THE SIGNIFICANCE OF AN ABNORMAL ELECTRO-ENCEPHALOGRAM

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ATTENTION has recently been focused upon the occurrence of abnormalities in the electro-encephalogram (e.e.g.) of apparently normal subjects, and upon the high incidence of these abnormalities in subjects with behaviour disturbances and in other members of their families. Davis (1941) analysed the variations in the e.e.g. of groups of normal subjects and the abnormalities in wave form and frequency which she found in epileptic and psychotic patients. Similarly Lindsley and Cutts (1940) measured the number of waves in different frequency bands in small groups of normal adults and children, and in groups of children considered to be "constitutionally inferior" or presenting definite behaviour problems. Previously Jasper, Solomon, and Bradley (1938) had studied the abnormalities seen in the e.e.g. of behaviour problem children, while Hoagland, Cameron, and Rubin (1937), and Davis and Davis (1939) showed that a relatively high proportion of psychotic, especially schizophrenic, patients had abnormal e.e.g.'s.

In a statistical evaluation of the e.e.g. in epilepsy made by Golla, Graham, and Walter (1937), abnormalities were found in the e.e.g.'s of 60 per cent. of a mixed group of epileptics. It has since then been generally accepted as the common experience of most workers that a proportion of undoubted epileptics have a normal e.e.g. between fits. Jasper and Kershman (1941) have recently reported abnormalities in the e.e.g.'s of over 95 per cent. of a large group of epileptic subjects, and in surveying the electro-encephalographic phenomena found in epilepsy they have excluded epileptic subjects with "normal" records as being atypical. Lennox, Gibbs and Gibbs (1940) found that with their methods of interpreting records about 3 per cent. of patients with overt seizures had normal e.e.g.'s. This discrepancy in the percentage abnormality rate of epileptics may possibly be due to a difference in the norm adopted, but as there are not comparable figures for control groups of normals in all the communications this point is obscure. Löwenbach (1939), Strauss, Rahm, and Barrera (1939), and Lennox, Gibbs, and Gibbs (1939 and 1940) have

carried the investigation into the families of epileptic subjects. All these workers demonstrated a high incidence of abnormal e.e.g.'s in the members of these abnormal families. In particular Lennox, Gibbs, and Gibbs (1940) found that although they considered the e.e.g. definitely abnormal in 10 per cent. of a group of otherwise normal subjects upon the basis of a norm which they defined, it was abnormal in 60 per cent. of the near relatives of epileptics, while 95 per cent. of the epileptic subjects were found to have one or more parents with an abnormal e.e.g., although only 20 per cent. gave a family history of epilepsy. Williams (1941*b*) compared the percentage abnormality in the e.e.g. of a group of normals with that of subjects suffering from a post-traumatic syndrome, the figures for the two groups being 8 and 50 per cent. The percentage abnormality was found to be three times as high in a group of psychoneurotics, and six times as high in a group with organic cerebral damage as in the normal group. Davis (1941) dealt with the definition of the normal in detail. She compared the characteristic features of the e.e.g. of groups of fully investigated normal subjects with those of subjects with an unknown past history, of unstable subjects living at home, and of patients in a mental hospital, and she was able to demonstrate an ascending scale of abnormality in these groups. Lindsley and Cutts (1940) found a similar ascending scale of abnormality in the e.e.g.'s of their groups of normal and abnormal children.

There is now close agreement between different workers upon the criteria selected in establishing the norm of the human e.e.g., but however meticulous the definition the limits of normality are so wide, the degrees of abnormality so variable, and the e.e.g. record itself so complex, that subjective interpretation becomes inevitable. In order to compare the results from different laboratories it is therefore necessary not only to specify the recording technique and the criteria of abnormality adopted, but also to apply these criteria to comparable groups of subjects. Furthermore the true biological significance of a single abnormal e.e.g. can only be assessed in relation to the percentage abnormality of the group. For example, the significance of a normal e.e.g. in a suspected epileptic is considerably greater if its incidence is less than 5 per cent. (Jasper and Kershman, 1941) and not 40 per cent. (Golla, Graham, and Walter, 1937), while the importance of an abnormal e.e.g. in a normal subject becomes much greater if it is possible by qualitative selection of normals to alter the quality of the e.e.g.'s in the selected groups. It is therefore necessary to have a constant and well defined norm in order to appreciate the implications of the deviation from that norm of any subject or group of subjects.

This present survey, which is based upon clinical and electro-encephalographic examination of 900 subjects, was undertaken with this necessity in mind. Its main purpose was to determine the relative significance of an abnormal e.e.g. in groups of normal subjects and in abnormal states, especially epilepsy. The value of the abnormal changes produced by overbreathing was assessed in relation to the abnormalities seen at rest.

METHOD

A standard three-channel ink-writing electro-encephalograph with condenser coupled amplifiers (Grass) was used. Time was marked in seconds, the paper speed being 1 inch per second. The amplification was maintained as nearly as possible at 1 cm. deflection for $50\mu\text{V}$ applied to the input. The time constant ($\frac{1}{e}$) of the apparatus was 1.1 second, the high frequency filter being maintained at position "3." This position appears to be standard in most laboratories using the Grass apparatus, and gives almost linear reproduction of frequencies between 1 and 50 cycles. These amplifier characteristics were used throughout, no system of filters, similar to those used by Davis (1941), being employed.

The recording technique, electrodes, and electrode placement, which do not differ fundamentally from those of most other workers in the same field, have already been described in detail (Williams, 1941*a*). The recording time was not less than 10 minutes, but was longer when an abnormality was encountered. Lennox, Gibbs, and Gibbs (1940) employed 20 minutes as a minimum, and Jasper and Kershman (1941) 30 minutes. Previous experience had shown that the longer periods of recording, obviously desirable but not always practicable, increase the likelihood in epileptics of observing a subclinical outburst, but it did not so greatly increase the incidence of slight abnormalities occurring in the resting or "between seizure" record.

Except in some of the psychoneurotic group, a period of hyperventilation was employed in all cases after records had been completed with the subject in the resting state. The subject overbreathed for 90 to 120 seconds, depending upon the respiratory exchange and the consequent change in the e.e.g. The record was continued after overbreathing had ceased until it had returned to its resting condition.

MATERIAL

Nine hundred and one subjects were studied. They were grouped as in Table 1:—

TABLE 1

Highly selected normals. (R.A.F. air crew at the completion of flying training)	100
Selected and known normals. (R.A.M.C. and V.A.D. personnel)	121
Psychoneurotics	148
Post-traumatic states—	
Over 3 months	132
1-3 months	105
Less than 1 month	100
Epileptics—	
All types	195
Clinically grand mal.	131
,, petit mal.	25
,, psychomotor	29
,, mixed	10

These subjects were all adults between the ages of 18 and 50, the great majority being in the third decade.

SELECTION OF MATERIAL

Clinical

Normals.—The R.A.F. flying personnel having passed the requisite medical and vocational tests had completed full operational training, and the more unstable and less efficient had thereby been selectively eliminated. Their medical documents were all scrutinized and the family history checked. The R.A.M.C. and V.A.D. personnel had undergone a less rigorous medical and environmental selection, but they had all been on active service for at least a year. The medical documents of this group were also examined.

Abnormals.—The psychoneurotic group were inpatients and outpatients in whom no organic abnormality could be found, but whose symptoms were thought to be psychological in origin. They were mostly constitutionally inferior people, with a personal or family history of instability. None were classed as psychopathic personalities or psychotics, and in a third of the cases no definite evidence of previous instability could be found, the precipitating causes of the illness being mainly exogenous. A few had had a trivial head injury or other illness to which the symptoms had been attributed. The groups of patients with post-traumatic symptoms have already been dealt with in detail (Williams, 1941*a* and *b*).

The subjects of epilepsy were inpatients and outpatients. The clinical diagnosis was made on the accounts given by the patients and other witnesses, but very few fits were witnessed in hospital, and it is fully realized that the differentiation into grand mal, petit mal, and psychomotor epilepsy is probably not so clear cut as the tabulated figures suggest. It was important, nevertheless, in spite of its limitations to handle the clinical evidence in a strictly impartial manner.

Electro-encephalography

The records were examined by two observers without reference to the clinical classification. At first, groups of doubtful normals and doubtful abnormals were isolated, but in order to clarify the issue these doubtful records were re-examined and a definite opinion of their status was given. This seemed more desirable than to have an indeterminate sub-group in each group of cases. The records at rest and after overbreathing were assessed separately.

Evaluation of the E.e.g.—The criteria of abnormality were adopted arbitrarily from a standard acquired during observations made in the past five years. Although largely independent, they are very similar to those described by Lennox, Gibbs, and Gibbs (1940) and Davis (1941), and in most particulars they coincide with those of Jasper and Kershman (1941). Random isolated fast waves of relatively high voltage, or runs of high voltage 10 a second waves were not included in the group of undoubted abnormalities. The selection was rather more rigid than that of Strauss, Rahm, and Barrera (1939).

The criteria are briefly tabulated below, but as has been stated previously,

subjective interpretation is inevitable, for the character of the whole record must be observed. Unfortunately this aspect of selection requires experience, apart from measurement of individual wave forms, which can be achieved with great accuracy by the method of electrical wave band analysis devised by Grass and Gibbs (1938).

Abnormal Features.

1. *At Rest.*—

- (i) A dominant frequency, if present, of less than 8 a second.
- (ii) A very unstable or asymmetrical dominant frequency.
- (iii) Disorganization of the dominant frequency by equally high voltage slower waves.
- (iv) A sequence of two or more waves with a frequency of less than 8 a second and an amplitude of more than half that of the dominant frequency in any lead. This includes all subclinical epileptic outbursts, and all general or local runs of slow waves, whatever their form.
- (v) Bursts of waves with any frequency over 14 a second whose voltage reaches more than half that of the dominant frequency.
- (vi) Random solitary waves with a frequency of less than 8 a second and a voltage greater than that of the dominant frequency from any lead.

Features which enhance the degree of abnormality are waves of long period, high voltage, and episodic or frequent occurrence. Abnormal wave forms have so frequently been illustrated in normal and abnormal subjects (Lennox, Gibbs, and Gibbs, 1940; Davis, 1941; Jasper and Kershman, 1941; Williams, 1941*b*) that no further example is necessary.

2. *After Hyperventilation.*—The only disturbance considered abnormal during a period of overbreathing was the appearance of typical epileptic outbursts of high voltage 2 or 3 a second sine waves, 2 to 3 a second wave and spike formations, 2 a second wave and hump formations or rhythmic outbursts of faster waves of an epileptic type (Gibbs, 1939). The response of the normal e.g. to changes in the pH of cerebral blood may be so great (Gibbs, Williams, and Gibbs, 1940) that no more rigid standard of abnormality than this could be adopted.

When overbreathing had ceased the record rapidly began to return to its former state. Any paroxysmal outbursts of waves of higher voltage or longer period which occurred after this improvement had begun were considered abnormal. These outbursts, common in epilepsy, usually began between 8 and 12 seconds after the cessation of overbreathing, with the readjustment in the acid base balance (Nims *et al.*, 1940). They were of the following types:—

- (a) Pure repetitive wave forms, usually of 2 or 3 a second, sometimes up to 6 or 7 a second.
- (b) Repetitive patterns—2 to 3 a second wave-and-spike or wave-and-hump.

- (c) Irregular discharges of many abnormally slow waves with varying wave form, voltage, and frequency.
- (d) A sudden increase in voltage of existing slow frequencies.
- (e) Very rarely a superimposition of fast waves (25 a second or more).
- (f) Persistence of the hyperventilation effect for more than 20 seconds after overbreathing had ceased.

Examples of these changes are illustrated (Fig. 1).

RESULTS

The results are presented in Table 2. The incidence of abnormal records in each group is expressed as a percentage of the total, the nearest unit percentage being stated.

TABLE 2

GROUP	NUMBER	PERCENTAGE WITH ABNORMAL E.E.G.'S		PERCENTAGE ABNORMAL AT REST AND AFTER OVERBREATHING
		RESTING	AFTER OVER-BREATHING	
Normal—				
Flying personnel	100	5	5	80
Army personnel	121	10	9	73
Psychoneurotic	148	26	—	—
Post-traumatic states—				
Chronic (over 3 months)	132	40	20	78
Subacute (1–3 months)	105	43	11	83
Acute (to 1 month)	100	58	31	84
Epilepsy—				
Total	195	60	55	73
Grand mal	131	55	50	72
Petit mal	25	60	72	61
Psychomotor	29	83	62	77
Mixed	10	90	80	87

DISCUSSION

The Norm.—The basis of the norm adopted in this investigation has already been described, and the proportion of otherwise normal subjects who attain to it is similar to that found by other workers in the same field. This is more significant because Davis (1941), Lindsley and Cutts (1940), and Lennox Gibbs, and Gibbs (1940) and the present author have each used different, methods of analysing the abnormal features they observed. The agreement of these workers has further significance because the limits of the normal e.e.g. are wide and ill defined, and its features are so complex that the experimental error of selection might be expected to be great. It is therefore apparent that

Fig. 1.—ABNORMAL TYPES OF RESPONSE TO HYPERVENTILATION.

Portions of the electro-encephalographic records from six subjects. In each case the arrow indicates cessation of 90 seconds of strenuous overbreathing. The samples show:—

1. A run of 3-a-second sine waves beginning 9 seconds after overbreathing had ceased.
2. Wave-and-spike activity beginning 9 seconds after.
3. A prolonged outburst of 6-a-second sine waves gradually slowing to 5, 4, 3, and then 2 a second.
4. An irregular outburst made up of a 7-a-second rhythm, well seen 11 seconds after overbreathing had ceased, with much irregular fast activity.
5. A long run of irregular slow waves of higher voltage than at the end of overbreathing.
6. Persistent activity with a frequency of 24 a second.

the norm is sufficiently distinct to permit an evaluation of the significance of the abnormal e.e.g.

Psychoneurosis.—The psychoneurotic subjects of this investigation are all grouped together, but obviously in some the constitutional factor in the neurosis predominated, while in others, probably a minority, exogenous factors were mainly responsible for it. The increase in the percentage abnormality of the e.e.g. from 10 per cent. of the normal group to 26 per cent. of the psychoneurotic reflects the presence of a constitutional abnormality in these subjects, since there is no evidence at all that psychological trauma can produce abnormal changes in the pattern of cerebral electrical potentials. On the contrary, Jasper, Solomon, and Bradley (1938); Gibbs, Gibbs, and Lennox (1938); and Lindsley and Cutts (1940), have shown that in problem children and even in the children of constitutionally inferior families the incidence of abnormalities in the e.e.g. is high. These children will furnish some of the constitutional psychoneurotics and psychopaths of their generation, and it is apparent that the high incidence of abnormal e.e.g.'s in unstable individuals, as well as in psychotics (Hoagland, Cameron, and Rubin, 1937) is related to the similar abnormalities seen in unstable and constitutionally abnormal children.

Epilepsy.—In epilepsy the position of the abnormal e.e.g. can be more clearly defined. The proportion of abnormal e.e.g.'s observed in this present series is very similar to that recorded by Golla, Graham, and Walter (1937), but it is lower than that found by Lennox, Gibbs and Gibbs (1940), and by Jasper and Kershman (1941). Although all the records were examined in the knowledge of this work, such a constant appearance of abnormality could not be observed in this series of epileptics, on the basis of the norm which had been adopted. On the contrary individual cases showed a great disparity between a profound clinical manifestation of epilepsy and an absolutely normal e.e.g. For example, a man of 22 (Case 320) had had fits since his second year, and he was having several grand mal attacks a month and at least two petit mal each day when examined. His mother, three siblings and one maternal sibling had epilepsy, but his e.e.g. showed a well sustained 10-a-second rhythm with normal characteristics, without any evidence of subclinical outbursts or of an abnormal response to hyperventilation.

The present observations are concerned with the incidence of "between seizure" abnormalities, including the presence of subclinical outbursts, so that the actual wave form encountered in clinical attacks has not been mentioned. Jasper and Kershman (1941) have recommended that Gibbs, Gibbs, and Lennox's (1937) division of epilepsy upon the basis of the e.e.g. into grand mal, petit mal, and psychomotor epilepsy, should be discarded because so many subjects who show specific types of disturbance do not have a similar constant type of clinical attack, so that the form of clinical seizure cannot be accurately predicted from the form of the e.e.g. They point out, for instance, that a subject of grand mal attacks may only show 3 a second wave-and-spike outbursts of the type seen in the e.e.g. in association with petit mal epilepsy. They have therefore analysed the epileptic disturbances

seen in the e.e.g. upon the basis of the wave forms and their cerebral localizations, without reference to the clinical form of epilepsy. This dissociation of the electro-encephalographic diagnosis from the clinical makes for lucidity, and is desirable, but the authors have neglected the fundamental observations made by Gibbs, Gibbs, and Lennox, that when an observed attack which could be recognized clinically as grand mal, petit mal, or an "epileptic equivalent" was associated with a disturbance in the e.e.g., the electrical disturbance was always true to type and was unmistakable (Gibbs, Gibbs, and Lennox, 1937). Thus the division of the electro-encephalographic phenomena, on the basis of their clinical correlates, into the three main types of epilepsy was perfectly valid, and must obviously remain. Jasper and Kershman's observations of the frequent lack of correlation between the form of the subclinical outbursts and the clinical fits which happen to be seen in any subject have repeatedly been made during the present investigations, and were the principal reason for the study of the effects of overbreathing. Gibbs (1939) wrote: "It is my policy to let the diagnosis depend largely on the clinical history and to report that the record shows the type of disorder seen during a particular type of seizure, grand mal, petit mal, or psychomotor." That has become the policy in this laboratory. A full clinical history is obtained and the presence of any abnormal wave form in the e.e.g., whether general or local, is ascertained. In many instances it is possible, in view of specific wave forms or rhythms, to describe the e.e.g. as typically epileptic. In this way the clinical diagnosis of epilepsy may be confirmed in 60 per cent. of the subjects, but the type of seizure resulting from the basic abnormality reflected in the e.e.g. is determined by clinical methods. When a report is given upon the remaining epileptic subjects who have normal e.e.g.'s it is clearly stated that the absence of demonstrable abnormality does not invalidate the clinical diagnosis of epilepsy. The most exact procedure seems therefore to be to establish a nonspecific diagnosis of epilepsy upon the findings in the e.e.g., when abnormalities are observed in a suspected epileptic, but to determine the type of epilepsy by clinical observation.

Hyperventilation.—The abnormal responses to hyperventilation which have been described occur in about the same proportion of the subjects as do abnormalities in the resting e.e.g., and there is about a 75 per cent. overlap in the incidence of the two types of abnormality in all the groups of subjects. This shows that the paroxysmal outbursts, which occur during the period of acid-base readjustment (Nims *et al.*, 1940), are usually related to some underlying metabolic abnormality of cerebral tissue, which is manifest in the dysrhythmia. The presence of these paroxysmal outbursts in each group of subjects indicates that they are not specifically epileptic, but rather that they are related to the underlying cerebral instability which seems to determine the appearance of epilepsy, psychopathy, or neurotic instability. The use of overbreathing to elicit the abnormality increases the likelihood of demonstrating an inborn constitutional defect in potentially abnormal subjects. Experience has shown that greatest instability after overbreathing is present in those

subjects who have normal or abnormal rhythms of high voltage in the resting e.e.g. This forms a link with the known lability of the wave-and-spike pattern in its response to changes in blood CO₂ tension, for this pattern is almost always associated with a well marked dominant frequency. The abnormal responses to overbreathing, particularly the wave-and-spike pattern, can readily be inhibited by a rise in blood sugar, so that the relationship of the investigation to the preceding meal should be noted in doubtful cases. It appeared from critical examination of the material, that the more rhythmic the disturbance after overbreathing, as, for instance, the wave-and-spike formation or rhythms of pure sine waves, the more likely was it to be associated with clinical epilepsy.

The Normal Groups.—Probably the most interesting data in Table 2 are those referring to the normal groups. These show that the incidence of abnormality in a perfectly normal group of subjects may be halved by further selection upon criteria having no apparent relationship to electro-encephalographic selection. These criteria were to some extent based upon medical examination, but both normal groups were selected by this means. The most important single difference between the two normal groups was the occupational stress to which the first group had been subjected. This stress, by causing the eradication of the less efficient and more unstable members of the group, had given rise to a group of relatively super-normal individuals by auto-selection. It thus appears that in at least half of the normal subjects with an abnormal e.e.g. the abnormality may have significance in terms of latent constitutional inferiority. Two of the five airmen with abnormal e.e.g.'s showed changes considered to be definitely epileptic, but they denied personal or family histories of faints or fits, and their work performance had been good. On the basis of the investigations into the heredity of epilepsy, notably that of Lennox, Gibbs, and Gibbs (1940) it is reasonable to conclude that they carry the genetic predisposition to epilepsy which may become clinically evident in their progeny, or even perhaps in themselves. Three of these highly selected hundred normal subjects therefore remain with inexplicably abnormal e.e.g.'s. It may be impossible for practical reasons to show that the dysrhythmia in these cases represents a latent constitutional defect, but the series of observations upon constitutionally inferior children, psychoneurotics, and the near relatives of abnormal individuals, to which reference has already been made, make it very likely that such is the case. In conclusion it may therefore be affirmed that the evidence of this investigation, co-ordinated with that of others, strongly suggests that an abnormal e.e.g., based upon a norm which excludes 10 per cent. of the healthy population, indicates an inborn constitutional defect which may find expression as epilepsy or a behaviour disorder such as a constitutional psychoneurosis, psychopathy, or psychosis, in the subject himself or his offspring.

SUMMARY

The electro-encephalograms of 900 subjects, divided into groups of highly selected normals, normals, psychoneurotics, epileptics, and subjects of a post-traumatic syndrome have been examined. The percentage abnormality has been determined, the subjects being at rest and having overbreathed, upon the basis of arbitrary norms which have been described.

The abnormality rate, detailed in Table 2, varied from 5 per cent. in the highly selected normal group to 60 per cent. in the epileptic. Seventy-five per cent. of the subjects with an abnormal response to overbreathing showed abnormality in the resting e.e.g. The percentage abnormality in epilepsy ranged from 55 in subjects of grand mal to 90 in patients with more than one type of fit. It is suggested that a non-specific diagnosis of epilepsy should be made upon the abnormalities seen in the e.e.g. at rest and after overbreathing, but that the recognition of the specific type of fit should be based on clinical observation.

On the basis of the present results and those of other workers it is concluded that:—

1. An abnormal e.e.g. in an otherwise normal subject is strong evidence of an inborn constitutional abnormality involving the central nervous system.
2. This abnormality appears to be non-specific, and may manifest itself in the subject or his offspring as a behaviour disturbance which may be psychoneurotic, psychopathic, psychotic, or epileptic in type.
3. On the basis of a norm which excludes 10 per cent. of apparently normal subjects, 40 per cent. of epileptics have a normal e.e.g. between fits, but the incidence of abnormality in epileptics showing more than one type of clinical fit was 90 per cent. The significance of this figure is discussed in relation to the findings of other investigators.

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