The Goulstonian Lectures

ON

A CONTRIBUTION TO THE LOCALISATION OF CEREBRAL FUNCTION, BASED ON THE CLINICO-PATHOLOGICAL STUDY OF MENTAL DISEASE.

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LECTURE I.

Delivered on March 1st.

MR. PRESIDENT AND GENTLEMEN,—In thanking you for the honour you have done me by your invitation to deliver the Goulstonian Lectures for the present year, I would at the same time apologise for my presumption in choosing as my subject such a vexed and intricate question as the localisation of cerebral function. I have but one excuse to offer—namely, that in my researches I have attacked this subject by a somewhat different method from those hitherto adopted, and have thereby obtained results which appear to me partly to confirm and partly to elaborate the conclusions arrived at by certain other and more experienced workers. As my present investigations have already occupied a considerable period of time, it being now 14 years since their commencement and 10 years since my first paper on cortical localisation was published, I think I may fairly claim that the conclusions at which I have arrived are neither hasty nor ill-considered, and I therefore trust that you will regard these, and also the evidence which I am about to lay before you, as not entirely unworthy of your attention.

HISTORICAL REMARKS.

I do not propose to enter into a historical retrospect of the investigations of the past 40 years, as for my purpose it is sufficient to refer briefly to those of the past decade. With regard to the earlier researches, I would remark that the experimental method of investigation, which was introduced by Fritsch and Hitzig and by Ferrier, and continued by numerous workers from whose names it would be invidious to make a selection, may be considered to have served its purpose with the publication of the researches of Sherrington and Grünbaum. These, by linking together the conclusions arrived at by the experimental and the histological methods, resulted in the belated recognition of the neglected histological investigation of Bevan-Lewis and Henry Clarke on the cortical localisation of the motor area, and gave an impetus to the latter method which has already been followed by a considerable amplification of our knowledge of the structure and functions of the cerebrum.

The last, but not the least important, of the researches to which I must refer before dealing with the published work of the past few years are those of Flechsig on the development of the human brain by a study of the process of myelination. The division of the cortex cerebri by this investigator into the two great classes of "sensory centres" and "centres of association" raised a storm of discussion and dissent which is almost unprecedented in the history of research, and which, but for Flechsig, would have overtaken the workers of the past decade. Though many of the results obtained by Flechsig have failed to obtain credence, largely perhaps through the frequency with which he modified them in successive publications, his broad generalisation has successfully withstood the fire of criticism, and forms the origin, if not entirely the basis, of our present knowledge of cortical localisation by histological methods. In my personal opinion, which is based on my experience of the great differences which exist in the degree of development of foetal and infantile brains of approximately the same age, Flechsig was injudicious in applying directly to the adult cerebrum the results he obtained from the investigation of such brains; but, of course, it is easy to be wise after the event, and it is

No. 4518.

probable that the researches of Flechsig would have attracted less attention had they excited less dissent.

During the past decade numerous publications have appeared on the subject of cortical localisation by histological methods. In these several publications the whole cortex cerebri of man, and in many orders of mammals, has been mapped out into various histologically different regions, and in some instances proof of the functional significance of these has also been adduced. Further, the mode of evolution and functional significance of the different cell laminæ of the cortex cerebri have been discussed from both the ontogenetic and the phylogenetic aspects.

As I purpose in these lectures to deal solely with the human cerebrum, it is unnecessary for me to refer, except as occasion serves, to such investigations as concern the cortex of the lower mammals. Amongst the publications which bear on cortical localisation in man, those of two authors stand out prominently—namely, the "Histological Studies" of Campbell and the series of monographs published since the year 1902 by Brodmann. These authors have independently and elaborately mapped out into histologically different areas the whole human cortex cerebri, as well as the cortex cerebri of certain orders of mammals. The human maps of these authors, whilst differing considerably in detail, agree with one another much more than either of them resembles the maps of Flechsig. I have already indicated one reason why the map of Flechsig cannot be applied directly to the adult cerebrum. It will also be evident to you that, owing to the low development in the foetus of the later evolved spheres of association, the projection areas must of necessity differ considerably in their relative size and distribution in the foetus and the adult. Further, without going so far as Elliot Smith, who from the point of view of causation closely correlates fissuration and histological differentiation, although these differ very considerably in the adult cerebrum, I certainly regard histological differentiation as one of the causes of fissuration, others being arterial supply, and probably also certain mechanical conditions of growth. It is hence not surprising that the projection areas of Flechsig, taking for granted their correctness in the foetus, do not bear the same relationship to the main cerebral fissures as do these areas in the adult cerebrum.

HISTOLOGICAL DIFFERENTIATION OF THE CORTEX.

I shall now show on the screen the maps of Flechsig, for comparison with the maps of Campbell and of Brodmann. (Fig. 1.) It will be noticed that the visuo-sensory area is much larger than in the adult, as is also the bodily sensibility projection centre, which in the adult lies entirely behind the fissure of Rolando. Flechsig, however, I may remark, expressly states that the majority of the sensory projection fibres pass behind the central fissure. At the period when the experimentally obtained Rolandic area was considered to be both pre- and post-Rolandic, and to be sensori-motor in function, its supposed distribution closely resembled the foetal bodily sensibility area of Flechsig, and the two were regarded as identical. Now, however, the "motor" and "sensory" areas are regarded as separate and as lying on either side of the furrow of Rolando. It is, by the way, necessary to remark in this connexion, lest I should appear to disregard a recent article by Sir Victor Horsley, that I intend to refer to this when dealing later with the structure and functions of the psychomotor area.

[On the plate which was then exhibited were arranged for comparison two sets of maps by Campbell, published in the years 1904 and 1905, and the maps of Brodmann.]

In view of the great difficulties involved in the cutting up, blocking, sectioning, orientating, and reproducing in diagram form of the cortex of entire human hemispheres, considerable differences might well be expected in maps prepared by two totally independent investigators. It is, however, difficult to understand the well-marked differences which exist in the case of the two pairs of diagrams of Campbell, one of which is contained in a preliminary communication and the other very shortly afterwards in his monograph, since the fissuration of the two is identical. In the case of the prefrontal, the frontal, the parietal, and the visuo-psychic regions, the differences in distribution are very considerable, in view of the fact that, in the case of a particular brain, either the lines of demarcation should be very exact or they should be left indefinite.

On the face of it, the maps of Campbell appear to be

the more diagrammatic and the less accurate of the two sets, and this impression has been confirmed from my personal acquaintance with many regions of the cortex, particularly the frontal lobe and the visual areas. I would also refer to a recent paper by Gordon Holmes on the histology of the post-central gyrus, in which the findings of Brodmann are confirmed. I am nevertheless of the opinion, without disputing in any way the entire accuracy of these particular maps of Brodmann, that the exact differentiation of the greater portion of the grey mantle into such rela-

FIG. 1 (AFTER FLECHSIG).

The "centres of projection" and "centres of association" of Flechsig. The small dots are placed in the chief focus of each centre of projection. Around these chief foci are the regions to which a smaller number of fibres of projection pass; these are indicated by larger dots. The areas, which represent the different cortical spheres indicated by Flechsig as the result of his embryological studies, are not directly comparable in either extent or distribution with the corresponding areas in the adult cerebrum.

tively precise areas as are the Betz-cell area and the visuo-sensory area, will be attended with great difficulty owing to the probability that considerable differences exist in the case of different individuals, and especially so in the case of the poorly developed brains which are often met with in asylum practice. As an illustration of my meaning I will show a diagram of six occipital regions in which many years ago I precisely mapped out and obtained proof of the functional significance of the visuo-sensory area. It will be noticed that both the shape and the apparent extent of this area differ considerably in the several cases, even when difference of age or the existence in some of long-standing blindness is allowed for. Case 1 is a normal male, aged 55 years; Case 2, a female, aged 17 years, is an example of chronic insanity with epilepsy; Case 3, a female, aged 27 years, is an example of chronic insanity with blindness from infancy; Case 4, a male, aged 30 years, is an example of chronic insanity with long-standing blindness; Case 5 is a normal infant, a male, aged three months; and Case 6 is an example of anophthalmos, aged one month. If such individual differences exist in a projection area of early evolution and stable organisation, it is, to say the least, likely that still greater individual differences exist in the later evolved and later specialised regions of association.

As another illustration, this time of probable individual variation only, I will refer in a few words to the recent researches of Marie concerning aphasia and the functions of the area of Broca. It may be accepted, as I have elsewhere remarked, that the thesis of this author with regard to the

intellectual impairment exhibited by all aphasics is true, at any rate, if such cases be studied by methods familiar to the alienist. It is not, however, probable that motor aphasia is invariably the result of anarthria + sensory aphasia, although, on the other hand, it is doubtless true that anarthria + sensory aphasia necessarily give rise to the symptomatology of classical motor aphasia. It is certain that in the case of many persons Broca's speech centre is rightly disrated by Marie, whereas it is extremely probable that in others Broca's area is part of the educated psychomotor area, in which case its permanent loss would result in temporary "motor aphasia" with temporary interference with voluntary thought. Such variability with regard to the individual distribution of the special part of the psychomotor area which subserves the evolution of speech is, in my opinion, the only possible explanation of the widely divergent views which are held by equally competent observers.

Before concluding my reference to the histological differentiation of the cortex I wish to mention quite briefly another question of importance. I have indicated the probability, if not certainty, that individual variations occur in the actual extent occupied by the several histologically differentiated areas which have been described. Whilst histological differentiation probably indicates the limits of possible educability, it does not, however, necessitate the existence of functional activity, as Bianchi appears to believe.

A very obvious illustration of this truth may be seen in the motor exhibitions evolved by the psychomotor area, which as you are aware constitute the sole objective indications of cerebral activity. Whether we consider the infinite variety of skilled movements, the numerous highly complex written and spoken languages, or the wonderful gamut of expression and gesture, of which the intelligent human subject is capable, we see in each case gross individual differences in educability. Histological differentiation probably supplies the key with regard to individual potentialities, but it is doubtful whether any single individual of the race has ever even approached the limits of possible educability.

I will trouble you with but one further illustration—namely, the remarkable manner in which such serious disabilities as congenital or early deprivation of the senses of hearing or sight may be compensated for by education. A person suffering from congenital or early loss of hearing is necessarily dumb, and, unless he live in association with other individuals suffering from the same disability or be educated by special means, his mental functions differ little from those of the anthropoid primates. In such persons under either of these conditions the auditory disability is compensated for by shrewdness of vision, and the speech disability by the evolution of descriptive mimicry to a high standard. The deaf and dumb think by mimicry, just as voluntary thought in normal persons occurs by the preliminary activity of the articulatory part of the psychomotor area, which is important evidence, if such be needed, in favour of the truth of the latter thesis. A normal individual may "think to himself" by means of invisible laryngeal and respiratory movements. A deaf and dumb person does not possess the same involuntary ability to hide the results of psychomotor activity during voluntary thought. Further, if such be taught lip-language they readily learn to communicate with normal persons inexperienced in the special mimicry of the deaf and dumb. On the other hand, the congenitally or early blind acquire language just as do ordinary non-reading and non-writing individuals, and in the absence of special education exhibit little or no defect of the mental functions. In such persons, however, loss of sight is usually compensated for by marked hyperactivity of the sense of touch, and by means of special type the blind are able to acquire education which is often little, if at all, inferior to that of many normal individuals.

After these general remarks I pass to the subject I propose laying before you—namely, the evidence which I have obtained from the clinico-pathological study of mental disease, with regard to the functional significance of certain special cortical areas.

I have hitherto confined my attention to four of the numerous regions into which the cerebral cortex is divisible: the visuo-sensory area, which is the best example of the sensory projection spheres; the visuo-psychic zone, which is one of the regions of special cerebral association; and the

prefrontal and precentral regions. As necessary preliminaries, I shall now describe in detail the method which I have employed, and also the manner in which the cortex cerebri undergoes evolution during foetal life and infancy.

METHOD OF INVESTIGATION.

The method which I am about to describe, and which I have employed for many years, is that of micrometric measurement of the primary cell and fibre laminae of the cortex. Neither in detail nor in results is it in any way comparable with the macro- and micro-metric mensuration of grey matter which has been performed by several workers for many years, and it is therefore not necessary for me to refer further to this.

For reasons which I shall indicate later I am accustomed to subdivide the cortex, for the purposes of measurement, into the five primary laminae from which it has been evolved—namely, (1) the outer fibre lamina or superficial layer; (2) the outer cell lamina or pyramidal layer; (3) the middle cell lamina or granule layer; (4) the inner fibre lamina or inner line of Baillarger, which in certain regions contains such bodies as the Betz cells and the solitary cells of Meynert; and (5) the inner cell lamina or polymorphic layer. These five laminae may more or less readily be identified in all parts of the neopallium, though they differ in their degree of development in different cortical areas. For example, in the psychomotor area the third lamina is of minimal depth and can only be detected by careful examination. On the other hand, in the visuo-sensory area the third lamina is of great depth, the granule layer being duplicated by the interposition in its midst of the fibre layer of Gennari, in which terminate the fibres of the optic radiations.

For the micrometric examination of the cortex it is, however, not sufficient merely to determine the laminae which it is proposed to measure. Granted that accurately vertical sections are obtained, it is further necessary to define the exact regions of the convolutions which are capable of measurement. In theory the flat external surface of the convolutions is the ideal region, and in certain foetal brains it is the only one which is available. In practice, however, its sole employment is impossible, if only for the sufficient reasons that a trustworthy number of situations is rarely available and that its degree of development varies greatly, being very different over broad and narrow convolutions. I consequently employ four regions of the convolutions, and from these prepare a general average measurement. These regions are the *flat surfaces* or external parts between fissure lips, the *apices* or fissure lips, the *bottoms* of fissures, and the *sides* of fissures at some point between the apices or fissure lips and the bottoms of the fissures. These regions are shown in the diagram (Fig. 2). It is, perhaps, hardly necessary to remark that in any given section, though it be cut ever so truly, many obliquities exist and only a certain number of regions can be selected. In fact, it is by no means easy to obtain the necessary number of regions for measurement, and it sometimes happens that cases of promise have to be rejected, even after all the sections have been cut and stained. The four well-defined regions to which I have referred are alone capable of accurate micrometric measurement, and for reasons which I shall now give it is possible, after a sufficient number of measurements from these have been averaged, to obtain a trustworthy general average measurement from the four which can be employed for the comparison of case with case.

[Reasons were then given for the choice of these special regions and for their conjoined employment for the preparation of a general average measurement. The methods employed for the preparation of material were referred to, and certain details were given with regard to the method of micrometric measurement.]

The special regions of the human cortex cerebri which I have hitherto dealt with by this method are the visuo-sensory, the visuo-psychic, and the prefrontal, as the most satisfactory examples available of projection, special associational, and higher associational cortex. The reasons for this selection will appear later. I have in all measured 54 regions in 38 hemispheres, which were obtained from 37 cases of various types, including 3 foetuses, 2 still-borns, 3 infants, 4 normal cases, and 25 examples of various types of mental disease, grading from the idiot with very deficient cerebral evolution, through imbeciles, recent chronic and recurrent non-demented lunatics, and partially demented

lunatics, to the gross dement with marked cerebral dissolution. Of the 54 regions measured, 15 are visuo-sensory, 15 are visuo-psychic, and 24 are prefrontal. The visuo-sensory and visuo-psychic results are from the same cases, and in theory it would appear desirable that all the regions should have been examined in every case. In practice, however, this has been impossible owing to the laborious nature of the work and the length of time it has been in progress. It has also been found to be unnecessary, on the one hand,

FIG. 2.

REGIONS OF CORTEX CHOSEN FOR MICROMETRIC MEASUREMENT

A' - APEX, B' - BOTTOM, F' - FLAT, S' - SIDE

MEASUREMENTS OF VISUO-PSYCHIC CORTEX OF NORMAL ADULT.

REGIONS OF CONVOLUTIONS	I	II	III	IV	V
SIDE AVERAGE OF 36	265	909	200	177	243
APEX AVERAGE OF 35	232	863	218	189	410
BOTTOM AVERAGE OF 12	345	737	163	067	166
FLAT AVERAGE OF 19	255	948	221	282	354
GENERAL AVERAGE IN MM:100	274	864	200	229	293

DITTO OF INFANT, AGED 3 MONTHS.

REGIONS OF CONVOLUTIONS	I	II	III	IV	V
SIDE AVERAGE OF 18	229	721	193	178	214
APEX AVERAGE OF 16	178	700	204	168	297
BOTTOM AVERAGE OF 6	327	496	149	069	180
FLAT AVERAGE OF 3	136	786	221	231	234
GENERAL AVERAGE IN MM:100	242	676	191	212	224

This figure illustrates the method of micrometric measurement. In the upper portion of the figure are shown the four regions of the convolutions, which alone are capable of satisfactory measurement. In the middle part the results of the micrometric measurement of the visuo-psychic cortex of the normal adult and of an infant aged three months are given. In the lower portion the different cortical laminae are shown graphically. These from above downwards are (1) the outer fibre or superficial lamina; (2) the outer cell or pyramidal lamina; (3) the middle cell or granule lamina; (4) the inner fibre lamina or inner line of Baillarger; and (5) the inner cell or polymorphic lamina. On the left hand side are shown the general average measurements obtained from a normal adult and an infant aged three months respectively; and on the right hand side the average "side," "apex," "bottom," and "flat" measurements from which these general average measurements are produced.

because the differences in measurement are well marked and definite, and on the other because the results of prefrontal measurement are of a different type from those obtained from the visuo-sensory and visuo-psychic regions. I may add that it has in consequence been possible up to the present to measure a much larger series of cases than would otherwise have been available. I have, however, specially selected a suitable well-marked case, and measured all the three regions, in order to obviate such a possible

criticism and to prove the points to which I have just referred.

I purpose demonstrating in the second lecture that the essential physical basis of mental disease consists on the one hand in an imperfect development of the cell laminae of the cortex, which is of the nature of a true sub-evolution, and on the other in degrees of decrease of the cell laminae which are of the nature of a true involution or dissolution, since such decrease in depth takes place in the converse order to that in which the cell laminae are developed during the process of normal growth. As one of the necessary preliminaries to this demonstration it is therefore desirable to describe in some detail the normal mode of evolution of the lamination of the cortex. For this purpose I shall employ the prefrontal region, since this is the portion of the cerebrum which is the last to be normally evolved, and also the area in which are present in maximum intensity those indications of sub-evolution and involution which occur in cases of mental disease.

EVOLUTION OF LAMINATION OF THE CORTIX.

The plates which I am now about to exhibit are intended to show from the general point of view the manner in which the lamination of the cortex becomes evolved. All the micro-photographs of this series are of exactly the same magnification.

[A photograph representing the right hemisphere of a human foetus of about four months was then exhibited. The fissure of Sylvius and a depression which occupies the site of the future fissure of Rolando are present, as also are numerous vascular grooves.]

In the micro-photograph (Fig. 3) is shown a section of the prefrontal cortex of this hemisphere. This will be seen to consist of a layer of undifferentiated neuroblasts covered by a superficial layer of neuroglia, into which irregular masses of neuroblasts project. The neuroblasts are most closely packed towards the surface and, at about the level of the lower trisection, indications exist of commencing differentiation of the nerve cells. The cortex has not begun to laminate, and its total depth is less than half of that of the normal adult.

[A photograph was then shown of the left hemisphere of a foetus of about six months. The brain is somewhat larger and firmer, and the main fissures are defined or appearing. The numerous vascular grooves seen in the previous hemisphere have largely or entirely disappeared, and the prefrontal region of the cortex consists simply of a flat external surface.]

The prefrontal cortex of this case, as is seen in the micro-photograph (Fig. 4), shows little increase in depth but definite signs of the commencement of the process of lamination. The inner cell lamina or polymorphic layer is being separated from the rest by the development of the inner fibre lamina or inner line of Baillarger. The middle cell lamina or granule layer is visible, owing to the shape and mode of aggregation of its constituent cells, and the outer cell lamina or pyramidal layer can also be made out, and exhibits a partially columnar arrangement of its constituent cells in its lower two-thirds and a massing together of the cells in its upper third. It will be at once evident to anyone familiar with the appearance of the adult cortex that development is taking place from within outwards and that the superficial laminae, especially the outer cell or pyramidal, are as yet of very deficient depth, the last being only about one-fourth of the adult normal.

It will be noted, on comparing the fourth and sixth months foetuses, that the development of lamination is coincident with greater firmness of the brain and disappearance of the numerous vascular grooves, rather than with any notable increase in the complexity or size of the hemispheres. Microscopically, however, an important advance has occurred—namely, the commencement of the process of lamination and a cleavage of the neuroblasts into an upper and a lower portion. In view of the evidence I shall produce with regard to the functions of the inner cell lamina I would remark that this early cleavage of the partially differentiated neuroblasts of the cortex into an upper and a lower portion is an occurrence of the greatest significance.

[A photograph was then shown of the right hemisphere of a foetus of seven to eight months. The magnification is somewhat less than that of the preceding and following brains. The fissuration is completed with the exception of

the less important subsulci, and the brain has a general resemblance to that of the adult.]

As is shown in the micro-photograph (Fig. 5) marked progress has taken place with regard to the development of the cortex and the differentiation of the nerve cells. The inner cell lamina is clearly marked off by the inner fibre lamina from the middle cell lamina, and the outer cell lamina or pyramidal layer shows a notable increase both in the depth of its lower part and in the degree of differentiation of the constituent cells of this. The upper portion of this lamina is still in a poorly differentiated condition, and the aggregation of its embryonic constituent cells is by contrast more visible than is the case in the foetus of six months.

[In the next photograph was shown the unstripped right hemisphere of a stillborn male infant. The resemblance to the adult appearance of the brain is now well marked.]

In the micro-photograph (Fig. 6) it will be seen that the cortex now exhibits a general resemblance to that of the adult. The nerve cells have largely taken their permanent form, and, being less embryonic and smaller, appear less crowded. A further important factor in causing less aggregation of cells is the increased superficial area of cortex and the consequent smaller number of cells in a section of the same thickness. The outer cell lamina or pyramidal layer is, however, still little more than one-half of the adult normal depth, and exhibits a very obvious aggregation of embryonic cells in its upper part.

In contrast to the preceding illustrations, the following micro-photograph (Fig. 7) shows the depth and general appearance of the adult normal cortex. The magnification is four-fifths of that of the preceding micro-photographs. The great increase in the depth of the outer cell lamina or pyramidal layer which has occurred is very evident.

It was originally my intention to follow the further development of the cortex in children of different ages, but I found that such notable individual differences in the degree of the development of the cortex occurred as precluded the possibility of obtaining definite results. This truth is the anatomical counterpart of the known great individual differences in degree of mental development which exist in infants and young children.

In the next diagram (Fig. 8) are shown, in percentages of the normal, the general average measurements which I have obtained from the prefrontal cortex of a number of cases. They very clearly indicate the point to which I have just referred. The second case, though it falls well into series with the remainder, exhibits certain differences in the depth of the fourth and fifth laminae which are due probably to the fact that all the measurements are from the flat external surface owing to the absence of fissures. The fourth and fifth cases exhibit the individual differences in degree of development which I found to occur in two stillborns; and the case in the sixth column, that of a marasmatic infant of retarded general development, is also interesting in that the outer cell lamina is of less depth than that of the second stillborn, whilst all the other laminae are of almost exactly the same depth as are those in the latter. Further, the diagram shows quite definitely that the laminae are evolved from within outwards, and that the inner cell lamina approaches the adult normal depth at birth, at which date the middle cell lamina is about three-fourths and the outer cell lamina still little more than one-half of the adult normal depth.

With regard to the date at which evolution of the cortical laminae occurs, I have at present merely sufficient evidence to show that it takes place earlier in the visuo-sensory area (projection sphere) than in the visuo-psychic (zone of special association), and earlier in the latter than in the prefrontal region (zone of higher association). This evidence is shown in the following diagram (Fig. 9), in which are collected a series of observations on the cortex of certain foetuses, infants, and adults. The following are the chief points illustrated in the figure. In the visuo-sensory area of the infants of 1 and 3 months the whole of the cell layers have attained to almost the normal adult depth, and the outer cell layer is rather better evolved in the former than in the latter, in spite of the existence of congenital blindness in that case. On the other hand, in the visuo-psychic zone none of the layers are so far evolved, and the outer cell layer of the infant of one month is much shallower than that of the infant of three months. The visuo-sensory cortex is thus obviously evolved earlier than is the visuo-psychic. A

FIG. 3.

FIG. 4.

FIG. 5.

FIG. 6.

FIG. 7.

FIG. 3.—The prefrontal cortex of a fetus of four months. $\times 94$ diameters. The cortex has not begun to laminate, and consists solely of a superficial layer and a layer of undifferentiated neuroblasts.

FIG. 4.—The prefrontal cortex of a fetus of six months. $\times 94$ diameters. The process of lamination has commenced. L.I. = outer fibre lamina; L.II. = outer cell or pyramidal lamina; L.III. = middle cell on granule lamina; L.IV. = inner fibre lamina; and L.V. = inner cell or polymorphic lamina.

FIG. 5.—The prefrontal cortex of a fetus of seven to eight months. $\times 94$ diameters. L.I. to L.V. as in FIG. 4. It will be noted that L.II., the outer cell or pyramidal lamina, though the latest to develop, has already become the deepest layer of the cortex.

FIG. 6.—The prefrontal cortex of a stillborn male infant. $\times 94$ diameters. The cortex has begun to lose its embryonic characters. The outer cell or pyramidal lamina (L.II.) is still less than one-half of the adult normal depth. L.I.-L.V. as in the preceding figures.

FIG. 7.—The prefrontal cortex of a normal adult. $\times 72$ diameters. The magnification is four-fifths of that of the preceding microphotographs. L.I.-L.V. as in the preceding figures.

further interesting point shown in the diagram is the low evolution of the middle cell lamina or receptive layer of the cortex of the congenitally blind infant of one month, and the almost adult development of this in the infant of three months. The same detail is visible in the case of the visuo-psychic region, and this is alone sufficient to hall-mark the visuo-psychic region as a zone of special visual association, especially when it is noted that this lamina is in the infant of three months of practically the adult depth, whereas the inner cell lamina of this case is by no means so well developed. In other words, the granule or receptive layer of the visuo-psychic zone follows the order of its evolution in the visuo-sensory area in being ahead of the inner cell lamina in its degree of development.

FIG. 8.

The figure shows, in percentages of the normal, the general average measurements of the prefrontal cortex of a series of fœtuses and infants. The laminae from above down are as in the preceding figures. The illustration indicates that the cortex evolves from within outwards, the inner cell lamina being the first to appear and rapidly attaining almost to the adult depth, and the outer cell lamina the last, this lamina at birth being still only about one-half of the adult normal depth.

In the case of the prefrontal region, though the results are not comparative, they are sufficient (especially when combined with other data, to which I shall refer later) to indicate that evolution is individually variable and occurs at a later date than is the case in either of the other two regions.

LAMINATION OF DIFFERENT REGIONS OF THE CORTEX.

I now propose to illustrate the lamination of the regions of the cortex which are under consideration, and in the case of the prefrontal area it is my intention, for reasons which I shall presently detail, to describe at some length its general structure. I would add that the micro-photographs I am about to exhibit are of different magnifications, as it is necessary that the whole depth of the cortex should be present.

[The lamination of the visuo-sensory and visuo-psychic regions was then described and illustrated.] One of these illustrations, taken from a fœtus of 7 to 8 months, is shown in Fig. 10. On the right hand side is seen the periphery of the visuo-sensory region, in the middle the abrupt passage of this type of cortex into the surrounding visuo-psychic, and on the left hand side the cortex of the visuo-psychic zone. It will be seen that the line of Gennari suddenly ceases and the two layers of granules run into one, which occupies the site of the inner, the outer cell or pyramidal lamina at the same time increasing to almost double the depth. A comparison

of this illustration with Fig. 5, which shows the prefrontal cortex of the same case, indicates that the last is in degree of development far behind the cortex of the visuo-sensory and visuo-psychic regions, which, particularly the former, much more closely resemble the adult type.

[The general fibre architecture of the cortex was then referred to, with the object of indicating that the horizontal fibre bands of the cortex bear no necessary relationship to the original laminae from which the cortex has been evolved. Finally, the prefrontal cortex was referred to in greater detail in consequence of the fact that the great delicacy and high complexity of the structure of this region have been denied.]

It has been definitely stated by Campbell in his recent

FIG. 9.

THE CELL LAYERS OF THE CORTEX
AND THE MANNER IN WHICH THEY DEVELOP.

The figure shows the mode of evolution of the cell laminae of the cortex of the visuo-sensory, visuo-psychic, and prefrontal regions. The bottom series represents the inner cell or polymorphic lamina, the middle series the middle cell or granule lamina, and the upper series the outer cell or pyramidal lamina. A description is given in the text, but in general the figure suggests that the visuo-sensory cortex develops before the visuo-psychic, and this before the prefrontal; that the inner cell lamina develops before the middle and the middle before the outer; and, finally, that in the visuo-sensory and visuo-psychic regions the middle cell or granule lamina is the receptive lamina of the cortex and develops more rapidly than does the inner cell lamina of these regions.

monograph, which has attracted great attention, that the prefrontal cortex is of slight structural and functional significance. He remarks: "The structural development of the 'prefrontal' cortex is exceedingly low. It presents an extreme of fibre poverty. All the fibre elements are of delicate calibre, and its association system is particularly deficient. Its cell representation is on a similar scale. The cortex is also shallow." There is no mistake, as has been suggested, with regard to the region under consideration, as a comparison of the diagrams of Campbell and of Brodmann at once indicates; and I purpose showing that the cause of the great discrepancy in the descriptions lies in the difference of method adopted. Campbell used throughout his investigations the Wolters-Kulschitzky method, which

as ordinarily employed I regard as quite unreliable for this especial purpose. The method, on the other hand, which I adopt for the staining of the fibres of the cortex is based on the results of a research which I conducted many years ago into the chemistry of the Weigert-Pal method. I found that this process is not a specific method for the staining of medullated nerve fibres with hæmatoxylin, but is a method of dyeing fibrils which comprises three distinct operations—the mordanting of the fibrils, the formation of a lake in them by the employment of a basic dye, and, finally, the removal of the stain by oxidation from nearly every other part of the complex tissue under treatment. I compared the method with what would occur were a fabric composed of different fibres interspersed with fine glass threads, stained by a commercial process. The glass threads would

The usual Weigert-Pal methods, however, are still in general use, and by means of these it is practically impossible to stain even imperfectly the delicate fibrils of the prefrontal cortex.

[Photographs were then shown illustrating the special method referred to. The first series indicated the results of staining different types of fibre architecture of the nervous systems of the frog, dog, and cat. The second illustrated the minute structures of the prefrontal region. The specimens indicated the high complexity of the fibrillar meshwork throughout the grey matter, since, by means of high-power micro-photographs, the whole depth of the cortex was illustrated.]

In view of these photographs it is impossible to deny the great complexity of the fibre architecture of the prefrontal region, and I may add that John Turner in 1907, the year

FIG. 10.

The cortex of a seven to eight months' fetus. 94 diameters. The microphotograph is prepared at the periphery of the visuo-sensory area, and shows the passage of the visuo-sensory cortex into the visuo-psychic. L. I. to L. V. are as in the preceding illustrations; L. III. A and L. III. C are the two layers of granules; and L. III. B is the intermediate fibre layer or line of Gennari, of which three layers the middle cell lamina consists in the visuo-sensory area. In the centre of the illustration it will be noted that the line of Gennari, L. III. B, ceases, and that the layers of granules, L. III. A and L. III. C, run into one to form the granule lamina, L. III., of the visuo-psychic cortex. A comparison of this figure with Fig. 5, which illustrates the prefrontal cortex of the same case, very clearly demonstrates that the visual cortex of this case is much more advanced than that of the prefrontal region in its degree of development. These figures thus afford a partial graphic illustration of the truth that the visuo-sensory cortex develops before the visuo-psychic and the latter before the prefrontal.

refuse the mordant and consequently the lake, whereas the fibres would retain the stain. In the case of human tissue, the more highly metabolic elements represent the fibres, and the more fixed and lowly metabolic elements the glass threads. Further, the process is applicable to any, and not solely to nervous tissue—e.g., kidney, involuntary muscle, &c., form beautiful low-power specimens. The mordanting of the tissue is the most important process, and osmic acid, iron alum and ammonium molybdate, used separately or in succession, are the strongest mordants. My results were independently and almost simultaneously confirmed by Herrick, and the method has for years been successfully applied to the staining of cortical fibrils by G. A. Watson, who in 1903 published details of the special mode of employment necessary to display them, and of the difficulties which attend the obtaining of positive results.

following the appearance of my paper on this subject, also combated the statements of Campbell and remarked that the prefrontal region, treated by a special method of his own, shows a wealth of intercellular fibres probably greater than in any other region of the cortex.

THE INVALID CHILDREN'S AID ASSOCIATION.—

The annual meeting of this association will be held, by kind permission of the Duchess of Marlborough, at Sunderland House, Curzon-street, London, W., on April 27th, at 3 o'clock. The Duchess of Marlborough will preside and the Bishop of Bath and Wells, Dr. Robert Hutchison, and Mr. D'Arcy Power will be among the speakers. Applications for tickets of admission may be made to the secretary, 69, Denison House, Vauxhall Bridge-road, Westminster, S.W.

ON THE FAILURE OF NERVE ANASTOMOSIS IN INFANTILE PALSY.

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FOR the last three years or so we have been watching with much interest the progress of several patients for whom, in consequence of the crippling from anterior poliomyelitis, a nerve anastomosis was performed. The observations are on five patients, four of whom suffered from infantile palsy; in two the upper limb was affected, in two the lower. The fifth case was a traumatic lesion of the great sciatic nerve, due to a dislocation of the hip. We may say at once that in none of these cases has any improvement, the direct result of the anastomosis, resulted. Improvement due to the natural processes of repair in the cord was observed to a considerable degree, quite sufficient to satisfy the parents of the benefit of the operation, but, as will be obvious, in no wise to be connected with the actual surgical interference undertaken.

We have not attempted a systematic review of the literature on this subject, but it may be confidently asserted that very few instances of a truly satisfactory nerve anastomosis for infantile palsy have been published. The failure of this method, which looked so full of promise, is particularly disappointing. Our experience suggests that as successful cases are certainly few failures may be more numerous, and it is of some importance that those also should be recorded. We consider such records gain in value when recorded by a physician as well as by the operator. The cause of failure may be either because (1) an inappropriate time is chosen for the operation; (2) the surgical technique is at fault; or (3) physiological reasons do not permit of recovery.

1. *The time for operation.*—No one has insisted more upon the power of recovery of muscles under proper treatment—rest, massage, postural fixation—than Mr. Robert Jones, and we venture to refer to the section on Treatment in a paper on Palsies of the Brachial Plexus, written by that surgeon and one of us (W. B. W.) in THE LANCET of Dec. 15th, 1906, where several cases are related of great improvement in infantile palsy as long as two years after the onset of the disease.

We consider that no operation should be contemplated unless for six months from the onset of the disease assiduous treatment has been directed to the palsied muscles to improve their nutrition and to assist the return of power by adequate postural support, and, further, that at the end of this time faradic irritability must be absent, although a strong current is used whilst the patient is anaesthetised. The following case well illustrates this rule:—

A woman, aged 27 years, seen in private practice and so circumstanced that the best of nursing, medical attention, with constant intelligent coöperation of herself and husband was obtained, was seized in the early part of August, 1906, with poliomyelitis anterior acuta, causing widespread palsy of both limbs. It was not until the lapse of six months that the patient recovered power enough to walk, and at the end of that time the flexors of the forearms feebly responded to voluntary effort and to the faradic current. The deltoids were powerless and gave no trace of faradic excitability. A year later all the muscles except the deltoid, which remained completely powerless, had practically fully recovered.

Experience, we think, shows that it is the deltoid which, in all acute peripheral palsies of the upper arm, shows the least response to the methods of nature or art, and some means of restoring the power of abduction of the arm is urgently required—possibly the circumflex nerve may be anastomosed to another nerve. When a patient has not been under the most favoured circumstances adequate treatment should be adopted at least for three months before surgical interference is attempted. At the end of these periods of time we think that in cases of infantile palsy some degree of certainty as to the impossibility of future natural recovery may be obtained.

In passing, it may be remarked that in obstetrical palsy and in spontaneous neuritis the natural tendency to complete recovery is greater than in infantile palsy, and we think that amongst recorded cases of surgical treatment in the former group of cases are to be found instances in which the operation was superfluous. In the paper just mentioned by Mr.

Robert Jones and one of us, of 6 cases of obstetrical palsy, 2 completely, 3 partially recovered, and of 4 cases of spontaneous neuritis, 3 completely recovered.

2. *The surgical technique.*—In every case the paralysed nerve was completely divided. In three cases the peripheral end of the nerve was engrafted into a longitudinal slit made in the sound nerve (Fig. 1). In two cases an end-to-end anastomosis was made. In one of these the divided external popliteal was joined to a flap raised from the sound internal popliteal nerve (Fig. 2); in the other case the spinal accessory

FIG. 1.

The external popliteal nerve E has been divided and grafted into a slit made in the internal popliteal nerve I.

FIG. 2.

An end-to-end anastomosis has been made by raising a flap from the healthy nerve.

nerve was completely severed and joined to the divided fifth cord of the brachial plexus. The suture material used was very fine silk. Care was taken in handling the nerves and in passing the sutures to bruise the tissues as little as possible. In no case was there any trouble whatever as regards the healing of the wound.

3. *Physiological considerations.*—The studies of Wichmann on the pathology of infantile palsy are the most valuable we have; they plainly show the widespread distribution of the lesion, that not only are the ventral cornual cells the site of disease, but also that the white tracts and pia mater are often affected. The final scar may, therefore, be most destructive, not so much in its extent as in its degree. Nevertheless, experimental work either on the effects of poisons on the nerve cells or on the results of various sections of peripheral fibres having origins in cells shows that the latter present a high degree of capacity for repair and that the *restitutio ad integrum* may be complete. The clinical evidence that we are using a functioning nerve for the purpose of grafting is, of course, the presence of voluntary power and of faradic excitability in the muscles supplied by it. But the nature of the pathological lesion suggests that though these signs are present, yet even in the segment in the spinal cord, from which the functioning nerve takes origin, recovery may be incomplete. Hence one cause of the lack of success may be that the effort is too much; there may be sufficient nerve cells left to supply one group of muscles, but insufficient to supply two. If this be the explanation, it appears that the operation must often fail in its object, yet the very valuable observations of Kilvington¹ have shown that after section of a nerve trunk the axons branch, hence the peripheral supply at least may be increased.

Further, the state of the peripheral apparatus must be considered. Many are the battles which have been waged on the field of the facts and theories of nerve regeneration. We consider that the evidence of Langley and Anderson,² Head and Ham,³ Mott, Halliburton, and Edmunds,⁴ conclusively show that axons are alone reformed by downward

¹ Brit. Med. Jour., vol. i., 1905.

² Journal of Physiology, vol. xxxi., p. 418.

³ Ibid., vol. xxxii.

⁴ Ibid., vol. xxxi., p. 7.