THE APPLICATION IN GENERAL MEDICAL CONDITIONS OF A VISUAL METHOD OF ASSESSING AND REPRESENTING GENERALIZED ELECTRO-ENCEPHALOGRAPHIC ABNORMALITIES

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Certain disorders, which do not primarily involve the brain, may interfere with its metabolism. If this metabolic dysfunction is sufficiently severe the patient may become confused or even comatose. The continuum from normality to coma will here be considered as one of increasing delirium. Such delirium may be produced by a variety of conditions which include those with alterations in blood chemistry, namely, hypoglycaemia, uraemia, and possibly hypokalaemia (Sherlock, Read, Laidlaw, and Haslam, 1958); certain of the collagen diseases (Leinwand, Duryee, and Richter, 1954; Clark and Bailey, 1956); pernicious anaemia (Walton, Kiloh, Osselton, and Farrall, 1954, Holmes, 1956); carbon dioxide narcosis complicating chronic bronchitis and emphysema (Westlake and Kaye, 1954; Conn, Dunn, Newman, and Belkin, 1957); and those forms of liver disease associated with encephalopathy (Adams and Foley, 1953; Summerskill, Davidson, Sherlock, and Steiner, 1956).

The electroencephalogram (E.E.G.) can define the extremes of this continuum. At one end, the wide range of normal is characterized by rhythmic activity predominantly within the alpha frequency band (8-13 c./sec.) and at the other, coma by delta waves (under 4 c./sec.) of varying regularity and amplitude.

In the zone between, however, the E.E.G. changes are less clear. It is very difficult by inspection to assess variations in the severity of a generalized abnormality and even more difficult to express such an assessment, except as an arbitrary statement of opinion. Not only is a method of assessment essential for any E.E.G. investigation of delirium but it is of practical clinical importance to be able to detect relatively small changes, and to have a language in which to explain them. First, because the E.E.G. provides an objective and often sensitive index of cerebral function and ought to be able to help by warning of clinical deterioration or measuring the efficacy of treatment. Secondly, because although the E.E.G. changes in disorders not primarily cerebral, such as those described, are not specific, the E.E.G. can help in diagnosis if it is possible to measure the effect of provocative or therapeutic tests.

This paper describes a method which has been developed to assist in the assessment and representation of such generalized abnormalities. Work on the E.E.G. during the transition from consciousness to coma is in progress and definitive results have not yet been obtained. Some description of this work is given and tentative hypotheses mentioned in order to clarify the scope and limitations of the method.

A number of patients, the majority with liver disease, have been followed with daily E.E.G.s as they recovered from or lapsed into coma or states of manifest confusion. Inspection of the records suggested:

(1) That the changes which occurred were not specific to any disease.

(2) That the most important change, with increasing delirium, was a slowing of frequency both as a slowing of the dominant frequency and as the introduction of random slow waves.

(3) That variations in the amount of rhythmic activity, particularly with the eyes open, were probably important.

(4) That during certain stages of delirium there were considerable intra-record variations which occurred both spontaneously and as a result of stimuli intended to influence the patient's state of attention.

(5) That slowing was usually seen first over the lateral and post-central parts of the scalp, and that although with advancing delirium very slow waves might be maximal anteriorly, if a single area of the scalp needed to be chosen for inspection, the posterolateral aspect of the non-dominant hemisphere gave the most satisfactory measure of the frequency changes over the whole spectrum of delirium.

The method was developed in order to quantitate and express graphically changes which had been
observed and which were considered to be associated with alterations in delirium. It was decided not to use an automatic frequency analyzer for two main reasons: (1) The apparatus, which is expensive and requires skilled maintenance, is seldom available outside special centres, and a method to be of use must be available in those units where general medical cases are found. (2) The present analyzers only record the energy at different frequencies, i.e., the product of amplitude (voltage) and number of waves. Frequency changes were considered of primary importance and it was felt that more weight should be given to a large number of moderate amplitude waves than to a smaller number of high amplitude ones. Further, a measure was required of the ratio of rhythmic activity to irregular and desynchronized parts of the record.

In 1944, Engel, Romano, Ferris, Webb, and Stevens described a simple visual method of frequency analysis. They counted the number of complete waves in each of 300 consecutive one-second periods, excluding those containing low-voltage fast activity, expressing the result as a histogram. A recent application of this method showed the E.E.G. effects of alcohol (Holmberg and Martens, 1955).

The method to be described is a development of Engel's and similar to one used by Brazier and Finesinger (1944) to study the normal E.E.G. It attempts to overcome, first, the disadvantage of forming a histogram from averages and so masking the occurrence of frequencies far removed from the mean and failing to give a measure of the degree of polyrhythmia, and secondly, the difficulty of dealing with irregular records and those containing a high proportion of low-amplitude fast activity. It must be emphasized that although it deals with frequencies and expresses them in mathematical and graphical form, it should not be thought of as a method of frequency analysis in the sense that an automatic analyzer analyzes frequency, but as a way of representing a generalized abnormality as a frequency pattern.

**Method**

Essentially, the principle is to measure the periods of as many individual waves as possible over a given epoch* to calculate the time occupied by each frequency, and to plot on a graph the frequency-time as a percentage of the epoch, against frequency, to give a frequency pattern (Fig. 4).

Scalp electrodes are placed as shown in Fig. 1 to give seven channels of E.E.G. The spare channel of an eight-channel machine may be used for other purposes such as an electrocardiograph lead or the recording of alerting stimuli. It has been found that the best measure of frequency changes is given from the postero-lateral aspect of the non-dominant hemisphere (channel 5 for a right-handed patient). Time constants of 0-3 sec. are suitable and have been used throughout in the work described.

All rhythmic and reasonably regular waves are counted. Certain parts of each epoch are excluded according to the following criteria.

(1) Those which are flat and desynchronized: with amplitude calibration at 1 cm. for 50 microvolts and paper speed of 6 cm. per second, a wave is considered flat if its height is less than a quarter of its width. If all the rhythmic activity in a record is of low amplitude this criterion may be modified.

(2) Very irregular activity when it is impossible to define a wave clearly. In practice very little of an epoch needs to be left out for this reason.

(3) Activity with a frequency above 20 c./sec. which is uncommon in the records which have been considered.

Only the wave which is dominant at any one time is measured. Thus a low-amplitude ripple superimposed on a large slow wave is ignored. It is usually quite easy to decide which wave form should be counted, but if there is difficulty, activity recorded simultaneously in other channels is considered.

The period of each wave, from trough to trough, is measured with the cursor shown in Fig. 2. The numbers at the top of the cursor give the frequency when the paper is run at the normal speed of 3 cm./sec. Unless the record consists of predominantly delta activity, measuring is easier if the gains are doubled and the paper run at 6 cm./sec.; at this speed the frequencies are given by doubling the numbers at the top of the cursor. The intervals between the measuring lines on the cursor

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*Although not strictly correct etymologically the word "epoch" can be used with advantage to mean "a period of time".
are each 1 cm. and very slow waves can be measured by making an appropriate combination of measuring line and interval, e.g., the measuring line for 3 with the intervals on either side of it measure 3 cm. and at 6 cm./sec. represent a wave at 2 c./sec.

Over the continuum from normal consciousness to coma, records tend to show a considerable variation from one part to another (part B in Fig. 3) and it is usually necessary to measure an epoch of 50 seconds. At the extremes of the continuum of delirium, where there tends to be less variation, the epoch may be shorter. If it is decided to attach significance to a certain degree of change in the frequency pattern, it is necessary to choose an epoch long enough so that if two epochs of this length are counted from the same record under similar circumstances, i.e., with the eyes shut or open, the variation between the frequency patterns from these epochs is appreciably less than the change to which significance is to be attached.

In most cases an epoch can be measured without any preparation and the frequencies called out to an assistant or a tape recorder; with practice a 50-second epoch can be measured in about 10 minutes. As a refinement (and for difficult records) it is sometimes useful to mark doubtful parts of an epoch with vertical pencil lines through the troughs of waves before measuring. This saves time in the end and allows a colleague to check. Fig. 3 shows examples of a normal record (A), a moderately abnormal record (B) from a patient, who although showing no clinical evidence of delirium, was in fact deteriorating and later became manifestly confused, and a severely abnormal record (C) from a patient in coma. The frequencies have been written in below the waves; those parts without subscripted numbers have been excluded according to the criteria given.

The number of waves at each frequency divided by the frequency gives the time occupied by that frequency. If a 50-second epoch has been measured, this time multiplied by 2 gives the frequency-time per cent. Since it is difficult, and not sufficiently important, quickly to differentiate frequencies over 10 c./sec. the faster waves are grouped together: those from 11 to 13 c./sec. as 11/13 and from 14 to 20 c./sec. as fast. When calculating frequency time these groups are divided by 12 and 15 respectively and are plotted on the frequency pattern as blocks not points.

Fig. 4 shows the frequency patterns derived from the records, of which specimens are shown in Fig. 3. It will be seen that whereas the patterns for the normal (A) and severely abnormal (C) records show sharp peaks with most of the activity at one or two frequencies, the moderately abnormal (B) pattern is more broadly based, demonstrating the polyrhythmia and intra-epoch fluctuation which was seen in Fig. 3 B.

Illustrative Material

Examples from two sets of serial records are shown in Figs. 5, 6, and 7. Specimens of the original E.E.G.s are seen to the left (the numbers referring to the channels marked in Fig. 1) and the corresponding frequency patterns on the right are each derived from 50-second epochs with the eyes shut. The area under the frequency pattern gives a measure of the amount of rhythmic activity, the time occupied by the rhythmic and reasonably regular waves which have been counted.

Figs. 5 and 6 (Case 1) show E.E.G.s recorded on six consecutive days from a patient with cirrhosis complicated by encephalopathy. At the time of the first record (A) she was manifestly confused. Five days later (D) she had returned to her usual state. The following points may be noted:

(1) There is a gradual increase in frequency throughout the series.

(2) Even after recovery from the acute episode there is a slight generalized abnormality as shown by an excess of activity at frequencies less than 8 c./sec.
Fig. 3.—Specimens of a normal (A), moderately abnormal (B), and severely abnormal (C) record. The frequencies of those waves which have been counted are subscripted.

Fig. 4.—Frequency patterns of the normal (A), moderately abnormal (B), and severely abnormal (C) records shown in Fig. 3.
There is less rhythmic activity after recovery than in the earlier records. In E and F rhythmic activity averages 57% of the epoch, in A to D inclusive the average is 79%.

Fig. 7 (Case 2) shows three records from a normal young male subject weighing 12 st. before (A) and 10 minutes (B) and 27 minutes (C) after the rapid ingestion of 75 ml. of absolute alcohol diluted five times with lemon-flavoured water. The following points of interest are seen: (1) All the records lie within the normal range and show normal frequency patterns with sharp peaks in the alpha band. (2) After alcohol there is a progressive shift of the frequency pattern as a whole towards slower frequencies and of the dominant frequency from 10 to 9 to 8 c./sec. This shift is demonstrated clearly in the patterns whereas it is less easy to see in the original records. (3) There is appreciably more rhythmic activity after alcohol.

In order to give some measure of the accuracy of assessment and of the significance to be attached to the shift in frequency pattern shown in Fig. 7, frequency counts from the same subject for six 50-second epochs are given in Table I and charted as frequency patterns in Fig. 8. There are two patterns from consecutive epochs immediately before alcohol was given and one...
from the same subject three weeks later (continuous line in Fig. 8) and three counts from epochs recorded 27, 29, and 41 minutes after ingestion of alcohol (broken line in Fig. 8) at which times the maximum E.E.G. effect of alcohol was obtained.

It will be seen that the patterns fall into two groups: the three control patterns uninfluenced by alcohol, group A corresponding to A in Fig. 7, and three patterns after alcohol, group C, corresponding to C in Fig. 7.

Each pattern in group A has a similar shape and dominant frequency at 10 c. sec.; they differ from each other in the area under the curve, a measure of the amount of rhythmic activity in the epoch, which is probably a function of the subject's state of attention. The group C patterns differ from each other very little and they each have a dominant frequency at 8 c. sec. It can be seen quite clearly that the inter-group difference is much greater than the intra-group one.
Fig. 8.—Case 2. Frequency patterns before alcohol (continuous line) and after alcohol (broken line). See text and Table I.

TABLE I

<table>
<thead>
<tr>
<th>Group</th>
<th>Percentage of Total Time of Rhythmic Activity at Different Frequencies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Before alcohol 1</td>
<td>A</td>
</tr>
<tr>
<td>Before alcohol 2</td>
<td>A</td>
</tr>
<tr>
<td>Three weeks later</td>
<td>A</td>
</tr>
<tr>
<td>27 min. after alcohol</td>
<td>C</td>
</tr>
<tr>
<td>29 min. after alcohol</td>
<td>C</td>
</tr>
<tr>
<td>41 min. after alcohol</td>
<td>C</td>
</tr>
</tbody>
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Discussion

Simple inspection of records shows clearly that in certain disorders, which do not primarily affect the brain, the E.E.G. can provide evidence of cerebral dysfunction. Further, if serial records are taken, changes in the E.E.G. abnormalities may be seen which give a measure of variation in the severity of this dysfunction, a measure which, because it is often more sensitive than physical or psychological examination, has considerable clinical value. The method which has been described for expressing a generalized E.E.G. abnormality as a frequency pattern was developed in order to improve on assessment by inspection and to provide a graphic form in which this assessment could be passed on to the clinician in charge of the patient.

The conversion of complex wave forms to percentages should not be allowed to suggest a spurious accuracy. The frequency patterns have no intrinsic theoretical significance: they have been derived empirically. They have proved useful in demonstrating the extent of manifest changes and in showing slight variations which were difficult to detect in the original records. Their simple graphic
forms are easy to compare and contrast and studies of these forms may emphasize variations not readily obvious in the more complex primary record. Starting as a method of representing frequency changes with known alterations in the degree of delirium, the use of frequency patterns has already suggested that variations in the amount of rhythmic activity, spontaneous intra-record fluctuations, and the extent of frequency changes produced by stimuli may be of importance and worthy of further investigation.

The limitations of visual methods are fully appreciated (Dawson and Walter, 1944), and it is not suggested that a frequency pattern so derived should represent the precise electrical changes which occur in the brain. However, the method has proved of practical value (Read, Haslam, Laidlaw, and Sherlock, 1958; Sherlock et al., 1958) and, although it takes time, it requires no complicated or expensive equipment. Preliminary work with visually derived patterns has shown that the assessment of small changes in generalized E.E.G. abnormalities has sufficient clinical and probably theoretical value to justify the development of an automatic method which will save time, increase accuracy, and, it is hoped, reveal new facts of importance. The present method has been described because it will form the basis for any new method and because it may be of interest to those concerned in the development of electro-encephalography as a tool in the investigation of general medical disorders.

Summary

Certain disorders, not primarily cerebral, may produce alterations in consciousness and generalized electro-encephalographic abnormalities.

A simple empirical method of assessing these abnormalities and representing them graphically is described. Two illustrative examples are given and the scope and limitations of the method are discussed briefly.

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References