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ELECTRO-ENCEPHALOGRAPHY IN CASES OF SUB-CORTICAL TUMOUR

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THE application of electro-encephalography to organic brain lesions has mainly been limited to the study of cases with involvement of the convexity of the hemispheres. In these an expanding lesion is usually associated with potential changes at a frequency well below the normal range—1 to 3 c/s. It is generally accepted that discharges at this frequency are pathological when their amplitude approaches that of the normal rhythms ($20\mu\text{V}$). When localized by multi-channel recording, even lower potentials indicate cortical abnormality. These low frequency or "delta" rhythms (Walter, 1936, 1937, 1938) are not specifically diagnostic of new growth for they are also seen in traumatic and degenerative conditions, and in idiopathic epilepsy.

One of the main difficulties in interpreting abnormal e.e.g. records is that the waveform is rarely simple or repetitive, as in the electro-cardiogram. Many observers have remarked that in cases of new growth, the waveform of the slow potential changes is particularly irregular and complex, whereas in cases of idiopathic epilepsy the discharge tends to be more stereotyped and rhythmic. An irregular and complex waveform is hard for the unaided eye to interpret, and it is also likely to contain many components. The e.e.g. [is simply a graph of voltage difference against time. The interpretation of such a graph depends upon the capacity of the eye and brain to analyse a sinuous line in a conventional co-ordinate system. Most people understand readily the meaning of a simple curve, and a little practice gives facility in appreciating a simple periodic one, such as a sine curve. When, however, a periodic curve contains several components, appreciation is more difficult and when the periodicity is irregular and the components variable, the efficiency of the direct visual analysis falls off and fatigue quickly sets in. Now in the case of the e.e.g. a simple periodic curve is an extreme rarity, for only occasionally are two con-

secutive waves exactly similar, and in the more common complex records the eye invariably compromises by attending only to those components which possess the greatest regularity and amplitude. It is this tendency which has led to the designation of certain basic rhythms such as the "alpha" and "delta" rhythms and thus to an over-simplification of the whole subject.

Various ways of supplementing primary inspection have been devised. Most are tedious and many are unreliable. The only principle which can be of value is to break the record up into segments and to analyse each segment into its component parts, as a prism displays the colour content of white light. This implies a mathematical wave analysis of a particularly clumsy type, but fortunately the computations can be made quite accurately by machinery. The first useful analyser for the e.e.g. was described by Grass and Gibbs (1938), and this has been used by the Boston workers for some years with good results. It has the disadvantages that a special photographic record must be made as well as the usual ink-traced one, that the analysis is not available until the photo-record has been processed and run through the analyser, and that the analysis curve cannot be immediately referred to the primary trace to which it applies. In order to produce an analysis without these hindrances, another type of instrument has been built. A technical description of it has appeared elsewhere (Walter, 1943a and b), and the details of design need not be gone over here.

Method

The apparatus traces a frequency histogram or band spectrum over the primary record. For this purpose an arbitrary epoch of ten seconds has been chosen to which each spectrum analysis applies. The analysis is performed automatically every ten seconds, and is traced over its primary record in the natural order of frequencies. In the first model the frequencies included were 2, 3, 4, 5,

6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 20, 22 c/s.; in a later model the range was extended to include in addition 1.5, 2.5, and 24, 27, 30 c/s. An arbitrary ordinate scale is used, corresponding approximately to (average—amplitude $\times$ duration) of oscillation at each of the frequencies during the ten-second epoch. Thus a 10 c/s. oscillation with an average amplitude during the epoch of half the possible maximum, lasting throughout the epoch, would be represented as a kick of the analyser pen of half the maximum at the 10 c/s. point in the frequency scale. An oscillation of maximum possible size, but lasting for only half the epoch would be represented by a kick of the same size. When oscillations at several frequencies are present simultaneously, all will be shown as kicks at the appropriate point on the frequency scale, each kick indicating the amount of "activity" at that frequency during that epoch.

To a first approximation the amplitude of any given oscillation in the e.e.g. is an indication of the number of neurones engaged in synchronous electrical activity at that frequency. The analyser kick, therefore, shows the temporal and spatial extent of electrical activity at any or all of the frequencies covered in the area of the brain from which the record was taken, during a ten-second epoch. Its great advantage over the unaided eye is that it is not deceived nor discouraged by the presence of a small intermittent rhythm close in frequency to a large regular one. Since the spectrum is traced directly over the primary record, the analytic summary may be used to attract attention to features of the primary record which would otherwise be overlooked, and an essential feature of the new technique is that the primary and spectral records are used to complement one another, and the combined data are immediately available to direct further recording or experiment.

It has been found that the introduction of this form of analysis extends the range and interest of the whole subject, a survey of which is in course of preparation. Advances have already been made in problems relating to diagnosis and neurophysiology. The complexity of records from cases of cerebral tumour was the first subject to be clarified. Analysis of these records shows that the irregular form of delta waves is due to the presence of components which are quite steady in their mean frequency, but very variable in their amplitude. It was found in the course of routine recording from many cerebral tumour cases that usually these other components had a frequency of from 4 to 7 c/s. and that the focus of this activity was often different from that of the slow delta discharges. It seemed probable that the association of these medium frequencies with the new growth was due to a different mechanism from that leading to the slower rhythms. It was suspected that this other mechanism was connected with involvement of the sub-cortical centres and material was gradually collected to check this hypothesis.

Material

Attention was first directed to a group of cases in which the nature and extent of the tumour had been verified either at operation or post mortem. There are 31 cases in this group. This number is too small for formal statistical treatment, and, indeed, less has been learned by this method than by study of each individual case and correlation of details. A much larger number of cases has been studied, but not all have been thoroughly investigated

pathologically. In general it was found that all these cases exhibited, among various other features, significant activity in the 4–7 c/s. band. In 21 cases there was good correlation between the superficial location of the 4–7 c/s. rhythm and the deeper effects of the new growth. In two cases the 4–7 c/s. rhythm was posterior and bilateral, and in these the lesion was in the posterior fossa. In eight cases the activity was more diffuse, and in these there were either multiple lesions or a grossly raised intracranial pressure.

Results

Considering the 21 cases in which the location data are trustworthy, these may be divided into:—

1. Those in which the tumour arose superficially and was spreading into or pressing upon the sub-cortical structures (5 cases).
2. Those in which the tumour arose in the deeper structures and was spreading outwards or compressing the cortex (5 cases).
3. Those involving the deeper structures to a much greater extent and affecting the cortex only indirectly (11 cases).

The records from Category 1 all showed a more or less prominent delta rhythm (1–3 c/s.), localized to the area around the superficial involvement of the tumour. In addition they exhibited in varying degrees activity in the 4–7 c/s. band. This was often masked in the primary record by the larger, slower rhythms and usually was wider in focus. In certain cases it arose from areas remote from the superficial aspect of the tumour (Fig. 1A, B, C). Typically, the delta rhythm was at 2 c/s., and the other at 6 c/s. That is, the higher frequency tended to be a multiple or third harmonic of the slower. This explains the delta waves with square or triangular forms. Both of the frequencies vary by about a half c/s. and also fluctuate in amplitude, so that the variety of wave-forms is very large.

The records from Category 2 all showed 4–7 c/s. activity which seemed most prominent where the tumour approached the surface. There was in addition a smaller delta rhythm, also indefinitely localized and varying from moment to moment in frequency and amplitude. In these cases the slower rhythms in the primary records tended to be masked by the faster ones (Fig. 2A and B). The 4–7 c/s. activity was often bilateral although its larger amplitude on one side and the co-existence of the delta rhythm usually served to lateralize it. In these cases the abnormal potentials are small, and they are often masked by the normal alpha rhythm of 8–9 c/s., so that in many cases the abnormal component would not have been suspected without analysis. Furthermore the 4–7 c/s. activity tends to show most clearly in the parieto-temporal regions on the more affected side, and careful location technique and analysis were needed to separate the pathological components from the alpha rhythm.

The records in Category 3 are more difficult to classify. In general the more restricted the new growth the less prominent the delta rhythms. The

FIG. 1.—(A). e.e.g. from case with tumour shown in Fig. 4. Distribution of rhythms in Fig. 5. (B). The same, using phase discriminating analysis. (C). e.e.g. from case with tumour shown in Fig. 6. Distribution of rhythms in Fig. 7.

For explanation of analysis, see text. The coloured trace is a frequency histogram drawn automatically by the analysing pen. Each kick represents the amount of activity during the ten-second epoch at the frequency indicated by the number at the base of the kick. The small double downward deflections indicate divisions between epochs.

FIG. 2.—(A). e.e.g. from case with tumour shown in Fig. 8 (X-rays) and Fig. 9. Distribution of rhythms in Fig. 10. (B). e.e.g. from case with tumour shown in Fig. 11 (X-rays) and Fig. 12. Distribution of rhythms in Fig. 13.

FIG. 3.—(A). e.e.g. from case with umour shown in Fig. 14. Distribution of rhythms in Fig. 15. (B). e.e.g. from case of tumour shown in Fig. 16. Distribution of rhythms shown in Fig. 17. (C). e.e.g. from case of tumour shown in Fig. 18. Distribution of rhythms in Fig. 19.

only cases exhibiting any really significant delta activity were those with a raised intracranial pressure (Fig. 3A). In the others the most prominent feature of the records was activity at about 6 c/s. from the post-central and parieto-temporal areas (Fig. 3B, C).

Turning now to the eight cases with more equivocal or complex clinical features, these showed correspondingly more diverse abnormalities in the e.e.g. All had lesions involving the sub-cortical structures, and all the e.e.g.s had one feature in common—activity in the 4–7 c/s. band. This activity was usually bilateral and most prominent in the parieto-temporal areas. It was often of low potential and therefore tended to be masked by the other larger rhythms.

Before discussing this material in general, a more detailed reference to the figures will help to clarify the picture.

Fig. 1A is a record from a patient who complained of headache, vomiting, and prolonged attacks of uncon-

sciousness for four months. Examination indicated a frontal lesion with fluctuating pyramidal signs on both sides. In the record, the dominant components from all areas are at 2 and 6 c/s. There is only a trace of normal alpha rhythm at 10 c/s. There are occasional waves at an even lower frequency than 2 c/s. The slow components frequently show a square or triangular waveform indicating the presence of third harmonics. This corresponds in the analysis to the peaks at 2 and 6 c/s. Location in this case was obviously difficult but was assisted by the method illustrated in Fig. 1B, whereby analysis is made of the components out-of-phase in channels 1 and 2, discriminating against those components which are in-phase in the two channels. In the first epoch the dominant out-of-phase component is at 6 c/s., while in the second epoch, both 2 and 6 c/s. are present. Comparative phase-discriminating analyses of this type were also made between the other channel-pairs. These revealed delta foci in the right frontal and left fronto-temporal regions, suggesting a large space-occupying lesion between these foci, obliterating the cortex and pressing inwards on the basal ganglia. The patient died shortly after operation. At post mortem a meningioma the size of a tangerine was found arising in the left frontal region, pressing both left and right frontal lobes apart, and reaching as far down as the basal ganglia and diencephalic structures. This deep involve-

FIG. 4.—Tumour location topogram of case with e.e.g. in Fig. 1A.

ment was probably responsible for the patient's prolonged attacks of unconsciousness and for the sudden death. Fig. 4 shows the tumour and Fig. 5 the e.e.g. topogram.

Fig. 1C is from a patient complaining of headache and

FIG. 5.—e.e.g. rhythm topogram of case with tumour shown in Fig. 4 and record in Fig. 1A.

- (1) 1-3 c/s Rhythms [Delta]. (2) 4-7 c/s Rhythms Prominent [Theta]. (3) 4-7 c/s Rhythms [Theta]. (4) 8-13 c/s Rhythms [Alpha].

The shading convention is the same for all e.e.g. topograms (Fig. 7, 10, 13, 15, 17, 19).

loss of vision for a year. The only neurological findings were bilateral optic atrophy and astereognosis of the right hand. The record shows an analysis similar to that of Fig. 1A, but there is less activity at the very low frequencies. The dominant feature is the peak at 6 c/s. There is also an irregular but high voltage alpha rhythm. The slow components and the 6 c/s. rhythms both focussed over the left fronto-parietal region. Operation revealed a nodular tumour in this area infiltrating the deeper structures below but not laterally. In this case there was less cortical damage and more localized interference with the basal ganglia than in the patient of Fig. 1A. Fig. 6 shows the tumour and Fig. 7 the e.e.g.

FIG. 6.—Tumour location topogram of case with e.e.g. in Fig. 1C.

topogram. Fig. 2A is from a patient complaining of headaches for several months. The only neurological finding was a doubtful extensor response on the right side. The record again shows a prominent 6 c/s. rhythm localized to the left parietal region and accompanied

by a smaller amount of 2-3 c/s. activity. In Fig. 8 are the X-rays showing a calcified mass below the left fronto-parietal region. This was found by biopsy to be an oligodendroglioma. The site of the tumour and

FIG. 7.—e.e.g. rhythm topogram of case with tumour shown in Fig. 6 and record in Fig. 1C.

(1)

(2)

FIG. 8.—X-rays of case with e.e.g. shown in Fig. 2A.

e.g. topograms are shown in Fig. 9 and 10. Fig. 2b is from a patient who has had epileptic attacks and headaches for 20 years. Examination showed anosmia and paresis of the left external rectus. The records

FIG. 9.—Tumour location topogram of case with X-rays shown in Fig. 8 and e.e.g. in Fig. 2A.

show a peak in the 6 c/s. band from the left temporo-parietal leads. The alpha rhythm is normal on the right side with a frequency of 9 c/s. It is present also, though smaller in potential on the left side. The

FIG. 10.—e.e.g. rhythm topogram of case with tumour shown in Fig. 8 and 9 and record in Fig. 2A.

activity in the delta bands is much less than in the previous case. The X-rays (Fig. 11) show a sharply defined egg-shaped calcified mass below the left parieto-temporal cortex. The mass location and e.e.g. topograms are shown in Fig. 12 and 13. Fig. 3A is from a patient complaining of headaches and mental deterioration for some weeks. There was a progressive right-sided hemiplegia with a raised intracranial pressure. The records show the widespread slow waves characteristic of raised pressure. On the right side these are smooth and fairly rhythmic and analysis shows few components between 3 and 10 c/s. On the left side the form of the waves is more irregular, triangular or square and analysis shows the presence of components at 6–7 c/s. chiefly from the left parieto-temporal region. Post mortem a metastatic tumour was found involving the left side of the hypothalamus and extending into the posterior fossa. The primary tumour was not found. The site of the tumour and e.e.g. topograms are shown in Fig. 14 and 15. Fig. 3B is from a patient complaining of blurring of vision in the left eye for three years, followed by sudden blindness of both eyes a month before. There was also vomiting and headache and a tendency to general obesity. The vision improved later, leaving a bitemporal hemianopia. The vision of the right eye was better than that of the left. X-rays showed an enlarged and eroded sella turcica. The records show asymmetry of the hemispheres and in the right frontal region the dominant peaks are at 6 and 12 c/s. This is a good example of the value of analysis since the primary trace of channel 1 in this record would be difficult to describe owing to the irregularity and low potential of the discharges. The twelve-cycle rhythm is the second harmonic of the 6 c/s. and is associated with it, the alpha rhythm being a separate component at 10 c/s. of low amplitude. This second harmonic alters the form of the 6 c/s. waves and masks them, tending to a spiky monophasic pattern. Inspection of the primary record shows

(1)

(2)

FIG. 11.—X-rays of case with e.e.g. shown in Fig. 2B.

FIG. 12.—Tumour location topogram of case with X-rays shown in Fig. 11 and e.e.g. in Fig. 2B.

FIG. 13.—e.e.g. rhythm topogram of case with tumour shown in Fig. 11 and 12 and record in Fig. 2B.

FIG. 14.—Tumour location topogram of case with e.e.g. shown in Fig. 3A.

FIG. 15.—e.e.g. rhythm topogram of case with tumour shown in Fig. 14 and record in Fig. 3A.

FIG. 16.—Tumour location topogram of case with e.e.g. shown in Fig. 3B.

FIG. 17.—e.e.g. rhythm topogram of case with tumour shown in Fig. 16 and record in Fig. 3B.

that the 6 c/s. and 12 c/s. components can occur independently of one another occasionally. This spectrum is abnormal for the frontal lobe and suggests a deep seated lesion. Operation revealed a bulging diaphragma sellæ pressing upon the optic chiasma. A portion of the new growth was removed. Fig. 16 shows the site of the tumour and Fig. 17 the e.e.g. topograms. Fig. 3c is

from a patient with a six-months history of headaches, vomiting, vertigo and personality change. There had been a radical amputation of the breast for malignancy two and a half years previously. The only abnormal signs were stupor and engorgement of the retinal vessels.

FIG. 18.—Tumour location topogram of case with e.e.g. shown in Fig. 3C.

The records show a prominent peak at 5 c/s. from the right side, focussing over the lower parietal and temporal regions. The alpha rhythm is of normal frequency and focus, though masked in the primary records from the right hemisphere by the slower rhythms. Post mortem

FIG. 19.—e.e.g. rhythm topogram of case with tumour shown in Fig. 18 and record in Fig. 3C.

five months later revealed a metastatic tumour involving the right cerebello-pontine angle with pressure effects in the mesencephalic structures. The tumour location and e.e.g. topogram are shown in Figs. 18 and 19.

Discussion

This detailed description serves to illustrate the way in which electrical activity at about 6 c/s. is associated with involvement of sub-cortical structures. A valid general criticism is that new growth anywhere in the brain is almost certain to affect these structures in some way since they are close to the ventricles and easily damaged by distortion. In most cases of brain tumour these rhythms do exist but in purely cortical lesions they are small and in basal ones they are large. Moreover, in different conditions they appear as a correlate of deep involvement. They are prominent in concussion without gross cortical damage where according to Holbourn (1943), the basal structures bear the brunt of the blow, and in children with behaviour disorders characterized by rage attacks and emotional lability, in whom the 4-6 c/s. waves are particularly large and rhythmic. Similar rhythms have been described by Hill and Watterson (1942) in aggressive

psychopaths. The location of this rhythm in the parietal and temporal regions is also characteristic. In tumours the more affected side shows more of this activity, but a tumour expanding on one side may displace the deeper structures so far to the other side that the disturbance is in effect bilateral.

Some of the material here described was discussed at a meeting of the Electro-encephalographic Society in 1943, and since then at other centres cases of cerebral tumour have been collected which show the 4-7 c/s. activity clearly enough to be seen in the primary record (Gibb and Turner, 1943). In a private report, Cobb (1943) agrees that these frequencies may have significance and suggests that they may "originate in structures adjacent to the third ventricle, more anterior than posterior."

With the analytic method rhythms at many frequencies can be appreciated simultaneously, and as each has its zone of dominance and physiological associations, classification by "cycles per second" becomes clumsy and inadequate. The term "alpha rhythm" is widely known and is clearly more convenient than "rhythm at about 10 c/s. from the occipital region tending to be blocked by visual and mental activity." Similarly "delta rhythm" is shorter than "waves at 1 to 3 c/s. of cortical origin signifying damage, dystrophy or degeneration." In the case of the 4-7 c/s. waves the term which we suggest is "theta."

These waves occur in the state just preceding or following natural sleep. Electrical exploration of normal waking subjects has revealed that with high amplification and phase-discriminating analysis a small peak of energy at 6 c/s. is almost invariable in the parieto-temporal areas, and this peak is augmented when the subject starts to feel remote and is on the verge of drowsiness. In some normal people this peak is large, though never as large as the alpha peak from the occipital region. Sometimes, it is diminished like the alpha rhythm by opening the eyes and mental alertness.

Kennard and Nims (1942) and Kennard (1943) found that in monkeys "lesions of the thalamus alter the pattern of cortical e.e.g.s in general, but most markedly in the post-central areas." These changes were usually the production of waves at 6-8 c/s. as distinct from the normal 8-10 c/s. rhythm, and this effect long outlasted the temporary local changes associated with experimental acute cortical trauma. Lesions of the caudate nucleus and putamen had most effect upon the precentral and frontal areas, while lesions of the thalamus affected most the post-central regions. If, as a working hypothesis, it can be assumed that the 4-7 c/s. oscillations resemble the 8-12 c/s. alpha rhythm in being physiological "rest rhythms," it would be expected that lesions interrupting the transmission of centripetal impulses through the thalamus would tend to augment the 4-7 c/s. activity, much as closing the eyes augments the occipital alpha rhythm. This conception has importance beyond tumour location, since normal maturation of the human nervous system also involves change in the thalamo-

cortical relations. Kennard and Nims (1942) have shown that, in the monkey, there is a progressive "increase in amplitude, rate and complexity of pattern" during the first year of life, but closer inspection shows the appearance first of 4-7 c/s. and then of 8-10 c/s. waves. This process is paralleled in human development where the details can be filled in more easily. In human children, analysis of local rhythms shows, even in the infant, activity at 2-3, 5-6, and 8-10 c/s. from the frontal, parieto-temporal and occipital areas respectively. In the first few months the slowest rhythms are dominant, later the medium frequencies, and finally the alpha becomes prominent, but at all times the various frequencies are present in their respective zones. It is not true therefore to say that "the e.e.g. is slower in children than in adults," but it is true that in young children the 4-7 c/s. rhythms are larger in their areas than the 8-12 c/s. are in theirs.

Further evidence that the basal ganglia affect the e.e.g. is given in the report of Gibbs and Gibbs (1941) that complex slow rhythms occur in cases of chorea and athetosis. This is not so, however, in all cases where the basal ganglia are known to be affected, notably in parkinsonism, where the e.e.g. is typically "normal." This discussion serves to emphasize the limits of knowledge of the electrophysiology of the forebrain which results from (1) the difficulty of deciding to what extent a given lesion, experimental or spontaneous is irritative or destructive; (2) inability to replace removed or damaged nervous tissue to complete an experiment; (3) The great flexibility of central nervous function leading always to extensive re-routing of impulses and consequent vicarization of function; (4) the limitations of electrophysiological technique which permit intimate study of one neurone group only if others are sacrificed; and conversely, in the intact brain reveal only the blurred outline of a possibly irrelevant statistical conglomeration. The last difficulty is in course of solution; the others are more subtle and more challenging but may be circumvented.

Summary

1. Special automatic analysis and accurate location procedure have been used in the electro-encephalography of cases with cerebral tumours affecting sub-cortical structures.
2. In 31 cases subsequent operation or post-mortem revealed the site and extent of the tumour.
3. In cases with superficial tumours spreading inwards, the site of the tumour exhibited 1-3 c/s. (delta) waves; the adjacent areas and parieto-temporal regions showed activity at about 6 c/s.
4. In cases with deep tumours spreading outward the main feature was 6 c/s. activity from the cortex above the tumour and/or from the parieto-temporal regions. A small delta rhythm was sometimes seen immediately above the tumour or as a general effect of raised pressure.

5. In cases with deep tumours not affecting the cortex, the 6 c/s. rhythm was the only significant abnormality. This was usually from the parieto-temporal region and often could only be distinguished from the normal alpha rhythm by analysis.

6. In cases with more widespread new growth, the 6 c/s. rhythm was seen whenever the basal structures were affected.

7. The occurrence of rhythms at about 6 c/s. from the parieto-temporal region in these cases is related to the similar rhythms found in other clinical and physiological conditions where the basal structures are involved, and also to the effect of experimental lesions of the basal ganglia in monkeys.

8. It is suggested that rhythms at about 6 c/s. should be termed "theta" rhythms and that such rhythms are characteristic of the resting, immature or isolated parieto-temporal cortex.

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