5-1-1942

Electroencephalogram : an example of the utilization of bioelectric potentials in diagnostic medicine

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The Electroencephalogram.

An Example of the Utilization of Bioelectric Potentials in Diagnostic Medicine.

by

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Senior Thesis

Presented to the College of Medicine

Omaha, Nebraska

April 6, 1942

Preface

The author wishes to take this opportunity to thank Dean C. W. M. Poynter for suggestions and guidance as to the choice of aims and purpose in the presentation of this paper. I also wish to thank Professor A. R. McIntyre and Professor A. L. Bennett for their suggestions and encouragement in this attempt at a logical and profitable undertaking of a new and confused subject. The association with them in related studies of peripheral nerve and medullary center activity has served as a valuable basis of understanding of the electrical principles involved. I am indebted to Mrs. L. L. Wagner for the careful preparation of the final paper and helpful criticisms in its arrangement.

Jacob C. Wagner

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Introduction

In recent years there has been a great acceleration in the degree of skill in medical diagnosis. A part of this is no doubt due to the accumulated observations of clinicians. Combining of careful clinical observation and notations, with confirmation or elucidation at autopsy, and, probably more important, experimental research by which conditions may be rigidly controlled and post mortem studies can be undertaken at any stage of a disease process undoubtedly plays a major role in the recent acceleration in medical knowledge. A considerable contribution, however, must be ascribed to the development of electrical diagnostic procedures.

The usefulness of the electrocardiograph is well established, as may be attested by its general usage. Electrodiagnosis of nerve lesions by the reactions of degeneration as determined by galvanic and faradic stimulation is a standard neurological procedure (1). Impedance measurement as a diagnostic procedure is less uniformly accepted as to its usefulness (2, 3, & 4). Of all the standard diagnostic procedures which employ changes in electrical activity of tissue, the newest, the electroencephalogram, is perhaps the most interesting because of the complex structure it represents. The complexity of the structure combined with the complexity of the recording apparatus has been a deterrent factor in its more general understanding.

Besides the attempt to evaluate the usefulness of the electroencephalogram, it is the purpose of this paper to attempt to simplify it both from the standpoint of principles of recording and the functional processes which these recordings represent. In order to do so most effectively, rigid restriction of material to clinical studies is impossible. A more fundamental understanding of the nature of biolectrical phenomena seems an essential to the interpretation of clinical studies. On the other hand an elaborate and technical presentation of the electrical principles involved would defeat the attempt at simplification. The introduction of elaborate circuits, meaningless to anyone unfamiliar with electrical symbols, and the presentation of complex mathematical formulae to express simple relationships have confused many not thoroughly grounded in such matters and made further perusal of the subject unattractive. Technical presentations are undoubtedly necessary to those who are investigating such phases of the subject.

In an attempt to present the subject in its simplest form, references to several related subjects have been utilized. Animal experimentation will be referred to wherever it is felt to be of possible usefulness in a better understanding. A special section related to the physiological basis will be undertaken. The references to other fields will serve the same purpose. The basic mechanisms operating to produce potentials in other active tissue have been investigated over a much longer period of time, and the presentation of pertinent points may serve a very useful end.

It is hoped that this presentation will be successful in bridging the gap between the specialty which it represents and the general physician interested in its practicability.

History

Volta corrected the misconception developed by Galvani as to the electrical reaction of frog muscle. He showed that the convulsion produced when a frog's muscle was touched by two dissimilar metals was a manifestation of the reaction of the animal to electricity produced by the metals and not due to electricity produced by the animal. The original conception thrived, however, with such speculation as to the nucleus of life processes being an electrical humor, etc., until relatively recent times (5).

Du Bois Reymond (1843) probably recorded the first potentials produced by animal tissue (6). By means of a crude galvanometer of the type consisting of a coil of wire suspended between the poles of a magnet, he was able to demonstrate that a difference in potential of about 50 mV existed between the intact skeletal muscle and the dead, crushed end. He demonstrated that when the muscle was stimulated a decrease by 10 mV in this potential accompanied the contraction.

A very popular field of investigation, attempts were soon made to record potentials from practically every organ of the body. The first successful recordings from the exposed brain were reported by Canton in 1875 (7). He found that the gray matter was positive to the cut surface. (Note the similarity of these findings to the findings of Du Bois Reymond on muscle.) He found further that stimulation of the retina by light produced a decrease in the positive potential of the intact cortex in the occipital lobe. He concluded from this that there is a negative variation in potential when any part of the cortex becomes active. Later others confirmed these findings.

The next step towards the modern study of brain potentials was taken by Neminski in 1913 (8). His contribution is important mainly because he showed for the first time that potential changes could be recorded through the intact skull, for which he is not generally accredited. This was made possible by the use of Einthoven's string galvanometer, a more sensitive instrument than had been available heretofore.

In 1929 Berger first reported the recording of waves of a constant pattern from the human skull (9). His first records were made by the use of steel needles as electrodes passed through the superficial structures to the skull, the same as Neminski. Later he found he could get the same findings by means of saline-soaked pads of gauze secured by bandages. Here again progress followed the application of a more sensitive recording system. It was the beginning of our knowledge of the modern electroencephalogram in man. The development of the various phases of the subject will follow a discussion of the development of recording systems which made it possible.

Technical Considerations

Electrically active tissue such as nerves and all types of muscle, skeletal, heart, and smooth muscle, can now be investigated by rather accurate instruments. Each type of tissue has characteristics which distinguish it as to the potentials maintained, the rapidity with which these potentials fluctuate during activity, and the ease with which these changes may be provoked, that is, its irritability. These characteristics limited the study of the respective tissue according to the development of apparatus suitable thereto.

Apparatus.--The development of apparatus suitable for EEG studies has been achieved only recently. Du Bois Reymond was able to measure the action potential of nerve and muscle since these are rather high; e.g., the action potential of a nerve trunk may range from 10 to 30 mV, and single isolated axons give rise to action potentials of 10 to 250 mV (10). When it is considered that the normal brain waves usually produce a voltage of less than 100 μV when recorded from the scalp, it is readily seen that their successful study awaited recent developments in methods of amplification.

Electrodes by which contact is made with active tissue have evolved from complex to simple types. Neminski (8) recorded potential changes from the intact dura and skull and demonstrated their similarity to potentials recorded from the exposed surface of the brain by means of steel needles as electrodes. Berger used this same type of electrode first and then used saline packs, as mentioned before. As other workers entered the field other more simple electrodes were developed with a constant tendency to a reduction in size and simplicity in application; e.g., Toman (11) uses platinum foil 4 mm. in diameter secured to the cleaned scalp by collodion. The smaller electrodes give better localization properties, important in the localization of source of abnormal potentials, as will be discussed later.

Only recently have attempts at standard placement of electrodes been attempted. In early work electrodes were placed practically anywhere on the scalp, usually in general reference to frontal, parietal or occipital regions (9 & 12). There are now two general methods of placing electrodes, the monopolar and bipolar. In the monopolar method the mastoid process or the lobe of the ear is used as a reference electrode and other electrodes placed at specific points on the scalp on each side indicate the potential changes developed at that point relative to the single fixed point. There is some difference in opinion as to the best point for the reference electrode. Davis (13) prefers the lobe of the ear to the mastoid process because she claims to have shown this point to be less electrically active than a point on the scalp.

The bipolar method of recording consists in placing electrodes at three points as frontal, parietal, and occipital and determining the electrical variations between these points; e.g., fronto-parietal, parieto-occipital, and fronto-occipital. Four points in a line may be used instead of the arrangement discussed for bipolar recording. Fig. 1 is taken from diagrams by Davis (13) illustrating these placements.

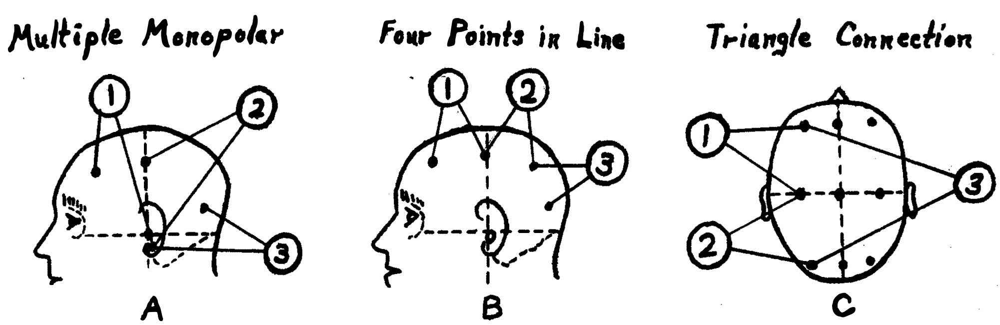


Fig. 1.--Placements on head representing different techniques of recording. The numbers represent the amplifiers.

Another system of electrode placement is presented by Woltman (14). He uses 5 pairs of electrodes numbered 1 to 10. The odd number of the pair corresponds to the left side, the even number to the right side of the scalp. Numbers 1 and 2 are placed in the frontal area, 3 and 4 are prerolandic, 5 and 6 are parietal, 7 and 8 are occipital, and 9 and 10 are temporal in position. Potentials are recorded in a line from anterior to posterior or between any two.

When pathology relative to a particular area is indicated, a more precise localization can be obtained by attempting to place the electrodes in such a way as to obtain the highest voltage of the abnormal waves.

Recording Systems.--Instruments used to measure potential differences between two points are called potentiometers. There are a considerable number of possibilities as to how these potentials may be measured. An adaptation of a movable coil suspended in a magnetic field was used by early workers. The current produced by the difference in potentials being measured gives rise to an electro-magnetic field in the coil at right angles to the magnetic field maintained between the poles of the magnets in which the coil was suspended, and a deflection of the movable coil results. The coil having a relatively high inertia failed to follow the rapid changes in potential ordinarily found in biological tissue.

Einthoven in 1903 developed a string galvanometer which improved the sensitivity of the system a good deal and made Neminski's work possible. It consisted of a very light quartz string suspended between the poles of a powerful electro-magnet. The magnetic field around this string when a current passed through it produced a deflection of the string according to the torque of the interaction of the two fields. Fig. 2 (15). For example, if the current is flowing down in the string

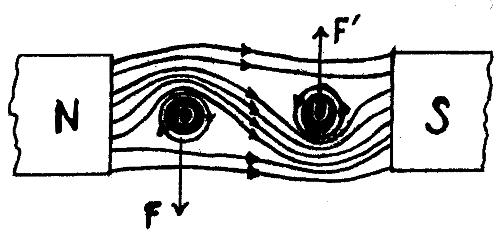


Fig. 2.--Torque on a current coil in a magnetic field.

between the two poles of the magnet, the magnetic fields would act to deflect the string in the direction F. If the current flows in the opposite direction, the string moves oppositely. By using a very light string with a high periodicity and low inertia, suspended in a powerful magnetic field, a markedly more sensitive instrument capable of following rapid changes resulted (6). Minute deflections could be detected by means of observing the movements of the string through a microscope placed at right angles to the string and in a bore through the holes of the magnet. These deflections could be photographed by means of projecting the movements of the string through the microscope on photographic film moving at right angles to the direction of the deflections. This instrument has been in general use since for studying changes in heart potentials, the records obtained being known as the electrocardiogram.

The electro-oscillograph was adapted to the studies of biological potentials by Erlanger and Gasser in 1922. The application and advantages of this instrument are more fully discussed by one of them (16). Fig. 3 represents the general principles of the instrument. Briefly,

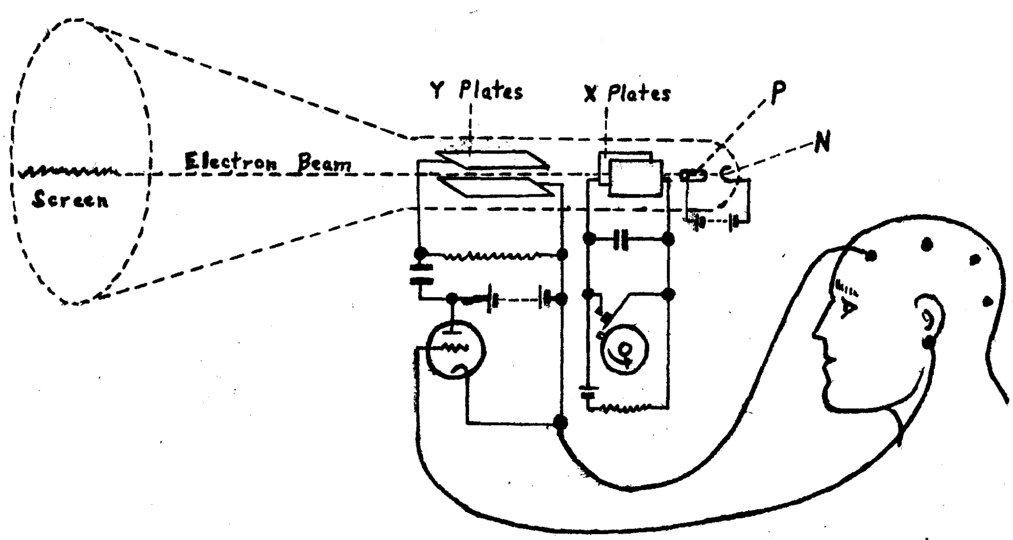


Fig. 3.--Simplified diagram of cathode ray oscillograph.

a negative pole "N" is the source of electrons attracted by the positive pole "P", maintained at several hundred volts, which is hollow so that the stream of electrons pass on through with great velocity to strike a flourescent screen on the inside of the face of the tube. This stream of electrons can be deflected by a positively charged plate to one side at any point in its course. By means of a condenser the voltage of a pair of vertically placed plates is made to fluctuate in a sweep circuit so that the potential of one plate rises linearly to a given heighth and then drops off instantaneously to 0 by means of discharge of the large condenser. The displacement of the beam of electrons follows this rise and fall of the voltage on the vertical plates. The rate of deflection of the beam can be varied at rates from a few to several thousand times a second or be held as a spot on the face of the tube to be subject to only vertical displacements by the horizontal plates, as explained below.

A second pair of plates placed horizontally to the stream of electrons is a part of a circuit of the biological tissue being studied. Variations in voltage of the electrically active tissue can be amplified several million times to produce a corresponding fluctuation of the beam passing between the horizontal plates. The displacement of the flourescent glow on the face of the tube then represents the rise and fall of the potentials produced by the electrically active tissue.

The adaptation of the electro-oscillograph awaited the development of the amplifying tube by Lee DeForest. The principles of the tube briefly are as follows (15).

Edison in 1883 found that a plate sealed into a tube with a filament heated by a direct current would produce a current when connected to the positive pole of the source of current to the filament, but there was no flow of current when the plate was connected to the negative pole. When a wire or lattice, called a grid, is placed between this pole and a heated filament, the tube becomes a triode (contains three electrodes). When the grid is positively charged, electrons flow freely from the filament to the plate maintained positive. When the grid is negatively charged, the electrons are retarded or turned back toward the filament depending on the magnitude of the grid charge. The intensity of the current between the filament and plate, therefore, fluctuates in unison and in proportion to the changes in potential of the grid. These changes in the current to the plate are far greater than the changes that produce the fluctuation in the grid potential. By connecting this plate circuit to the grid of a second tube, the potential changes of the grid of the second tube become still greater than those of the first. Therefore, the plate current of the second tube is made to vary much more than the first. By continuing this procedure the amplification may be increased indefinitely. Tube design and adaptation of types of tubes to meet certain conditions have been so successful that, as Adrian (5) has said, the development of amplifying systems has exceeded the needs of the biological laboratories.

By means of adaptation of the oscillograph with amplifier to the study of biological potentials, several advantages result. The beam of electrons has no inertia; therefore, accurate reproductions of fluctuations of voltage have been followed at frequencies of over two-hundred million per second. Accurate reproductions of changes in voltage have been amplified at frequencies of about six thousand per second. The most rapid variation in frequency in biological tissue is on the order of 0.1 sigma (one-tenth of one one thousandth of a second) (10). It can be seen from this that reproduction of potential changes can be practically perfect.

As adapted to the reproduction of brain waves, such an accurate system is not necessary. As will be seen later, the fastest waves which it is ordinarily practical to record probably do not exceed 50 per second, as best shown by the Grass analyzer (17). Accordingly, it has been found more convenient to record brain potentials by means of ink writers. A very nearly perfect reproduction with frequencies up to 100 per second has been claimed by various instrument houses. The general principles are as follows (18):

Instead of photographing an electron beam, the amplified voltage variations are passed through a coil connected to an ink-writing arm. This coil is supported over the pole of a powerful electro-magnet. As the magnetic fields in the coil change, the coil is attracted or repelled by the powerful magnetic field to which it is approximated. The ink-writing arm, constructed as lightly as possible to reduce its inertia, follows these fluctuations. Other modifications of this principle are used in ink-writing recording systems.

A good many technical problems have been met relative to the successful recording of brain waves. The amplifying system is extremely sensitive to noise, induction of potentials from sources outside the system as 60 cycle a.c. on the light and power lines, and potentials arising from muscle activity of the individuals studied and due to displacement of electrodes on slight motion.

Building the amplifiers on rubber supports will minimize induced potentials due to vibrations of sound. Muscle action potentials have a very high frequency and can be eliminated as well as a.c. inductance by means of tuned electrical filters. By including these filters, the range of frequencies of waves passed is limited to a narrow range (13). Thus a ten-cycle filter will pass only frequencies in the neighborhood of 10 per second; that is, from 7 to 13 per second. The width of the band varies with the apparatus of different workers.

The Grass Analyzer.--Recently an adaptation of the Fourier transform to electroencephalography by Grass (17) has opened important possibilities as to the analysis of records. The record is analyzed by this instrument as to the relative proportion of waves of a given frequency. It has been compared to the breaking up of light into its color component by a prism (19). A record is easily classified as to frequency characteristics and has been used to more accurately determine differences in records of different psychotic types (20). Differences not readily observed by ordinary methods are revealed, and a more accurate classification of records should be possible.

Recording from Exposed Brain.--There have been a good many studies of potentials derived from the exposed surface of the brain in experimental animals and some in man. The apparatus for such studies is the same as has been described above, except for such modifications as to sterile electrodes and design of electrodes. Adrian and Matthews (21) have studied the problem of electrodes in some detail in their studies on experimental animal. They object to the use of the co-axial electrode in which a fine metal wire, as one electrode, is passed through a large hypodermic needle, the other electrode, and insulated from it. They claim that if similar metals are used in the construction of the electrode a high resistance results. If different metals are used, confusing local currents are produced. They prefer the use of a large indifferent electrode somewhere on the surface of the animal's scalp, and a single enameled silver wire with the bared tip coated with silver chloride in the brain. Others still find the co-axial electrode very useful.

On man various types of electrodes which may be easily sterilized are used. Probably the most versatile recent adaptation is that of Rahm (22). He is able to adjust the position of the electrodes by means of a "mechanical stage" mounted at the end of a rigid support. Fine accurate movements in all directions were possible thereby. The electrodes were fine silver wire made more flexible by the introduction of coils near the fixed end.

By placing the electrodes so that the points move perpendicularly, large artifacts due to movement of the electrodes by the pulsation of the brain surface were avoided. A consideration of technical difficulties introduced by recording from the human brain surface are not within the scope of this paper.

Control of Conditions.--It was found by Berger that in order to obtain good records conditions had to be controlled rather carefully as to the subject being studied. He was placed in a quiet, nearly dark room on a cot. Adrian and Matthews (23) later felt it was better to have the individual in a semi-sitting position. then, various recommendations on conditions of recording have been made. There are few of these of critical importance beyond those specifications Berger originally suggested. Relaxation with a minimum of muscular action is important in reducing artifacts. At the same time the mental and physical condition of the individual must be known. The individual must be mentally alert since waves which may be confused with abnormal waves may arise if he is allowed to doze off (24).

The Normal EEG

Our knowledge of what constitutes a normal EEG has been slow in developing and further elucidation may be expected in view of the progress already made. It is perhaps well to consider some recent specifications as to what constitutes the normal individual as defined by Davis (13), who has had considerable experience in EEG studies, and then study the normal EEG in more detail later. In a study of over eleven hundred individuals in the last five years she has suggested the following conditions to be satisfied to meet the requirements of a selected normal:

1. A chronological age of over 15 years.

2. Extensive and reliable medical and social history as to: (a) A history of only the usual childhood diseases without unusual sequelae. (b) There is no history of a single convulsion regardless of cause. (c) There have been no psychiatrical problems requiring care, nor have there been questionable relationships with others. (d) The behavior has been normal and wholesome at home, at work, at school, or at play. (e) They should be known to be free of drugs, even aspirin, for several days before recording, not only because of the possible effect of the drug but also because the presence of a drug suggests that the individual is not in a perfectly normal condition.

Such a rigid selection has not always been exercised in the past. The development of our knowledge for the selection of normals and the components of their records will be considered.

Early Studies.--Berger in 1929 (9) described the first EEG from the human scalp. He demonstrated that only the amplitude of the recorded waves varied when recordings were taken from the scalp surface by means of saline packs as compared to hypodermic needles thrust through the scalp near to the periosteum. In a series of publications (25, 26, 27, 28, 29, and 30), he has established the presence of an alpha rhythm of 8 to 12 cycles per second, and a beta of 30 to 50 cycles per second. Adrian and Matthews (19) and others have since confirmed these findings and tried to determine the origin of the two wave frequencies.

Origin of Wave Groups.--Berger and others have convinced themselves that the typical wave patterns obtained arose from the cortex and not from heart or voluntary muscle action potentials (31), etc. Berger originally had considered the origin of the alpha and beta rhythms as being from the entire cortex. Adrian and Matthews showed that the alpha waves were stronger from the occipital area. They found that an individual's alpha waves disappeared when his eyes were fixed on a visual pattern. In individuals who have been blind for years, there was no alpha rhythm. They assumed, therefore, that when an area in the occipital lobe was not occupied by a pattern of vision, it took up a beat at a fixed rate and in unison. Afferent stimuli, as light, act to break up the synchronism of the cells of the occipital lobe and eliminate the alpha rhythm. In the blind, the area is subjugated to other areas of the cortex. These authors also observed that any condition requiring attention as a problem in arithmetic, noise, light touch, etc., decreased the alpha rhythm while muscular effort increased it, observations supporting the origin by synchronous beating of neuronal units.

Jasper and Andrews (32) have recently reinvestigated the source of alpha rhythm. They found that the autonomous activity of each cortical area is rather complex and each area has a characteristic activity. The alpha range is placed at from 8 to 13 cycles per second, the beta at 17 to 30 per second, and a possible gamma at 35 to 48 per second, the latter being obscured by the slower higher voltage waves. They postulate two distinct origins for the alpha, an occipital and a precentral, on the observations that: 1. There are spontaneous appearances of alpha waves in one region of the scalp independent of another region, usually, though not always, of the same frequency. 2. Their reaction to stimuli may be independent of each other in the two regions. 3. There is a greater preponderance of beta rhythm from the precentral area. 4. The precentral alpha is depressed by tactile stimuli and not affected by light. The occipital alpha is affected by light and not by tactile stimuli. Therefore, the rhythms represent activity of the sensorimotor and visual systems respectively. Both are affected similarly by sleep, excitatory conditions and general metabolic conditions as temperature, etc.

Rubin (33) earlier had also proposed a separate origin of occipital and frontal alpha rhythm on the observations that: 1. The occipital alpha is very stable from time to time, while the frontal alpha is very variable. 2. Bursts of alpha of the occipital lobes are not synchronous with those from the frontal lobes. 3. The alpha rhythm from the two hemispheres are relatively independent of each other. He concluded that the alpha rhythm may arise from any part of the cortex.

Evidence from the Exposed Brain.--Evidence as to the origin of the different rhythms from the exposed brain by Scarf and Rahm (24) is elucidating. They classified the wave groups as to frequencies into slow waves of under 8 cycles per second, an alpha rhythm of 8 to 12 per second, and over 12 per second as beta rhythms.

In no cases were they able to demonstrate absolutely constant localization of spontaneous rhythms. However, the alpha rhythm seemed to be confined to the occipital, parietal, and temporal lobes. They were obtained from the frontal lobes in only one case. The central sulcus seems to be the anterior limit of the alpha rhythm. An alpha rhythm of 10 per second was obtained from the optic nerves in one case in which they were exposed.

The beta rhythms occur predominantly in the frontal lobes and with much decreased amplitude in the parietal and occipital lobes. The amplitude is greatest in the anterior parts of the latter lobes. Slow waves could be found in any part of damaged cortical tissue.

Evidence from Animal Experimentation is of interest in regard to the origin of the rhythms. Gibbs et al (34) in 1936 demonstrated a marked similarity in the EEG of the cat to that of man. This relationship is to be expected in view of other evidence to be discussed later. In a study of the interrelationship of the thalamus, cerebrum, and cerebellum, Spiegel (35) found a marked similarity of the waves from the thalamus and cerebrum. No constant differences could be demonstrated between different thalamic nuclei. They are present in the curarized animal under artificial respiration and vary only quantitatively with superficial ether anesthesia, indial sleep, and bulbocapnine catalepsy. They are absent in the dead animal. Exterpation of the cortex or cauterization of it affects only the slow waves of the electrothalamogram. On the other hand, the independent activity of the cortex relative to the thalamus is indicated by the persistance of waves in isolated sections of the cortex and after the thalamo-cortical fibers have been severed.

The electrocerebellogram was very similar to the electrocorticogram and also remained unaffected by section of the midbrain or section of the inferior and middle cerebellar peduncles. The amplitude only is affected as the distance between electrodes is increased. Except for the findings on the electrocerebellogram, this experimental study substantiates the work on humans, already discussed, as to the possible independent origin of rhythms from nearly any part of the cortex. Scarf and Rahm could get no consistent rhythms from the cerebellum.

One study attempting to fix the origin of certain waves, especially slow waves, has been made (36). An attempt to prove a dominance of the hypothalamic over the cortex was undertaken by Grinker and Serota. By means of an intranasal electrode which could be used both as a stimulating and recording electrode, they attempted to show that conditions as cold, electrical stimulation, and strong emotions produced waves arising in the thalamus and followed in the cortex. Masserman (37), in an analysis of the hypothalamus as the center of emotion, pointed out that these intranasal electrodes used by Grinker and Serota were really nearer to the pons and medulla. He questions the validity of the recordings indicating hypothalamic activity. In experimental studies he planted small electrodes directly into the hypothalamus and, some weeks after the animal had apparently recovered, records taken gave the following results. Only occasional slow 2 to 4 per second waves could be recorded. Light, sound, painful stimuli, and stimulation through the imbedded electrode to the point of producing sham rage failed to produce any characteristic results. Giant waves of 3 to 4 per second were obtained from the cortex. He suggests that Grinker and Serota were really recording cortical waves and that variations they reported were very similar to those he found produced by very slight facial movements. He also found that the hypothalamic reacted the same as the cortical areas to various stimuli, as opening eyes, etc. He questions dominance of hypothalamus over cortex in emotional conditions, and questions that the hypothalamus is anything more than a path in the production of autonomic changes during emotions.

The question of blindness and the relation of flicker to the alpha rhythm observed by Adrian and Matthews has since been investigated by others. A powerful dominance by the optic cortex over the rest of the cortex as to alpha rhythm is suggested by these observations. Serota (38) has suggested the possibility of ruling out possibilities of malingering on this basis. Recent observations by Loomis et al (39) bring questionable significance as to the validity of this adaptation by finding a normal alpha present in three blind subjects.

Jasper (40) has reviewed the experimental evidence of optic relationships rather extensively with possible considerations of the basic functions of vision. It seems waves of conducted impulses have been recorded from the optic nerve, the geniculate body, and the cortex. The desynchronization of cortical alpha by an optic nerve impulse has been observed as well as a secondary facilitation having a phasic relationship with the alpha rhythm.

Toman (11) in a recent study on man made correlative observations. Rubin (33) had shown that the apparently normal individuals vary in the per cent-time alpha; that is, some have an alpha rythm present a high per cent of the time, others only a very small per cent of the time. Toman, using monopolar recording from frontal, temporal, and occipital regions, found that those who had a low per cent-time alpha had the widest range of flicker-following, and once synchronization was established after a short period it continued for some time after the flicker was stopped. In other words, they showed a high degree of facilitation. In those having a strong alpha rhythm, a variation of frequency with flicker was hard to induce. Certain other relationships were studied:

1. The frequency of alpha varied from 9.4 to 12 per second, flicker-following varied from 4 to 22.5 per second.

2. The distribution of alpha was: (a) 13 of 21 subjects had the greatest activity over the occipital region; (b) 7 of the 21 had an equal temporal and occipital activity; (c) 4 of the 21 studied had alpha activity equal in all three leads; (d) one showed the greatest alpha activity in the frontal lead. Flicker-following, on the other hand, occurred in the occipital region in 10 cases, occasionally in the temporal, and never in the frontal region.

3. Factors reducing flicker potentials were: any reduction in the visual field--especially any part of the macula, or either half of one eye, or absence or blindness in one eye. Toman discusses the findings of

some investigators of critical fusion frequencies up to 40 to 50 per second according to the basic alpha rhythm of the individual. Some have claimed flicker-following at other than multiples of the alpha rhythm but this only by alternation. By using a light of 1.25 millilamberts intensity, about the maximum possible without producing marked discomfort, Toman was able to produce flicker-following at a practically continuous increase in frequency, especially in those with a weak alpha rhythm, that is it was not limited to doubling or alternation of the alpha rhythm. Evidence considered en toto suggests a very strong relationship of the alpha rhythm to the visual cortical area of the cerebrum, flicker-following being considered a succession of overlapping "on" responses to optic nerve stimulation demonstrated in experimental studies indicated above (40).

Classification According to Basic Rhythms.--Early workers observed differences in frequencies, amplitudes, and persistence of brain waves of individuals. Such variations occur in apparently normal individuals. Lemere (41) classified individuals in two groups, those giving good alpha waves, i.e., over 50 μV and of high regularity, and those giving poor alpha waves, i.e., under 50 μV and of poor regularity. In general, those showing poor alpha waves showed better beta waves. Rubin's division of groups according to per cent-time alpha has already been mentioned. The attempt at uniformity of classification and evaluation of records has been requested by the editors of the American Journal of Psychiatry (42). Various forms have been suggested. A classification advanced by Davis (13) is already in common usage. Under such conditions, as monopolar occipital recording, a record of at least 100 cm. in length at 3 cm. per second begun at least 10 seconds after the eyes were closed, the alpha index is taken as that percentage of time the alpha frequency appears in the record. At least 3 waves must appear in a group of an amplitude of at least 7 μV. Subjects are classified as to "dominant" in which the alpha index was 75 to 100 per cent, "subdominant" from 50 to 75 per cent, "mixed" from 25 to 50 per cent, and "rare" from 0 to 25 per cent. In a series of over four hundred "presumably normal" individuals (less complete information is had than in "normals" defined earlier), the peak of the distribution was at 70 to 80 per cent. Only frequencies between $8\frac{1}{2}$ and 12 cycles per second were considered. Beta activity does not seem to be so important in the evaluation of an EEG. However, if generally applied in the future, the Grass analyzer (43) may differentiate more critically groups according to other than alpha frequency. On a considerable series of cases maximal peaks of energy have been placed at $9\frac{1}{2}$, 19, $28\frac{1}{2}$, 33 1/3, and 43 cycles per second in the normal.

The records are then classified as to pattern. They are briefly:

A.--A regular and clearly countable alpha rhythm reveals a proportional distribution over occipital, pre-frontal, and frontal areas when recorded simultaneously. Other frequencies are regular and consistent in their distribution. The pattern may have a low alpha index and low voltage, the average fluctuation being between 30 to 80μV.

B.--The activity is predominantly of rapid frequencies of low voltage, i.e., 14 to 20 cycles per second of 10 to 30μV amplitude.

M.--M is composed of mixed frequencies, none clearly dominant. Slow, alpha, and fast frequencies are represented with a voltage range of 20 to 60μV.

MF.--This indicates a mixture of frequencies in the alpha and fast frequency range whose voltage fluctuates in a consistent manner within a narrow range. Alpha is usually over 10.5 per second.

MS.--The counterpart of MF contains frequencies in the alpha and slow frequency ranges. Alpha is usually 9 to 10 per second and blunted or deformed by the interference of slower frequencies.

Each of these groups are normal if they maintain a consistent stability of voltage and frequency range for their type. The A and MF are most frequently seen. Rigid classification into any of these patterns is often difficult. (See Fig. 4 in the Addenda for samples of normal tracings.)

Individual Variations.--The question of the consistency of an individuals brain waves has been investigated by Travis (44 and 45). Four individuals with some experience in reading EEG's first attempted to identify 352 isolated strips of records taken on 44 individuals. They were correct in 94 per cent of the time with only a 4.5 per cent chance of being correct on the basis of mathematical probability. Later they identified parts of 11 records of 6 different individuals taken on different days, and at no regular time of the day, only the conditions as to the room, lighting, noise, etc., being controlled. Ninety-one per cent were placed correctly. The EEG from a given individual, therefore, seems to be quite constantly the same. They feel the individual can be recognized by his electroencephalographic tracing.

EEG's of normal individuals vary rather consistently with certain groups. Characteristics which distinguish these groups are:

Age.--Although a variation in the frequency of alpha rhythm of a normal individual may vary from 1 to 2 per second under supposedly constant conditions (46), especially immediately after "eyes closed" is ordered (13), significant average frequency variations can be shown on a statistical basis in children. Berger (28) first mentioned the difference in the EEG of children as having a slower alpha rhythm. Lindsley (47), in a large series of children, first found an alpha rhythm appearing at 3 to 4 months at a frequency of 3.5 to 4.0 per second. The increase to the adult level, 8.0 to 12.0 per second, was gradual and attained at 8 to 10 years. At the ages of 10 to 12 years, the average rate is 8.5 to 14.0 cycles per second, higher than in the adult. They return to the adult frequency at about 12 to 14 years of age.

He speculates as to the following relationships: (a) The child first perceives objects at 3 to 4 months, about the time the first alpha waves appear. (b) At the age just prior to puberty, 10 to 12 years, the frequency is greater than the average adult. Marked glandular adjustments and changes are occurring at this time. The course of myelinization is suggested by these findings.

Smith (48) in 1937 studied the EEG in children and substantiated the findings of Lindsley. He also recorded slow random waves in children under 3 months of age. Amplitudes of up to 50μV may be seen by 2 months. The waves are usually over the Rolandic area. During sleep waves of 8 to 15 per second appear of a similar nature to the waves of the adult during sleep. The correlation of waves to Rolandic and occipital areas at about the time central perception in these areas occurs seems significant as to possible functional relationships of the brain to the EEG findings.

Metabolic Conditions.--Changes in the basal metabolic rate have been correlated with EEG findings. Here again Lindsley (49) first published findings as to a general increased alpha frequency in those with hyperthyroidism as compared to normal and hypothyroids. Rubin (50) reported that in three hyperthyroids with BMR's of + 26.5 to + 47.7 the alpha frequency was increased from 4.9 to 17.2 per cent. Another patient given thyroid had an initial rise with the BMR, then a fall to the premedication level despite a continued high BMR. He suggests that the data supports the hypothesis of a quantitative relationship between the alpha frequency and the carbohydrate metabolism of the brain. Later Ross and

Schwab (51) compared 80 records against the BMR's of 12 myxedematous and 22 hyperthyroid patients. A good correlation existed between the whole group ($\rho = 0.668$) but a better relationship was found when compared to the total calories per hour ($\rho = 0.903$). The EEG was found to be best soon after eating, i.e., not under basal conditions.

The relationship of general increased metabolism to alpha frequencies was also shown to follow Dinitrophenol medication in four individuals by Hoagland et al (52). Since vitamin B_1 is related to carbohydrate metabolism, the results of Takaji and Gerard (53) are of interest. In pigeons avitaminotic as to B_1 the alpha rhythm was unchanged, but the slow 2 to 5 per second waves of the normal pigeon were increased in amplitude by 100 per cent, while the fast 35 to 50 per second rhythm was decreased in some. The rhythms returned to normal within two hours of the administration of vitamin B_1 intravenously. No effect was seen on the EEG when vitamin B_1 was given to normal pigeons. This agrees with the findings of Rubin (54) when he attempted to alter the record and clinical course of schizophrenics. The schizophrenics simply were not vitamin B_1 deficient. Enormous doses by mouth and finally intravenously were given without EEG changes.

Psychological Considerations.--Various problems of interest psychologically have been investigated. Kreezer (55 and 56) studied the EEG of subjects mentally deficient on a hereditary basis (either parent or both or no reason found) and correlated them with the mental age found in standard Intelligence Quotient tests. Mental ages down to 4 years were the same as normal as to presence of about 10 per second alpha rhythm, a normal beta rhythm, and response of alpha to visual stimuli. In the Mongolian idiot no distinctive findings were found down to a mental age of 5 years. Below this there was a very low alpha index, and the appearance of large slow 1 to 5 per second waves. The average alpha index in his series of normals was 52 per cent. In 6 Mongolian idiots of a mental age 6 to 7, the alpha index was 48 per cent; in 13 of a mental age 4 to 5 it was 21 per cent; in 12 of a mental age of less than 4 years it was 19 per cent. A slight increase of the alpha index in the last group (mental age under 4 years) corresponded slightly with chronological age, i.e.; ages 7 to 9 years had an alpha index of 17 per cent; in the ages 18 to 45 the alpha index was 21 per cent. The results were similar in the hereditary mentally deficient group with mental ages under 4 years.

Lateral dominance as determined by normal activities, such as right or left-handedness, etc., tends to have waves of higher amplitude from the non-dominant half of the hemisphere according to Raney (57). In a more extensive study of 48 right-handed, 8 left-handed, and 9 ambidextrous children, Lindsley (58) found that the alpha waves of the two hemispheres were out of phase a greater proportion of time in left-handed and ambidextrous individuals. Unilateral blocking of alpha rhythm was greatest in the left hemispheres in right-handed individuals, and greater in the right hemispheres in left-handed individuals. The degree of asynchronism of the two sides in two stutterers was comparable to the asynchronism of the left-handed and the ambidextrous group, with no increased asynchronism during speech. Unilateral blocking, however, was increased in all groups during speech and occurred both in the occipital area and over the speech area in stutterers. It seems that both asynchronism and unilateral blocking of alpha may interfere with speech formulation and becomes important in those lacking a definite and complete laterality.

Perseveration, defined as the temporal after effect of a stimulus, was studied by Travis (59), who considered its duration as the length of time between the removal of a stimulus and the return of the brain potentials to their prestimulus value. Three stimuli and their perseveration time were given as: (a) a standard printed word = 4.6 seconds; (b) a nonsensical printed word = 4.8 seconds; (c) a light field of slightly higher intensity than the word chart = 3.1 seconds. He concludes that meaning has a physiological basis. The evaluation of a word possesses the activities of the brain for a longer time than a simple light stimulus. The abolition of rhythm by other adequate stimuli has been referred to.

The psychogalvanic response to novel stimuli, as a startling buzzer, an electric shock, a 500 cycle tone, etc., was found to be independent of EEG changes (60). Waves from different areas of the cortex showed changes only in the premotor area preceding and accompanying the voluntary erection of body hair in an individual capable of voluntary autonomic control (61). In this individual, at least, the premotor area seems related to the basal autonomic nuclei.

Personality as classified into introverts and extroverts has been spoken of as related to schizoid and cyclothymic types from a psychiatric standpoint. Gottlober (62) has studied 7 women and 21 male introverts, and 11 women and 28 male extroverts to determine the characteristic brain waves of the groups. The extroverts had a per cent-time alpha of 50 to 100 per cent as a group, whereas the introverts tended only slightly toward a lower than 50 per cent-time alpha. Lemere (41) substantiates these findings. These findings as compared to findings in the major psychoses are of interest.

The hereditary factor has been studied more extensively in the mentally ill group. The study of twins is of interest in regard to normals. Raney (57) claims identical twins have more similar tracings than unrelated children only when treated as a group. Davis (63) finds a more significant relationship, getting very similar records from three pairs of identical twins. Raney may have been misled by his findings that opposite bilateral differences may be found in a pair. This seems significant in itself in consideration of the common findings of opposite bilateral differences as to hair whorls, laterality, etc.

Factors Effecting an Individuals EEG:--Temperature. Hoagland (64, 65, and 66) has studied the effects of changes in temperature from 98.6° to 105.0° produced by diathermy in normals and paretics. He finds an increase in alpha rhythm consistent with the Arrhenius equation of critical thermal increment. He found increases from an average of 9 to 10 per second to 13 per second for the whole group and analyzes these increases in basic serial chemical process relationships, and the direct effect on cortical cells considered acting as relaxation oscillators. Libet and Gerard (67) found Q_{10} = 2.3 in the frog where changes in temperature of from 5^{o} to 30^{o} could be conveniently produced. In general, a direct functional relationship to the rate of chemical reactions is suggested.

CO_2, O_2, Glucose, Ionic Concentration Changes.--Brill (68) in a study of 100 normal children found that hyperventilation tended to produce dysrhythmias, the tendency being greater the younger the children. The adult seldom had the characteristic outbursts of 3 per second slow waves with hyperventilation. They are found, however, in adult epileptics and in organic disease. Further reference to epileptic conditions will be considered later.

In the normal adult acapnia increases the fast waves and the slower waves become slower, more regular, and of greater amplitude. Increased CO_2 and decreased O_2 (the latter probably playing a small part in hypercapnia) intensifies the faster waves and disturbs the rhythm of the slower ones (69). Oxygen and glucose level changes have to be extreme to produce changes in alpha rhythm (70). As Neminski had shown (8), the waves in an animal disappeared after four minutes of asphyxia but persisted longer if hyperventilation preceded asphyxia.

Changes in ionic concentrations are significant only when they become extreme. In the cat isotonic KCl applied to the cortex rapidly abolishes spontaneous rhythm. This is reversed slowly by Ringer's solution, more rapidly by $CaCl_2$. (Note similar effects on contractility of the heart (1).) Intravenously KCl exaggerates the rhythm of the anesthetized animal. $CaCl_2$ again reverses the effects. These changes were all with concentrations beyond the usual normal. Perhaps less marked concentrations would have a similar effect to a lesser degree.

Voluntary Muscle Activity in Normal, Epileptic, and Paralysis Agitans.--The accentuation of alpha rhythm by voluntary muscle activity has been mentioned before. A basic rhythm of 10 per second during muscle activity had been observed frequently. Hoffman and Stronghold (71) found the frequency of action potentials from the forearm during rhythmic stretching to be 55 per second with a basic modulation at 10 per second. Jasper and Andrews (72) studied several individuals with simultaneous recordings of the cortical action potentials, tension rhythms of the forearm, and muscle action potentials. The tremor frequencies were found to correspond closely to the cortical potentials anterior to the central fissure with a major 10 per second and a minor 25 per second rhythm. During sleep both changed to a major 5 per second rhythm and a minor rhythm of 13 to 14 per second. Sensory stimulation may depress both or produce a dissociation, i.e., the amplitude of the tremor becomes greater, whereas the cortical waves are depressed.

In the epileptic, cortical seizure waves were often associated with corresponding bursts of muscle potential at 3 per second with a latency of about 50 milliseconds. The authors conclude that since the typical waves appear sometime before an attack, and since there is a lack of correspondence of seizure waves and clonic waves, other centers, probably subcortical, may be set into autonomous activity and take over control of certain major pathways during an attack.

The 4 to 5 per second tremor of two cases of paralysis agitans, did not appear in the cortical rhythm. In more advanced cases the 4 to 5 per second rhythm would appear periodically in the cortical rhythm. They conclude therefrom that in derate involvement of the strio-pallidal motor system, functional integration is disrupted, whereas, in severe inv lvement, the subcortical centers may take over the cort cal rhythm.

The study suggests that there is an interrelation between cortical and subcortical centers which determines the rhythm of impulses in the final common path. Ordinarily the cortex probably determines the rhythm of lower centers. In conditions of sensory stimuli, or general excitement when the cortex is activated or possessed, subcortical centers may take over control both of the cortex and the final common path.

This work has been severely criticized (see discussion of 69) especially in view of studies which indicate a quantitative relationship of the frequencies of impulses to the degree of contraction of a muscle (5). However, this criticism is not altogether valid since these studies were related to variations in degree of voluntary activity, whereas the studies of Jasper and Andrews (72) concerned only frequencies found in the muscle at rest. Schwab and Cobb (73), however, could find no relationship in the muscle tremor frequency and cortical rhythm in 37 cases of paralysis agitans.

Sleep, hypnosis and trance states have similar patterns of cortical activity and will be considered together. The importance of recognizing the fact that a confusing record is apt to appear with sleep has been referred to. Davis et al (74) have described five stages with the onset of sleep: (a) Interrupted alpha--the normal alpha rhythm of 10 per second dominates the picture with slight interruptions. (b) Low voltage--the alpha rhythm disappears. (c) Spindles--short groups of spindles (waves of 14 to 16 per second, waxing and waning in amplitude) appear and also random delta waves, i.e., large slow waves of 0.2 seconds duration. (d) Spindles and random--both types of waves increase in amplitude and the delta become longer. (e) Random--the 14 per second waves become inconspicuous but the delta waves continue to increase in voltage and wave length.

In subjects with a strong alpha rhythm, the depression or loss of alpha occurred at the "drifting off" point as signaled by the subject. Slow delta waves appeared here also. In subjects with few alpha waves, depression of the beta, 15 to 20 per second, waves occurred at this time also with the appearance of delta waves. "Real sleep" was always acknowledged when the slow waves had reached an amplitude of 150μV or more and persisted for 0.5 minutes. Spindles were a sure sign of sleep. Dreams occurred in stages (b and c). It was impossible to clearly define the beginning or end of sleep.

Loomis et al (75) point out that only the waking pattern clearly defines an individual, stages (b to e) being very similar for all individuals. The 14 per second spindles appear predominantly from the vertex while the large delta waves appear from all parts of the head. They find that any disturbance during sleep, whether it restores alpha or not, is apt to give rise to large 7 per second waves, or K waves, appearing with an initial negative then positive swing with small 8 to 14 per second waves superimposed. These waves are possibly a forerunner of the delta of stages (d and e). They result regularly from a tone stimulus.

Some interesting observations on EEG's during hypnosis have been made. Gerard (69) reports a case in which a regular 10 per second alpha rhythm was found when "darkness" was suggested to the individual although he was in a brightly lighted room. Another subject hypnotized by Dr. David Slight into a state of cataleptic rigidity retained a normal pattern of waves. No waves characteristic of sleep appeared during hypnosis, but such waves did appear in this individual during normal sleep. The subject was hypnotized with his eyes fastened open by adhesive tape. When he was told, "You are blind," the alpha rhythm appeared, as in a normal with eyes shut. When he was told, "You can see," the alpha waves disappeared, as occurs in a normal with eyes opened. Waves could not be started in an unhypnotized person with his eyes open in a lighted room. Abolition of the alpha rhythm in a normal individual has occurred on the suggestion that he was observing some object in a totally darkened room, indicating some of the possibilities of the power of suggestion. It can be concluded from these studies that hypnotism is not a state of sleep (39).

A case of self-induced trance gave an EEG record suggesting a condition related to sleep. Slow 2 to 2.5 per second waves of 30 μV appeared during the trance state with changes in the alpha rhythm (76).

Drugs Not Generally Used in Psychiatrical Conditions.--Davis (13) in her specifications for the choice of a normal individual has emphasized the necessity of ascertaining the presence or absence of drugs. The effect of drugs not generally used in the treatment of mental conditions will be briefly explored, not only to determine the possible effects of such drugs on the "normal" EEG, but also to further elucidate their actions.

Depressants.--Adrian and Matthews (21) had observed that in the anesthetized rabbit the EEG was characterized by large slow waves as compared to the normal with some small brief waves. They were more regular the deeper the anesthesia. The anesthetic seemed to affect the afferent and efferent paths more than they did the general electrical activity of the cortex. Beecher (77) found that a drop in blood pressure by cardiac tamponage produced changes in the electrical activity of the cortex comparable to an increased depth of anesthesia. The significance of this finding is well appreciated in modern surgical procedures.

Rubin and Freeman (78) found that during cyclopropane anesthesia the alpha decreased by 20 per cent in frequency and increased by 100 per cent in amplitude after 1 to 2 minutes of induction. Opening the eyes at this stage still interrupted the rhythm. When large 3 per second waves appear, the subject is in surgical anesthesia. Occasional bursts of alpha still occur here. Recovery produces a reversal of changes with the appearance near complete recovery of 12 to 14 per second waves typically seen in sleep. When the alpha rhythm returns dominantly, the subject can be easily aroused.

In a case of bromide intoxication (79) the alpha frequency rose as the bromide level fell from 59.6 mg. per cent to 0.0 mg. per cent. The possible relation of the bromide ion to a general depression of the metabolic activities of the cells of the nervous system, and the possible use of the EEG to ascertain the presence of toxic substances are suggested.

In a study of the effect of sodium amytal on the EEG and the associated psychological condition of several normal subjects, Fowler (80) found a significant increase in the mean frequency of alpha rhythm with associated mental depression. Anderson (81), in a study of 50 morphine addicts and 50 addicts in whom the addiction had been terminated for several years, found an abnormal alpha distribution curve for both groups. An abnormally high alpha frequency was seen in addicts which persisted some time after withdrawal. The persistence of high alpha output during withdrawal is not consistent with the abolition of alpha during similar high degrees of emotional tension in normals.

Mescaline produces a reduction in the amplitude of alpha waves and an augmentation of silent periods which last for many hours (82). Speculation as to the associated trance-like condition may be of general interest.

Stimulants.--The effect on the frequencies of the alpha rhythm were inconstant with Cocaine (80). In the isolated frog brain, Gerard (83) found that caffeine applied locally produced large repeated waves which traversed the hemisphere and continued into adjoining cortex though all neuronal connections had been severed by transsection. A caffeinized brain was capable of inducing these waves in an adjoining normal brain also.

Convulsants.--Thujone injected intravenously into an anesthetized rabbit produced large pulsations which spread widely over the cortex (21). Strychnine produces similar effects, the spreading waves not being localized to the area to which it was applied locally (84). Strychnine injected into a curarized animal produces increased generalized oscillating activity (35).

Autonomic Drugs.--Adrenaline injected into several normal individuals decreased the alpha frequency of only one. Mecholyl produced a significant increase in alpha frequency in 3 of 7 cases, but the authors explained this on the basis of O_2 and CO_2 changes secondary to cardiovascular changes (80). Miller et al (85) found that local application of either 1 per cent eserine or $1:10^5$ acetylcholine to the cat or rabbit cortex reduces the amplitude of slow waves and large fast waves. 0.2 to 1.0 per cent acetylcholine applied to eserinized cortex produces typical spikes with more marked motor effects. Atropine abolishes these effects. Pilocarpine produced no effects. The authors relate these changes of eserine and acetylcholine to the facilitation of synaptic transmission to produce a combination and synchronization of neuronal units.

Evaluation of the Total Record.--Having considered the variations in normal records and possible factors producing changes in the supposedly normal records, a discussion of the evaluation of the total record is in order. The tabulation of Davis (13) is recommended as a very suitable form.

Tabular headings for gross analysis

(The author used the following headings consecutively on a ten-inch card).

Serial no.	Type of Pattern	Volt.	Reg.	Alpha		Resp. to "O & Cl"	Asymmetry	
	A, B, M, MS, or MF	Ave. (+) High (++) or Low (-)	Ir., Int., or Reg.	Per cent	Freq.	Good (+) Poor (-) or Ir.	Yes (+) No (-)	More α on right or left

Abnormal activity					Freq. band of Dysrhythmia			Location of Dysrhythmia	Rating	Remarks
E	R	Sp.	Diff.	Local	δ 1-3	SF 4-8	FF 16+	If not diff. give the order of prom. by area	Based on total record	

Key

Ir. = irregular, meaning frequencies are irregular and distorted.

Int. = interference, meaning good wave form but other frequencies interfere with its appearance or superimpose themselves.

Reg. = clearly regular without distortion or superimposed frequencies.

Alpha per cent is measured on 100 cm. of record.

Alpha frequency is counted and determined from speed-up following eyes closed (see text).

Resp. to "O and Cl" is appearance of alpha following eyes open and closed. Slight delay in response is secondary.

Key (Cont'd)

<u>Sp</u>. = specifically recognized complex such as petit-mal or grand-mal complex or variant.

<u>Diff.</u>= diffuse.

Local= localized to an area or side.

= episodal dysrhythmic interference.

- "rambling" dysrhythmic quality as opposed to clear episode, usually in the slow range.

Other forms have been suggested (42), but a final generally adopted form will probably not be used until more is known about the EEG. This form is suggested as very suitable for evaluation of normal and abnormal records. Before undertaking the study of abnormal EEG's, reference to sample tracings of normal records is recommended. All tracings, normal and abnormal, being grouped together should make comparisons more convenient.

Tumors, Lesions, and Associated Conditions

One of the most valuable applications of the EEG has been made relative to the localization of tumors and intracranial lesions of other types. It is well known that the neurological symptoms presented are not always reliable (86). Secondary stimulation of centers distant from the cite of the lesions may produce symptoms masking those which might arise from neurological centers near to the lesion. Encephalography has been a great aid to localization of the lesion. Even this fails at times. Case (87) has pointed out that the value of the EEG is especially appreciated when there are lesions in neurologically silent areas. The principles of localization and the possibilities and limitations of the EEG will be briefly explored.

Principles, Possibilities and Limitations of Localization.--Berger (26) reported finding irregularities in frequency and amplitude of the alpha activity in cases of cortical degeneration of dementia. He reported marked dissimilarity between homologous areas. Walter (12) first reported an accurate localization procedure. In general it is desirable to have simultaneous records from different areas. At least three independent units should be used. He discusses the limitations of localization due to the spread of potential changes in an area by the dura, skull, and scalp beneath the electrode as pointed out by Toennies in 1933. He estimates the limits of accurate localization to be near 4 cm. Williams (88) gives an excellent discussion of method and localization by the Walter method. Jasper (89) in 1938 first analyzed localization principles more extensively in applying what he called "triangulation" to determine the foci of epileptic seizure waves. By placing three electrodes in a triangular relationship to a suspected focus of seizures, simultaneous tracings give important clues as to the exact location by the amplitude and phasic relationships of the recorded waves.

The principle is really an application of Einthoven's triangle used in determining the electrical axis of the heart. This principle of Einthoven's triangle is discussed so well in Best and Taylor's Textbook of Physiology and is felt to be of such importance that it is presented here.

Fig. 5.--Einthoven's Triangle

Theory of Electrocardiographic Interpretation (applied to EEG). Description in text.

"First let a geometrical proposition be considered. Let an equilateral triangle, ABC, be described and a straight line, DE, be drawn in any direction within it, and let this line be projected perpendicularly on to the three sides (P_1, P_2 and P_3, fig. 5, I). Then the longest projection (which in the illustration is P_2) equals the sum of the other two (i.e., P_1 and P_3) in the instance depicted. This is true no matter what may be the direction of DE.

"Next let a plate of conducting material be fashioned in the form of an equilateral triangle (fig. 5, II) and let any two apices of the triangle be connected through a galvanometer so that when the fall in potential is from A to C either through B or directly to C the galvanometer deflection is upward, i.e., positive, and when the fall in potential is in the opposite direction, deflection is downward or negative. When an electromotive force, whose magnitude and direction are represented by one or other of the two central arrows shown in the figure, is developed within the triangle, then the potential difference between any two of the latter's apices will be proportional to the length of the projection of the arrow upon the side connecting these apices; the length of the projection on a given side of the triangle, and so the recorded potential change which it represents, will vary, of course, with the angle which the arrow makes with that side. Whether the central EMF will produce an upward or a downward deflection will depend upon its general direction. In the figure all the projections of the solid arrow are positive; two of the projections of the arrow drawn in interrupted lines are negative and one positive. But the arrow might point in any direction, and depending upon its direction in relation to a given side of the triangle its projection upon that side will be of positive or of negative sign. It will be found, nevertheless, that in whatever direction the arrow points, the algebraic sum of its projections on the sides AB and BC will equal its projection on AC.

"Finally, let the three electrocardiographic leads be imagined as forming an equilateral triangle about the heart (fig. 5, III); let the electrical axis of the heart be represented by the arrow, and the potential differences, negative or positive, which are recorded (as deflections) in the electrocardiogram in the three leads, be taken to correspond to the projections of the arrow upon the respective sides of the triangle. Then the potential difference between any two points upon the body represented by the apices of the triangle will vary in magnitude according to the angle which the arrow (electrical axis) makes with the lead joining these points, and be proportional to the projection of the arrow upon the line of the lead."

Instead of the electrical axis of the heart, consider potential differences recorded from the brain spreading from a point of origin over the adjoining brain substance. The similarity in principle and practice is immediately apparent. Fig. 6 (see Addenda) illustrates the principles of localization by consideration of the phasic relationships and amplitude of waves in an EEG.

The importance of these principles is seen in attempts to localize lesions of the cerebellum and lesions deep in the subcortical centers. Since the electrodes are nearly as close in one position of the head as another due to the spherical nature of the skull, localization becomes very difficult (90).

Having considered the major factors in localization, the question may arise as to the accuracy of such localization. In 66 cases of focal epilepsy studied in which 60 of these showed discrete lesions on operation, Penfield and Jasper (91) report the following results: In 85 per cent of the cases localization was accurate to within 2 to 3 cm. of the location found at operation. In 90 per cent of the cases localization was within 4 to 6 cm. Whereas this may not appear to be very accurate, it must be remembered that other localizing signs may be negative and the pneumo-encephalogram in such cases may be entirely negative or indicate a much larger lesion than exists.

In reporting the success of attempts of localization in 105 cases, Williams (88) presents the following summary. In 50 cases in which the pathological process was demonstrated on operation, there was a close correlation with the EEG findings. In 41 cases in which the EEG was negative, operation indicated by clinical symptoms revealed no lesion. Lesions were suggested by the EEG in 14 cases in which subsequent pathological studies failed to substantiate the findings. From these studies, ascribing a definite value to the EEG as supporting evidence to other findings is certainly justified.

Evidence from the exposed brain is very elucidating as to factors to be considered in the accuracy of localization. Only a few such studies have been undertaken as reviewed by Rahm (22). His report and that of Sachs et al (92) will be drawn upon for evidence as to the following:

1. Tumor tissues of all types, glioblastoma, astrocytoma, meningioma, supersellar cysts, and metastatic carcinoma, are electrically inactive.

2. Abnormal waves arise from the tissue adjacent to the tumor. The greatest dysfunction is observed in those regions of the cortex being actively invaded by the tumor. The electrical activity of the cortex becomes more and more nearly normal as the distance from the site of the tumor is increased. Thus, the benign encapsulated

lesions show remarkably little abnormal electrical activity. Of course, electrical activity of the cortex ceases when sufficiently damaged.

3. Large slow waves arising in cortical tissue in cases of internal hydrocephalus disappear immediately when the pressure is reduced by aspiration unless the cortex has been severely damaged.

4. Cerebellar tumors and lesions produce little or no characteristic electrical changes from the cerebellum itself but may produce irregular activity in the adjacent occipital lobes.

5. Large slow waves were obtained from cortical tissue adjacent to a cortical scar resulting from skull fracture.

6. Diffuse pathological disease of the brain shows normal brain rhythm interspersed by slow waves over the entire area of the cortex.

Summary of Limiting Factors.--It can be seen from this that the following are all factors which limit the localization of a brain lesion.

1. The necessary size of the electrode.

2. Spread of the electrical activity by the tissue overlying the origin of the abnormal waves.

3. The fact that the lesion itself is electrically inactive and the abnormal activity arises from around the lesion.

4. Confusion may arise as to the origin of slow waves by the diffuse effects of possible raised intracranial pressure.

5. The proximity of the lesion to the surface of the cortex.

With so many limiting factors it is perhaps surprising that the instrument has such usefulness as has been demonstrated and at the same time emphasizes the necessity of using the EEG only in conjunction with other findings. A few studies with characteristic findings in various brain lesions are presented. (See Fig. 7 in the addenda for a sample tracing.)

Findings in Tumors and Lesions.--Frontal Lobe.-- Lemere (93) reports the following: A stronger abnormal rhythm was found in the affected side in three cases of frontal lobe tumor, in one case of which there was an increased intracranial pressure.

Parietal lobe.--In two cases of parietal lobe tumors without an increased intracranial pressure, he found a rhythm stronger on the affected side. In one case of a parietal tumor with an increased intracranial pressure, abnormal waves arose with equal strength from the two sides.

Temporal lobe.--A tumor located deep in the temporal lobe gave much stronger waves from the affected side.

Temporo-parietal tumors gave stronger waves from the affected side. In two cases where the optic radiation was completely severed, the waves were the same with eyes open or shut.

Occipital lobe.--A cyst and a tumor with no increased intracranial pressures produced a complete absence of alpha rhythm on the affected side where the hemionopia was complete. In two cases of posterior cerebral artery thrombosis the alpha rhythm was absent in one and depressed in the other with corresponding findings in vision.

Basal ganglian lesions produced markedly better alpha rhythm on the affected side in three cases.

Thalamic lesions, three of which were vascular and one of which was a tumor, produced a depression of the alpha rhythm on the affected side. In one vascular lesion the two sides were similar in the EEG.

Cerebellar Tumors.--Two cases producing mild intracranial pressure produced no difference in the EEG of the two sides. Smith et al (94) reporting seven cases of posterior fossa tumors found focal pathological 2 to 3 per second waves symmetrically over the occipital area of each side. In two cases operated, marked improvement in the EEG resulted. The results indicate that the cerebellum produces effects in the EEG from the occipital lobes secondarily to a compression in them through the tentorium.

Bilateral Lenticular Lesions.--The alpha rhythm was found stronger in the least affected side in two cases, and less difference was seen in the other of the three cases of Wilson's disease reported by Lemere. In a comparative study, Weatherby (95) found marked evidence of cortical damage, especially in the right side, in the pneumoencephalogram of a case of Wilson's disease. The changes in the EEG substantiated the findings of extensive cortical damage. Outbursts of high voltage 6 per second waves, occasional 9 per second, and also runs of 15 per second waves were recorded and were especially marked from the right side.

Pituitary Tumors.--In Lemere's two cases in which there was no increased intracranial pressure but severe amblyopia, the alpha rhythm was present in both sides and was little affected by opening or closing the eyes.

Pontine Tumor.--In one case of a pontine tumor, Smith et al found abnormal waves mostly prefrontally in the left hemisphere. The cause may have been the secondary enlargement of the left hemisphere which was demonstrated.

General Paresis.--An increased alpha rhythm in proportion to the severity of the dementia was shown by Hoagland (64). Berger had found similar results with a marked dissimilarity between the two sides and improvement in the EEG with clinical improvement following medication. Hock and Kubis (96) found slow 3 to 6 per second waves in most of 17 cases. Only in 4 patients did the frontal area seem most involved electrically. The general cortical involvement in general paresis is indicated in all studies.

Vascular Lesions.--In hemiplegia slow waves on the side of the lesion were usually found by Hock and Kubis (96). Walter (12) had found no changes in one case. In three cases of traumatic hemorrage localization by EEG was reported (97). Clinical and electroencephalographic improvement followed operative correction of the difficulty.

In a left carotid artery ligation for a sacular aneurysm in the left side of the circle of Willis, Yeager and Walsh (98) reported a loss of alpha and the presence of many delta (1.5 to 6 per second) waves from the left side and occasional delta waves from the right side after the operation. The EEG was normal some time before the operation, but just before the operation some irregularity of the alpha rhythm was found.

Other Dementias and Deteriorations.--*Disseminated sclerosis* gave an average or poor alpha rhythm in 13 of 19 cases (41 and 93). In 5 of 6 others in whom early emotional instability was a uniform complaint, a better than average alpha rhythm was found. *Senile dementia* is characterized by an alpha frequency lower than normal in proportion to the severity of the dementia. As low as 4 per second alpha waves were found (96). The frequency was lower than in *alcoholic psychosis*, in which only the *Korsokoff* type showed abnormal slow 3 to 6 per second waves. Those classified merely as *paranoid* and *hallucinosis* types had normal rhythms. Cases of *deteriorated epileptics*, *cerebral arteriosclerosis*, *diffuse sclerosis*, *progressive muscular atrophy*, and *olivo-ponto-cerebellar disease*, all showed poor alpha rhythm (93). Localization of *cerebral atrophy* with associated conditions, as schizophrenia and manic-depressive psychosis, was possible by the distribution of "per cent-time alpha" (99). The pneumoencephalogram confirmed the EEG findings. Three of 6 cases of *amyotrophic lateral sclerosis*, showing marked cerebral involvement clinically, gave abnormal findings in the EEG (100). Slow sinusoidal waves of high amplitude from the frontal lobes, episodes of waves of a frequency greater than the normal beta, and rare alpha waves from the occipital lobes unaffected by light stimuli characterized these cases.

Increased Intracranial Pressure.--The effect of increased intracranial pressure may be surmised from the cases discussed above. Berger (26) first mentioned the presence of slow 3 per second waves in this condition. Lemere (93) substantiated these findings but prefers to call these waves delta rather than slow alpha as Berger had designated them. Williams (101) has ascribed these findings as being due to the edema of the cerebral tissue and not a pressure effect per se. Increased pressure caused by the injection of petressin in which oedema is slight or absent does not produce EEG findings. He could find little correlation between the EEG and the state of consciousness, or the degree of intracranial pressure.

Frontal Lobotomy.--Davis (102) reports three cases of bilateral frontal lobotomies and the EEG findings. One showed abnormal EEG's before operation. The indication for operation was alcoholism with restlessness and anxiety. The record two weeks later was unchanged. Another developed a generalized overactivity with giant delta (500μV) episodes from the left side over a period of two years with manic trends clinically. He was markedly improved by the operation, and the EEG became nearly normal. In the third case, an agitated depression, the EEG contained low voltage fast waves and slow waves of the alpha pattern. He was markedly improved by the operation psychologically, although the EEG showed greater instability temporally and frontally but greater stability in the occipital lead.

The Epilepsies

Perhaps of equal or greater importance than the localization of intracranial lesions has been the application of the EEG to the study of epilepsies. The principles of localization of epileptic foci are the same as those used in locating lesions (89). Many successful localizations of foci have been reported in the last few years (103 and 104). These localizations have been proved correct by pneumoencephalographic studies or by operation. Casamajor (105) reports lateralization of abnormal waves of a diffuse nature in 14 of 17 cases in which the pneumoencephalogram failed to indicate any lateralization. Here again the usefulness of the EEG has proved itself where other methods have failed.

Berger (27) first noted the variation from the normal in records from epileptic patients.

various types of epilepsies have been classified according to their EEG findings, and the word "epilepsy," from the Greek word meaning "falling sickness," no longer expresses the general understanding we now have of this condition. Instead, Gibbs et al (106) in 1937 suggested calling it a condition of "paroxysmal cerebral dysrhythmia". Characteristic patterns are found in the different types. They base their conclusions on 900 hours of tracings from 400 patients, including records during 120 seizures. Their findings were:

1. Seizures involving the cortex show distinct characteristic fluctuations in the EEG.

2. Rhythms distinctive of the three main types of epilepsy are: (a) grand mal--fast waves, (b) petit mal--slow and fast waves, and (c) psychic variants--predominantly slow waves.

3. Subclinical seizures are seen during sleep, especially in petit mal.

4. A lack of control of the cerebral rhythms in general is noted.

5. Grand mal seizures can be predicted several hours in advance by the appearance of the characteristic waves.

6. The characteristic appearance of the waves in one area for a given individual gradually spread to other areas.

7. The type of pathological activity tends to be characteristic of the area which produces it.

8. The effect of therapy as seen clinically can be correlated with the suppression of the abnormal activity in the EEG.

9. In one case, a frontal lobotomy cured the patient and was correlated with the absence of abnormal waves which were seen to arise from this frontal area in the EEG before operation.

Characteristic tracings found in epileptic patients are presented in the addenda, Fig. 8.

Classification of epileptic seizures on an EEG basis has been undertaken by Jasper and Kershman (107) from 468 cases studied. Sudden outbursts of high voltage waves, called paroxysmal hypersynchrony, were the distinguishing features. Localization was found to be the best basis of classification. They were either (a) localized unilateral cortical outbursts, (b) bilaterally synchronous from homologous areas, or (c) a diffuse wave form and were important for detailed analysis. Classification of the record into (a) random waves of three types--(1) spikes, (2) sharp waves, and (3) delta waves, and (b) paroxysmal rhythms of six forms--(1) 3 per second waves and spikes, (2) 3 per second waves, (3) 6 per second waves, (4) 10 per second waves, (5) 14 per second waves, and (6) 25 per second waves was found very useful.

Abnormality localized to a discrete area of one hemisphere was found in 50 per cent of the cases. These were usually of the form of random spikes, random sharp waves, or random delta waves in paroxysmal rhythms. The most common rhythm found was random spikes. They were usually seen in patients with seizures characterized by a focal onset and a gradual march of the seizure to other areas. The type of focal onset was related to the function of the cortex involved.

Bilateral synchronous abnormality appeared in 35 per cent of cases usually bifrontal or bitemporal in location though occasionally bioccipital. The principal forms of waves in records in this group were: (1) 3 per second waves and spikes, (2) random sharp waves, (3) 3 per second waves, and (4) 6 per second waves in random groups. Three per second waves and spikes and 3 per second dome-shaped waves were usually seen bifrontally in the same patient, and these usually were the petit mal type of epileptics or the grand mal types with an initial loss of consciousness. Sharp waves characterized the records of patients with the onset of major or minor seizures referential to centers in the temporal lobes. Many had visceral aura with complex disturbances of behavior and thinking. Six per second waves, often associated with 3 per second waves if from the bifrontal area or with sharp waves from bitemporal areas, occurred in patients with visceral aura and epileptic automatism.

The remaining 15 per cent of the cases gave records characterized by a diffuse abnormality without synchrony. Three forms were seen: (1) diffuse multiple spikes, (2) diffuse multiple sharp waves, and (3) diffuse multiple delta activity. Patients of this group who had records of the first two forms usually had major cortical seizures with no consistent focal cortical onset.

These authors are not impressed with the etiological factors as determining the type of record. The location of specific neurones of excessive discharge and the relations of this primary focus to the rest of the brain evidently determine the type of EEG found and the form of clinical seizure.

As was seen in this study above, 50 per cent of the cases were characterized by bilaterally synchronous waves or generalized dysrhythmia. These were generally associated with grand mal or petit mal types of convulsions. These findings corroborate previous findings of other workers as Gibbs et al (108), who described the waves and spike pattern as being pathognomonic of petit mal epilepsy. The importance of the EEG has been in the correlation of the suppression of pathological waves by drugs and other means.

Drugs and Control of Epilepsy.--Thus Cobb et al (109) observed that hyperventilation in petit mal patients preceded the appearance of delta waves and corresponded to the incidence of attacks. If hyperventilation with CO_2 was undertaken, no abnormal waves appeared and no attacks occurred. Also 150 grains a day of NH_4Cl for four days decreased the effectiveness of the production of abnormal waves with hyperventilation. If $3\frac{1}{2}$ grains of Dilantin were given each day for three days, with the above dosage of NH_4Cl, hyperventilation was even less effective in producing abnormal waves. Dilantin alone was not as effective. They suggest, therefore, that acidosis-producing drugs be given with Dilantin in the control of petit mal. The importance of hyperventilation in the detection of epileptic conditions will be discussed later.

Gibbs et al (110) showed that high blood sugar increased and low blood sugar decreased the wave and spike form of petit mal epilepsy but did not affect the abnormal crescendo bursts of grand mal nor the high voltage 6 per second waves characteristic of psychic epilepsy. They found that hyperventilation was equally specific in its effects on these same waves of the different types. Thus an Insulin reaction would produce an amelioration of petit mal epilepsy for from 1 to 3 days.

Lennox et al (111) had noted the effects of hyperventilation in 1936 and also found that phenobarbital and NaBr in doses without effect on normal waves, produced marked depression of abnormal waves. Camphor injected intravenously in a normal person produced waves and a convulsion typical of epilepsy.

From these studies it may be seen that Dilantin is of great general usefulness in the epilepsies, especially the petit mal and focal types. The specificity of therapy for the type of epilepsy is indicated by the studies of Grinker et al (112). In a case of myoclonic epilepsy characterized by waves faster than normal, without a loss of consciousness but with muscular twitchings, a counterpart to petit mal clinically and electroencephalographically, he suggests depressing drugs as phenobarbital. In petit mal stimulating factors as occupation by sound or visual stimuli, attention, etc., are indicated. Schwab (113) had found sound stimuli to be more effective. On the other hand, Strauss (114) found doses of phenobarbital up to 70 grains a day ineffective in the control of a case of reflex epilepsy. The case was cured by applying Cocaine to the right eye over a period of months, presumably by allowing the cortex to readjust itself while the peripheral irritating focus was eliminated.

Epileptiform Records from Non-epileptics.--Epileptic-like waves may be obtained in cases in which no seizures occur. Jasper et al (115) found typical waves in 64 cases of head injuries without seizures. In some cases the abnormal records were obtained years after the injury associated clinically by changes in personality, irritability, etc. Of course, cortical injury may serve as a source of epileptiform waves and cause seizures especially of the Jacksonian type as shown by Penfield and Jasper (91) in 66 cases. Usher and Jasper (116) pointed out that the EEG patterns very similar to those found in epilepsy are found in Sydenham's chorea, where no specific lesion has been found responsible.

Records from an individual diagnosed as psychoneurotic contained 3 per second waves from a fronto-motor lead, as was reported by Bennett and Cash (117). Jasper et al (118) first reported an analysis of records from behavior problem children. Later Cutts and Jasper showed that, whereas Benzidrine sulphate had no effect on the per cent-time alpha or the slow waves in form or amplitude in these children, it was associated with clinical improvement in those with a 6 per second rhythm. Phenobarbital made 9 of 12 such patients worse whereas it decreased the number and amplitude of the slow waves and increased the number and amplitude of the beta waves. In these children, the records were very suggestive of epilepsy. Lindsley and Cutts (120) again emphasize the importance of taking records after hyperventilation in behavior problem children. It induced abnormal waves in many children in which the record appeared normal under standard conditions.

Inheritance and Epilepsy.--A good deal of interest has been aroused in the consistent findings of investigators of abnormal records in relatives of epileptics not dissimilar to those, i.e., individuals who actually have epilepsy. Lennox et al (121) first reported that 54 per cent parents or siblings of 138 epileptics had abnormal records, although only 1 in 5 of the patients knew of any relative similarly affected. In a control group only 6 per cent had epileptiform records. In 46 epileptics both parents were examined. In 28 per cent of these relatives both parents had abnormal records, and in 94 per cent at least one of the parents had an abnormal record. They point out the importance of the EEG in the selection of mates in eugenics and advise that if two individuals have abnormal records they should not marry. Since only 2.4 per cent of the relatives of a large group of epileptics studied actually had seizures, whereas 60 per cent of this group had abnormal records (a ratio of 25 to 1), the authors (122) conclude that since only 0.5 per cent of the general population have epilepsy 12 per cent of the population probably have a disposition thereto as might be determined by EEG findings. Robinson (123) presents similar findings and points out the importance of taking records after hyperventilation to detect abnormalities which might not be seen without hyperventilation. Strauss (124) also substantiates these findings in general and points out that in 71.5 per cent of close relatives of 10 epileptics some related symptom as, migraine, epileptoid personality, etc., are found.

Major Psychoses

The EEG has been applied to the study of the major psychoses with very little success from the standpoint of diagnosis. Berger had mentioned that abnormal waves were obtained from some cases of schizophrenia, but later Kreezer (125) in 1936 reported that his studies indicated that no definite statement could be made as to the diagnostic value of the EEG in such cases. A series of conflicting reports then followed. The statement by Knox and Campbell (126) seems applicable as a summary to the whole problem. They decide that a uniform type of abnormal record can hardly be expected where such a variety of clinical pictures are seen. Although a type of diagnostic tracing representing a type of psychoses cannot be defined, some interesting observations have been made.

At one time a possible relationship to the epilepsies was indicated by the works of Gibbs et al (127) and of the Davis's (128 and 129). They speak of the conditions, schizophrenia and psychomotor personalities, as being a cerebral dysrhythmia which is perhaps better represented by the EEG than by the clinical manifestations. They admit that no diagnostic form of tracing can be ascribed however.

Davis (130) in a later study of the manic-depressive group reported that in 42 depressive manic-depressives an alpha rhythm of less than 10 per second was usually found, whereas in 22 manic manic-depressives the alpha rhythm was usually over 10 per second. She found no changes of alpha rhythm with changes of the individual from a manic to a depressed state or vice versa, however. She suggests that in a normal person, when an individual has a record of high alpha activity of over 10 per second ("A" type of normal), he is most apt to be diagnosed as a manic manic-depressive if he becomes psychotic, and depressive manic-depressive if he has a MF or B type of record. (See classification of normal records and sample tracings, Fig. 4, addenda, from reference (13).) She bases these predictions on the case histories of the patients studied.

Knox and Findley (127) have studied 500 schizophrenics and classified their tracings as compared to 215 normals into five patterns: a. A uniform normal frequency of 8 to 12 per second made up of sine cycles undistorted by cycles outside the normal range; b. Similar to pattern "a" with an occasional distortion by superimposed rapid low voltage activity, slow waves, or both; c. characterized by a great variety of patterns, an absence of an organized frequency, could either be called a questionable normal or questionable abnormal; d. a significant quantity of rapid waves of 25 μV or more superimposed on slow waves and occasional short runs of abnormally slow waves; e. well organized rapid activity of 50 μV or more, or a predominantly slow pattern of 75 μV or more, or a combination in varied form. They found that 70 per cent of the normals and 40 per cent of the schizophrenics had patterns of the "a" or "b" type. Only 22 per cent of the normals and 34 per cent of the schizophrenics had patterns of type "c". The remaining

7 per cent of normals had patterns of type "d", whereas 25 per cent of the schizophrenics had patterns of this type and 3 per cent had patterns of type "e". No clinically adjudged normals had patterns of type "e". A definite dissociation of normals from schizophrenics is seen as to the relative preponderance of individuals in patterns of the normal and abnormal types. In classifying the schizophrenics as to simple deterioration, catatonic-hebephrenia, paranoid, or other heterogenous groups, it was found that the 47 per cent of the 500 cases with patterns of the "a" type were simple deteriorations, whereas the catatonic-hebephrenics were predominantly of pattern "b", the paranoids in pattern "c", and the heterogenous group was in patterns "d" and "e". Manic-depressives were similarly distributed as schizophrenics except that fewer had patterns of the "c" type and more had patterns of the "d" type. Epileptics showed more abnormal and less normal tracings than any other group. There was no relationship found in EEG tracings of schizophrenics with similar histories, nor did similar cases have similar EEG patterns. They feel that the EEG may be a valuable measure of the basic biological forces acting in schizophrenic disorders, but differ with earlier investigators as to any similarity of the EEG records found in cases of epilepsy and major psychoses.

With such poor consistency in findings, the EEG is certainly of questionable value diagnostically in the major psychoses. Perhaps the Grass frequency analyzer already referred to (20 and 43) may make for a more uniform basis of classification. It is in such groups as this that it may be of greatest value.

Grinker and Serota (36) claim to be able to demonstrate differences in normals and major psychotics in the EEG records taken during action or conditions of stress. They argue that it is in such conditions that the schizophrenic breaks down and reveals his psychological instability. They claim that three provocative tests have revealed real differences in EEG reactions of the two groups. 1. Cold--normals show a definite response in both hypothalamic and cortical leads. The schizophrenic showed no response to cold or hyperthermia in either lead. 2. Intramuscular injections of adrenalin produced prompt and striking electrical and subjective effects in the normal. Intravenous injections were necessary to produce changes in schizophrenics. 3. Electrical stimulation through the hypothalamic lead produced profound EEG changes in the schizophrenic and none in the normal. Other provocative tests as, verbal stimulation and intravenous sodium amytal, produced less pronounced differences.

Drugs and Shock Therapy.--The EEG has been of value in investigating the value of and elucidating the mechanism of shock therapy. Hoagland et al (131) in 1937 found that during Insulin shock therapy there was a progressive drop in alpha frequency with the fall in blood sugar. The normal alpha frequency returned along a smooth curve as intravenous glucose was given at any point. The alpha frequency is shown to be directly proportional to the rate of sugar metabolism. Lemere (132) a year later found that the alpha frequency of a group of schizophrenics was strengthened in the initial excitatory stage, and was replaced by 1 to 5 per second delta waves during coma, indicating depressed cortical activity. A rebound strengthening of the alpha waves followed by 1 to 3 hours the termination of the hypoglycemia. Although clinical improvement was maintained in 9 of the 15 cases, the alpha frequency reverted to its pretreatment level in 1 to 4 weeks. The alpha frequency had been lower than normal in 12 of the 15 cases before treatment, and 6 of the 15 had 1 to 5 per second delta waves present before treatment. These authors also found that small non-convulsive doses of Metrazol enhanced the alpha activity and a temporary enhancement was also found during the post-convulsive depression. Later the alpha frequency returned to its pretreatment level. In summary, he found the alpha rhythm improved by intravenous sodium amytal, Metrazol, Insulin hypoglycemia, CO_2 inhalation, and emotional stimulation. They conclude that a weak alpha rhythm seems an inborn neurophysiological characteristic of schizophrenia.

Davis (133) made some interesting observations on a 33 year old schizophrenic during the course of 24 Metrazol treatments of which 20 treatments produced convulsions. In the 4 attempts in which the usual or increased dosage failed to produce a convulsion, large positive waves persisted in the EEG until the next treatment ended in a convulsion. During these periods the patient was in a confused state and failed to respond as well as otherwise. No confusion followed a successful convulsion. During the course of treatment abnormalities which become more marked with successive treatment appeared. Clinically his catatonic psychomotor manifestations, negativism, hallucinations, paranoid system, and insight and judgment relative to his condition remained the same. The patient regressed during the latter part of his treatment. Five months later Insulin therapy improved him somewhat. The EEG remained abnormal. Six other patients showed the same effect of prolonged Metrazol treatment. The author concludes that the EEG precedes symptoms and indicates the progress and ultimate prognosis of the patient.

Davis's observations are corroborated by Finley and Leska (134). They found that of 9 cases treated, in the 4 of the 9 in whom 6 or less injections were given, except in 1 of these where 11 injections were given, there were no temporary or permanent changes in the EEG except during injection. In 3 cases given 9 to 14 injections, improvement in the EEG was seen for a few days. In 2 cases given 18 to 20 injections permanently abnormal patterns in the EEG developed. They suggest, therefore, that the number of injections of Metrazol be limited to 10 or under.

Changes in EEG During Shock Treatment.--Various authors have reported changes seen during shock treatment. Of the more recent, Goodwin et al (135) in 1940 reported two main stages in the rabbit with Insulin and Metrazol. 1. Occasional spikes appear in the record in the preconvulsive stage. 2. During coma, the record consists predominantly of slow waves. The thalamus, midbrain and cerebellum show abnormal waves during Metrazol shock. Metrazol applied locally produced similar changes. They conclude that Insulin produces its changes by depriving the brain of metabolic requirements. Metrazol produces an activity of the neurons which exceed the immediate possibilities of fulfillment. Thus both produce an eventual neuronal depression characterized by slow waves.

Except for the latent periods of response, Finley and Leska (134) find the same stages present in humans where the stages are somewhat longer. An intermediate stage between "1" and "2" above is described as characterized by the appearance of high voltage spikes of 15 to 20 per second gradually dropping in frequency and becoming synchronous in groups of 2 or 3 with the clonic jerks. A final stage 4 is described during which slow random waves gradually decreasing in amplitude and increasing in frequency are replaced by the preconvulsive record. This is the recovery stage from the convulsion.

Electrically induced convulsions were studied in the rabbit by Löwenback and Lyman (136). Essentially the same stages were seen here as those described above. Whereas in Metrazol a latent period and a period of variable length and severity of convulsions are seen, in electrically induced convulsions the convulsions begin immediately and can be made shorter and milder than with Metrazol. The author speculates as to the value of better controlled convulsions, and, remembering the appearance of abnormal waves with too numerous Metrazol convulsions as shown above, his arguments are certainly worth considering. Such studies as these are probably of the greatest practical importance as compared to the other studies relative to the major psychoses.

Value of EEG as to Functional Activity of the Nervous System.

A lengthy discussion of the value of EEG studies as to our knowledge of the functional activity of the nervous system is not indicated in a presentation of a subject primarily of a clinical nature. A periodic perusal of such studies should certainly be of value to anyone interested in the development of his understanding of the EEG. The yearly reviews such as the one by Jasper (40) is very enlightening. Visual, auditory, vestibular, and tactile mechanisms are all related to the final EEG recorded from the scalp. The interrelation of all parts of the brain, the effects of metabolic changes, drug, and environmental changes can be better studied experimentally. Progress made in the various phases of clinical applications are reviewed and interpreted.

Briefly, an integral activity of neuronal units is observed by which rhythms or waves will wax and wan larger and slower or smaller and more rapidly according to the synchrony of the cells. Disintegration into irregular, rapid, feeble waves occur as synchrony is destroyed. A "pacemaker" enhances synchrony. Afferent impulses and depression in various forms may enhance or disrupt it. The recorded waves seem to be an envelope of many single units, the units being discharged by a trip of any one of them. Their profile, frequency, and temporal relationships depend on the interrelationships of the individual units and the conditions of their environment. Rate of metabolism seems to be intimately related. The unification of the beats of many units must depend on the propagation of nerve impulses or on electric fields and currents.

Factors favoring unison, as already suggested before, are high temperature, Ca^{++}, low Na^{+} and K^{+}, diminution of afferent impulses (recall the effect on the alpha rhythm of opening the eyes, etc.), increased polarization, and drugs such as nicotine and caffeine. A strictly electrical mechanism can control nerve cell beats and cause a spreading activation as shown when two cortical units isolated as to neuronal connections are placed next to each other. One producing large spreading waves, due to locally applied caffeine, will activate the adjoining non-caffeinized to a synchronous state (83). The ultimate enlightenment by such studies promises great progress in our future understanding of the functional activity of the nervous system.

If this prediction seems carelessly chosen, we have only to remember the progress made since 1934 when

Bishop (137) predicted the nature of some of the studies since undertaken. At that time he discussed some of the possible contributions to come from neurophysiological investigation especially to our ultimate understanding of psychiatrical problems.

"Two types of mental derangement may then be recognized, or rather two causes of abnormal function: one due to specific anatomical or physiological defect, as from accident, intoxication, drugs, or disease, and the other due to 'purely mental' causes, such as suggestion, anxiety, or repression. * * * * In the second type of case, a solution of the problem involves knowing what is right with the patient; i.e., it involves a differentiation between two manners of functioning both physiologically normal, but one of them socially or personally undesirable. * * * * If, as seems possible, mental derangement can result from an alteration of the functional relationships of normally active and healthy neurones, the fundamental approach to a study of this derangement must involve a study of these functional relationships, and this study lies very properly within the province of neurophysiology. * * * * The more complicated functions of the nervous system, including mental activity, differ from the simpler in the degree of specificity of action. Mental activity differs from reflex activity--that is to say--in the ease with which it can be altered and in the variety of actions (not to say choice) of which it is capable. In physiological terms, this implies that the pathways through networks of neurones which a nervous impulse may take are more complicated in the higher centers, and the conditions that determine which of possible pathways shall be traversed are still more complex. It may mean further that the forces required to direct such impulses are actually less in the higher centers, and that slighter disturbances will send such impulses astray, with a more consequent derangement of mental activity. * * * * In acquiring the ability to respond to these sensory impressions as elaborately as we do, the nervous system has obviously succeeded at the expense of specificity of action; in physiological terms, this means that neurones have become less particular about their associates. In a complex society of neurones the results of such individual departures from the paths of conventionality might be disastrous. What is more to the point here is that they might also be capable of physiological investigation. * * * * We have discussed two general fields in which the writer believes research in neurophysiology to have a direct interest for psychiatry: (1) a comparative study of the neurone as such, at various levels of function, corresponding to the current study of the various types of nerve-fiber, and (2) a study of the electrical responses of neuronal groups or patterns as normally functioning in the various structures of the intact brain." It is the latter of the two approaches which concerns the EEG, and the potentiality of which has only been touched.

Evaluation of the Applicability of the EEG.

There is probably no real value in attempting to ascribe a total accuracy or usefulness to the EEG. Bennett and Cash (117) have estimated it to be from 85 to 90 per cent accurate. Hyland and Goodwin (138) caution against too great reliance on the EEG. They feel it is useful only where the cerebral cortex is in some intermediate stage of degeneration.

Ultimately the value and applicability of the EEG must be considered relative to specific problems and conditions. At the present it is certainly of a considerably greater value applied to localization of brain lesions than as a diagnostic procedure applied to psychotic conditions.

Its value in modern military selection of individuals suitable as pilots has already been referred to (19 and 38). It seems to be of proved value already if the statement that Great Britain is using it routinely in its selection of pilots is correct. Five hundred students were tested at Pensacola, Florida, as early as the summer of 1940, and preparations were being made then to test students at other large training centers.

Lemere (139) has referred to the use of the EEG to differentiate between true and hysterical or malingered blindness. The importance of this application to military and industrial problems, especially compensation claims, needs no further comment.

Whether the EEG will be applied to the selection of individuals suitable for marriage as suggested (121 and 122) is a problem for the future. The problem is one of social sanction of control of eugenics rather than a question of value. Perhaps in a future more settled social state such problems will be given thorough consideration.

Further discussion as to the total worth of this procedure is hardly indicated in a study of such a limited scope as this. Such discussions are more sensibly allocated to those with more experience and understanding. Accordingly, it is felt that a concise and conservative summary based merely on the total opinion of investigators is indicated.

Summary

1. A reliable, accurate method of recording variations in brain potentials has been developed.

2. Normal variations of activity and electrical activity of the brain under constant conditions have been established.

3. The EEG is a measure of intelligence only at extreme levels.

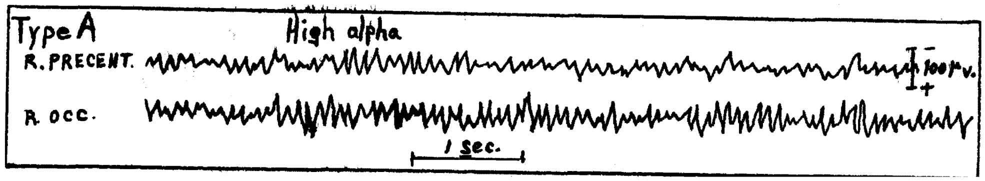
4. The functional activity of the human brain has been clarified somewhat, and the action of certain drugs has been more closely studied by means of the EEG.

5. The localization of brain lesions of various types can often be determined by the EEG.

6. The epilepsies have acquired a new meaning, and in these conditions the effectiveness of medication can be closely followed by means of the EEG.

7. The EEG is of little diagnostic value in non-organic psychoses. Some insight as to their nature has been gained and suggestions as to limitations of shock therapy have been obtained.

8. Indications are that the EEG may be of value in the selection of the most suitable individual for activities requiring considerable skill and mental control.



Normal EEG patterns. The two most common types taken under standard conditions. Unfiltered monopolar recording. MF A

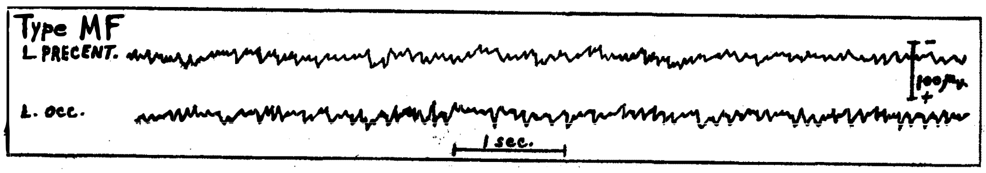


Fig. 4.--from Davis (13).

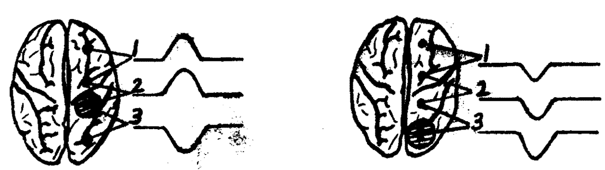


Fig. 6.--Four electrodes are connected to three amplifying and recording systems in the same manner in each case. An electrical discharge of constant sign under each electrode causes a deflection of the recording pen in the direction shown. It is therefore possible, by studying the phase relationships of the waves recorded, to determine under which electrode the disturbance has occurred.--from Williams and Gibbs (88).

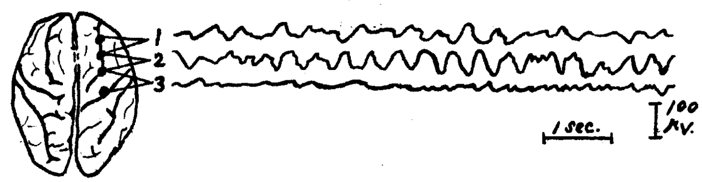


Fig. 7.--High voltage 3 per second "subclinical" seizure waves with a focus near the second electrode. They do not affect the third record, which shows a 10 per second frequency. The electrodes are less than 2 cm. apart over an area of cortical damage.--from Williams & Gibbs (88).

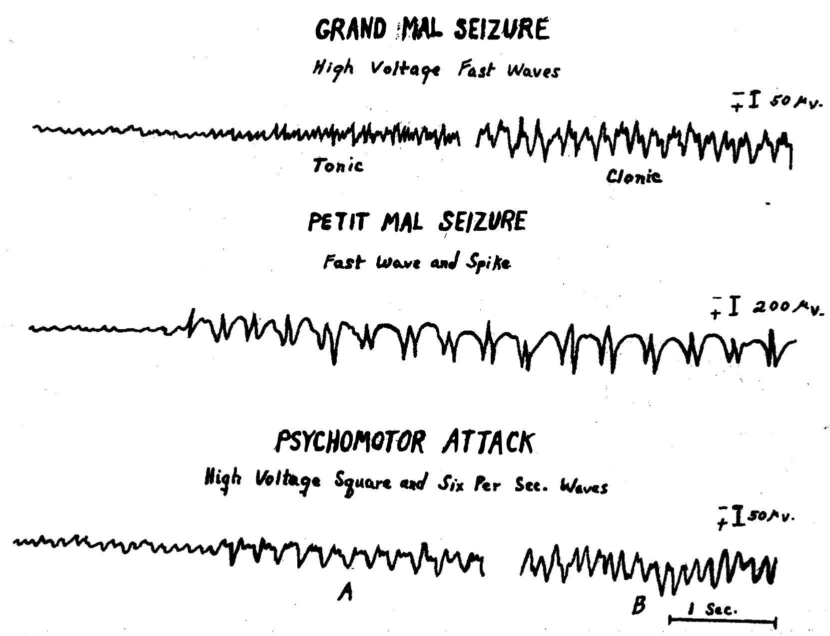


Fig. 8.--Types of abnormal activity encountered in epilepsy and the variety of seizure with which each is associated. Grand Mal Seizure: Typical pattern, with electrodes on the left frontal region and ear. Petit Mal Seizure: Typical pattern, with electrodes on the left frontal region and ear. Psychomotor Attack: Typical pattern, with electrodes on the left occipital region and ear. A represents the onset; B, a later phase. These abnormal patterns can appear without, as well as with, clinically obvious seizures.--from Gibbs et al (110).

Bibliography

1. Best, C. H. & Taylor, N. B. The physiological basis of medical practice. The Williams & Wilkins Co., Baltimore, 1939.

2. Brazier, M. A. B. The impedance angle and thyroid disease. Endocrinol., 20:621-627, 1936.

3. Horton, J. W. & Hertz, S. The significance of electrical impedance measurements on the human body. Endocrinol., 20:831-838, 1936.

4. Schrumpf, A. Beitrage zur beleuchtung des klinisches wertes der impedanzmessung. Zeitschr. f. Klin. Med., 133:139-167, 1938.

5. Adrian, E. D. The mechanism of nerve action. Uni. of Penn. Press, Philadelphia, 1932.

6. Howell, W. H. A textbook of physiology. W. B. Saunders Co., Philadelphia, 1915.

7. Canton, R. Electrical currents of the brain. Brit. Med. Jour., 2:278, 1875.

8. Neminiski, W. W. Ein versuch der registrierung des elecktrischen gehirnerscheinungen. Zentralb. f. Physiol., 27:951-960, 1913.

9. Berger, H. Electroencephalographic reactions in man. Arch. f. Psychiat., 87:527-570, 1929.

10. Erlanger, J. & Gasser, H. S. Electrical signs of nervous activity. Uni. of Penn Press, Philadelphia, 1937.

11. Toman, J. Flicker potentials and the alpha rhythm in man. J. Neurophysiol., 4:51-61, 1941.

12. Walter, W. G. The location of cerebral tumors by electroencephalography. Lancet, 2:305-308, 1936.

13. Davis, P. A. Technique and evaluation of the electroencephalogram. J. Neurophysiol., 4:92-114, 1941.

14. Woltman, H. W. & Craig, W. McK. Altered behavior caused by removable tumor of the brain: site suggested by electroencephalogram. Proc. Staff. Meet., Mayo Clin., 16:49-51, 1941.

15. Foley, A. L. College Physics. P. Blakiston's Son & Co., Inc., Philadelphia, 1937.

16. Gasser, H. S. & Erlanger, J. S. A study of the action current of nerves with the cathode ray oscillograph. Am. J. Physiol., 62:496-521, 1922.

17. Grass, A. M. & Gibbs, F. A. The Fourier transform of the electroencephalogram. J. Neurophysiol., 1:521-526, 1938.

18. Rahm, W. E. Electroencephalography. Electronics, 12:11-13, 1939.

19. Minderman, E. Pilots tested by brain wave analysis. Med. Rec., 153:292, 1941.

20. Gibbs, F. A. Cortical frequency spectra of schizophrenic, epileptic, and normal individual. Tr. A. Neurol. A., 65:141-144, 1939.

21. Adrian, E. D. & Matthews, B. H. C. The interpretation of potential waves in the cortex. J. of Physiol., 81:440-471, 1934.

22. Scarf, J. E. & Rahm, W. E., Jr. The human electrocorticogram. J. Neurophysiol., 5:418-426, 1941.

23. Adrian, E. D. & Matthews, B. H. C. The Berger rhythm: potential changes from the occipital lobes in man. Brain, 57:355, 1934.

24. Davis, H., Davis, P. A., Loomis, A. L., Harvey, E. N., Hobart, G. Changes in human brain potentials during the onset of sleep. Science, 86:448-450, 1937.

25. Berger, H. Electroencephalography. Med. Welt., 4:911-913, 1930.

26. Berger, H. Über das elektrenkephalogramm des menschens. Arch. f. Psychiat., 94:16-60, 1931.

27. Berger, H. Electroencephalography in man. Arch. f. Psychiat., 97:6-26, 1932.

28. Berger, H. Electroencephalography in human beings. Arch. f. Psychiat., 98:231-254, 1932.

29. Berger, H. Electroencephalography in man. Arch f. Psychiat., 101:452-569, 1935.

30. Berger, H. Human electroencephalogram. Arch. f. Psychiat., 106:577-588, 1937.

31. Cervello, F. Electrical activity. Arch. Opth., 14:992-1019, 1935.

32. Jasper, H. H. & Andrews, H. L. Electroencephalography differentiation of occipital and precentral regions in man. Arch. of Neurol. & Psych., 39:96-113, 1941.

33. Rubin, M. A. The distribution of the alpha rhythms over the cerebral cortex of normal man. J. Neurophysiol., 1:313-323, 1938.

34. Gibbs, F., Lennox, W., & Gibbs, E. Electroencephalogram in diagnosis and localization of epileptic seizures. Arch. of Neurol. & Psych., 36:1225-1235, 1936.

35. Spiegel, E. A. The electrothalamogram. Tr. A. Neurol. A., 62:53-55, 1936.

36. Grinker, R. R. & Serota, H. M. Electroencephalographic studies of corticohypothalamic relations in schizophrenia. Am. J. of Psychiat., 98:385-392, 1941.

37. Massermann, J. H. Is the hypothalamus a center of emotion? Psychosom. Med., 3:3-25, 1941.

38. Serota, H. M. Applicability of the electroencephalogram (EEG) to military medical problems. Mil. Surgeon, 87:537-539, 1940.

39. Loomis, A. L., Harvey, E. N., Hobart, G. Brain potentials during hypnosis. Science, 83:239-241, 1936.

40. Jasper, H. H. Electrical activity of the brain. Am. Rev. Physiol., 3:377-398, 1941.

41. Lemere, F. The significance of individual differences in the Berger rhythm. Brain, 59:366-375, 1936.

42. (Editorial Comment). Indexing electroencephalographic records. Am. J. Psychiat., 96:979-981, 1941.

43. Gibbs, F. A. Spectra from eight cortical areas of normal adults, epileptic, parents of epileptics and schizophrenic individuals. Tr. A. Neurol. A., 66: 211-212, 1940.

44. Travis, L. E. Do brain waves have individuality? Science, 84:532-533, 1936.

45. Travis, L. E. & Gottlober, A. How constant are an individual's brain potentials from day to day? Science, 85:223-224, 1937.

46. Jasper, H. H. Cortical excitatory state and variability in human brain rhythms. Science, 83:259-260, 1936.

47. Lindsley, D. B. Brain potentials in children and adults. Science, 84:354, 1936.

48. Smith, J. R. The electroencephalogram in infancy and childhood. Proc. Soc. Exper. Biol. & Med., 36:384-386, 1937.

49. Lindsley, D. B. & Rubenstein, B. B. Relationship between brain potentials and some other physiological variables. Proc. Soc. Exper. Biol. & Med., 35: 558-563, 1936.

50. Rubin, M. A., Cohen, L. H., & Hoagland, H. The effect of artificially raised metabolic rate on the electroencephalogram of schizophrenic patients. Endocrinol., 21:536-540, 1937.

51. Ross, D. A. & Schwab, R. S. The cortical alpha rhythm in thyroid disorders. Endocrinol., 25:75-79, 1939.

52. Hoagland, H., Rubin, M. A., & Cameron, D. E. Brain wave frequencies and cellular metabolism. Effects of Dinitrophenol. J. Neurophysiol., 2:170-172, 1939.

53. Takaji, E. & Gerard, R. W. Avitaminosis B_1 and pigeon brain potentials. Proc. Soc. Exper. Biol. & Med., 41:653-655, 1939.

54. Rubin, M. A. The electroencephalogram of schizophrenic patients during administration of vitamin B_1. Proc. Soc. Exper. Biol. & Med., 42:440-441, 1939.

55. Kreezer, G. Electric potentials of the brain in certain types of mental deficiency. Arch. of Neurol. & Psych., 36:1206-1213, 1936.

56. Kreezer, G. Intelligence level and occipital alpha rhythm in the Mongolian type of mental deficiency. Am. J. Psychiat., 52:503-532, 1939.

57. Raney, E. T. Brain potentials and lateral dominance in identical twins. J. Exp. Psychol., 24:21-38, 1938.

58. Lindsley, D. B. Bilateral differences in brain potentials from the two cerebral hemispheres in relation to laterality and stuttering. J. Exp. Psychol., 26: 211-225, 1940.

59. Travis, L. E. & Knott, J. R. Brain potential studies of perseveration: perseveration time to visually presented words. J. Exp. Psychol., 21:302-326, 1937.

60. Forbes, T. W. & Andrews, H. L. Independent control of alpha rhythm and "psychogalvanic" response. Science, 86:474-476, 1937.

61. Lindsley, D. B. & Sassman, W. H. Autonomic activity and brain potentials associated with "voluntary" control of the pilomotors (MM. Arrectores Pilorum). J. Neurophysiol., 1:342-349, 1938.

62. Gottlober, A. B. The relationship between brain potentials and personality. J. Exp. Psychol., 22: 67-74, 1938.

63. Davis, H. & Davis, P. A. Action potentials of the brain. Arch. of Neurol. & Psych., 36:1214-1224, 1936.

64. Hoagland, H. Temperature characteristics of the "Berger Rhythmn" in man. Science, 83:84-85, 1936.

65. Hoagland, H. Electrical brain waves and temperature. Science, 84:139-140, 1936.

66. Hoagland, H. Pacemakers of human brain waves in normals and general paretics. Am. J. Physiol., 116:604-615, 1936.

67. Libet, B. & Gerard, R. W. Control of the potential rhythmn of the isolated frog brain. J. Neurophysiol., 2:153-169, 1939.

68. Brill, N. Q. & Seidemann, H. The electroencephalogram of normal children. Am. J. Psychiat., 98:250-256, 1941.

69. Gerard, R. W. Factors influencing brain potentials. Tr. A. Neurol. A., 62:55-60, 1936.

70. Gibbs, F. A., Williams, D., & Gibbs, E. L. Modification of the cortical frequency spectrum by changes in CO_2, blood sugar, and O_2. J. Neurophysiol., 3:49-58, 1940.

71. Hoffman, P. & Stronghold, H. Ein beitrag zur frage der ozillationsfrequenz der willkürlichen innervation. Z. Biol., 85:599-603, 1927.

72. Jasper, H. H. & Andrews, H. L. Brain potentials and voluntary muscle activity of man. J. Neurophysiol., 1:87-100, 1938.

73. Schwab, R. S. & Cobb, S. Simultaneous electromyograms and electroencephalograms in paralysis agitans. J. Neurophysiol., 2:36-41, 1939.

74. Davis, H., Davis, P. A., Loomis, A. L., Harvey, E. N., & Hobart, G. Human brain potentials during the onset of sleep. J. Neurophysiol., 1:24-38, 1938.

75. Loomis, A. L., Harvey, E. N., & Hobart, G. A. Distribution of disturbance patterns in the human electroencephalogram with special reference to sleep. J. Neurophysiol., 1:413-430, 1938.

76. Thomson, M. M., Forbes, T. W., & Bolles, M. M. Brain potential rhythmns in a case showing self-induced apparent trance states. Am. J. Psychiat., 93:1313-1314, 1937.

77. Beecher, H. K., McDonough, F. K., & Forbes, A. Effects of blood pressure changes on cortical potentials during anesthesia. J. Neurophysiol., 1:324-331, 1938.

78. Rubin, M. A. & Freeman, H. Brain potential changes in man during Cyclopropane anesthesia. J. Neurophysiol., 3:33-42, 1940.

79. Rubin, M. A. & Cohen, L. H. The electroencephalogram in bromide intoxication. Arch. Neurol. & Psych., 40:922-927, 1938.

80. Fowler, O. D. Neurophysiological and psychological changes induced by certain drugs: electrocortical changes. J. Exp. Psychol., 28:37-52, 1941.

81. Andrews, H. L. Brain potentials and morphine addiction. Psychosom. Med., 3:399-409, 1941.

82. Chweitzer, A., Geblewiez, E., & Liberson, W. Action de la mescaline sur les ondes alpha (rythme de Berger) chez l'homme. Compt. Rend. Soc. de Biol., 124:1296-1299, 1937.

83. Gerard, R. W. & Libet, B. The control of normal and "convulsive" brain potentials. Am. J. Psychiat., 96:1125-1152, 1941.

84. Dusser de Barenne, J. G. & McCullock, W. S. Some effects of local strychninization on action potentials of the cerebral cortex of the monkey. Tr. A. Neurol. A., 62:171, 1936.

85. Miller, F. R., Stauraky, G. W., & Woonton, G. A. Effects of eserine, acetylcholine, and atropine on the electrocorticogram. J. Neurophysiol., 3:131-138, 1940.

86. Wechsler, I. S. A textbook of clinical neurology. W. B. Saunders Co., Philadelphia, 1939.

87. Case, T. J. & Bucy, P. C. Localization of cerebral lesions by electroencephalography. J. Neurophysiol., 1:245-261, 1938.

88. Williams, D. & Gibbs, F. A. Electroencephalography in clinical neurology. Arch. of Neurol. & Psych., 41:519-534, 1939.

89. Jasper, H. H. & Hawke, W. A. Electroencephalographic localization of seizure waves in epilepsy. Arch. of Neurol. & Psych., 39:885-901, 1938.

90. Holland, C. G. Changes caused by cerebellar neoplasm in the electroencephalogram. Virginia M. Jour., 68:459-462, 1941.

91. Penfield, W. & Jasper, H. Electroencephalography in focal epilepsy. Tr. A. Neurol. A., 66:209-211, 1940.

92. Sachs, E., Schwarz, H. G., & Kerr, A. S. Electrical activity of the exposed human brain. Tr. A. Neurol. A., 65:14-17, 1939.

93. Lemere, F. Berger alpha rhythmn in organic lesions of the brain. Brain, 60:118-125, 1937.

94. Smith, J. R., Walter, C. W. P., Laidlow, R. W., & Casamajor, L. Posterior fossa neoplasms in children: an electroencephalographic study. Tr. A. Neurol. A., 65:149-152, 1939.

95. Weatherby, H. Progressive hepatolenticular degeneration with electroencephalograms and pneumo-encephalograms. Am. J. Roentgenol., 45:714-717, 1941.

96. Hock, P. & Kubis, J. Electroencephalographic studies in organic psychoses. Am. J. Psychiat., 98:404-408, 1941.

97. Glaser, M. A. & Sjaardema, H. Electro-encephalographic diagnosis of extradural and subdural hemorrages. Proc. Soc. Exper. Biol. & Med., 47:138-140, 1941.

98. Yeager, C. L. & Walsh, M. N. Changes in the electroencephalogram from ligation of the carotid artery. J. A. M. A., 114:1625-1627, 1940.

99. Rubin, M. A. Electroencephalography in the psychoses. Am. J. Psychiat., 96:961-975, 1941.

100. Guillan, G., Bertrand, I., & Godet-Guillain, J. Modifications de l'electroencephalogramme au cours de la sclerose laterale amyotrophique. Compt. Rend. Soc. de Biol., 134:462-464, 1940.

101. Williams, D. The abnormal cortical potentials associated with high intracranial pressure. Brain, 62:321-334, 1939.

102. Davis, P. A. Electroencephalographic studies on three cases of frontal lobotomy. Psychosom. Med., 3:38-50, 1941.

103. Goldensohn, L. N., Marmor, J., & Meyer, B. C. Pneumo-encephalographic and electro-encephalographic localization of an eleptogenic focus. J. A. M. A., 114:1345-1346, 1940.

104. Gibbs, F. A., Gibbs, E. L., & Lennox, W. G. Cerebral dysrythmias of epilepsy. Arch. of Neurol. & Psych., 39:298-314, 1938.

105. Casamajor, L., Smith, J. R., Constable, K., & Walter, C. W. P. The electroencephalogram of children with focal convulsive seizures. Arch. of Neurol. & Psych., 45:834-847, 1941.

106. Gibbs, F. A., Gibbs, E. L., & Lennox, W. G. Epilepsy: a paroxysmal cerebral dysrythmia. Brain, 60:377-388, 1937.

107. Jasper, H. & Kershman, J. Electroencephalographic classification of the epilepsies. Arch. of Neurol. & Psych., 45:903-943, 1941.

108. Gibbs, F. A., Lennox, W. G., & Gibbs, E. L. The electro-encephalogram in diagnosis and in localization of epileptic seizures. Arch. of Neurol. & Psych., 36:1225-1235, 1936.

109. Cobb, S., Sargent, W. W., & Schwab, R. S. Simultaneous respiration and electroencephalographic recording in petit mal. Tr. A. Neurol. A., 65: 137-141, 1939.

110. Gibbs, F. A., Gibbs, E. L., & Lennox, W. G. Influence of the blood sugar level on the wave and spike formation in petit mal epilepsy. Arch. of Neurol. & Psych., 41:1111-1116, 1939.

111. Lennox, W. G., Gibbs, F. A., & Gibbs, E. L. Effect on the electro-encephalogram of drugs and conditions which influence seizures. Arch. of Neurol. & Psych., 36:1236-1258, 1936.

112. Grinker, R. R., Serota, H., & Stein, S. I. Myoclonic epilepsy. Arch. of Neurol. & Psych., 40:968-980, 1938.

113. Schwab, R. S. The influence of visual and auditory stimuli on the electroencephalographic tracing of petit mal. Am. J. Psychiat., 97:1301-1316, 1941.

114. Strauss, H. Jacksonian seizures of reflex origin. Arch. of Neurol. & Psych., 44:140-152, 1941.

115. Jasper, H. H., Kershman, J., & Elvidge, A. Electroencephalographic studies of injury of the head. Arch. of Neurol. & Psych., 44:328-380, 1940.

116. Usher, S. J. & Jasper, H. H. The etiology of Sydenham's chorea. Electrographic studies. Canad. M. A. J., 44:365-371, 1941.

117. Bennett, A. E. & Cash, P. T. The present status of electro-encephalography and some of its practical applications. Nebraska M. J., 25:435-440, 1940.

118. Jasper, H. H., Soloman, P., & Bradley, C. Electroencephalographic analysis of behavior problem children. Am. J. Psychiat., 95:641-658, 1938.

119. Cutts, K. K. & Jasper, H. H. Effect of benzidrine sulfate and phenobarbital on behavior problem children with abnormal electroencephalograms. Arch. of Neurol. & Psych., 41:1138-1145, 1939.

120. Lindsley, D. B. & Cutts, K. K. Electroencephalograms of "constitutionally inferior" and behavior problem children. Arch. of Neurol. & Psych., 44: 1199-1212, 1940.

121. Lennox, W. G., Gibbs, E. L., & Gibbs, F. A. The inheritance of epilepsy as revealed by the electroencephalograph. J. A. M. A., 113:1002-1003, 1939.

122. Lennox, W. G., Gibbs, E. L., & Gibbs, F. A. Inheritance of cerebral dysrythmia and epilepsy. Arch. of Neurol. & Psych., 44:1155-1183, 1941.

123. Robinson, L. J. Cerebral dysrythmias in relatives of epileptic persons. Arch. of Neurol. & Psych., 44:1109-1111, 1941.

124. Strauss, H., Rahm, W. E., & Barrera, S. E. Electroencephalographic studies of relatives of epileptics. Proc. Soc. Exper. Biol. & Med., 42:207-212, 1939.

125. Kreezer, G. Electrical potentials in certain types of mental deficiency. Arch. of Neurol. & Psych., 36:1206-1213, 1936.

126. Knox, H. F. & Campbell, C. M. Electroencephalography in schizophrenia. Am. J. Psychiat., 98:374-381, 1941.

127. Gibbs, F. A., Gibbs, E. L., & Lennox, W. G. The likeness of the cortical dysrhythmias of schizophrenia and psychomotor epilepsy. Am. J. Psychiat., 95:255-269, 1938.

128. Davis, P. A. & Davis, H. The electroencephalograms of psychotic patients. Am. J. Psychiat., 95:1007-1025, 1939.

129. Davis, P. A. Evaluation of electroencephalograms of schizophrenic patients. Am. J. Psychiat., 96:851-860, 1940.

130. Davis, P. A. Electroencephalograms of manic-depressive patients. Am. J. Psychiat., 98:430-433, 1941.

131. Hoagland, H., Rubin, M. A., & Cameron, D. E. The electroencephalograms of schizophrenics during insulin hypoglycemia and recovery. Am. J. Physiol., 120:559-570, 1937.

132. Lemere, F. Effects on electroencephalogram of various agents used in treating schizophrenia. J. Neurophysiol., 1:590-595, 1938.

133. Davis, P. A. & Sulzback, W. Changes in the electroencephalogram during Metrazol therapy. Tr. A. Neurol. A., 65:144-149, 1939.

134. Finley, K. H. & Lesko, J. M. EEG studies of nine cases with major psychoses receiving Metrazol. Am. J. Psychiat., 98:185-191, 1941.

135. Goodwin, J. E., Kerr, W. K., & Lawson, F. L. Bioelectric responses in Metrazol and insulin shock. Am. J. Psychiat., 96:1389-1405, 1940.

136. Löwenbach, H. & Lyman, R. S. The electroencephalogram in electrically induced convulsions in rabbits. J. Neurol. & Psych., 3:336-342, 1941.

137. Bishop, G. H. Electrophysiology of the brain from--The problem of mental disorder. McGraw--Hill Book Company, Inc., New York, 1934.

138. Hyland, H. H., Goodwin, J. E., & Hall, G. E. Clinical applications of the electroencephalograph. Canad. M. J., 41:239-246, 1939.

139. Lemere, F. Electroencephalography as a method of distinguishing true from false blindness. J. A. M. A., 118:884-885, 1942.