they marked the centres for neck, fore, and hind limb. The stimuli used were single shocks from a galvanic apparatus. Induced currents they thought were not so reliable because of spread and later Hitzig attacked Ferrier's researches on this ground. Extirpation of the fore and hind limb areas led to weakness of the expected limb. Because of the well established belief in the corpus striatum as a centre for movement we might expect Fritsch and Hitzig to have something to say on that rival apparatus. They investigated its claims by sinking insulated needles into the brain and applying the galvanic current to their butts. Twitchings only occurred when the needle point was so deeply sunk as to be, they estimated, in the region of the cerebral peduncle. (This observation will recall Todd's report.) The contractions were quite unlike those obtained from the cortex, requiring much stronger currents and affecting many more muscles in a convulsive sort of way. They concluded that the subcortical areas played no part in the cortical stimulatory effects that they had seen, for if they had, the muscle twitches should have become more easy to produce the deeper the electrode penetrated. The reverse was the case.

FIG. 6.—Diagram of centres for movement and especially epilepsy.

FIG. 7.—Diagram of excitable motor points: 1, dog; 2, rabbit; 3, guinea-pig; 4, rat; 5, pigeon; 6, frog; 7, carp (Ferrier).

In 1873 Hitzig, who from then on published alone, described further researches in the dog, adding more details, and in 1874 he demonstrated the excitability of the monkey's cortex and in the same year did an important piece of work in the identification of the physiological equivalents of the excitable convolutions in dogs, monkeys, and men.

David Ferrier's experiments were first published in 1873 and are so well known that they require little special description. Both he and Hitzig used minimal currents, just strong enough to be felt on the tongue, the one faradic the other galvanic. From the first Ferrier's observations were vastly more detailed and informative than those of Hitzig. One cannot but admire the energy, persistence, and success of that young man on his excursion into a field where so many had failed. As we have seen, nothing short of a very gross movement or even of a convulsion had satisfied the earlier research workers. Hitzig's and Ferrier's evidence was of a much finer quality. It must have been singularly interesting to see a twitch of an eyelid, a slight elevation of the angle of the mouth, a flick of an ear, a clutching movement of a paw, and the protrusion of the claws produced by weak electrical stimulation of the cortex with the electrodes only a millimetre or so apart.

In 1875 Ferrier, like Hitzig, moved onto the monkey's cortex and from that day forwards the exploration of the brain surface became almost a British preserve. Burdon-Sanderson, Victor Horsley, Beevor, Schaefer, Yeo continued to parallel Ferrier's work, until they were joined by the master of them all, Sherrington. So it came that the flood that Fritsch and Hitzig had let loose submerged their discovery without in any way detracting from its merits, which remain secure for all time. Ferrier, it must be added, contributed something that helps us to understand better the failures of the ardent and intelligent workers of the earlier decades of the nineteenth century. The explanation arose out of his use of comparative physiology, a variant on the comparative anatomy of his forerunners. It will be remembered that many of Flourens' most telling experiments had been done on birds. Ferrier showed that the brains of birds, frogs, and fish were difficult to stimulate, often gave no replies and, when they did so, never in form of local movement. These results solved a puzzle. Added to the causes of cortical inhibition already mentioned they gave us a comprehensive answer to a worrying question.

It must not be supposed that the new discoveries

FIG. 8.—Excitable points in internal capsule (François-Franck and Pitres).

which destroyed the long cherished concept of a physiologically homogeneous cortex were accepted without demur. Much prejudice remained to be overcome. Hughlings Jackson writing as late as 1886 said: "When I first began the investigation of nervous disease I supposed, as most other physicians then did, and as perhaps most still do, the seat of epilepsy to be in the medulla oblongata". The impressive things are the words "as most still do" and the year, 1886. These men would remember the publication in 1859 by the New Sydenham Society of a translation of Schroeder van der Kolk's book "On the minute structure and functions of the spinal cord and medulla oblongata and on the proximate cause and rational treatment of epilepsy". In this it was made clear that a state of exalted sensibility in the medulla made it liable to discharge by the operation of causes either organic or psychological. They might even recollect the impressive writings of Marshall Hall "On the neck as a medical region" (1850) in which he proved (he thought) that medullary reflexes led to closure of the glottis and that it was cerebral congestion that excited a fit. Tracheotomy was the rational answer and it was applied. Time would be needed to break down the barriers erected by doctrines such as these, doctrines which, though they had not brought complete conviction, were at least in line with the thinking and experimentation of the previous decades. It took time to persuade the critics that the electrical excitability of the cortex was an inherent quality of its own. Some bodies, such as one in New York, set up a committee containing two professors of physiology to make new experiments to test the disturbing new theory. They reported favourably. Putnam followed in Boston (1874) with a similar concurrence, as did Luciani and Tamburini (1878). But many said that the movements were due to the spread of currents into the deeper central nuclei. They were encouraged by Burdon-Sanderson's

discovery that the white matter subjacent to the motor strip could be made to give very similar motor replies to faradism. But this was a shortlived check because very soon François-Franck and Pitres repeated the experiments and by brilliant timing were able to show that there was a delay after stimulating the grey matter which disappeared when the white alone was stimulated. François-Franck became in fact a European champion of the new physiology. Not only did he map the arrangements of the motor fibres in the internal capsule, but he and his school demonstrated autonomic visceral results such as changes in pulse rate, blood pressure, and respiration. It was to be expected that the French school would turn their eyes to the visceral effects of cortical stimulation since they had been revived by that master physiologist, Claude Bernard, and in Marey they had a man who had invented new tools, the tambour and the smoked drum, permitting more accurate analysis. Bochefontaine (1876) saw salivation, rise of blood pressure, contractions of the intestines, bladder, and Fallopian tubes, on stimulating the sigmoid gyrus of the dog. His observations received little credence until the hypothalamus and visceral brain were born in our own lifetime. How right Ferrier was when he wrote (1886) "there is no reason to suppose that one part of the brain is excitable and another not. The question is how the stimulation manifests itself". Many years were to pass before the truth of this could be more amply confirmed by neuronography by electronic recording systems, and by looking for results not in the skeletal musculature but in autonomic reactions. These men of long ago had had something to say even there.

The Localization of Tumours

I have been concerned with the anatomy and physiology of brain function and have been forced to omit the running commentary on the manifestations of cerebral pathology that might have been expected. We can imagine that although the cortical localization of movements, of sensation, of vision and the special senses must have been very interesting to everybody, the wider appeal would be made by two other things. First that different forms of epilepsy began to have a meaning that they had lacked and, second, that quite superficial injuries to the brain, as Nothnagel showed, caused paralysis or numbness or hemianopia. Surely these facts must have deeply impressed all men. Certainly no less did the demonstration by Roberts Bartholow (1874) in Cincinnati and by Sciamanna (1882) in Rome that movement or convulsions could be caused in man by stimulation of the brain. They

pushed needles through holes in the skull, holes made in one case by an epithelioma, in the other by injury. At the time of Godlee's famous operation there was already in existence a considerable body of convincing evidence that gross cerebral lesions could be accurately localized in the brain. Hitzig himself published (1874) a beautiful case of subacute brain abscess in a French soldier wounded at the battle of Sedan which had given its site away by localized fits and aphasia. The difference between this observation and Macewen's very similar one in 1876 was that the latter had strongly urged operation. A thoroughly convincing series of cases was collected by Ferrier in his book "The Localization of Cerebral Disease" (1878); he included Hughlings Jackson's cases.

The student of this epoch can feel the pressure rising: the time was ripe for surgery. What, we may ask, were they waiting for? Perhaps fear of the consequences of inflicting operative injury on the human brain? The experimenters had not had much success in keeping the larger animals alive after ablation of brain tissue until Ferrier arrived. Then there was the very real danger of infection and this did in fact carry off Godlee's patient eventually but not before the real point of his operation had been proved. Both Bartholow's and Sciamanna's patients had died of intracranial suppuration a few days after the stimulating electrodes had been pushed into their brains. Although the patients already had infected fungi there had been outspoken criticism of such experiments on men. It must have required great resolution to face the storm that would break if a brain tumour that gave no sign of its presence by local swelling of the skull bones was looked for and not found, or if the patient died immediately. By great good fortune, in the last quarter of the nineteenth century, the correctness of Lister's views were being vindicated. The dangers of infection, though present even now, were diminishing. Macewen was the first to move, using the new physiology in the practical treatment of brain abscess, injury, and dural tumours. Lister had been Macewen's early teacher; he was Rickman Godlee's uncle. Lister had apt pupils in these two. Evidently all that was needed now was knowledge, a full sense of responsibility, and courage. Fortunately for us Godlee possessed these qualities in high degree as he stepped over the threshold into a future unknown—but how rich in fulfilment!

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