THE STRUCTURE AND FUNCTIONS OF THE CEREBELLUM EXAMINED BY A NEW METHOD.

By SIR VICTOR HORSLEY, F.R.S., F.R.C.S.,

AND

R. H. CLARKE, M.A., M.B.

(*From the Laboratory of Pathological Chemistry, University College, London.*)

PART I.—METHODS.

I.—INTRODUCTION.

THE methods and experiments described in the following pages are the direct outcome of an investigation into the anatomical relations of the cortex of the cerebellum to its nuclei and peduncles, and to the rest of the brain and spinal cord. An account of that research was published in *Brain* in the spring of 1905.

When we began that work (1903) the view had been gaining ground that there was no direct path from the cortex of the cerebellum to the peduncles or to the spinal cord, and had been advanced by distinguished observers, especially Ferrier and Turner, Risien Russell and Thomas, who expressed themselves more or less definitely in favour of this opinion, and supported it with observations furnished by their own experiments. But although the evidence adduced established a strong probability we did not consider that it amounted to proof, as the conclusions were founded on lesions involving both cortex and nuclei, or complicated with injuries to other parts. Nor were all the conclusions of the authors absolutely definite. Marchi originally described a direct descending path in the spinal cord derived from the cerebellum. Ramon y Cajal spoke of this tract in a rather ambiguous way, leaving the reader in some doubt whether he recognized the tract himself or was merely quoting Marchi by calling it the *via descendente*. Ramon y Cajal also described some fibres passing from the cerebellar cortex to the superior peduncle.

Thomas in his classical work ("Le Cervelet"), though generally supporting the view that no direct cerebello-spinal path existed, yet gave illustrations of a case of cerebellar lesion exhibiting degenerated (tecto-spinal) fibres in the spinal cord; and though he stated that there was an accidental lesion of the posterior colliculus which might have produced degeneration of such a spinal tract, Thomas was of opinion that these fibres were derived from the cerebellum.

The later illustrations of Probst all showed more or less injury to the nuclei, and though he made the deduction that the amount of degeneration seen in the peduncles or beyond them was proportional to the amount of injury to the nuclei, and was therefore derived entirely from them, the lesions were not sufficiently defined to justify these conclusions.

Considering this position of the subject was unsatisfactory, and that besides the anatomical question the much broader one of the respective functions of the cerebellar cortex and nuclei was as yet wholly undetermined, we resolved to try and find some more conclusive evidence by which to decide these points. The failure of previous experiments to afford absolute proof appeared to be due in all cases to the fact that the lesions had not been sufficiently limited, and it seemed most probable that if special precautions were observed to avoid this defect in a series of cortical lesions, following the resulting degenerations by Marchi's method, definite information regarding the course and destination of the cortical fibres would be afforded.

The results justified these anticipations. Small lesions of the cortex were made by one of us (V. H.) in anæsthetized animals—monkeys, dogs and cats. In thirteen cases the cerebellar nuclei were absolutely untouched, the lesions being strictly confined to the cortex; and of these cases, though there were abundant well-stained fine fibres passing to the adjacent folia (arcuates) and to the intrinsic nuclei, none showed degenerated fibres in any of the peduncles or in the spinal cord; this evidence appeared to us conclusive.

We did not think it necessary to perform any more experiments for the purpose of accumulating evidence on this question, but accepting the data as correct have endeavoured to follow up the indications they afforded. This view was corroborated by the appearance (after the publication of our paper) of an important research by van Gehuchten, who quite independently came to the same conclusion from experiments on another species of animal, viz., the rabbit.

As a result of these experiments we were led to the conclusion that the cerebellar cortex is essentially a recipient organ (Edinger); its efferent

fibres passing to neighbouring folia and to the cerebellar nuclei, the latter being regarded as stations interposed between the efferent cortical fibres and the rest of the nervous system. Collectively, therefore, these nuclei might be considered the focus of cerebellar activity, and regarding this as the standpoint from which further investigations of their structure and function must proceed, we resolved upon a systematic inquiry into the function of the cerebellar cortex and nuclei respectively.

On making a general survey of the subject before us, and considering the most promising methods of research, we were confronted with the following preliminary difficulty : The nuclei of the cerebellum in monkeys, dogs, and cats are small, deeply situated, and not very accessible for excitation experiments, while it is evident that to get results of any value by Marchi's degeneration method, lesions must be precisely limited to the nuclei, or, if possible, to parts of them, and that such lesions must not only be accurately localized but also produced without noteworthy injury to other structures, for we had already observed the difficulties and confusion which such complications have introduced into the discussion of the subject. An essential preliminary, therefore, to further progress was to find some method which would satisfy these conditions, viz., a means of producing lesions of the cerebellar nuclei which should be accurate in position, limited to any desired degree in extent, and involving as little injury as possible to other structures (*see* fig. 20A, p. 98). Neither puncture with a small knife, nor galvano-cautery, nor the injection of acids or other fluids appeared to us to fulfil these conditions adequately, and we therefore discarded them. At this time (1904) we were unaware of the experiments of Sellier and Verger (see p. 86), in which insulated needles were used for the production of electrolytic lesions in the brain, and we arrived independently at the same point after a number of preliminary experiments which will be referred to presently. At first, although the application of an electrical current to the nuclei by means of needles insulated to within a short distance of their points appeared most likely to serve our purpose, we were doubtful whether it would be better to employ two insulated needles and a current of high tension, thus obtaining destruction ·by sparks, or to use a single needle and a surface electrode with faradism or electrolysis ; it is sufficient to say here we soon abandoned both the spark and faradism. The former was too violent and difficult to regulate, and the latter set up vigorous convulsive movements which are too severe to allow of the application being maintained long enough to produce an

effective lesion; but the electrolytic method appeared promising from the first, and after several years experience we regard it as satisfactory. The conditions under which a lesion should be made, and which we have enumerated already, are not very exacting, but, such as they are, electrolysis fulfils them in a way which leaves little to be desired. As we shall explain more fully later, electrolytic lesions of the brain, especially anodal ones, are quickly and easily produced with very slight injury to any other parts; their size can be accurately regulated, their form depends on the nature of the electrode, they are precisely defined, and the necrosed tissue passes in all directions almost abruptly into the uninjured tissues, which do not appear to be even temporarily affected by the lesion; while, finally, with the stereotaxic instrument we are going to describe, we are able to direct a protected stimulating and electrolytic needle to any desired part of the brain with very fair accuracy. All these particulars are included in the method which in this paper we propose to explain fully before giving in a separate communication the results we have obtained with it on the cerebellum. We shall begin with an account of our method of cranio-encephalic topography and measurement, followed by a brief discussion of the subject of electrolysis of central nerve tissue, including the physical and chemical characters and microscopical structure of the lesions, the different effects of anode and cathode, concluding with a discussion of the methods of electrical stimulation we have employed on the cerebellum. In a second communication we shall describe the results obtained by these methods on the structure and functions of the various parts of the cerebellum and cognate centres; this will include an account of the anatomical position of a great number of lesions, the course of the degenerated fibres and tracts they have produced, and an analysis of the functional changes and clinical symptoms which have been associated with them.

A preliminary account of our methods and of the stereotaxic instrument was published by one of us (V. H.) at the meeting of the British Medical Association at Toronto, August, 1906.

II.—RECTILINEAR CRANIO-ENCEPHALIC TOPOGRAPHY.

The first requirement in a research of this kind is the establishment of the relations existing between the exterior of the head in animals and its encephalic contents, especially in the monkey, but also in orders as far apart as the carnivora, insectivora, and birds.

As yet relatively little information exists on this question, although it is of fundamental importance in anatomy.

For the higher vertebrates the valuable drawings (especially fig. 9, p. 69) in the text-book by Flatau and Jacobson [3] are useful indications, but for our purpose it was necessary to have not only a precise knowledge of the proportionate relations, but a means of reaching any definite spot in the encephalon, and we were therefore compelled to begin *de novo*, and, as will be seen directly, have adopted a method in which the objective is determined by measurement from a zero inside the encephalon, and not by the usual projection on the exterior and measurement from it.

On the question of correct technique in making cutting lesions in the central nervous system, the most important communication that has recently appeared is that by Wilhelm Trendelenburg [24]. After quoting the well-known methods of Longet, Nawrocki, Dittmer, Cyon, Woroschiloff, Probst, and Corona he points out that it is possible to devise an apparatus which consists of two parts: first, a model in brass foil of a sagittal section of that portion of the nervous system in which it is desired to make a lesion; and, second, a knife ingeniously devised of stout steel wire, so that it is possible to guide its one extremity by a hole in the brass plate (such hole representing the desired lesion), while the other extremity enters the brain. It will be understood that the model is fixed above the brain in which the lesion is to be made, that the knife is made to follow the outline in the model, and that its parallel movements and adjustment are cleverly obtained by a lazy-tongs arrangement, for movements in two planes, frontal and horizontal, that in the vertical plane being provided by sliding up and down an upright. It will be seen, of course, that this *myelotom*, as Trendelenburg names it, does not fulfil the conditions we feel must be satisfied. It is, however, a great advance on the cannulæ and hook-like stilettes, devised by Veyssière and subsequently employed by Bechterew, Probst, and other workers, since it includes an accurate control of the cutting point during the whole operation.

To meet our immediate necessities, and at the same time to provide a plan of general application to the whole encephalon, a method of rectilinear topography and a stereotaxic instrument for applying it to direct an insulated needle to any desired point in the brain for excitation or electrolysis were devised by one of us (R. H. C.), and we have employed them for the last three years for the study of the structure and functions of the cerebrum and cerebellum in various animals.

Topographical Data and Measurements.

The difficulty of arriving at the precise localization of a point in the deep structures of the brain is due to several causes which have been generally recognized but not hitherto satisfactorily met. The first and most obvious one is that of making accurate measurements of the curved surface of an irregular sphere, like the head, especially when there are few constant and trustworthy features to serve as fixed points, while of these the precise definition is obscured, and their value more or less impaired by the mobile integument and muscles which cover the cranium. The initial difficulties are much enhanced when the ultimate objective to be localized is not on the surface, but deeply situated and probably at an uncertain distance within the cavity of the skull, and when allowance must be made for variations of thickness of the bones and their coverings, and of the size, shape, and symmetry of the structures concerned. We find, however, that a practicable and, on the whole, satisfactory solution of this problem may be attained by dividing the cranium into eight segments, by three section planes at right angles to each other, *e.g.*, sagittal, horizontal, and frontal. As a result of these sections, each segment presents the three internal surfaces of a cube, and every point in it can be identified by recti-linear measurements from those surfaces or section planes, *i.e.*, from their *internal* boundaries. By this means the irregular curved surface, which corresponds to the three outer sides of the cube, is not involved in any way and needs no further consideration.

In short, instead of employing the usual method of endeavouring to project the detailed structure of the interior of the encephalon on to the surface of the head, we measure the position of the deep parts of the brain by their relation to three section planes.

The advantage of applying this principle, which, so far as we know, is new in the topography of the brain, to the localization of structural detail for the identification and record of lesions, and for the mechanical direction of an insulated needle for excitation or electrolysis, is obvious, and its utility will become more evident as we proceed to consider the details of its practical application.

The essential points of this principle may be briefly summarized as follow :—

(1) Any irregular solid may be divided by three section planes in three dimensions into eight segments, in each of which the three in-ternal surfaces are those of a cube.

(2) In any solid body a constant point which can be measured from plane surfaces, representing the three dimensions of a cube, can be identified by three perpendiculars of correct length dependent from those surfaces, and it is the only point where those perpendiculars can meet.

(3) A needle may be substituted for any of these perpendiculars, and in order that it may be directed mechanically to any required point in any of these rectilinear segments, an instrument is necessary which will introduce it in a direction perpendicular to one surface, and therefore parallel to the other two, to any required distance from the first surface, any required distance from the others, *i.e.*, the needle must have a regulated movement in three dimensions.

The Determination of the Three Section Planes of the Head.

These principles are applicable to the identification of any point within the brain of a living animal and to the direction of a needle to it, provided that the conditions as defined are fulfilled. Now it is obviously practicable to divide the cranium by three section planes, which in the living animal are imaginary (definition 1). We can construct an instrument which meets the requirements of definition 3. The only difficulty lies in the determination of "constant points which can be measured from plane surfaces representing the three dimensions of a cube" (definition 2). This measurement cannot be effected in the living animal; the distance of a selected point must therefore be known from the measurement of other heads, and can be trusted only so far as these data are constant. Hence it is essential to find a method of determining section planes, which are themselves constant and can be proved by experiment to have a constant relation to any selected point within the brain.

The simplest method of selecting section planes of the cranium would be to bisect its longest diameters in three dimensions by planes perpendicular to them. This is not practicable in the case of the vertical diameter because of the structures of the neck, and in order to determine the frontal and median sagittal planes, by bisecting the longitudinal and transverse diameters of the cranium, we must first define those diameters. But there are no landmarks on the surface of the skull beneath the integuments which are sufficiently clear and precise to determine an accurate longitudinal diameter, though for transverse diameters we can utilise such prominent features as the eye and ear. The simplest method, therefore, is to begin with these structures and adopt the centre of the

external auditory meatus and the centre of the lower margin of the orbit
on both sides for the definition of the horizontal plane, or a basal plane
to which the horizontal section plane is parallel but about 10 mm. nearer
the vertex.

Beginning with this basal plane we can define the frontal section
plane as perpendicular to the horizontal and passing through the centres
of both meatus, and the sagittal section plane as bisecting the cranium
perpendicular to the other two (section planes).

It will be seen (p. 63) that this order will be followed in the applica-
tion of Clarke's stereotaxic instrument. The horizontal frame is adjusted
and fixed to the four points (eyes and ears) of the basal plane. By the
same process the frontal zero plane is brought into place perpendicular
to the horizontal plane and cutting the centres of both meatus, and the
sagittal zero plane, perpendicular to the other two, is made to correspond
with the median sagittal plane of the cranium by four graduated lateral
clamps.

We consider the above are the most satisfactory section planes; we
have verified them by the methods of drilling and passing ivory needles
and making frozen sections as described elsewhere (p. 59), and, as far as
our experience goes, their relations to the most important structures of
the brain are constant, with such corrections for size and symmetry as
are necessary, and also quite practicable (*vide* p. 82).

Various anatomical features, such as sutures of the cranial and facial
bones and surface markings of the brain, will be found useful for verifica-
tion of the accuracy of adjustment of the instrument.

It will be noticed that the centre of the external auditory meatus
corresponds to the auricular point of anatomists, and the basal plane
differs very slightly from the Frankfort-Munich plane, the latter being
determined by the upper margins instead of the centres of the external
auditory meatus.

Reference has been made to the situation of the zero horizontal section
plane being about 10 mm. above the basal plane; the object of this is to
make it more central. The advantage of making the section planes as
central as possible is not only that it brings them into closer relation
with the most important structures of the brain, but as all measurements
are made in both directions from each of the three section planes which
count as zero, the margin of error in measurement is reduced.

The precise position of the zero horizontal section plane is therefore
a level determined by what has been found convenient in practice in
the animals we have used. Thus in the average *Macacus rhesus* the

distance from the centre of the auditory meatus to the vertex, per-
pendicular to the base line, is 40 mm.; in the cat it is about 30 mm.;
in the hedgehog about 20 mm.   But whilst in the *Macacus rhesus* the
inter-aural line (that is a line passing from the centre of one meatus
to the other) passes through the pons, in the cat it touches the
inferior surface of the pons, while in the hedgehog it is still further
ventral and lies in the basi-occipital bone.   This has suggested to us that
the zero-horizontal section plane in the *Rhesus* should be placed at one-
fourth of the distance from the meatus to the vertex, that is 10 mm.
on the average above the basal plane (passing through the auricular
point in the meatus and the orbital border).   In the cat one-third of the
distance from the meatus to the vertex, and in the hedgehog one-half
the distance, places the zero horizontal plane at proportionately the same
region of the encephalon.   In all these animals. the horizontal section
plane will then be about 10 mm. above the base line and convenient for
measurements above and below it.   For these animals, therefore, we have
adopted this arrangement, but possibly future investigators employing
different animals may find other proportions more convenient.

The Subdivision of the Encephalic Segments into Lamellæ and
Cubic Millimetres.

As already described, the whole encephalon is divided by the three zero
section planes into eight segments, which are, we designate, right and
left frontal, occipital, temporal and cerebellar, and each segment of
the encephalon presents on its inner aspect three rectilinear surfaces
corresponding to the three section planes—sagittal, frontal, and hori-
zontal.   On frozen sections of an animal's head, the preparation of
which will be presently described, the distance from any point of these
three surfaces of any segment can be measured and then, for an actual
experiment, by means of the stereotaxic instrument, which is adjusted
by these indications and carries an excitation and electrolyzing needle
travelling on graduated guides in each of the three planes, it is easy to
direct the latter to a similar point in an intact head.   The identification
of the desired point and the direction of the needle are made practicable
by finally subdividing the segments into cubic millimetres as follows :
Each segment is theoretically subdivided into slices or lamellæ 1 mm.
thick in each plane, and each lamella is divided by lines parallel to the
other two planes into millimetres.   For the study of the topographical
detail and structure of each lamella working " charts " are made by

cutting frozen heads in a special instrument into lamellæ in all three planes. To secure the identification of the section planes perpendicular to the lamellæ thus prepared fine ivory knitting needles are previously introduced by a drill. For instance, for lamellæ in sagittal sections, two fine ivory rods are passed transversely from the auditory meatus and orbital margin of one side to the corresponding points on the other ; each sagittal lamella therefore shows a section of the two ivory needles, a line joining which is our base line. A glass plate (fig. 1), divided by ruled
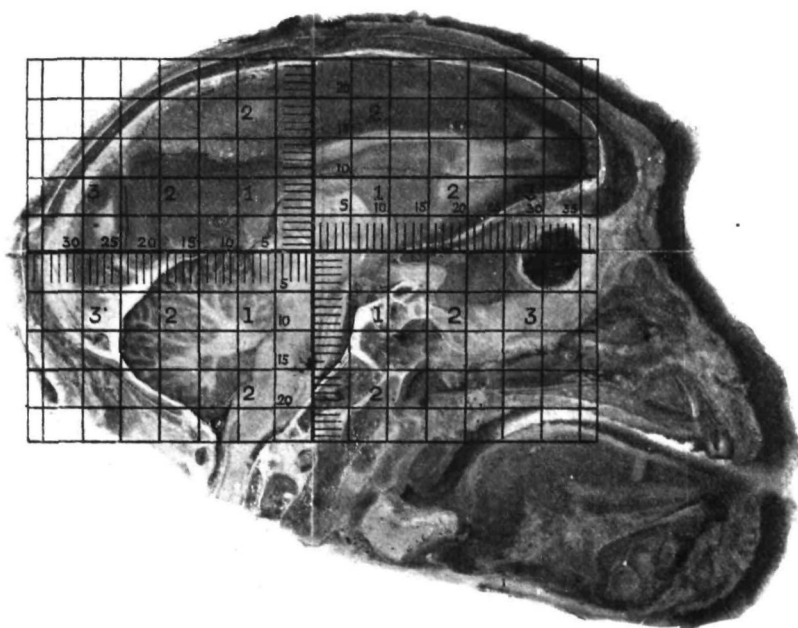
FIG. 1.

Sagittal section of frozen head of Rhesus, and millimetre glass plate.

lines into square millimetres and by two bold lines crossing in the middle into four parts, is then placed on the surface of the lamella, and with the aid of the centres of the ivory points the glass plate is adjusted so that the two bold lines coincide with the frontal and horizontal lines or section planes. The distance of any point in the lamella from these lines can then be directly read off, and as the number of the lamella indicates the number of millimetres from the median

section plane, the exact[1] distance of the selected point from the three inner surfaces of the segment in which it lies is known. Though it is useful to have several series of lamellar sections cut in all three planes, it is best to make records and references as far as possible to one plane only, and the sagittal plane is the most convenient for this purpose.[2] Further advantages of such limitation are : much less confusion and greater brevity of reference. If it is understood that all lamellæ not otherwise specified are situated in the sagittal plane, the word sagittal is superfluous. Lamella vi. then signifies a lamella in the sagittal plane 6 mm. from the median sagittal plane. It is also convenient to indicate the ordinates, *i.e.*, distances above or below the zero horizontal plane in the ruled plate, and so in the lamellæ by letters of the alphabet, while the abscissæ or distances in front or behind the zero frontal (inter-aural) plane are denoted by numerals. If the sagittal plane is adhered to, one soon learns that letters refer to millimetres above and below the horizontal line and numerals to millimetres before and behind the frontal line. At first the use of letters to indicate numbers is rather confusing, but after a little practice one remembers the numbers the letters correspond to without much difficulty. The advantage of having a short and easily recognized reference to any cubic millimetre will be appreciated in practice. Thus a rhesus' brain contains about 200,000 c.mm., and yet by the method described any given cubic millimetre can be identified by a reference as short as the following : *Left frontal segment, lamella* v. *J.* 6. Such a statement refers to a cubic millimetre in the left frontal segment 5 mm. to the left of the median sagittal plane, 10 mm. above the zero horizontal plane, and 6 mm. in advance of the inter-aural or zero frontal plane. With that reference it is easy to select from the frozen sagittal sections lamella v., and by applying the ruled glass plate with the help of the points marked by the ivory, so that the cross coincides with the frontal and horizontal lines, to identify the deep structures which correspond to J. 6.

This sketch of the principles of what may be called rectilinear topography may serve to explain the measures required for its application, which must now be rather more fully described.

Working " charts."—These consist of a series of sections of the

---

[1] For corrections due to size, &c., see p. 82.

[2] Probably, too, most investigators visualize the encephalon sagittally, *i.e.*, as a lateral view, the head being in the anatomical position with the visual axes horizontal, although it has unfortunately been the stereotyped custom to make the large majority of anatomical researches by sections in the frontal plane only.
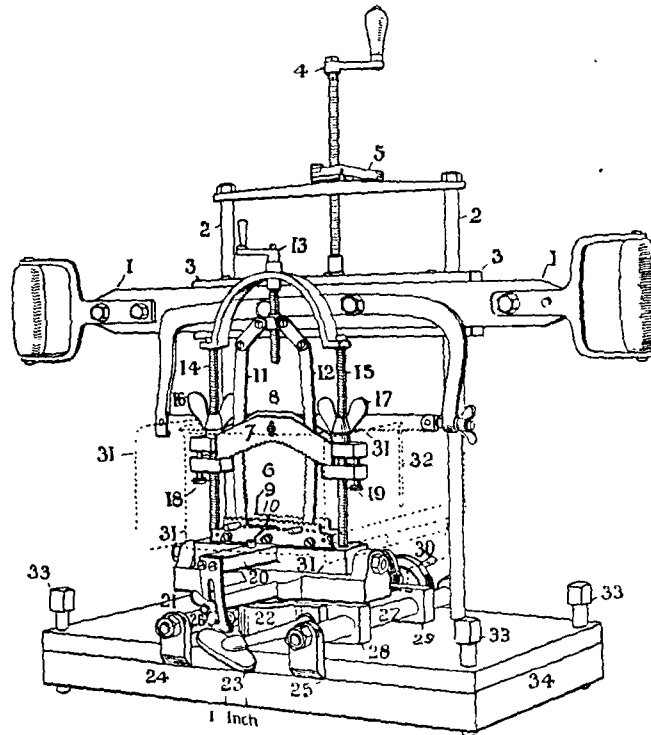
FIG. 2.

Clarke's Saw for cutting sections of frozen heads 1 mm. or 2 mm. thick.

1 Hack saw working on horizontal and vertical guides.
2 Vertical guides for saw.
3 Horizontal guide for saw.
4 Screw for raising and lowering saw.
5 Grip with spring catch, in which screw 4 works.
6 Placed in centre of head vice.
7 Posterior blade of upper jaws of head vice.
8 Anterior blade of upper jaws of head vice.
9 10 Anterior and posterior lower jaws of head vice.
11 12 Vertical jaws of head vice.
13 Screw for approximating vertical jaws of head vice.
14 15 Screw guides for upper jaws of head vice.
16 17 Fly nuts for depressing upper jaws of head vice on screw guides (14, 15).
18 19 Screw for adjusting upper jaws of head vice.
20 Rocking adjustment of head vice.
21 Fly nut for clamping rocking adjustment (20).
22 Rotatory adjustment of head vice.
23 Screw for clamping rotatory adjustment (22).
24 25 Fixed brackets supporting guides of travelling stage of vice.
27 Right guide of travelling stage of vice.
28 29 Travelling stage of head vice.
30 Graduated wheel for moving travelling stage of vice on guides—One complete turn = 2 mm. movement of stage.
31 Zinc tray (shown by dotted lines) to confine CO² snow.
32 Dotted lines show gap in sliding side of tray for saw.
33 Levelling screws of foot-plate.
34 Foot-plate.

frozen head of an animal of the same species, and as nearly as possible of the same size as that which is to be used for the experiment. These sections are cut with a saw in a special instrument (Clarke) (*see* fig. 2) 2 mm. thick, parallel to one of the section planes, and mounted in glycerine jelly between glass plates. Each section shows two lamellæ, one surface of each lamella being visible under the glass plate which covers it. The lamellæ are measured and numbered from the section plane to which they are parallel. Thus they will be right and left sagittal, superior and inferior horizontal, anterior and posterior frontal lamellæ in their respective planes, and the number of any lamella indicates the number of millimetres from the zero section plane to its distal surface, *i.e.*, lamella i. lies between the section plane and a section 1 mm. from it. It is convenient to have a series of lamellæ in each plane, but the sagittal is most important, since we make, as already stated, all records and references in it unless otherwise indicated.

Preparation of the head.—Heads of different sizes are injected with warm 10 per cent. formalin, or equal parts of this and Müller's fluid. If not injected before the vessels have time to contract, the injection should be put off for several hours till the contraction of the vessels has begun to pass off; only moderate pressure should be employed, 0·5 to 1 metre of water is sufficient. After the injection is completed two or three holes are trephined in the skull, and the head is suspended in equal parts of 10 per cent. formalin solution and Müller's fluid of double strength ; it is ready to cut in a few days.

Drilling.—It has been explained already that the directions of the section planes are identified by passing two ivory knitting needles (size No. 13 or 14) in one of the section planes perpendicular to that in which the sections are made. For this purpose, and for the attachment of the stereotaxic apparatus later, it is necessary to obtain an accurate centreing of the external auditory meatus, which is accomplished as follows. Fig. 3 represents the drill, which is passed through the auditory meatus in the following manner : The same ear plugs which are used for subsequently adjusting the head in the stereotaxic instrument are employed for the drilling, being bored for this purpose. These ear plugs are made by modelling from casts of the external auditory meatus, conical plugs of different sizes so as to fit different meatus, and bent 3 mm. or 4 mm. from the base at an angle of about 20°. The floor of the meatus in the rhesus and in most animals forms a slight elevation a little internal to the external orifice and, in the rhesus, is then directed downwards and forwards. The bend in the conical plug divides it into two
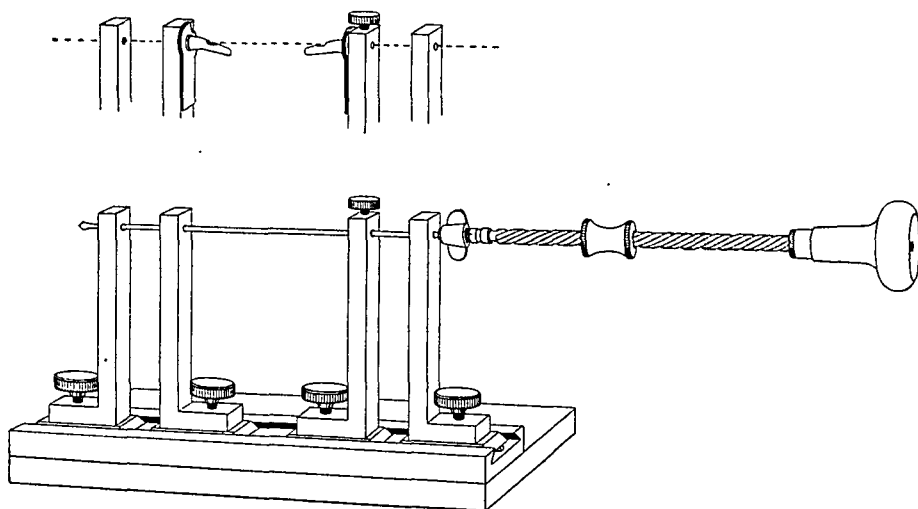
Fig. 3.

Clarke's drilling instrument.—For defining the relation of external to internal structures and determining section planes by means of ivory needles passed through corresponding points on opposite sides of the cranium and cut in frozen sections.
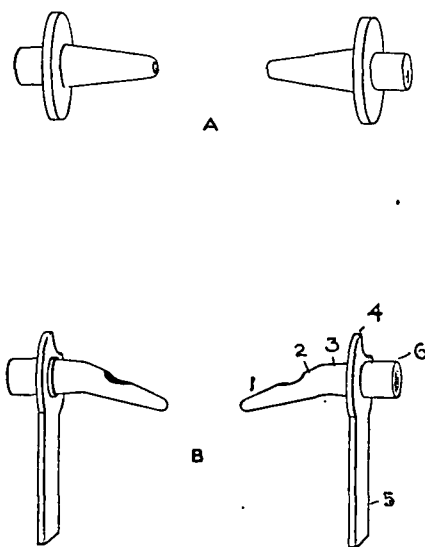
A

B

Fig. 4.

Ear Plugs.

1, cone ; 2, angle ; 3, barrel ; 4, disk ; 5, flange ; 6, funnel.

parts, an inner conical part (the cone) and a short outer cylinder, the barrel (fig. 4). A disc and flange are attached 3 mm. or 4 mm. from the bend, and the barrel is continued and expands slightly to a few millimetres beyond the external surface of the disk to form the funnel (fig. 4), which admits the cylindrical end of the aural pivots in the stereotaxic instrument or the nipples of the drilling apparatus. For passing the ivory needle and marking the inter-aural line, the ear plugs are introduced into the meatus and the two inner uprights of the drilling apparatus (*see* fig. 3) are brought together in the slide till the nipples enter the funnels of the ear plugs; they are then pushed home and clamped, the head being supported by the ear plugs and nipples on the two inner uprights. The drill is passed first on one side and then on the other through the perforation in the two uprights, by which accuracy of direction is secured, the petrous bone being drilled through on each side to the middle line; then a steel needle is passed the whole distance from one outside upright to the other (fig. 3), and finally the ivory needle. For drilling between the malar margins of the orbit the points are marked on each side, then the head is fixed in a clamp between the two uprights and drilled from each side as before, and the ivory needle can then be passed in the place of the drill. The points at which the drills are entered for different section planes should be marked by putting the head in the stereotaxic instrument, and it is desirable to do this and to drill when the head has been but recently fixed (*i.e.*, before it has been rigidly hardened), so that the soft parts of the auditory meatus are practically in a natural condition.

Cutting.—The instrument for cutting frozen sections has been altered from time to time, but its general construction can be seen in the illustration (fig. 2). It consists of a hack-saw working in vertical (2) and horizontal guides (3), the saw being raised or lowered by a screw which can be released by a catch (4). The head is carried on a travelling stage which is moved in guides at right angles to the saw by a graduated wheel (30), one complete turn of which moves the block 2 mm. The stage (28) carries a head vice (6) on a plate with rotating and rocking adjustments (20-22) by which the head can be adjusted in two dimensions after it is fixed in the clamp. Two zinc plates (31) are fixed to the front and back of the travelling stage (28), and two lateral ones, attached by a sliding movement to its sides (32), confine the frozen CO_2 which is used to freeze the head, and the lateral plates have a gap (32) directly beneath the saw in which it descends. Some of the frozen snow escapes through these gaps, but not much. The head can be gripped in the clamp by one

side, by the face, or by the base for sections in the sagittal, frontal, or horizontal planes. Having been secured it is next aligned by the adjustable plate guided by plummets suspended from the ends of the saw and by the surface markings on the head. A superficial saw cut is made to begin with in the median section plane, *i.e.*, for sagittal sections in the median sagittal line, and the distance from this line to the limit of the furthest sections to be cut is measured and marked. The head is then packed with frozen CO_2 moistened with ether. Freezing usually takes about half an hour. If frozen too hard the sections are too brittle and apt to break. If too soft they are apt to bruise and tear, but the right degree is soon learned with a little practice. When freezing is apparently complete the screw is worked till the position chosen for the first saw cut is brought directly under the saw and the first slice removed. If the surface, which can now be seen, is properly frozen its distance from the median section plane is measured with a depth gauge, the plate of which is applied to the cut surface, while the sliding bar of the gauge terminates in a knife edge which fits into the superficial saw cut previously mentioned, and gives the distance in millimetres of the cut surface from the section plane, that is to say, the number of the lamella which that surface represents. A glass plate is then smeared with gum and applied to the cut surface, to which it immediately freezes and protects the next section while it is being cut. The block is now moved forwards 3 mm. by the screws, so that the saw cut and *débris* being equivalent to 1 mm., the section will be 2 mm. thick. As soon as it is sawn through it is placed in a dish of water, the number of the section and the distance of its surface being written on the glass plate. The same operation is repeated till all the sections are cut. They must then be carefully cleaned from the saw dust and *débris* in water, and left for a couple of days in equal parts of glycerine and water to dissolve out some of the formalin and chromates, as these have a tanning effect on the gelatine of the glycerine jelly which is apt to be troublesome. The sections are permanently mounted in glycerine jelly.

It is right to mention that there is a difficulty in mounting in glycerine jelly owing to the shrinking of gelatine produced by formalin and chromates, even after soaking the sections in glycerine and water. The most convenient way of mounting them is to make cells with glass plates large enough to include the section, and walls of square glass rods 3 mm. or 4 mm. diameter. When dry the cell is filled with warm glycerine jelly, and the section introduced with care to avoid bubbles. After a time the gelatine shrinks, air may find its way in, and occasionally the shrinkage

breaks the glass plates and the sections have to be remounted. The number of the lamella should always be immediately written on the glass covering the section with enamel paint.

General Conclusions on the Topographical Relations of the Encephalon in the Macacus rhesus.

From a large series of measurements of heads of *Macacus rhesus* and in a few cases of *Macacus cynomologus* we have been able to construct a
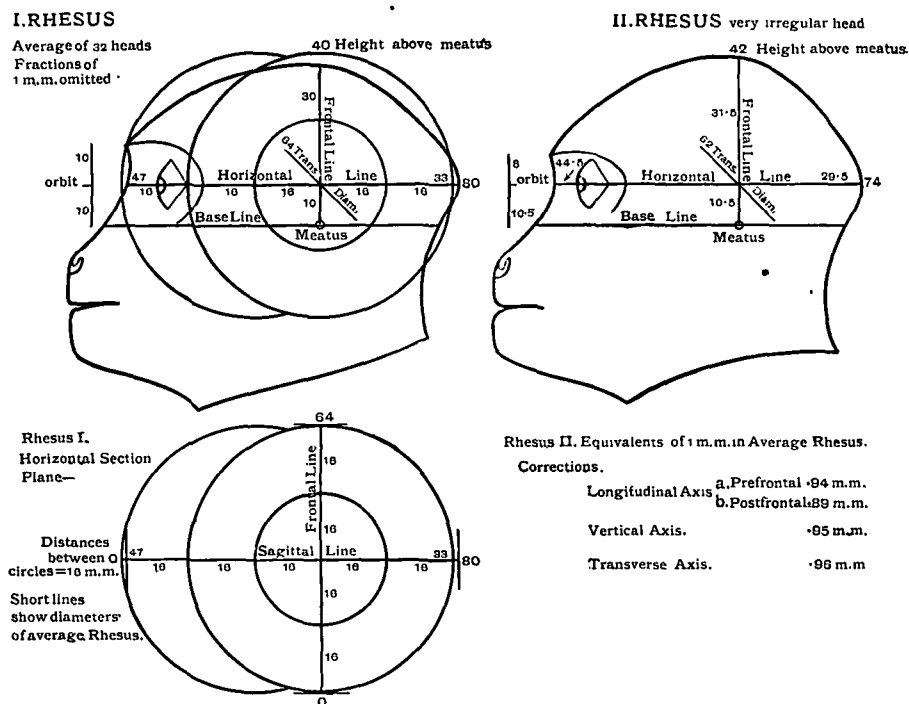
FIG. 5

Drawing of sagittal sections of heads of two Rhesus. I. Average size, and II. an irregular head. To illustrate measurements.

scale of averages for the former animal, and before describing the stereotaxic instrument we use for excitation and electrolysis we may perhaps with advantage first recount the general dimensions of the head in a *Macacus rhesus*, whose total body (head and trunk) length is about 320 mm. This being the commonest and most convenient size, we have as far as possible employed it only.

In fig. 5 is a reduced outline from a drawing on millimetre ruled paper showing the dimensions of a rhesus' head taken from an average of between .thirty and forty specimens (avoiding fractions of 1 mm.). The base line passes through the centre of the lower margin of the orbit and the centre of the auditory meatus. Its length longitudinally is not used for calculation. Perpendicular to the base line is the frontal line, representing the (inter-aural) frontal section plane and erected from the centre of the meatus to the vertex; in the average rhesus it is 40 mm. in length. The greatest vertical diameter of the orbit is next taken and found to be 20 mm. on the average, or exactly half the height of the frontal line. On this point the constancy of the dimensions of the orbit in *Macacus rhesus* deserves some attention in view of opinions prevailing among craniologists on the value of orbital measurements. It is not a little remarkable that in examples of this species of monkey about 320 mm. long, the greatest vertical height of the orbit should rarely vary more than 0·5 mm., or at the outside 1 mm. from a total (greatest depth) of 20 mm., and in the large majority of cases not at all.

Further as regards symmetry any difference between the two orbits when present (and this is extremely rare) never exceeds 0·5 mm. It follows, therefore, that the determination of the lowest point in the lower margin of the orbit gives very satisfactorily the anterior point for the construction of the base line. To obtain the next convenient dimension, namely, the horizontal zero section plane, it will be seen that half the orbital height and one-fourth of the average frontal line are in both cases 10 mm. on the average. At this level, therefore, viz., one-fourth of the frontal line, we draw parallel to the base line the horizontal line representing the zero horizontal section plane, which extends from about the nasion to the occiput. Level in front with a line joining the two inner canthi, from nose to inter-aural plane it measures 47 mm. on an average, and from this plane to occiput 33 mm., making an average total length of 80 mm. Finally the greatest transverse diameter of the frontal plane is taken with callipers and found to be maximal at about the level of the horizontal plane and 64 mm. on the average. The point where these section planes meet in the median plane is zero, and all measurements are reckoned from it, as we have already indicated on p. 50. Two interesting points may be noticed in the above measurements: one is that the frontal line (the median section of the inter-aural plane) is exactly double the vertical diameter of the orbit, the other is the relation of the number 16 to several of the average measurements; thus it is

one-fifth of the longitudinal and one-fourth of the transverse diameter in the horizontal plane.   In some animals with the same total longitudinal measurements the frontal line is 1 mm. further back, making the division of the longitudinal diameter 48 and 32 instead of 47 and 33 mm., these being also multiples of 16 in the proportion of 3 : 2, and in the horizontal section plane itself the relations of this number are still more striking, for the section of the skull at this level is almost exactly represented by one circle with a radius of 32 mm. and its centre at zero and half a circle with the same radius at a point 16 mm. further forward on the median sagittal line.   Probably the average of a still larger number of (320 mm.) rhesus monkeys will differ a little from this, but the relative proportions are not likely to alter much, and accumulated experience proves that the above-stated figures will continue to be accurate guides.

III.—Description of Clarke's Stereoscopic Instrument Employed for Excitation and Electrolysis.

The application of the foregoing facts to our experimental investigations has been effected by an instrument, the general plan of which will be most easily obtained by an examination of the illustrations. It would be very tedious to follow a minute description of every screw and detail, and the purport* of any of these can be ascertained by referring to the figures and letterpress, consequently no more will be attempted in the text than a short explanation of the essential features and their direct application to the animal's head.

The foundation of the stereotaxic instrument is a rigid quadrilateral rectangular frame (the " horizontal frame ") the ends of which (the "nasal" and "occipital" bars) can be approximated by joints which slide on the lateral bars. The lower border of this frame, which is in the same plane on all four sides, is adjusted so as to correspond accurately with the zero horizontal section plane of the head and is fixed in this position on the skull by four lateral screw points all furnished with millimetre scales, so that in addition to fixing the frame they make the median sagittal line of the frame coincide with the sagittal section plane of the head.   It will be seen directly that the horizontal pivot bars articulating with the ear plugs in the auditory meatus, on which the topographical adjustment of the horizontal frame primarily depends, also indicate the points of incidence of the perpendiculars to the horizontal

¹ The instruments were made by Messrs. Swift and Son, Tottenham Court Road.
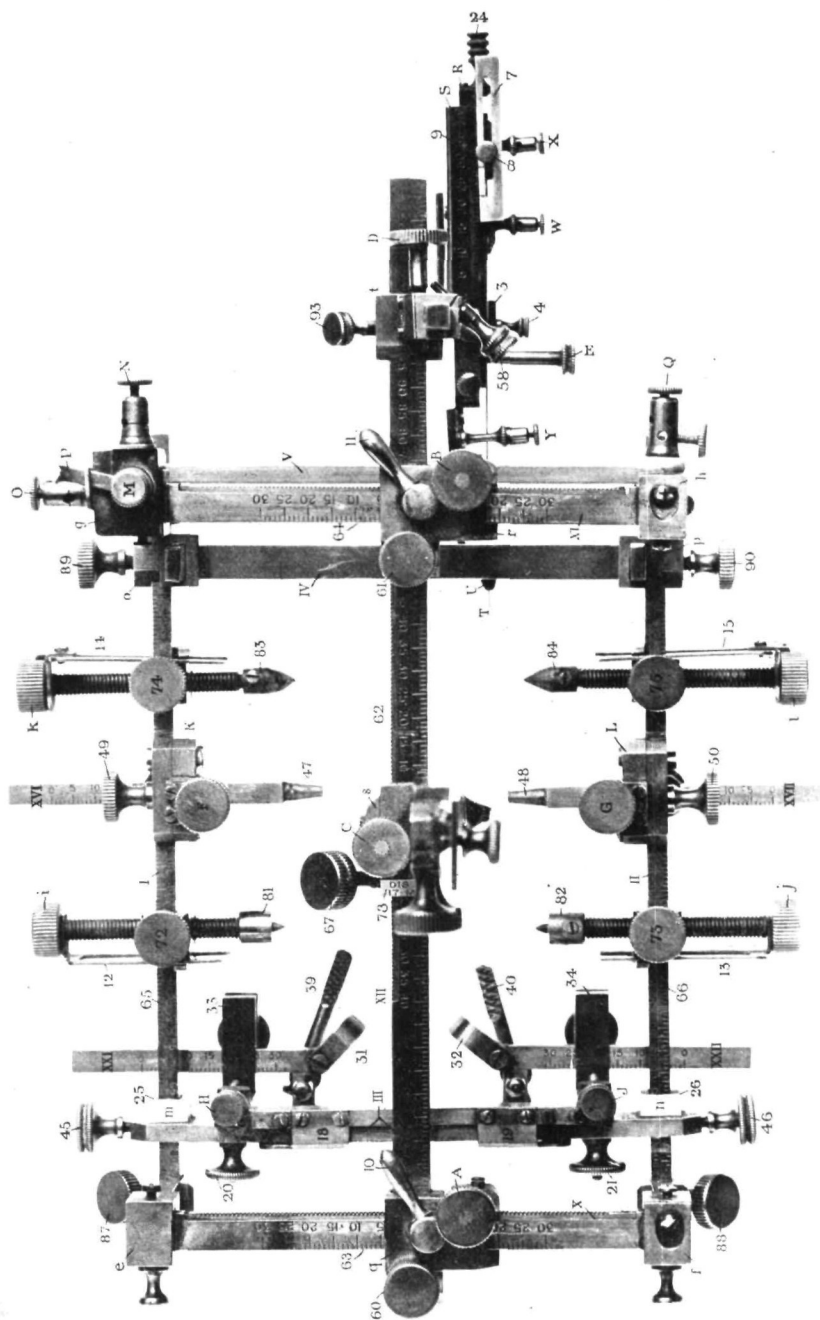
Fig. 6.

I. —*Clarke's stereotaxic apparatus for directing an insulated needle by graduated movement in three planes.*

I.—Plan.

No. I. Plan.—Roman Numerals.

I & II   Right and left lateral bars of horizontal frame.
   III   Frontal bar, comprising nasal and orbital plates.
   IV   Occipital bar.
   V   Occipital stay.
X   XI   Anterior and posterior transverse guides.
  XII   Sagittal guide.
XVI XVII   Right and left aural pivots, horizontal.
XXI XXII   Right and left infra-orbital bracket bars.

Capital Letters.

A & B   Anterior and posterior pinions for racking sagittal guide on transverse guides.
   C   Pinion for racking needle carrier on sagittal guide.
   D   Pinion for racking sheath on vertical guide.
   E   Pinion for racking bed of needle forward on sheath.
F   G   Right and left screws for aural adjustment of horizontal frame.
H   J   Right and left screws for orbital adjustment of horizontal frame.
K   L   Right and left aural adjustment fitting.
   M   Terminal for cathode lead from battery or coil.
   N   Terminal for cathode lead to needle.
   O   Terminal for cathode lead to live stop.
   P   Switch.
   Q   Terminal for anode leads, battery and needle.
   R   Vulcanite bed of needle holder.
   S   Sheath of needle holder.
   T   Needle.
   U   Stop.
   W   First needle terminal.
   X   Second needle terminal.
   Y   Live stop terminal.

Small Letters.

  e f   Right and left terminal joints of anterior transverse guide.
  g h   Right and left terminal joints of posterior transverse guide.
  i j   Right and left anterior lateral frame clamps.
  k l   Right and left posterior lateral frame clamps.
  m n   Right and left sliding joints of nasal plate.
  o p   Right and left sliding joints of occipital bar.
  q r   Two-way travelling joints of anterior and posterior transverse guides.
   s   Needle carrier travelling joint.
   t   Vertical guide two-way joint rack and slide.

Ordinary Numerals.

   3   Vulcanite clamp on needle holder.
   4   Screw for vulcanite clamp.
   7   Adjustable index on bed of needle.
   8   Screw for fixing index on bed of needle.
   9   Millimetre scale on sheath graduated 40·0 mm.
10 & 11   Clamps to lock travelling joints on anterior and posterior transverse guides.
12 13   Millimetre scales on right and left anterior lateral frame clamps.
14 15   Millimetre scales on right and left posterior lateral frame clamps.
18 19   Right and left millimetre scales of orbital adjustment.
20 21   Right and left screws for fixing orbital adjustment.
  24   Screw to adjust vulcanite bed for second needle.
25 26   Right and left bevelled edge indices on slots of nasal plate.
31 32   Right and left infra-orbital brackets.
33 34   Right and left sliding clamps for infra-orbital bracket bars.
39 40   Right and left horizontal maxillary rods.
45 46   Right and left screws for clamping sliding joints of nasal plate.
47 48   Tapered ends of right and left aural pivots.
49 50   Right and left fixing clamps of aural adjustment.
  58   Clamp for fixing rack movement of vertical guide.
60 61   Right and left clamps to fix sagittal guide in longitudinal slots of travelling joints of transverse guides.

Ordinary Numerals (continued).

	62	Millimetre scale on sagittal guide.
63	64	Millimetre scales on anterior and posterior transverse guides.
65	66	Millimetre scales on lateral bars of horizontal frame.
	67	Clamp to fix travelling joint of needle carrier (vertical).
72	73	Right and left fixing screws for sliding joints of anterior lateral frame clamps.
	78	Bevelled edge index of travelling joint of needle carrier for scale on sagittal guide.
81	82	Terminal points of right and left anterior lateral frame clamps.
83	84	Terminal points of right and left posterior lateral frame clamps.
87	88	Right and left anterior corner clamps for horizontal frame.
89	90	Right and left clamps for occipital sliding bar.
	93	Clamp for posterior sliding joint on sagittal guide.

frame which coincide with the frontal section plane. When, therefore, the horizontal frame is accurately adjusted, by erecting two perpendiculars of equal length on the centres of the nasal and occipital bars and joining their upper and lower extremities with two straight lines, we can obtain a rectangular quadrilateral figure which represents the sagittal section plane. A similar figure representing the frontal section plane can be constructed from perpendiculars to the lateral bars which fall through the centres of the auditory meatus; in short, by the adjustment of the horizontal frame we secure data for constructing a rectilinear framework or cage corresponding to the three section planes of the head, which can be used for measurement and to direct a needle to any depth perpendicular to any section plane and at any distance from the other two, or, in other words, to any point of known distance from the three inner surfaces of any of the segments into which the head is divided by the three section planes.

These considerations show that the adjustment of the horizontal frame is of primary importance, and the means by which it is effected require some explanation. It has been mentioned that the base line is drawn through the middle of the lower margin of the orbit to the centre of the auditory meatus on each side and that the zero horizontal line is drawn parallel to the base line but at a convenient distance above it, namely, one-fourth of the height of the inter-aural frontal line. The adjustment of the horizontal frame to the zero horizontal plane is effected by two little pieces of mechanism called the aural and orbital adjustments, which enable the operator to bring the lower border of the horizontal frame to the correct height above the base line at these two points without difficulty.

(1) *The Aural Adjustment.*—In the illustration (fig. 7) two upright columns will be seen on the upper surface of the lateral bars. Each of them has a screw (G) at the top which raises and lowers a short vertical rod graduated in millimetres on its outer surface (XIX); this
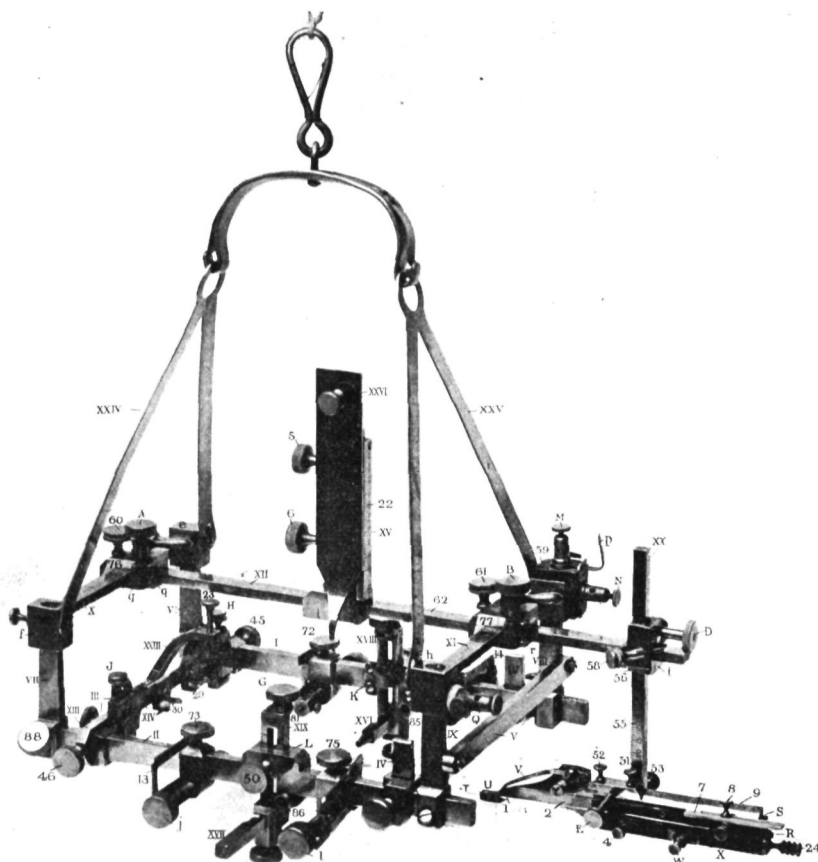
FIG. 7.

Side Elevation of Clarke's instrument.

Roman Numerals.

I II	Right and left lateral bars of horizontal frame.
III	Frontal bar.
IV	Occipital bar.
V	Occipital stay.
VI VII VIII IX	Right and left anterior and right and left posterior corner columns.
X XI	Anterior and posterior transverse guides.
XII	Sagittal guide.
XIII	Nasal plate.
XIV	Orbital plate.
XV	Needle carrier, vertical.
XVI XVII	Right and left aural pivots, horizontal.
XVIII XIX	Right and left aural pivots, vertical.
XX	Vertical guides.
XXIII	Supra-orbital stay.
XXIV XXV	Anterior and posterior slings.
XXVI	Dummy needle.

Capital Letters.

A	B	Pinions for racking sagittal guide on anterior and posterior transverse guides.
	C	Pinion for racking needle carrier on sagittal guide.
	D	Pinion for racking vertical guide.
	E	Pinion for racking needle bed on sheath.
	G	Screw of left aural adjustment of horizontal line.
H	J	Right and left screws of orbital adjustment of horizontal line.
K	L	Right and left aural adjustment fitting.
	M	Terminal for battery lead ; cathode.
	N	Terminal for needle lead ; cathode.
	P	Switch.
	Q	Terminal for battery and needle leads ; anode.
	R	Vulcanite bed of needle holder.
	S	Sheath of needle holder.
	T	Needle.
	U	Stop.
	V	Live stop.
	W	Needle terminal, first.
	X	Do. do. second.
	Y	Terminal for live stop.

Small Letters.

e	f	Right and left terminal joints of anterior transverse guides.
	h	Left terminal joint of post, transverse guide.
	j	Left anterior lateral frame clamp.
	l	Left posterior lateral frame clamp.
q	r	Two-way travelling joints on anterior and posterior transverse guide.
	t	Two-way joint rack and slide on vertical guide.

Ordinary Numerals.

|		
	1	Neck of sheath of needle holder.
	2	Shoulder of sheath of needle holder.
	4	Screw of vulcanite clamp on needle holder.
5	6	Screw for clamping needle holder in vertical carrier.
	7	Adjustable index on bed of needle.
	8	Screw for fixing adjustable index.
	9	Millimetre scale on sheath of needle holder.
	13	Millimetre scale on left anterior lateral frame clamp.
	14	Millimetre scale on left posterior lateral frame clamp.
	22	Millimetre scale on needle carrier.
	23	Screw to depress forehead on supra-orbital brackets.
	24	Screw to adjust sliding bed of second needle.
29	30	Right and left supra-orbital brackets.
45	46	Screws for clamping right and left sliding joints of nasal plate.
	50	Fixing clamp of left aural vertical adjustment.
51	52	Screws for fixing needle pinion.
	53	Screw for attaching needle holder to vertical guide.
	55	Millimetre scale on vertical guide.
	56	Bevelled edge of index millimetre scale of vertical guide.
	58	Clamp for fixing rack motion of vertical guide.
	59	Vulcanite insulator of cathodal terminal.
60	61	Clamps to fix sagittal guide in sliding joints of anterior and posterior transverse guides.
	62	Millimetre scale on sagittal guide.
72	73	Fixing screws for sliding joints of right and left anterior lateral frame clamps.
	75	Fixing screw for sliding joint of left posterior lateral frame clamp.
76	77	Bevelled edge indices for scales on anterior and posterior transverse guides.
	81	Terminal point of right anterior lateral frame clamp.
85	86	Right and left slots for posterior lateral frame clamps for small animals.
	88	Right and left anterior corner clamps for horizontal frame.
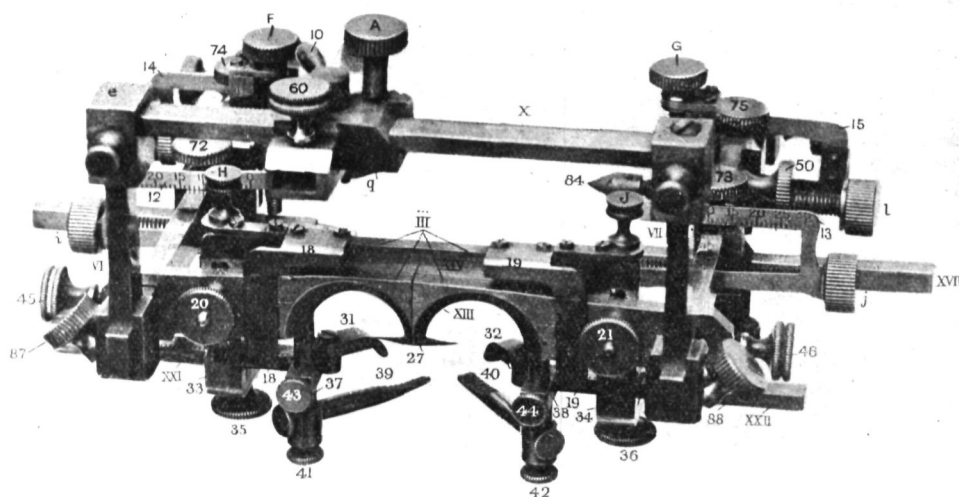
FIG. 8.

Front Elevation (anterior half) with orbital adjustment for various animals.

Roman Numerals.

III   Frontal bar.
VI VII   Right and left anterior corner columns.
X   Anterior transverse guide.
XIII   Nasal plate.
XIV   Orbital plate.
XVII   Left aural pivot, horizontal.
XXI XXII   Right and left infra-orbital bracket bars.

Capital Letters.

   A   Pinion for racking sagittal guide on anterior transverse guide.
F   G   Screws for right and left aural adjustment of horizontal line.
H   J   Screws for right and left orbital adjustment of horizontal line.

Small Letters.

   e   Right terminal joint of anterior transverse guide.
i   j   Right and left anterior lateral frame clamps.
   l   Left posterior lateral frame clamp.
   q   Two-way travelling joint of anterior transverse guide.

Ordinary Numerals.

   10   Clamp to lock travelling joint on anterior transverse guide.
12   13   Millimetre scales on right and left anterior lateral frame clamps.
14   15   Millimetre scales on right and left posterior lateral frame clamps.
18   19   Right and left millimetre scales of orbital adjustment.
20   21   Right and left screws for fixing orbital adjustment.
   27   Needle indicating lower border of nasal plate, and therefore anterior limit of horizontal frame.
31   32   Right and left infra-orbital brackets.

Ordinary Numerals (continued).

33	34	Right and left sliding clamps for infra-orbital bracket bars.
35	36	Screws for clamping right and left sliding clamps for infra-orbital bracket bars.
37	38	Right and left vertical maxillary rods.
39	40	Right and left horizontal maxillary rods.
41	42	Screws for clamping right and left horizontal maxillary rods.
43	44	Screws for clamping right and left vertical maxillary rods.
45	46	Screws for clamping right and left sliding joints of nasal plate.
	50	Fixing clamp of left aural adjustment vertical.
	60	Clamp to fix sagittal guide in travelling joint of anterior transverse guide.
72	73	Right and left screws for fixing sliding joints of anterior lateral frame clamps.
74	75	Right and left screws for fixing sliding joints of posterior lateral frame clamps.
	84	Terminal point of left posterior lateral frame clamp.
87	88	Right and left anterior corner screws of horizontal frame.

is the vertical bar of the aural pivot. Its lower end terminates in a clamp which carries another graduated rod at right angles to it, the horizontal bar of the aural pivot (XVI XVII); this bar slides in the clamp perpendicularly to the sagittal plane and can be fixed by a screw in the clamp. Its inner extremity tapers slightly (fig. 6, 47) and fits accurately into the funnel of the ear plug. These conical plugs have been described on p. 57; they are fitted into the meatus, and the frame lowered over the head of the animal sufficiently to allow the horizontal aural pivots to engage the ear plugs. They are pushed into the funnels to exactly the same distance measured by the millimetre scales on the horizontal bars of the pivots, and when these are the same length they are fixed by the screws. Thus in practice these are the first lateral adjustments made, and by their equality these pivots first approximately centre the head in the sagittal plane. If the height of the horizontal line above the base line is known—suppose it is 10 mm.—the vertical aural pivot bar is set at 10 mm. by its scale and screw, and this brings the lower border of the frame 10 mm. above the centre of the meatus; but generally the height of the vertex above the meatus is not known and has to be measured in the apparatus, and the first adjustment of the vertical height of the aural pivots is only approximate and provisional. The measurement of the frontal line is made by provisionally fixing the aural pivots at 10 mm. and then dropping a dummy needle (fig. 7, XXVI) vertically by the needle carrier (fig. 7, XV) on to the vertex. The scale on the needle carrier gives the distance from the vertex to the horizontal plane, and this, plus the provisional setting of 10 mm., gives the whole height. If this exceeds or is less than 40 mm. then corrections are made accordingly in the aural and orbital adjustments (*see* figs. 5 and 7).

(2) *The orbital adjustment* for the monkey is somewhat different from that which is employed for other animals, and will be described first.
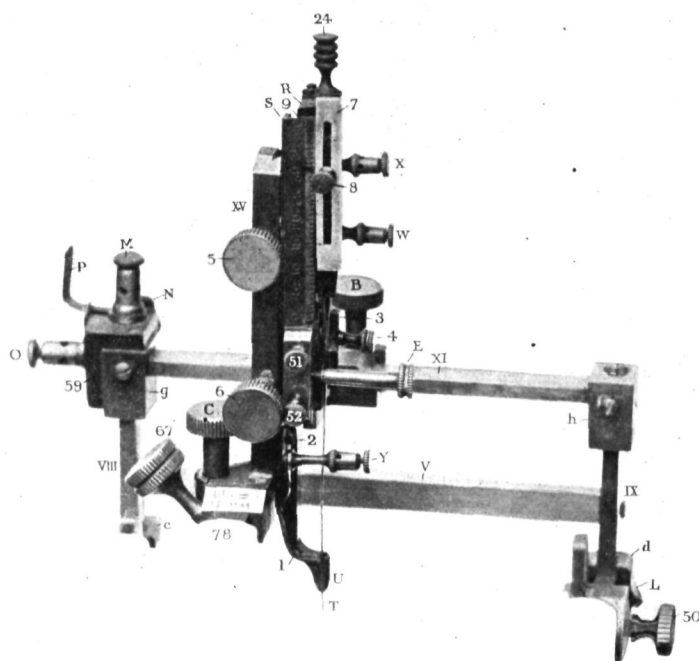
FIG. 9.

Front Elevation (posterior half), with needle mounted for vertical insertion.

Roman Numerals.

V   Occipital stay.

VIII IX   Right and left posterior corner columns.

   XI   Posterior transverse guide.

   XV   Needle carrier, vertical.

Capital Letters.

B   Pinion for racking sagittal guide on posterior transverse guide.

C   Pinion for racking needle carrier on sagittal guide.

E   Pinion for racking bed of needle holder in sheath.

L   Left aural adjustment fitting.

M   Terminal for battery lead ; cathode.

N   Terminal for needle lead ; cathode.

O   Terminal for live stop lead ; cathode.

P   Switch.

R   Vulcanite bed of needle holder.

S   Sheath of needle holder.

T   Needle.

U   Stop.

W   Terminal of first needle ; anode.

X   Terminal of second needle ; cathode.

Y   Live stop terminal.

Small Letters.

c   d   Right and left posterior corner joints of horizontal frame.

g   h   Right and left terminal joints of posterior transverse guide.

Ordinary Numerals.

  1 Neck of sheath of needle holder.
  2 Shoulder of sheath of needle holder.
  3 Vulcanite clamp on bed of needle holder.
  4 Screw for clamp on bed of needle holder.
 5 6 Screws for clamping needle holder in vertical carrier.
  7 Adjustable index on bed of needle.
  8 Screw for fixing index on bed of needle.
  9 Millimetre scale on sheath of needle holder.
  24 Screw to adjust sliding bed for second needle.
  50 Fixing clamp for left aural adjustment.
  59 Vulcanite insulator of cathodal terminal.
  67 Clamp to fix travelling joint of needle carrier.
  78 Bevelled edge index on travelling joint of vertical needle carrier for scale on sagittal
    guide.

The front of the horizontal frame is formed by the frontal bar, which consists of two thin plates, one in front of the other, and held together by two screws (fig. 10, 20 21). They are called nasal (the front one, XIII) and orbital plates (the rear one, XIV) respectively; their connection permits a vertical sliding movement between them, regulated by the screws (fig. 10, H J) and indicated by the millimetre scales (18-19) on the face of the nasal plate. The latter is extended laterally and slotted near its extremities, which thus form sliding joints on the lateral bars (fig. 10, m n). As the upper surfaces of these latter are graduated in millimetres backwards and forwards from a point opposite the centre of the auditory meatus, which is marked zero (and the posterior edges of the slots are bevelled as indices), the distance of the posterior surface of the orbital plate from the inter-aural frontal line is read off at once. The orbital plate is brought into contact with the forehead by sliding the whole adjustment backwards on the lateral bars, to which the nasal plate is fixed by the clamping screws as described (fig. 10, 45 46). The lower border of the nasal plate, of course, has, with the rest of the horizontal frame, to coincide with the horizontal section plane. This is effected as follows: Where the orbital plate is in contact with the forehead there are attached to it on each side small horizontal slightly convex plates, the superior orbital brackets (fig. 10, 29-30), which project backwards about 6 mm. beneath the supra-orbital arches. An arm (XXIII), the "supra-orbital stay," which extends back about 2 cm. over the forehead and carries a vertical screw (fig. 10, 23), affords a simple means by which the supra-orbital arches are kept in contact with the orbital brackets on which they rest. The brackets and stay, therefore, like the blades of a pair of forceps, hold the frontal bone to the orbital plate, and the vertical movement and millimetre scales between this and the nasal plate enable the operator to see and regulate the height of the supra-orbital arch above

the lower edge of the horizontal frame, *i.e.*, of the nasal plate. As the vertical diameter of the orbit is taken beforehand with callipers (in the average Rhesus, as already stated, it is 20 mm.), if the distance of the edge of the frame below the supra-orbital arch is known its distance above the lower margin of the orbit is known also. The lower border of
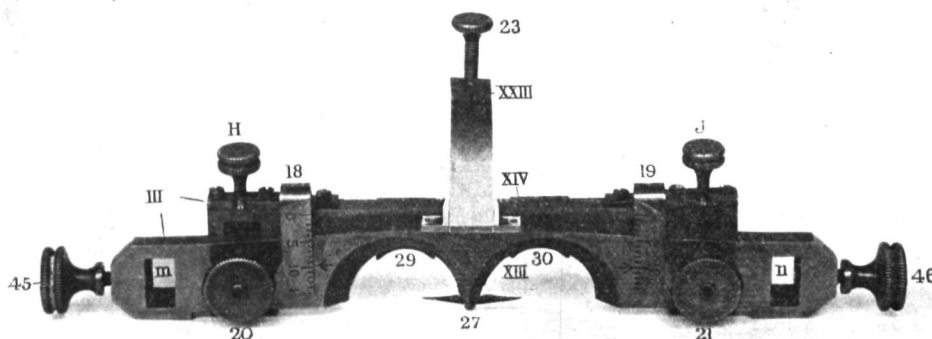

Fig. 10.

Orbital Adjustment for Monkey.—Front Elevation.

Roman Numerals.

III	Frontal bar.
XIII	Nasal plate.
XIV	Orbital plate.

Capital Letters.

H J Right and left screws for orbital adjustment of horizontal frame.

Small Letters.

m n Right and left sliding joints of nasal plate.

Ordinary Numerals.

18	19	Right and left millimetre scales of orbital adjustment of horizontal frame.
20	21	Right and left screws for fixing nasal and orbital plates.
	23	Screw to depress forehead.
	27	Needle indicating lower border of nasal plate, and therefore horizontal frame.
29	30	Right and left supra-orbital brackets.
45	46	Screws for clamping right and left sliding joints of nasal plate.

the horizontal frame is therefore made to coincide with the horizontal section plane at the specified height (one-fourth of the frontal line) above the lower margin of the orbit by the screws (fig. 10, H J) and then fixed by the screws (20 21). The orbital adjustment being thus completed, the bevelled edges (fig. 6, 25 26) behind the nasal bar slots will

now on the average read 47 mm. on the pre-aural scales of the lateral bars on both sides, and the nasal plate is fixed by the screws (fig. 10, 45 46). The occipital bar (fig. 6, IV) is next brought forwards into contact with the occiput, the bevelled edges of its sliding joints (fig. 6, o p) reading on the average 33 mm. on the post-aural scale of the horizontal frame bar, and it is also clamped.

The scale of the aural (fig. 7, XVIII XIX) adjustments is set at 10 mm. (if this be one-fourth of the frontal line), and then the four lateral frame clamp points (fig. 6, 81 82, 83 84) are screwed in sufficiently to secure the head firmly in its position. Each clamp is provided with a millimetre scale to ensure that the corresponding pairs, preaural and post-aural, are screwed into the same distance on each side. Since the same precaution was observed in adjusting the aural pivots the sagittal centreing of the head is adequately provided for by these six lateral supports thus accurately measured to corresponding lengths. After the clamping points have been fixed the occipital bar can be removed to give free access to the cerebellum. The horizontal frame has thus been accurately adjusted so that its lower border coincides with the zero horizontal line, and it now constitutes the foundation of a frame which corresponds with the three section planes and provides for directing a needle by them. Before describing the needle mechanism a few words are required on the adjustments for various other animals besides monkeys and on corrections for size, for hitherto we have only considered the average rhesus. As the measurement of the head in the apparatus, in correcting for size, &c., involves the use of some parts which have *not been described it will be best to complete the description of the instrument and then consider the remaining questions of measurement.*

Adjustment for animals below primates.—The instrument can be applied to any moderately sized mammals and to the larger birds, such as geese and ducks. We have not attempted to enlarge it so as to include dogs because in almost every respect the cat's brain is superior to the dog's for elementary neurological purposes; the nerve tracts are better marked, the size of the encephalon is more convenient for serial sections, and, most important of all, cats' heads are of much more uniform size and shape than those of dogs ; in fact, the endless variations in the size and shape of dogs' heads make them unsuitable for a research involving accurate cranio-encephalic topography. The orbital adjustment is the only one that needs modification to suit the heads of animals below the primates, for in all cases the range of movement in other parts of the apparatus is sufficient for any variation of size that is required, the aural
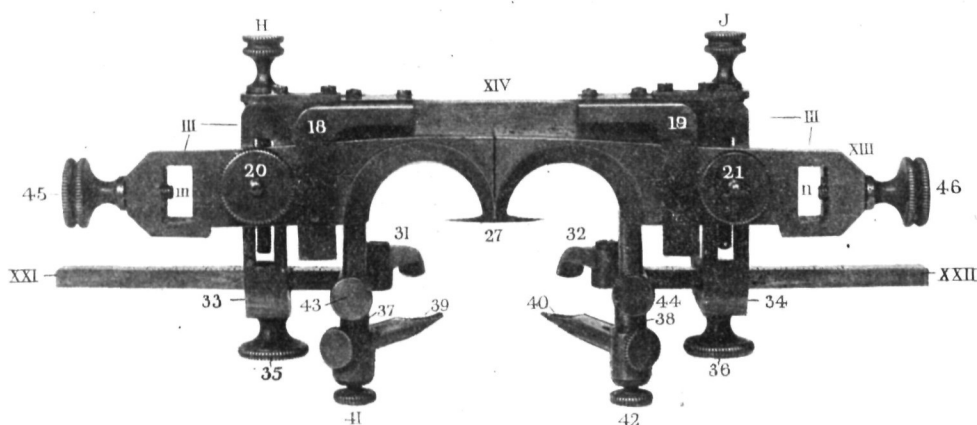
FIG. 11.

Orbital Adjustment for various Animals.—Front Elevation.

Roman Numerals.

III	Frontal bar.
XIII	Nasal plate.
XIV	Orbital plate.

Capital Letters.

H   J   Right and left screws for orbital adjustment of horizontal frame.

Small Letters.

m   n   Right and left sliding joints of nasal plate.

Ordinary Numerals.

18	19	Right and left millimetre scales of orbital adjustment of horizontal frame.
20	21	Right and left screws for fixing nasal and orbital plates.
	27	Needle indicating lower border of nasal plate, and therefore horizontal frame.
31	32	Right and left infra-orbital brackets.
33	34	Right and left sliding joints for infra-orbital bracket bars.
35	36	Right and left screws for fixing sliding joints (33 34).
37	38	Right and left maxillary rods, vertical.
39	40	Right and left maxillary rods, horizontal.
41	42	Right and left screws for clamping horizontal maxillary rods.
45	46	Right and left screws for clamping sliding joints of nasal plate.

adjustment fitting the form of ear plug which may be required for any species of animal.[1]

Though the modification of the orbital adjustment we suggest as more useful[2] for animals below the monkey looks different (*see* fig. 11),

---

[1] It should be mentioned that in the cat the orifice of the meatus is so covered by the pinna that division of the latter is necessary to admit the ear plugs; the incision should be made in the line of the postero-inferior edge of the tragal portion of the pinna.

[2] Possibly for any species.

anyone who has followed the description of the adjustment for the monkey will find the principle the same and the modifications easy to understand. The head, and therefore the lower border of the orbit, is raised and lowered in relation to the lower border of the frame (*i.e.*, of the nasal plate, fig. 11, XIII) by a vertical sliding motion between the nasal and orbital plates regulated by screws (fig. 11, H J) and indicated by millimetre scales (fig. 11, 18 19) on the face of the nasal plate—all this is the same in plan as before. The only difference is that while the orbital plate is connected to the forehead of the monkey by the superior orbital brackets and stay, which grasp the frontal bone like the blades of a pair of forceps, in this pattern the orbital plate is attached to the superior maxilla by inferior orbital brackets (fig. 11, 31 32) and horizontal maxillary bars (39-40). The former project a few millimetres into the orbit over its lower edge, the latter similarly into the mouth, and both together hold the superior maxilla, grasping it like a pair of forceps by the lower edge of the orbit and the upper teeth. In birds the horizontal maxillary bars pass under both mandibles instead of between them. The maxillary bars consist of vertical (fig. 11, 37 38) and horizontal (39 40) portions freely adjustable in all directions; they and the orbital brackets are supported on graduated arms (fig. 11, XXI XXII), supported and sliding in clamps (fig. 11, 33 34) which allow them a transverse motion; the clamps are fixed to the orbital plate, and thus, being attached to the nasal plate, have a longitudinal motion on the lateral bars. Both infra-orbital brackets and maxillary bars have therefore a transverse and longitudinal movement by which they can be adjusted to heads of any size.

Mechanism for Directing the Excitation or Electrolytic Needle.

We have pointed out the data for the mechanical direction of a needle in any plane by the adjustment of the horizontal frame, and the illustrations (fig. 6 and 7) show how one method of giving effect to the principles of localization we have described are carried out in the instrument. Four rigid perpendiculars, the corner columns (fig. 7, VI VII VIII IX), are fixed to the corners of the horizontal frame and joined in pairs by two transverse graduated bars, the anterior and posterior transverse guides (figs. 6 and 7, X XI) ; the centre of each bar corresponding to the median sagittal plane is marked zero and graduated in millimetres from that point on each side. Each transverse guide carries a travelling two-way joint (figs. 6 and 7) with rack and pinion motion.

These joints travel on the transverse guides and at the same time support and carry with them a long graduated bar, the sagittal guide (figs. 6 and 7, XII). This bar is fixed in the slots of the two-way joints in such a position that the zero marked on it corresponds to the inter-aural frontal line, and the sagittal guide is graduated forwards and backwards from this point. The only movement of the sagittal guide is a lateral one, by means of the travelling joints on the transverse guides; longitudinally it is a fixed base on which the arm carrying the horizontal needle slides by a simple joint and on which also the vertical (*see* fig. 7, XV) needle carrier connected perpendicularly to it by a travelling joint moves forwards and backwards from the zero inter-aural frontal plane. The excursions of the needle carriers are indicated by the milli-metre scale on the sagittal guide.

The Needle Holder and its Movements.

(1) The needle, which may be single or double, consists of an iridio-platinum wire insulated nearly to the point in a capillary glass tube, and is clamped on a vulcanite plate, the bed. The glass is held by a vulcanite clamp, from which it is separated by a small piece of soft rubber. The proximal end of the projecting wire is fixed in a metal clamp secured by the terminal, which is screwed firmly down upon it, and electrically connects the needle with the lead from the coil or battery as the case may be. The bed slides by a bevelled edge on each side on a sheath, which tapers in front into a shoulder and neck, and the latter terminates in a small flattened vulcanite cylinder, the stop, perforated to permit the passage of the needle, which can be advanced and withdrawn through the stop by a rack and pinion movement of the bed on the sheath, registered by an adjustable index on the bed, and a graduated millimetre scale on the sheath. This gives the needle an excursion of 40 mm. The perforation in the stop is formed by a lateral slit open on one side to admit the needle and then closed by a fine brass rod which projects a little beyond the stop, and at its proximal end is attached to the shoulder of the sheath by a terminal which receives a lead if required and makes contact with the rod; this rod then constitutes what we call a "live stop," and may be used for so-called unipolar excitation. It also serves the purpose of exercising slight pressure on the needle in its groove, steadying it, and serves as an electrode when required. It is convenient when a single wire is employed. As we show later, in deep punctures faradization of the brain by a long arc stimulation is highly objectionable,

since if one electrode is formed by a needle point and the other by some form of surface contact the current traverses many excitable areas and may produce confused and misleading results, but in making electrolytic lesions the single needle is almost indispensable, and as we never electrolyze without at least one faradic excitation, and generally several, the difficulty is to get a satisfactory stimulation when the single needle is used. It was to meet this that the "live stop" was devised, and in practice we find that as it makes a small surface contact close to the needle, the current is notably confined to its track, thus very much diminishing the escape of current and irregular effects of wider and more distant surface contacts. The disadvantage electrolytically is the exaggeration of the needle track.

The essential parts of the needle holder are thus the bed and the sheath, the latter including the neck and stop. As the needle is carried forwards through the stop the adjustable index attached to the bed indicates the excursion of the needle on a scale on the sheath, which is so graduated that as the needle is advanced the index approaches zero. The object of this is that as the needle penetrates the brain perpendicular to either the horizontal or frontal zero section planes, it is convenient that the index should arrive at zero when the point of the needle reaches the zero plane.

The instrument is constructed to direct the needle at will into any part of the brain from two positions: (1) Vertical from above, and (2) horizontal from behind.

(1) In the vertical position the sheath of the needle bed slides in a slot in the carrier, where it can be fixed with two screws. It is perpendicular to the sagittal guide, and, of course, to the horizontal section plane. It has been explained that the carrier travels longitudinally on the sagittal guide from a zero, which corresponds with the inter-aural frontal section plane, and laterally on the transverse guides to right and left of the median sagittal plane. By these two movements the needle can be brought over any square millimetre in the horizontal plane. For the vertical movement the connection between the sheath and the carrier is used as a coarse adjustment. For this purpose there is a scale on the carrier and an index on the sheath (figs. 9 and 7). The scale is originally graduated as follows: The sheath is pushed downwards till the distal surface of the stop is level with the lower border of the horizontal frame. This point is marked zero on the scale, and the graduation is made as the sheath is drawn up. This scale therefore always indicates in millimetres the distance of the stop above the

zero horizontal line.   In use the sheath is pushed down till the stop is at a convenient point, commonly the surface of the brain, and it is fixed there; the scale on the carrier (XV) then shows how many millimetres separate the stop from the horizontal line.   The needle is then advanced till its point is exactly flush with the surface of the stop, and the adjustable index on the bed is set at the same figure on the scale on the sheath.   If the stop, according to the scale on the carrier, is 30 mm. above the horizontal line, and the ivory index is set at 30, then as the needle penetrates the brain the figure on the sheath scale will always show the distance of the point from the horizontal section plane, and when it arrives there the index will be at zero.

(2) In the second or horizontal position the needle holder is connected to the sagittal guide in a different way.   In the illustration it is shown connected to the hinder end of the sagittal guide as follows: The sheath carrying the bed and needle is fixed at right angles to the lower end of a vertical guide (fig. 7, XX) by two screws (fig. 7, 53).   The vertical guide is connected with the sagittal guide by a two-way joint, one slot of which (horizontal) slides over the sagittal guide and can be fixed at any point by a screw (fig. 6, 93).   The other slot of the joint is vertical and the vertical guide is worked up and down in it by a rack and pinion (fig. 7, D).   The vertical guide is graduated in such a way that when the point marked zero is opposite the bevelled edge of the joint (fig. 7, 56) which serves as the index, the needle is on the horizontal line, and the graduations above and below zero show the vertical distance of the needle above or below the horizontal line.

The transverse movements of the sagittal guide to right and left of the median sagittal plane convey the same motion to the needle, and the vertical and sagittal guides in this way afford the two movements required to bring the needle opposite any square millimetre on the frontal plane.   The third movement, that of the needle towards the frontal plane, is a double one as in the first position, but differently arranged.   The coarse adjustment is the movement of the whole needle holder and stop towards the frontal section plane.   This is effected by the sliding joint (fig. 6, t) on the sagittal guide.   The bevelled edge of the joint is an index for the graduated scale on the guide and indicates the distance of this edge from the interaural plane, i.e., zero on the sagittal guide.   The distal surface of the stop (U) is 50 mm. in front of the bevelled edge.   As the distance of the bevelled edge from the frontal line is known, that of the stop from this line is known also.   For example, if the bevelled edge is at 80, the anterior surface of the stop

is 30 mm. behind the frontal section plane. The point of the needle is racked flush with the surface of the stop and the adjustable index (fig. 6, 7) set at 30. As the needle advances towards the frontal line the index travels towards zero on the scale on the sheath (fig. 6, 9), and when it reaches zero the point of the needle arrives at the zero frontal inter-aural plane.

Needles.—These are made of iridio-platinum (20 per cent. iridium), about 10 cm. long, pointed and of various calibres, according to the size of the electrolytic lesion required, which depends on various considerations. For stimulation fine needles are required (30 to 32 on the English standard wire gauge), about 0·22 mm. in diameter; they are fitted into the smallest glass tubes which will take them, about 25 to 26 gauge. We have not found it desirable to use finer needles than this as a rule. In every excitation experiment there are some points which must be marked by a small electrolysis, sometimes to record a noteworthy response, and in any case to serve as indicators to verify or correct the position of the part investigated after the brain has been fixed and sectioned. Owing to the high resistance, however, there is a limit to the calibre of needles which can be employed with advantage for electrolysis. Illustrations of the needles which we are at present using, and showing both the actual size and enlargement, are given in fig. 12. They represent three varieties: the single, the double-barrelled, and the concentric. In all cases the insulation is by a capillary glass tube. The following are measurements of needles in use at present showing the relations of needles and glass tubes. The measurements are given in millimetres and in the English standard wire gauge:—

	Wire gauge	mm.			Wire gauge	mm.
1 Single needle, fine ...	32 ...	0·19	...	Glass tube ...	27 ...	0·34
2 Single needle, large ...	25 ...	0·45	...	Glass tube ...	21 ...	0·70
3 Double barrel ...	30 ...	0·27	...	Glass tube ...	24 ...	0·50
	30 ...	0·27	...	Glass tube ...	24 ...	0·50

The single needle is the most convenient when only an electrolytic lesion is required; it gives a better point, is most easily introduced, with the least effect on the tissues, its track being scarcely recognizable in sections; its size and the amount of platinum exposed are very easily regulated and consequently the size of the lesion; the latter, when the needle is an anode, is generally spherical, circumscribed and precisely defined. For preliminary stimulation to verify the position, &c., of the

needle, it is best to employ it with the live stop, but this must not, of course, be used for any subsequent electrolysis or it will produce a kathodal lesion on the cortex.   When stimulation is the principal object a single needle is undesirable, since even the live stop gives too large an area of excitation, and a short arc stimulus is far more satisfactory. Either the double-barrelled or concentric needle shown in fig. 12 may be used for short arc stimulation.   The double-barrelled needle penetrates well, makes a small wound and has good rigidity.   It was a
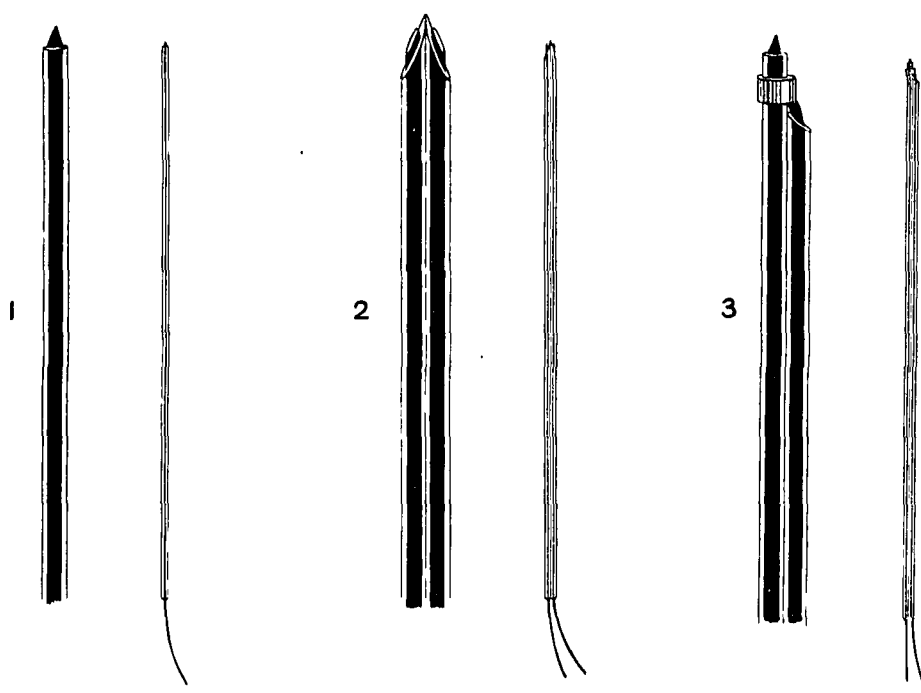
FIG. 12.

Iridio-platinum needles insulated in glass tubes.

1 Single needle.   2 Double-barrelled needle.   3 Concentric needle.
(Actual size and enlarged.)

long time before we succeeded in getting two capillary glass tubes fused together, and we have to thank Professor Jackson, of King's College, for the suggestion which made it practicable. This was to fuse two ordinary glass tubes together for a short distance, and then

heat them and draw them out together. This gives excellent results; the tubes are fused together like the barrels of a gun and can be drawn out quite straight and as long and fine as can be wished. They are ground to a point and wires inserted, which are cut parallel to the slanting orifice which terminates in the point. The ends of the wires are thus separated completely from one another by a glass point, round the edge of which the current must pass.

The concentric needle gives the most constant effects, especially where groups of cells in a nucleus are stimulated. It is rather difficult to make, and, unless very well finished, is rather clumsy, less easy to introduce, and makes a larger track than the others. Mr. Rittershaus,[1] who makes them for us, has much improved them, and is now making them with the double-barrelled glass sheath which diminishes these drawbacks. As will be seen from the illustration, they consist of two fine single insulated needles. The wire of one projects about 0·75 mm. beyond the glass, while of the other the wire is drawn out of its glass tube sufficiently to make a little collar round the glass of the first about 0·75 mm. behind the edge of the glass. The end of the needle, therefore, consists of wire, glass, and collar, each 0·75 mm., or about 2 mm. in all, and the current flows backwards and forwards from the point all round to the collar, giving an equally diffused stimulus for a small area round the point of the needle. When an electrolysis is required the point or the collar can be used alone, the point making a very minute, the collar a moderate-sized, and both together a large lesion.[2]

Corrections for Size and Symmetry.

In describing the adjustment of the instrument to the head of the rhesus it was assumed that the animal was a typical example of average measurements. In practice there are nearly always some variations, and they may be considerable; every head, therefore, must be carefully measured and corrections made for irregularities. The procedure we have adopted is as follows: We first take the maximal longitudinal and transverse diameters of the cranium, *i.e.*, above the level of the zygomatic arch as well as the greatest vertical diameter of the orbit, with callipers before applying the instrument; an outline drawing of the head is made to scale on millimetre paper, and all the measurements filled in as they

---

[1] Of Huntley Street, Tottenham Court Road.
[2] Mainly kathodal.

are taken (*see* specimen of such outline, fig. 5). The callipers are necessarily not as accurate as the apparatus, and the preliminary measurements with them are checked by reading on the instrument after the head is fixed. The measurements, including the true height (fig. 5, I and II) of the horizontal line shown in the outline sketch, are all filled in, and a chart frozen section which shows the required lamella is selected, and the dimensions of each segment in the experimental animal and the chart section compared. If the error of difference is less than 10 per cent., we usually treat it as negligible, but if it amounts to 1 in 10 or more we make the necessary correction according to a table of equivalents. With such corrections and careful adjustment of the apparatus the results are generally accurate in the rhesus. If there is a great difference between the absolute dimensions of the animal's head and the chart section, there is, of course, more likelihood of error, but discrepancies can be in a great measure avoided ; thus if there is only one series of frozen sections to work by, animals must be selected which approach it in size, and, of course, if two or three series of sections of different sized animals are available the operator is less restricted. On the question of symmetry the measurements depend on the assumption that the positions of the bony landmarks, *i.e.*, the meatus and orbits, are generally symmetrical. Moderate variations of proportional measurement can be corrected, and though, of course, the fewer such necessary amendments are the better, they are not necessarily inconsistent with accuracy provided they balance, but an irregularity which prevents the inter-aural plane being perpendicular to the sagittal plane is a grave fault. We do not find that such serious forms of asymmetry occur in monkeys. Of other animals we cannot speak from much experience, but cats' skulls are less regular than monkeys, and more care will be necessary in their selection.

Asepsis.

It is hardly necessary to say that in degeneration experiments every care to maintain asepsis must be observed. It need not be alluded to further here except in relation to the instrument ; this is too delicate to bear repeated boiling, and as some portions of it are of vulcanite efficient sterilization by heat is precluded. We keep the whole instrument in absolute alcohol, which does not injure it and has proved satisfactory. The glass and platinum needles are easily sterilized in strong acids. The small wounds and the protection from contact afforded by the instrument are very favourable to asepsis and infection ought not to occur.

Preparation of Tissues.

As Marchi's method is so well known and described in text-books we need not do more than mention a few points. We inject the brain of the animal just killed, from the aorta preferably, with Müller's fluid (or Müller and formalin) and preserve in Müller alone, since we think any continued use of formalin interferes with osmic acid staining. It is very desirable when employing this method to cut the brain parallel to the section planes which have been defined in the use of the apparatus •
(*vid. inf.*), and such section blocks should never be more than 2 mm. thick, cut as soon as the brain is fixed.
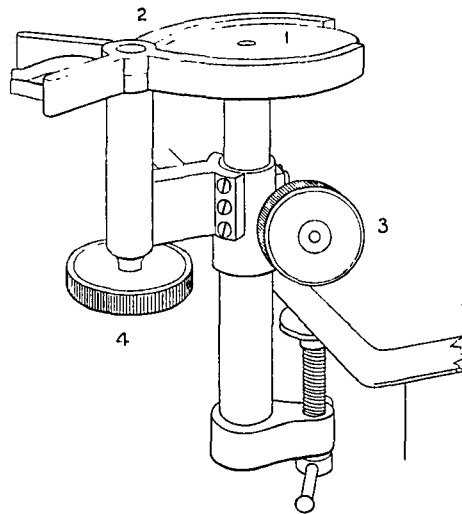
FIG. 13.

Macrotome for cutting brain in slices of known thickness.

1   Plate, raised or lowered by pinion 3.
2   Jaws.
3   Rack and pinion movement to raise and lower plate 1.
4   Clamp to fix jaws 2.

Macrotome.

An illustration is given in fig. 13 of a section instrument, or macrotome, which is useful for this purpose. The brain is divided in one of the section planes. The cut surface is then applied to the plate (1), and the jaws (2) adjusted 2 mm. above the plate. While the brain is well moistened with water, successive slices are cut with a brain

knife, keeping the edge of it on the jaws with a short sawing movement. In the sagittal plane the median section can be judged by the eye, but for the other two planes it is necessary to mark the brain; at present the only way of doing this accurately is to adjust the head in the stereotaxic instrument and mark it before it is removed. Thus when it is in the instrument four to six points can be marked by the dummy needle on both sides of the head in either frontal or horizontal planes (preferably in the inter-aural plane); the skull is removed or drilled at these points and the brain marked with a red-hot needle. After the brain, removed from the skull, has been suspended by Retzius's method in Müller's fluid for twenty-four hours, the desired section can be carried through these marks.

We will now proceed to discuss the electrolytic lesion as produced by the instrument just described, and next the procedure of stimulation, since the use of these methods led us to consider and experimentally investigate a number of points of procedure which bear directly on the question of the accuracy to be obtained in all investigations of this kind.

Although a natural order of these two subjects would be (1) stimulation, (2) electrolysis, for that is our experimental procedure, it will be more convenient historically to deal first with the application of electrolysis to the production of localized lesions in the encephalon.

IV.—THE ELECTROLYTIC LESION.

Historical References.

Attention was early directed to the electrolytic method; thus Mr. William Brande, Sir Everard Home, and Sir H. Davy in the *Philosophical Transactions of the Royal Society* for 1809, give an account of some experiments on the electrolysis of animal fluids undertaken by Mr. Brande for Sir Everard Home. In some of these experiments Mr. Brande was assisted by Sir H. Davy.

Various albuminous fluids were employed, including blood and serum, the former of these being in one experiment contained in the vessels of a freshly killed deer.

The general results may be summarized by saying that with strong currents there was always rapid coagulation at the kathode, none with weak currents. With both currents there was slight coagulation at the anode. Davy's explanation of this was that the albumen was kept in solution by alkali, and when this was liberated coagulation of the

albumen followed. Brande showed that while strong currents are required to liberate the alkali sufficiently to coagulate the albumen, there is more tendency for slight coagulation to occur at the acid pole with weak currents. With fresh human blood kept at 100° F. and a current from twenty 4 in. double plates employed for fifteen minutes, there was no coagulation nor any change, but a slight difference of colour and the production of acid and alkali at the electrodes.

In experimenting on deer's blood in a blood-vessel, and with serum, strong currents caused a rapid coagulation at the kathode, but a slow and slight deposit of albumen at the anode. Employing a weak current for fifteen minutes, a filament about $\frac{1}{4}$ in. long was seen adhering to the positive wire, but nothing at the kathode.

Thus the existence of polar differences in the establishment of a coagulation necrosis have long been known. The direct use of electrolysis as a method of causing localized lesions in the central nervous system seems to have been first described by J. Sellier and H. Verger (1898), who produced electrolytic lesions of the thalamus in five dogs with two insulated needles. A current of 9 ma. to 12 ma. being employed for from seven to ten minutes, the lesions obtained were about the size of a pea or grain of maize.

Gustave Roussy [17] also produced a lesion of the thalamus in two cats, two dogs and one monkey. Following the method of Sellier and Verger, he gives a more precise description of the procedure he employed as follows:—

Current.—A battery of 20 elements with galvanometer in circuit using 8, 10, 12 ma., for eight or ten minutes.

Needles.—Iridio-platinum sheathed in glass. Wire not exceeding 8 cm. long, 0·3 mm. calibre and 1 mm. exposed. They were mounted on a vulcanite plate to carry terminals, one in a slot so that the needles could be separated or approached.

The resistance was observed to fall during the passage of the current (*vide* p. 97 in present paper for reference to this point). The circuit was opened and closed by degrees to avoid movements of the animal.

Roussy reached the thalamus in the cat and dog by taking the middle point of the median sagittal line, *i.e.*, a line extending from the superciliary ridge to the occipital protuberance and trephining $\frac{1}{2}$ cm. to 1 cm. behind this point.

Owing, however, to unavoidable want of precision in this method of localization, Roussy found that of twenty experiments, but five, *i.e.*, one-fourth, were available for the research.

Roussy states that Golsinger, of St. Petersburg, in 1895, was the first to employ this method for destruction of the deep tissues of the brain. He used or advocated unipolar electrolysis, one pole being connected with an insulated needle in the brain, the other attached to an indifferent plate electrode on the abdomen. The current he employed varied from 20 to 40 ma., and, according to his measurements, 8 coulombs gave a lesion the size of a pin's head, 36 coulombs a lesion the size of a cherry. Golsinger showed at the Conférence des Médecins de la Clinique des Maladies Nerveux et mentals (St. Petersburg, 1895), the brains of six dogs with isolated lesions produced by this method. Unfortunately we have not been able to see the report of this communication.

Production of the Electrolytic Lesion.

Having determined on electrolysis as the control to electrical excitation we began by investigating the effects of the various forms of electrical currents on the central nervous (cerebral) tissue, and we arrange the results obtained as follows :—

(A) The Lesion as Produced by Sparks from High Tension Currents.

We first endeavoured to obtain lesions by the use of sparks from high tension currents with an interruption of about 100 per second. The electrolytic action of such sparks on water (steam) has been investigated since Perrot's original observations and has received thorough reinvestigation by Professor J. J. Thomson [23] and others. Lesions of the brain so produced we have found to consist of combined electro-thermic, electro-chemical and mechanical effects.

When two needles, 4 mm. apart, were introduced into the cerebral substance to a depth of 5 mm. and the coil started, the result was to cause a rapid swelling and illumination of the superjacent cortex by reason of the passage of sparks causing practically a subcortical deflagration. Macroscopically and microscopically the resultant lesion proved to be a combined laceration and cauterization with no determinate border. The site of one needle pole was crateriform and empty, that of the other was more tubular and filled with gas bubbles, which were present in a diminishing degree along the narrow line of destruction which marked the shortest paths between the needle points.

The restriction of the effects of such a lesion was proved as in the case

shown in fig. 14, for, on faradic excitation, the excito-motor cortex imme-
diately in front of the destroyed area was found to be physiologically
active close up to the margin of the lesion.

Although the combined effect was thus fairly localized it appeared to
us that the degree of destruction by sparks is not sufficiently controllable
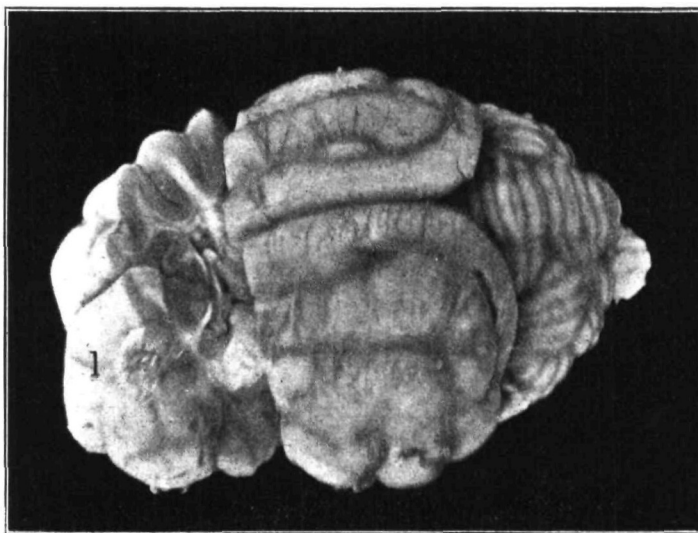to be useful for our purpose and we gave it up on this ground.

FIG. 14.

Lesion of cerebral cortex made by use of high tension sparks.

1 Spot on normal cortex just in front of the lesion and where
excitation proved that the cortex in question was functionally active.
(Cat.)

(B) The Lesion as Produced by Constant Currents.

Electrolysis by a constant current is, of course, a familiar subject, but
little has been written on the immediate question, namely, the destruc-
tion of brain or central nerve tissue by its means, and when we were
endeavouring to estimate its qualitative and quantitative effects we found
that practically no description of the products obtained from cerebral
tissue by the action of each pole existed. We have had therefore to
spend a very considerable time in clearing up several points, not only
chemical but also mechanical, which attracted our attention early in the
research as well as attempting, with the kind assistance of Dr. Gordon

Lane, to form an opinion as to the basis of the chemical changes.   We may therefore group the effects under the headings of : (1) *Mechanical ;* (2) *Chemical.*

(1) *Mechanical effects.*—(a) *Transference.*—The knowledge of the migration of ions prepares one for the acceptance of the fact that in a compound tissue like that of the brain the lesions show a separation and localization of the chemical constituents of the tissues electrolyzed.
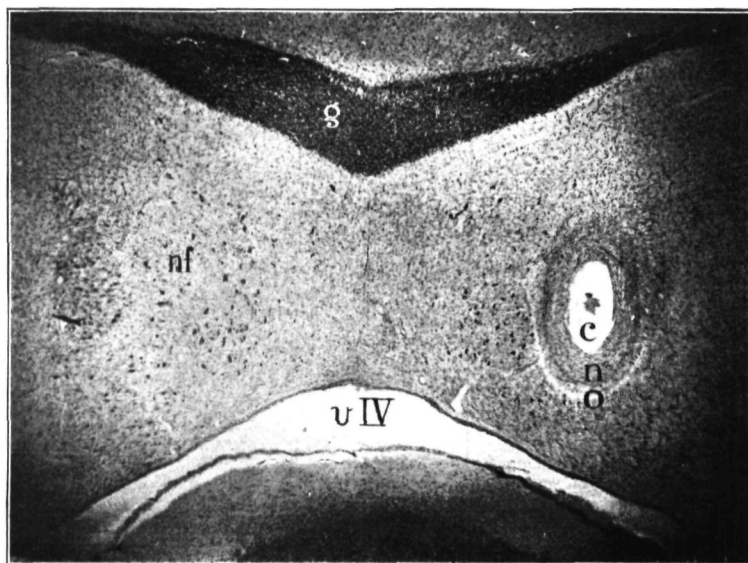

FIG. 15.

Anodal lesion made in the nucleus fastigii (outer group of cells) just before death.   (Methylene blue.)

c   Cavity of lesion.
n   Necrotic zone.
o   Œdema zone.
g   Granule layer of a pyramid folium.
nf Nucleus fastigii. (Note [with lens] that the nerve corpuscles near the lesion stain more deeply and appear somewhat smaller than the normal cells on the opposite side, and that the layers of necrosed tissue exhibit concentric distension.)
vIV   Fourth ventricle.   (Dog.)

It is obvious that since as it has been shown that the conductivity of serum hardly differs from a 0·7 per cent. solution of NaCl, and that the rapidity of ionization in a gelatinous solution varies with the concentration of the latter (Leduc [8]), so the dissociation of the

FIG. 16.

Anodal lesion, twenty-two days old, in the lateral region of the bulb. (Osmic acid.)

IV   Fourth ventricle.
VIII Descending vestibular tract.
l   Lesion cavity.
li   Lingula.
l.p.   Inferior peduncle.
plb   Posterior longitudinal bundle.
r   Raphe.
my   Columns of myelin. (Note their radial arrangement.)
n   Necrotic zone.
o   Œdema zone.

cerebrospinal fluid of the blood and serum and of the neuroglia and
nerve elements will proportionately differ and result in separation.

Our knowledge of this interesting phenomenon of convection, first
demonstrated by Hittorf in respect of the greater velocity of the anion
compared to that of the kathion, has been extended by Kohlrausch, who
showed that if the kathion of different molecules remained the same the
velocity would further vary according to the anion.

Finally, all investigators have shown that large complex molecules
are more retarded than smaller ones.

From all these considerations it followed that a definite, if coarse,
separation of the constituents of the nerve tissues might be looked for.
Such is the case, and the centre of the lesions (*see* figs. 15 and 16) shows
the complex fat-protein molecules as though left behind during the
extension of the electrolytic processes; intermediately are the collagenous
tissues, and furthest of all is a watery zone.

(*b*) *Distension.*—But in addition to this chemico-physical disarrange-
ment by convection there is another mechanical effect which in our
opinion is as powerful, and that is the distension or compressing effect
of the gases developed in the lesion. These are present both in the ·
anodal and kathodal lesions, but as for the same strength of current
there is a greater volume of gas at the kathode than the anode, the
mechanical destruction effected by the kathode is greater (in the propor-
tion of 4 or 5 to 3) than that produced by the anode.   In each case,
however, there is an obvious disruption by the current of the tissues
attacked and in each the pressure of the gas produces a condensation of
the tissues as they are necrosed, this condensation resulting in the tissues
being compressed concentrically with the axis of the lesion.   This is
exceedingly well shown in figs. 15 and 16, which represent respectively
the condition of a lesion made (*a*) just before the death, and (*b*) three
weeks before.   When we first observed this mechanical distension effect
of the gases and could not find that attention had been particularly
directed to the point, we thought it was worth while to investigate the
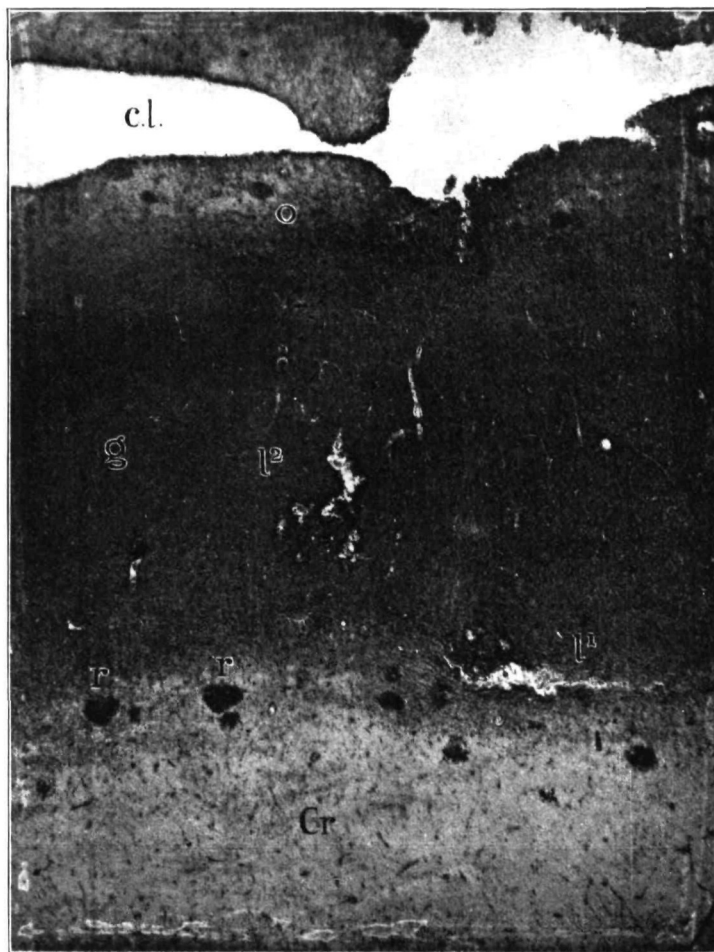question a little further and to see how far destructive effects could be

FIG. 17.

Experimental production of a lesion by injecting gas under pressure in water.

c.l. Central cavity of lesion.
o   Œdema zone.
l¹ l² Lesions at a short distance produced by the gas and water
following the perivascular lymphatics.
r r   Thrombosed blood-vessels.
Cr   Corona radiata.
g   Section of the bottom of a sulcus, *i.e.*, grey cortex.   (Dog.)

produced in living brain substance by gases under pressure and in solution.
We therefore made sundry injection experiments, using hydrogen or
carbonic acid gas and water under pressure.   The result is shown in the
accompanying photograph (fig. 17), from which it is evident that there

are considerable effects even at a distance from the source of pressure and further that the mischief spreads because the gas and water tend to force their way into and dilate destructively the perivascular lymphatics.
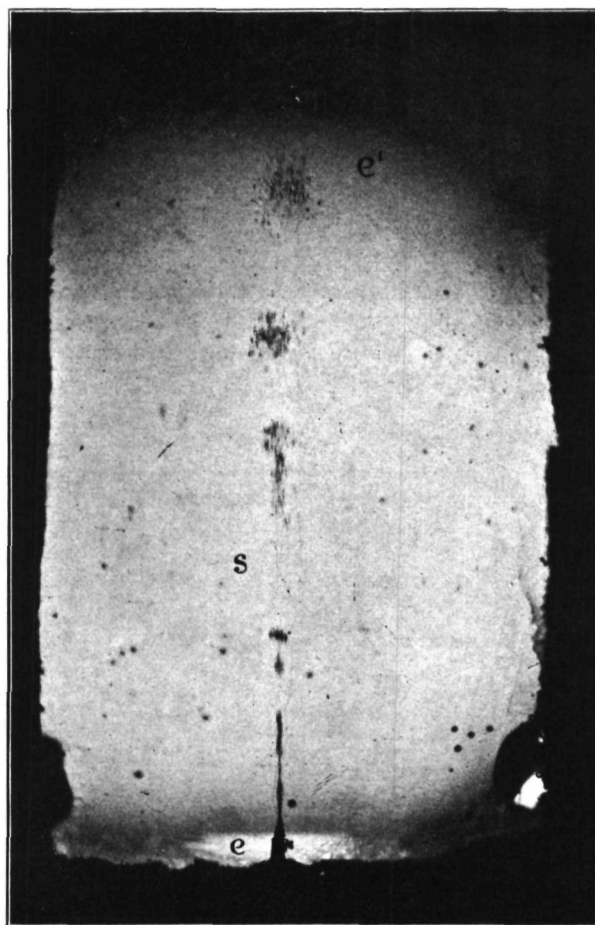

FIG. 18.

Instantaneous photograph of stream of gas, emanating from the point of the needle electrode, e, when it is a kathode. (The opposite electrode is just above, e'.) The solution, s, is transfusion saline fluid containing phenophthalmein. The colour developed by the reaction is shown as streaks left by the ascending bubbles

On this point, further, we have made comparative experiments with anode and kathode respectively to show, if possible, graphically a comparison between them when a moderate current (2 to 5 ma.)

is employed.   For this purpose we fixed in a water cell, as shown in figs. 18 and 19, the positive and negative needle electrodes, and obtained, as seen in the instantaneous photograph, the proportionate amount of bubbles of gas developed by each.   The character also of the evolution

FIG. 19.

Similar photograph, showing the much less quantity of gas developed and with less ebullition when the electrode, e, . is an anode.

of the gas is seen to differ in the two cases, being more explosive and ebullitional from the kathode.

(2) *Chemical effects.*—The first and most striking contrast between anodal and kathodal lesions is the reaction, the kathodal lesion

being strongly marked by deep blue, whereas the anodal lesion in the brain tissue simply bleaches litmus; but as Dr. Lane has shown with di-methylamido-azo-benzol there is outside the bleached point a ring of acid reaction.

The anodal lesion.—The histological changes in the anode are so characteristic and useful for our purpose that we endeavoured to ascertain what chemical effect was produced there. The anodal bleaching effect is due to the chlorine dissociated from the NaCl, and the particular form of anodal coagulation of proteins and tissues is attributed by Leduc and others to the combination of the chlorine with the water and formation of HCl. Dr. Gordon Lane, however, was unable to estimate in anodal lesions of the brain the exact quantity of the acid, though in a solution of saline electrolytes resembling the inorganic constituents of serum, he was able to make the estimation accurately.

The kathodal lesion.—The chemical condition of the kathodal lesion as estimated by Dr. Lane is that a definite amount of alkali is developed, but when we compared the degree of tissue destruction in the lesion with the trivial effect produced in a normal living brain by the injection at any given point of a similar amount of alkali it was obvious that the latter, whether nascent or not, could not be a practical factor in the production, of the destructive effects.

(3) *Quantitative relations.*—On the question of the quantity of electrolytic destruction varying directly with the quantity of electricity employed, Dr. Gordon Lane has kindly made for us a very large number of titration experiments with electrolytic solutions resembling serum, the details of which will be published in full by him in this Journal.

The solution in the first set of observations was of two different degrees of quantity of electrolytes. Nevertheless, the same current, namely, 1 ma. for ten minutes duration, with a 23 gauge electrode, gave 0·00248 increase of alkalinity in the one, and the same current, time and electrode gave from the other solution 0·0026642, practically identical figures.

The next set of observations had relation to the duration of the application of the electrical current. In these the solution was electrolyzed for five, ten and twenty minutes, and the gain of alkalinity was respectively 0·0136, 0·00264, 0·00588.

It is evident that the relationship of time and quantity cannot be closer.

In Dr. Lane's third series of observations he compared different sizes

and different lengths of the electrolytic needle ; it was found that results practically true to the fourth figure were obtained, and showed that for constant current strength and duration the resultant gain in alkalinity was the same whether the electrode needle was fine or coarse, short or long.

A fourth table of great quantitative interest was the proportionate gain in alkalinity evoked by different milliamperage. The average obtained was as follows : 1 ma. gave 0·0012, 2 ma. gave 0·00248, 4 ma. gave 0·00488.

The last point of more special interest is the relative action of the kathode and anode. We have repeatedly drawn attention to the ana-tomical changes produced by the gas pressures, but these do not fully indicate that the volume of the gas liberated at the kathode exceeds so largely that derived from the anode. Thus, in one of Dr. Lane's observations, a measured volume of gas was evolved by the kathode in twenty-four and a half minutes, but by the anode in only 108 ; hence in this experiment more than four times the volume of gas was liberated at the kathode.

To sum up, the determination of the electrolytic products in a simple solution of electrolytes is a certain and accurate process, because the relationship between quantity of current and effect produced is also very definite.

For full discussion, however, of the points involved reference must be made to Dr. Lane's full paper.

The Size and Nature of the Lesion.

(a) *Size and outline of the electrodes.*—The size and shape of the lesion depends in the first place upon the size, outline and position of the electrodes.

Unipolar needle.—The most restricted globular lesions we have obtained by employing a unipolar needle with but 0·5 to 1 mm. of platinum exposed, the other " indifferent " electrode being formed by all the points of contact of the instrument (*e.g.*, the frame fixing screws, aural pivots, &c.) with the head, or by insertion in the wound, or by a large indifferent plate electrode applied to the body.

With such an arrangement and an extremely fine wire as the unipolar needle it is easy to obtain destruction limited to very small groups of cells or bundles of nerve fibres. On this question of limiting the uni-polar lesion it is important to note that when the other electrode has

been formed by the " live stop " or other termination in the wound it
has appeared as though there was a certain extension of the electrolytic
change along the track of the needle, the path of least resistance for the
current, exactly as noticed in excitation experiments.

This also is demonstrated by the average shape of the lesion, espe-
cially when maximal currents are used and for a considerable time.
Under such conditions the proportionate diameter of the lesion in the
line of the axis of the needle to that at right angles is nearly as 2 to 1.

Bipolar needles.—Of the two forms of bipolar needles shown in
fig. 12 that which we have called the concentric pattern produces a lesion
the outline of which is a repetition of the form of the whole of the end
of the electrode even when only the collar portion is employed, *e.g.*, as a
unipolar anode.   Similarly the other form of bipolar needle produces a
lanceolate or flame-shaped lesion. It is thus quite clear that, as might be
supposed, the area of nerve tissue which is damaged by the pressure of
the point of the needle yields first to the necrosing effect of the current,
and thus the shape of the electrode is of considerable importance for
precise topographical limitation of the lesion.

(*b*) *Quantitative production of the lesion.*—In the second place the
size of the lesion depends on the amount of the current employed.
We originally hoped that we should be able to regulate the degree of
destruction entirely in accordance with Faraday's law, and that the
quantity of decomposition of the tissue would be directly proportional to
the quantity of electricity employed (Arrhenius).   In this we have only
been partly successful, the reason being that the factor of time carrying
with it also the alteration of resistance deprives the method of mathe-
matical accuracy.   We have, however, by accumulating a large number
of experiments, been able to arrive at a clear understanding as to what
is necessary to produce a given effect.   On this point the diminution of
resistance to which allusion has just been made must first be referred to.
The readiness of living tissues to polarize has long been recognized, and
the fall of resistance, which has been a striking and constant phenomenon
in our experiments, is proportional to the ionization and coagulation
obtained.   It can be readily compensated, and by a sliding resistance we
have thus kept the experimental condition constant as far as possible
during the process of making the lesion.   The quantity of electricity we
have used (*i.e.*, milliamperage and duration of application), and especially
in its first factor, which has varied during the last two years only between
1 and 5 ma., is much smaller than that employed by our predecessors,
hence we cannot enjoy the advantage of comparison with their results.

Moreover the wide difference of effect according to the contrast in polar action such as we are about to describe has not been employed by other experimenters; this has influenced us so much in favour of the anode that any comparison between the size of the lesion and the quantity of electricity required to produce it ought in future to be considered as referring to an electrode used as an anode.

High milliamperage is wholly unnecessary; thus 1 ma. produces an adequate effect in a few seconds (fifteen) on a single group of cells, but 2 ma. give a more constant result, and a hyper-maximal effect is reached with 5 ma.
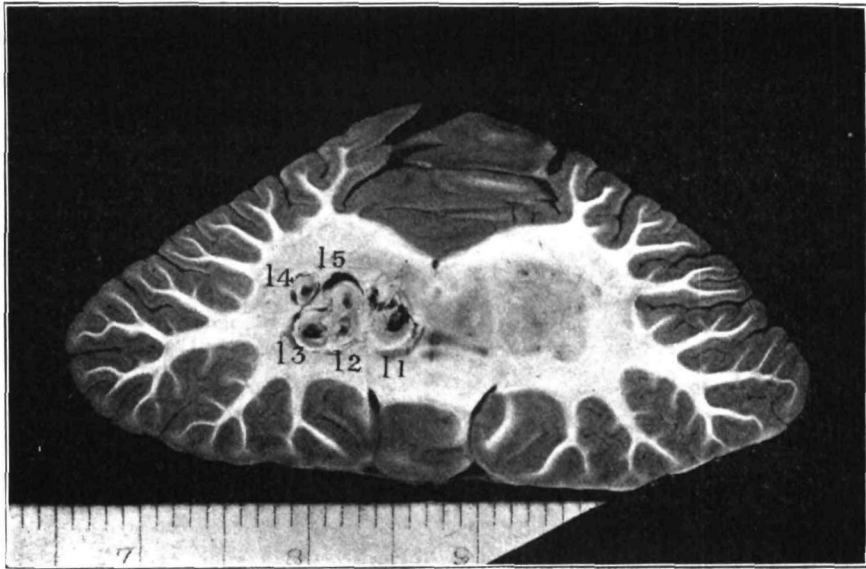
FIG. 20A.

Five anodal lesions, 11—15, made three weeks before death to destroy the nucleus dentatus, embolus, globosus and outer part of nucleus fastigii. (Note that the lesions have been made by successive insertions of the needle, and that the object of the procedure is attained with minimal injury to surrounding parts. The smaller scale divisions are millimetres.) (Macacus rhesus.)

Next, as regards the influence of time, which must be considered directly with that of milliamperage, our experience has been that although a notable effect is produced within a few seconds, the amount of further destruction proportionately diminishes as the time is prolonged. We have not, however, worked out any definite curve of this diminution, but in a number of preliminary observations we found

FIG. 20.

Margin of a large kathodal lesion made just before death.

ca Central cavity of lesion. Below the letters is a large mass of necrosed tissue and clot. To the left is the advancing necrotic border, n, showing numerous gas bubbles, bu, and largely consisting of altered, *i.e.*, electrolyzed, blood-corpuscles.

o Œdema zone.

g Normal gyrus.

s Normal sulcus.

that it was so marked[1] as to render any increase of the time above five minutes purposeless. For practical purposes a rough average of quantities and proportional effects may be drawn up as follows :—

Kind of lesion.	Size of lesion.	Quantity of current.	Duration of electrolysis.
Simple anodal lesion ...	2·7 mm. ...	3 ma. ...	1·8 min.

Combining many observations together it is evident that for a unit of time, e.g., one minute, there will result about 1 mm. breadth of destruction for each 1 ma. of current employed. This, of course, is only approximate, and only true within about 5 ma.

We will next describe the structural changes wrought in the cerebral and cerebellar tissues by the electrolytic processes.

Macroscopical Anatomy of the Lesion.

From what has been already stated it will be realized that, whether anodal or kathodal, the lesion presents three zones on naked-eye examination, i.e., a central cavity (containing gas, watery fluid, myelin, &c.), a zone more or less broad of necrosis, and outside that a narrow zone of œdema. All these three zones are extremely obvious within a month after the lesion is made, but we have not yet examined the ultimate fate of the lesion after longer survival periods. To the naked eye the differences between the polar effects are very obvious and coincide with the descriptions given of and results obtained by electrolysis of the blood. Thus the anode produces a small central cavity surrounded by a compact, greyish pink coagulation or necrotic area; the kathode causes, on the contrary, the production of a larger cavity filled with a rosy pink fluid, often almost gelatinous in its viscosity, the walls of the cavity showing the presence of bubbles of gas and consisting of necrosed tissue, which is whitish yellow, soft and diffuse. These differences are shown in the accompanying photographs, figs. 20, &c.

Similarly the œdema border around the kathodal lesion is proportionately wider than that bordering the anodal injury.

Microscopical Anatomy of the Lesion.

The microscopical details of the changes produced are of the highest importance, and especially because they show at once the great

[1] As an example we may quote the figures obtained from an experiment on this point, as follows : Needle, 22 gauge; amount exposed from glass sheath, 2·5 mm. ; place, dentate nucleus ; pole, kathode ; amount of current, 5 ma. ; duration, thirty minutes; result, lesion 8 mm. in line of needle ; 6 mm. at right angles to same.

advantage of this method of making experimental lesions, namely, that the injury produced is sharply delimited from the surrounding tissues, and consequently the loss of physiological function is strictly confined to the seat of electrolysis.   As a side fact, a physiological proof of this may conveniently here be stated.   It is that when, during an excitation
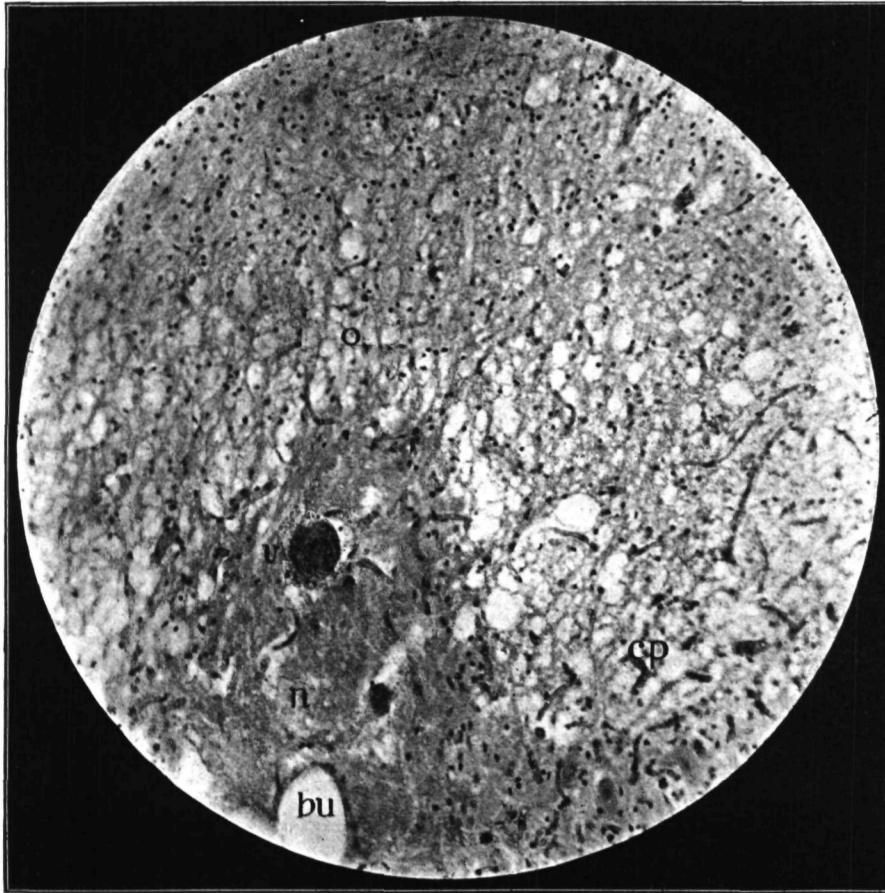
FIG. 21.

Section of margin of kathodal lesion made just before death, showing the dissociation of the neuroglia by the gas and fluid forming the œdema zone, o; the edge of the necrosed tissue, n; a gas bubble, bu; congested capillaries within which thrombosis has occurred in some, cp.

experiment, a restricted electrolytic lesion has been made to mark some spot from which a definite response has been obtained, we have found, on advancing the needle another millimetre, that the uninjured tissue immediately adjoining is normally excitable.
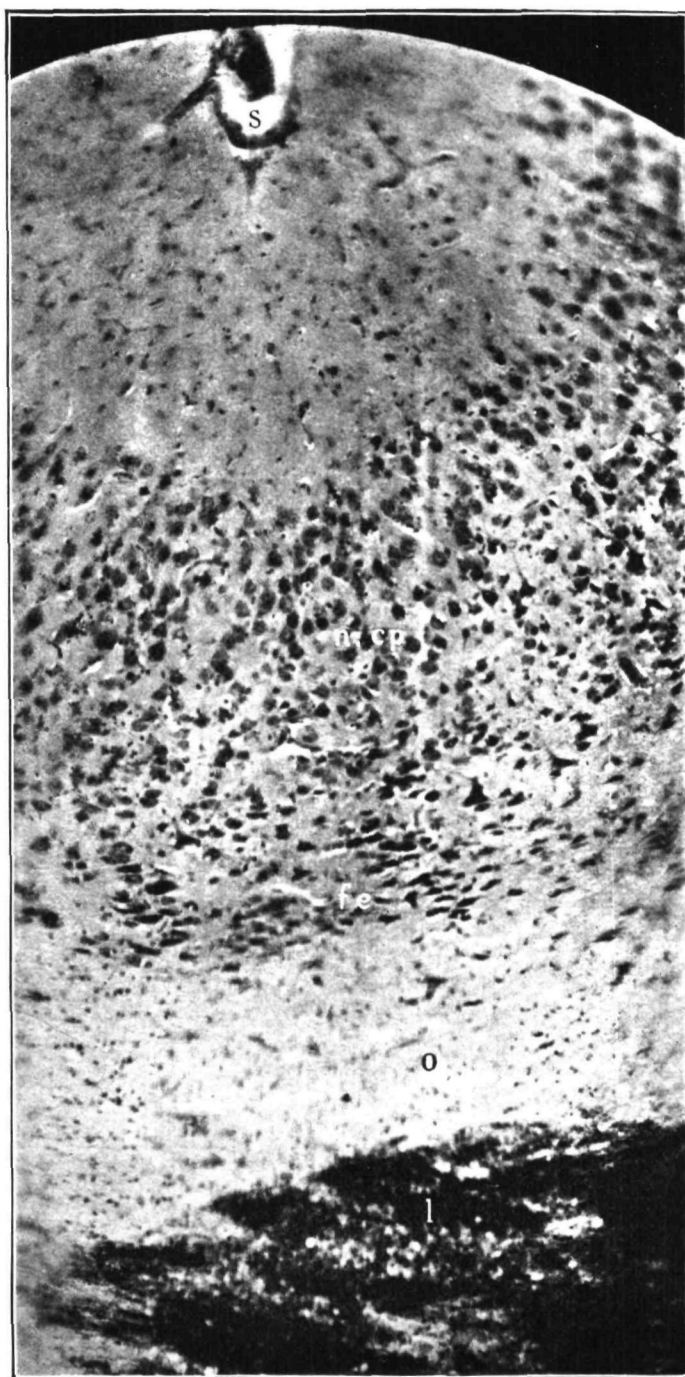
FIG. 22.

Vertical section of gyrus and kathodal lesion just below it, l, made just before death. The lesion shows laked blood and numerous very small gas bubbles. The œdema border, o, extends to the cortical layers of cells, of which the lower layers, fc, are flattened by the gas pressure, whereas the upper layers, n. cp, are normal; s = bottom of a sulcus. (Cat.)
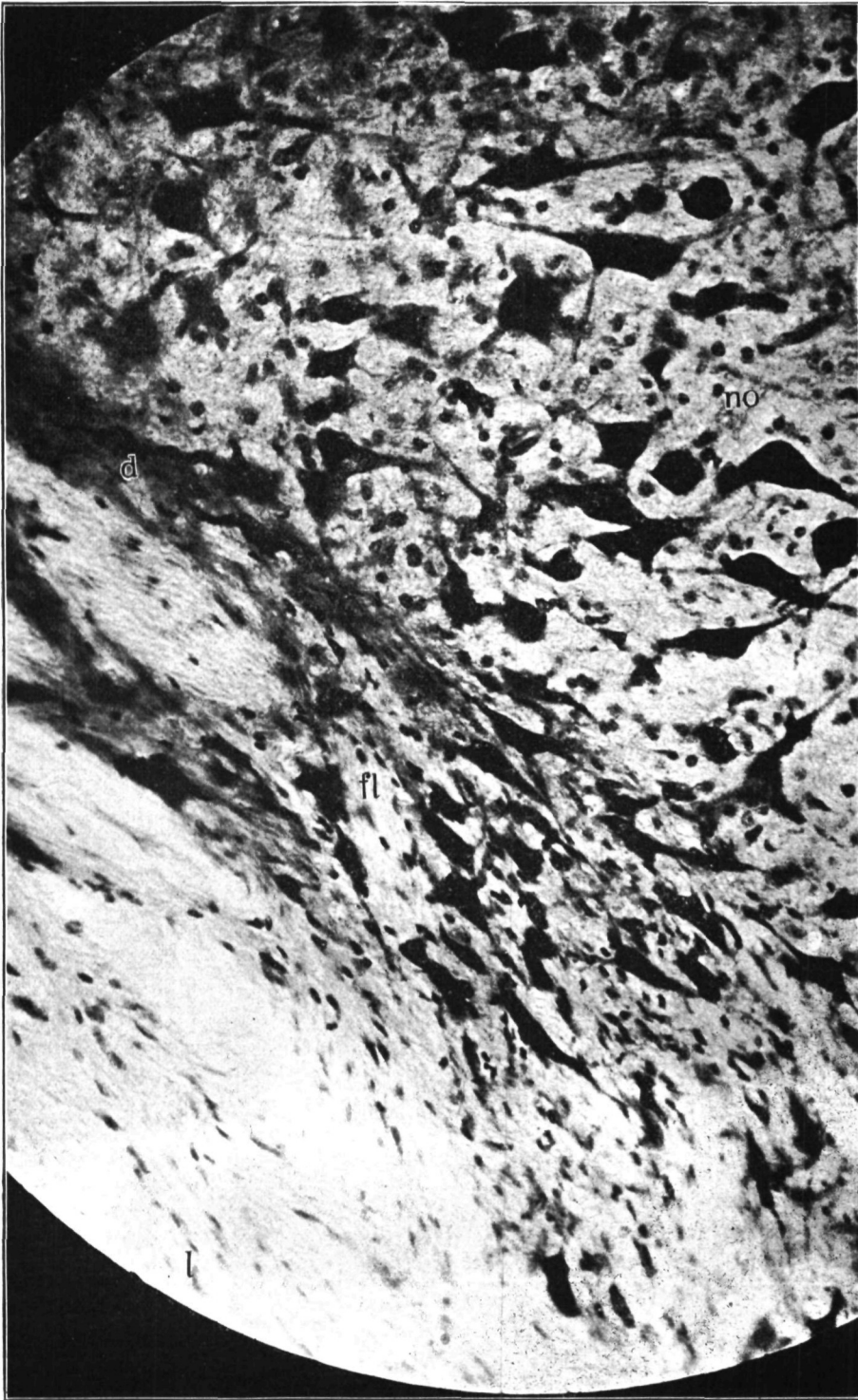
Fig. 23.

Margin of an anodal lesion made just before death in the bulb close to the motor nucleus of the fifth cranial nerve, no, showing the compression and destruction effects of the electrolytic lesion on a portion of a nucleus. The neuroglia, partly in solution, is shown at the bottom left hand corner at l. The nerve cells involved are seen flattened and distorted at fl, whereas the cells in the rest of the nucleus, n o, are still functionally active.

To proceed now to the details of the microscopical changes observed, we can most conveniently condense the large amount of material we have collected by grouping the facts under two heads : (1) lesions created just before systemic death; (2) lesions created three weeks before death.

The second class naturally only presents as additional features the phagocytic processes of removal of the necrotic tissues and products, as well as certain stages of commencing repair.

(1) *The Histology of the Electrolytic Lesion when Made just before Death.*

Although the first and principal change in the entire living brain is the electrolysis of the blood and lymph, the nerve tissues begin to break down very soon, and the fate of the different components may be taken separately.

(a) *Changes in the neuroglia.*—The changes in the neuroglia must be considered according to the degree of destruction.

(1) *Zone of necrosis.*—The nuclei of the neuroglial cells rapidly lose their capacity for staining with basic dyes, though the nuclei of leucocytes still stain readily.

Similarly the neuroglia fibrils refuse to stain, and in differentiating polychrome methylene blue stained sections the compressed nerve tissue (which subsequently necroses) decolorizes before the normal from which it is sharply marked off.

Before disappearing the nuclei become distorted and shrunken, though for a long time their outlines or nucleolar contents can be recognized in the necrotic coagulum. The fibrils and " punkt-substanz " of Retzius become fused into an amorphous mass, which under a high power looks like a coagulated precipitate, but is notably denser than the precipitate in the cavity of the lesion, which is certainly altered blood-plasma and has a loose floccular and granular appearance.

(2) *Zone of œdema.*—In the zone of œdema which immediately surrounds the necrotic core and separates it from the normal surrounding tissue the meshes of the neuroglia are simply torn open, thus forming spaces. The stages by which this is produced are seen in the photograph, fig. 21, where the small holes showing themselves in the section bear a relation to the cell spaces of the tissue generally, and, moreover, are exactly similar to the small cavities produced by the injection of hydrogen into the cerebral tissue.

The nuclei of cells of the all connective tissue type become granular,

the protoplasm of the body of the cell ceases to stain, the nuclei begin to shrink, and as they shrink often take the dye excessively and appear almost as black points.

A coagulation precipitate (exceedingly fine) can be seen between the fibres forming the œdematous border òf the tissue which is necrosing and which will form the zone of necrotic tissue.

(b) *Changes in nerve cells.*—The earliest change is a general fusion tigrolysis. The cell bodies stain darkly, ultimately intensely darkly, and then proceed to shrink, the contraction naturally being most marked at first between the dendrites.

This general change applies to all nerve cells.

The details of the change merit further investigation. As far as we have seen the tigroid bodies first contract and the intervening cell substance tends to stain diffusely.

With the shrinking of the tigroid body (which renders it very narrow in longitudinal section of the cell and point-like in transverse section) there is also intenser coloration of it.

While this alteration is proceeding in the body of the cell the axone and dendrites are undergoing a disappearance of fibrillar structure followed by swelling and paling, and this again by shrinkage and deformation.

The cells thus degenerating in the zone of necrotic compression also show very interesting mechanical defects by torsion, especially in the large dendrites and axone (*see* fig. 23).

Further, by reason of the contraction of the tigroid bodies, spaces like vacuoles appear in the protoplasm of the cell, and often are strictly circular in outline as though holding fluid. In many instances the remaining chromophile substance is aggregated at the border of the cells, in others more rarely round the nucleus.

The nucleus does not move towards the side of the cell, but as it shrinks it becomes more deeply stained and shrivelled on the nucleolus until it stands out in sections as an intensely dark point.

(c) *Changes in nerve fibres.*—Nerve fibres attacked by the electro- lytic process are apparently simply dissolved. In accordance with the like changes in the connective tissue protoplasm the axis cylinders within the neurotic zone refuse to stain with polychrome methylene blue, but they can readily be distinguished and particularly as they do not swell before disintegration.

The myelin of their sheaths flows in the liquid in the lesion cavity as the fibres undergo dissolution. Indeed, in some preparations (*see*

fig. 16, 25) it appears as though the compression of the necrotic zone by the gases in the cavity caused the myelin to ooze out and be left in trails radiating from the centre of the lesion, *i.e.*, arranged in columnar fashion as though along lines of electrolytic convection.

The fate of the myelin will be discussed later, but attention should here be drawn to the fact that as it escaped from the fibre sheaths it is but little altered and consequently it gives to osmic acid practically the same reaction stain as a normal fibre.
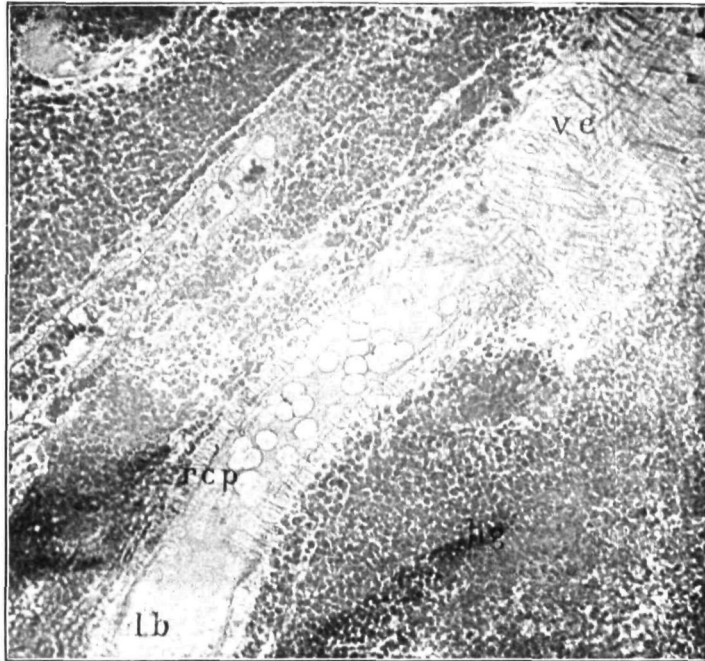

FIG. 24.

Electrolytic changes in a vein and blood.   Kathodal lesion.

v e   Vein wall undergoing dissolution.
r c p   Stromata of red corpuscles swollen and lying in blood, which is completely laked at l b.   Surrounding the vessel are shrunken blood-corpuscles, h g, lying in the cavity of the lesion.

In summary it may be said that the alteration of the nerve fibres indicates the destruction to consist of a progressive solution, so that there is practically little interval between the disappearance of the structure and the complete fibre.

(*d*) *Changes in the blood-vessels.*—The altered condition of the blood-vessels first evinces itself in the immediate neighbourhood of the lesion

by thrombosis of the smallest vessels. The blood slightly coagulated shows no change in the corpuscles.

Later, the muscle fibres in the wall of the vessel undergo a cloudy swelling metamorphosis and then show considerable hyaline changes. A vessel in this condition is often seen hanging in the lesion cavity and undergoing at its free end a solution of its elements. Such a vessel while intact contains a thrombus consisting of altered corpuscles, but as the next result of the electrolytic process is a liquefaction, such thrombi are very fragile and partial.

The dissolution of the elements of the vessel wall is not without interest, as the most resistant are the endothelial layer and elastic lamina, and further because there is a very short stretch between the point of complete destruction and that of a fairly complete vessel.

(e) *Changes in the blood.*—The changes in the blood commence with the dissociation of the red corpuscle in the manner indicated by Brücke forty years ago. The pigment holding protein compound (Brücke's zooid) escapes from the stroma and consequently aggregations in the neighbourhood of the lesion of partly decolorized stromata within the vessels are a characteristic feature of the electrolytic process. Such stromata stain a greenish purple with polychrome methylene blue.

This results in an early laking of the blood, and the decolorized stromata soon become invisible in the highly tinted plasma. Nuclear stained sections often show the vessels containing thoroughly laked blood in which are floating practically unaltered leucocytes (*see* fig. 24).

The next stage affords a highly interesting instance of convection, for the colouring matter (protein compound) is carried through the wall of the vessel and collects in nodular masses, leaving the contents of the blood-vessel evidently little more than water, as there is frequently no protein precipitate in it.

The blood in large vessels passing through the lesion affords interesting points for study of the corpuscles apart from the convection phenomenon above mentioned. The red corpuscles become crenate and irregularly shrunken, showing bright particles of hæmoglobin without arriving at the later stage of hæmosiderin, but granules of the last-named substance are seen in quantity in the *débris* in the lesion.

(2) *The Histology of the Electrolytic Lesion Three Weeks After.*

The chief differences between the lesion immediately examined and that in which the animal has been kept alive three weeks before death are essentially summed up in the word phagocytosis, for all the conditions

as just described are present, namely, the necrotic zone, its central cavity and the zone of œdema. We will therefore begin with the phagocytic cells (*see* fig. 25).
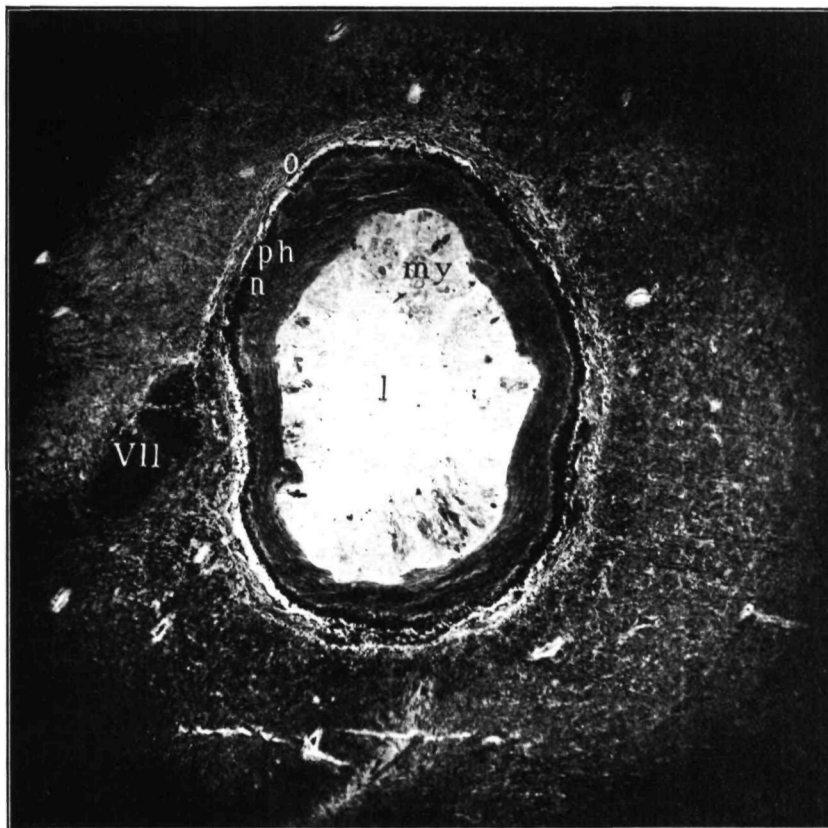
FIG. 25.

The lesion, made three weeks before death, in fig. 16, more highly magnified.

l Cavity of lesion, containing a few leucocytes and much myelin in radiating columns, my. The necrosed tissue, examined with a lens, shows well the distension effect of the gas content of the lesion. The dense black ring of phagocytes, ph, closely surrounds the necrosed tissue and the two other subzones of the œdema zone, o, are well marked.

VII The seventh cranial nerve totally degenerated, being divided by the lesion.

(1) *Distribution of phagocytes.*—A very interesting characteristic is noticed where a restricted globular lesion has been made deep in the substance of the organ and where consequently the wall of necrosis is unbroken. It is then seen that though the phagocytes are thickly aggregated in the œdema zone they nowhere succeed (within twenty-five days) in
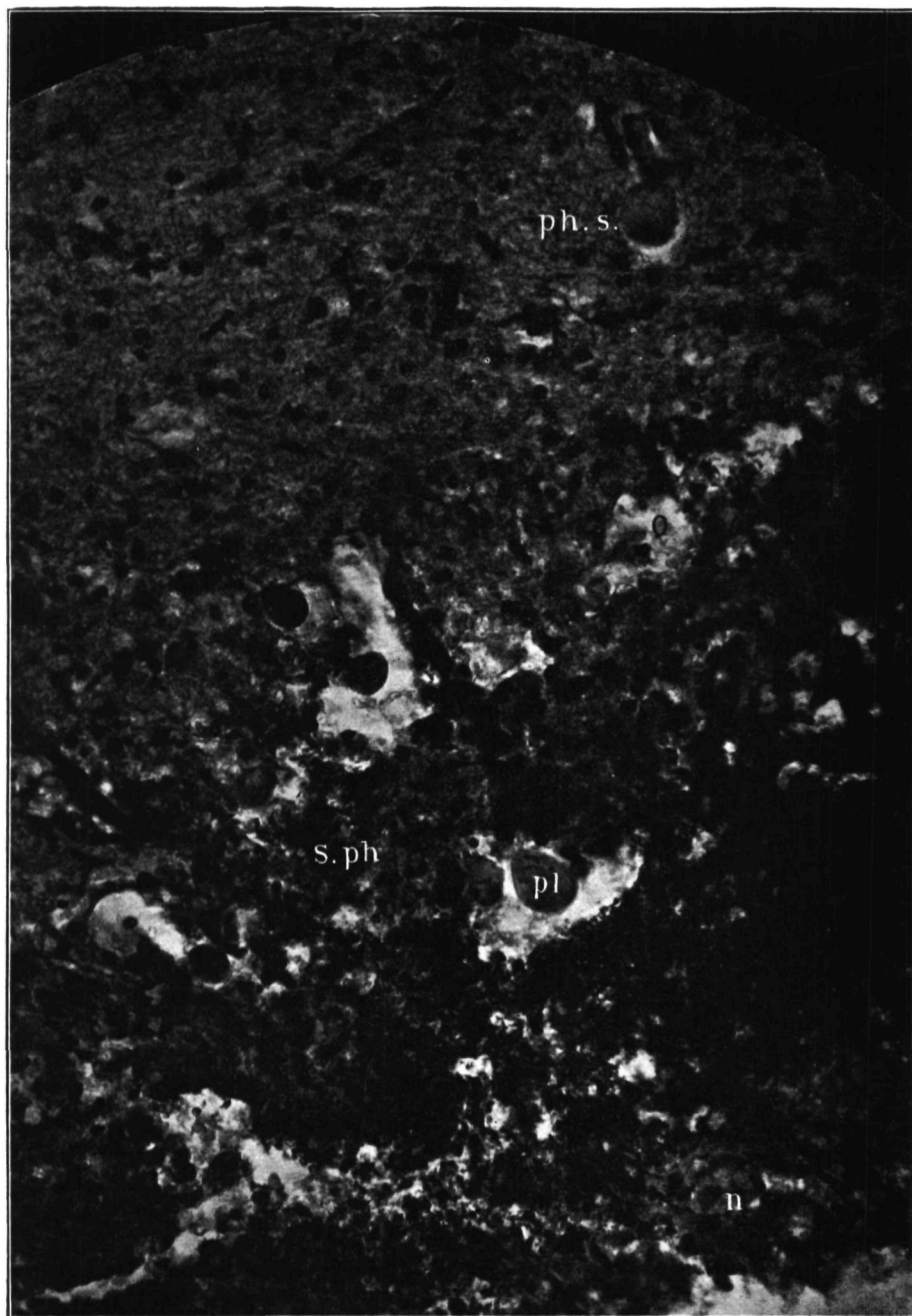
FIG. 26.

Section (methylene blue) showing the margin of a kathodal lesion made four days before death.

ph.s, indicating the genesis of a large phagocyte, is placed on the normal neuroglia at the extreme border of the œdema zone.

O is placed in the middle subzone in a (watery) space.

S.ph marks the line of phagocytes, the innermost subzone.

pl is a large phagocyte abutting on the necrotic tissue which lower down is marked n. (Dog.)

penetrating the necrosed tissue or coagulum or gaining the cavity of the lesion. The few stray cells occasionally met with on the inner side of the wall are obviously surviving leucocytes. On the disputed question of the genesis of Gluge's corpuscles it is interesting to note that these scattered
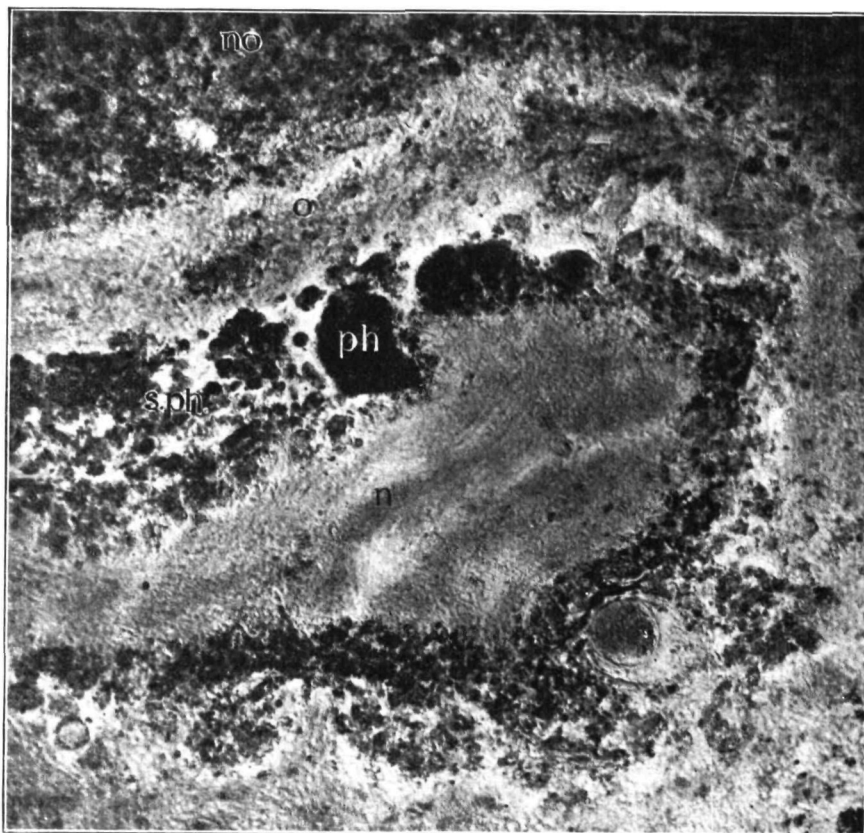

Fig. 27.

Margin of an anodal lesion twenty-two days old, showing the subzones of the œdema zone and the two classes of phagocytes.

    n   Necrotic tissue.
    S.ph   Innermost subzone, containing many small phagocytes.
    o   Middle œdema subzone.
    ph   Giant phagocytes
    n o   Outermost œdema subzone, showing now only infiltration, with small granules stained black by osmic acid. All the phagocytes are full of such granules. (Macacus rhesus.)

cells only take up a few particles of blood-pigment or very little myelin. They are not comparable, therefore, with the ordinary phagocyte or Gluge's corpuscle. Consequently the distribution of the phagocytic cells

(the true Gluge's corpuscles) in the œdema zone is extremely easy to map out.

For this purpose the œdema zone may be divided into three concentric zones: an innermost, a middle and an outer subzone (*see* figs. 25 and 26).

(*a*) The innermost subzone consists of a layer of phagocytes arranged column-wise in three or four concentric rows, but closely packed together and full of fine granules staining intensely black with osmic acid.

(*b*) The middle subzone is a watery layer in which float phagocytes and neuroglial *débris*, half destroyed vessels, blood partly clotted in various stages of absorption, myelin droplets, &c.

(*c*) The outer subzone contains very few phagocytes, but consists of the slightly affected edge of the normal tissue, that part of the œdema zone in which from the first a fine precipitate can be seen in the meshes of the neuroglia.

(2) *The character of the phagocytes.*—The shape, arrangement and contents of the cells differ in the three subzones, and may best be described *seriatim*.

(*a*) *Innermost subzone.*—The phagocytes which attack the outer surface of the necrotic coagulum resemble plasma cells in every particular. As a rule they are small, narrow and club-shaped, owing to their radial and packed arrangement in the œdema zone. At points in this ring of phagocytes giant-cells appear and many intermediate shapes, but the large protoplasmic masses, though staining a very dark brown, rarely contain more than a few granules (*see* fig. 27). The smaller the cell as a rule the more completely is it filled with myelin granules, obscuring the nucleus. In some the granules fuse into two or three large vacuoles filled with feebly staining myelin.

(*b*) *The middle subzone.*—In this layer, which is the true (separation) line of the necrosed tissue, we find large spaces filled with clear fluid or altered blood; the phagocytes floating freely are, as a rule, spherical in outline (*see* fig. 28). These are comparable to those found in extensive ischæmic softenings in man (*see* fig. 29).

(*c*) *The outer subzone.*—Running outwards from the edge of the œdema cavity are degenerated fibres which arose from the nerve cells destroyed by the lesion or are the peripheral portions of those which have been severed. The neuroglia between them is no longer water infiltrated, but there is a fine granular precipitate, which stains brown with bichromate of potash and osmic acid, as well as numerous fine black granules.
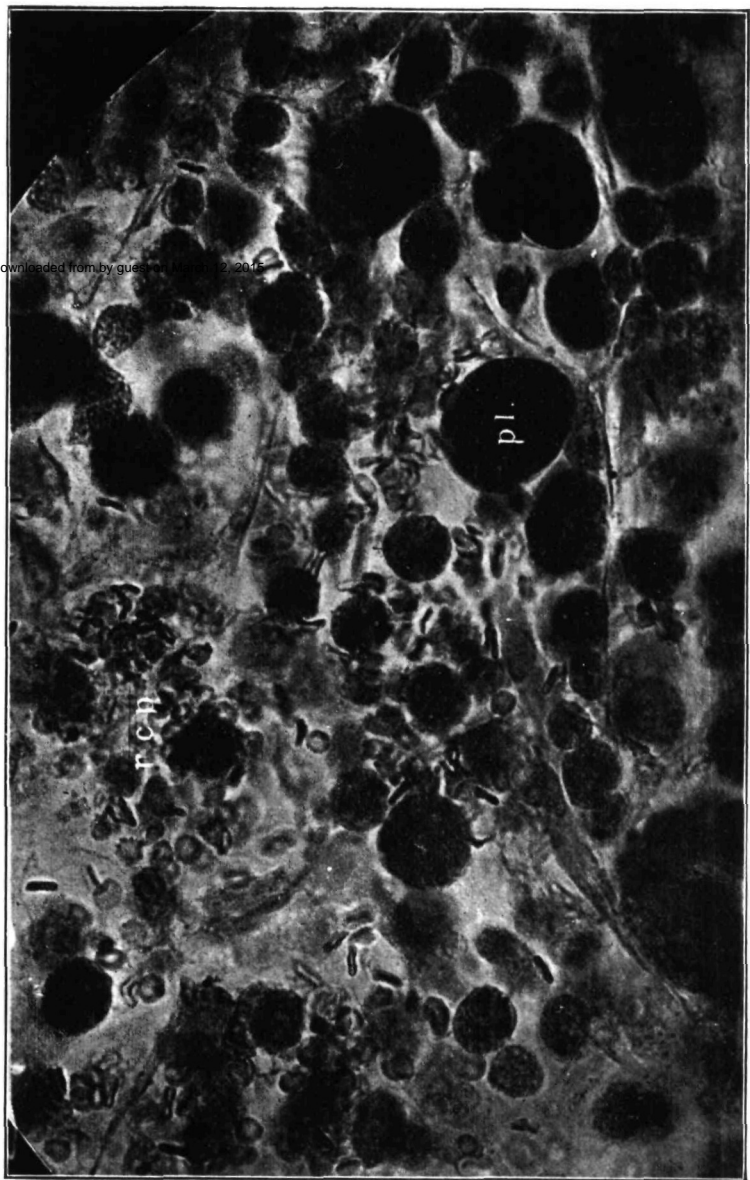
FIG. 28.

Phagocytes in an anodal lesion on the border of the fourth ventricle.

All the phagocytes contain many granules, which stain deeply with osmic acid. The large cells, p l, do not take up the red blood-discs, however altered. Of the red corpuscles, r c p, many still preserve a normal outline. (Macacus rhesus.)

V.—THE METHOD OF EXCITATION.

The systematic investigation of the functions of the cerebellum by the excitation method has been attempted by relatively few observers and only of the cortex cerebelli. The first was Ferrier [1], who employed the faradic current, and explored the cerebellum in different

FIG. 29.

Phagocytes (Gluge's corpuscles) large and medium size, from a cerebral ischæmic lesion, to compare with fig. 26.   (Man.)

classes of animals. He was followed by Hitzig, Nothnagel and Dupuy, the first of these using the constant current, the latter mechanical irritation, which had already been attempted by Leven and Olivier and Weir-Mitchell. In later years, Sherrington, Löwenthal and Horsley, and

Rijnberk, Lewandowsky, Pruss and Lourié have contributed short communications on the subject.

We will refer to the results obtained by those observers later in our second paper and here only discuss the following points of practical interest, which appear to us to govern the whole subject, and which certainly afford a test of the value of any particular method of investigation. These are :—

(1) Excitability of the cortex cerebelli.

(2) Relative excitability of the cortex cerebelli compared to that of the cortex cerebri.

(3) Relative excitability of the cortex cerebelli compared to that of the nuclei cerebelli and efferent tracts therefrom.

With the means described in this paper the functions of all these parts can now be adequately examined and differentiated, provided that some general principles are fulfilled.

(1) *Excitability of the Cortex Cerebelli.*

We begin by raising a fundamental question, viz., whether the cortex cerebelli is strictly speaking excitable to electrical stimuli. Ferrier records that in his experiments, using the interrupted current as stimulus, he obtained positive results in but a relatively small proportion of experiments, and to those who, like Nothnagel (*cf.* Pagano), employed a mechanical stimulus, viz., a needle point (sometimes heated), negative results were extremely common.

The explanation commonly given of these facts is that the difficulty of the operative procedure for exposing the cerebellum causes shock effects to the delicate cortex from loss of blood, &c., and so lowers its excitability.

We may most conveniently dismiss now this question of hæmorrhage and what is, in our opinion, the equally important matter of cooling. Though these adverse conditions have evidently occurred very frequently in previous researches on the cerebellum, they can be completely avoided by suitable care in operation, *e.g.*, by careful study of the situation and grouping of the blood-vessels, the use of lenses,[1] reflected illumination, constant irrigation with warm saline solution, large hot water trough support, &c., and finally by the instruments and topographical methods already described.

---

[1] For exact adjustment of the apparatus used we have found magnifiers, as very kindly arranged for us by Mr. Henderson (viz., Sp. +7 combined with prisms +6 and fixed in a strong spectacle frame carrying mesially a concave mirror), quite essential. All the blood-vessels are strikingly revealed by such glasses and the topographical identification of any spot which has been determined by measurement is rendered easy.

Given all the operative conditions just stated, the negative results obtained by previous observers are, in our opinion, the genuine expression of what we have found to be characteristic, namely, that the cortex cerebelli is relatively inexcitable. This, of course, raises a new issue regarding the cerebellum, and we will now proceed to discuss the evidence in our possession. The first factor to be considered is the kind of stimulus employed. We will take the various methods and procedures which have been tried and begin with the less exact.

(a) *Mechanical stimulus.*—The cortex cerebelli itself has not been carefully examined with mechanical excitation, but Leven and Olivier, Weir-Mitchell, Hitzig, Nothnagel, and Dupuy have stated that mechanical puncture of the cerebellum sometimes causes movements which other methods suggest may be represented in the organ, but whether in the cortex or nuclei was not in the minds of these authors. Dupuy observed in addition to movements definite indications of algesia.

On this last point our observations are not strictly parallel, as they have all been made on anæsthetized animals, but as regards the question of mechanical excitation during the insertion of the insulated needle we have noted very exceptionally distinct motor effects which we believe are due to excitation of the subjacent nuclei or efferent paths from them. But though an effect may be observed to follow a puncture or slight stab of the cerebellum, that does not afford any proof that the cortex cerebelli as such has been excited, since every puncture of necessity involves the subjacent fibres, and in many cases the nuclei also.

The immediate effects observed by Pagano with injections of curare are similarly explicable and do not, we think, admit of interpretation as restricted and localized stimuli. Indeed, Pagano recognizes that the cortex cerebelli is very resistant to excitation, and that the general effects produced by his method are of diffuse origin is proved in his demonstration that excision of the opposite excito-motor cerebral cortex abolished the results.

(b) *Constant current stimulus.*—Hitzig found that the cerebellum (*i.e.*, as a whole) was definitely excitable to the constant current, but he naturally at that period did not discuss the present question of how far the motor response is ascribable to the cortex. In accepting his facts we cannot but deduce from our own experiments that there is a very sharp contrast between the reactions of the cerebrum and cerebellum to a galvanic and faradic stimulus respectively. The "shock" character of the galvanic excitation ("make" and "break") renders this mode of stimulation applied to the central nervous system much less precise than the faradic current in differentiation of reaction.

In fact, Hitzig's interesting observation that when by stimulating the "upper lobes" skew deviation of the eyes resulted, the direction of such deviation was reversed with the reversal of the current, seems to us to show that the excitation effect was not limited to the spot of application of the cortical electrode. Our own observations lead us to believe that as a stimulus the constant current cannot be ranked for accuracy and limited localization with the induced current, and further, that no proof is yet to hand that the cortex cerebelli has been excited alone in any experiments so far published.

We have during the past three years accumulated a large number of facts on excitation with the constant current in comparison with the interrupted current, since by our method when we proceed to mark by electrolysis a spot which has just given a certain response to faradic stimulation we cause both an opening and closing effect on the same tract or nerve centre as the case may be.

The results have fully borne out the foregoing statement as to the disadvantages of the constant current excitation, and especially its diffuse and shock-like effect. We need not, therefore, dwell further on this point, but turn to another interesting phenomenon which we have also observed and which appears to us to be explained simply as another form or demonstration of the principles of complex representation of Hughlings Jackson and of reciprocal innervation of Sherrington.

It is that if a definite motor response, e.g., flexion of the elbow of the same side, is evoked by faradic stimulation of the dentate nucleus the antithetical or reciprocal movement, e.g., extension, will be the response to galvanic excitation.

An indication of the same phenomenon we have also occasionally seen while employing the same (e.g., faradic) stimulus if the nuclei are fatigued, and when contractures have already set in.

This is a further instance of the special modification of a motor response, as one of us (V. H.) showed ten years ago, for spinal centres [5].

(c) *Interrupted current stimulus.*—We have followed Ferrier in employing the faradic current as the most reliable stimulus (furnished by a Kronecker coil with one or two Obach dry cells in the primary circuit), and we have used it both by bipolar and unipolar application.

Our final conclusion is that though the cerebellum, *i.e.*, cortex and nuclei, *as a whole* responds to the faradic stimulus the presumed excitability of the cortex cerebelli is extraordinarily low compared with that of the cortex cerebri and that, comparatively speaking, the former is

inexcitable. Further, that, as will be seen presently, the values obtained for different depths of insertion of the electrodes show not only that the cerebellar cortex is not directly excitable, but the cerebellar nuclei are, and to a high degree. The preliminary point of difference in the character of the effect according to the method of stimulus, *i.e.*, whether " unipolar "[1] or " bipolar," also requires very careful consideration. This is especially necessary since, although the unipolar[2] method offers at first sight special advantages in the exploration of deeply situated central mechanisms, it theoretically and actually conduces to errors of observation.

(*d*) *Bipolar excitation.*—When the bipolar method is employed with the electrodes 1 to 2 mm. apart the cortex cerebelli gives no response on the average until the 4,000 or even the 8,000 point on the Kronecker scale is reached. It was soon obvious to us in exploring by means of the unipolar method the posterior surface of the cerebellum, covered as it is by the strong arachnoid membrane forming the posterior and lower limit of the large cerebrospinal fluid *cisterna* opposite the lower third of the cerebellum and obex, that lateral escape of the stimulus to the margin of the fourth ventricle[3] and to the trunk of the spinal accessory nerve frequently occurs. Probably most previous descriptions of representation of trunk muscle movements in the cerebellar cortex based upon excitation experiments are to be accounted for by this accidental error.

This erroneous effect is composed primarily of movements of the upper shoulder group of muscles, so that its topography is obvious, while the character of the response is so sharp that it definitely displays itself as the effect of a peripheral nerve excitation rather than that of nerve centres such as in the cortex cerebelli.

We have made a series of experiments to compare in this respect of causing local error the unipolar and bipolar methods of excitation respectively. The results are not only striking as showing what very special care must be used in employing the " unipolar " method for localization experiments, but the subject is also of such vital importance to the present investigation that we devoted much time to investigating with the faradic current the whole question of the absolute and relative excitability of the cerebellar cortex.

---

[1] *Cf.* Sherrington [22].

[2] The expression unipolar frequently applied to faradic current is really scarcely accurate although perhaps convenient. We have therefore made special investigation of the use of one electrode, and the full discussion of the question is given subsequently. (*See* pp. 119-121.)

[3] *I.e.*, region of nucleus gracilis, nucleus cuneatus, the tubercle of Rolando, &c.

In the first place we established as standards the excitability of the frontal and occipital cortico-cerebral areas for the movement of conjugate deviation of the eyes, and as an example of the comparisons obtained here subjoin the results of a typical experiment, which shows the minimal stimulus required to evoke the movement of *conjugate deviation of the eyes*, from the different chief points in the encephalon in which that movement is represented.

	CEREBRUM.				CEREBELLUM.	
	1	2	3	4	5	6
	Inferior frontal gyrus (Conjugate deviation of eyes centre.)	*Corona radiata cerebri beneath No. 1.*	*Occipital lobe, upper and outer surface.*	*Corona radiata cerebri beneath No. 3.*	*Left half of vermis pyramid.*	*Left nucleus fastigii region.*
Minimal stimulus in Kronecker coil - units of current	... 100	... 30	... 200	... 50	... No effect at 2,000	... 10

We next proceed to study the relative effects of unipolar and bipolar stimulation. To the bipolar method of faradic excitation, the electrode points being either 1 mm. or 2 mm. apart, we have found that the cortex cerebelli is unquestionably not excitable, *i.e.*, no muscle response followed the application of the electrodes even when the coil distance represented 4,000 units of the Kronecker scale, and in some cases even 8,000, *i.e.*, at a point when the tension of the current was sufficient to cause frequent sparking between the electrodes when separated 1 mm.

When the whole surface of the cerebellum was thus explored with a hypermaximal stimulus the trapezial group of muscles began to contract with gradually increasing force as the electrodes were gradually brought down towards the edge of the fourth ventricle, and lower still to the neighbourhood of the spinal accessory trunk.

The delimitation of the spinal nuclear representation of the trapezius and other cervico-scapular muscles has not to our knowledge been specifically determined.

We have therefore made a few observations on this point as follows:

(a) *Anatomy.*—The most oral root of the *spinal* accessory nerve takes superficial origin from the bulb in the :—

(1) Cat. In the zonular level of the angle of the posterior border of the external arcuate fibres.

(2) Dog.   In the zonular level of the same point.

(3) Monkey (*Macacus rhesus*).   In the zonular level of practically the same point, *i.e.*, about 1 mm. above the obex.

Thus the bulbo-spinal representation of the shoulder muscles must be regarded as extending headwards as far as the large celled vestibular nucleus and consequently all excitation of the posterior cervical roots, and of the columns and nuclei of the obex region, will theoretically respond by contraction of the muscles named.

(*b*) *Physiology.*—Risien Russell [18], by excitation of the anterior cervical roots, showed that the first cervical nerve supplied the trapezius with other muscles. We have obtained the same response on stimulation of the bulb : (1) Nucleus gracilis.   (2) Nucleus cuneatus.   (3) Tubercle of Rolando.

That these results are due both to direct excitation of the bulbar representation and escape to the accessory trunk itself is proved by the fact that excitation after section of the highest roots is followed by the trapezial group movement though weaker.

With unipolar excitation the errors due to escape of current appear much earlier than with the bipolar method, and we will now give further facts which show the misleading character of the response to unipolar excitation of the surface of the cerebellar cortex.

For unipolar excitation we employed as the localizing (or as Sherrington terms it the " stigmatic ") electrode the glass-insulated needle before described, and for the other either the wide attachments of the brass head piece or a broad metal plate expansion, which was inserted beneath the skin of the back or applied to any other selected spot. We also tried as a diffusing electrode a large area of wet linen applied to the shaved surface of the skin of the lumbar region.

When the surface of the cerebellar cortex was explored with the single insulated needle point and one of the above-named " indifferent " electrodes, the first effect was observed when the Kronecker coil strength reached 1,600 units. The response that then followed was invariably contraction of the trapezius, usually of the same side, but with stronger currents, *e.g.*, 2,000, &c., it easily became bilateral.

The degree of this typical response always steadily increased as the exciting electrode point was brought down towards the nucleus cuneatus. The natural conclusion follows that the effect was an " escape " phenomenon, and therefore such unipolar responses cannot be accepted as evidence of function.

To test this further, and to get if possible some idea of the amount of

the error produced by the conditions of application of the electrodes, we next tried several variations of the unipolar excitation method. In the first place we found that the muscle response was notably diminished by
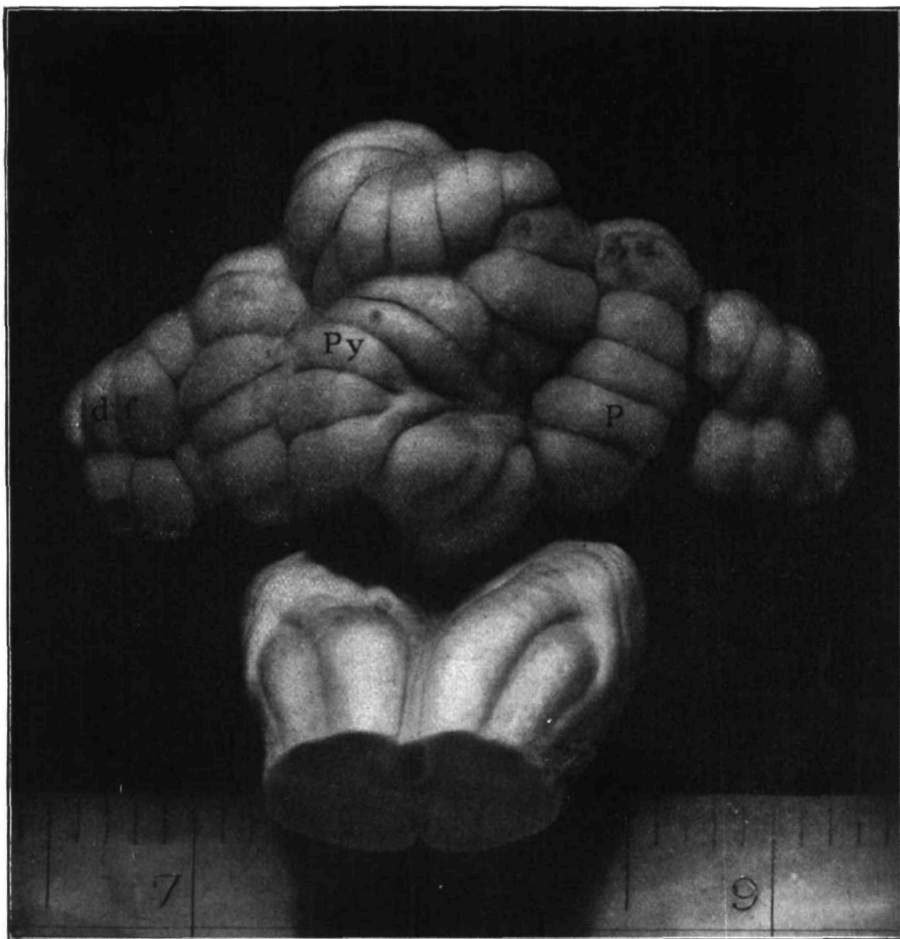
FIG. 30.

Normal cerebellum in the cat enlarged to show how the white fibres in the paramedian fissure (between Py and P) lie on the surface, and consequently exposed to any stimulus applied in the region of the sulcus.
df   Dorsal paraflocculus.
Py   Pyramidal lobe.
P   Paramedian lobe.
The smaller divisions on the scale are millimetres.

shifting the other (the so-called " indifferent ") electrode from the lumbar region of the spine to the frontal bone.

In the second place when the unipolar electrode was placed on the surface of the pyramidal lobe of the cerebellum, and surrounded by either (1) a copper ring, or (2) the same ring covered with absorbent wool, or (3) a circle of amadou, the response was in each case very greatly diminished, *i.e.*, to about one-third of its former value.

An additional important (physiological) point is that even in all excitations of the free surface of the cortex with the marked escape to the trapezial group just described, we never, except when the localizing electrode was placed on or close to the paramedian sulcus, observed unequivocal concurrent movements of the eyes or conjugate turning of the head. The reason for the positive result occasionally obtained from the paramedian sulcus region must now be considered, and will be found to depend upon the anatomical conditions of the region which enable the stimulus to reach the subcortical structures most readily at this particular point.

The paramedian sulcus, which is so strongly marked in the carnivora and well developed in the macacque monkey, is a deep furrow filled only with loose pia mater. The cortex of the ends of the folia of the vermis, and to a similar degree of those of the paramedian lobe, ceases close to the surface of the organ; consequently the white fibres leading to the subjacent nuclei are, at this point, actually freely exposed within 2 mm. of the surface (*see* fig. 30).

Indeed in the dog and cat, where the pyramid constitutes the extreme sigmoidal flexure of the vermis, it can be seen with the operating lenses that the white fibres are often actually exposed on the free surface of the organ. In such a case obviously the response to excitation at that point would not be of cortical but nuclear origin.

The positive effects from excitation of the paramedian sulcus, which Nothnagel, Ferrier, and Hitzig have found comparatively easy to obtain, and which we also have seen, are therefore more correctly explicable as due to stimulation of the nuclei and not of the cortex.

A simple demonstration of the fallacious evidence yielded by unipolar excitation is given by first obtaining the usual false trapezial response with the unipolar electrode, and then immediately changing this for bipolar electrodes with the same coil ; the result is immediate absence of any muscular contraction.

Our general conclusions from the whole of these facts are as follows

(1) The unipolar method of excitation is not accurate for investigation of the localization of function in the cerebellum.[1]

---

[1] While this paragraph was being composed a second communication by Lourié [10] appeared, also proving that the unipolar excitation gave results which were wholly explicable as escape of current, and therefore that the above-stated conclusion is true.

(2) The bipolar method of excitation shows that the cortex cerebelli is not like a "motor" centre intrinsically excitable to the electric stimulus.

The cortex cerebelli is therefore in accord with Edinger's views to be considered wholly as a sensory organ which is in relation with certain lower, *i.e.*, basal centres, viz., the dentate, roof and emboliform nuclei these act as the motor equivalent to the sensory representation in the cortex.

We have shown before (*Brain*, 1905) that the anatomical architecture of the cerebellum exhibits no provision of direct efferent paths from the cortex except to the neighbouring nuclei, therefore our present conclusions regarding the functional activity of these two great divisions of the small brain are in full accord with the anatomical facts.

Relative Excitability of the Cortex Cerebelli compared with that of the Cortex Cerebri.

The question of the comparative excitability of the cerebellar and cerebral cortex respectively is interesting from the general physiological aspect, and although the two organs are commonly regarded as similar in design it seems to be forgotten that the structure of the cerebellar cortex is very specialized and not like that of any other nerve centres, *e.g.*, cerebral pallium, which have been similarly investigated.

Assuming the commonest movement represented in the cerebellum to be that of deviation of the eyes, it is worth while to compare the degree of response when the cerebrum and cerebellum are respectively excited. Reference back to the table on p. 118 shows that the response which was readily evoked from the cortex cerebri by a stimulus of 100 units is hardly to be obtained from the cerebellum until such a strong stimulus is applied that it obviously excites the nuclei of the cerebellum directly, and indeed all nuclei in the neighbourhood.

It will, of course, be conceded that while every sensori-motor centre must be excitable, notable differences of degree of excitability exist even between those in the cerebral cortex : *e.g.*, the visuo-sensory occipital cortex cerebri compared to that of the præcentral gyrus. It appears to us that a parallel though greater functional separation exists between the cortex cerebelli and the intrinsic nuclei.   Consequently whatever be the kinds of movements represented in the cortex cerebelli in their preliminary sensory stage, it is not probable that they are localized in the manner generally understood as motor localization in the cerebrum.

There are, moreover, two more points which in our opinion add weight to the view we are now pressing, viz., that the cortex cerebelli ought not to be regarded physiologically as of the same class of nerve centre as the cortex cerebri.

These two points are (1) stimulation after-effects, (2) intra-vital methylene blue reduction, and must be considered separately.

(1) *Stimulation after-effects.*—Perhaps the most striking feature of difference between the functions of the cerebral and cerebellar mechanisms as a whole is that while the cerebral excito-motor cortex is so essentially productive of very gross after-effects (epilepsy), excitation of the cortex of the cerebellum is not followed by any such phenomena. It is the consideration of the absence of this mode of discharge of nerve energy that led us to a series of experiments with another vital test, viz., that of methylene blue by Ehrlich's method, since the experience of one of us (V. H.) of a large series of experiments in 1893 showed that the cerebral cortical discharge (as originally discovered by Ehrlich) caused an active reduction of the blue in proportion to the degree of development of the epileptic after-effect.

(2) *Comparison of the cerebral and cerebellar intra-vital blue reaction.*—Before stating the contrast between the two organs which we have found, it is necessary to point out that, as shown by one of us and by Eve, there is a slight but distinguishable reduction of methylene blue by a strong (*i.e.*, hypermaximal for excitation of the cortex) faradic current between electrodes 2 mm. apart. But in this method of investigating the cerebral cortex the most striking feature of the activity of the nerve centre is that apart from any slight change due to the current itself the blue colour only materially fades out when the epileptic discharge commences, and then the nerve centre, the seat of the excitation, is left pale white. The method thus offers a valuable means of physiological comparison between the cerebral and cerebellar cortex respectively.

In our experiments specially on this point we have investigated the excitation of these two parts of the encephalon in dogs and cats. The total quantity of 5 per cent. solution of methylene blue injected intra-vitally has been on the average 400 c.c. to 500 c.c. when employed subcutaneously, or about 60 c.c. when infused into a vein direct.

Stimulation of the cortex cerebelli produced either no change in its blue tint or a slight and doubtful one, and offered a strong contrast to the clear paling on exciting the "motor" region of the cortex cerebri. It follows, therefore, that according to this evidence there is no

maximal outflow of energy from the cerebellar cortex comparable to that of the cerebral " motor " cortex.

(3) *Relative excitability of the cortex cerebelli compared to that of the nuclei cerebelli and efferent tracts therefrom.*—Perhaps the most concrete result of our method of investigating the cerebellum is the revelation of the motor functions of the intrinsic cerebellar nuclei as demonstrated by excitation. As already stated the negative result of bipolar excitation of the cortex cerebelli gradually changes into a positive effect as the needle passes forwards among the axones of the Purkinje cells running to the nearest nucleus until the stimulus is directly applied to the nucleus itself, or to the paths and tracts issuing from it when the result becomes maximal with even a very weak excitation.

The full detail of the representations of function which this method has revealed in the cerebellar nuclei we will give in Part II. of this communication.

BIBLIOGRAPHY.

[1] FERRIER. " Functions of the Brain," 1886.
[2] *Ibid. West Riding Asylum Reports*, 1873.
[3] FLATAU and JACOBSON. " Handbuch der Anatomie und vergleichenden Anatomie des Centralnervensystems der Saügethiere," Berlin, Karger, 1899.
[4] HITZIG. " Untersuchungen über das Gehirn," Berlin, 1874.
[5] HORSLEY. *Brain*, 1898, vol. xxi., p. 547.
[6] HORSLEY and CLARKE. *Brit. Med. Journ.*, 1906, vol. ii., p. 1799.
[7] *Ibid. Brain*, 1905, vol. xxviii., p. 13.
[8] LEDUC. " Les Ions," *Monographies Cliniques*, No. 48, January, 1907.
[9] LEWANDOWSKY. *Arch. f. Anat. u. Physiol.*, 1903.
[10] LOURIÉ. *Neurol. Centralbl.*, 1907, Bd. xxvi., S. 652; also *ibid.*, 1908, p. 102.
[11] LÖWENTHAL and HORSLEY. *Proc. Roy. Soc.*, 1897, vol. lxi., p. 20.
[12] NOTHNAGEL. · *Virchow's Archiv*, 1868.
[13] PAGANO. *Arch. Ital. de Biol.*, 1902, T. xxxviii., Fasc. 2.
[14] PRUSS (quoted by LOURIÉ). *Poln. Arch. f. d. med. u. biolog. Wissenschaft*, 1901.
[15] RIJNBERK, V. *Arch. di Fis.*, 1904.
[16] *Ibid.* "Lokalisation im Cerebellum," 1907. (Preischrift.)
[17] ROUSSY. " La Couche Optique," Paris, 1907.
[18] RUSSELL, RISIEN. *Brain*, 1897, vol. xx., p. 35.
[19] SELLIER et VERGER. *Arch. de Phys. norm. et path.*, 1898, p. 706.
[20] *Ibid. Comptes rendus de la Soc. de Biol.*, Paris, 1903, p. 485.
[21] SHERRINGTON. *Proc. Roy. Soc.*, 1897, vol. lxii., p. 183.
[22] *Ibid. Journ. of Physiol.*, 1902, vol. xxviii., p. 14.
[23] THOMSON, J. J. "The Electrolysis of Steam," *Proc. Roy. Soc.*, 1893, vol. liii., p. 93.
[24] TRENDELENBURG. " Studien zur Operationstechnik am Zentralnervensystem," *Arch. f. Anat. u. Phys.*, 1907, S. 83.
[25] " Verständigung über ein gemeinsames craniometrisches Verfahren" (Frankfurt-München), *Arch. f. Anthropol.*, 1884, Bd. xv., S. 1.
[26] WEIR-MITCHELL. *Amer. Journ. Med. Sci.*, 1869, p. 320.