CRITICAL REVIEW

THE TECHNIQUE AND APPLICATION OF ELECTRO-ENCEPHALOGRAPHY

BY

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THE rate at which scientific knowledge is accumulated depends upon a number of factors the relative importance of which is not the same in the various branches of science. The history of physiology and medicine suggests that their development is becoming increasingly dependent upon the progress of the physical sciences. This is not merely because the physiologist and clinician prefer to describe their observations in physical and chemical terms ; the link is apparent in the first stage of the scientific method, the manner in which the observations are made. The number of new facts discovered with the unaided senses grows smaller ; the range of perception is extended by more and more elaborate tools. This growing dependence of the biologist on the physicist is familiar, but it has been emphasized here because it suggests some reasons for the difficulty of integrating the facts collected in the last ten years by many observers of the electrical activity of the human brain.*

The use of modern electrical techniques in electro-physiology has made the collection of facts easier and more rapid, but the subjects in which the facts have been most satisfactorily built into a coherent theoretical structure are those which were most developed before the introduction of the new methods. In lines of study which spring directly from technical advances the tendency is for more problems to be created than can be solved ; worse still, the avalanche of new observations produces a chaos in which a problem can be stated only in the most indefinite terms. An atmosphere is soon created which is congenial to empiricism and deductive speculation ; while the ascetic principles of inductive logic are forgotten in the search for facts and applications. The apparent incoherence of the factual premises is likely also to lead to a cynical individualism in the attitude of the various workers toward their subject, and variations of method and terminology arise which make it hard for those who should be colleagues to understand one another, and almost impossible for a new-comer to understand any of them.

The short history of electro-encephalography illustrates this process in detail. The electrical phenomena associated with nervous activity were observed almost as soon as there were instruments capable of detecting them, early in the last century, and Caton (1875) showed that electrical changes

* The reviews by Jasper (1937) and Fessard (1938) were found most useful as guides to the literature.

occurred in the exposed brain of an animal both when resting and during stimulation and motor activity. Fleischl von Marxow (1883), Beck (1890), Gotch and Horsley (1891), and several others contributed information which suggested that the central nervous system of animals possessed electrical properties related to those found in peripheral nerve and muscle. Prawdicz-Neminski (1913, 1925) described six types of wave in what he called the " electrocerebrogram " of the dog, and was the first to attempt to classify his observations.

The experiments of all these workers were made on the exposed brains of animals, using galvanometers to detect slow changes and string galvanometers or capillary electrometers for the rapid ones. The comparative lack of interest in the electrical activity of the brain may seem surprising until it is remembered that the electrophysiology of nerve and muscle was still in its infancy, though rapidly developing, and the clearer problems of excitation and propagation in these simpler tissues afforded ample scope for those whose interest was attracted to such subjects.

In 1929 Berger published the first record of the electrical activity of the human brain. This was taken through the unopened skull with a Siemens galvanometer, and the deflections were therefore small and unconvincing. For this reason, and perhaps also because he was known to have been looking for the phenomena he described, Berger's " elektrenkephalograms " were almost disregarded and his entirely original, painstaking work received little recognition until Adrian and Matthews (1934) supplied thorough respectable confirmation. By this time Berger had published eight papers ; since 1932 his records have been with an amplifier and oscillograph, and he has applied his technique to the study of many pathological conditions. He also worked out a theory to account for his observations, and this will be discussed later.

Since Adrian and Matthews confirmed that, given adequate technical equipment, the electrical waves of the human brain could be observed with less trouble than the action potentials from the single nerve-fibre preparations of modern electrophysiology, electro-encephalography has become one of the most popular laboratory subjects. The normal electro-encephalogram was soon found to be, in Adrian's phrase, " disappointingly constant," and the attention of many workers was diverted to the study of nervous disease. This was found a rich field, and the surprising state has been reached wherein what may be called the electropathology of the brain is further advanced than its electrophysiology ; while there is still a great variation of opinion as to the precise nature and significance of the features of the normal electro-encephalogram, its usefulness in the study of diseases of the brain is widely accepted.

A body of knowledge which comes into existence in this way, rather from the technical ease with which it was begotten than from its necessity in the general scheme, is likely to suffer not only from congenital deformities but also from the further handicap that if a large number of observations are made in a short time, some of them are likely to be false ; and when the observers are armed with a weapon as powerful as the equipment used in electro-encephalography, the errors may be greatly magnified ; so that it becomes hard enough to sift true from false, let alone compound the true into a consistent and enlight-

ening whole. Just as in microscopical anatomy the fixation of a tissue or the aberration of a microscope may produce artefacts which mislead even experienced histologists, so in electro-encephalography both the subject and the apparatus may produce spurious electrical discharges which are almost indistinguishable from those associated with the brain. Accordingly, the requirements and limitations of the technique will be discussed before considering the information which it has yielded.

Technical Considerations

The upper limit of size of the brain potentials as led off through the skull approaches that of the electrocardiogram ; about one millivolt and potentials even greater than this are obtained when leads are placed directly on the exposed cortex. Discharges of this magnitude are rare, however, and in fact are only found in abnormal conditions. The commonest features of the human electro-encephalogram (E.E.G.) usually have a potential of less than 50 microvolts, and significant discharges can be recognized which are as small as 5 microvolts. If there were no limit to the amplification which could be used, even smaller cerebral potentials might be detected, but for physical reasons the greatest sensitivity which can be used is such that an input of 5 microvolts produces a measurable deflection of the recording instrument, which should be capable of responding at the same time to an input of twenty times this size without damage or adjustment. The time relations of these small potentials are, by ordinary physiological or electrical standards, very slow ; their effective duration varies from one second down to perhaps 20 milliseconds. Sometimes they are rhythmic, sometimes they occur as pulses or transients. Rohracher (1935, 1937*a*) has described frequencies as high as 1,000 per second associated with intellectual activity, but their existence has not been confirmed. Even more doubtful are the discharges reported by Cazzamalli (1936, 1937). These are claimed to appear during emotional excitement and have a frequency of the order of megacycles !

There is no oscillograph or galvanometer capable of dealing unaided with such potentials, and thermionic amplification is essential ; even then careful design is necessary, for the frequency-band on which the brain appears to work, having no æsthetic or commercial importance, falls below the range of the conventional audio-frequency amplifier. The ideal arrangement would be a direct-coupled amplifier with a circuit such as that described by Matthews (1938). This will reproduce faithfully all frequencies, even steady differences of potential, and has the added advantage that it cannot be choked by overloading with a very large transient at high sensitivity. The very virtues of this system, however, make it tiresome for electro-encephalography, since with electrodes on the skin, slow swings of potential are picked up. These are often of considerable size and when amplified would result in violent base-line fluctuations. For most purposes a condenser-coupled circuit can be used provided that the overall time constant is not less than one second.

For reasons which will be discussed later, it is generally necessary to use several independent channels of amplification at the same time, therefore particular attention must be paid to the input stage. Amplifiers in which one side of the input is a common earth line cannot be truly independent, so a " balanced " input stage must be used. There are several possible arrangements, but the simplest is probably that described by Matthews (1938) and originally due to Tönnies. Like the earlier circuit designed by Matthews (1934), this is relatively immune to radiated interference, such as that from alternating current mains, so that in most cases elaborate screening arrangements can be dispensed with. It has the considerable practical advantage that the batteries, being earthed, can be common to the several channels, and that the subject too can be at earth potential and may therefore be touched without producing electrical disturbances. In electro-encephalography the parasitic potentials set up in the subject's skin and in the electrodes are usually greater than the valve noise of the amplifier,

and the base-line may legitimately be smoothed considerably by filtering out the audio-frequency components of the background noise which lie above the highest frequencies produced by the brain. None the less, it is sound practice to have as quiet a first stage as possible. The special " quiet " triodes, Marconi A537 and MH40, are specially suitable. The input leads and early stages of the amplifiers should, of course, be electrostatically screened.

The output from a balanced input stage has one side earthed, and thereafter a conventional design may be adopted. The amount of amplification necessary depends, of course, upon the sensitivity of the recording system. This may be of any type provided that it will respond faithfully at the frequencies concerned and permit continuous observation or visible recording over a long period. Whatever type of oscillograph is used, it is important that provision be made for multiple-channel recording. Mirror oscillographs have been used by many workers. (For example, Berger, 1930 *et seq.* ; Adrian and Matthews, 1934 ; Jasper and Andrews, 1936.) These are relatively cheap and are convenient for multiple recording. Their disadvantages are that they require a power output stage and that observation of the slow waves by the usual rotating mirror system is unsatisfactory, since at these speeds visual persistence fails to give the illusion of a standing wave. The cathode-ray oscillograph is a highly satisfactory instrument for use with photographic recording. Multi-channel records may be obtained either by using several tubes with mirrors (Walter, 1937) or by commutation of the several channels on to one tube (MacMahon and Walter, 1938). Old-fashioned gas-focused tubes may be used, and these require only about 50 volts output and negligible power from the amplifier. Recently double trace (Cossor) and triple trace (Western Electric) vacuum tubes have been produced, and these would be ideal for electro-encephalography. Tubes fitted with an afterglow screen make the form of even the slowest deflections easily visible. Provided that frequencies above about 30 per second are not encountered, the ink-writing oscillograph is by far the most convenient, particularly when long records are taken. The " Polyneurograph " of Tönnies (1933), which has five writers, each with a natural frequency of about 50 per second, is probably the finest equipment of this type, but it has not been manufactured commercially. The piezo-electric writer of Offner and Gerard (1936) has a higher natural frequency than most electro-magnetic systems, but the size of the deflection obtainable with it seems rather small. The " undulator " of Garceau and Davis (1935) has given excellent results and a four-channel instrument of similar type has been used by Gibbs, Gibbs, and Lennox (1938) for some years in their studies of epilepsy. The peculiar advantage of writing oscillographs for continuous recording is illustrated by the work of Loomis, Harvey, and Hobart (1935) on sleep, in which continuous records were taken for periods up to eight hours. Most ink-writing oscillographs are very expensive and naturally require considerable power, but a simple and cheap way of obtaining a direct record is to adapt a moving-coil loud-speaker or relay for tracing on the smoked paper of a kymograph. This device was used by Golla, Graham, and Walter (1937) for the study of a number of epileptic patients. With a large kymograph, recording can be carried on for about thirty minutes.

The details of the recording apparatus, then, are unimportant, providing that the following four conditions are fulfilled :

1. Sensitivity must be such that an input of 5 microvolts will produce a measurable deflection.

2. The response must be uniform and undistorted from a frequency of one cycle per second up to 50 cycles per second, and should not be grossly deficient for some way beyond these limits.

3. Several recording systems should be used simultaneously, and must be entirely independent of one another.

4. Facilities must be provided for continuous observation and recording.

Another technical matter in which there has been considerable variation, but which is not actually very important, is the type of electrodes used and the manner in which

they are held on the head. Berger's original records were taken with silver wires inserted into the scalp under local anæsthesia with the help of ground-down hypodermic needles. This proceeding has not been found to have any particular advantage, and of course is positively dangerous when the subject is uncoöperative. Berger himself now uses silver foil and cotton-wool moistened with saline, held on with rubber bands. An elaborate and theoretically sound electrode was described by Jasper and Andrews (1936), but they have abandoned this (1938) for a simpler design consisting merely of chlorided silver and felt and stuck on the scalp with collodion. A similar pattern was described by Walter (1936) and the silver-silver chloride pad seems the most practical form for ordinary purposes. These are not truly non-polarizable, but if they are regularly chlorided and kept out of direct sunlight, they produce no visible distortion of the brain potentials and generate only a minute e.m.f., which is important if no blocking condensers are used in the leads to the amplifiers. The attachment to the scalp depends upon the type of observation which is being made. For a long session the electrodes must be moistened with jelly saline and stuck on firmly with collodion, but for shorter studies they may be held in place with a hairdresser's wave-setting cap and dampened with saline as described by Walter (1937). This method is quick and flexible, but is unsuitable if the subject is likely to move a great deal or if rapid drying of the pads is likely. In any case, the grease of the scalp should be removed with alcohol from the places where the electrodes are to be applied. The hair need not be shaved, but care should be taken that the electrode is in firm contact with the skin. If the scalp has been recently shaved or if electrodes have been placed in a great many positions, the natural insulation of the sebum will have been entirely removed and replaced with a film of electrolyte which, by considerably lowering the inter-electrode resistance, can produce an apparent reduction in size of the potentials. If observation has to be continued in these circumstances, the scalp must be liberally rinsed with water and a small quantity of vaseline rubbed in between the electrodes. In general it may be taken that whatever pattern of electrode is used it should be relatively non-polarizable and should not hurt the subject.

For leading off directly from the human cortex, wick electrodes may be used, or, for localizing, a small concentric silver electrode is convenient and if held in an anglepoise holder can do no damage to the tissue.

The manner of leading off has a great effect upon the results obtained and the interpretation which can be put upon them. When Berger's discoveries first came to be taken seriously, a dispute soon arose as to the respective merits of " Bipolar " and " Unipolar " leads. Berger's arrangement was bipolar, consisting of one electrode on the forehead and one on the occiput, thus including most of the brain between the electrodes. Adrian and Matthews (1934) also used bipolar leads, but with an important difference which will be explained later.

Tönnies (1934) pointed out that with both electrodes equally near to presumably active cortex, a complex record would be obtained due to all the discharges originating in the large mass of tissue, and advocated an " indifferent " electrode attached to the two ears with an exploring electrode on the scalp. With multi-channel recording the indifferent-ear electrode is connected to the common earth line and the exploring electrodes are placed over the parts of the brain which are to be studied. Location of the discharges is accomplished by comparing the size of the deflections from the various channels, presuming that the amplification is exactly the same in all and that the potentials picked up by the electrode nearest the active area are always larger than those picked up by electrodes further away from it. This argument seems fairly convincing and unipolar leads have been used successfully by many observers, including Gibbs, Davis, and Lennox (1935), Gibbs, Lennox, and Gibbs (1936), Gibbs, Gibbs, and Lennox (1937), and Loomis, Harvey, and Hobart (1935 *et seq*).

There are certain fallacies, however, in the argument for unipolar leads, the two chief being, first, that no electrode position is truly indifferent, since no part of the head is either infinitely far from the brain or in contact with the inside of it (as is the

" indifferent " electrode used for obtaining monophasic action potentials from nerve or muscle), and secondly, that, treating the brain and its envelopes as a source of potential and an ohmic resistance network respectively (*cf.* Tönnies, 1933), the potential developed between two points (the electrodes) is a function not only of the resistance (or distance) between one of the points and the potential source, but also of the resistance between the points. In practical terms this means that in the first place some electrode arrangements will result in the " indifferent " electrode being nearer to the point of activity than any of the " active " ones, and in the second place the active electrode which seems to be picking up the largest potentials may be doing so not because it is nearest to the focus of activity but because it is furthest from the common indifferent electrode. The situation is made even more difficult by the fact that the electrical discharges of the brain are not always in the same sense as are those of nerve and muscle, in which an active or injured region is always electro-negative to an inactive or normal one. This irregularity makes location virtually impossible with only one channel. A technique to overcome these obstacles was devised by Adrian and Matthews (1934) and perfected by Adrian and Yamagiwa (1935). With it they were able to prove that the focus of origin of Berger's " alpha rhythm " was usually in the occipital region and that it wandered over an area of several centimetres. By placing a source of feeble alternating potentials inside the skull of a cadaver they were able to show that location was possible to within a centimetre. The method involves the use of three or more separate channels, each starting with a " push-pull " or balanced input stage. If three channels are used the input leads are connected to four electrodes in such a sense that a potential change at an electrode common to two of the channels will produce deflections which are out of phase in the two channels. Location of a focus of activity is achieved by observation of the phase relations of the deflections in the several channels, and the accuracy is equal roughly to the distance between the electrodes. This technique has been used for the location of cerebral tumours by Walter (1936, 1937, which contains illustrative diagrams), for the location of abnormal foci in epileptics (Golla, Graham, and Walter, 1937), and to determine the region of onset of cardiazol convulsions (Cook and Walter, 1938).* It appears to be the most trustworthy method of location available at present, though it has certain disadvantages. The chief of these, which is absolute rather than relative to other methods, is that, as stated above, the record from any one channel represents the electrical activity of the tissue in the neighbourhood of both electrodes. If sufficient channels are used, the discharges may be sorted out by analysis of the records, but this becomes very laborious when there are more than two active foci or when there is a generalized discharge.

The last matter to be considered before discussing the electro-encephalogram itself is the recognition of various distortions and artefacts. Distortion of the brain potentials by the amplifiers and oscillographs can be avoided only by observing the physical rules of thermionic amplification and by allowing for the properties of the recording system used. For example, the valves must be worked on the linear portion of their characteristic curves, and the oscillograph, if mechanical, must be critically damped and have a natural frequency above that of the fastest component of the discharges to be studied. These conditions are, of course, the same whatever the subject of investigation and need not be specially considered here.

The chief sources of artefacts in electro-encephalography are seven in number.

1. Radiated interference. The various forms of this can only be learned by experience and are most easily tracked down with a portable radio set. The balanced input reduces them considerably, but in some cases the subject has to be enclosed in a screen. The radiation from diathermy apparatus is probably the worst form. Movement of any electrostatically charged body, such as a rubber tube or celluloid ruler,

* The " triangulation " sometimes used by Jasper and Hawke (1938) (in which three channels lead off from three electrodes placed so as to form a triangle around the area under observation) is essentially the same method, and owes little to trigonometry.

in the neighbourhood of the input will produce large deflections unless the subject is earthed, as is possible with the input circuit recommended above.

2. Movements. The extent to which these interfere with recording depends upon the method of electrode attachment, since their transformation into electrical potential changes depends upon variation of electrode contact resistance. To lessen the drag upon the electrodes the leads to the amplifiers should be light and may conveniently be suspended from a flexible stand. If violent movements of the jaw or scalp or convulsions are expected, the electrodes should be held on the scalp with collodion or surgical strapping, but for ordinary purposes a cap is adequate.

3. Photo-electric potentials. Most metallic electrodes either change their resistance or develop an e.m.f. when exposed to light, and silver-silver chloride exhibits this property. For this reason the damp part of the electrodes should not be exposed to light of fluctuating intensity, particularly if the effect of this upon the brain potentials is to be studied.

4. Skin potentials. A small, steady e.m.f. exists between any two electrodes placed on the skin, due to slight differences in polarization and differences of ionic concentration in the tissue fluids and the electrolyte used. These steady potentials will only interfere if the resistance of the electrode system changes owing to movement or drying of the electrodes, both of which should be avoided. In some subjects the so-called " psycho-galvanic reflex " can be picked up from the scalp, and since conditions which produce this reflex also tend to affect the brain potentials, this source of error should be controlled by taking simultaneous records from the hands when any doubt arises.

5. Blinking of the eyelids is probably the commonest single source of artefacts. The potentials are very large—several hundred microvolts, and in nervous subjects may be rhythmically produced. They can, however, be easily recognized, since they are always in the same sense for a given direction of movement. Flutter of the eyelids produces a large quasi-sinusoidal discharge which can be recognized as an artefact only by localizing in the same way as any other potential is localized, or by recording the lid movements by some other means. Movements of the eyeballs are also frequent sources of confusion, and are probably an associate cause of the blink artefacts. This phenomenon may be put to use for recording nystagmus. It is particularly prominent in certain classes of psychotic patient as an habitual movement, and in these cases the movements sometimes are very difficult to detect by inspection of the eyeball. Potentials which seem to originate from the extreme frontal pole should be suspect until they are proved not to be eye-artefacts. One helpful point is that the eye movements are nearly always conjugate, though the lids may, of course, be winked separately.

6. An artefact of uncertain origin is a small rhythmic discharge which can sometimes be detected in the fronto-temporal region. This is in rhythm with the heartbeat and occurs at the same moment as the pulsation of the arteries of the head. It is usually best seen in cases of hypertension, but is not apparently due directly to the mechanical effects of the pulse, since electrodes placed on the radial artery where the pulsation is much greater are not similarly affected. It is not an electrocardiogram, since by simultaneous recording this can be shown to be over before the artefact occurs. From its position on the head it seems probable that it is associated in some way with pulsation of the middle meningeal artery, but further study is required. When better understood it may conceivably be found useful as a criterion of the effective intracranial arterial pressures.

7. The last class of artefact is that due to bio-electric potentials. Nerve action potentials are too small and far away to influence electrodes for electro-encephalography, but muscle action potentials are nearly always present to some extent, particularly in records from the frontal region. Their presence helps to identify potentials due to movement of the scalp and clenching of the jaws, which are not easily noticed. The time relations of these potentials are usually much shorter than those of the brain potentials, and they can therefore be eliminated by electrical filter circuits. In very powerful tonic contraction the almost synchronous volleys of action potentials may

produce a smooth, rhythmic discharge which would be hard to distinguish from some of the brain rhythms were it not always accompanied by a considerable amount of asynchronous activity in the form of a small, rapid discharge of sharp spikes. The electrocardiogram is practically never seen with electrodes on the head, since the neck tends to form an iso-electric isthmus.

The spurious potentials from these various sources have naturally been remarked on by most observers, but they are responsible for a certain number of fallacious statements, and constant vigilance is necessary to exclude them from electro-encephalographic records, the features of which may now be described.

The Electro-Encephalogram

Berger's first papers described two electrical rhythms. The first, which he called " alpha waves " and which was referred to five years later by Adrian and his collaborators as the " Berger rhythm," consists of an almost sinusoidal discharge with a frequency of about 10 per second and with a potential varying irregularly from zero to about 100 microvolts in some subjects. With his five years' start, Berger was able to build up without dispute a theory to account for his observations on both normal and abnormal subjects, and for the reasons mentioned earlier his attitude was conditioned to a great extent by his preconceived notions and the shortcomings of his technique. Nevertheless, the priority in nearly all the problems connected with electro-encephalography is certainly his, though his opinions are not shared with the majority of those who have followed him. Strange though it may seem, the extreme, perhaps excessive, simplicity of his methods led to a puzzling indefiniteness and complexity of theory. The explanation for this is that since he used only one channel, and placed his electrodes as far apart as possible on the head, his records are of what has been called the " global " electro-encephalogram, that is, they show the electrical activity of the brain as a whole. Berger's conviction that the rhythms which he found represented a basic function of the whole cortex was strengthened when he found that approximation of his electrodes reduced the size of the potentials. Such a reduction in size could, of course, have been foretold from Ohm's law, and has no other theoretical significance. Since, moreover, the rhythm of each individual was characteristic both in rate and regularity and seemed to him adversely affected more by general psychological factors such as nervousness and attention rather than by any specific sensori-motor activity, Berger considered it reasonable to build up a hypothesis of the significance of the alpha rhythm in terms of a holistic theory of central nervous action. The difficulty of understanding the theoretical portions of his later papers is partly responsible for the general scepticism regarding the facts which Berger was attempting to explain, and the impression made by his work was confused by his neglect to attempt the second process of the inductive method, that of classification of his observations. When Adrian and Matthews (1934) and Adrian and Yamagiwa (1935) had verified the existence of the alpha rhythm they compared it to the spontaneous electrical rhythms which Adrian had previously demonstrated in the central nervous systems of various animals (Adrian, 1930*b*, 1931, 1932 ; Adrian and Buytendijk, 1931) and in injured mammalian nerve fibres (Adrian, 1930*a*). By classification with these phenomena the alpha rhythm gained in respectability what it lost in strangeness,

though only a most tentative explanation could be given of the rhythmic activity even in the nervous system of a caterpillar.

In the subjects who happened to be used by Adrian and his colleagues one property of the alpha rhythm, which has since become a classical demonstration, was particularly well marked. This is its inhibition by visual activity. Furthermore, unlike Berger, Adrian was able to locate the focus of the alpha discharge, which in his subjects was restricted to the parieto-occipital region of both hemispheres. He also confirmed Berger's discovery that the rhythm was decreased or abolished, even when the eyes were shut, by intellectual concentration such as that required for mental arithmetic, and also by a startling noise or sensation. These facts suggested that the alpha rhythm was a sign of physiological rest in the occipital cortex in the neighbourhood of Vogt's Area 19, which is supposed to be associated with the integration of sensation and particularly of visual stimuli. The mechanism of the discharge was supposed to be fundamentally the same as that proposed for the slow bio-electric rhythms in other organs ; the electrical summation of slightly asynchronous volleys of action potentials, the rhythm of these volleys being set by some pacemaker either in the cortex or elsewhere. This hypothesis is still by no means out of court, although many new facts have been collected since it was first put forward, and it has the great merit that no special assumptions need be made about the properties of central grey matter.

The focal nature of the discharge may be accepted since it has been confirmed by all workers who have used suitable equipment. Discharges resembling the alpha rhythm are not restricted to the occipital regions, however, even in normal subjects. Jasper and Andrews (1938) report that in a few subjects a frontal alpha rhythm is more prominent than an occipital one and is not " blocked " by visual activity. There are certainly great variations in the size of the focus, both between individuals and in the same individual from time to time, but a precentral focus is extremely rare among normal subjects. In the author's experience, which includes the observation of upwards of 1000 subjects, normal and otherwise, only four cases have been found to have an alpha focus in the precentral regions and these were all either in pathological conditions or normal subjects in unusual circumstances. The foci in the two hemispheres are nearly always symmetrical and the rate is usually the same on both sides, and moreover the waves are in phase in both foci. Fluctuations in size, either spontaneous or induced by stimulation, are also the same on both sides, which seem to be closely linked. It must be supposed, therefore, either that one hemisphere drives the other, or that both are regulated by a common pacemaker or escapement. Of these two possibilities, the latter seems to fit in better with the fact that the discharges on the two sides are exactly in phase, for a slight delay would be expected if one side were driven by the other. Very little is known, however, about resonance in the central nervous system, and if two areas were accurately tuned to the same natural frequency only a small amount of " feed-back " would be necessary to keep them in phase, and if the synchronization were accomplished by nerve impulses in the callosal white matter, the delay would be very short.

The " blocking " of the alpha rhythms by visual stimuli offers an excellent subject for study. Durup and Fessard (1936) report that an interval of from 0·1 to more than 0·5 second elapses between a visual stimulus and the disappearance of the waves. The latency varies with the intensity and duration of the light stimulus and the relationship is logarithmic over the middle range. This has been confirmed by many observers, notably Jasper (1936), Jasper and Cruickshank (1936, 1937), Loomis, Harvey, and Hobart (1936). These workers report also that the latency of inhibition of the alpha rhythm is shorter than the motor reaction time measured simultaneously. The reaction times in these experiments seem very long, however (0·45 second average in Jasper's work and 0·35 second in that of Loomis, Harvey, and Hobart), compared with the usual figure of 0·1 to 0·2 second, and in the experience of the author the reaction time has nearly always been found *shorter* than the blocking time of the alpha rhythms —a great disappointment, since it had been hoped to discover a sign of activity midway between the afferent and efferent paths. If a movement can be made in response to a visual stimulus before the alpha focus is aroused, the region of this focus must be in the nature of a detour for the impulses concerned. In these unpublished experiments the latency was found to vary by more than 100 per cent. in the same individual in the same conditions.

As mentioned before, the frequency of the alpha-rhythm is remarkably constant in each individual, and provided normal health is maintained does not vary by more than 5 per cent. to 10 per cent. over a period of years (Berger, 1930 ; Davis and Davis, 1936 ; Loomis, Harvey, and Hobart, 1936 ; Jasper and Andrews, 1936 ; Travis and Gottlober, 1937). Berger (1932) found no activity in infants under one month old, and an alpha rhythm with adult features is not seen until the age of 5 or 6 years ; until that time the discharge is slower, and is first seen at about one year as an irregular sequence of waves at about 6 per second which resembles more the E.E.G. of sleep and some pathological states in adults. In an unpublished series of observations on the E.E.G. of people of all ages, Golla, Graham, and Walter found that if the alpha frequencies are plotted against the ages, a smooth, flat-topped curve is obtained ; the plateau extends from about 10 years to 65 years and the drop at both ends is fairly abrupt. Ontogenetically, then, the alpha rhythm starts typically as a discharge at about 6 per second in the early years of childhood, and rises steadily to a maximum frequency of 8 to 13 per second, at which it remains constant until in old age it again declines to about 6 per second, even if the individual retains his faculties more or less unimpaired.

Individual differences between mature subjects are, it should be repeated, very great, and observation of a few people, particularly if they happen to belong to any well-defined psychological or even racial group, may supply misleading data. The various controversies and disputes about the nature and significance of the alpha rhythm may be traced to this fact, and a good example is found in the opinions expressed by different authors on the E.E.G. in blind persons. Impressed by the dramatic inhibition of the alpha rhythm by visual stimuli in their few subjects, Adrian and Matthews (1934) postulated a specific connection between pattern-vision and this inhibition. They were therefore

not surprised when they found the alpha rhythm to be absent in the blind subjects whom they tested, and explained this by supposing that the visual cortex in a person who had been blind since birth or for some years could never have the same function as that of a normal person who was only temporarily in darkness. Berger (1935), however, published quite normal alpha rhythms taken from several blind subjects, and pointed out that in the peculiar circumstances of an electro-encephalographic examination a blind person, being unable to see what was being done to him, would be in a state of greater anxiety and apprehension than a normal subject, and that therefore greater care must be taken to allay his fears and gain his confidence, so that he could reach the state of general emotional and intellectual relaxation necessary for the appearance of an alpha rhythm, and which Adrian and Matthews' normal subjects, being mostly accustomed to laboratory methods, had easily attained.

The existence of an alpha rhythm in the blind can easily be verified, and it has been shown by Loomis, Harvey, and Hobart (1936) to be very easily " blocked " by an auditory or tactile stimulus. In an experiment of the author on a congenitally blind youth the alpha rhythm was found to be easily and regularly suppressed by the silent opening of a door which produced no change in the sound-level detectable by those unaccustomed to use such clues in their daily life.

In general, the conditions in which the alpha rhythm is found are those which for the subject in question imply the least degree of stimulation, interest, and anxiety. The onset of sleep, however, is associated with a fall in frequency and finally with disappearance of the alpha rhythm. The discharge may be inhibited by almost any internal or external stimulus to an extent varying enormously in different subjects. A homely example of the efficacy of internal stimuli is the " cat-box " effect described by Rheinberger and Jasper (1937) in their study of the discharges in the cat's brain. The desire to defœcate or urinate was reflected in a suppression of the spontaneous rhythms. A similar effect can be seen when young children are being examined in such circumstances. The most effective unconditioned stimuli are usually those with the greatest significance or " arousal value " (Jasper, Cruickshank, and Howard, 1935 ; Bagchi, 1937), but the inhibition is easily conditioned, and such conditioning obeys the classical laws of conditioned reflexes ; such phenomena as extinction and time reflexes may be demonstrated, and this is a subject which would probably repay the patient experimenter. Thus, by treating the inhibition of the alpha rhythm as a " response," it may be used to some extent to study a subject's " type " and idiosyncrasies. In this it resembles in some ways the " psycho-galvanic " skin reflex (*cf.* Forbes and Andrews, 1937).

Conditions in which the alpha rhythm is extremely prominent usually border on the pathological, and in the author's experience, those cases which have presented an alpha discharge which was both large in size and resistant to inhibition have complained either at the time or later of some nervous or mental symptoms. This subject will be approached later from the direction of the pathology of the E.E.G.

The possibility of controlling the frequency of the alpha rhythm by inter-

mittent visual stimulation was suggested by Adrian and Matthews (1934). They showed that when some subjects looked at a large, brightly lighted, flickering field, rhythmic potentials could be recorded from the occipital region which followed the flicker frequency up to about 25 per second. This has been confirmed by several experimenters (Durup and Fessard, 1935 ; Loomis, Harvey, and Hobart, 1936 ; Jasper, 1936). Whether this phenomenon should be described as " driving the alpha rhythm " (Adrian and Matthews) or as a succession of the " on " and " off " effects observed by Jasper and Cruickshank (1937), and whether these two descriptions are not the same cannot yet be decided. Jasper (1937*a*) and Jasper and Andrews (1938) stated that potentials can be detected from the occipital region which follow flicker frequencies up to 60 per second and they explained this (1937*b*) with the help of the concept of " alternation." Taking the mean amplitude of the spontaneous alpha rhythm as unity, the size of the evoked potentials was one half at twice the alpha frequency, one quarter at four times, and so on, while at frequencies midway between multiples of the fundamental frequency the response was greatly diminished, suggesting some sort of harmonic response. The significance of these findings cannot be assessed until they are confirmed, since the possibility of confusion with artefacts is considerable owing to the small size and high frequency of the evoked potentials.

Hoagland (1936, *a*, *b*, *c*, and *d*) has shown that the alpha frequency rises with an increase of bodily temperature, and Jasper (1936) and Jasper and Andrews (1938) have confirmed this. The critical thermal increments appear to be from 7000 to 8000 calories, but the accuracy possible in the measurements is not great enough to give the calculation much significance.

Although the alpha discharge is by far the most prominent feature of the normal E.E.G., it is not the only one. Berger has described and discussed rhythms of a frequency of 20 to 25 per second and has called them " beta rhythms." In certain of his records by his own admission these have been radiation artefacts and Walter (1937) has pointed out that artefacts due to electromyograms often give rise to similar rhythmic potentials. This is particularly evident when a recording instrument is used which has a low natural frequency, such as a writing oscillograph, for its response to a series of transients each with an effective frequency higher than its own will be a small oscillation at its own frequency. The same criticism applies to records taken with tuned amplifiers, for the more efficient a resonant circuit, the more it will tend to produce oscillations at its own frequency in response to transients. Wrinkling the brow and clenching the jaws can produce a very good imitation of a beta discharge, even with high-frequency oscillographs, and in the author's experience the beta rhythms found in most records taken without special precautions are spurious. When, however, they appear in records taken by experimenters with a full knowledge of the sources of error and ways of controlling them, their true existence as a character of the E.E.G. cannot be doubted. Marinesco, Sager, and Kreindler (1938*c*) suggest that the beta rhythm is due chiefly to layer V of the precentral cortex, since it is absent in cases of amyotrophic lateral sclerosis, when this layer is degenerate. Jasper and Andrews (1938)

have made a special study of the beta rhythms. They conclude that they are the predominant components of the precentral E.E.G., have an average frequency of 25 per second, are independent of the alpha rhythm, though similarly affected by the same " general excitatory conditions," tend to be inhibited by tactual stimulation, and that their relation to the sensori-motor areas is probably analogous to that of the alpha rhythm to the occipital visual association regions. This point of view seems to have more to commend it than that of Berger and Rohracher (1937), who both regard the beta rhythm as the accompaniment of psychical activity. There is, of course, no *a priori* reason why the precentral regions should not have a rhythm of their own, and undoubtedly a disproportionate amount of attention has been given to the superficial features of the occipital discharges by many workers. Jasper and Andrews also mention tentatively the appearance of even faster rhythms at about 50 per second, which they propose to call " gamma rhythms," but whose significance they do not attempt to discuss. Dietsch (1932) made a Fourier analysis of several electroencephalograms and found many components between 10 and 50 per second. This does not, however, mean that the irregularities of the record are actually due to the existence of such components. Rohracher (1937*a*, 1938), using a similar method, states that a normal alpha rhythm has no harmonics and is therefore a pure sine wave. For reasons which are not quite clear he infers that the alpha rhythm is an expression of vegetative rather than psychical processes in the cortex. Rohracher (1935) has described frequencies up to 1,000 per second which, like the beta waves, he finds to accompany mental activity. No one else has succeeded in recording these discharges, and they must therefore be suspect, though Rohracher appears to have taken great trouble to control his experiments.

By placing the subject close to the antenna of a short-wave oscillator, Cazzamalli (1935) claims to have detected radiations with a frequency of several millions per second proceeding from the head during emotional crises and efforts of imagination. Although the experiments take place in a leaden chamber, control of the possible sources of interference does not seem to have been very thorough, and precise details of the apparatus are not forthcoming. It is possible that, if genuine, the effect might be due to variable damping of the local oscillator by the subject. At present a benevolent scepticism would seem the correct attitude to these picturesque claims.

The alpha and beta rhythms are the only discharges which can quite confidently be ascribed to the brain in healthy human subjects, but by analogy with other animals there must be other electrical phenomena. The work of Kornmüller (1937), Adrian (1933, 1936*a*, 1936*b*), Adrian and Matthews (1934*b*), Bartley (1933*a*, 1933*b et seq.*), Bartley and Bishop (1933 *et seq.*), Gerard, Marshall, and Saul (1936), Rheinberger and Jasper (1937), Marinesco, Sager, and Kreindler (1938*a*), and many others indicates that many potential rhythms can be found in the cortex of animals. The significance of these potentials and their relation to cyto-architectonic structure and function are still matters for experiment and conjecture, but it is probable that if leads were taken directly from the human cortex a similar diversity of discharge would be revealed (*cf.* Foerster

and Altenburger, 1935). With electrodes on the scalp the cortical potentials are attenuated, appearing only 1/50 to 1/100 the size of directly recorded discharges. This means that the comparatively small local " Eigenströme " would be swamped by background noise and artefacts, leaving only the largest rhythms visible in the record. There is also the possibility that the greater complexity of function of the human cortex entails less synchronization than in the case of experimental animals. The opportunities for direct recording under a local anæsthetic from normal human brains are of course very limited.

The foregoing descriptions apply to the electro-encephalogram of normal waking human subjects. Intermediate between these and the abnormal conditions which must presently be discussed is the state of *natural sleep*, most extensively studied by Loomis, Harvey, and Hobart (1937), whose special technique permits the continuous observation of a subject throughout the night. These workers find that from the electro-encephalographic standpoint there are five stages of sleep. The first, in which the subject is still conscious but feels drowsy, is characterized by normal alpha waves at the usual frequency. The second stage, which they call " floating," is the first of true sleep, and is negative in the sense that no definite rhythms can be detected. In the third stage, which may last much longer than the previous ones, intermittent bursts of waves appear at 14–15 per second. These are called " spindles." In the fourth stage there are both spindle and slow, random " delta " waves. When the author reported the location of cerebral tumours by the slow discharges produced in adjacent cortex (1936) the name " delta waves " was suggested for the abnormal rhythms. Loomis and his collaborators and most other workers have adopted this term and used it—probably quite rightly—to describe the slow waves discovered in sleep and in many other conditions. The fifth stage is characterized by an increase in size and duration of the delta waves. These observations have been confirmed by Blake and Gerard (1937).

As will be seen, the E.E.G. in the fifth stage of sleep resembles in some ways that found in certain pathological conditions. During the second stage, arousal stimuli which in the waking subject would tend to inhibit the alpha rhythm may be followed by a train of alpha waves, that is by a transient emergence from the second to the first stage. By arranging that the subject should press a key on awakening from a dream it was found that many dreams occur with a burst of alpha waves in the second stage. This facinating study is difficult to interpret, since there is so little information on other aspects of sleep.

Jasper and Andrews (1938) have found that the " spindles " are developed from the precentral beta rhythm as sleep progresses and suggest that the slower potentials are slowed alpha waves. Since there appear to be stages of electrical inactivity between the alpha-dominant first stage and the random delta fifth, this interpretation seems difficult to accept. There has been a very general tendency to describe the slow waves which occur in many abnormal conditions as " slow alpha rhythm," and certainly all the electrical manifestations of the brain may be of the same fundamental nature, but at this stage of development

it would seem more useful to reserve the term alpha rhythm for discharges between 8 and 13 per second in normal conscious subjects.

The E.E.G. in *hypnosis* has been studied by several workers. Loomis, Harvey, and Hobart (1936) found that hypnotic sleep has little electro-encephalographic resemblance to natural sleep. They found the alpha rhythm slightly slowed ; suppression of the alpha rhythm by a painful stimulus continued even when anæsthesia was suggested and no sign of pain was visible, but on the other hand, the rhythm could be stopped and started by suggestion that the subject could or could not see, provided that in the latter case the " effort to see " associated with opening the eyes was minimized by strapping the eyes open. Marinesco, Sager, and Kreindler (1937) also found a reduction in the alpha frequency. In a few unpublished experiments, Golla, Graham, and Walter found no abnormality in hypnotized subjects. In *auto-hypnosis* as practised in certain Eastern cults the author has found that the alpha rhythm may be considerably increased in size and persistence. Records taken from an Indian engaged in meditative abstraction showed an almost continuous train of normal alpha waves, which were very resistant to inhibition by external stimuli, though in the same subject shutting the eyes without meditation produced a normally irregular discharge.

Changes in the *ionic and gaseous environment* of the brain naturally affect its electrical activity, but investigation of this subject in human beings is difficult and dangerous. Voluntary hyperpnœa was found by Gibbs, Davis, and Lennox (1935) and Lennox, Gibbs, and Gibbs (1936) to produce some slow waves in normal subjects and to enhance the slow discharge already present in abnormal ones, while inhalation of CO_2 or administration of ammonium chloride reduced the tendency to produce slow waves. These effects have also been found by Golla and Walter (unpublished). It is not possible to decide whether they are due to a direct influence on the nerve-cells or to the well-known action of CO_2 as a cerebral vaso-dilator. Golla and Walter also found that the quiet period induced in an epileptic by breathing CO_2 was always followed by a reactive phase, during which bursts of large slow waves appeared, and sometimes also by a fit or fugue. This evidence seems rather in favour of the vascular theory of the action of CO_2 on the E.E.G., since a slow " overswing " is more characteristic of the blood vessels than of the blood itself. On the other hand, the phenomenon may be related to the " rebound " observed after inhibition of a spinal reflex.

The sensitivity of the E.E.G. to slight changes in the acidity of the blood has been compared by Gibbs, Gibbs, and Lennox (1938) and Gibbs (1937*a* and 1937*b*) to that of the respiratory centres to the same stimulus, and the mechanism of the response, whatever it is, may be the same in both. Three objections may be made to the comparison, however. First, that the observations which most strongly suggest the similarity have been made on abnormal subjects ; secondly, that there is no evidence that the electro-encephalographic changes are due to a direct effect on the cerebrum ; and thirdly, that the effects of changes of acidity appear to be directly opposite in the respiratory centre and the cortex ; over-ventilation, which reduces the CO_2-content of the blood and results in inactivity

of the respiratory centre and apnœa, is associated with an increase in the electrical activity of the cortex. This paradox and the other difficulties resulting from argument by analogy will be discussed later.

Changes in the *glucose concentration* of the blood are not accompanied by alteration of the E.E.G. unless they are so great as to produce profound general effects. Hypoglycæmia induced by insulin in the treatment of schizophrenia is characterized by a reduction in frequency and increase in amplitude of the alpha waves (Berger, 1937 ; Hoagland, Rubin, and Cameron, 1937 ; Marinesco, Sager, and Kreindler, 1938*b*). In deep hypoglycæmic coma, large slow waves are found. The technique of the workers responsible for these observations was not very advanced, and it is possible that the apparent change in the alpha rhythm during the early stages of hypoglycæmia is really the first sign of the slow waves found in the later stages.

The effect of *drugs* upon the E.E.G. has attracted considerable interest.

Alcohol, consumed in the customary amounts, tends to make the alpha rhythm more prominent, and in large quantities lowers the frequency (Loomis, Harvey, and Hobart, 1936). In acute alcoholic poisoning large slow waves are usually seen. In Korsakow's syndrome also Berger (1933) reports irregular slow waves with a duration of 130 to 190 milliseconds.

Administration of the volatile fat solvent *anæsthetics* produces a marked effect on the E.E.G. Berger (1929) reported an increase in frequeency during the excitation phase of chloroform anæsthesia, and in the cat the first effect of ether was found to be the production of a small high-frequency discharge (Bremer, 1936). During deep ether or chloroform narcosis large, slow, rhythmic waves appear over the whole cortex (Berger, 1929 ; Walter, 1937). The frequency of these waves is 2 to 3 per second, and their amplitude may reach several hundred microvolts. Loss of consciousness due to inhalation of nitrous oxide, carbon monoxide, or other substances resulting in anoxæmia is also accompanied by the appearance of slow waves in the E.E.G., but they are not usually as regular as those seen with ether and the other fat solvents. These slow waves are usually in phase in corresponding areas of the two hemispheres.

The effect of derivatives of barbituric acid is entirely different. For example, injection of evipan is followed by a large discharge over the whole cortex at a frequency of about 8 per second (Berger, 1933, 1934 ; Walter, 1937). This begins abruptly with the onset of unconsciousness and dies away rapidly as the subject returns to normal. The appearance of this discharge is so similar to the normal alpha rhythm that it is tempting to suppose that it is due to an interruption of the afferent pathways for sensory impulses to the cortex. Bremer (1936), arguing chiefly from the similar results which he has obtained in animals, postulates a block in the thalamus which frees the cortex from the upsetting effect of the inflow of sensations—a true anæsthesia. Barbiturates, which are more used as sedatives than as narcotics such as luminal, do not have this effect in the usual doses ; in fact, they may actually diminish the alpha rhythm.

Drugs of the *alkaloid* group do not appear to have any regular effect upon the E.E.G. in the usual doses, but Berger (1932) reports abolition of the alpha rhythm by administration of scopolamine and morphine.

Apart from the anæsthetics, the analeptic and convulsant drugs have the most dramatic effects upon the E.E.G. These have been studied in animals by Fischer (1933), Fischer and Löwenbach (1934*a* and 1934*b*), Bartley (1933*b*), Kornmüller (1937), Adrian and Matthews (1934*b*), Dusser de Barenne and McCulloch (1936*b*), and Gozzano (1936). The changes which occur in the human E.E.G. on administration of convulsants has been studied in epileptics by Lennox, Gibbs, and Gibbs (1936), and Cook and Walter (1938) have recorded and localized the large waves which precede and accompany the convulsions induced by cardiazol in the treatment of schizophrenia. These various observations will be discussed again in connection with epilepsy, but the general results may be outlined here.

1. Local application of a drug such as strychnine or thujone to an animal's cortex produces a local discharge of large waves at a frequency of 2 to 6 per second. The concentration required to produce this effect varies for different areas of the cortex. In the motor regions the local outburst of waves is accompanied by convulsive movements of the limbs concerned. The local discharge is often grouped, that is, two or three waves may appear in a fraction of a second, to be followed by a second or so of quiet before another burst of waves appears.

In certain conditions the waves may be conducted for a few centimetres from the point of application at a rate of 15 to 20 centimetres per second (Adrian and Matthews, Dusser de Barenne and McCulloch). Gozzano states that when a local discharge is produced in a given cortical region in one hemisphere the corresponding area in the opposite hemisphere also shows a discharge at the same rate which can be abolished by section of the corpus callosum.

2. Injection of a convulsant drug in man results in the appearance of waves at a frequency of about 5 per second over the whole cortex. If a convulsion follows, a sudden greater outburst occurs in the frontal region, and this spreads over the greater part of the cortex, increasing in size and decreasing in frequency as it does so (Cook and Walter).

Mescaline was found by Chweitzer, Geblewicz, and Liberson (1937) to produce two effects, first a transient augmentation and then a prolonged depression of the alpha rhythm. They also found, as did Golla, Graham, Guttmann, and Walter in some unpublished observations, that even with the eyes shut a subject with mescal hallucinations produces only a very few rather rapid alpha waves, whatever his normal degree of activity.

Drugs whose action is supposed to be related to functions of the *sympathetic* nervous system produce no definite direct effect upon the E.E.G. in normal persons. The abnormal discharges associated with " pyknolepsy " in children were found by Golla, Graham, and Walter (1937) to be abolished by administration of benzedrine sulphate in small doses, and this drug may also make the alpha rhythm less persistent in subjects whose normal rhythm is particularly prominent. This effect may be connected with the well-known arousal effect of benzedrine.

The effect of *endocrine secretions* upon the E.E.G. has not been fully investigated. Lindsley and Rubinstein (1937), Jasper (1936), and Gerard (1936)

report that administration of thyroid extract is followed by a slight increase in the alpha frequency in some cases, but the significance of this is doubtful.

In brief, the agencies which have the greatest effect upon the E.E.G. are those which are known to affect the central nervous system directly. Those affecting consciousness produce the most dramatic results, and the change usually consists of the appearance of large waves which are slow in the case of cerebral narcotics, faster in basal narcotics and convulsants.

Abnormal Conditions

The study of *nervous and mental disease* has naturally tempted the majority of workers away from a closer investigation of the normal electro-encephalogram. Berger's original intention as a neurologist and psychiatrist was to apply his methods to diagnosis, and there is scarcely a condition on which he has not reported some observations.

The possibilities of error and misinterpretation have already been emphasized, and it is unfortunate that many original discoveries reported by Berger and others who have used a single-channel technique must be given a low assessment, either because artefacts were not excluded or because observation is entangled with opinion.

When the *intra-cranial pressure* is raised by such agencies as obstruction of the ventricles, concussion, meningitis, or cerebral tumour, a slow discharge at about 3 per second is found over the whole cortex (Berger, 1930 ; Walter, 1936, 1937). The waves are often as large as 100 microvolts and may resemble in their regularity the potentials found during ether anæsthesia. In the writer's series of cases no correlation was found between the actual pressure of the cerebrospinal fluid and the degree of prominence of these slow waves, which seemed more closely connected with the extent to which cortical function was impaired. In several cases the slow diffuse discharge associated with a raised intracranial pressure was greatly reduced by intravenous injection of hypertonic solutions, but much less affected by withdrawal of fluid from the ventricles. Cases of cerebral œdema with no change in ventricular pressure also show a slow discharge, and it seems likely that the œdema is the important factor rather than the increase in hydrostatic pressure. The E.E.G. in infants with hydrocephalus is difficult to interpret, since the normal rhythm is slow in very young children.

Cases of *cerebral tumour* provide one of the most dramatic illustrations of the interest of clinical electro-encephalography. Berger (1933) reported some cases in which the E.E.G. gave signs of local abnormalities consisting either of slow waves or of an abnormal independence of the alpha rhythm on the two sides. Walter (1936, 1937) described sixteen cases in which records taken with three channels enabled a focus of delta waves to be localized to within a centimetre or so. In all cases a tumour was later found in the region of the focus. This series has now grown to over 100 cases, and the possibility of locating cerebral tumours by electro-encephalography may be considered definitely established. The general results are as follow. Confirmation of these findings has recently been supplied by Case (1938) and Case and Bucy (1938).

1. The great majority of tumours which affect the cortex either directly by

infiltration or indirectly by other means produce in it a condition in which a delta discharge occurs.

2. The new growth is entirely inactive electrically (*cf.* Foerster and Altenburger, 1935).

3. Tumours several centimetres below the surface commonly give rise to a delta discharge in the cortex directly above, which may also show some local flattening or œdema.

4. When the local electrical signs of a tumour are masked by a general delta discharge due to raised pressure, a focus may be revealed by a reduction of the pressure by osmotic means.

5. The greater and more acute the abnormality produced in the cortex, the slower are the delta waves. Meningiomata and deep, slow-growing gliomata may be associated with a discharge approaching the alpha rhythm in frequency. A meningioma which compresses the cortex may produce a discharge which is slow in the centre of the affected area and faster towards the periphery.

6. In about 3 per cent. of cases found to have a cerebral tumour, no abnormality has been noticed in the E.E.G. The tumours in these cases have been either small meningiomata or astrocytomata. A normal E.E.G. is not conclusive evidence that no tumour exists.

7. In a few cases of cerebellar tumour a delta focus has been found on the side of the tumour by leading off from just behind the mastoid process. Midbrain tumours cannot be localized and usually produce no abnormality except by raising the intracranial pressure. Griffiths, Nevin, and Walter (to be published) found a very large regular general delta discharge in a comatose case of hypothalamic tumour in which the pressure was normal. The E.E.G. resembled that found in deep sleep, and may possibly be due to destruction of a " waking centre " in the hypothalamus.

Circulatory disorders are not usually associated with change in the E.E.G. Even the most severe cases of arteriosclerosis present no abnormality, and *cerebral hæmorrhage* and *thrombosis* are not detectable except for a short period immediately following the catastrophe (Berger, 1931 ; Walter, 1936). Berger has reported one case of aphasia following thrombosis in which the beta rhythm was more prominent than normal and declined as the condition improved. It can only be supposed that in cases of cerebral arterio-sclerosis the symptoms are due to a general depression of the cortex, no part of which is sufficiently affected to give rise to a delta discharge.

Injury to the cranial contents has not been studied extensively. Deliberate surgical trauma produces a transient local delta discharge which passes off in about a week. This would probably be found also in cases of accidental injury, but in the recovery stages nothing definite has been reported.

Diseases of the *Meninges* are sometimes associated with a general delta discharge. Delta foci have been found by the author in a few cases of localized *Arachnoiditis* and these may sometimes mimic cerebral tumours very closely. In two cases there was a delta discharge from both frontal poles which declined as the clinical condition improved.

Infections of the central nervous system are associated with electro-encephalo-

graphic abnormalities chiefly when the cerebral cortex is directly affected. *Cerebral abscesses* may be located in the same way as cerebral tumours, and some types of encephalitis appear to be associated with a general delta discharge. The E.E.G. in *Encephalitis lethargica* was found to be normal in the resting stage by Berger (1931, 1933), but Jasper (1936) found slight abnormalities in a few cases. A mesencephalic lesion would not, of course, be expected to produce a very definite change in the cortical E.E.G. (Jasper, 1936*b*, found no abnormality in two cases of *Paralysis agitans*.) Indefinite abnormalities have been reported (*e.g.* Berger, 1931) in cases of *disseminated sclerosis* and *general paresis*, but there has been no satisfactory confirmation of these findings, and the position is uncertain also with regard to *encephalomyelitis* and *poliomyelitis*.

Disorders of voluntary movement, such as *torsion spasm*, *chorea*, and *athetosis*, do not seem to be associated with abnormalities in the E.E.G., and recording is very difficult if the movements are violent. Negative evidence of this sort is not conclusive, but it would suggest that the movements in these conditions are not cortical in origin.

Congenital disabilities, such as hemiplegias and diplegias, do not present abnormalities unless the cortex is affected, and then only apparently in such cases as suffer also from convulsions. This is probably an illustration of the general truth that a definitely abnormal E.E.G. is found only when the cortex is in some intermediate stage of degeneration and not when it is completely atrophied. Thus, in degenerative diseases such as *Alzheimer's disease* abnormalities may be found, but they are not necessarily greater in the terminal stages (*cf.* Berger, 1931).

Intoxications of the cerebral hemispheres have been considered already in relation to narcotics. Jasper and Andrews (1936) describe irregular slow waves in cases of lead encephalitis, and this sort of discharge is characteristic of all sorts of conditions in which the hemispheres are poisoned : the degree of electro-encephalographic abnormality is an indication of the extent and severity of the intoxication rather than of the nature of the poison. The fact that, particularly in the case of anæsthetics, the condition is reversible, indicates that a prominent delta discharge is produced by cortex in a state when no permanent damage has been done. It has been observed, moreover, that intoxication may go beyond the delta stage, and that then recovery is impossible or at best incomplete.

The group of *paroxysmal and convulsive* disorders is of unique interest from the electrical standpoint. The mystery which surrounds the nature and origin of the epilepsies is as humiliating to the physiologist as it is exasperating to the clinician, but there is reason to hope that the spell may eventually be broken with the help of electro-encephalography.

In some of his quite early papers Berger (1931, 1933) reported a large, slow discharge in cases of epilepsy complicated by dementia or feeble-mindedness, and he showed also that a minor attack is accompanied by very large waves at about 3 per second, while during the period after a fit the E.E.G. is remarkably quiet. These observations have been confirmed and extended by several workers. The E.E.G. during seizures has been studied in great detail by Gibbs,

Gibbs, and Lennox (since 1935) and they have recently presented a useful summary and interpretation of their results obtained by multiple recording from over 400 patients (1938 *a* and *b*). Their conclusions are as follow :

" 1. Seizures involving the cortex are accompanied by distinct and characteristic fluctuations in the action potentials of the brain.

" 2. The rhythm which obtains during seizures is distinctive for the three main types : *grand mal* has a fast, psychomotor attacks (psychic variants) a slow, and *petit mal* an alternating fast and slow rhythm. The exact pattern of the seizure tends to be characteristic for each patient.

" 3. Antecedent to these gross abnormalities of rhythm is the lack, in epileptics, of a competent control of cerebral rhythms.

" 4. Some patients have sub-clinical seizures which are typical short disturbances of rhythm, not attended by subjective or objective evidence of a seizure. *Petit mal* may occur during sleep.

" 5. There is evidence that *grand mal* may be predicted many hours in advance.

" 6. In some patients abnormal activity begins in one area of the cortex and spreads to involve other areas. . . ."

Gibbs, Gibbs, and Lennox also suggest that sedatives are more effective in *grand mal* than in *petit mal* because they slow the cortical rhythms, while the *petit mal* rhythms may be temporarily abolished by a rise in the CO_2 tension or glucose concentration of the blood.

Some amelioration was produced in two cases out of three in whom a frontal lobectomy was performed on the basis of abnormalities in the E.E.G.

These observations suggest to Gibbs and his associates that epilepsy is a " Paroxysmal cerebral dysrhythmia."

The electro-encephalogram is often abnormal between seizures also. Golla, Graham, and Walter (1937) found that out of 214 cases of epilepsy, 91 showed a definite abnormality in the E.E.G. between fits. These observations have been continued and the number of cases examined is now approaching 1,000. It would seem that of all patients under 40 years old who complain of fits, about 50 per cent. show some abnormality in the E.E.G., and of these the majority are cases of idiopathic *grand mal*. For some reason few patients over the age of 40 show any abnormality, whatever the diagnosis, and the disappearance of the discharge at about that age has been watched in a few cases, in whom, however, the fits continued. In most abnormal cases the discharge resembles that found in cases of cerebral tumour, and may accordingly be described as a delta discharge ; it is not often more than 1/10 the size of the smallest seizure waves. The focus can usually be located by three-channel recording, and in cases of *grand mal* is most often in the region of the superior frontal gyrus on either or both sides. In cases complaining only of minor attacks the focus is usually post-central, and in the so-called pyknolepsy of children is in the occipital poles. The position of the focus appears to have some connection also with the character of the attack in *petit mal*, though not with the nature of the aura in *grand mal*. When a patient has a fit during examination the seizure waves can be seen to start as an increase in the focal

resting discharge which spreads, often quite suddenly, to involve other parts of the cortex, becoming at the same time larger, slower, and more regular. The " subclinical seizures " of Gibbs and his co-workers can be recognized in cases of *petit mal* as a period of less pronounced augmentation and expansion of the resting delta discharge.

The resting delta activity may be restricted but not diminished by drugs effective in controlling fits, although in some cases of pyknolepsy the fits and the focus have both disappeared during administration of benzedrine sulphate. There are, however, spontaneous fluctuations in the size of the discharge and these are correlated with changes in the frequency of the fits.

There is evidence that the cortical area responsible for the delta discharge also shows slight but definite histological abnormalities. In some cases the delta focus was associated with gross atrophy.

From the clinical point of view it is important that cases of traumatic epilepsy do not show a resting abnormal focus, though the seizure waves in these cases are the same as those in idiopathic epilepsy. Cases diagnosed as hysteria show no abnormality, either between or during fits, except when the attack is accompanied by voluntary hyperpnœa. These facts make possible the differential diagnosis of idiopathic and other types of epilepsy, though only positive results are completely trustworthy, since a certain proportion of idiopathic epileptics give normal records.

These observations and those of Gibbs and his colleagues fit together admirably, and the whole forms an imposing addition to the facts about epilepsy, but the data are very much harder to integrate than they are to collect. Jasper and Hawke (1938) have recently published work confirming these observations. There is no doubt that in most cases of idiopathic epilepsy a part of the cortex is in an electrically abnormal condition, and that when a fit occurs this abnormality is enormously increased. There is, however, no proof that the electrical phenomena indicate a truly cortical origin for the condition preceding and accompanying the epileptic symptoms. The results of cortical excision are not promising from the therapeutic standpoint, and the failure to stop fits by enlightened surgical intervention suggests that the cortical manifestations may have only a secondary association with the true cause of epilepsy. Golla, McKissock, and Walter (to be published) found that the excision of a delta focus in epileptics was followed by a few months of comparative freedom from fits, but the patients slowly returned to the pre-operative condition. The treatment seemed no more effective than any other major operation.

The importance of the information obtained about epilepsy by electroencephalography lies first in its use in empirical diagnosis and secondly in its value as a stimulant to the experimenter. For example, the frequency with which delta foci are found in the superior frontal gyrus in idiopathic major epilepsy and the fact that convulsions induced by cardiazol (Cook and Walter, 1938) are associated with a high-potential electrical discharge in the same region suggest that this area of the cortex has something to do with convulsive movements. In general, a delta discharge indicates inactivity of the area concerned, and if this is true also in epilepsy, it might be argued that integrity of the pre-

frontal area is essential for the control of voluntary movements and the prevention of convulsions. This hypothesis accounts for the therapeutic ineffectiveness of removal of this area and suggests that much remains to be learned about its function and connections.

The E.E.G. in *narcolepsy* usually shows little definite abnormality, but there is often a very prominent alpha rhythm from a large focus, and the same has been found in some cases of *cataplexy*. The alpha rhythm becomes normal when the sleepiness is controlled by benzedrine (Walter, unpublished). No definite abnormality has been reported in cases of *migraine* or *vaso-vagal attacks*. In one case at first diagnosed as *myoclonus* and later as *epilepsia partialis continua*, the author found a large discharge from the right superior frontal gyrus in rhythm with involuntary movements of the left side of the body. The discharge resembled that found during the clonic stage of a fit, but involved only a comparatively small area, and this patient had never had a general seizure of any sort. This is further evidence for the connection between frontal areas and involuntary movements, but the temporal relation between the cortical discharge and the action potentials of the affected muscles was not constant (*cf.* Jasper and Andrews, 1938, and Travis and Cofer, 1937). The movements in this case resembled a *tic*, but in cases of true *tic* no abnormality is found.

The *neuroses* have so far proved a sterile field for electro-encephalography. The alpha rhythm reflects to some extent changes in the mood of a subject and seems particularly sensitive to fluctuations in his attention, but a highly neurotic individual usually gives a normal record. Exceptions are sometimes found in " problem " children, who may give records similar to those of epileptics. Solomon, Jasper, and Bradley (Jasper, 1937) found a correlation between the degree of abnormality of the patients' behaviour and the abnormality of the record, both in different patients and in the same patient from time to time. In the author's experience such children are actually suffering from an almost continuous series of *petit mal* attacks and usually develop true epilepsy later (except in cases of pyknolepsy which clear up spontaneously). In these cases electro-encephalography has been found useful as an aid to diagnosis and prognosis. After a painstaking survey, Travis and Knott (1936) have shown that the E.E.G. in *stutterers* is not significantly abnormal.

The E.E.G. in the *psychoses* has been studied by Berger (1931, 1933*a*, 1933*b*, 1937*a*, 1937*b*, 1938). Lemere (1936), Travis and Malamud (1937), none of whom report any definite abnormality in schizophrenia or manic-depressive psychoses. Berger (1937*b*) emphasizes the frequency of artefacts when leading from insane patients and concentrates on the E.E.G. during hypoglycæmic shock treatment. Lemere considers that schizophrenic patients usually have a poor alpha rhythm as compared with normals or manic-depressives. Hoagland, Rubin, and Cameron (1936, 1937*a*, 1937*b*, 1938) claim that a significant proportion of schizophrenics give slow swings of the base-line which they propose to class as delta waves. They have devised a measure of the incidence of these delta waves in a record, which they call the " delta index " and state that this is significantly higher in untreated schizophrenics than in normal subjects, and that the index in schizophrenics drops during treatment or spontaneous remis-

sion. MacMahon and Walter (1938) have followed up this question and find that there is indeed a certain amount of slow random activity in some types of schizophrenia, but suggest that many of the large waves to which Hoagland and his collaborators attach importance are in reality due to eye-movements, which are particularly common in this class of disorder, and moreover diminish with clinical improvement. MacMahon and Walter also find a different sort of abnormality ; an alpha rhythm which persists during all forms of visual and mental activity. This was found in patients with symptoms of volitional weakness, and they suggest that a perpetual alpha discharge may be associated with the patient's inability to mobilize his sensory resources or to relate afferent impressions to internal associations.

It is clear from what has already been done that interpreting the E.E.G. in psychoses will be a difficult and controversial problem, made still harder by the uncertainties of clinical diagnosis. In no other branch of electro-encephalography is greater vigilance required to escape the three enemies of precision—artefacts, statistics, and analogies ; and in no other branch are the rewards to be gained by clinical application so tempting and so meretricious.

The foregoing survey of facts must now be still further condensed into compact generalizations. The most obvious one is that the chief sign of cortical abnormality is the appearance of slow delta waves, and as an empirical guide to interpretation the presence in a record from a waking adult subject of discharges at a frequency of less than 7 per second may be taken as definitely pathognomonic. In children the normal limit is lower. The other criterion of abnormality is the persistence of a seemingly normal rhythm through all stages of activity and attentiveness.

We do not know how or why delta waves are produced, but it seems most likely that they represent a true change in the natural electrical period of the cortical neurones, a change which is usually ominous but yet reversible if the cause is removed. During delta activity no useful work can be done by the neurones concerned. Sometimes the delta waves are so large that we may suspect them of paralysing the cortex by electrocution, as it were, and we may speculate as to whether this may not be their special function in certain conditions, just as the function of pain is sometimes to immobilize an injured part. In order to explain the occasional great size of the slow waves it may be necessary to invoke a series connection for the cortical cells, similar to that evolved from muscle cells in electric fish. The rhythmicity of the discharge need cause no wonderment, but nor should it be taken as an excuse for free speculation. Parables and analogies are valuable stimulants but bad food for thought, and the fact that a terminology designed to classify phenomena observed in simpler systems can be used to describe certain features in the behaviour of the central nervous system proves nothing except that it can be so used. Nevertheless one phase of scientific reasoning permits description of the new in terms of the old, and if we look for something in simpler tissues that will help us to understand the normal and abnormal electrical rhythms of the brain, the phenomena which seem most likely to be not merely similar but homologous are the slow electrotonic potentials of the spinal grey matter described in detail by Barron and

Matthews (1935, 1938). A discharge of impulses from a spinal neurone is accompanied by a slow potential swing similar in its time relations to the cortical rhythms, and altogether different in form from the action potentials of peripheral nerve. Moreover, a discharge of impulses may be evoked by a small externally applied current in the right sense, and reversal of this current inhibits the discharge. There is also evidence that such slow electrotonic potentials produced by nerve cells may influence conduction even in fibres to which they are not directly connected. These observations of Barron and Matthews suggest the possibility of translating Sherrington's " C.E.S." and " C.I.S." into terms of katelectrotonus and anelectrotonus in the grey matter, and since the cortex contains chiefly grey matter it would not be altogether fantastic to suppose that the E.E.G. is a record of rhythmic cortical alternations of kat- and anelectrotonus rather than of cortical action potentials, a term which should probably be restricted to the electrical features of a propagated disturbance. It can easily be understood that in normal circumstances the frequency at which a cell in the cortex can produce electrotonic alternations will be fixed within narrow limits by the physical dimensions of the oscillating system and that when a certain number of cells oscillate in synchrony the potentials will be detectable as an alpha or beta rhythm. The apparent size of the rhythms will depend upon the number of cells beating together, and this agrees with the practical observation that a high-potential rhythm indicates a large focus. The normal rhythms are associated with some degree of inactivity in the cortex, and it seems probable, therefore, that the less the activity of a part of the cortex, the greater the degree of synchronization of the cells concerned, but it is not certain whether the electrical quiet associated with cortical activity is due merely to desynchronization of cells which are still oscillating at their natural frequency, or whether the discharges of each cell are damped. The former explanation seems the more probable.

Returning to the discharges in abnormal conditions we may suppose that a focal disturbance such as a neoplasm results in a reduction of the natural period of the cells in its neighbourhood and that their discharges are synchronized in the same way as the normal ones. Dusser de Barenne and McCulloch (1936*a*) have shown that laminar coagulation of the upper layers of the cortex abolishes the local characteristic currents and leaves a delta-like discharge which they presume emanates from the lower layers. The origin of the delta-foci in epileptics remains a subject for speculation. The change in time relations of the affected area may account in part for its inability to participate in normal activities, which may require some sort of isochronism of several areas or levels. The disappearance of characteristic local discharges in narcosis and their supersession by a general slow discharge has been studied in animals by Drohocki (1938), who refers to this state as the " Echostadium." It is remarkable that in man whenever consciousness is lost the normal local rhythms vanish and are replaced by a much larger, slow, general discharge, and that a similar delta rhythm appears locally when only a part of the cortex is affected, though the first signs of interference may be slowing, persistence, or irregularity of the normal resting discharges if any are detectable.

Electro-encephalography has developed as a technique rather than as a science, but since the phenomena have turned out less like others than was expected, fresh theories must eventually arise. At present the sorting and classification of data is only beginning and there must be many facts still to be discovered. Meanwhile, as interpretation becomes more confident and more detailed, the usefulness of electro-encephalography will increase, and we may hope that in time a precise neurophysiology will develop from the marriage of electro-physiology and clinical neurology.

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