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Part I.—Original Articles.

THE ELECTRO-ENCEPHALOGRAM IN EPILEPSY.

By F. GOLLA, F.R.C.P., S. GRAHAM, M.B., B.S., D.P.M., and W. GREY WALTER, M.A.Camb.

(From the Central Pathological Laboratory of the London County Hospitals for Nervous and Mental Disorders.)

IN 1929 Berger (1) discovered that changes of electrical potential in the human brain could be detected through the unopened skull. Since that time the study of electro-encephalography has occupied the attention of many workers, and the literature is already too extensive for adequate review in this place. A brief description of the technique for obtaining an electro-encephalogram, or "EEG", and a summary of its normal and pathological characters may be found in a communication by one of us (2) on the relation between the EEG and the presence of intracranial neoplasms. The cortex in the region of a tumour was found to produce abnormally slow potential waves, which were provisionally called "delta" (δ) waves to distinguish them from the normal "alpha" (α) waves which are the original "Berger rhythm". In the same paper a case was reported in which a focus of δ waves was found in the left parieto-occipital region associated with an area of degenerating cortex. The history in this case was of occasional minor attacks and one major fit and an indefinite severe illness in infancy, the only sign being a right homonymous hemianopia in accordance with the left-sided focus. Ether and nitrous oxide anæsthesia are also accompanied by the production of slow waves, but in this condition there is no fixed focus, the whole cortex being engaged in abnormal electrical activity. Since the publication of the above-mentioned results, a case of cerebral abscess has been examined, and the EEG was found to indicate a δ focus similar in character to those which have been found in cases of new growth.

These findings suggested strongly that the production of slow electrical oscillations is characteristic of cortex in some stages of dystrophy or degeneration, whether this condition be set up by new growth, inflammation or any other cause.

In the course of the experiments at the Hospital for Epilepsy and Paralysis, Maida Vale, which resulted in the above observations, there was opportunity to examine 97 patients who complained of various sorts of epileptiform attack (Table I). In 39 of these patients the electro-encephalogram was found to be abnormal in so far as it exhibited a discharge similar to that associated with organic lesions of the cortex.* In 34 of these the abnormal discharge had a well-marked focus, while in 5 it consisted of a more generalized activity. In 25 cases the EEG could not be interpreted, either because a technical fault was suspected, or because the patient was so restless that no satisfactory records could be obtained. The majority of these restless patients were children less than five years old. Thirty-four patients gave EEGs which were within the normal range. The concept of the norm in electro-encephalography is discussed in the paper previously referred to ; briefly, we regard as normal an EEG which shows no regular waves of a potential greater than 5μV with the subject alert. The appearance of α waves in the parieto-occipital cortex when the eyes are open is not regarded as abnormal, although it is unusual, but the appearance of waves of this frequency (8–13 per second) anywhere but in the parieto-occipital region, or in this region when the subject is reading, is taken as an abnormal sign, since it has been found only in abnormal subjects. Actually, the only criteria which we have used to determine the abnormality of an EEG in this study of epileptics are : (*a*) The appearance of waves in any part of the cortex having a frequency of less than 6 per second and a potential with the routine leads of more than about 10μV, which are not affected by visual or mental activity ; (*b*) the appearance of waves resembling the α rhythm, but not originating in the parieto-occipital cortex and not affected by visual or mental activity. These criteria are, of course, empirical in that they are based on the fact that the characters concerned have not been found in any clinically normal subject under physiological conditions.† In the absence of an inductive explanation of the normal character of the EEG we must be content with the unsatisfactory state of the pathology of the subject. Nearly all the cases in this series were examined on several occasions. Several were examined every week for some months.

Although the number of cases included in this series is too small to provide material with statistical significance, examination of Table I yields some facts which are, at least, suggestive. Before discussing these, some explanation must be given of the terms used.

(1) " Positive heredity " indicates that the patient or a relative admits to the existence of an epileptic in the family. It is well known that comparatively few of those with a family history of epilepsy will admit it, even if they know of it, and many sufferers from epilepsy have not been told that

* This abnormal discharge should be clearly distinguished from that described by Gibbs, Lennox and Gibbs (9) as occurring during the actual course of a fit.

† Although Berger still considers that the α rhythm arises from the whole cortex, the balance of general opinion is strongly against this view.

TABLE I.—*Electro-encephalograms of "Epileptic" Patients, Series* 1. *Total Number Examined*, 97; *EEG Doubtful*, 25.

	Number of cases.	Cases with abnormal EEG.								Cases with normal EEG.
		Total number.	Position of focus.						Diffuse.	
			Frontal.			Occipital.				
			Left.	Right.	Bilateral.	Left.	Right.	Bilateral.		
Total	72	38	9	6	8	4	3	4	4	33
Heredity positive	4	4	1	2	..	..	..	..	1	..
,, negative	68	35	8	4	8	4	3	4	4	34
Age: 1–9	7	6	1	..	1	1	..	2	1	1
10–19	21	13	2	4	2	2	1	2	..	8
20–29	22	10	4	2	2	..	..	..	2	12
30–39	17	9	2	..	3	1	2	..	1	8
40–49	3	1	..	..	..	..	..	..	1	2
50–59	2	..	..	..	..	..	..	..	..	2
Nature of fits:										
Major only	28	16	4	2	6	..	..	1	3	12
Major/minor	6	4	2	..	2	..	..	..	..	2
Minor/major	10	6	..	..	..	3	1	..	2	4
Minor only	23	11	2	4	..	1	1	3	..	12
Uncertain	5	2	1	..	..	..	1	..	..	3
Age at onset:										
Childhood	31	24	5	4	3	3	2	3	4	7
Adolescence	17	6	1	2	2	..	..	1	..	11
Later life	11	2	..	..	1	..	..	..	1	9
Uncertain	13	7	3	..	2	1	1	..	..	6
Clinical diagnosis:										
Idiopathic major	15	15	5	2	2	1	2	1	2	..
,, minor	8	5	..	3	1	1	..	..	..	3
Pyknolepsy	6	6	1	..	1	..	..	3	1	..
Narcolepsy	1	..	..	..	..	..	..	..	..	1
Congenital or early lesion	5	4	2	..	..	2	..	..	..	1
Traumatic	4	..	..	..	..	..	..	..	..	4
Syphilitic	1	..	..	..	..	..	..	..	..	1
Toxæmic	2	1	..	..	..	..	..	..	1	1
Functional	17	..	..	..	..	..	..	..	..	17
Doubtful	13	8	1	1	4	..	1	..	1	5

others in the family have been afflicted with the same disease. For this reason the figures in this group should be suspected, though it may be significant that the four patients who gave a family history also gave abnormal EEGs.

(2) The majority of the cases were out-patients, so that the description of the fits was obtained from the patient or a relative. This fact undoubtedly admits of a certain amount of error.

(3) The age of onset, again, is derived from the patient or a relative. In many of the cases with onset in adolescence there was a history of suspicious convulsions as a baby, so that the number of cases with an onset in childhood is probably larger than is apparent.

(4) The clinical diagnosis is that applied by the out-patient physician or, in the case of the in-patients, the final diagnosis on discharge. Cases of cerebral tumour are not included in this series.

(5) The position of the focus in the cases with abnormal EEGs was determined with the triple amplifier cathode-ray oscillograph set-up as described in the paper mentioned above. The centre of the focus can be located to within about 1 cm., but this degree of accuracy was not attempted in all the cases, since it involves the taking of a considerable amount of film. It was considered adequate to establish in which part of which lobe the abnormality was to be found. The frontal foci were nearly all in the upper part of the frontal lobe, over the "area 6 a β" of Vogt. It is interesting that Foerster (3) attributes considerable importance to this area in the pathogenesis of epilepsy. Bilateral foci are those in which *symmetrical points* in the two hemispheres exhibit abnormal activity. The occipital foci were mostly in the regions of "area 19" and "area 7" of Vogt, except in the cases of pyknolepsy, when they were more posterior. The "diffuse abnormalities" were those with either multiple foci or with a general abnormal discharge over the whole cortex. A considerable degree of dementia was presented by two of these cases, of which one had a marked epileptic heredity; the third was in *status epilepticus*; the fourth was toxæmic, and the fifth was of doubtful diagnosis.

The fact which this table illustrates most clearly is that the majority of the cases with abnormal foci are those with an early onset of major fits to whom the diagnosis of idiopathic epilepsy had been applied, and who at the time of examination were less than forty years old. All 15 of the cases of major idiopathic epilepsy exhibited foci; none of the 17 functional cases did so. On the other hand, all 6 of the pyknolepsies also gave foci, and the fits in these cases must certainly be classed as minor. There is a marked difference, however, between the records from pyknoleptics and those from a typical idiopathic epileptic. Fig. 1 shows the discharge from the frontal cortex of an epileptic girl, æt. 12. The focus is in the region of "area 6 a β" of Vogt. The discharge is of irregular frequency and amplitude. There was a less well-marked focus in the same area on the other side. This patient had chiefly major fits, as many as three a day without sedatives, and one a day or so while

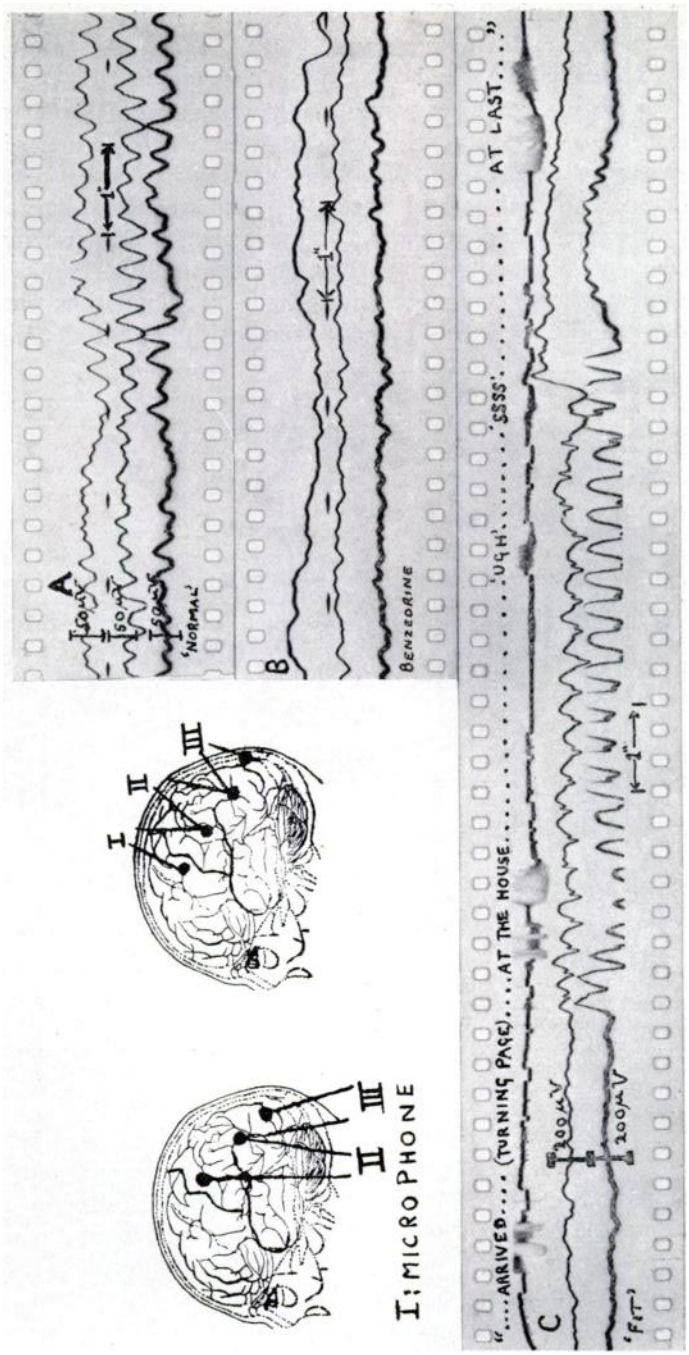

FIG. 1.—EEGs from a girl, æt. 12, with a history of frequent major fits. A. Normal, sitting quietly with eyes open. B. After 2 minutes' hyperpnœa.

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taking 2 to 3 gr. of luminal. The fits started at the age of three and had become more and more frequent and severe. There was an aura of spatial contraction. Clinically and electro-encephalographically this is a case representative of the group of young major idiopathics. Fig. 2A shows the discharge from the occipital cortex of a child of seven. This originates in the region of " area 18," and consists of large (50μV) smooth waves of a frequency of 3½ per second. This patient had very slight and frequent attacks consisting merely of vacancy and lasting for a few seconds. She usually had about ten of these slight attacks in an hour, and two or three rather more severe attacks in which she was quite unresponsive to stimulation, but still did not fall down. Fig. 2C shows the development of one of the slighter

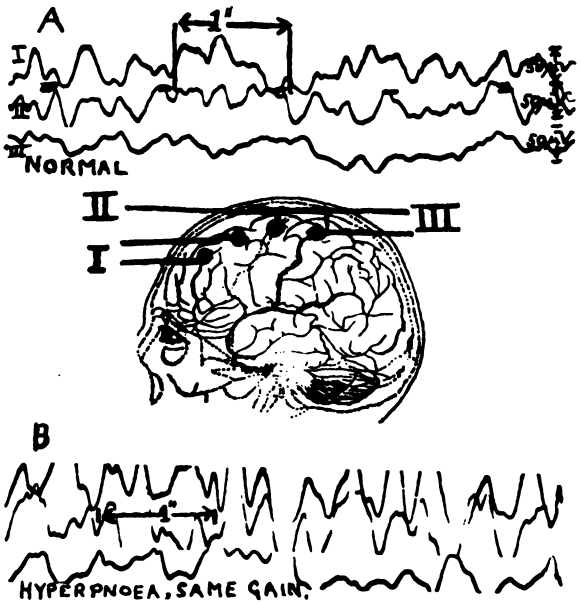

FIG. 2.—EEGs from a girl, æt. 7, with a history of frequent " pyknoleptic " fits. A. Normal, sitting quietly with eyes open. B. The same after 3 days' treatment with benzedrine. C. During the same examination as A, but with less amplification, showing the development of a minor fit. The top oscillograph shows the sounds uttered by the patient.

attacks. The top tracing is of the sound of the child's voice picked up by a microphone as she read aloud from a story-book. The second and third are oscillograph records of the EEG from the left occiput, as in the diagram. The amplification is too small to show the resting discharge. From the region of " area 18 " large waves (300μV) start, and as they spread forward the voice stops. After a few seconds the waves die down and, shortly after, the voice starts again. The patient was unaware of her lapse, and went on reading as if there had been none. In form these waves are similar to those from their

area of origin in this patient between fits, but they are about four times larger. Both " resting " and " fit " discharges resemble the waves produced by ether anæsthesia in the normal subject, and this resemblance may be connected in some way with the fact that these attacks are completely resistant to sedation with luminal, suggesting rather that a cortical stimulant might be required in this condition. Acting on this, the effect of administering benzedrine sulphate 2 mgm. *b.d.* was tried. After three days of this treatment the fits stopped completely and the abnormal waves also vanished (Fig. 2, B). This experimental treatment and the significance of its results is discussed later, and will be dealt with in full in another paper.

The next point of interest is that none of the four cases with a history of trauma gave an abnormal EEG. One case, which was examined at the suggestion of Dr. Knight, of St. Bartholomew's Hospital, was supposed to have fits as the result of a blow in the right frontal region, but showed a focal abnormality in the right occipital cortex. Although this might have been the result of a *contre-coup* injury, it seemed an anomalous finding, so the early history of the case was gone into and was found to suggest that fits had, in fact, occurred before the accident.

The cases with a congenital or early organic lesion and abnormal EEG belong to a different group. One of these was the case previously reported, which showed a left parieto-occipital focus corresponding with a multilocular cavity communicating with the ventricle. Two cases had a history of early encephalitis, and one had a congenital nævus in the left frontal region. The history of the case with a normal EEG is obscure. The single case with a history of congenital syphilis had attacks which involved the right hand and arm only, and were preceded by a definite sensory aura in this region. In spite of the most careful and repeated examination of the area in the left parietal region suggested by the nature of these attacks, no abnormality could be discovered.

Of the two cases of toxæmic convulsions, one showed a generalized abnormality in the EEG similar to that found in cases of raised intra-cranial pressure. This case has been previously described (Walter (1937), Case 8). The other showed no abnormality and the diagnosis of toxæmia was somewhat uncertain.

Of the cases with doubtful diagnoses, the majority of those with abnormal EEGs were considered by their physicians to be probably idiopathic, while most of those with normal EEGs seemed to be of the functional type. These thirteen do not, however, contribute as yet to the attempt to correlate diagnosis and prognosis with the electro-encephalogram.

Although the conditions at the Hospital for Epilepsy and Paralysis, Maida Vale, were excellent for the continuous and repeated study of a few patients, it was realized that the examination of larger numbers of well-classified epileptics was required before these results could be seen in their correct proportion.

The material offered by the London County Mental Hospitals was accordingly drawn upon, patients being conveyed to the Central Pathological Laboratory by omnibus.

Technique.

Since at least 100 patients were to be examined, the apparatus used was designed to give a quick result at the expense of accuracy of location. Two amplifiers were used, both similar in design to those at Maida Vale, but the output stage in both was a low-frequency pentode driving writing oscillographs. These were made up from scrap Weston moving coil relays (Model 30). By fitting a stronger control spring and adding a light straw lever, these instruments were made suitable for writing on a large Palmer kymograph. Their undamped natural frequency was about 40 per second, and they were critically

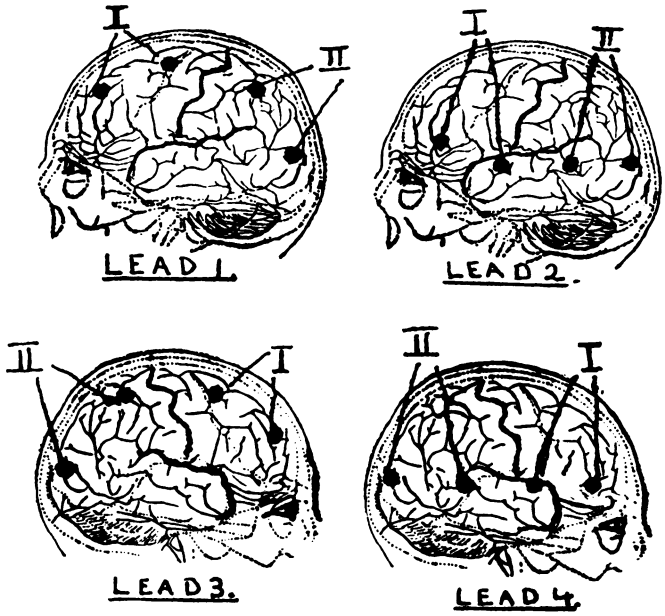

Fig. 3.—The routine electrode arrangements for the examination of patients in Series 2.

damped with oil. The overall time constant of the amplifiers was of the order of 1 second, so this arrangement was appropriate for recording electroencephalograms, the potentials of interest in this work having frequencies between 2 and 10 per second. The electrodes and the manner in which they were held on the patient's head were similar to those used in the first series of observations.

With only two recording systems the accuracy of location with the routine leads is to about 5 cm., and this was judged adequate for the purpose of these observations. It was at least possible to determine in which lobe and on which side a discharge was taking place. It is of interest to note that in one case (57 F.) in this series the accuracy of the double-writer system could be

checked against that of the triple cathode-ray set-up, and was found to be completely satisfactory, the centre of the focus being correctly placed. The only difference was that with the triple machine it was possible to delimit the extent of the focus, which in this case was unusually small.

The time taken for the complete examination of a patient was from 15 to 20 minutes and a provisional interpretation of the records could be made at once. As a routine, at least four records were taken (Fig. 3), and usually the effect of opening and shutting the eyes was studied, particularly when a discharge was found in the post-central region, but not all the patients were able to co-operate in this respect.

Statistical Survey of Records.

One hundred and seventeen cases in all were examined on a single occasion, all of them residents in mental hospitals and all but two certified. They were unselected except in so far as behaviour went, only the reasonably docile and manageable type of case being sent up for examination. The medical officers of the respective institutions from which these cases were culled were requested to send typical cases of epilepsy, both major and minor, who would be likely to co-operate sufficiently well for records to be obtainable from them.

The records were studied independently by three observers, and were ultimately classed as positive, negative and doubtful, according to whether they did or did not show the type of curve which has come to be associated with epilepsy. The "doubtful" group consisted of records about which the observers were unable to come to an agreement or which, although not normal, did not show the characteristic features sufficiently clearly to be classed as positive. These records, ten in all, are not taken into account in the present survey.

Of the remaining 107 cases, 52 gave positive and 55 negative records; in other words, about 52% of insane epileptics selected at random give normal electro-encephalograms.

In order to discover any possible factors which would tend to make for positive and negative curves respectively, the case-histories of all patients were subjected to careful scrutiny, attention being paid, amongst other things, to hereditary factors and to the kind of treatment (notably sedatives) which the patients were receiving.

The results of this investigation can briefly be set out as follows:

(1) Minor epilepsy is far more frequently associated with negative records than major epilepsy. Only a small proportion of cases were exclusively one or the other, the majority showing a preponderance of either major or minor attacks. The exact numerical data will be found in the tables, but on the whole cases with exclusively or predominantly minor attacks belong to the negative group.

(2) The more a case tends to conform to the type known as idiopathic epilepsy, the more likely the record is to be positive. As criteria of idiopathic epilepsy were used: (*a*) Data from the family history so far as obtainable,

notably incidence of epilepsy in parents and siblings ; (*b*) age at onset of attacks, infancy to puberty being regarded as the commonest age-group during which idiopathic epilepsy might manifest itself ; (*c*) absence of other causal factors and complications, such as trauma, cerebral tumours or operations and specific infections ; (*d*) some weight was given to congenital mental deficiency as indicating a tainted heredity. Cases with positive family histories and with no complicating conditions, in whom epilepsy manifested itself at or before puberty, provide the bulk of the typically positive records.

(3) Other things being equal, the greater the age of the patient at the time of examination, the more likely the record is to be negative. This only partly implies that the curves are negative, because the older the patient the more long-standing the disease. As a matter of fact, it is very difficult to assess the effect of duration of disease alone as a factor ; our group of middle-aged epileptics with negative curves includes a variety of cases, cases where there is an overlapping of factors as it were, so that it is difficult to make an unqualified statement as to influence either of age or of duration of disease separately. On the whole, however, as will be seen from the tables, the age-group 40 to 60 tends to show far fewer positive curves than the age-group 20 to 40. In trying to discover the possible reason for this, one might speculate along two different lines : firstly, is it that degenerative changes in the cortex incidental to age or to repetition of attacks over a period of years tend to obliterate signs of activity, both normal and abnormal ; secondly, is it that we are dealing with an accidental contributory factor—that, for example, a certain kind of epileptic tends to live longer than another, and that our middle-aged group therefore represents a picked population. There would seem to be some evidence in favour of this view ; as we have seen, more than one type of case tends to give negative records, notably cases with predominantly minor fits and cases in whom epilepsy first appeared in adult life. As major epilepsy does have a mortality, in *status*, one could quite fairly assume that cases who are less liable to develop *status epilepticus* are correspondingly more liable to survive to old age. In that case age as a factor in itself ceases to be of significance, and we are left with minor epilepsy and epilepsy due to other than hereditary causes as the two chief groups with normal electro-encephalograms.

(4) Administration of sedatives, principally bromides and luminal, does not appear to affect the electro-encephalogram in any way. With a very few exceptions all the patients were receiving bromide or luminal, some both, and the total dosage in the positive group is only a trifle higher than that in the negative group. This is, if anything, the reverse of what might be expected, considering the effect of these drugs on the frequency of fits ; but it is hardly significant, inasmuch as both the heavier dosage and the greater incidence of positive records are effects of a common cause, namely, a predominance of major attacks.

TABLE II.

Clinical classification of all cases.	Total 52 positive records.		Total 55 negative records.	
(1) Nature of fits :				
(*a*) Major only	12	37	1 (æt. 62)	19
(*b*) Major chiefly	25		18	
(*c*) Major and minor	12		10	
(*d*) Minor chiefly	3	3	19	26
(*e*) Minor only	..		7	
(2) Age of onset of fits :				
(*a*) Infancy	13	38	9	26
(*b*) Childhood	25		17	
(*c*) Adult life	4		22	
(*d*) Unknown	10		7	
(3) Present age :				
14–18	1	42	1	17
19–28	20		6	
29–38	21		10	
39–48	4	7	18	38
49–58	3		14	
59–68	..		6	
Unknown	3		..	
(4) Presence and nature of aura :				
(*a*) None	3		25	
(*b*) Diffuse (dizziness, faintness)	5		15	
(*c*) Fright	1		1	
(*d*) Sensory—vague (choking)	6		3	
(*e*) Headache	1		5	
(*f*) Sensory—local	1	1	4	6
(*g*) Motor—local	..		2	
(5) Causation :				
Presumed idiopathic	42		13	
Due to focal lesions	2		23	
Cause unknown	8		19	

These tables were examined statistically, using the χ^2 method, and they show that in every case a definite relationship exists between the type of electro-encephalogram and the factor tested.*

The contentions made on page 145 are therefore substantiated, and it might be of interest to analyse the main group of exceptional cases of presumably true idiopathic epilepsy which yet gave negative records (Table III). We find that they represent instances of overlapping of significant factors, as has already been suggested, and it would appear that two such factors, namely, age of patient and nature of attacks, seem to dominate over the factor of causation of disease.

It will be seen that out of the total of 13 cases only 2 remain which show clinical features such as should place them in the positive group. One of them, a woman, is described by the medical officer in charge as a hysterical personality, and there is some doubt as to the true nature of the fits ; the other is one of the

* Thanks to the courtesy of Dr. Julian Blackburn we are able to quote the actual factors, which show that the odds against a chance relationship are as follows : Groups (1), (2), (3), (5) as 100,000, 4,000, 33,000, 1,000,000 to 1 respectively.

TABLE III.—*Analysis of Cases of Presumed Idiopathic Epilepsy with Negative Records. Total Number of Cases,* 13.

Identification number.	Present age.	Nature of fits.	Age of onset of fits.	Remarks.
24/F.	53	..	..	..
43/F.	53	..	..	..
28/M.	50	..	..	..
9/F.	44	..	..	..
16/F.	42	..	..	..
41/M.	40	..	..	..
58/F.	39	..	..	..
13/M.	39	..	..	..
20/M.	39	..	..	..
48/M.	37	Minor only	..	..
51/F.	33	Minor +++	..	..
54/F.	27	Major and minor	Infancy	Hysteria
10/M.	23	Major ++	16	Focal aura

very few presumed idiopathic cases that show a local sensory aura—tingling in the feet. The rest of the cases would fall into the negative group on account of age and the nature of their fits.

Table IV is an analysis of the negative cases of Group 1, (*a*), (*b*) and (*c*)—

TABLE IV.—*Negative Cases with Major Fits. Total Number of Cases,* 29.

Identification number.	Details of fits.	Present age.	Age of onset of fits.	Remarks.
42/M.	Major +	65	..	..
26/M.	Major only	62	..	..
31/M.	Major +	58	..	..
23/M.	,, +	57	..	..
3/F.	Major and minor	57	..	..
25/M.	Major ++	53	..	..
28/M.	,, +	50	..	..
5/F.	,, +	50	..	..
21/M.	,, +++	49	..	..
16/M.	,, ++	47	..	..
20/F.	,, +	47	..	..
55/F.	,, ++	45	..	..
9/F.	,, +	44	..	..
11/F.	Major and minor	42	..	..
16/F.	,, ,,	42	..	..
35/F.	Major +	41	..	..
25/F.	Major and minor	41	..	..
41/M.	,, ,,	40	..	..
20/M.	Major +	39	..	..
40/M.	Major and minor	39	..	..
17/F.	,, ,,	37	23	Non-idiopathic
19/M.	,, ,,	37	15	..
52/F.	,, ,,	36	1	..
44/F.	Major ++	36	25	Non-idiopathic
38/F.	Major and minor	34	25	,,
54/F.	Major ++	27	Infancy	Hysterical
37/F.	,, +	26	13	..
10/M.	,, ++	23	? 16	..
2/M.	,, +	14	6	Meningitis

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—cases, that is, with major fits who should, on that factor alone, belong to the positive group. These also are presented in order of decreasing age, clinical data being given only in those under 39, who are therefore exceptions in a more strict sense of the word.

It will be seen that there are 5 cases which seem to be in every way exceptional, and two of them (54/F., 10/M.) are the same two which appeared as exceptions in the previous table. Two others again are reported as hystero-epilepsy in whom some of the fits are entirely hysterical. The remaining case (19/M.) had had a fit on the morning of the examination, so that it is just possible that the record was taken during the "silent period"—an interval following a major fit during which abnormal activity seems to subside so that very few or no potentials can be led off.

It is interesting to note that earlier authors (Gowers (10), Binswanger 13)) describe two groups of cases differentiated on the basis of high or low incidence of a local aura and focal features generally. The two groups correspond strikingly to our groups of negative and positive cases respectively, the former being those that are not instances of essential or idiopathic epilepsy and in whom minor fits predominate; the latter, having a clinical history which strongly suggests idiopathic epilepsy, and suffering predominantly from major attacks.

The group of positive cases gives records as follows:

Diffuse δ activity over the whole cortex . . .	6
Bilateral δ foci	26
δ focus on left	10
δ focus on right	10
Total	52

None of the cases with unilateral foci have a local aura or show any localizing features clinically; their case-histories differ very little from those that show bilateral foci and diffuse abnormality, and they all, with two known exceptions, belong to the class of idiopathic cases. One of the exceptions is a woman, aged 27, who has had fits for six years and who shows a well-defined focus in the left parietal region; the other is a case of exophthalmic goitre (woman, aged 37) who has had fits for the last two years only and who shows an extensive abnormal focus on the right side. These two cases seem to suggest that there might be an early or "acute" stage of the disease, during which the electro-encephalogram of the symptomatic case resembles that of the idiopathic one. It is noteworthy that both cases have relatively short histories of fits—actually the shortest in the entire series here described.

Discussion.

At the present stage no definite pronouncement is possible as to the significance of the δ-wave foci in epilepsy. These foci may merely represent

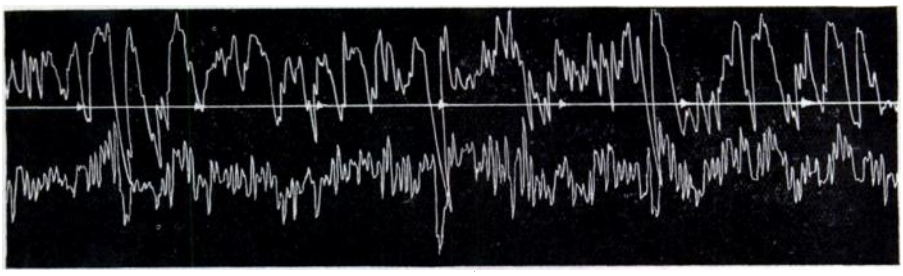

FIG. 4.—Case No. 57/F. Left parietal δ focus. Record taken from left (top line) and right (bottom line) parietal regions. Irregular 4-second δ waves shown on the left. From a symptomatic case, æt. 27, who has suffered from major fits for the past six years (one of the exceptional cases referred to below). Centre line. Time, 1 second.

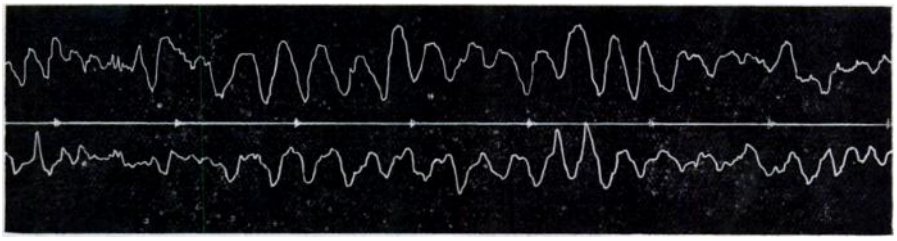

FIG. 5.—Case No. 10/F. Diffuse bilateral δ focus. Leads taken from left fronto-parietal (top line) and left parieto-occipital (bottom line) regions. Fairly regular 4-second δ waves shown in both leads. From a typical idiopathic case with predominantly major fits and no aura, æt. 21. Centre line. Time, 1 second.

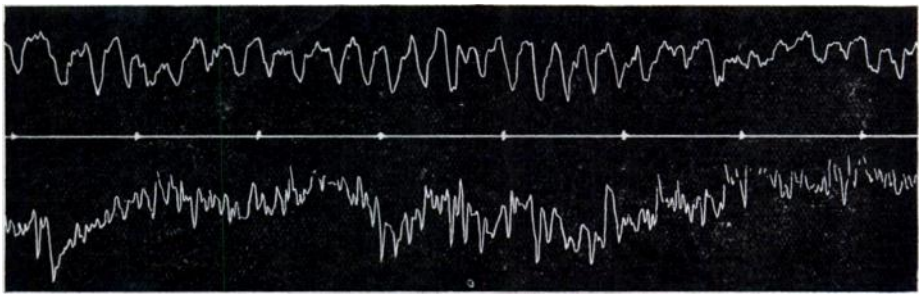

FIG. 6.—Case No. 46/M. Left frontal δ focus. Record taken from left fronto-parietal (top line) and left parieto-occipital (bottomline) leads. Top lead shows almost persistent 3–4-second δ waves. From an idiopathic case, æt. 34, with major fits only. Centre line. Time, 1 second.

the electrical signs of degenerative processes in the cortex occurring as a result of epileptic fits, or they may indicate the existence of epileptogenic areas from which the fits are originated when appropriate conditions obtain.

There is no lack of evidence that the epileptic state may occasion extensive anatomical disturbance in the cerebral cortex, and some histological changes are found in about 50% of cases of epilepsy. It is unanimously agreed that the changes in the cornu ammonis and the cortex of the cerebellum described by all histo-pathologists who have investigated the pathology of epilepsy are attributable to the circulatory disturbances accompanying the fit. They possess no pathogenic significance other than that of being evidence of previous anoxæmia of the central nervous system.

The significance of the marginal gliosis first described by Chaslin, in 1889 (4), is apparently similar to that of the sclerosis of the cornu ammonis and the cerebellum. Both the marginal gliosis and the ischæmic generalized nerve-cell degeneration that precedes it and was described by Alzheimer (5) are found not only in essential epilepsy, but in cases of symptomatic epilepsy of some duration, in familial chorea, whooping-cough with convulsions and eclampsia gravidarum. The changes in the cerebral arterioles described by Weber (6) are interesting as affording some additional support to the view that these sclerotic changes are all of ischæmic origin and are sequelæ of the epileptic fit. The cortical sclerosis is always diffusely distributed—the whole of the cerebral hemispheres and the mid-brain may be involved, or random patches of sclerosis may be found over both hemispheres. In none of the cases that have been described is it unilateral or confined to a single area.

The fact that δ-wave foci were found almost exclusively in undoubted cases of essential epilepsy and not in the cases of symptomatic epilepsy is a strong argument against the view that they are related to these secondary sclerotic changes. In the group of epileptics investigated at Maida Vale four cases of symptomatic epilepsy occurred, and in those from the mental hospitals twenty-five cases were considered to be symptomatic. None of the four cases from Maida Vale and none, with two exceptions, from the mental hospitals exhibited the ∂ waves. So far as the evidence of histopathology goes, the sclerotic changes secondary to ischæmia should have been at least as frequent in these cases as in those of essential epilepsy.

The fact that in a number of cases the ∂ foci were well defined and single is again presumptive evidence against their association with the diffuse secondary ischæmic changes. The evidence on this point is, however, far from conclusive. The nerve-cell changes originally described by Alzheimer (5), and confirmed by a number of recent observers, would undoubtedly appear to precede the gliosis, and at some stage such early cellular changes may be confined to the epileptogenis zones. Some observations by Penfield (7) tend to show that at any rate in some cases the vascular disturbance at the

beginning of a fit is confined to the " trigger " area from which the fit originates. It is not impossible that an early sign of the ischæmic lesion may be the production of δ waves by the damaged cells in cases of essential epilepsy, whereas in the case of symptomatic epilepsy such vascular disturbances do not occur.

The fact that δ-wave foci are found more frequently in early life and become rare after forty would fit in with this view, for Scholtz (8) shows very definitely that the ischæmic nerve-cell changes seen in the young epileptic brain are not seen after the age of thirty, when the secondary gliosis has become the leading pathological feature. Evidence from two angles of observation might be of capital importance in any attempt to estimate the pathological importance of the δ-wave foci. Firstly, evidence as to the association of the δ-wave area with the epileptic discharge, and secondly, as to the relation of the area to the prodromal symptoms and focal beginnings of fits.

It must be premised that only those cases showing either a single well-defined δ area or one with a less well-defined mirror image on the opposite hemisphere would be available for these considerations, and this limits the number of cases of evidential value very considerably. In the nature of things, too, only a small number of cases are likely to exhibit epileptic discharges during the electrical examination. Gibbs, Lennox and Gibbs (9) have recently published some observations in which such discharges were recorded in the electro-encephalogram. They do not, however, appear to have made any attempt to localize the area from which the discharges arose. On ten occasions it has been possible to observe the electrical concomitants of such discharges in patients with well-defined δ-wave foci. In two of these cases it has been possible to demonstrate that the discharge arose either from the δ-wave area or in its immediate vicinity. The first of these cases was that of a girl, aged 12, with a δ-wave focus situated in the left frontal area. The patient suffered from both major and minor fits, and during the course of the examination epileptiform discharges were noted which could only have arisen in the proximity of the δ-wave area or in the area itself. The second case is that of the girl of 7 years described on p. 142. In two adult cases the discharge again appeared to arise in the immediate vicinity of the δ focus. In two other cases it was only possible to affirm that the epileptiform discharge originated in the same hemisphere as the δ waves. Four cases of the type usually diagnosed as pyknolepsy showed frequent discharges which could be demonstrated to arise either from or in the immediate vicinity of well-defined δ areas.

The second case furnished additional evidence pointing to an epileptogenous significance in her δ-wave focus which, if confirmed in other cases, should be of decisive importance. Considerations alluded to above, and which will be dealt with in detail in another paper, led us to try the effect of administering a daily dose of benzedrine (β-phenylisopropylamine) sulphate to a number of epileptic patients, one of whom was the little girl in question. During a fortnight whilst receiving this drug she was entirely free from fits, which had

previously occurred many times an hour, and the δ-wave focus disappeared. Cessation of the drug was followed, after a few days, by reappearance of the fits and of the δ-wave focus. This concomitant appearance and disappearance of both fits and focus was verified again by observations over a second and third period of drug treatment, with a control interval.

The attempt to correlate the focal δ-wave areas with prodromal symptoms or local beginning of fits met with no success. We were unfortunate in having few cases with well-defined aura and none with a Jacksonian type of discharge among the cases with δ-wave foci. Although an aura is by no means a rare occurrence in cases of essential epilepsy, it is relatively infrequent when such cases are compared with those of symptomatic epilepsy, and focal motor beginnings are exceedingly rare in the idiopathic form. Cases showing δ-wave foci belong exclusively to the idiopathic group, and hence it will only be from examination of far larger numbers that information as to the correlation of aura and δ focus is likely to prove of value.

It must further be borne in mind that the electro-encephalogram only gives information as to electrical events originating in the cortex in immediate contact with the skull. It is probable that any foci of δ waves occurring on the base or the mesial surface of the hemispheres will be missed with our present methods. Thus the cortical area explored in our electro-encephalograms does not by any means represent the whole potential source of δ-wave foci. If the aura of epigastric sensation, which is, according to Gowers (10), the commonest form of aura, be, as Penfield suggests, localized in the posterior inferior mesial portion of the frontal lobes near the ventral nuclei of the tuber, its presence could not be signalized by the occurrence of a δ-wave focus in the electro-encephalogram.

Any attempt to correlate the δ-wave foci with an epileptogenic or "trigger" area in cases of essential epilepsy may appear to be unwarranted when the existence of such "trigger" areas is not susceptible of direct proof. The hypothesis that such areas may exist in all cases is, we think, justified by the admitted occurrence of occasional cases of essential epilepsy with definite sensory or motor prodromata or of a definite local motor commencement of the fit. Experiments have abundantly shown that such definite prodromata are related to the existence of a "trigger" cortical zone, stimulation of which will evoke either the aura or the fit. Once such epileptogenic zones have been admitted to exist in the cases with definite prodromata, the fact that only a small minority of cases of essential epilepsy exhibit strictly localized prodromata is readily understandable. The area of the cortex from which localized responses can be elicited by stimulation is only a small portion of the whole. If localized δ-wave foci correspond to epileptogenic areas, their study will be of the greatest importance as affording the only means of discovery of such areas in the "silent" portions of the cortex.

Inasmuch as the aura or local beginning of a fit remains constant for very

long periods, one would expect a similar constancy in the delimitation of the δ area if there be any relation between the two series. In the cases with well-defined δ-wave foci which were repeatedly examined for several weeks at Maida Vale the position of such foci has remained constant. In two cases of epileptic children and in all the cases of pyknolepsy the δ-wave foci never exhibited any other electrical discharge than that of the slow δ waves. All the other cases of similar foci only showed interrupted periods of δ-wave activity, varying from bursts of a few seconds' duration to an occasional group of three or four waves. This irregularity is very reminiscent of the spasmodic production of bursts of the *a* waves from the area 19 in normal subjects.

No conditions of cortical activity or stimulation such as influence α-wave activity have been found to have any influence on the occurrence of the δ waves. In the intervals between the bursts of δ waves the cortical discharge is not distinguishable from that of the surrounding normal area. Observations on a few cases have furnished evidence of occasional slight shifting of a δ-wave focus, such as has been shown by Adrian (11) to occur in the α-wave focus.

The frequency of these large slow δ waves varies in the course of a single examination; bursts of waves with a frequency of 2 per second may be succeeded by others with frequencies mounting up to 5 or 6 per second. In cases of pyknolepsy, however, the frequency of the δ waves remained constant. In these cases the commencement of an epileptogenic discharge was heralded by the slowing of the constant δ-wave frequency. The slowing was generally from about 4 to 3 beats per second. The amplitude of the waves is increased by over-breathing, but in a single series of experiments was not found to be affected by amyl nitrite inhalation or by carbon dioxide in the inspired air.

Further experiments on the effect of drugs will be dealt with in a subsequent publication. At this juncture we only wish to note that there was no evidence that the administration or withholding of bromides or barbiturates in the doses used in attempting to control epilepsy had any influence on the electro-encephalogram.

The localization and number of δ-wave foci is illustrated in the accompanying tables. Single foci or single foci with a "mirror" focus on the opposite hemisphere are noted most frequently in the young children and early cases in Maida Vale Hospital. The occurrence of a "mirror" focus in a number of cases is consonant with the observations of Gozzano (12) on rabbits, in which a localized epileptic discharge produced by application of strychnine to the cortex evoked a "mirror" discharge in the opposite hemisphere which could be abolished by section of the corpus callosum. In many of the cases, however, and particularly among the essential epileptics from mental hospitals, multiple foci are noted, although there is no apparent relation between the occurrence of multiple foci and the degree of dementia. In some of the cases the impression was given that the whole cortex was liable to display δ-wave discharges at intervals.

It is an old observation that in long-standing cases of epilepsy there is a tendency for strictly localized prodromal symptoms to be lost, and for fits to occur either without prodromal symptoms or with such symptoms varying from one fit to another, suggesting a multiplication and scattering of the hyperexcitable cortical areas. The infrequent occurrence of δ-wave foci in cases of essential epilepsy after forty is illustrated in both the Maida Vale and the mental hospitals cases.

Summary.

(1) Electro-encephalograms have been taken from two series of epileptic patients, comprising 214 cases altogether. In 91 of these the EEG was considered to be abnormal, in most cases on account of a discharge of slow δ waves.

(2) In both series a correlation was found between the type of EEG and the clinical diagnosis, idiopathic epileptics with a history of major fits providing most of the abnormal EEGs.

(3) A correlation appears to exist also between the EEG and the age of the patient, few abnormal EEGs being found in patients over the age of forty.

(4) In most of the cases in the first series the abnormality was found to be persistent and localized.

(5) EEGs have also been taken during the onset and course of fits. In some cases the discharge characteristic of the fit was found to start in the same region as the persistent abnormality.

(6) The significance of these findings is discussed.

We wish to record our thanks to the medical superintendents and medical officers of the London County Mental Hospitals, and to the medical staff of the Hospital for Epilepsy and Paralysis, Maida Vale, for their kind help in supplying us with clinical material, and for putting such information as we required at our disposal.

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