CONCERNING ELECTRO-ENCEPHALOGRAPHY.

M.D., Thesis.
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INTRODUCTION.

It has long been known that nervous activity is accompanied by changes of electrical potential. As early as 1875, Caton(1.) using a string galvanometer demonstrated electrical activity in the exposed brain of animals.

In 1913, Prawdicz-Neminski (2) described six types of electrical rhythms in the "electro-cerebrogram" of the dog. This was the first serious attempt to classify observations of this type.

In 1929, Berger (3) published his first report of characteric electrical rhythms detectable through the intact cranium in man. It is surprising that physiologists paid so little attention to his earlier reports, for it was not until 1934, by which time Berger had already published some eight papers, that Adrian and Matthews (4) undertook a series of experiments to confirm his work. The importance of the work of Adrian and Matthews cannot be overestimated. They demonstrated clearly that in principle the claims of Berger were correct; namely, that it was possible to detect certain characteristic electrical changes through the intact cranium, and that these changes could only be due to nervous activity within the skull. By the introduction of important refinements into the technique which will be referred to later in more detail, they were able to localise the source of the changes which were referred to by Berger as the α rhythm.

Furthermore, they were able to make important deductions as to the origin and nature of these changes: deductions. which were a distinct advance over the more holistic concept which had been put

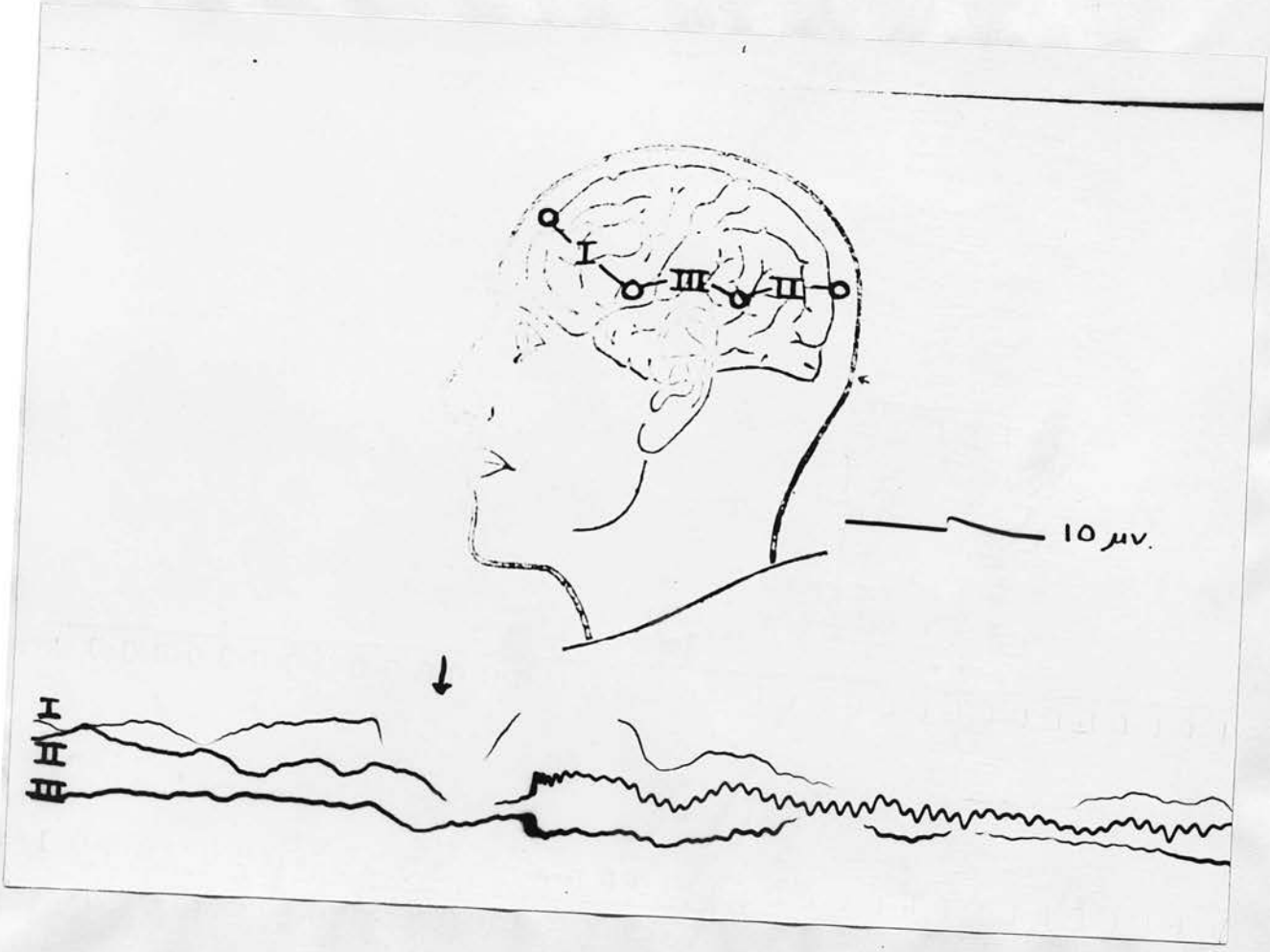


Fig. 1.

forward by Berger. The main points brought to light by the work of Adrian and Matthews were that, in normal individuals, there is a characteristic electrical rhythm which originates from the region of the occipital lobes in each hemisphere. The rate of the changes were shown to be remarkably constant for different individuals, usually in the neighbourhood of 10 - 11 per second, with extreme limits ranging between 8 - 13 per second. For any single individual, however, the changes were found to be constant in nature and rate. They did find that the exact foci of origin of the changes were liable to shifts of a centimetre or two from time to time.

Adrian and Matthews also found that the α, or Berger rhythm as they designated it, was inhibited by visual stimuli, or by mental concentration. They also described the so-called "flicker response" in which rhythmical alterations of light stimulus would, within certain strict limits, produce alterations in the rate of the Berger rhythm.

Fig. 1. has been included as a matter of general interest, and also because it demonstrates rather nicely the effect of the closure of the eyes on the Berger rhythm. The eyes were closed at the point indicated by the arrow on the record. The Berger rhythm is seen to appear as soon as the eyes were closed. The rhythm is best seen in the centre lead of the record, the chart appearing with the record showing the electrode positions, explains the reason for this.

More recently the work of Kornmuller (5), Adrian (6), Adrian and Matthews (7), Gerard (8), Jasper (9), and others, indicates that numerous electrical rhythms, or discharges, arise from

various areas of the brain, and the the type and nature of these rhythms are in some way related to variations in the cyto-architecture.

It would appear that within the central nervous system there are an infinite number of potential changes, as many changes as there are active neurones, but it is only when certain groups of units because of like activity in the physiological sense, or because of a common cytoarchitecture, act in unison, or "beat" together, that it is possible to pick up characteristic changes on the surface of the brain.

When one endeavours to study these events through the intact cranium, many of the changes become masked, and there is very little apart from the Berger rhythm which might described as characteristic. As Adrian pointed out, the normal electro-encephalogram was soon shown to be disappointingly constant, with the result that the attention of many workers was diverted to the study of pathological states in the central nervous system.

It soon became apparant that this was going to prove a worth-while field for the electro-physiologist.

In 1936, Walter (10) showed that he was able to recognise gross deviations from the normal electrical behaviour, in certain pathological states. He also claimed to be able to localize accurately the site of intracranial tumours, using a technique similar to that devised by Adrian and Matthews for their study of the Berger rhythm. About the same time Gibbs, Lennox, and Gibbs, (11) published their first paper describing the electrical behaviour in certain epileptic states.

Electro-encephalography was by this time very much "on the map".

Bremer (12) produced a series of papers showing the effects of various depressant and stimulant drugs on the electro-encephalogram of animals.

Bucy and Case (13) published a paper purporting to confirm the work of Walter. The nature of the records published by these authors throws some doubt on the accuracy of the particular work. Cazzamalli (14) claimed that there were high frequency components of the order of megacycles in association with emotional states, But it is hardly necessary for me to add that confirmation of this work has not yet been forthcoming.

Jasper, and Andrews (15) made a special study of the electrical changes apart from the α rhythm, the so-called beta rhythm. It would appear that they were not able to find anything really characteristic, and they concluded that the predominant components of the pre-central electro-encephalogram, in the intact cranium, have an average frequency of about 25 per second.

Physiological states were studied, and the work of Loomis, Harvey, and Hobart (16) on the electrical changes associated with normal sleep is worthy of mention.

No further evidence confirming the claims of Walter with regard to the localization of intracranial tumours was forthcoming until quite recently, when Gibbs and Williams (17) working at Boston, and Krynauw (18) working at Oxford, produced, as was stated in a leading article in the British Medical Journal, August 26. 1939.,,"complete and systematic confirmation of his claims!

My own interest in electro-encephalography was aroused after the first publication of Walter. With the institution of the

Nuffield Department of Surgery at Oxford, it became possible for me to undertake a detailed survey of the electrical changes associated with certain well-defined pathological groups.

The period of work can be divided into three stages; (a) a period entirely devoted to technical considerations, (b). a preliminary stage lasting some six months during which earlier confirmed work such as the observations of Adrian and Matthews were repeated as very necessary technical exercises, and (c) the last period during which an electro-encephalographic study was made in conjunction with the clinical investigation of certain well-defined pathological groups of nervous disease. This work has now unfortunately been interrupted because of "evil things " which have upset the channels of normal endeavour.

I propose for the scope of this thesis to review the work of the last six months.

METHOD.

The amplifier has become such a commonplace feature of the modern physiological laboratory that there is little need to discuss in detail the design of the apparatus. There are, however, several special features wherein amplifiers designed for electroencephalographic work differ from most other amplifying systems, and I shall make reference to these in the following brief description of the apparatus.

For the localization of electrical disturbances associated with intracranial pathology, the method introduced by Adrian and Matthews, and later modified by Walter (19) is employed. This introduces the complication of multiple channels of amplification. Even when the so-called unipolar method of leading off is employed, multiple channels are essential because of the large area which has to be surveyed electrically..

Most workers in this field are still employing the "unipolar" method of leading off, and there is a considerable difference of opinion as to the relative merits of the two methods. It will be necessary to make some further reference to this aspect of the subject later.

Amplifiers.

The amplifiers consist of three separate channels, and each channel is composed of two parts; (1) the preamplifier: this this consists of a balanced input stage carefully screened. The circuit was described by Matthews (20), and was originally due to Tonnies. The tubes in the input stage are indirectly heated triodes with a low noise ratio. The preamplifiers are independent units, each in its own metal box, which is earthed, and contains

its own low, and high tension battery supply, thus further enhancing the effectiveness of the screening. The input stages are relatively immune from radiated interference.

(2) the main amplifiers, one for each channel, are mounted on a metal rack 5'8" high, and 21" broad. Each amplifier consists of three stages of resistance-capacity coupled pentodes, the last stage being a paraphased "push-pull"output.

Condenser values are large so as to give the amplifiers a slow time constant of the order of 1 cycle per second.

Another point which I consider to be important, is the inclusion of a variable frequency filter circuit. This is important for several reasons. As I pointed out, the changes which have been recognised in the normal electro-encephalogram, are the 10 per second Berger rhythm, and the so-called β rhythms which have a frequency of the order of about 25 per second, that is if we exclude the work of Cazzamalli already referred to, and Balado (21) who claim that there are much faster components.

So far as I have been able to judge, the rate of flux associated with pathological changes in the brain seldom, if ever, exceed 20 per second, usually being within 1 - 10 per second. The filter circuit is, therefore, designed so as to give a cut-off at about 25 - 30 cycles. There is much to be gained from this arrangement; firstly, with apparatus well screened, and earthed, there is no need to have the patient earthed, or in a screened room, nor is there any need to exclude A.C. from the room for lighting purposes. Furthermore, the high tension and sweep circuits of the recording oscillographs can be "mains driven" which is a great advantage. Any A.C. which the subject picks up is rejected

by the filter circuit; secondly, the most objectionable and unwanted biological potentials, namely, muscle action potentials from muscles attached to the skull are similarly rejected; and thirdly, the background noise or "valve mush" is also smoothed out, so that the final trace is free of numerous unwanted electrical effects, thus making the interpretation much easier.

Many of the published records where the filter circuit with a low cut-off has not been used, are, to my mind, difficult or almost impossible of interpretation.

The final adjustment of the amplifiers is such that an input of 10μV from the calibrating circuit gives a 2 cm. deflection on the oscillograph tubes at full working gain; and at the same time an input of several millivolts does not produce jamming of the amplifiers.

Recording System.

Three cathode ray tubes are used for recording. The tubes chosen are the gas focussed type with a long afterglow. The reasons for the choice of the old gas tubes are,(a) they have a greater sensitivity than high vacuum tubes, so that there is no need to increase further the degree of amplification which is already critically high; (b) that for the purpose of recording changes as slow as we are encountering, a very slow sweeping time is necessary, the spot traversing the 7 cms. of the screen in a matter of 3 -4 seconds. With gas focussing tubes the arrangement of a circuit of a "sweep time" as slow as this affords no very great difficulties, but with the high vacuum tubes the problem is much more difficult, and has not to my knowledge been satisfactorily solved. The filament, high tension, shift, and scanning

circuits are all mains driven, each circuit having separate transformers, and rectifying circuits. Shift circuits in both the X, and Y, axes are included.

The oscillograph tubes are vertically mounted. The backs of the screens are used for viewing, and a mirror system throws the image from the front of the tubes into the recording camera. The camera is a moving camera, and the standard 35 mm. bromide paper is used. When the shutter of the camera is opened, and the paper starts to move, the X plates of the tubes are automatically earthed, the sweep circuit is thereby cut off, and the spots centred over the appropriate mirrors.

The rate of travel of the paper is the same for all records being 2.4 cms. per second. This is checked from time to time by recording a wave of known frequency. In this way we are able to keep the record which is already sufficiently complicated, free (~~free~~) from the extra record of a time marker.

Electrodes, and method of leading off from the patient.

The potential changes from the patient's skull are picked up by means of saline pad electrodes, the so-called silver-silver chloride electrodes which were described by Walter. The electrodes are held in place by means of a special cap. The area of scalp to which the electrode is to be affixed is cleansed with alcohol to remove grease, the hair is parted at the selected spot, and the electrode slipped into position under one of the bars of the cap.

The electrodes are arranged on the skull in pairs, the connection with the amplifiers being made in such a manner that in the event of a change of electrical potential occuring beneath

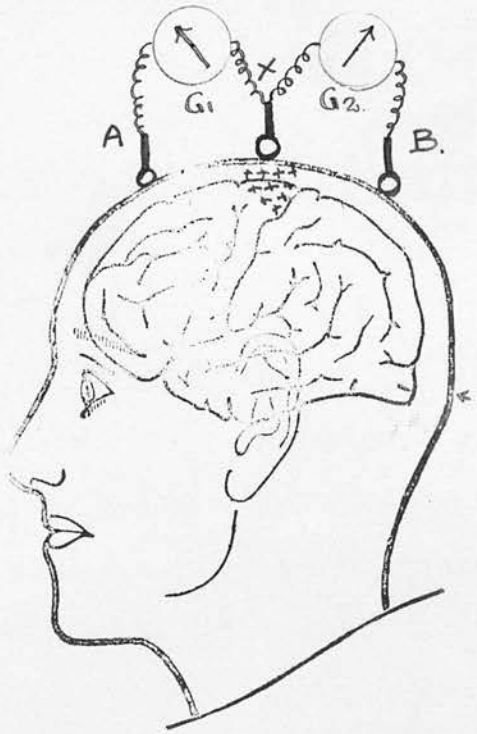


Fig. 2.

A,X,B represent three electrodes placed over the skull. When a change of potential occurs under the centre electrode X, the hands of the two galvanometers G1 and G2 move in opposite directions as indicated in the diagram.

any one of the electrodes, the recording apparatus of the adjacent two amplifiers will be caused to operate in opposite directions. The electrical events as they are recorded are then said to be out of phase. The accompanying diagram Fig.2. will serve further to clarify this point.

This, it will be recognised, is the method of localization of electrical events within the cranium which was introduced by Adrian and Matthews.

For the analysis of the exact nature of the changes this method has very distinct limitations. It will be obvious by referring to Fig.2. that the final behaviour of either of the recording devices G1. or G2. will be a function of the electrical changes occuring beneath not only the electrode X, but also beneath the electrode A, if G1. be considered. It is obvious, therefore, that such an arrangement would not faithfully reflect the behaviour of any single disturbance. Therefore, to study the exact nature of the changes emanating from any single point, another electrode arrangement is necessary. We have introduced a special technique for this latter purpose, the description of which will be deferred until later.

Calibration.

A calibrating circuit is included in the input leads of all the amplifiers. This is so arranged that potentials varying from 1 to 100 μV can be injected into the circuit at will. Comparison between the deflection produced by the events being studied, and that produced by a known input is then easily made.

There is a considerable variation in the amplitude between

the normal physiological changes detected, such as the α and β rhythms, which are usually between 2 - 10μV, and the changes encountered in pathological states which may reach an order of several millivolts in an epileptic seizure. For the most part, however, potential shifts of the order of 100μV may be considered to be of high amplitude.

Artefacts.

The question of artefacts assumes great importance when one is working with high gain amplifiers, and no discussion of the technical considerations would be complete without mention of some of the sources of artefact, together with some mention of the ways and means employed to counter them. I am, of course, considering the question of artefacts quite apart from those which may arise from any instability of the amplifiers themselves.

(1) Radiated interference. Mention has already been made of the precautions taken to eliminate radiated interference. If one has to work in close proximity to other electrical equipment, then some screening of the room may be necessary. Working in an operating theatre in which there is an endothermy necessitates hte disconnection of such apparatus from the mains supply because of the great interference set up in the proximity of thw fields of the transformers etc.

(2) Movements. Complete relaxation of the subject is essential, because movements imparted to the electrodes greatly alters the resistance of the contacts, resulting in great distortions of the base line. Where movement on the part of the subject cannot be obviated as in epileptic seizures, or in very restless people such as those with athetoid movements, arrangements for the

attachment of electrodesother than those described, must be made. In such cases small flat silver electrodes, about 3 mm. in diameter, moistened with saline jelly and fixed in place with colloidion, are usually quite satisfactory.

(3) Skin potentials.

Slow shifts of the base line may be due to alterations in the resistance of the skin of the scalp, such as may occur in the presence of increased sudomotor activity; or may be due to the actual presence of skin potentials,the so-called psychogalvanic response. Usually,however, the potential shifts in such instances are of such a slow order that the amplifier fails to respond to the changes.

(4.) Eye movements.

Movements of the eyelids and eyeballs are productive of the most persistent and troublesome of artefacts. In certain subjects it is quite impossible to prevent a continuous flutter of the eyelids. This flutter is often worse when the subject is asked to close the eyes, and in such instances one may overcome the difficulty, should the subject be sufficiently co-operative, by keeping the eyes open and ensuring fixation on some distant object. In other cases in which there is a persistent nystagmus, it is impossible to carry out the investigation, as all the events are by the larger potentials consequent upon the eye movements. I do not know of any way of overcoming this difficulty.

(5) Muscle action-potentials.

These can become very troublesome if the patient persists in contracting the muscles of the jaw. As a rule, with a little

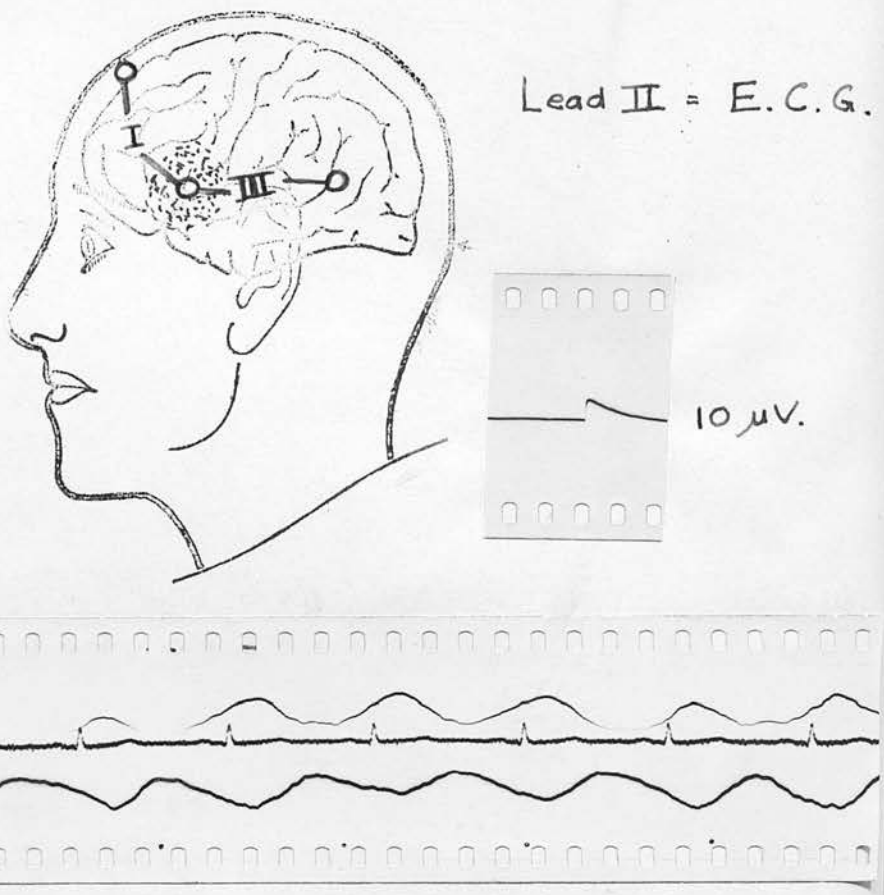


Fig. 3.

patience, one is able to overcome this difficulty; and a moderate degree of relaxation on the part of the subject, together with the low cut-off filter already mentioned, reduces to negligible proportions an otherwise formidable source of interference.

(6) Walter has described an artefact which he considers may be in some way related to the pulsation of the middle meningeal artery. It is a slow regular wave of characteristic appearance, and bears a direct time relationship to the heart rhythm. We have encountered this on many occasions.

Fig. 3. is an example of such an instance with a simultaneous electrocardiographic record. I am unable to agree with Walter as to the origin of this rhythm. After several experiments with a view to determining the cause, I have come to the conclusion that it is due to a rhythmical rocking of one of the electrodes by the pulsation of a superficial vessel with consequent rhythmical shifts of interelectrode resistance.

(7) Other possible sources of artefact such as those due to alterations of temperature, and photoelectric potentials, need only be mentioned, as their avoidance requires only reasonable care in the technique.

The Records.

With each record there is included a chart showing the electrode positions when the record was taken. The amplifier to which the electrodes are connected is indicated on the chart, and the trace from the corresponding amplifier is also marked on the record.

The rate of travel of the recording paper is the same for all the records, namely 2.4 cms. per second.

With regard to amplifier gain, a slip of record showing the deflection produced by 10μV at the same gain, is included with each record.

RESULTS & CONCLUSIONS.

The objects of the investigation have been:-

(1). To determine whether a particular pathological state is, or is not, associated with a detectable abnormality when considered in terms of the cortical potentials.

(2). In the presence of abnormal changes to determine whether these changes can localized to a particular area.

(3). To determine the topographical relationship between the focus of electrical disturbance, and the site of the pathological disturbance.

(4). To discover whether different pathological states are associated with recognisable differences of electrical behaviour.

Electrical behaviour

The study of "electrical behaviour" entails a detailed examination of the nature of the changes emanating from a focus of disturbance, with regard to amplitude, rate of change, rhythm of change,etc. To put it more simply it amounts to examining one's records from the point of view of the "wave form" produced. We have to consider the rate of the waves, their regularity or otherwise, with due regard to the degree of amplification which has been employed.

Ideally to study the many factors implied by the term electrical

behaviour, one would localise the disturbance using the method already indicated, and then use a standard "set up" in the technical sense for the detailed study of the wave form.
To do this, one electrode would have to be placed over the centre of the disturbance; and for the other electrode, some neutral point which would be common to all intra-cranial electrical events would have to be found. A grounded "pad electrode" from the ear is used by nearly all workers for this purpose. The choice of such an arrangement does not strike me as being satisfactory. It is not, in my opinion, inactive in the sense of being common to all intra-cranial events; its distance from the other electrode varies from case to case, depending upon the site of the focus; and finally it is a point on the very system of resistances through which we are trying to measure the changes.

A point within the ventricular system would be free from these objections, and I have now examined several cases using such a point for the "common electrode".
Method. For the "common electrode" we have devised special silver ventricular needles. The needles are coated with insulating enamel except for the first centimetre, and the back end to which contact is made with the amplifier.
The standard burr holes for ventriculography are made, and the special needle is inserted into the lateral ventricle on the side opposite to the lesion. The surgical reasons for the choice of the contra-lateral ventricle are sufficiently obvious. The ventricular fluid is not allowed to escape, the stilette only being withdrawn momentarily from the needle to ensure that the needle is in the ventricle. The results employing the intra-

ventricular electrode have been most encouraging, and we are now using the same method for exploration of the exposed cortex at operation.

As already indicated I am confining the analysis of the work to those cases which were examined in the six month period March - August 1939. During this period 154 cases were examined. The series is still to small to make anything in the nature of a statistical survey worth while. This will be better appreciated if it is realised that the 154 cases are made up of widely differing pathological states.

I have divided the cases up into the following pathological groups:-

(A). Expanding intra-cranial lesions.

(B). Head injuries.

(C). Vascular accidents, and abnormalities.

(D). The Epilepsies.

Interest has been mainly centered in the group of expanding lesions, so that the analysis of the work in this section can necessarily be more detailed than in the other groups.
It will be recognised that in the group of expanding lesions we are dealing with a complex group of pathological states.
It has been found necessary to subdivide the group on a clinico-pathological basis. For instance, we have considered all the posterior fossa tumours together, regardless of the intimate nature of the causal lesion, whereas the hemisphere lesions are considered under more detailed pathological headings.
The reasons for this arrangement will become apparant when we come to consider in detail the findings in relation to each pathological group.

(A). Expanding intra-cranial lesions.

Fifteen cases which were later verified as posterior fossa lesions have been examined. Some of the cases in this group showed normal cortical activity, while in others there was a considerable generalised disturbance which may well have been related to raised intra-cranial pressure. The disturbance when present takes the form of slow, 1 - 3 per second, often high amplitude shifts of potential with no definite focus of origin. In these cases there appears to be a generalised instability of the entire cortical activity.

Walter(22) claimed that in some cases of posterior fossa lesions he was able to detect a focus of activity from the region of one or other mastoid process. I have not been able to confirm his contentions in this respect.

The relationship of the electrical disturbance to the raised pressure is interesting, but is by no means clear, for in some instances in which there was undoubted rise of pressure as shown by manometric readings of the intra-thecal, and intra-ventricular pressures, no abnormality could be detected. On the other hand, in some of the cases in which gross electrical changes were encountered, and in which the pressure was raised, the administration of hypertonic saline intravenously reduced considerably the electrical activity for short periods.

(2). Pituitary Tumours.

Five cases of pituitary and Rathke pouch tumours are included in the series. In two of these cases in which there was considerable extension of the tumour into the third ventricle, I found generalised instability of the cortical activity without any localisable focus. In another case, in which at autopsy we found

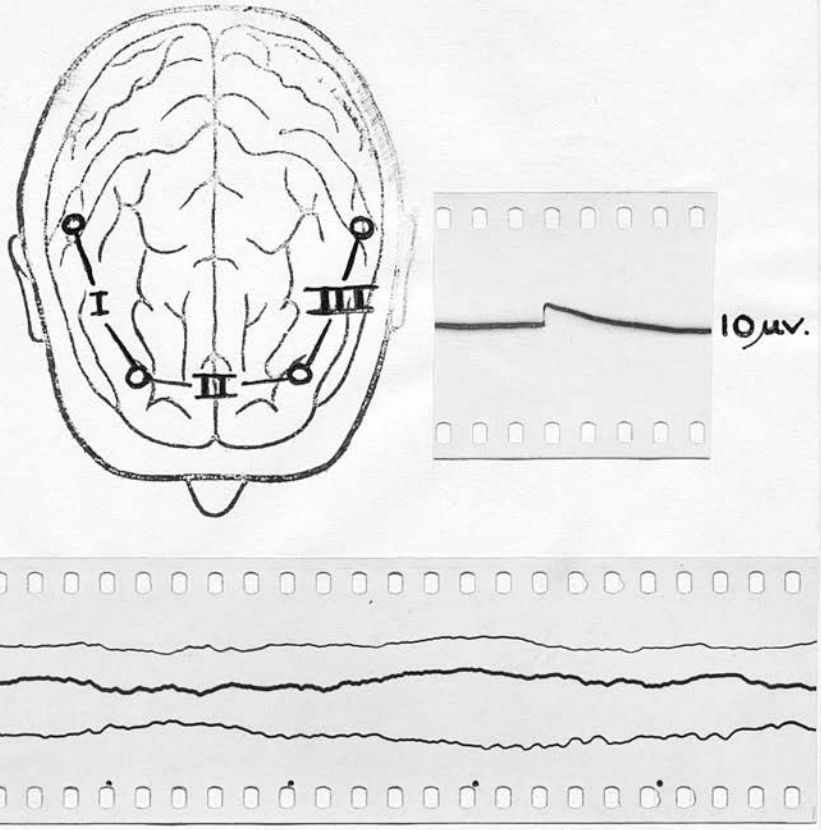


Fig. 4.

PATHOLOGICAL GROUPS.

(a), Multiforme Group.

(b). Meningiomas.

(c). Abscesses.

(d). Astrocytoma Group.

(e). Oligodendrocytomas.

(f). Porencephalic cyst.

(g). Tuberculoma.

(h). Subdural Haematomas.

Fig. 5.

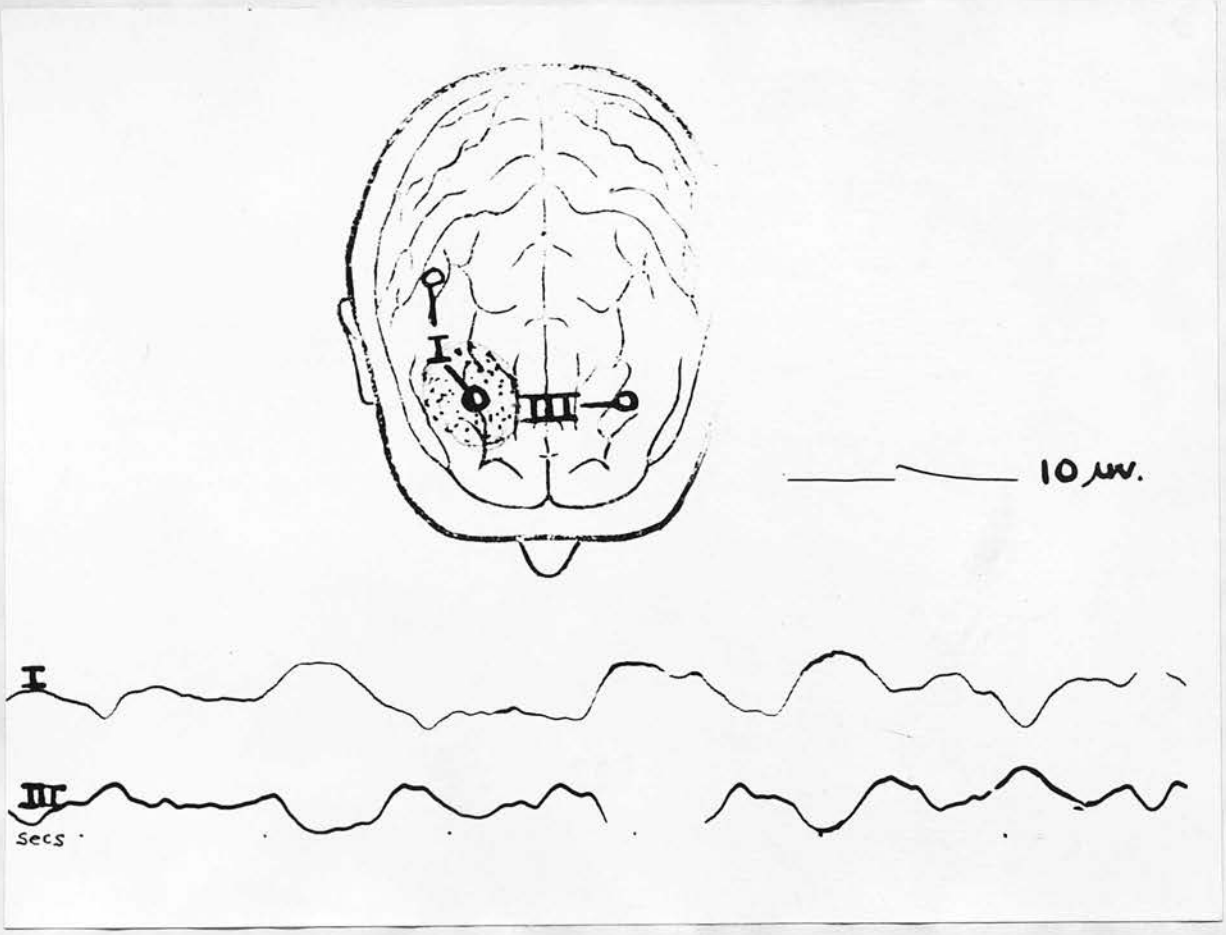


Fig. 6.

expansion into the third ventricle, and into the middle fossa, no abnormality was detected.

In the remaining two cases which were purely intra-sella lesions, no abnormality of the electrical behaviour was encountered.

Fig. 4. is the record taken from one of these. I have included the record because it represents what I consider to be a normal electro-encephalographic record, and it will, therefore, serve as a basis for comparison with the records of abnormal cortical activity.

(3). One tumour of the third ventricle, and septum pellucidum without gross hydrocephalus was examined. Here again no abnormality of the electrical rhythm was detected.

(4). Hemisphere Tumours.

Forty eight cases of hemisphere tumour were examined during the period under review. These include tumours due to neoplasms, and also those due to other causes.

The table, Fig. 5., indicates the pathological groups into which I have subdivided these lesions. The reasons for the particular arrangement are; that they are clinically convenient, and they are the groups in which I have found differences or similarities of electrical behaviour.

(a). Multiforme group.

Fig. 6. This is the record taken from C.H. a man of 38. He had a short history of headaches and vomiting. On examination he was found to papilloedema, about 4D, in both eyes, slight left lower facial weakness, and some mental deterioration. The record shows the slow high amplitude potential changes,

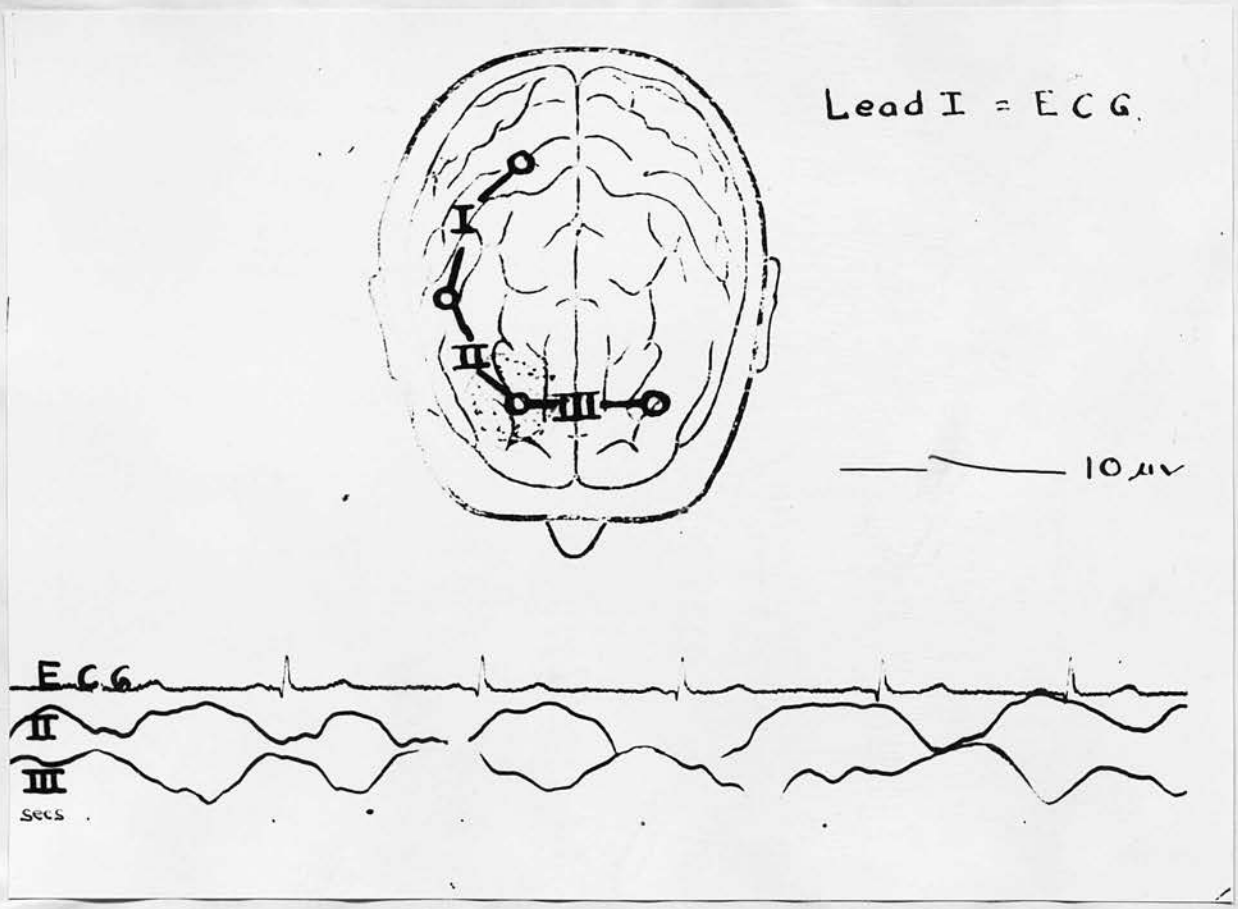


Fig. 7.

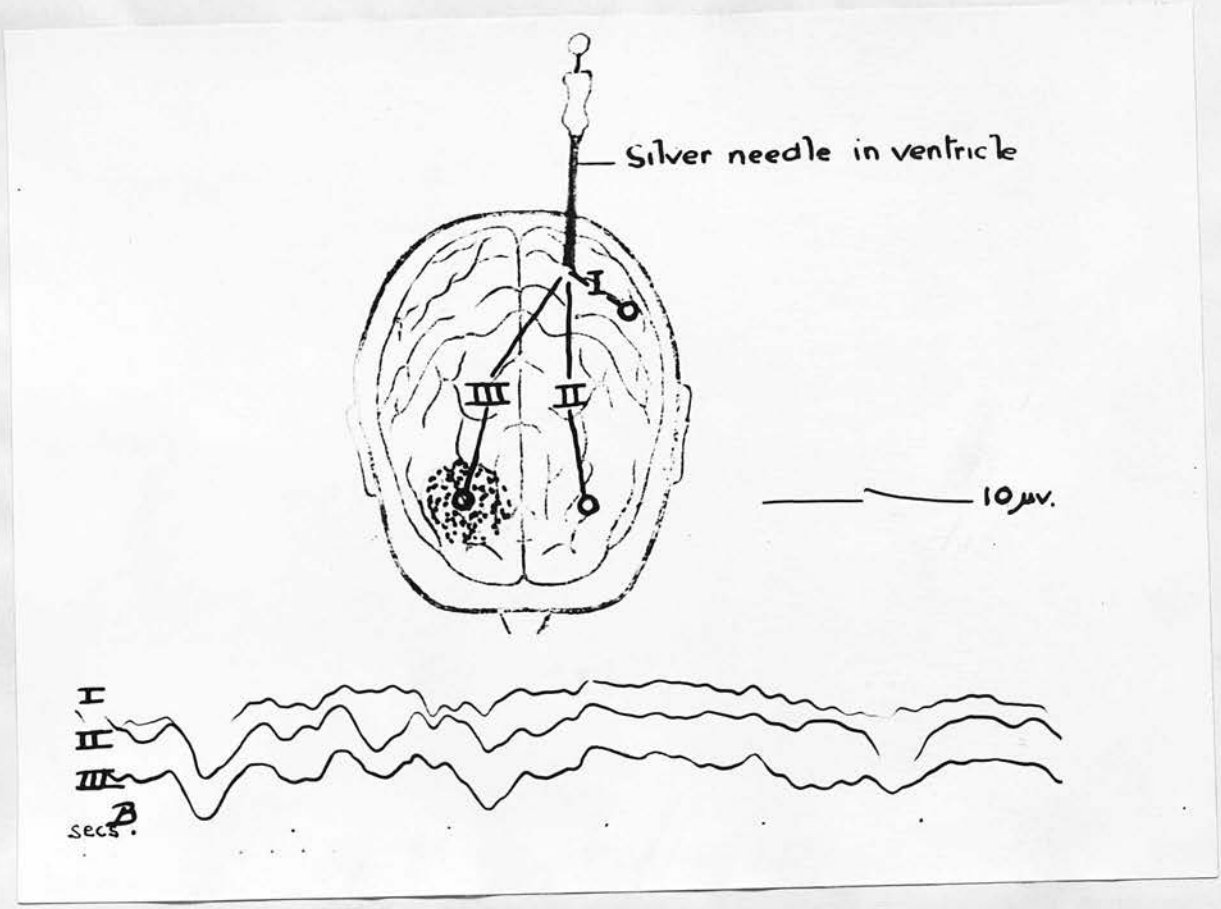


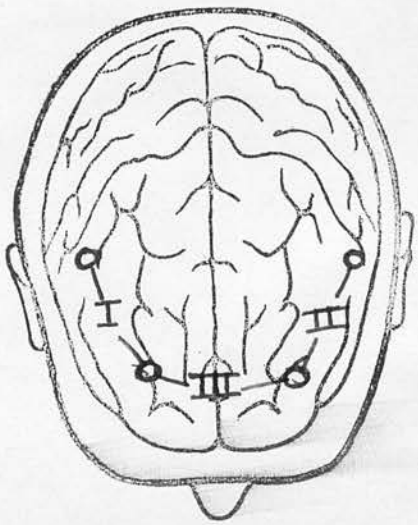
Fig. 7a.

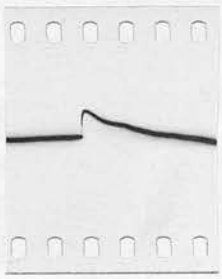
typical delta waves, and is highly characteristic of the electrical disturbance which one finds in association with tumours of this group. The record is also a very good example of the phase relationship, the waves being 180° out of phase, which determines the localization of the electrical disturbance. The focus of abnormality is seen to be in the region indicated in the chart accompanying the record.

The waves are very slow, about 1 per second, and are of considerable amplitude, as can be judged from the deflection produced by 10μV at the same amplification.
At operation a large subcortical neoplasm was partially removed. Histologically this revealed itself as a glioblastoma multiforme.

Fig. 7. Record from R.M. aged 56. He was admitted with signs, and symptoms suggestive of a right hemisphere neoplasm.
The record clearly shows the slow high amplitude waves out of phase between amplifiers II, and III. A simultaneous electrocardiogram, lead I, was taken to make sure that the abnormal rhythm bore no relationship to the cardiac rhythm.

Fig. 7a is another record taken from R.M., but in this instance the intraventricular electrode has been employed. It demonstrates two points; (1), that the wave form is rather more complex than is suggested by the "bipolar" method of leading off; and (2), that it would not be possible to determine whether Lead II, or Lead III, was nearer to the focus of disturbance. This experiment, which I have been able to repeat on several occasions, does I think show, contrary to the contentions of most workers in this field, that it is not possible to localize the focus of disturbance by the unipolar method of leading off.





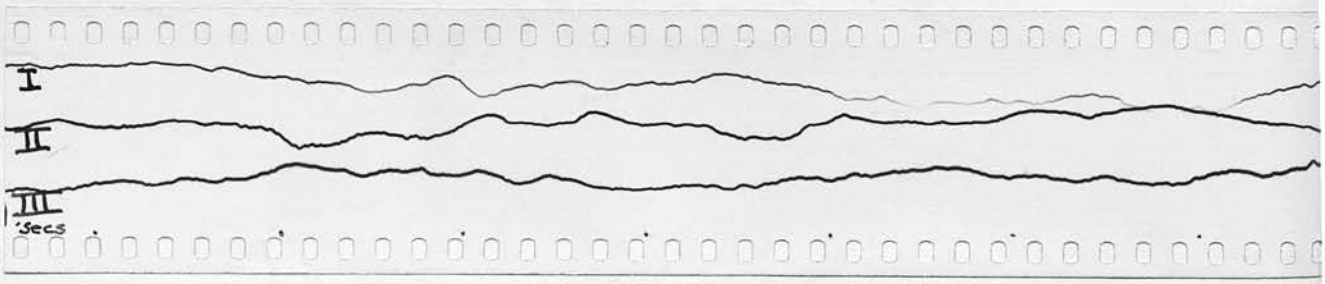


Fig. 8.

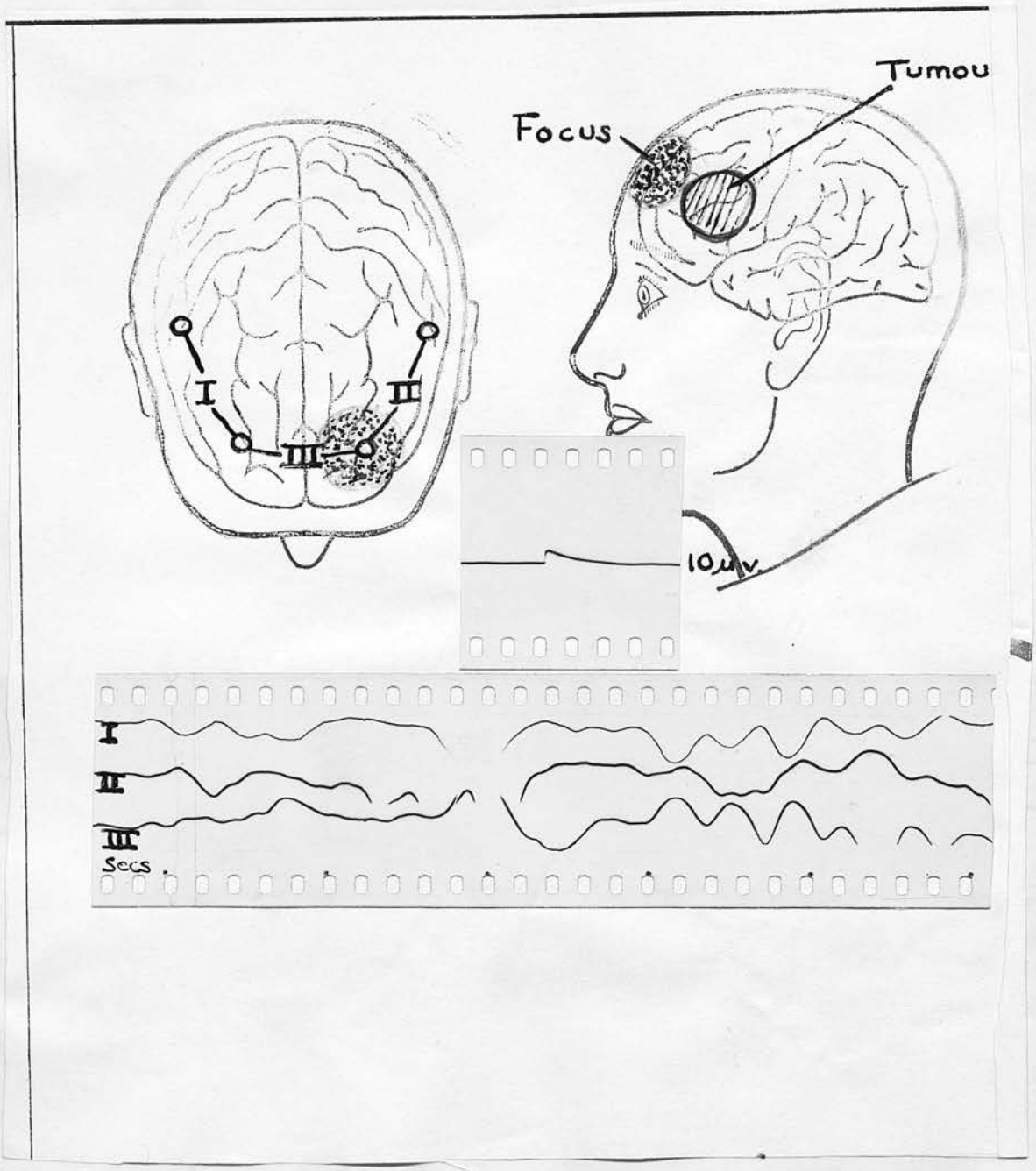


Fig. 9.

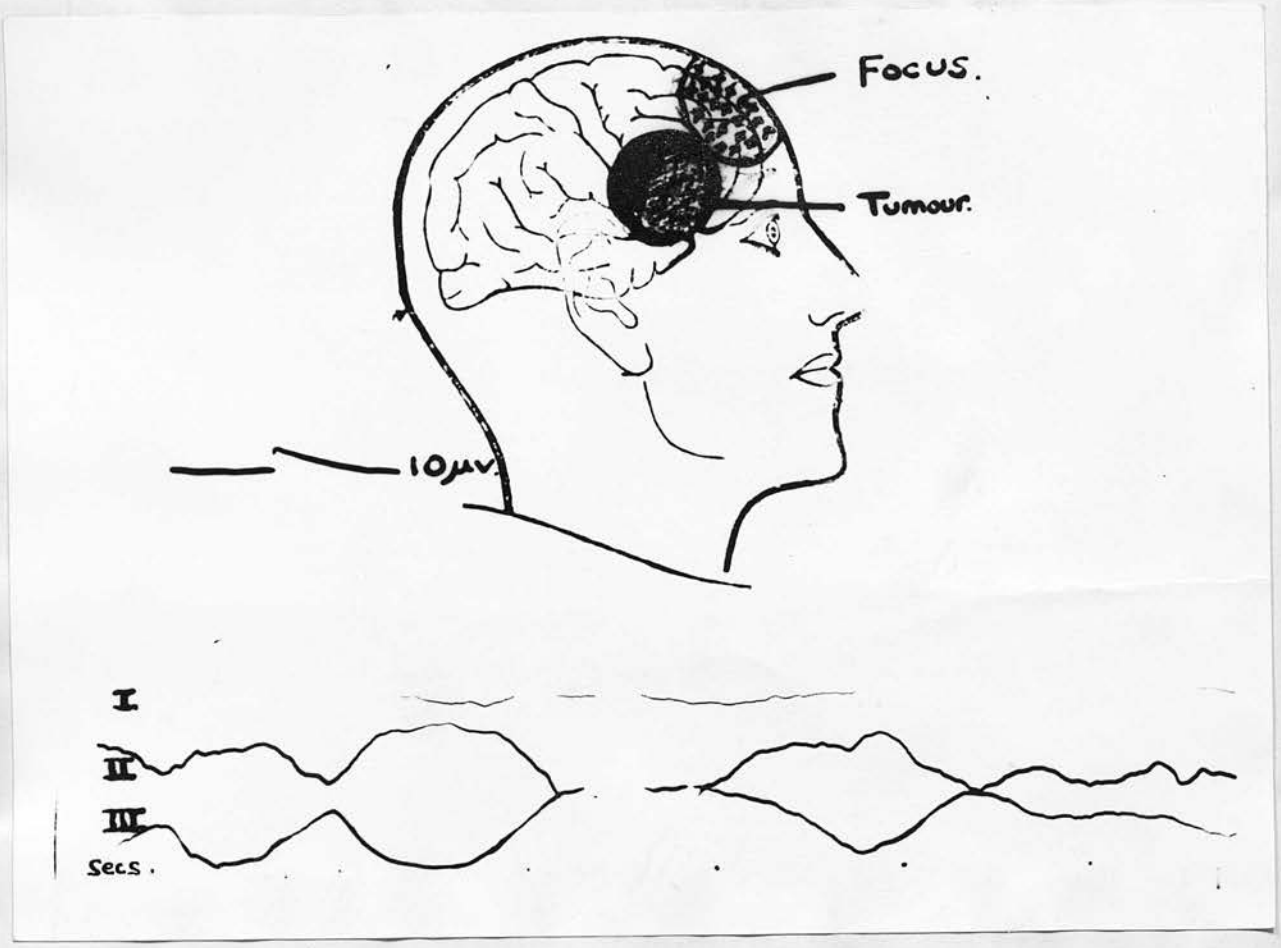


Fig. 10.

Allthat one would be able to say with regard to localization, would be that a disturbance of about the same magnitude was coming from the region of both frontal lobes. The findings illustrated in the previous record, and the subsequent operative confirmation, show the fallacy of this. At operation a right frontal multiforme was revealed. So far as it could be assessed, the tumour was completely removed. Two months after operation the electrical findings were much the same as before operation. Clinically he made an excellent recovery, and now 5 months after operation the cortical action potentials are well within normal limits, as is shown by Fig. 8., which is the record taken five months after operation.

Fig. 9., is the record taken from M.W. a girl, nine years of age, who was admitted suffering from headaches and vomiting. On examination she was found to have papilloedema, and a slight sensori-motor hemiplegia down the right side.
A focus of electrical disturbance was found at the left frontal pole. The waves were slow, and of high amplitude. The site of the focus is indicated in the chart accompanying the record. At operation a left frontal flap was turned, and a large partially superficial glioma was found just behind the focus of electrical disturbance. Histologically this was shown to be a multiforme.
The relationship of the disturbance to the actual site of the tumour is noteworthy, and to my mind raises some interesting points. I have seen the same sort of thing on several occasions. The record Fig. 10., is another example of discrepancy between the electrical focus and the actual site of the lesion.

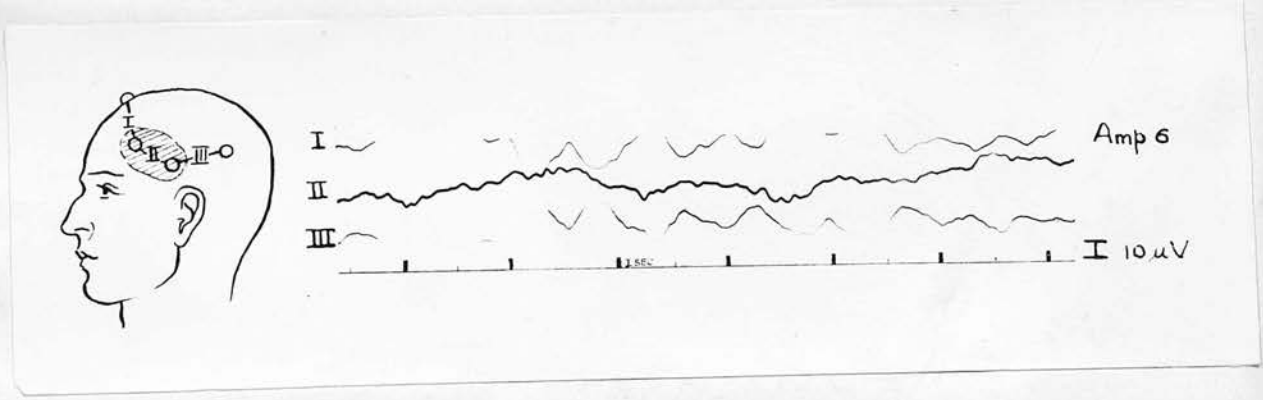


Fig. 11.

Why in each of these cases was the disturbance in front of the lesion? I am inclining more and more to the view that oedema of the tissues adjacent to the lesion is the main factor responsible for the abnormal potentials encountered in association with the expanding lesions. The tumours themselves we know to be electrically inactive, therefore the main factor responsible for the abnormal changes encountered, must be a function of the reaction of the surrounding tissue to the presence of the neoplasm. Referring again to Figs. 9. & 10., one would then have to try and explain why in each of these cases there is more reactive oedema in front of the lesion than behind it. One possible explanation is that lesions in the sites indicated in these instances, modifies to a greater extent the the vascular supply in the region of electrical disturbance. The question of the effect of interruption of the long projection tracts, is one which also has to be borne in mind. There is some experimental evidence that interruption of the long projection tracts per se, produces distortions of electrical activity in that part of the brain from which the particular track originated.

Fig. 11. C.S. a man aged 51 years was admitted, with fits, headaches, and vomiting. Objectively he had papilloedema, nominal aphasia, and a right sensori-motor hemiplegia.
The slow high amplitude waves out of phase bteween amplifiers II. and III, are clearly seen. This indicated a disturbance of wide area, beyond the bounds of the area encompassed by amplifier II. Clinically this was obviously a very unfavourable case. A burr hole was made over the centre of the focus, and

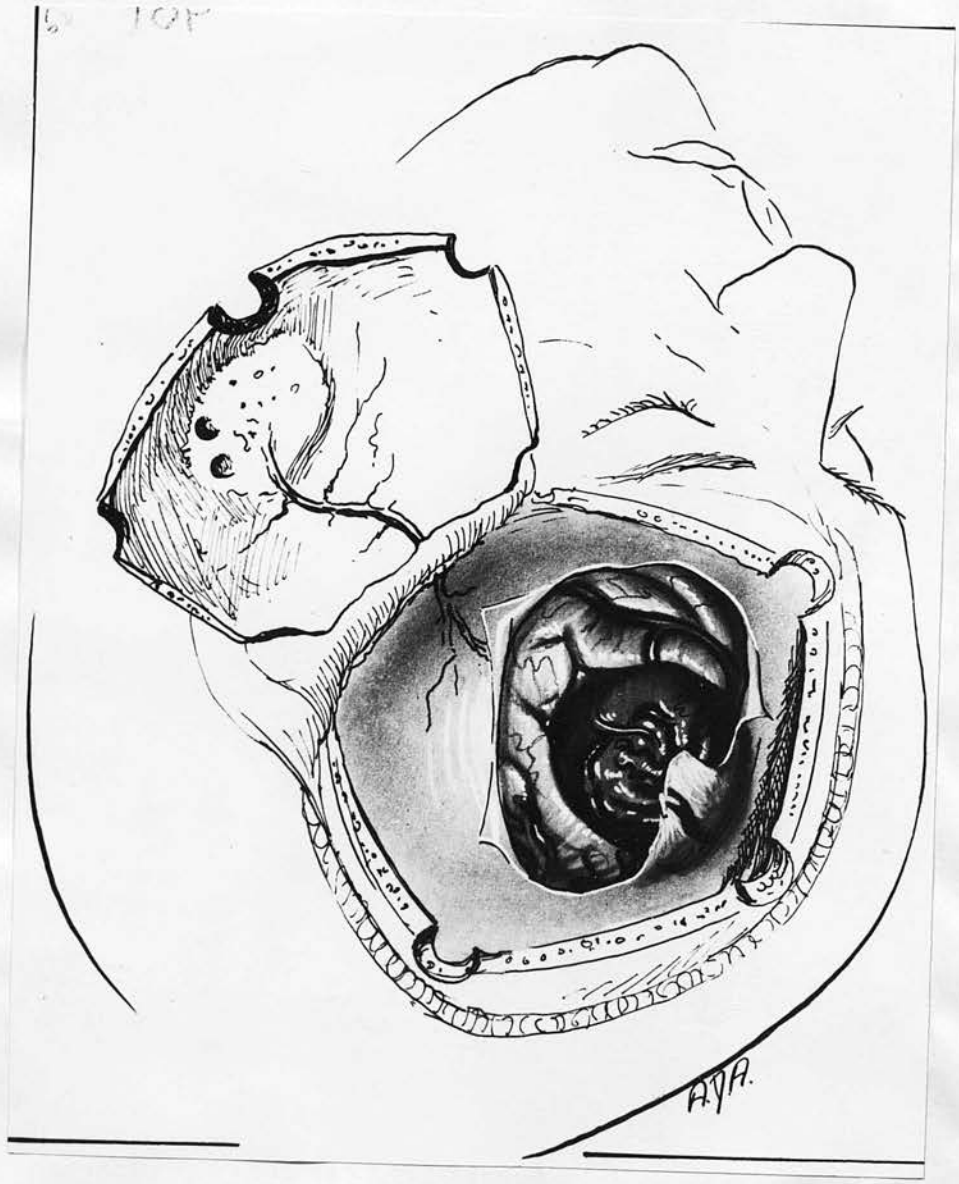


Fig. 12.

a portion of tumour tissue aspirated from a depth of 6 cms. Microscopically this was seen to be a very malignant type of glioma, and therefore nothing further was done.

We have now examined 23 cases of the multiforme group which includes also the spongioblastomas, the astroblastomas, in fact all the glioma forms apart from the astrocytomas, and the oligodendrocytomas which will be considered separately.

In all the cases in the multiforme group there was a profound disturbance of the electrical rhythm. Accurate localization was made in 21 out of the 23 cases. In the two instances in which localization was not made, the tumours were very large, and the patients were in extremis on admission. Grossly abnormal waves but without localizable focus, were picked up in both. The administration of hypertonic saline intravenously would probably have quietened things down sufficiently to enable localization to have been made.

I have come to consider that the electrical changes as exemplifed by the above records, are highly characteristic of the malignant gliomas. It will be seen, however, when we have considered the meningiomas and the abscesses, that the pathological diagnosis is in each instance modified by a consideration of the clinical history.

(b). Meningiomas.

Three cases of meningioma are included in the series. The electrical changes have been found to be in all respects similar to those encountered in the multiforme group. In two of the cases the tumour was very large, but in the

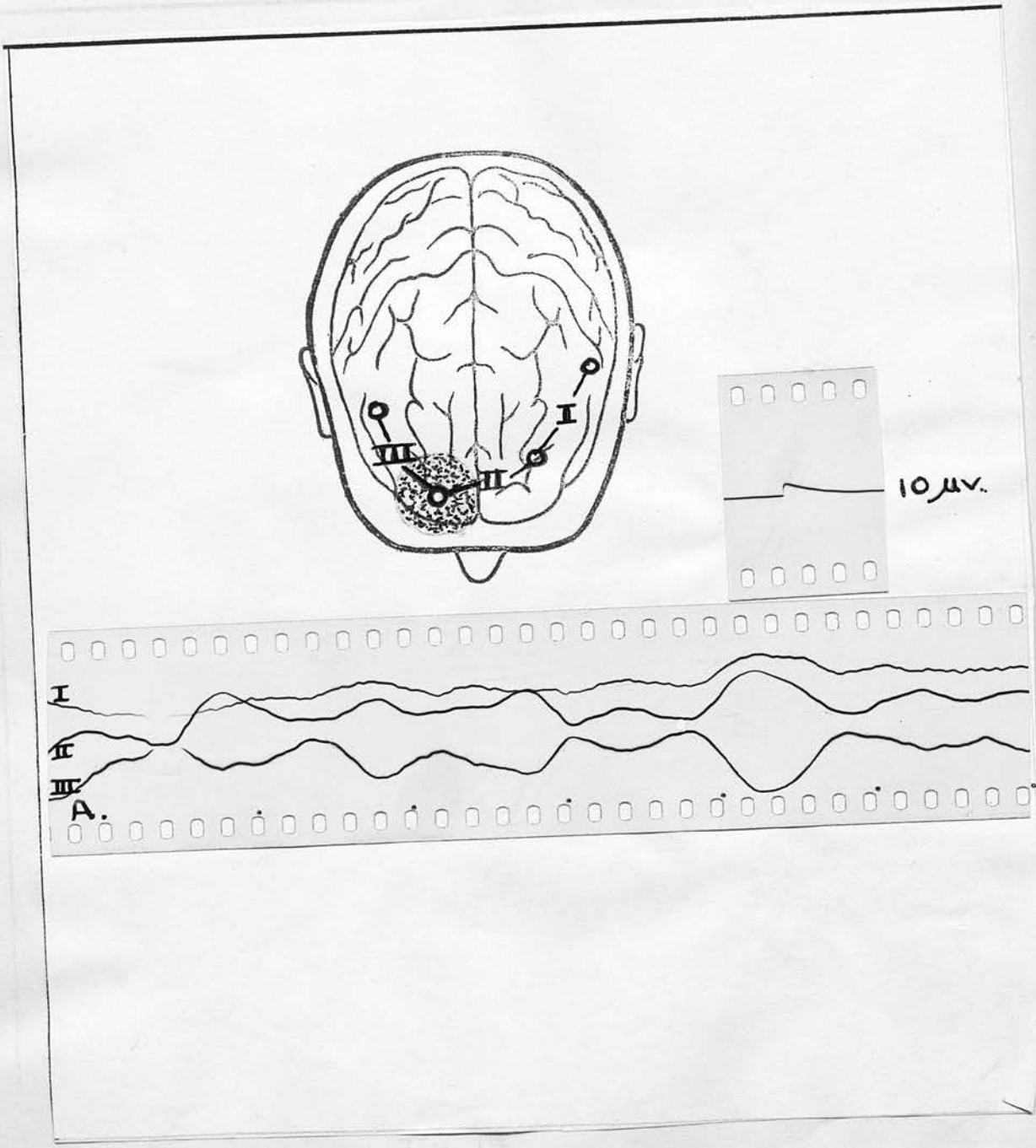


Fig. 14.

third was quite small as can be seen in Fig. 12., a sketch made at operation.

Fig. 13., is the electroencephalographic record made before operation. The localization, and the large slow delta discharge are clearly demonstrated in the record. The patient K.W. aged 45, had a history dating back some three years.

The significance of these findings will be more apparant when we have considered the astrocytoma group.

(c) Abscesses.

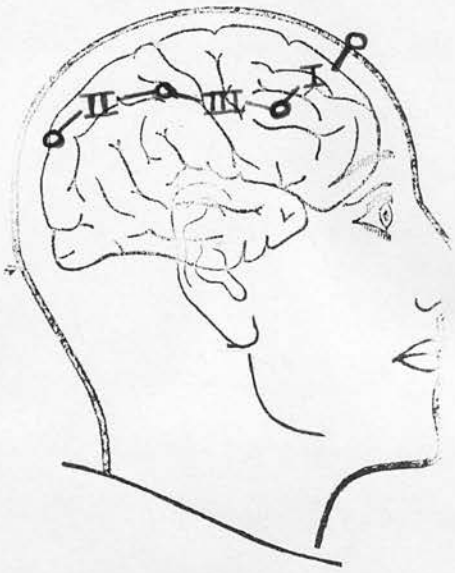
Three cases of brain abscess were examined. Here again the changes are very similar to those found in the multiforme group. Localization was accurately established in all three cases, and, clinically, abscess was suspected in each.

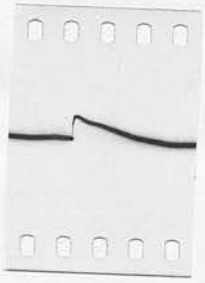
Two were of otogenic origin, and in the other the infection was probably blood borne.

Fig. 14. Record from a young man aged 19, who was sent up with a history of scarlet fever 5 weeks previously. His convalescence had been characterised by headaches, and in the fortnight before admission, these had become increasingly severe, and he had become progressively more drowsy. On admission he was difficult to rouse, and was quite unco-operative.

He had intense bilateral papilloedema. There was a very slight left-sided motor weakness, the left abdominal reflexes were absent, and both plantars were extensor in type.

Clinically, one was not able to do more than to place the lesion in the right hemisphere. The electro-encephalogram Fig. 14., showed a slow , high amplitude δ discharge from the right frontal pole. Operation was carried out immediately, a right frontal





10 μV.

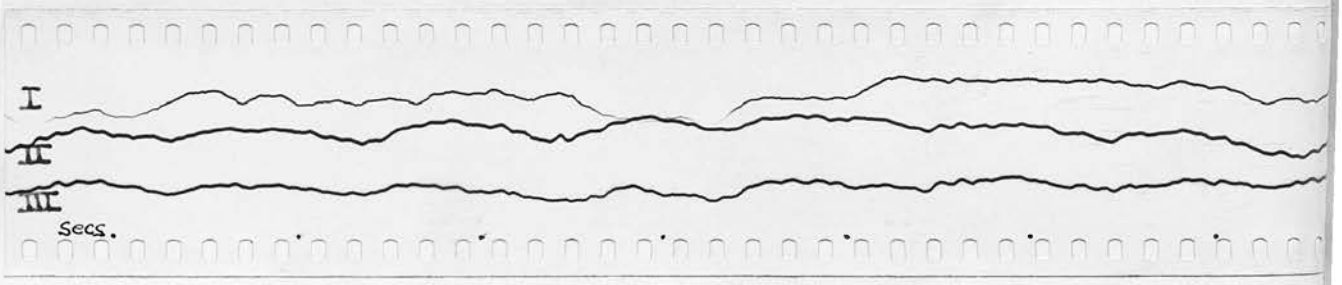


Fig 15.

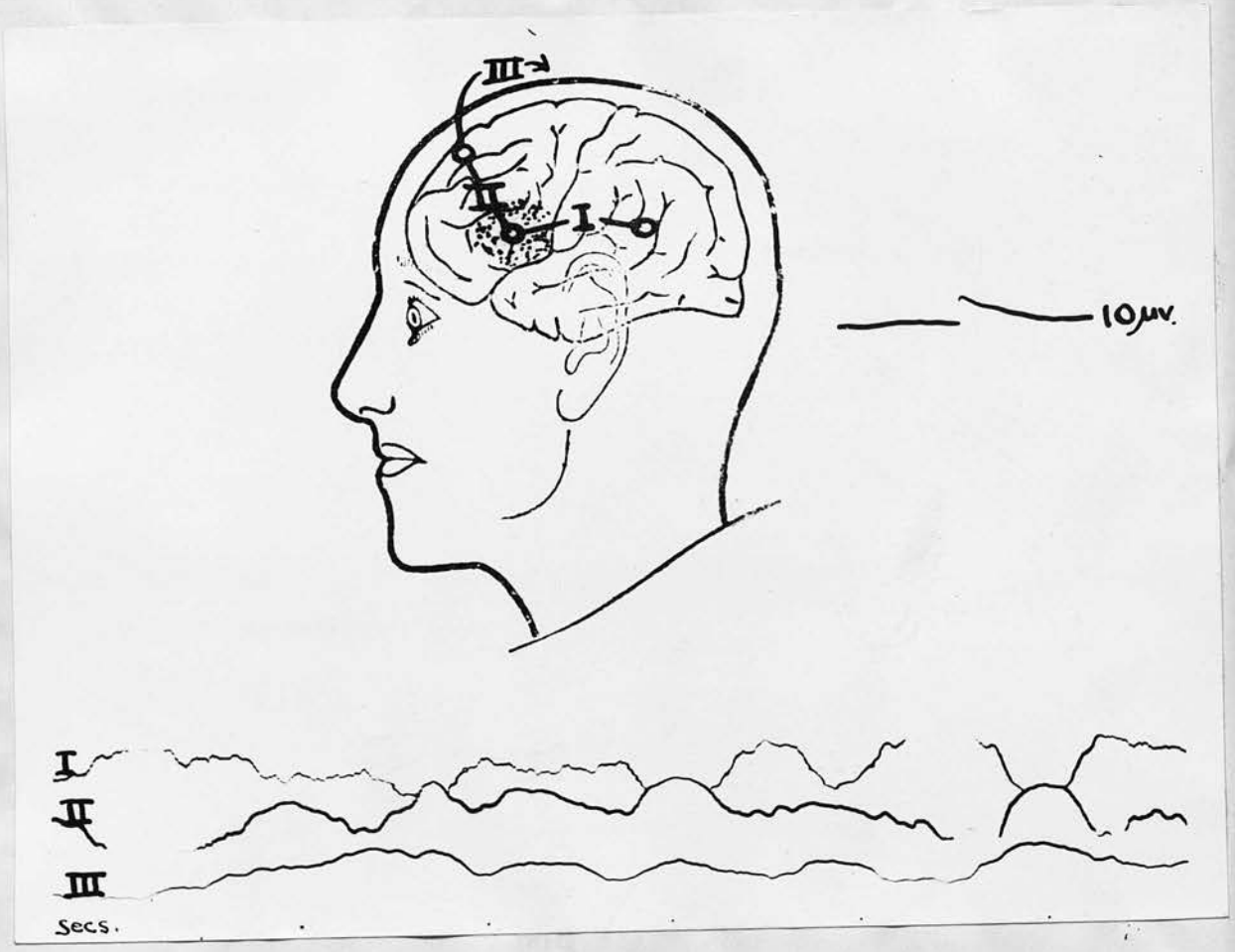


Fig. 16.

flap was turned and a large abscess found and aspirated. At a later stage the abscess was completely removed, and the boy made an uninterrupted recovery.

1) Astrocytoma Group.

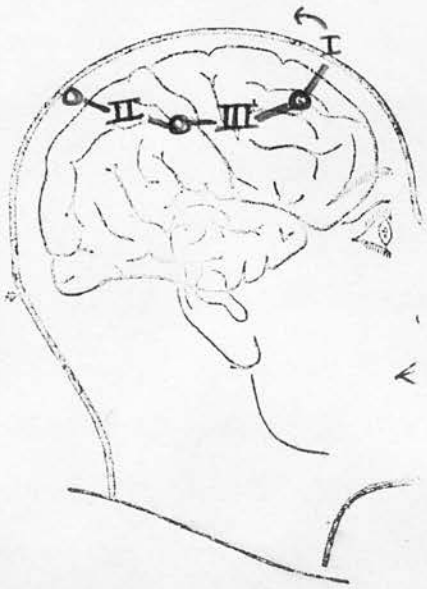
Seven astrocytomas have been examined. In two of these in which the tumours were very large, and associated with cyst formation, changes not unlike those associated with the previous groups were encountered. The findings in the remaining five cases were quite different as will be seen from the following examples.

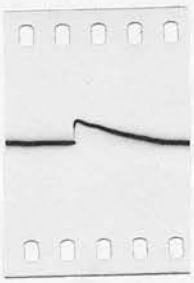
Fig. 15. J.D. a man of 32 years, had been having Jacksonian attacks for about 18 months. The attacks always started in the fingers of the left hand, and would go on to involve the left side of the body. There was no loss of consciousness associated with these episodes.

Previous air studies pointed to a right post central lesion. I was not able to detect any abnormality of the cortical potentials even after repeated examination. At operation a post central astrocytoma, in part superficial, but extending to a depth of 5 cms. was removed.

The next example indicates the sort of change encountered in the the other four cases of astrocytoma.

Fig. 16. J.H. a male, 52 years of age. He was admitted complaining of headaches vomiting and fits. On examination he was found to have papilloedema, and some mental deterioration, but no localizing signs to indicate the site of the lesion. On the basis of the mental changes, and the absence of other signs it was thought that the tumour was frontal, but there was not the





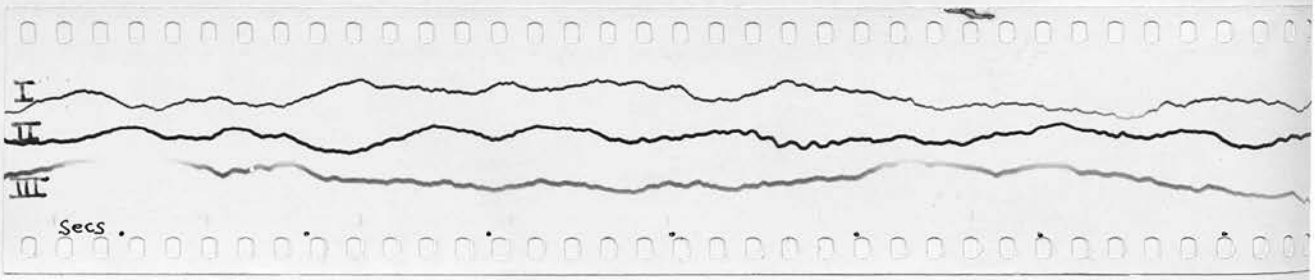


Fig. 17.

slightest clinical evidence of its lateralisation. The electro-encephalogram showed a slow low amplitude originating from low down in the left frontal lobe. Very high gain had to be employed to detect the abnormal changes, and if the searching electrode was moved a couple of centimetres one way or another, no abnormality could be detected. At operation, later, the site of the lesion was verified, and a firm astrocytoma was completely removed.

(e). Oligodendrocytomas.

Up to the present time we have had the opportunity of examining only two cases of this group. Calcification was visible in the X.rays in both instances. The one was an extremely large left hemisphere lesion extending from the frontal pole right up to Rolando. In this case a small focus of low amplitude was found low down in the frontal region. As in the previous case, if the searching electrode was moved even a small distance from the focus, no abnormality could be detected.

The other case was also a left frontal lesion, but of smaller dimensions. No abnormality of the electrical rhythm could be found.

(f). Porencephalic cyst.

Fig. 17. M.R. a woman aged 48 years. She had been having Jacksonian attacks starting in the left arm for the past four years. At times the attacks were associated with loss of consciousness. Air studies in this case revealed a large post-central porencephalic cyst in the right hemisphere.

I had the opportunity of examining her on many occasions, both before and after attacks, but was not able to detect any

abnormality of the electrical behaviour.

(g). Tuberculoma.

One case of supra-tentorial tuberculoma has been examined electrically. The lesion was a paraventricular tumour lying adjacent to and bulging into the anterior horn of the left lateral ventricle. At operation a left frontal flap was turned, and a small very hard tumour which proved to be a tuberculoma was removed. The cortical action potentials were normal in all respects. I do not know whether the absence of abnormal electrical changes can be related to the site of the lesion, or to its pathological nature.

h). Subdural Haematomas.

Two cases of subdural haematoma have come under the electrodes. Both were confirmed at operation. The cortical potentials were normal in both instances despite the fact that in both cases there were gross focal and general neurological signs.

The one case was particularly interesting. The patient was a man of 31. There was no history of head injury, and clinically a left temporal multiforme was suspected. Against the diagnosis of multiforme was the fact that the electro-encephalogram was normal. The fact that at operation this turned out to be a subdural haematoma is, I think, a point of some significance.

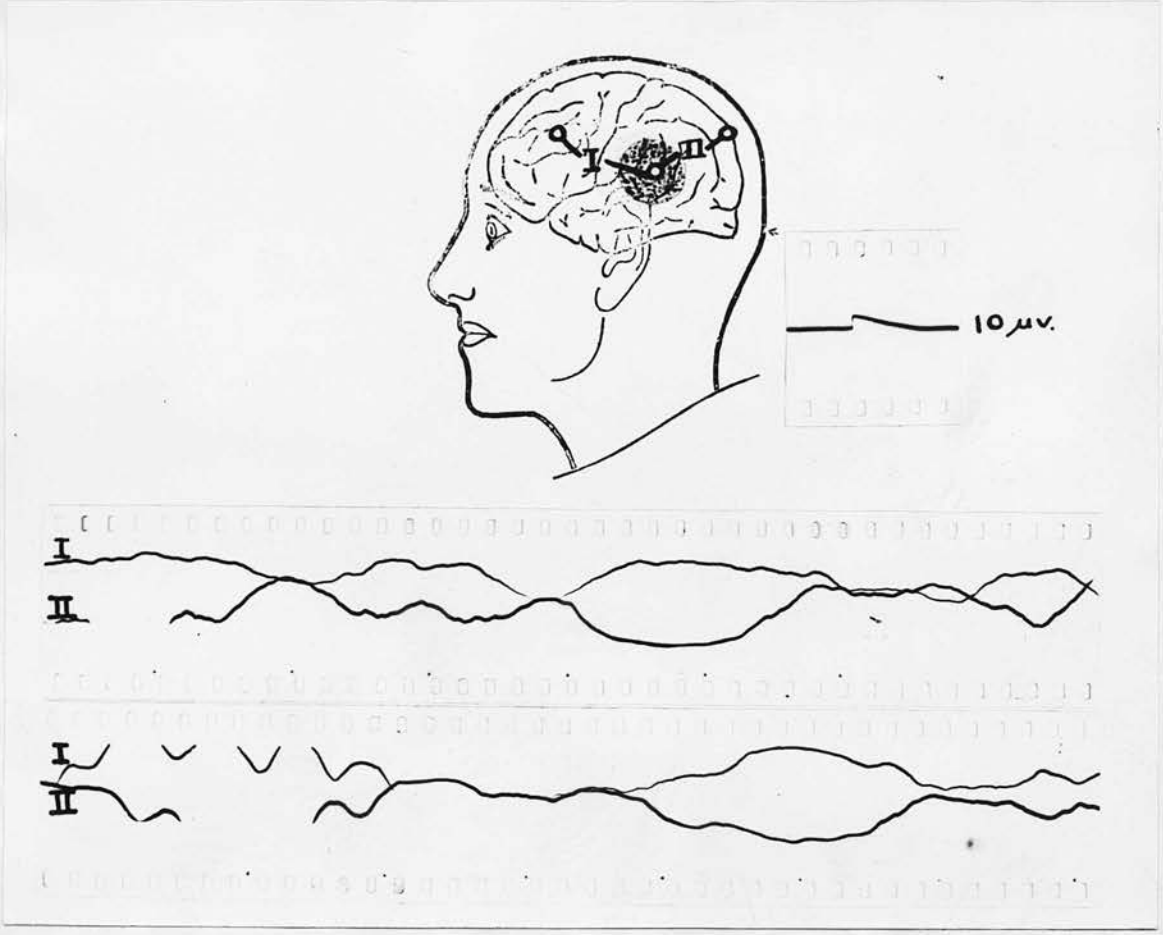


Fig. 18.

(B). Head Injuries.

Nineteen head injuries have been examined electrically. I have not yet reached the stage of being able to make a detailed analysis of this group. There are too many variants, and the series is still much too small to cover the many points which would arise in a critical survey. For instance, the examination of a case of simple concussion would necessitate a consideration of the cortical potentials while the subject was still unconscious, and again at fixed intervals after consciousness had been regained. It is an aspect of the work which I think would well repay further study. I had hoped to devote most of my time during the coming year to a detailed consideration of the head injuries, but there is now very little chance of my being able to do so.

It has been claimed that no abnormalities, or at least detectable abnormalities of electrical behaviour, are to be found in association with the head injuries. We have found, however, that in a certain percentage of recent head injuries, namely, those in which there is evidence of focal damage; there are definite, though exceedingly slow, alterations of potential which can be localised to the region of the damaged cortex.

The following is an example of such a case:- Fig. 18., I have chosen this particular example because the patient came to operation, so that we have actual and not presumptive evidence of the pathological state. The record is taken from L.K., a man of 28, who was admitted to hospital having been involved in a road accident. He was unconscious on admission, and only regained consciousness after some 24 hours. X. rays demonstrated fractures of the vault of the skull. On examination it was

found that he had a profound degree of expressive aphasia. This was evidence of focal damage in the left hemisphere, probably in the region of the temporal lobe. The electrical changes encountered are seen in the record. The outstanding feature is the extremely slow rate of the potential flux. The rate of the changes is much slower than my amplifiers can be expected to handle with any degree of accuracy. The picture, therefore, apart from indicating that very slow potential shifts are occuring, does not in any way represent the true nature of these changes when considered in terms of the wave form. I have encountered similar changes in several cases in which there was evidence of focal damage. Considerable modification of the amplifier system will be necessary before continuing the investigation of this group of cases.

With regard to the late complications of head injuries, up to the present I have confined my attention to those cases in which epilepsy has developed as a sequel to the injury, and propose, therefore, to discuss the findings when considering the question of the epilepsies.

The very slow potential shifts which we have found in association with recent focal cortical damage, is, I think, further evidence that there is, within certain limits, an electrical pattern which is more or less characteristic of pathological differences.

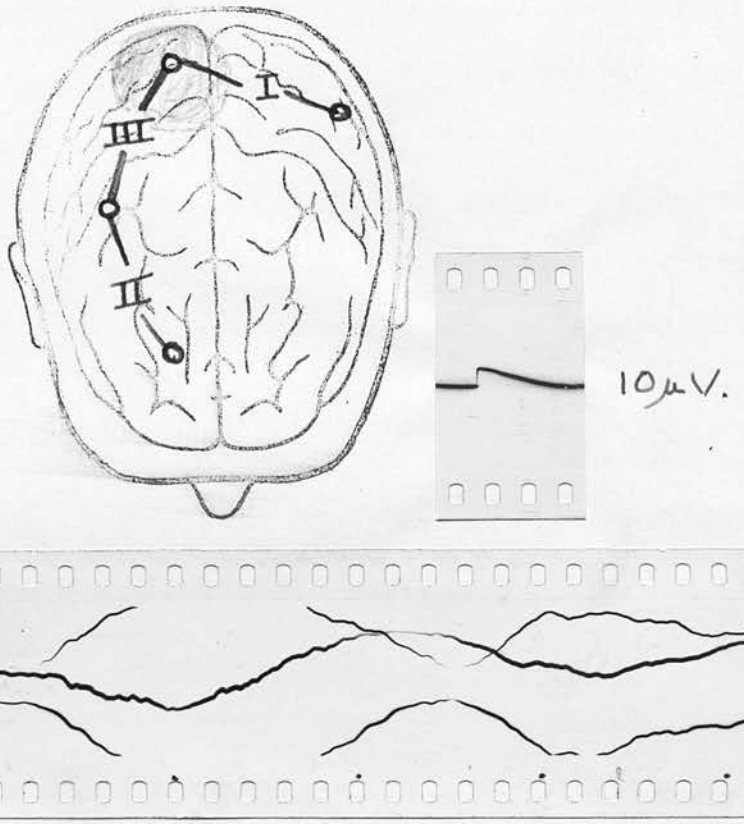


Fig. 18.

(C). Vascular abnormalities and accidents.

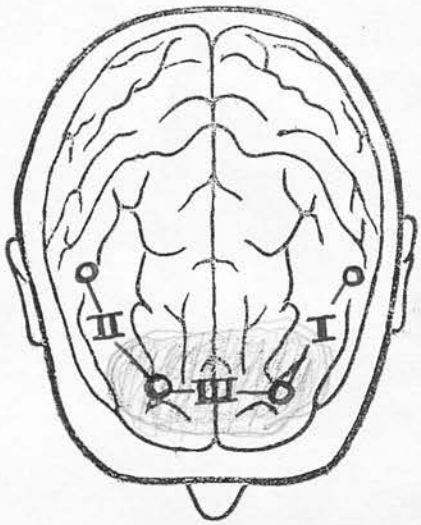
Several patients with known vascular abnormalities, and some who have had vascular accidents have been examined. Here again the series is too small to allow of a detailed analysis. The results in this group have been most erratic, varying from no detectable abnormality on the one hand, to very dramatic changes on the other hand.

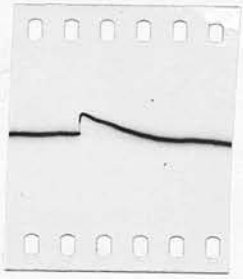
Two cases of ruptured aneurism with profuse subarachnoid haemorrhage were examined, and both were normal from the electrical point of view.

One young man with a profound but recovering hemiplegia, was found to have very large delta waves coming from the whole of the affected hemisphere.

One man with a large left parietal angiomatous malformation was electrically normal, while another patient with a similar condition in the right occipital region was found to have very slow large alterations of potential from that region.

Fig. 18., is the record taken from this last case. Another patient with a profound almost pure nominal aphasia following on what was probably a thrombosis, had a definite focus of abnormal activity situated over the left temporal region.





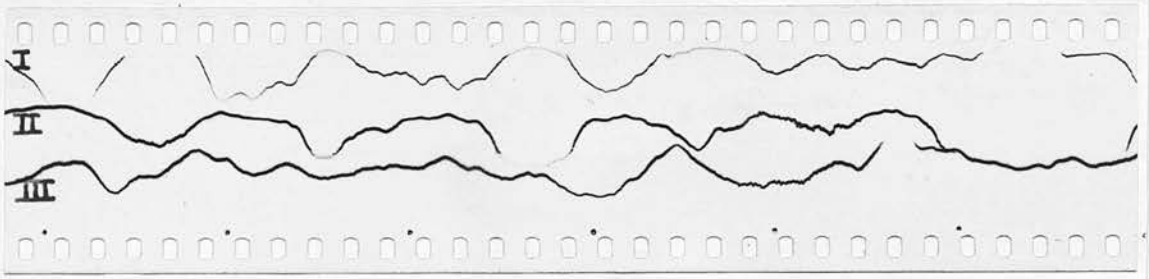


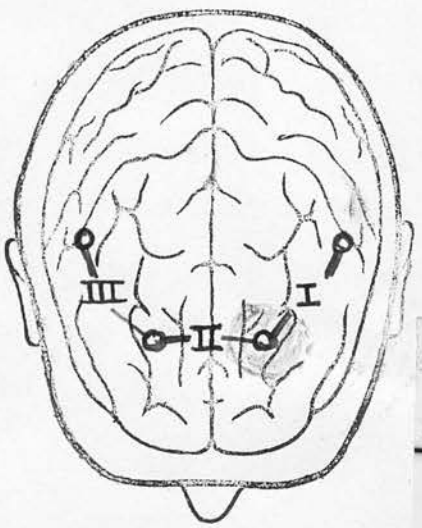
Fig. 19.

(D). Degenerative Processes.

I do not intend dwelling at any length on this aspect of the subject; but there is one record, Fig. 19., which is of interest in the light of the pathological findings.

The disturbance, as will be seen from the record, is in all ways similar to those which we have come to associate with the multiforme group. The disturbance in this case can be seen to be coming from both frontal lobes which appear to be acting in unison. After a protracted illness, in which she became progressively more and more demented, the patient, a woman of 48, died. At autopsy, an advanced degree of cortical atrophy was found in both frontal lobes. The brain in the atrophied area was tough and shrunken. It is certain that oedema could not have played a part in the production of the abnormal potential shifts which were encountered in this instance. I am not prepared, at this early stage, to advance any hypothesis as to the cause of the abnormal changes encountered in this case. The case is interesting in the light of our experience with epileptics; for we have found that young epileptics who show clinical evidence of mental degeneration, are invariably those who show abnormal electrical changes. The potential shifts in these cases are always of high amplitude, sometimes appearing to come from the entire cortex, and at other times showing multiple foci of origin.

Fig. 20. R.B. a boy of 19, who for ten years had been having numerous grand mal seizures. There were unmistakable signs of a slowly progressive dementia. Several foci of disturbance could be detected. The most obvious and persistent focus was



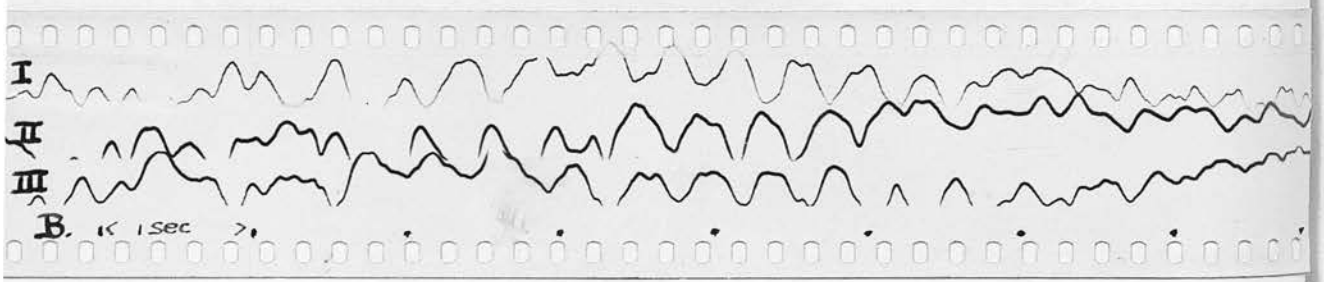
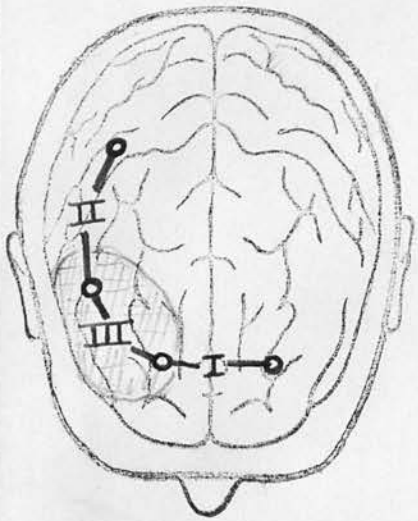


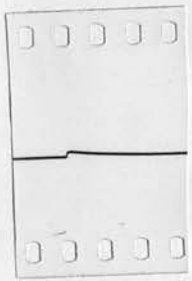
Fig. 20.

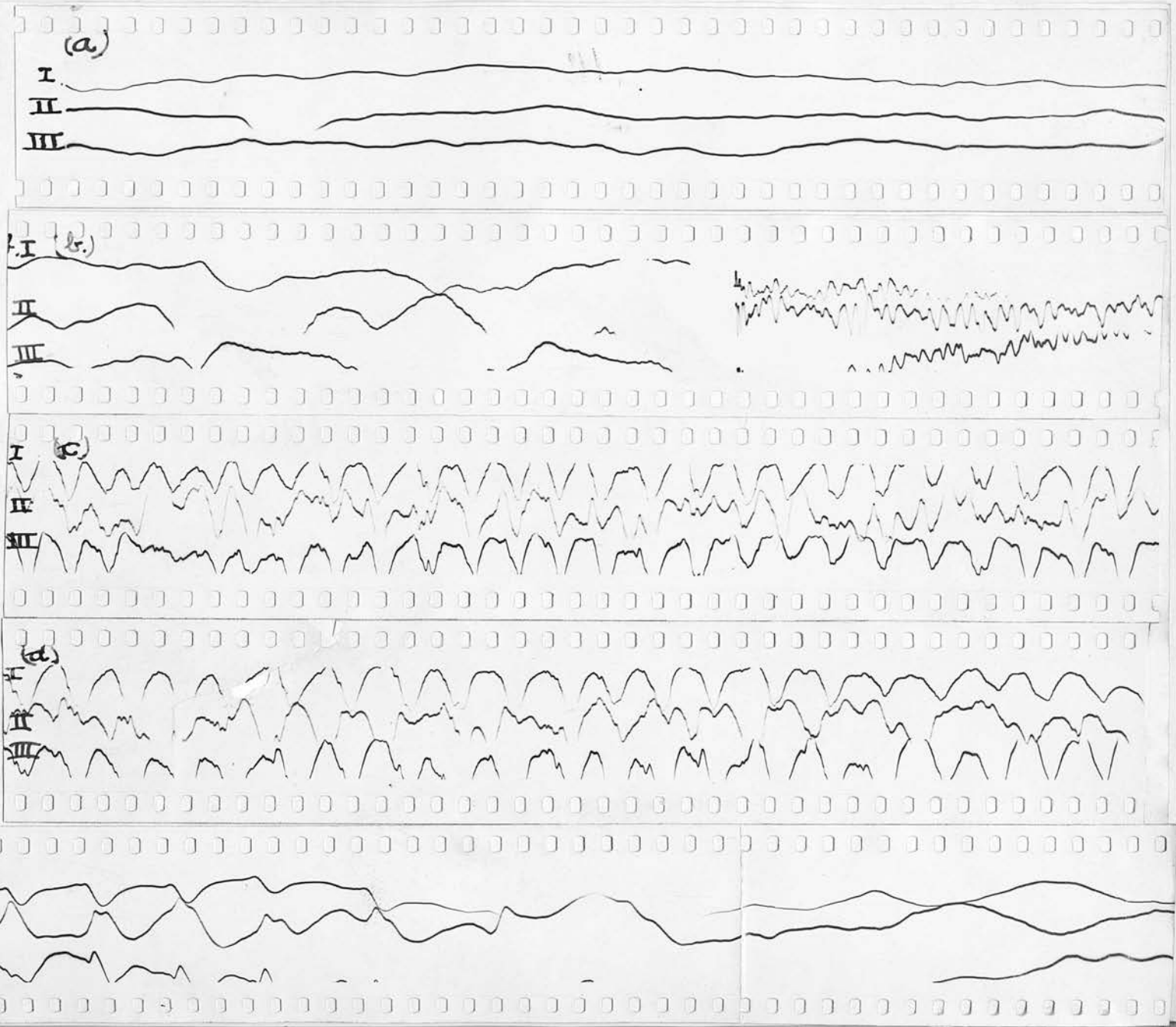
in the region of the left frontal adversive field, but even this was liable to sudden shifts of several centimetres. At other times the focus would suddenly appear in a corresponding position in the opposite hemisphere.

So marked have been the changes in those cases with evidence of degeneration, that I am inclining towards the view that the " resting focus " in the so-called idiopathic epilepsies is an index of localised degeneration, rather than of a pre-epileptic electrical instability. In other words the focus is a "post hoc" affair, and is not the local form of a major electrical catastrophy.

Fig. 21.







(E). The Epilepsies.

A full consideration of this group is not within the scope of this thesis, the object of which is to show that, within certain limits, there is an electrical pattern associated with pathological differences.

I propose, therefore, to limit the discussion to the types of changes encountered in various epileptic manifestations.

The most characteristic electrical pattern encountered in this group, is the dramatic change associated with an actual seizure.

Fig. 21., is the electrical record of a fit, taken from a man of 50, who was admitted to the ward having numerous major seizures. The clinical course of the fit was as follows:- there was no aura, and no cry at the commencement of the episode: the first indication of an attack was deviation of the head and eyes to the left: after a second or two, this was followed by a stiffening of the left arm and leg. Then clonic movements would suddenly start in the left arm, and spread rapidly to involve the entire left half of the body. Loss of consciousness occured with the initial deviation of the eyes to the left. Before the end of the fit the clonic movements spread to the right half of the body. After this the movements gradually became slower, and finally passing off, but persisting longest in the left arm.

The record has been cut into strips for convenience of reproduction. The amplifier gain used was extremely low, as will be seen from the gain strip which indicates the deflection produced by an input of 25μV.

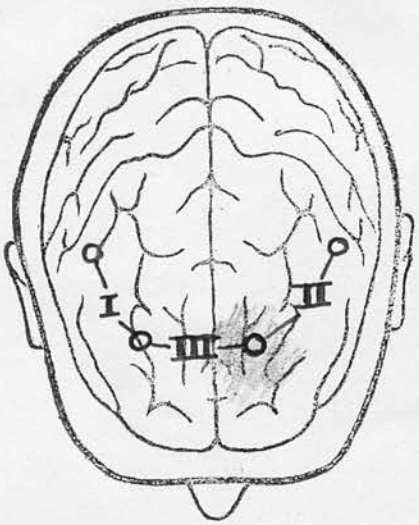
The top strip, (a) shows the normal quiet activity prior to

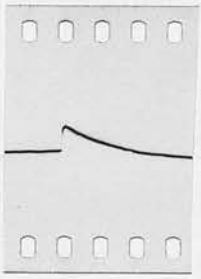
the onset of the fit: in (b), there is at first a slow irregular flux, and then, quite suddenly, and coincident with the deviation of the head and eyes, we see the onset of the rapid seizure waves. It will be noticed that the waves in the top two traces, (amplifiers I, & II.) are out of phase, thus indicating the origin of the disturbance to be from a large area, as is indicated in the diagram. In strip (c), we see the progress of the fit in the clonic stage when the whole cortex is firing in unison, the waves in all three leads being"in-phase".
In strip (d), we see the continuation of the clonic stage, but with the difference, that leads I, & II, are again out of phase, and clinically at this stage the twitching was confined to the left half of the body. In the final strip (e), we see the gradual slowing down of the discharge finally trailing off into relative quiescence.

Idiopathic grand mal.

It has been claimed that many, if not most, patients suffering from that form of epilepsy known as idiopathic grand mal, show, even in the intervals between seizures, a focus of delta discharge. This "resting focus", as we have termed it, is usually found in one or other frontal adversive field, (area 6aβ of Vogt.), although at times the focus may be found far back in the parietal, or occipital regions.
Walter pointed out that such a focus was seldom present in people over the age of forty.

Our experience is that relatively few cases of idiopathic epilepsy in which there is no evidence of degeneration, exhibit any " resting focus" of abnormality. As I have already indicated





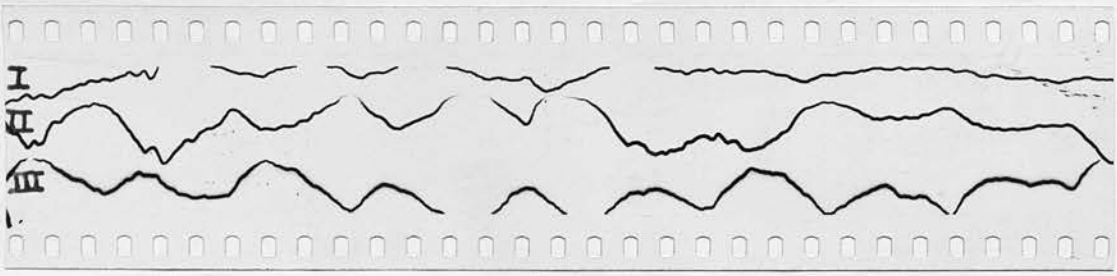
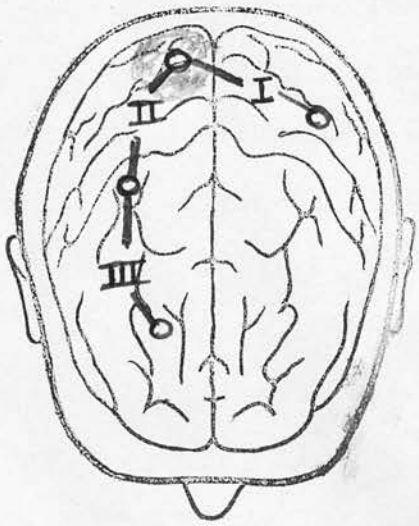


Fig 22.

the focus when present, may be an indication of some degenerative state secondary to damage done at the time of the seizures.
We have, however, encountered many cases in which there was no definite evidence of cortical degeneration, and in which a "resting focus" was encountered in one or other adversive field.
Fig. 22., is the record taken from a boy of 16. He had been having major seizures for about five years. The focus of delta waves emanating from the region of the left area 6aβ of Vogt is clearly seen in the record.
The presence of a resting focus is , I think, an indication of the point at which the main force - speaking electrically, - of the seizure strikes.
It has been shown that the actual seizure discharge starts from the region of a resting focus, before spreading to involve the entire cortex.
Whether the presence or absence of a resting focus has any prognostic significance it is still too early to say. It is certain, however, that this aspect of the subject is full of interesting possibilities.

Petit mal.

The electro-encephalographic findings in people suffering from petit mal have been well described by Gibbs, and his co-workers. These workers have considerable stress on the wave form in these cases.
It would appear that, in petit mal, there is an almost constant electrical flux with occasional sudden bursts of increased activity which have been described as larval, or subclinical seizures.



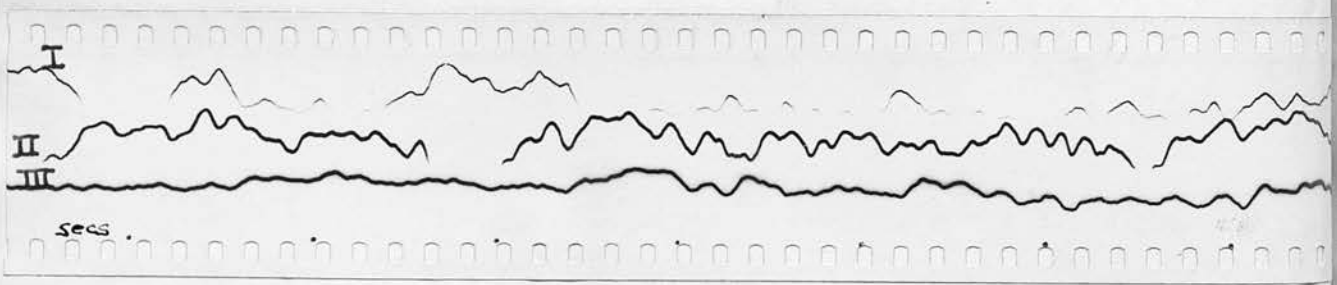


Fig. 23.

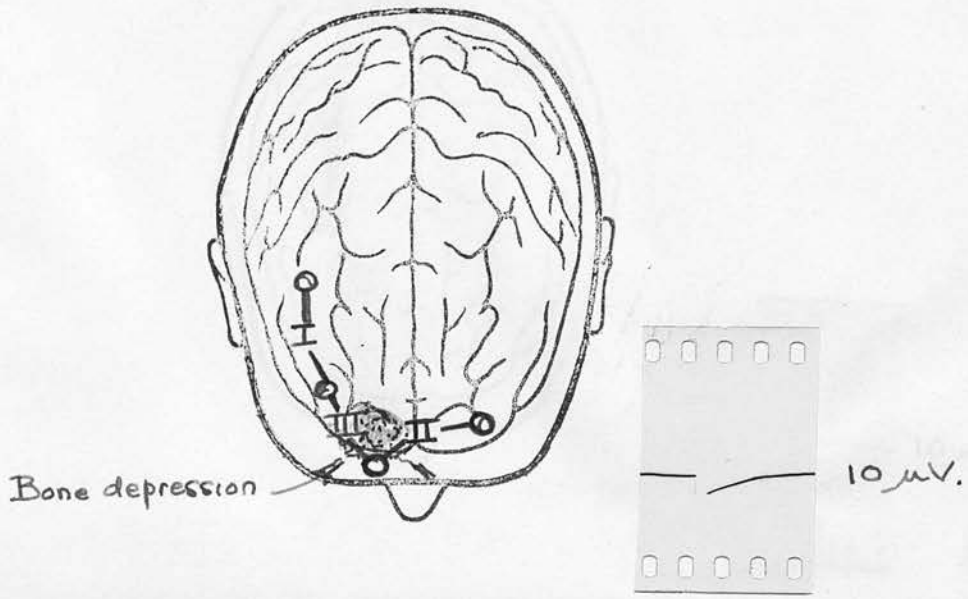


Fig. 24.

Fig.23., R.G., a boy of 12, who was having numerous petit mal attacks during the course of each day. The focus of disturbance was found far back in the occipital region.

Traumatic Epilepsies.

It has been claimed that in the group of epilepsies which occur as a sequel to head injuries, there is never a resting focus of abnormality. Walter has claimed that it is in this respect that the traumatic epilepsies differ as a group from the idiopathic epilepsies. Such generalisations are apt to be misleading, and, should they be accepted as authoritative, might lead to considerable confusion in cases where it is of legal importance to establish a diagnosis. Our experience would indicate that too few idiopathic epilepsies have a persistent abnormal rhythm to make its presence diagnostic of the group, or its absence indicative of a specific etiology. We have now seen several cases of epilepsy where trauma has undoubtedly been the responsible etiological factor, and in which there was a persistent and localizable focus of delta discharge. The following records are examples of such instances.

Fig.24., H.B., a man aged 40., who had sustained a compound fracture of the skull some twenty years previously. For about 15 years he had been having fits at intervals of 2 - 12 months. On examination, he was seen to have (a depressed fracture) in the centre of his forehead in the region of the frontal air sinuses. The electro-encephalogram revealed a focus of abnormal discharge of low amplitude from the tip of the right frontal pole. The focus, did, in fact coincide with the centre of the depression. I considered this to indicate an area of underlying

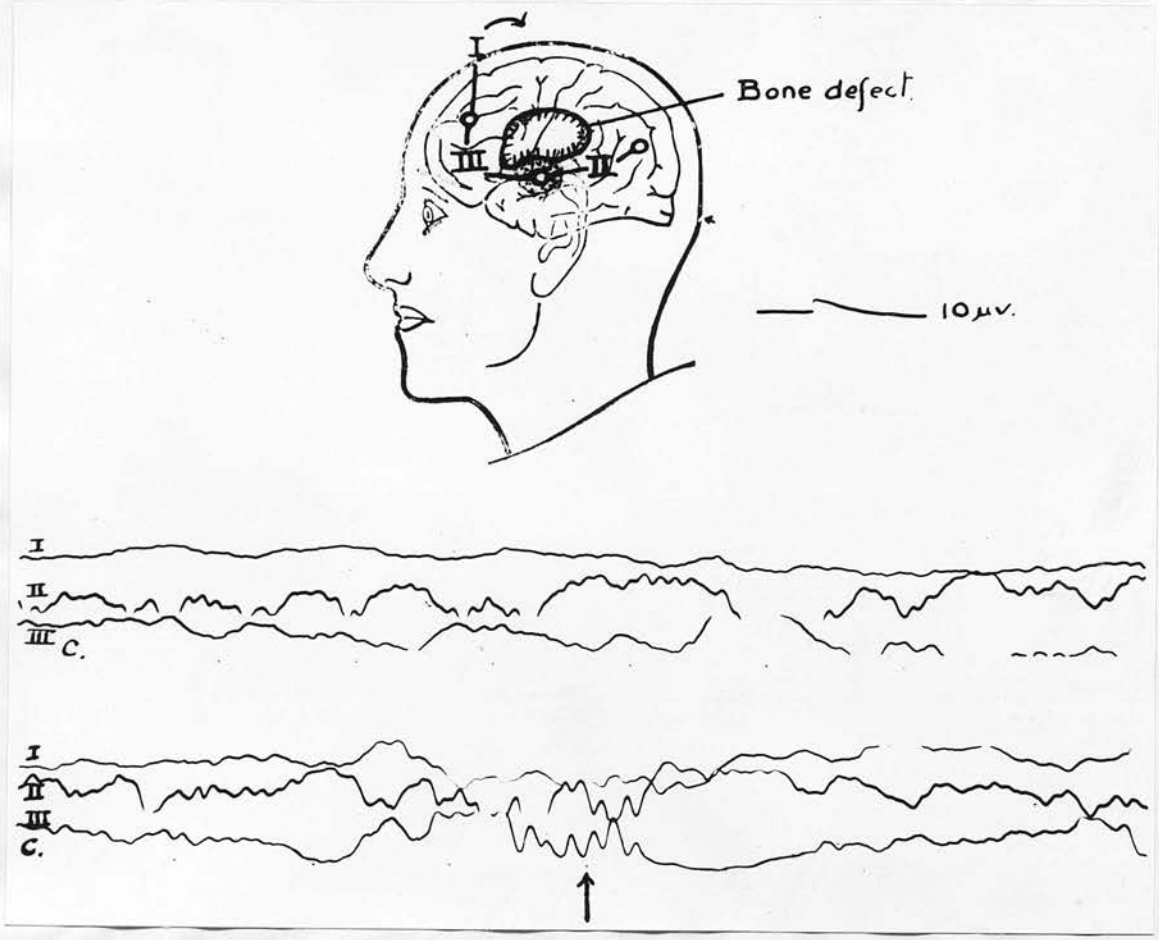


Fig. 25.

gliosis which in turn was producing a degenerative effect on adjacent nerve cells. With this in view an operation was decided upon with the idea of excising the area of gliosis.

A right frontal flap was turned . When the dural was opened, it was found to be adherent to the cortex at the right frontal pole, over an area 3 X 3.5 cms. The area of cortex was seen to be shrunken and atrophic, and was accordingly excised to a depth of about 3 cms.

Fig. 25., this record was taken from a young man of 25 who had had a penetrating injury in the left temporal region five years previously. Depressed bone fragments were removed at the time of the injury, leaving a bone defect on the left side of the skull, as is indicated in the diagram accompanying the record. A year after the injury he started having fits which recurred at intervals of 1 - 3 months. Apart from these major episodes he was almost constantly troubled, but more especially when he was alone and in the dark, by word hallucinations. To use his own words, "it is just as though hundreds of haphazard meaningless words are running through my head".

On examination, he was found to have a slight but definite nominal aphasia. The record shows a definite focus of abnormality emanating from just below the lower margin of the bone defect. The point which particularly interested me was that, on examining the record, one saw, every now and again, sudden bursts of waves which suggested to my mind the subclinical seizures of petit mal. The arrow on the record indicates one of these bursts of waves. An area of this sort, with its sudden electrical exacerbations, was, to my mind, clearly

an epileptogenic area, probably consequent upon cyst or scar tissue formation.

Operation was decided upon, and a left lateral flap was turned. The superficial tissues in the region of the bone defect was adherent to the underlying cortex. Below this, and in the region of the superior temporal gyrus, a multilocular cyst formation was encountered. A complete excision of the lesion would have been the procedure of choice, had not the site necessarily precluded anything in the way of radical surgery. We had to content ourselves with opening up, and aspiration of the cysts.

REFERENCES.

(1). Caton,R. (1875). Brit.med.J., 2,951.

(2). Prawdicz-Neminski,W.W.(1913). Zbl. Physiol., 27,951.

(3). Berger, H. (1929).Arch.psychiat.Nervenkr., 87,527.

(4). Adrian,E.D.,and Matthews,B.H.C.(1934).Brain, 57,355.

(5). Kornmuller,A.E. (1937). Die Bioelectrischen Erscheinungen der Hirnindenfelder. Georg Thieme, Leipsig.

(6). Adrian,E.D., (1933). J.Physiol., 83,32.
(1936). Ibid. 87,83.
(1936). Ibid. 88,127

(7). Adrian,E.D.,and Matthews,B.H.C.(1934).J.Physiol.81,440.

(8). Gerard,R.W. (1936). Arch.Neurol.Psychiat., 34,1133.

(9). Rheinberger,M.B.,and Jasper,H.H. (1937). Amer.J.Physiol., 119,186.

(10).Walter,W.G. (1936). Lancet, 2,305.

(11).Gibbs,F.A.,Lennox,W.G.,and Gibbs,E.L. (1936). Arch.Neurol.Psychiat.,36,1225.

(12).Bremer,F.(1936).Compt.rend.Soc.de biol., 121,861.
(1936). Ibid. 122,464.
(1936). Ibid. 123,90.

(13).Case,T.and Bucy,P.C.(1938).J.Neurophysiol.,1,245.

(14). Cazzamalli,F. (1935). Arch.int.Neurol.,54,113.

(15).Jasper,H.,Andrews,H.L.(1938).Arch.Neurol.Psychiat.39,96.

(16).Loomis,AL.Harvey,E.N.,Hobart,G.(1937).Science,86,448.

(17).Gibbs,F.A.,Williams,D.(1939).Arch.Neurol.Psychiat.41,519.

(18).Krynauw. R.A. (1939). Brit.med.J., 2,160.

(19).Walter,W.G. (1938). J.Neurol.Psychiat.,1,359.

(20).Matthews,B.H.C. (1938). J.Physiol., 93,25P.

(21).Balado,M. (1939). Arch.Argen.de Neurol.

(22). Walter,W.G. (1938). J.Neurol.Psychiat.,1,359.