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Part A. Cellular Processes and Brain Potentials, 1973
Part B. Electroencephalography and Human Brain Potentials, 1974
Part C. Receptor and Effector Processes, 1974

Bioelectric Recording Techniques

PART B

Electroencephalography and Human Brain Potentials

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General Preface

The major approaches used to characterize the organization and functions of the brain can be grouped into four categories of techniques—electrophysiology, anatomy, chemistry, and behavior. All these approaches to the study of the brain and its functions will be treated in this series on *Methods in Physiological Psychology*. The series begins with the present treatment of bioelectric recording techniques in three volumes (Parts A, B, and C). Much that has been learned about the brain is due to the development of bioelectric recording techniques. Perhaps more important, the basic processes among neurons that underlie all aspects of brain function and behavior, from simple reflexes to relativity theory, are fundamentally bioelectric in nature—they result in potential and current changes across membranes.

Bioelectric recording techniques currently offer one great advantage over anatomical and chemical procedures—they minimize the "uncertainty" principle. An electrode placed on the surface of the scalp can record human brain activity with minimum perturbation of the system. Activity of the heart can be recorded by placing wires on the arms; the autonomic signs of brain activity and behavior such as the galvanic skin response can similarly be measured by peripheral electrodes. However, we cannot infer central events from peripheral measures without basic knowledge of the cellular processes underlying the generation of bioelectric activity. Part A treats the analytic techniques used to study the basic bioelectric phenomena of neural tissue in animal preparations. Part B deals with electroencephalography and peripheral recording of brain events in man. Part C treats receptor and effector processes.

Brain electrical activity was first recorded by Caton in 1875, and the human EEG was described by Berger in 1929. However, the major developments in bioelectric techniques have come in the past 30 years. Recording techniques and methods of analysis have grown almost exponentially over this period. There is no up-to-date review of the methods of bioelectric

recording; hence these three volumes. All of the articles here are original contributions written by experts. Each author is a recognized authority in his or her area, who is actively engaged in the use of the techniques described.

The best and perhaps only way to understand properly a method or technique is to use it; the next best way is for an expert to describe it. The authors of these chapters have succeeded very well in presenting the techniques of bioelectric recording clearly and in sufficient practical detail to be of immediate use. Moreover, their chapters go well beyond details of technique and provide an analysis of experimental and theoretical issues as well. In our opinion, these volumes provide an outstanding synthesis of what we know and where we stand today in our understanding of the bioelectric aspects of brain function and behavior. The authors of these chapters have done their job very well indeed.

We express our very sincere gratitude to the many contributors who have written this work. We also acknowledge the invaluable editorial assistance of Nancy M. Kyle, and the help of the UCLA Brain Information Service, and Information Services, Pacific Southwest Regional Medical Library Service for providing the bibliographies of technique articles listed at the end of each volume.

RICHARD F. THOMPSON

Preface to Part B

The electroencephalogram (EEG) and human brain potentials are treated in this volume. Modern understanding of brain function really began with EEG recording in animals and man. The measures of human brain activity described in this volume are peripheral in the sense that electrical activity is recorded from the surface of the scalp rather than from the brain itself. They are obviously central in importance. Most of the information we have about the electrical activity of the human brain has come from peripheral measures such as the EEG. The widespread clinical use of EEG techniques for the diagnosis of brain malfunction attests to the success of this approach. In terms of current research on human brain activity, the application of averaging techniques and computer analysis of evoked activity has resulted in a data "explosion." Techniques for scalp recording of brain activity are deceptively simple—in essence, wires are glued to the scalp and attached to recording devices. However, there are many traps for the unwary—these techniques involve a number of methodological problems and theoretical issues. Partly for this reason we have included discussion by several authors on the same and related topics. Each expert has his or her preferred methods and emphasizes particular aspects of technique and interpretation.

The first section deals with EEG recording in animals and man. Lindsley and Wicke set the stage for the remainder of the volume with a fascinating historical review of EEG recording and a comprehensive discussion of modern techniques and experimental problems in recording brain potentials. Stevens focuses on techniques of human EEG recording, including discussion of abnormal brain activity.

The second section deals with evoked human brain potentials. Goff provides a very comprehensive discussion of procedures for stimulation and recording of human averaged evoked potentials. Vaughan emphasizes methods of analysis of EEG and evoked activity. In the last chapter of this section, Buchsbaum treats the critically important influence of psycho-

logical variables and processes on the human averaged evoked scalp potential.

The final section of Part B treats the contingent negative variation (CNV). This scalp recorded response has occasioned much recent interest, in part because it appears to correlate with "psychological" processes. Special technical problems exist which are somewhat analogous to those treated by Arduini and by Rowland and Dines in their discussions of slow potentials in animal brain recording in Part A. In the first chapter of this section McAdam provides an overview of the history and methods. Cohen emphasizes the interpretation and physiological significance in the next chapter. Hillyard deals with methodological issues and behavior correlations of the CNV in the last chapter.

Contents of Parts A and C

EFFECTOR PROCESSES

Chapter 1

The Electroencephalogram: Autonomous Electrical Activity in Man and Animals

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I. Introduction

A great deal of what we know about the functional activity of the brain and nervous system has been learned from studies of its electrical characteristics and properties by electrical stimulation and by recording its electrical activity. The discovery that the brain manifests continual electrical activity during sleep as well as during waking states, as revealed by the electroencephalogram, and that it is not merely a stand-by organ awaiting stimulation and emitting responses, has served as a tremendous impetus to further study by all available methods. In view of the great utility of investigating brain and nervous system activity in terms of its electrical properties and signs, it is perhaps pertinent to review briefly some of the steps by which we came to know about, and seek the meaning of, its electrical changes. As we trace some of this history it will become evident that technical developments in instrumentation by scientists and engineers, and a constant alertness to the applicability and adaptability of new physical instruments and methods by biologists, has made much of the progress in this field possible.

II. Historical Background

Late in the eighteenth century, about 1790, Luigi Galvani, an Italian physiologist, and his wife Lucia, became curious as to why the muscles of a frog twitched periodically when hung by a copper hook from the iron balustrade of their home. Galvani, alert to developments in the physical world of his time, hypothesized that the twitching was due to electric current generated by two dissimilar metals in contact with the moist tissue of the frog. He proposed that muscles and nerves are excitable tissues which react to an electric current. He demonstrated that touching the bared crural nerve in the leg with two metal probes of different composition caused the muscle attached to the nerve to contract. He correctly concluded that the nerve conducts an electrical impulse, and that it is not simply a tubule through which fluidlike vital or animal spirits flow as had been thought for many centuries, a view which was espoused also by Rene Descartes less than 150 years before.

Alessandro Volta, a contemporary Italian physicist, disagreed with Galvani's interpretation of his results, and vigorous arguments followed. As it turned out, perhaps both were correct, and no doubt Volta was stimulated to develop in 1800 the first electric battery, known then as a voltaic pile. Through electrochemical action the battery generated and stored electricity. The process by which this came about was called galvanism and the direct current which flowed from the battery was called, after

Galvani, a galvanic current. A few years later when Michael Faraday invented a method for interrupting and reversing the flow of current with his electromagnetic inductorium, the resulting alternating current was called faradic current. With these sources of d.c. and a.c. current available, physiologists began to stimulate nerves and muscles. Du Bois-Reymond utilized electrical stimulation to study spinal reflexes, Bell and Magendie established the law of independence of sensory and motor roots, Marshall Hall distinguished between reflex and voluntary movement, Johannes Müller defined his law of specific energy of nerves and Helmholtz figured out a way to measure the velocity of the nerve impulse.

Volta not only developed the first battery, but he invented a means of detecting and measuring the flow of current from it and the potential difference which existed between its poles, hence the terms volts and voltage. The device for doing this was called an electroscope or an electrometer, and much later a voltmeter. Other electrical measuring devices soon appeared; some of these were called galvanometers after Galvani, others were modified forms of Volta's original electrometer.

With the availability of instruments to detect and measure electrical current flow and potential differences, Nobili in 1827 became the first to measure "animal electricity" in a frog muscle, but Matteucci and du Bois-Reymond were the first to demonstrate and explain, in the early 1840's, the nature of the negative variation in the electromyogram. Whereas muscle potentials may be of the order of millivolts, brain potentials are often of the order of microvolts, which probably accounts for the fact that there were no reported studies of the electrical activity of the brain, until Richard Caton, an English physician, published the first account of the recording of electrical potentials from the brain of rabbits, and monkeys in a British medical journal in 1875. He observed two phenomena, surprisingly enough, even though he had available only a rather insensitive galvanometer and relied upon optical magnification for "amplification." One was the change in electrical activity at the surface of a sensory region of the brain when a sensory stimulation was given, the other was a continually changing background electrical activity. His was a very brief report without figures to illustrate his records, so we are left with sparse details of his findings. During the last quarter of the nineteenth century and the first quarter of the twentieth, several other investigators in Russia, Poland, Austria, and elsewhere confirmed Caton's results showing that electrical changes can be recorded from the exposed surface of the brain of animals when sensory stimuli are applied (presently called evoked potentials), and even in the absence of special sensory stimulation (so-called "spontaneous" or "autonomous" electrical activity). Not only were their instruments for recording

and measuring these electrical phenomena too insensitive, but they were also too slow to record faithfully the rapidly changing flux of the currents.

By 1903 Willem Einthoven, a Dutch physiologist, had invented and perfected a string galvanometer for recording the electrical beat of the heart as manifested by the volume-conducted EKG. This instrument was comprised of a threadlike metallic "string," usually of quartz, strung between two poles of a permanent magnet or of a sizable electromagnet. As the weak currents from the heart, or from nerves and muscles, passed through this string and changed strength and direction of flow in the magnetic field, the string was caused to deflect one way or the other in proportion to the magnitude of the electrical change. The shadow of the string cast by a focused light upon sensitive photographic paper moving at a constant rate traced these oscillations of current flow, or differences in potential, at the points of contact on the surface of the body or from electrodes attached to nerves or muscles.

From about 1910 to 1925 several young physiologists became interested in the electrophysiology of muscles and nerves, and fortified by Einthoven's development of moderately sensitive string galvanometers, or modifications of Volta's electrometer in the form of a capillary electrometer, they began to record from nerves and muscles. Principal among these were Alexander Forbes at Harvard Medical School, Keith Lucas and E. D. Adrian of Cambridge University, and Joseph Erlanger and Herbert S. Gasser at Washington University in St. Louis. Forbes used the string galvanometer, and in 1920, together with Thacher, was the first to employ and describe the use of electronic amplification with it, following the development of the vacuum tube for radio amplification during World War I. Lucas and Adrian employed the capillary electrometer and later, when electronic amplification became available, Adrian and collaborators employed a moving-iron, electromagnetic, mirror-type oscillograph developed by B. H. C. Matthews. Erlanger and Gasser were the first to employ the Braun tube, a forerunner of the cathode ray oscilloscope, in about 1924, which required amplification. Technical developments moved along quite rapidly during the 1920s, but the early applications of electronic amplifiers had limitations because the circuits employed in radio were adapted primarily for audio amplification and were not very adequate or stable in the lowest bandwidths or frequency ranges. This may have accounted for the fact that the classical electrophysiologists of those early days did not see or concern themselves with slow electrical changes and as a consequence were not prepared to accept the slow electrical events later reported by Berger. They were convinced that the only electrical changes of consequence were those of the brief spikelike potentials associated with the nerve impulse and with muscle action potentials.

It was over 50 years after Caton's (1875) first report of the recording of brain electrical activity in animals that Hans Berger, a rather obscure German neuropsychiatrist at the University of Jena, published for the first time an extensive account of the recording of electrical activity through the scalp and skull of human subjects. Because Berger was known mainly as a clinician rather than a scientist and electrophysiologist, and because his first report appeared in a psychiatric and clinical journal, the electrophysiologists of that day were slow to become aware of it and those that did treated it skeptically, until Adrian and Matthews in 1934 repeated and confirmed the validity of the observations Berger had made.

Berger (1929) pointed out in his electrical brain recordings that there were regular rhythmic sequences of waves at about 10 per second in the relaxed adult subject and that these were best seen with the eyes closed in the absence of stimulation or other mental activities such as imaging or problem solving. He called these "alpha" waves. He also observed smaller amplitude waves ranging in frequency from about 18 to 50 per second. These he called "beta" waves. Berger called the entire electrical record of the brain's activity the Elektrenkephalogramm, abbreviated EEG, in keeping with the EKG acronym for the Electrokardiogramm.

Berger had attempted to record electrical activity from the brain of animals with a string galvanometer from about 1902 to 1910, with relatively little success due to the fact that the potentials were small and no doubt further depressed by anesthesia. Also, his string galvanometer at this time was rather insensitive and probably inadequate to the task. His first report in 1929 told about his attempts since 1924 to record the human EEG using a more sensitive string galvanometer without amplification. He was successful in this, but soon acquired electronic amplifiers to augment the sensitivity of the string galvanometer and eventually the galvanometer-type mirror oscillograph developed by Siemens (and by Westinghouse and General Electric in America).

At first, in order to lead off the potential changes from the head, Berger placed two large pad electrodes soaked in saline on the surface of the skin over the forehead and over the back of the head, near the occiput. Later, he even found opportunity at time of surgery on the brain to record directly from the brain substance and was able to confirm that the activity recorded from the surface of the scalp was the same as that from the surface of the brain or within the gray matter, except that the voltage was lower on the scalp.

During the next 10 years, until his death in 1939, Berger published a series of papers on the EEG in human subjects, mainly relating to diagnostic and clinical goals, but steeped in a philosophical theorizing about the organization and role of the various layers of the cerebral cortex. Most of

Berger's principal papers have now been translated into English by Gloor (1969) and brought together in a book entitled *Hans Berger on the Electroencephalogram of Man,* with an interesting introduction and commentary on his work. Berger dealt with problems of attention, imagination, perception, problem solving and thinking, but mainly in a qualitative and clinically anecdotal fashion related to his theories, which had been derived principally from his clinical observation of patients. As was true of other workers in the field, he found that the EEG often revealed electrical aberrations in patients with neurological difficulties such as epilepsy, brain trauma, tumors and so forth, but revealed relatively little that was different from the EEG of normal subjects when he investigated psychiatric patients. The range of psychiatric disorders rarely showed marked abnormalities unless there were also associated neurological disturbances and there were no pathognomonic EEG signs as in some neurological disorders.

III. The Electroencephalogram during the 1930s

A. Instrumentation for Research

Berger's discovery of the human EEG in 1929 brought on a flurry of excitement in laboratories around the world during the era of the 1930's. It was a period of rapid growth and improvement in instrumentation and methodology. Differential or balance input amplifiers, often referred to as "push–pull" amplifiers, were developed and described by Matthews (1934, 1938) and Tönnies (1938). Among other things, these had the advantage that they would reject in-phase signals and thus reduce greatly the effect of unwanted interference such as 60-Hz oscillations radiating from power lines. They also permitted recording from two active sources on the brain or scalp, or one active and one inactive source, without grounding one electrode as was characteristic in the case of single-ended input amplifiers.

It soon became evident that more than one region of the brain should be examined simultaneously and that long continuing records would be needed for the study of sleep and waking states. This led to the development of multiple recording channels, both photographic and inkwriting. At that time, in the early or mid-1930s, dual-trace or multiple-trace cathode ray oscilloscopes did not exist. Multiple-element mirror or galvanometer-type oscillographs were available and were put to use (Travis & Dorsey, 1932; Jasper & Andrews, 1936) for multiple recording. Inkwriting oscillographs were developed (Garceau & Davis, 1935; Loomis, Harvey, & Hobart, 1936a, b), but were mainly one or two channel units, until Grass and Offner began to produce commercially three or four channel units in the late

1930s. In the early 1930s most laboratories had to build their own amplifiers for there were no commercial suppliers then. It is interesting that in most of the early publications authors published a circuit diagram of the amplifier, described its characteristics, and even published records of input-output function tests (overall frequency response curves), often using different time constants (see Travis & Dorsey, 1932; Jasper & Andrews, 1936).

There was much experimentation with electrodes. In order to record from various areas of the brain and in the hope of recording from more isolated regions, electrodes had to be smaller, usually about 5–7 mm in diameter. Some investigators used flattened pellets of solder; others used gold or silver disks, cup-shaped and chlorided, for there was concern about polarization when using long time-constant amplifiers, as there is today using d.c. amplifiers, though the problem was not nearly so serious.

It is difficult to explain to a modern generation of research workers in neuroscience and electrophysiology what the early days of electrophysiology and electroencephalography were like. Today we are heirs to 30 years of vast technological development, with many choices of fine amplifying and recording equipment and ample funds to buy it ready-made. The 1930's was an era of economic depression with almost no funds available for research, and even if money had been available, the equipment, or the parts to make it, would not have been, for radio and electronics were in their infancy and there were few manufacturers of electronic parts and equipment. Consequently, the period of the early 1930s was one of "blood, sweat, and tears" for the electrophysiologist and electroencephalographer. But they were days of hope and inspiration and improvisation; and they were days of cooperation and collaboration.

One "begged or borrowed" condensors, tubes, resistors, and other components necessary to build an amplifier. The input tubes of the amplifier were not very noise free and had to be carefully shock mounted against building vibration and even sound waves; the amplifiers often had to be shielded in a copper-lined and sound-attenuated box and suspended by screen door springs. Voltage amplifiers were operated from batteries, with separate batteries for filament, plate, and screen-grid voltages. The batteries were large and cumbersome; the transformers supplying voltage for the power stages of the amplifier were large and heavy and together with the vacuum tubes generated much heat.

Nevertheless, some EEGs in the 1930s were recorded with more adequate band width and time constants than are some EEGs today, for the latter are often subject to many built-in constraints or limitations to satisfy special purposes such as bandwidth gating, antiblocking features, filtering, etc. Although these special features often serve very useful purposes, one must

be aware of the limitations they introduce and must know the electrophysiological characteristics which one wishes to preserve in order to have a valid and undistorted record. That is to say, if one wishes to record slow potential changes he must use amplifiers with an appropriate, long time constant, or a d.c. amplifier. If he wishes to look at a particular part of the frequency spectrum unencumbered by other phenomena of lower or higher frequency, he may do so by an appropriate choice of bandwidth filtering, but he must be aware that he pays for this advantage by some distortion or attenuation of the signals remaining.

B. Direction of Research

After Berger's discovery became known, the subsequent investigation of the electroencephalogram took several directions. Three of the major directions were: (1) animal studies seeking to identify the source and nature of the EEG; (2) human studies seeking psychological and physiological correlates of the EEG; (3) human studies seeking pathological correlates of EEG.

1. Animal Studies of the EEG

It was natural to want to study the electrophysiological activity of the brain more directly and this led mainly to animal studies, for in the early 1930's it was not yet feasible to probe the human brain at time of operation. Furthermore, human brain surgery was not yet commonplace, nor had it developed the degree of sophistication and finesse that it enjoys today. The first extensive EEG animal studies of this period were by Fischer (1932) and Kornmüller (1932) in Germany and by Bartley and Bishop (1932, 1933) and Travis and Herren (1931) and Travis and Dorsey (1932) in the United States. These were soon followed by other significant animal studies (Adrian, 1936; Dusser de Barenne & McCulloch, 1936; Gerard, Marshall & Saul, 1933, 1936; Rheinberger & Jasper, 1937; Bremer, 1938). Except for the one by Rheinberger and Jasper, all of these studies were on acute preparations under anesthesia, whereas today it is common to do combined electrophysiological and behavioral studies using implanted electrodes.

2. Human Studies: Physiological and Psychological Correlates

As previously mentioned, Adrian and Matthews (1934) were the first to confirm Berger's human EEG results. Human EEG studies soon followed in the United States by Jasper and Carmichael (1935) and Gibbs, Davis and Lennox (1935), and in France by Durup and Fessard (1936). By that time a number of new laboratories for human EEG work had been started and it seemed logical to search for psychological and physiological variables

related to the EEG and its varied patterns. One approach was to study the EEG in relationship to psychological and physiological state factors. Loomis, Harvey, and Hobart (1935, 1936b) studied sleep and hypnosis. Bagchi (1936), Travis (1937) and Davis and Davis (1936, 1939) initiated studies of psychological and physiological changes associated with variations in conscious state. Lindsley (1936, 1938, 1939) and Smith (1937, 1938, 1939) investigated the ontogenetic development of the brain and behavior in relation to the EEG and found that alpha wave frequency increases as a function of age. Hoagland (1936) studied the EEG in relation to temperature. Lindsley and Rubenstein (1937) correlated the EEG with a number of physiological variables and found it highly correlated with total oxygen consumption. Other physiological studies were concerned with blood sugar level, acid–base balance, metabolism, drugs, and anesthetics and fatigue. There were many psychologically oriented investigations of the EEG in an effort to determine experimentally in what way the EEG correlates with, or relates to, sensory experience, perception, learning, emotion, motivation, and other factors.

3. Pathological Correlates of the EEG

In his early studies Berger had already called attention to the fact that epilepsy and other neurological disorders produced unusual and characteristic changes in the EEG whereas for the most part psychiatric disorders did not. In addition to the extensive studies by Berger and Kornmüller in Germany, the work of Gibbs and collaborators and of Jasper and associates in the United States and Walter in England highlighted the importance of the EEG and its applications in neurology and neurosurgery. It soon became evident that clinical patients with neurological disorders such as epilepsy in its several forms, brain tumors, brain trauma, and other brain-damaging factors caused the brain to produce striking electrical patterns in the EEG very different from those characteristic of the normal brain. This led to an important application of the EEG which has continued to grow and expand over the years to the point where almost every major hospital has an active EEG laboratory today.

Early summaries of these applications of the EEG in neurology and related fields are to be found in publications by Gibbs and Gibbs (1941), Jasper (1941), and Walter (1938). Extensive reviews of the whole field of endeavor in EEG during the 1930's were prepared by Jasper (1937) and Lindsley (1944). Ellingson (1956) did a special review on the EEG and problems of psychology.

Research and communication with respect to the EEG was markedly attenuated during World War II due to enforced preoccupation with other matters, but following the war there was a marked resurgence of interest.

Scientific and professional societies were formed and an international federation of EEG societies and an international journal were started. Progress in studying the EEG, and on a broader scale the electrical activity of the brain, has been rapid and extensive over the past 25 years. It has become possible to study important aspects of the EEG other than the spontaneous or autonomous rhythms first noted by Berger in 1929. Dawson (1951) described a technique for bringing out the evoked response of the brain to sensory stimulation. Augmented by computer technology during the 1960's, these average evoked potentials have become a very important by-product of the classical EEG and the methodology and procedures are described by Goff in Chapter 3. Another important development occurred when Walter, Cooper, Aldridge, McCallum, and Winter (1964) first described slow negative potential shifts associated with anticipation or expectancy and called them the Contingent Negative Variation (CNV). Both the average evoked potentials and the slow dc potential shifts offer great promise in the study of cognition and higher mental functions, and progress is already being made along these lines.

Hopefully, the future will bring a better understanding of the sources and mechanisms of the ongoing spontaneous EEG rhythms and their thalamic pacemakers, and of the relationships between the EEG, average evoked potentials and the CNV, which together constitute the three principal aspects of the electrical activity of the brain which can be recorded from the surface of the scalp of man.

IV. The Nature and Origin of the Electroencephalogram

The electrical activity which may be recorded from the surface of the scalp of man and which is known as the electroencephalogram (EEG) consists of continuous rhythmic oscillations. These alternating current potentials manifest amplitude modulations, rhythmic variations, and certain irregularities. The surprising feature of the EEG, when first reported by Berger in 1929, was its spontaneous or autonomous character. That is, the rhythmic electrical activity of continuing nature is not dependent upon special stimulation such as light, sound or touch, although of course there is always a continuous background of afferent flux from interoceptors and proprioceptors. Usually we are not aware of this afferent activity but we now know that it provides a synaptic drive for the reticular formation, as well as other structures, and this nonspecific sensory system activated by these impulses and by circulating neurochemical activators provides a tonic activating background for the cerebral cortex, keeping it awake and active. It in turn has feedback capability to the reticular formation. Phasic

surges of afferent activity from interoceptors and exteroceptors provide additional activation via the nonspecific sensory system, including the reticular formation and nonspecific thalamic nuclei. The generators of the rhythmic potentials recorded in the EEG from the surface of the scalp reside in the cortex, but the mechanisms by which their rhythmic activity is maintained and regulated are probably to be found in subcortical pacemakers, apparently in nonspecific nuclei of the thalamus.

As originally described by Berger, the normal EEG during a relaxed waking state without special sensory stimulation consists of two principal rhythms which he called the alpha and beta waves. The much lower voltage and higher frequency of the beta waves, plus the fact that they are easily confused with scalp muscle electrical activity, made them poor candidates for study, especially in the early days of EEG when amplification was a problem. Even to this day relatively little attention has been paid to the beta activity. On the other hand, the ubiquity of the alpha waves, their greater prominence, and their reactivity to sensory stimulation tended to focus interest on them from the beginning.

Berger (1930, 1931) soon discovered that visual stimulation and mental arithmetic caused a blocking of the alpha waves. When he found that other types of sensory stimuli also block the alpha waves and that voluntary movements or the intention to move an arm or a leg would do the same thing, he concluded, apparently quite correctly, that the effect of stimulation in reducing the alpha waves all over the head was related to attention and represented a generalized reaction of the brain. He thought that changes in the EEG with attention were in agreement with the notion that perception takes place through only one sensory channel at a time and that energy directed into the corresponding part of the cortex tended to inhibit temporarily all other parts. Although Berger's ideas were highly speculative and not very well founded at the time, it is interesting that his notions were not far different from some of our present conceptions except that we now have a better understanding of some of the mechanisms involved.

Forty years or more after Berger's discovery of the human EEG, we still do not know precisely where and how these rhythmic potential oscillations originate and how they are regulated (see Andersen & Andersson, 1968). It has been pretty well determined that their generators reside in the cortical mantle, but where precisely? Do they arise from particular types of cells or networks? Are they due to processes in dendrites, axons, synaptic junctions, along cell membranes, in neuropil, in granular or agranular regions, in glia, or in combinations of these? One thing certain is that alpha activity is more or less continuous and is found over all regions of the cortex (see Fig. 1-1). More prominent alpha waves are found over the sensory and association zones of the posterior half of the cortex, but they are also found

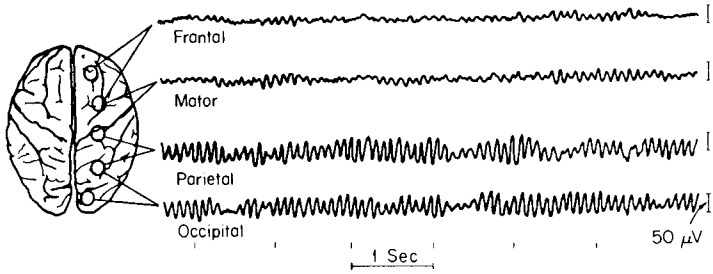


FIG. 1-1. Electroencephalogram of a normal human adult. Alpha waves at about 10 per second predominate in all regions but are largest posteriorly. Only a few smaller and faster beta waves are visible in the anterior regions. (From Lindsley, 1948.)

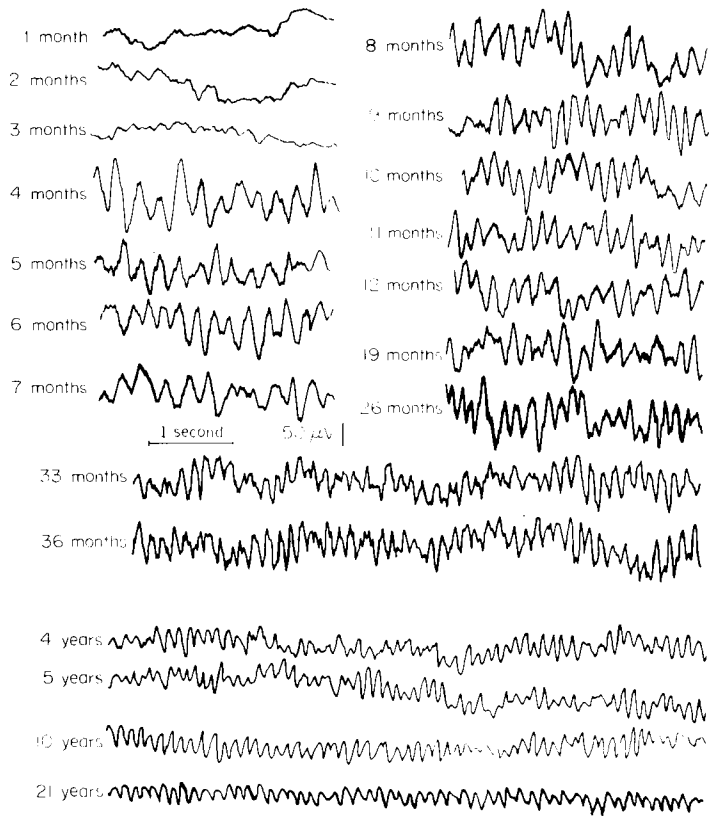


FIG. 1-2. Development of the occipital alpha rhythm. Serial recordings from the same subject. Persistent alpha rhythm first appears at 4 months of age at 3 or 4 waves per second, increases to 5 to 6 per second at 1 year and to an adult frequency of 10 per second by 10 years of age. No further increase in frequency occurs at 21 years. All records scaled to same size and time dimensions. (From Lindsley, 1960.)

over motor, premotor, and frontal association areas. There seems to be a voltage gradient from front to back. The potentials are usually largest over the occipital or occipito-parietal region and visual stimuli are usually more effective in blocking or desynchronizing the alpha waves than are other sensory stimuli. This may be due to the fact that visual stimulation characteristically is more demanding of attention and requires more frequent shifting of attention in daily experiences.

If alpha waves originate in the cerebral cortex, what is responsible for their rhythmicity and, more particularly, their continual rhythmic beat at about 10 per second? The frequency of the alpha rhythm ranges from about 8 to 12 per second in different individuals. The frequency is not exactly the

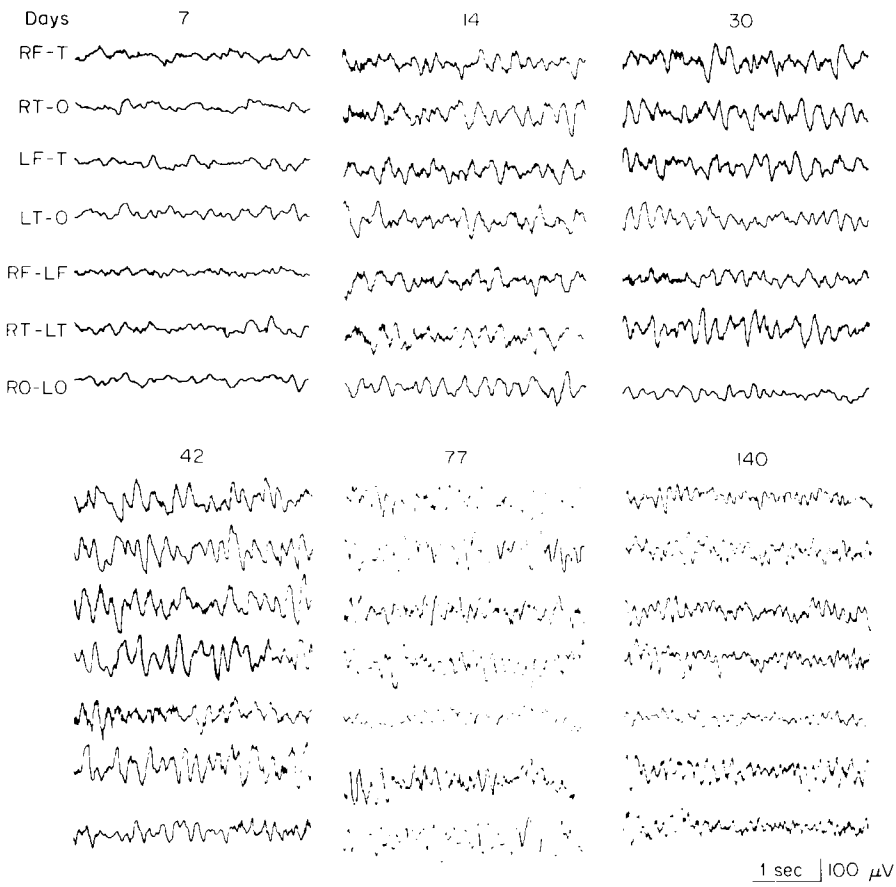


FIG. 1-3. Development of EEG in monkeys. Alpha rhythm present in all regions by 14 days at about 4 per second and gradually increases to about 8 per second by 140 days. (Courtesy of W. F. Caveness.)

same over all regions of the head but it is usually very similar. The mean value of the occipital alpha rhythm for a large group of normal adults was 10.2 per second (Lindsley, 1938, 1939). In any given individual the frequency of the alpha rhythm may vary typically by about one-half cycle, and it may, under conditions which modify the rate of chemical reaction and metabolism, vary considerably more. For example, in hypothyroid conditions or in other metabolically depressed states the alpha frequency is markedly reduced; also under conditions of severe lowering of temperature, as in the case of open-heart surgery. When the body temperature is elevated by fevers or artificially by diathermy treatments the alpha frequency may be elevated by one or two cycles or more, and similarly it may be lowered by severe cooling. Despite these and other possibilities of modifying the alpha rhythm, under normal circumstances it remains surprisingly constant day in and day out, and month by month, as Lindsley and Rubenstein (1937) showed when they studied the EEG of 4 young adult women for 32 consecutive days along with other physiological and metabolic indicators. They found that the standard deviation of the alpha frequency for any one

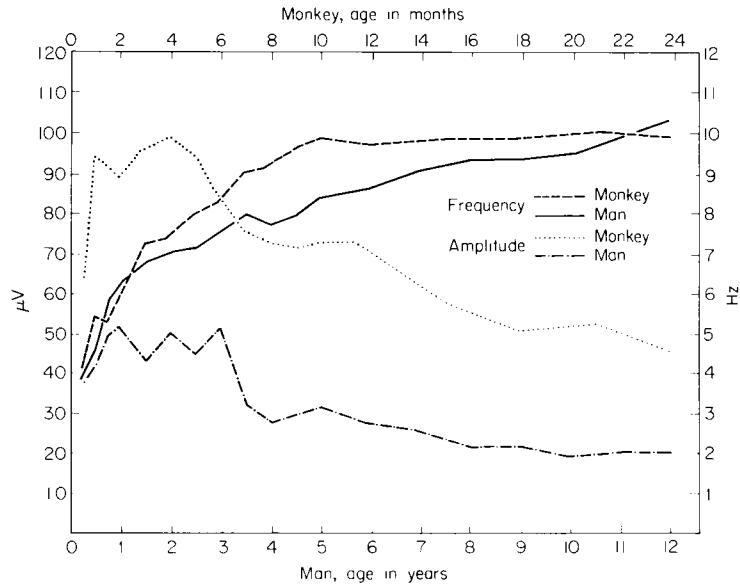


FIG. 1-4. Comparison of EEG data in man and monkey. Occipital alpha wave frequency and amplitude plotted as a function of age with life spans equated on a 6 to 1 ratio. Note parallel growth of frequency and reduction in amplitude of alpha rhythms. Human curves based on data from Lindsley (1939). (From Caveness, 1962.)

subject did not exceed .47 per second and that daily variations were for the most part less than 1 Hz.

Whereas the occipital alpha rhythm is about 10 per second in older children and adults, it has a much lower frequency in infants and young children. It is not present in newborn and very young infants. The onset of a regular rhythm over the occipital region first occurs at 3 or 4 months of age at a frequency of 3 or 4 waves per second. The frequency increases to about 5 or 6 per second at the end of the first year and thereafter increases at a slower rate to reach the adult frequency level of 10 per second at about 10 years of age. This is illustrated in Fig. 1-2 which shows the development of the occipital alpha rhythm in serial recordings made from the same child from 1 month of age onward. No regular alpha rhythm was present during the first 3 months but thereafter it was consistently present and can be seen to increase at first rapidly and then more slowly to the age of 10 where the frequency was about 10 per second and had a lower amplitude. At 21 years of age the pattern, frequency, and amplitude of the alpha waves were about the same as at 10 years of age.

In monkeys, whose life span is about one-sixth of that of man, the alpha rhythm over the visual area appears at about 15–20 days of age (see Fig. 1-3). This corresponds to its onset in the human infant at about 3 or 4 months of age. The growth in frequency of the alpha rhythm as a function of age in both species follows a similar curve when age span is equated (see Fig. 1-4). In both monkey and man the onset of the rhythm seems to mark the beginning of functional activity in the cortex and integration with subcortical centers. Its onset corresponds with the time of change in prenatal and neonatal reflex patterns, such as the Babinski, Moro, and grasp reflexes, to a more mature and normally integrated state. Along with these reflex changes at about 15 to 20 days in the monkey and at about 3 or 4 months in the human infant come changes in behavioral development which involve integrated responses to visual stimuli, such as the fixation and following of a dangling ring in the visual field (Lindsley, 1964, 1967).

Anencephalic monsters, that is, infants born without a cerebral cortex, who fortunately do not survive more than about 2 months, while living manifest the same reflex development essentially as the normal infant of the same age. This suggests that the normal human infant of 2 months has a cortex which is not yet functionally integrated with the rest of the brain and only becomes so at the age of 3 or 4 months when the onset of a persistent alpha rhythm occurs. All cortical brain cells are believed to be present at birth but have not matured sufficiently and have not developed connections with nonspecific projection systems so as to be rhythmically active and are apparently not electrically and behaviorally functional. An exception to this appears to be the motor cortex which structurally is more advanced

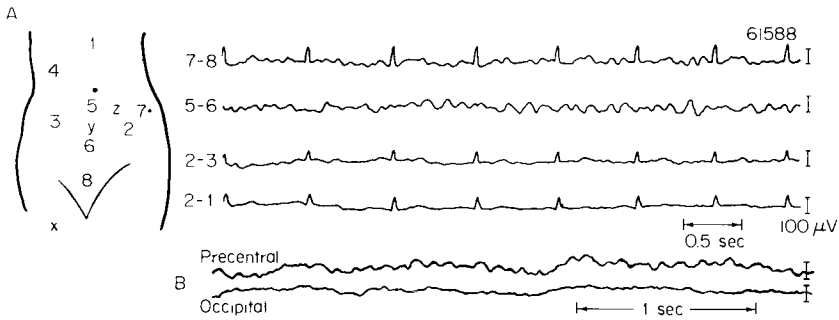


FIG. 1-5. Fetal and infant electroencephalograms. (A) Fetal EEG recorded in seventh month of pregnancy through abdominal wall of mother over palpable head of fetus—trace from electrodes 5–6 with maternal EKG absent shows 6–7 per second rhythm; also seen in 7–8. (B) EEG from same infant 3 weeks after birth. Precentral (motor) area tracing shows same type of rhythm as prenatally, but now increased in frequency to 7 or 8 per second. No rhythm has yet developed in the occipital area. (From Lindsley, 1942.)

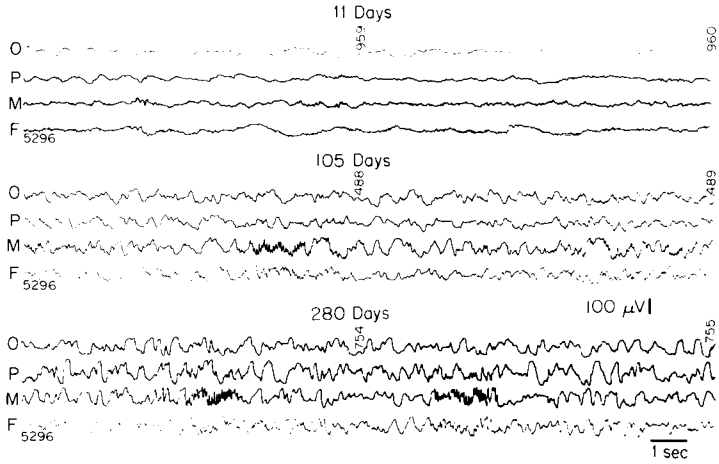


FIG. 1-6. Sleep EEGs recorded from the same child at different ages. During the first 15 days only incipient slow waves and very small spindle bursts in the motor region are seen. By 1 month of age a fairly well-developed sleep pattern is present and appears similar to those seen at 105 and 280 days when slow waves of sleep are widespread and 14 per second spindle bursts occur periodically about every 8 to 10 sec. (From Lindsley, 1960.)

than sensory and association areas, according to Conel (1939, 1947) and others. Lindsley (1942) showed that some cortical rhythms could be recorded prenatally through the abdominal wall of the mother during the seventh month of pregnancy, and that after the birth of the child the same type of rhythms could be recorded over motor cortex in the region of the anterior fontanelle or soft spot when the infant was relaxed and drowsy. These

results are shown in Fig. 1-5, but the waves seen prenatally and 3 or 4 weeks after birth are not believed to be forerunners of the alpha rhythm for they have a frequency of about 6 to 8 per second. It seems more likely that they may be the anlage of the sleep spindle bursts which eventually attain a frequency of about 14 per second and are often seen in the motor area shortly after birth, and which, by one month or so of age have developed, together with much slower waves, into a full-blown sleep pattern. The sleep records in a child at 11, 105, and 280 days of age are shown in Fig. 1-6. In the latter two records sleep spindle bursts in the motor area are well developed and recur about every 10 to 12 sec whereas the associated slower waves at the onset of sleep are widespread. At 11 days of age in the same child the slow waves are just beginning to emerge and also incipient spindles in the motor region. The fact that any waves at all are present probably means that some groups of cortical generators are present and active in a partially synchronized manner. The absence of organized rhythms in the sensory zones of the cortex until 3 or 4 months of age suggests that either the generators there are not sufficiently mature or that thalamocortical pacemakers are not yet functionally operative, or both. In addition to general pacemakers regulating the alpha rhythms all over the cortical surface there is some reason to believe that specific pacemakers operating through specific sensory relay nuclei (and possibly also posterolateral association nuclei of the thalamus) are capable of influencing the rhythmicity of generators in specific cortical regions.

A. Terminology

Berger called the record of the electrical activity recorded from the surface of the scalp over the head of man an Elektrenkephalogramm. The English version is electroencephalogram, abbreviated EEG. It means a graph or record of the electrical activity from the encephalon, or brain. Alternative terms used in the literature are brain potentials and brain waves. As time has gone on there has been a tendency to call any record of electrical activity from the brain of man or animal an EEG, except possibly microelectrode recordings. It was once recognized that this is probably incorrect and that the EEG, perhaps by analogy with the EKG, should be restricted to the recordings obtained from the scalp or skull over the brain of man or animal, that is, recordings at a distance and not in direct contact with the brain. For a while there was a tendency to refer to direct recordings from the surface of the brain as electrograms, qualified or specified as cerebral or cortical electrograms, cerebellar electrograms, thalamic electrograms, etc., depending upon the specific region of the brain from which they were derived. As more and more of the localized regions of the brain have been

explored, both on its surface and in its interior, this has become rather complicated terminology to employ with the result that there is no uniform terminology employed. Some authors use EEG as a convenient and brief designation for electrical recordings from any region of the brain, often naming the structure recorded from if a nucleus with a name or a designated pathway, or providing stereotaxic coordinates in order to give even greater specification.

Over the years advances and refinements in method and procedure have required that many electrodes be placed over the surface of the human scalp in order to attempt to localize and differentiate particular regional or local areal electrical activity or responses to stimulation. In these instances authors have specified occipital EEG, parietal EEG, temporal EEG, motor or premotor EEG, frontal EEG, etc. but it was soon recognized that this was an inadequate way to localize the site of an electrode or electrodes over a region. Usually more specification was given in terms of measurements with respect to landmarks on the skull. For example, a right occipital EEG recorded with a single electrode over the right occipital area and referenced to some so-called "indifferent" or "neutral" electrode, perhaps on the earlobe or mastoid process, might have the site of the electrode stated as 2.5 cm above the inion and 2.5 cm to the right of the midline. Obviously such a specification for the electrode would not necessarily represent the electrical activity for the entire right occipital lobe, but it would indicate the site from which the electrical activity in question was recorded.

Recording Conventions

Berger initially used large pad electrodes placed on the forehead and on the rear of the head, but soon came to use more localized recording electrodes. Both the extensive clinical use of the EEG and its use experimentally soon required that some standardization be developed with respect to electrode siting. This was necessary if the results of various studies reported in the literature were to have any meaning to other investigators and if results were to be compared and experiments replicated for verification. This standardization was difficult to accomplish because each laboratory had its own preferred procedures for recording, for siting electrodes, for evaluating records, and even preferred terminology for designating electrode sites, etc. Following the founding of the American Electroencephalographic Society in 1949 and the International Federation of EEG Societies, a great effort was made to standardize equipment and the specifications for equipment, recording speeds, electrode sites, terminology, etc. Although this has never succeeded, to the extent that it has with respect to the EKG, a

great deal more order has been developed than originally existed during the exploratory years of the EEG, roughly from 1930 to 1950.

Most clinical EEG laboratories now conform to the International EEG system of electrode placements, referred to as the International 10-20 System (Jasper, 1958). This system, based on proportional distances between anatomical landmarks of the skull or head in order to compensate for different head sizes defines electrode sites as 10% or 20% of distances along the midline from inion to nasion in a longitudinal or midsagittal plane, and along a line in a transverse or coronal plane which halves the distance between inion and nasion in the plane of the auditory meatuses. In a similar manner other circumferential lines have been defined. Hence the designation 10-20 system. The percentage values were chosen so that electrode sites would have some relevance to underlying brain area designations anatomically and functionally and at the same time would provide for a reasonable coverage of the total area. The scalp electrode sites for the 10-20 system are illustrated in Chapters 2 and 3.

Many clinical electroencephalographers find it necessary to augment this standard array of electrodes by others of intermediate location when they wish to localize some abnormality, and it is often necessary to do so in connection with experimental studies utilizing the EEG. When this is done, the location can either be designated as so many millimeters or centimeters from a 10–20 electrode site or between two or more such sites. It can also be specified with respect to head and skull landmarks or with respect to the area of the brain over which it is sited when that area can be designated in terms of an architectonic brain map, such as that of Brodmann (1909, 1925), which has come to be used rather extensively (see Fig. 1-7). The 10-20 system uses letters and numbers. The letters have meaning with respect to brain lobes, for example, O, P, C, F, and T standing for occipital, parietal, (central), frontal and temporal lobes. The associated numbers also have meaning—the odd numbers are over the left hemisphere, the even numbers over the right, and within limits they tend to define certain circumferential or coronal paths across the head.

Another terminological area relates to a matter which once caused vigorous arguments among certain advocates of one system of recording or another. At one time it was customary to specify whether the recording was bipolar or monopolar. The latter refers to the recording from a single electrode on some given site on the scalp over a region of the brain supposed to be "active" in generating electrical activity, and which is referenced to another region of the head or body which is presumed to be relatively "inactive" so far as the generation of electrical activity is concerned. That is, it is presumed to be an "indifferent" or "neutral" site with respect to

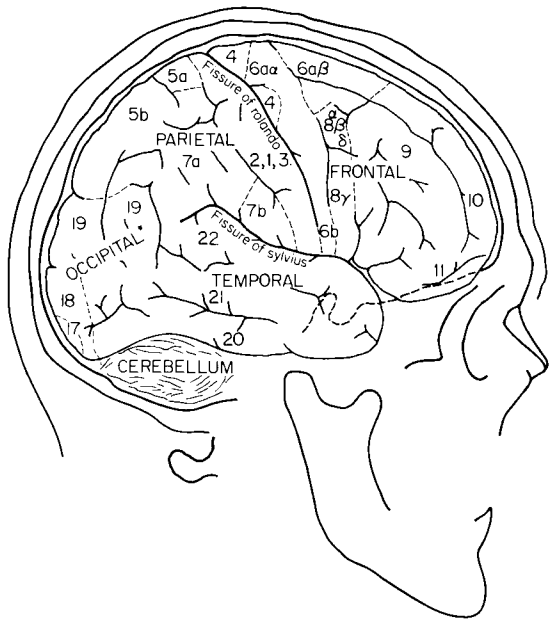


FIG. 1-7. Brain map fitted to tracing of X-ray photo of head. It shows relative thickness of scalp and skull through which EEGs must be recorded; also, principal lobes are labeled and some of the architectonic areas are designated, after Brodmann and the Vogts. (From Lindsley, 1948.)

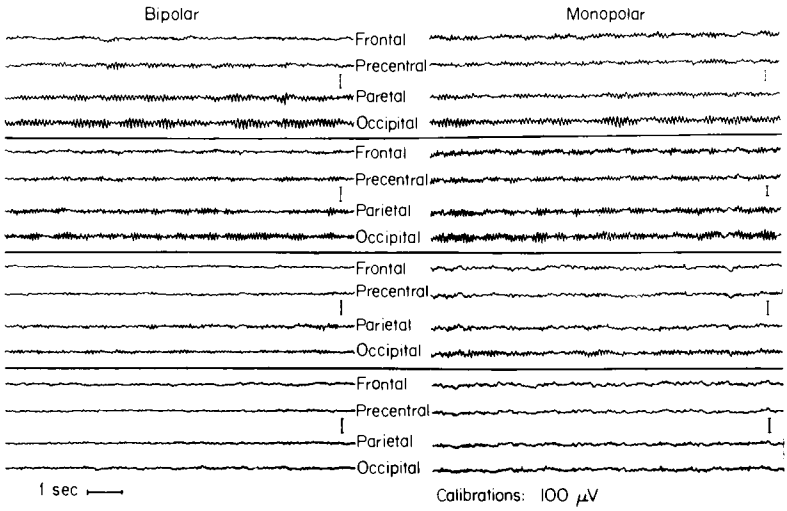


FIG. 1-8. Typical normal adult electroencephalograms recorded by bipolar and monopolar methods. These range from continuous and prominent alpha rhythms (top record) to almost no alpha rhythms (bottom record). Note that bipolar records show smaller amplitude waves and greater differences between regions, indicating a more localized recording. (From Lindsley, 1944. Copyright 1944, Renewed © 1972 The Ronald Press Company, New York.)

brain electrical activity. The earlobe, the mastoid process, the bridge of the nose, and the sternum of the chest wall have variously been used for this purpose, though it is generally admitted that none of these is truly "indifferent" or "neutral" in the sense that there is no "leakage" of currents to them from the head or heart or other sources of potential.

The other method of recording, employing two electrodes on the scalp over "active" brain tissue, is called the bipolar method. This method is supposed to have some advantages over the monopolar method. With the two electrodes over the scalp, fairly close together, it is presumed to provide a more localized recording, and indeed it seems to do this (see Fig. 1-8). Another localizing feature of a bipolar array of electrodes across the head is that they can be connected in tandem so that any given electrode has a connection to the input of two amplifying channels but in opposite orientation so that a negative signal generated under that electrode will cause the tracing to deviate in one direction in one channel and in the other direction in the other channel. This is called the phase reversal method of localizing the source or area from which a particular pattern or response arises.

A disadvantage of the bipolar method, in contrast to the monopolar, is that "in-phase" signals arising in the region under two closely spaced electrodes which lead to the input of a differential or push-pull amplifier tend to be cancelled out as do extraneous interferences such as 60-Hz field currents. Another disadvantage is that two scalp electrodes, separated by some distance, may span two or more functional or anatomical regions and thus sample and mix different functional activities. Also, when two electrodes are placed too close together (less than about 2.5 cm), the size of the potentials is markedly attenuated.

In clinical EEG literature the terms monopolar and bipolar have tended to be replaced in recent years by the terms scalp-to-earlobe (or other reference) and scalp-to-scalp, respectively. For deep electrodes in the brain, however, there is still a tendency to use "monopolar," "unipolar," or "single-ended" as an indication that only one electrode tip is being used to record the electrical activity generated in its neighborhood, while referenced to a distant "neutral" electrode. If two bared tips, insulated from one another, either in a side-by-side or a concentric electrode probe, are used, they are called "bipolar." Usually such recording electrodes have their bared tips only 0.5–2 mm apart in order to serve a localizing purpose. On the other hand, they could be considered "bipolar" if two separate electrodes perhaps a centimeter apart were connected to the same amplifying channel.

In the case of the "reference" electrode for the human EEG, some investigators connect the two earlobe electrodes together and refer to it as a linked earlobe reference. Some laboratories have used a system recommended by Offner (1950) in which all of the other electrodes on the head

serve as a "reference" for a given electrode but with about 0.5 to 2 MΩ of resistance introduced between each of these electrodes and their common connection. In animal preparations, both acute and chronic, several electrodes may be tied together to serve as a reference for a given recording site. This does not mean, however, that they are strictly "neutral" so far as contributing potentials is concerned. Often, in the case of the cat, where there is considerable space over the frontal sinuses, a screw electrode in the bone may serve as a reference, hopefully without picking up too much brain activity. The grounding of a distant "reference" electrode may make it a more neutral reference, but in the case of differential or balanced input amplifiers, it denies the advantage of the common mode rejection ratio (CMR) that such an amplifier provides for the elimination of in-phase signals such as 60-Hz interference. There are no easy or perfect solutions to these problems and each investigator must work out his own solution and salvation, depending upon the circumstances and the goals, but whatever method he uses should be made clear in his publications. Likewise, there should be specification of the polarity orientation of the amplifying and recording system so that any published records clearly indicate whether negative or positive gives an upward deflection when the recording electrode concerned becomes "negative" or "positive" with respect to the reference electrode. With bipolar recording, with both electrodes in active tissue, this is difficult, if not impossible, to specify since one electrode may be going positive while the other is going negative with respect to some distant reference or with respect to the brain as a whole, and direction of the deflection would be the same. Also, the region in which two electrodes are located may go negative with respect to distant regions, but one electrode site may be more negative than the other.

B. Types of Waves and Their Characteristics

For many years, before the days of frequency analyzers, computers and other means of resolving some of the characteristics of the electroencephalogram, three principal measures of the EEG were made by hand and eye. These were frequency, amplitude (voltage), and the percent of time that a particular type of wave or rhythmic activity existed in the EEG. These measures were often very laboriously made from sections of a record taken at representative times during the course of a recording session. This meant that one had to define in some manner the types of waves for which such measures would be applicable. For example, an alpha rhythm might be defined as three or more waves of equal duration (corresponding to the alpha range) occurring in uninterrupted sequence. There were other reasons, of course, for attempting to differentiate the types of waves. One

was to be able to say what various psychological or physiological states were associated more with one type of wave or rhythm than another. Another reason was that some types of waves were considered "normal" whereas others, observed only in persons with particular symptoms or under certain conditions, might be considered aberrant or pathological. Still another reason was that some types of waves might be characteristic of one region of the brain whereas another type might be found mainly over other regions. Table 1-1 provides information about various types found in the EEG.

Berger gave a good deal of thought and attention to the alpha and beta waves which he discovered, defined, and named. He speculated considerably about the source (what layers of the cortex) and functions (psychophysical, attentional, vegetative, or metabolic) of the alpha and beta waves and changed his mind as new evidence became available. In 1937 he argued that the upper three layers of the cortex serve "psychophysical" functions and that the beta waves were reflections of this. Previously he had held that the small and rapid beta waves were related to brain metabolism. From the beginning he regarded the alpha waves to be associated with certain levels of awareness or conscious states and their blocking by sensory stimuli, voluntary movements or intentions to move, and problem solving as an indication that they were related to attention. The fact that alpha waves were recorded from all over the head and that when they were blocked by a specific sensory stimulus they were blocked in all regions convinced him that alpha waves have a general function and are affected by generalized brain reactions.

Some of his theorizing and speculating was quite remarkable and showed an intense interest and preoccupation with matters psychological and how they might be accounted for in terms of brain structure and function. His early studies of brain temperature and cerebral circulation at the beginning of the century had started him thinking along these lines and his early attempts to record electrical activity in the brain of animals, and his persistence until he did so in humans, was undoubtedly strongly motivated by his desire to explain psychological events in terms of brain structure and function. For this he deserves much credit, for there were few men in those days who had the interest, courage, and fortitude to face up to the problems of relating brain, behavior, and mental activity, and indeed this is still true today, despite the many avenues that such approaches might take due to vast improvements in technology and to a wealth of accumulated data.

1. Alpha Waves

These prominent oscillations at about 10 per second in the 10- or 12-year-old child and in the adult are present in the EEG when the subject is fully awake and relaxed physically and mentally in an environment rela-

TABLE 1-1

TYPE OF WAVES AND RHYTHMS IN THE HUMAN ELECTROENCEPHALOGRAM AND THEIR APPROXIMATE AND RELATIVE SPECIFICATIONS AND DISTRIBUTIONS, INCLUDING CONDITION WHEN PRESENT AND WHETHER NORMAL[a]

Type of wave or rhythm	Frequency per second (range)	Amplitude or voltage (μV)	Percent of time present	Regional or diffuse	Region of prominence or maximum	Condition when present	Normal or abnormal
Alpha	8–12[b]	5–100	5–100	Diffuse	Occipital and parietal	Awake, relaxed eyes closed	Normal
Beta	18–30	2–20	5–100	Diffuse	Precentral and frontal	Awake, no movement	Normal
Gamma	30–50	2–10	5–100	Diffuse	Precentral and frontal	Awake	Normal—sleep deprived
Delta	0.5–4	20–200	Variable	Diffuse	Variable	Asleep	Normal
	0.5–4	20–400	Variable	Both	Variable	Awake	Abnormal
Theta	5–7	5–100	Variable	Regional	Frontal and temporal	Awake, affective or stress	Normal(?) Abnormal
Kappa	8–12	5–40	Variable	Regional	Anterior and temporal	Awake, problem solving?	Normal
Lambda	Pos-neg spike or sharp waves	5–100	Variable	Regional	Parieto-occipital	Vis. stim. or eye opening	Normal(?)
K-Complex	Pos. sharp wave + other slow pos-neg + other	20–50	Variable	Diffuse	Vertex	Awake-aud. stim.	Normal(?)
		50–100	Variable	Diffuse	Vertex	Asleep-var. stim.	Normal
Sleep spindles	12–14	5–100	Variable	Regional	Precentral	Sleep onset	Normal

[a]From Lindsley (unpublished data). [b]Lower for infants and young children.

tively free of stimuli. The subject may be sitting or lying comfortably in a dark and soundproof room, or with eyes closed in a dimly lit room. In general he must try to keep his mind free of thoughts or concerns. However, recent biofeedback and alpha conditioning procedures, which have become popular, suggest that considerable imaging can go on without marked disturbance of trains of alpha waves. This is true provided that faint auditory feedback signals, indicating the presence of alpha waves, furnish a continuing uniform background guide for minimal awareness and attention.

The voltage of the alpha waves ranges from a few microvolts to about 100 μV depending upon the state of the individual, i.e., whether apprehensive, tense and anxious, or relaxed. The voltage also varies from one individual to another. Some persons show almost continuous trains of quite uniform amplitude alpha waves of 50 to 100 μV, whereas others may have very low level alpha waves of the order of only 5 to 10 μV or less. The pattern varies greatly from one of almost sinusoidal character to quite irregular waveforms. In some persons there is an abundance of waves of quite rhythmic and regular character, whereas in others there is continual periodic or irregular amplitude modulation and in still others frequent interruptions in the rhythm and the regularity of the pattern of the waves. Often the characteristics manifested in the EEG of a person seem to be quite consistent from one recording session to another even when spread out over months or years. Each person's EEG pattern seems to be quite unique, although there are of course many who have similar patterns.

The alpha wave patterns of a normal adult can change in a matter of minutes as his attitude changes from one of apprehensiveness about the procedure and what his record might show to one of relaxation and satisfaction when assured that the first record has been taken and all is well. Initially the alpha wave voltage is very low and the rhythm irregular, but as the subject's apprehensiveness wears off and he is put at ease, the alpha activity may more than double in the size of the waves and the percent of time present. This is something every EEG worker soon learns, namely, that a subject must be put at ease and assured that no harm will come from the procedure. Otherwise the sensitive alpha mechanism will not generate the optimal alpha rhythm for that subject.

It is now known that the alpha rhythm and its underlying pacemaking mechanisms in the thalamus are closely linked with the ascending reticular activating system, so that nonspecific sensory activation results in desynchronization of the alpha rhythm, often to the extent of blocking it completely, although in other instances only depressing it partially. It is sensitive to unexpected sensory stimuli, to factors which modify the state of arousal and alertness or vigilance, and events which elicit or demand specific atten-

tion whether they be external events or internal events such as thoughts, ideas, worries, etc.

In animals there are waves comparable to alpha waves in the human subject. In monkeys, when relaxed and quiet, there are alpha rhythms similar to those in humans although the frequency on the average tends to be a little lower. In cats, normally very vigilant animals and seldom completely relaxed unless asleep, poorly developed alpha rhythms of about 7–8 per second may be seen but are usually not as rhythmical and regular as in man and monkey. In rabbits 5–6 per second alpha waves of good rhythmic quality can be obtained rather easily under the right environmental conditions.

In cats and monkeys, when alpha waves are present, it can easily be demonstrated how natural arousal stimuli will block the waves, and how artificial electrical stimulation of the reticular formation will quickly block or desynchronize the rhythmic waves. This is called an activation or arousal response. The anesthetic state induced by barbiturate anesthesia reduces activity in the reticular formation and accordingly reduces the state of cortical activation, allowing the cortical activity to be dominated by slow waves and periodic spindle bursts like those seen in the onset stages of sleep. In a relaxed animal in a very light state of anesthesia, without pain or stimulation, alphalike waves tend to return.

2. Beta Waves

Berger defined beta waves as low amplitude fast rhythms ranging from 20 to 50 per second and even higher. Later Jasper and Andrews (1938) referred to beta waves as ranging in frequency from about 18 to 30 per second and called waves in the range of 30 to 50 per second gamma waves. The voltage of beta and gamma waves is of the order of 1 or 2 to 10 μV, although sometimes they may attain a level of 20 μV. As previously mentioned, their small amplitude relative to the alpha and other types of activity, the tendency to confuse them with muscle potentials, amplifier noise or 60 cycle interference, plus the fact that when studied by spectral analysis methods they have not been particularly revealing, has often resulted in their being ignored. Probably more systematic effort should have been devoted to the study of beta and gamma waves. Jasper and Andrews (1938) studied them over the motor and frontal regions, where they are often larger and more evident because the alpha rhythm there is lower than over sensory zones. There is some indication that they may be affected by tactual, auditory, and emotional stimulation. Jasper and Penfield (1949) found that beta waves in local regions of the exposed precentral motor cortex of man under local anesthesia were blocked by voluntary effort.

3. Delta Waves

This term was introduced by Walter (1937) to describe slow waves of large magnitude, usually 2 or 3 per second or less, observed in the region of brain tumors. Slow waves of 0.5 to 5 per second are often generated diffusely over the head when intracranial pressure is increased, either by expanding lesions such as tumorous growths or due to blockage of the cerebrospinal fluid system. Figure 1-9 illustrates delta waves associated with a brain tumor in a 12-year-old girl and in the lower section demonstrates localization of the tumor by phase reversal technique. In the deep or slow wave stages of sleep in normal persons, waves of this character are typical and have also been called delta waves. Similarly, the low frequency alpha waves at 3 or 4 per second in an infant of 3 or 4 months of age fall in the range of delta frequency, but as Fig. 1-2 shows, there seems to be a continuous growth in frequency of these waves as a function of age and therefore it seems appropriate to call them alpha waves rather than delta or theta waves as they pass through the 3–5 or 5–7 per second frequency bands. Delta waves are common during unconsciousness, whether induced by sleep, syncope, anesthesia, a blow on the head, or following a major convulsive seizure. Slow delta waves may range from 20 to 30 μV to several hundred microvolts.

4. Theta Waves

The term theta waves or theta rhythms was also introduced by W. G. Walter in about 1943. In a popular book, entitled *The Living Brain,* Walter

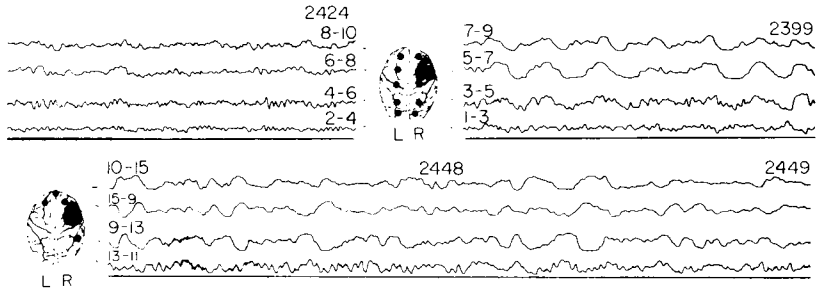


FIG. 1-9. Localization of a brain tumor in a 12-year-old girl by electroencephalography. Large slow *delta waves* arise from around the region of the tumor in the right frontal lobe. Brain surgery confirmed the location of a large oligodendroglioma. In bottom record electrodes were arranged in a line around the right side of the head so as to localize the disturbance by phase reversal procedure. Note that the two tracings with electrode 9 in common, but connected to each channel of the EEG in opposite orientation, show the delta waves reversed in phase. (From Lindsley, 1944. Copyright 1944, Renewed © 1972 The Ronald Press Company, New York.)

(1953) speculated that alpha waves scan for information and theta waves scan for pleasure. In human subjects, especially children and adolescents, theta rhythms of a frequency of about 5 to 7 per second are frequently observed over temporal and frontal regions of the head. Because they are especially characteristic of the hippocampus (Green & Arduini, 1954) and the limbic system, it is often assumed that their presence in the frontal and temporal EEG of humans bears some relation to the functioning of the limbic system. Theta waves in the human EEG are usually very rhythmic and occur in runs of several seconds in duration with periods of relative quiescence between runs. In other instances they may be more continuous.

Numerous studies have shown that waves and rhythms in the range of frequencies of both the delta waves and theta waves are often common in children with behavior disorders (Lindsley & Cutts, 1940; Lindsley & Henry, 1942). The magnitude of these waves is usually in the same range of voltage as the alpha waves. It seems likely that such aberrant activity (but also observed in the EEGs of some "normal" children) may represent pathophysiological activity in some way related to periods of physiological instability during the course of development, and perhaps augmented by psychological difficulties and maladjustments, in the course of "growing up." Figure 1-10, from Lindsley and Cutts (1940) illustrates some of the foregoing types of waves in the EEG of a "normal" child and in two children with "behavior disorders." Record (A) from a normal 11-year-old boy shows well-regulated alpha rhythms of about 10 per second in the occipital, parietal, and central regions and a mixture of alpha and faster beta waves in the frontal region. Record (B) is the EEG of an 8-year-old boy with a behavior disorder whose EEG shows abnormal slow wave activity (low to moderate amplitude deltalike activity) in all regions, but especially in the parietal region. Alpha rhythms are visible mainly in the occipital area. Record (C) is the EEG of a 10-year-old boy with a behavior disorder whose frontal EEG tracings show prominent bursts of 6 per second (theta rhythm) activity; the central tracing shows a mixture of low amplitude alpha and theta activity and the occipital tracing shows mainly alpha activity with occasional intrusion of a longer duration wave. Both of these children with behavior problems were otherwise healthy and had a normal physical and neurological examination.

Several studies have shown that approximately 75% of children with behavior disorders manifest one of these types of "abnormalities" in their EEG. The aberrant waves and rhythms are much less prominent both in voltage and in percent of time present than in children with convulsive disorder or other types of neurological problems. The EEGs of "normal" children show a small amount of these slower than alpha rhythms, but generally form a sharp contrast with the behavior problem groups in terms

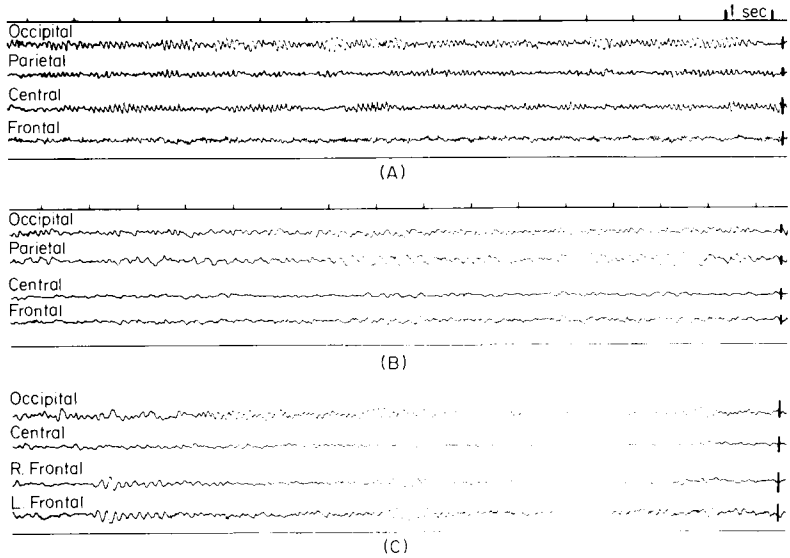


FIG. 1-10. Electroencephalograms from a normal child and two children with behavior disorders. (A) EEG of normal 11-year-old boy showing well-regulated alpha rhythms at about 10 per second in occipital, parietal, and central regions and a mixture of small amplitude alpha and beta waves in the frontal regions. No abnormal waves present. (B) EEG of an 8-year-old behavior problem child showing abnormal delta waves of 4 per second, most marked in the parietal region. Child is not asleep; alpha waves are mixed with delta waves in the occipital region. (C) EEG of 10-year-old behavior problem child showing rhythmic spindle like runs of 6 per second theta waves in both frontal areas, but with normal alpha rhythms in the occipital region. (From Lindsley & Cutts, 1940. Copyright 1940 American Medical Association.)

of the incidence and amount. Much of the time behavior problem children appear like normal children, but their behavior may be rather intensely disturbing at times and aberrant behavior seems to have a lower threshold for the effects of environmental stress, both physiological and psychological. On the other hand, as is well known, so-called "normal" children can on occasion manifest behavior disruptions, tantrums and the like. The EEG disturbances in children with behavior disorders seem to be more a matter of degree and persistence than a pathognomonic feature, and probably reflect physiological instabilities of the autonomic and central nervous systems rather than an organic pathology.

5. KAPPA WAVES

Kennedy, Gottsdanker, Armington, and Gray (1948) described an alpha-like rhythm at the temples which they thought to be associated with intellectual processes. It has a frequency of 8 to 12 per second and is of about 20 μV. It tends to occur in spindle-shaped bursts and is increased by reading,

mental arithmetic, difficult discriminations, memory tasks, and problem solving. It could be found in only about half of the subjects tested. The kappa rhythm is believed to arise in the temporal lobe, but most others who have searched for it have not found it or become convinced of its validity. It seems possible that oscillatory eye movements, of which there is a wide range, may be responsible since in thinking and problem-solving efforts people often tend to move their eyes and readjust their fixations frequently. A recent study of kappa and alpha activity during learning and problem-solving tasks by Chapman (1972) suggests that there are great individual differences, but in those subjects who show the kappa rhythm, it seems to be a reliable effect.

C. Clinical and Experimental Uses of the EEG

From what has been said heretofore about the normal spontaneous or background EEG, comprised typically of alpha and beta waves during the waking state, with some degree of theta activity occasionally exhibited under some conditions of stressfulness psychologically or physiologically, one might conclude that the EEG is a complex affair, which indeed it is, and not subject to very clear and precise definition. To some extent this is true, for alpha waves vary with physiological and psychological state, as has been pointed out, but this should be expected. If the alpha waves and other EEG wave patterns originate in cortical neurons and their meshwork of circuits, it must be realized that these cells, like other body cells, are subject to the variations of the fluid and chemical environment in which they are bathed and from which they derive their nourishment. Brain cells are known to be especially sensitive to such variations and the lack of oxygen for a very brief time will damage them irreparably. Fluctuations of the blood sugar level above or below the range of roughly 80 to 120 mg per 100 ml of blood, or perhaps an even greater variation beyond the limits of 60 to 140 mg can have serious consequences leading to coma, convulsions, and even death if not remedied, as is well known in the case of diabetics without insulin or following an overdose of insulin without access to sugar. Normal babies frequently manifest convulsions when their body temperature exceeds 104 or 105 degrees due to fevers accompanying illnesses. Fortunately, compensating endocrine, autonomic, and other physiological and chemical mechanisms permit a certain amount of homeostatic adjustment to such stressful factors, but there are limits beyond which the sensitive nerve cells of the brain will not perform normally and may even succumb. Similarly too, psychological factors can be stressful and interact with physiological and chemical factors to produce aberrant neural and behavioral performance. Even subtle conditioning and learning influences of

a normal environment may be reflected in the affective, emotional, and attitudinal behavior of the person and in the way his nervous system performs its important integrative and controlling activities.

Table 1-2 represents an attempt to view behavioral and EEG phenomena or parameters in terms of a continuum. Empirically this has seemed justified providing one accepts such a model only as a working hypothesis and with full realization that the model or parts of it must be subject to change if subsequent results do not bear it out. Lindsley (1952) proposed this model and acknowledged that some of it was based on empirical fact and some of it on fiction or speculation. Some of it, conscious states or states of awareness, as correlates of the more substantially determined and objectively observable behavioral and EEG states, are based only on what might appear to be everyday or commonsense interpretations of subjective experiences and consciousness. Until we have more objective indicators of these states, like electrophysiological events or behavioral responses, the matter of dealing with mental life will remain in the speculative and fictional vein. But the EEG, CNV, and average evoked potentials provide some hope of a liaison between the more objective and the less objective.

The notion of an EEG continuum, ranging from fast, low-amplitude waves (desynchronization, activation, or arousal, to use some overworked and somewhat indeterminate terms and concepts) during emotion and/or attentiveness, to synchronized alpha waves of intermediate frequency, and then gradually lower and lower frequency waves as sleep and its deeper stages follow, seemed to be a generally recognized and acceptable empirical observation. It seemed to fit in with the general concept of the role of the reticular activating system which was emerging in the late 1940's and early 1950's. To be sure, there have been numerous specific exceptions to the general and broad conceptions of the role of the reticular formation and of arousal mechanisms, but withal, the reticular system and arousal concepts have been useful in stimulating further thought and research. Indeed, the basic ideas involved have yet to be overthrown. For the most part what has been attacked and in some instances demolished are the extrapolations of the basic notions sometimes far beyond where the initiators of the original work and ideas would have gone.

At more prosaic levels of consideration, the background spontaneous EEG in both man and animals has been a useful index of the state of the organism, especially as influenced by its brain. Like electricity, one can use the EEG as an index or measure of something without knowing precisely what it is or how it works. Even though one is studying or measuring something else, the degree of synchronization of the EEG or its opposite, desynchronization or activation response, can be useful to warn when a change has taken place in the state of the brain's condition. One notes this

TABLE 1-2

PSYCHOLOGICAL STATES AND THEIR EEG, CONSCIOUS, AND BEHAVIORAL CORRELATES[a]

Behavioral continuum	Electroencephalogram	State of awareness	Behavioral efficiency
Strong, excited emotion (fear) (rage) (anxiety)	Desynchronized: Low to moderate amplitude; fast, mixed frequencies	Restricted awareness; divided attention; diffuse, hazy; "Confusion"	Poor (lack of control, freezing-up, disorganized)
Alert attentiveness	Partially synchronized: Mainly fast, low amplitude waves	Selective attention, but may vary or shift. "Concentration" anticipation, "set"	Good (efficient, selective, quick, reactions). Organized for serial responses
Relaxed wakefulness	Synchronized: Optimal alpha rhythm	Attention wanders—not forced. Favors free association	Good (routine reactions and creative thought)
Drowsiness	Reduced alpha and occasional low amplitude slow waves	Borderline, partial awareness. Imagery and reverie. "Dreamlike states"	Poor (uncoordinated, sporadic, lacking sequential timing)
Light sleep	Spindle bursts and slow waves (larger). Loss of alphas	Markedly reduced consciousness (loss of consciousness). Dream state	Absent
Deep sleep	Large and very slow waves (synchrony but on slow time base). Random, irregular pattern	Complete loss of awareness (no memory for stimulation or for dreams)	Absent
Coma	Isoelectric to irregular large slow waves	Complete loss of consciousness, little or no response to stimulation; amnesia	Absent
Death	Isoelectric: Gradual and permanent disappearance of all electrical activity	Complete loss of awareness as death ensues	Absent

[a] From Lindsley (1952).

repeatedly when working under barbiturate anesthesia, for the EEG is often a sensitive indicator of the depth or lightness of the anesthetic state even before an animal manifests by behavioral signs that there is a need for supplemental doses of the anesthetic. Similarly, in humans subject to seizure states, the EEG often provides premonitory signs before convulsive activity actually begins, or in the case of petit mal epilepsy there may be no behavioral indications of a seizure but highly distinctive and pathognomonic signs in the EEG. The fact that a sensory stimulus will block the alpha rhythm repeatedly but after a time habituation of the blocking response sets in, is indeed an indication that the EEG has value in the attempt to understand psychological processes and in judging whether, for example, in a psychophysical experiment, the data are worth collecting beyond a certain point in the experiment. We have learned much about the stages of anesthesia and sleep, and about the processes of perception and attention that we did not know before. We may not yet have learned enough, but we have benefited by having the EEG as an extra indicator.

1. Use of the EEG to Determine Effectiveness of Anticonvulsant Drugs

In the case of petit mal epilepsy which has a unique spike-and-slow-wave signature, it is not always possible to know from behavioral evidence when a seizure occurs. There is no loss of consciousness and falling to the ground in convulsive jerkings as in grand mal epileptic attacks. There may only be a few seconds hesitation in the flow of speech, momentary fixation of the eyes as if staring into space, or perhaps no ready indication at all that one of several hundred spells a day has occurred. The EEG made it possible to know not only when the brain manifested a spike-and-slow-wave seizure discharge but also when there was a subclinical attack with no external manifestations at all and no awareness on the part of the patient that an attack had occurred. This is illustrated in Fig. 1-11 showing three EEG records from a 7-year-old boy subject to petit mal epilepsy attacks. The top tracings show the EEG from occipital and precentral (motor) regions of the brain during a preseizure period. To the unpracticed eye the record looks almost normal, and indeed it is compared to the other records, but an experienced EEG reader would detect at once that there are incipient spikes and slow waves in the precentral traces and, in addition to alpha waves in the occipital traces, there are some slower than normal waves. None of these is of large amplitude at this stage. A few moments later the patient's EEG produced the middle record, labeled a subclinical attack. There were still no behavioral signs of a seizure, but the left occipital tracing has now developed continuous 3 per second slow waves with occasional suggestions of spikes, and some of the effect has spread to the right occipital area,

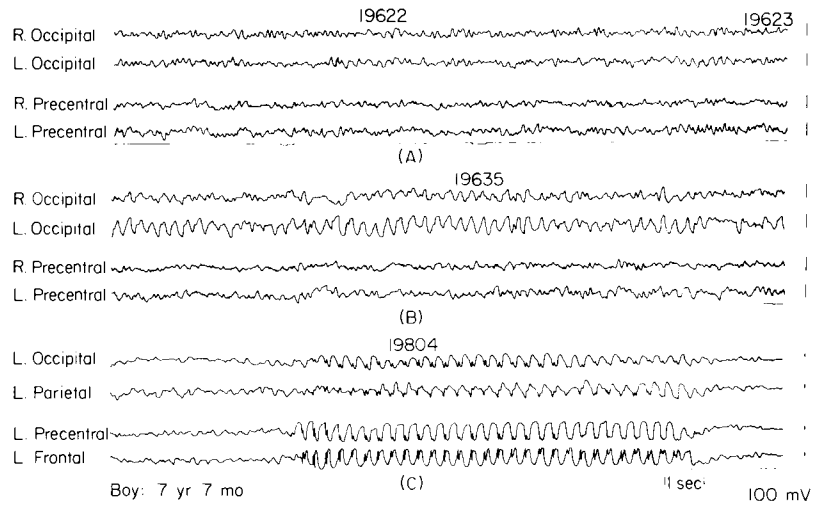


FIG. 1-11. Electroencephalogram from a 7-year-old boy with petit mal epilepsy, showing spike and slow wave patterns at 3 per second during full-blown seizure (bottom), a partial seizure (middle) and a preseizure record showing subthreshold attack abnormalities. (From Lindsley, unpublished data.)

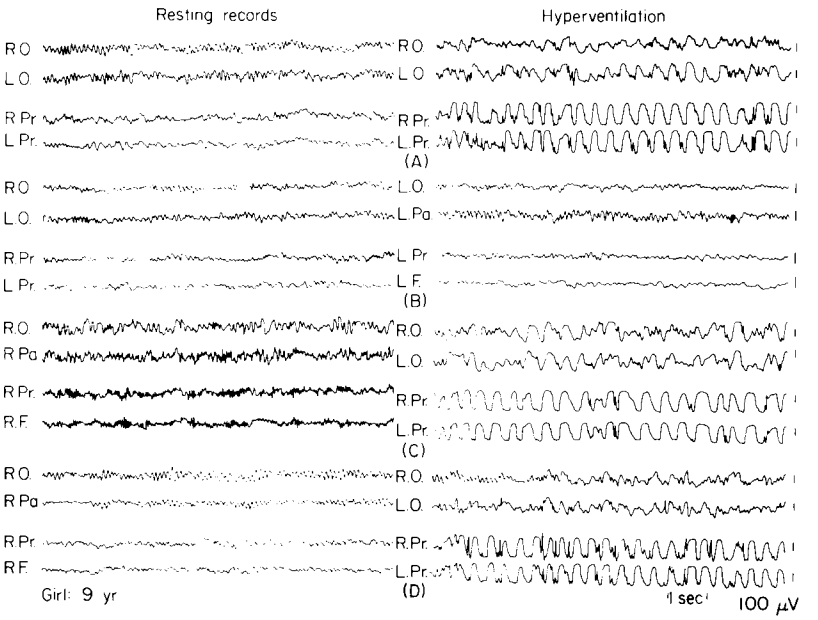


FIG. 1-12. Use of EEG to test the effects of anticonvulsant drugs on a 9-year-old girl with petit mal epilepsy. Left column shows resting EEG and right column the activated EEG (seizure discharges induced by hyperventilation or overbreathing) under the following conditions: (A) without medication, (B) Tridione, 1500 mg daily, (C) Phenobarbital, grains 1 three times daily, (D) Dilantin, grains ½ daily. Only Tridione prevented seizure discharges during hyperventilation but in that dosage suppressed somewhat the normal alpha waves of the resting occipital tracing. Phenobarbital induced fast activity in all tracings during the resting state and did not protect against a seizure discharge during hyperventilation. Dilantin was not effective in this case in blocking seizure discharges. See text for further comment. (From Lindsley, unpublished data.)

though the precentral or motor areas are yet relatively unaffected. Could the left visual area process information while such aberrant slow waves are present instead of the normal alpha waves? It would be interesting to know. In all likelihood some aspect of the visual perceptual process would have been adversely affected.

But let us look at the full-blown seizure in the lower record showing spike and slow wave patterns in all traces on the left side: occipital, parietal, precentral, and frontal, with the precentral and frontal traces showing a phase reversal indicating that the focus of the seizure (as it often is in petit mal epilepsy) is in the premotor region. Records such as these may be taken any time and repeatedly, without trouble or travail. It should be evident that they can tell the pediatrician or neurologist a good deal more about the way the brain of his patient is functioning than he can learn from taking a history from the parents, who may or may not know that the child has "spells" or "fits" as seizures are sometimes called. A neurological examination may or may not reveal them, depending upon the nature and overtness of the attacks. The EEG is not a substitute for a neurological examination or for other medical investigations. It is an adjunct, but sometimes, as in this kind of epilepsy, a very important one for under prolonged study one may learn how frequently the attacks occur and with what variations, how many occur during a day, or during a month. Furthermore, periodic EEGs by a time-sampling method can be a more accurate gauge of the effectiveness of treatment by either anticonvulsant drugs or diet, and one more economical of time than waiting for the parental report or other indications while the child is at home or in school. Also, the EEG can help to select the most effective drug for the particular case. This is illustrated in Fig. 1-12 where three different drugs were compared for their effects upon the tell-tale pathognomonic spike and wave pattern of petit mal epilepsy.

Rather than just waiting for the pattern to occur spontaneously during the resting record, a procedure of hyperventilation was employed as well. In this procedure, a 9-year-old girl breathing deeply for 30 sec or so was enough to set off a spike and wave seizure discharge, as is shown in the top record without medication. The resting records show essentially normal alpha rhythms in the occipital regions and only low amplitude slow waves in the precentral regions; during hyperventilation there is continuous seizure discharge. The second record under Tridione, a medication sometimes effective in petit mal epilepsy, shows that both the resting and the hyperventilation portions were completely free of seizure discharges. It is to be noted, however, that the normal activity (alpha rhythm) of the occipital regions was depressed compared to the resting record with no medication. Thus the abnormal feature, the spike and wave activity, had been suppressed,

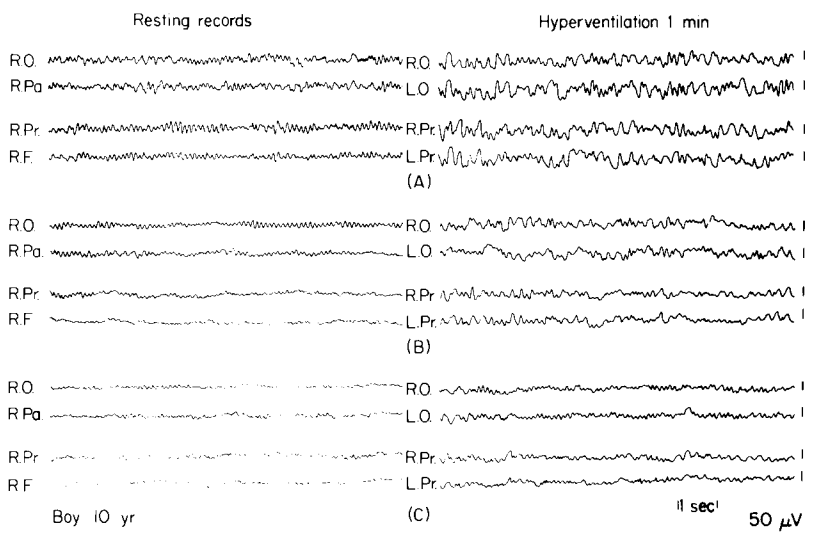


FIG. 1-13. Use of EEG to find the most effective dosage of an anticonvulsant drug in the case of a 10-year-old boy with petit mal epilepsy. Left column shows resting EEG, right column one minute after hyperventilation started. (A) without medication, (B) Tridione, 900 mg daily, (C) Tridione, 1200 mg daily. Only the latter completely suppressed slow wave seizure-like discharges during hyperventilation, but it also reduced the amplitude of normal alpha rhythms in the resting EEG. See text for further comment. (From Lindsley, unpublished data.)

but with it some of the normal activity as well. The conclusion to be drawn from this is that Tridione is effective in this patient but the dose is probably a little too high. Phenobarbital did not suppress the seizure activity and furthermore introduced an undesirable amount of fast activity (beta or gammalike waves) in the resting record. Dilantin left the resting record looking quite normal with good alpha rhythms in the occipital and parietal regions but did not prevent the seizure discharges during hyperventilation.

In another patient with petit mal seizures, a boy of 10 years, Fig. 1-13 shows how the most effective dosage of Tridione was determined using the EEG to reveal what was happening to the electrical activity of the brain during resting and hyperventilation periods. Here it will be observed that 900 mg daily left the resting record looking very normal but did not quite suppress all of the seizure activity during hyperventilation. Tridione in the amount of 1200 mg daily gave essentially a normal EEG during hyperventilation, but depressed slightly the normal alpha activity during the resting period. On the basis of this test one would judge that a dose between 900 and 1200 mg would probably be about right. There are many other instances of this kind where the EEG can be of aid in evaluating treatment procedures because it is sensitive to changes in the brain's activity which

may or may not be reflected always in the behavior and performance of the individual as clearly, or it may not be as easily assessed.

2. Experimental Studies of Perception and Attention in Animals and Man Using the EEG

Experimental studies are often more demanding than clinical studies as specific information is sought and usually some particular hypothesis relating to a conceptual model or a theory is up for test and appraisal. Often rigid controls are employed so as to limit the observed data to the specific stimulus conditions being studied.

Let us first consider briefly two animal experiments which used combined electrophysiological and behavioral observations. Both studies were concerned with perceptual discrimination and stimulus conditions which were limiting in one way or another. Both studies replicated essentially what had already been done with human subjects in our laboratories. In the case of the humans the EEG and average evoked potentials were recorded while the subject was making judgments about the stimuli, utilizing psychophysical methods. These results were very satisfactory and the EEG and judgmental data reinforced one another, but there was a feeling that we needed to learn something more about the underlying mechanisms by recording along the visual pathways from the eye to the visual cortex. This could not be done in our human subjects, so we turned to animals, cats and monkeys, where we could implant electrodes in the optic nerve or tract, lateral geniculate body, and visual cortex. Figure 1-14 shows one stage in the process of implanting electrodes and cryogenic probes for cooling and blocking reversibly the functional activity of pathways or nuclei. We see here a cat with its head in a stereotaxic instrument which will serve to guide our needlelike electrode probes to the exact site where we wish to record, the coordinates of the structure having previously been determined from a stereotaxic atlas. The cat is, of course, under deep anesthesia, either a barbiturate such as pentobarbital injected intraperitoneally with supplements administered as needed through a cannula in a leg vein, or by a fluothane gas mixture administered by an anesthesia machine through a snout mask.

In the case of the visual system, it is possible to ensure that each electrode is located in its appropriate structure as intended by the stereotaxic coordinates by flashing a light in the eyes of the cat and recording the response or looking at it in the oscilloscope. If necessary it can be readjusted to secure an optimal response before sealing it in place. Usually these implantations have been preceded by a number of "acute" experiments in which one not only identifies the appropriate site for the electrodes but becomes familiar with the type of responses that can be obtained.

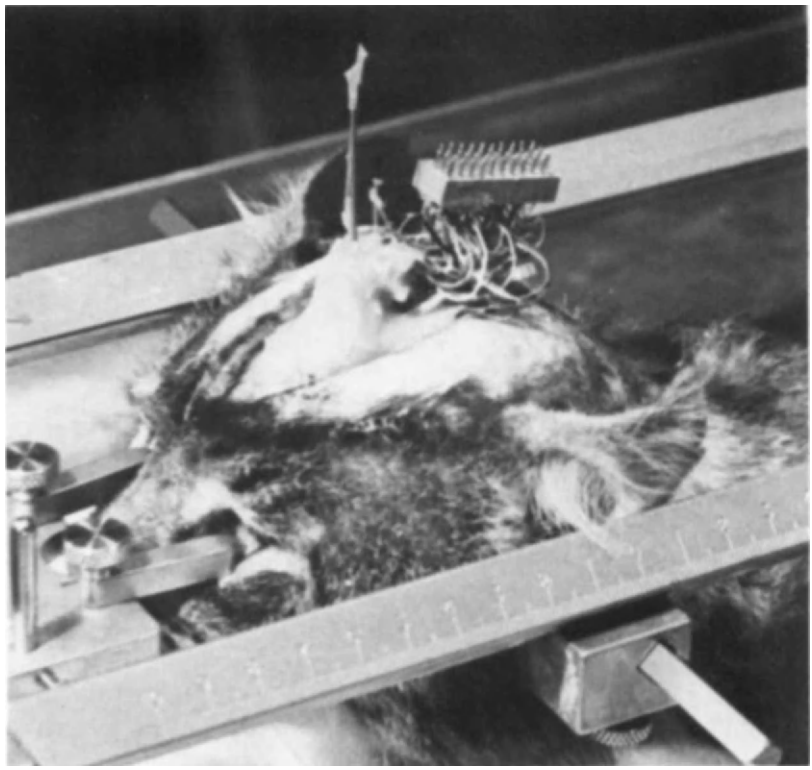
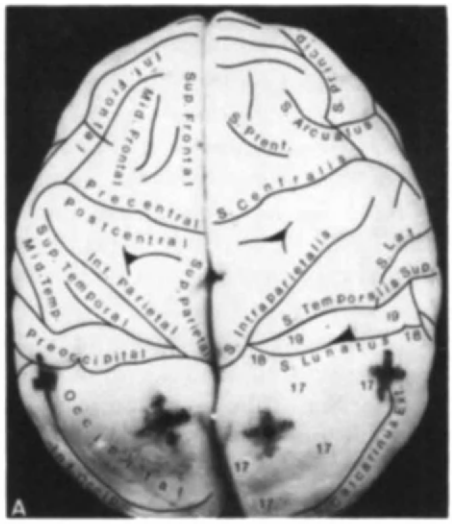


FIG. 1-14. Cat's head in stereotaxic frame during a stage in the implantation of many recording electrodes and a cryoprobe in the brain. All electrodes are now in place and their wires connected to the many-pronged plug which will be sealed in with dental acrylic, forming a mound on the head. When the cat recovers from the operation it will perform behaviorally and have the electrical activity of its brain recorded simultaneously. A connector plug and cable will be attached to lead the electrical responses to a recording instrument, either CRO or EEG, or both.

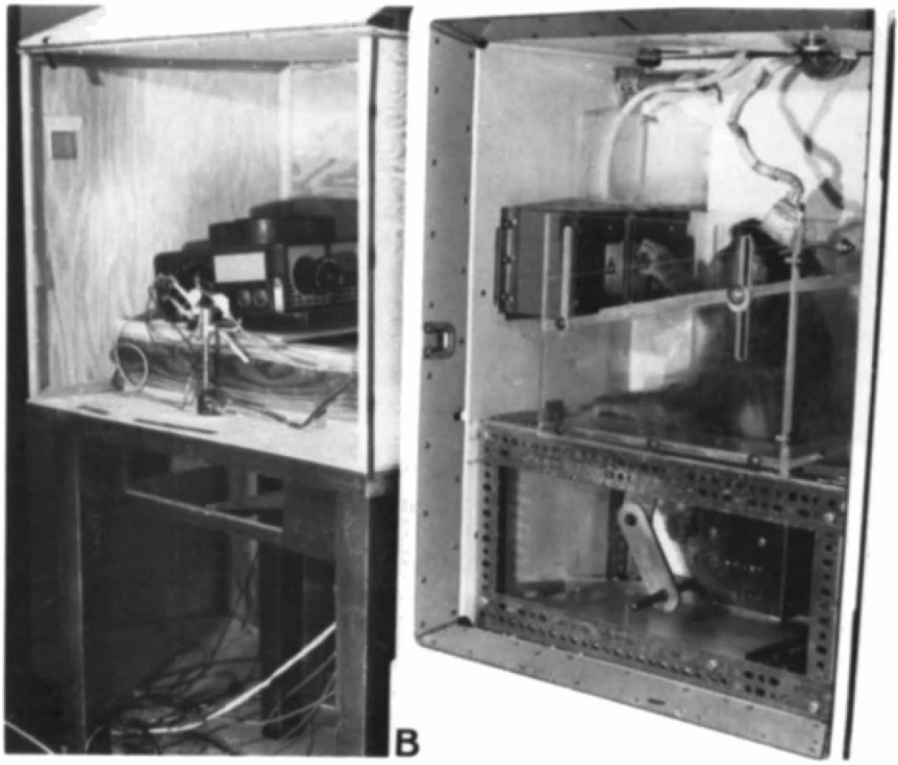
FIG. 1-15. (A) Photo of *Macaca nemestrina* brain with gyri labeled on left and sulci on right. Crosses show location of electrodes over the occipital region in primary visual area 17. The laterally placed electrodes were near the foveal projection area and the medial ones about 6 degrees out, according to the Talbot and Marshall (1941) data for cortical representation of the retina.

(B) Recording electrophysiological and behavioral responses of a monkey during performance of a visual pattern discrimination. Monkey has correctly discriminated "square" from "triangle" and is pressing the panel where the square appeared. See text for details. Door of chamber and optical projection box would normally be closed and the stimulus presentation would last only 10 msec. (From Fehmi, Adkins, & Lindsley, 1969.)

Figure 1-14 shows a stage where all electrodes have been sited over the visual cortex and in the deep visual structures for recording and perhaps others for stimulating elsewhere in the brain, such as the reticular formation in the lower brainstem. The connections from each electrode have been made with the appropriate jacks or prongs in the connector plug shown


A
Inf. frontal
Mid frontal
Sup frontal
Precentral
Postcentral
Sup temporal
Mid temp
Inf parietal
Sup parietal
S. Centralis
S. Lat.
S. Temporalis Sup.
S. Lunatus
Occipital
17
18
19

(A)


B

(B)

FIG. 1-15

ready to be cemented into place on the skull by means of dental acrylic. The wires will all be covered over by the mound of acrylic which is further anchored by stainless steel skull screws at its base. The tubes sticking up are part of the double cannula system which carries cooled alcohol under pressure to the tip of the cryogenic probe where local cooling takes place (see Skinner & Lindsley, 1967, 1968, 1971). When the whole implantation procedure is complete and experiments are ready to begin in the "chronic" behaving animal, these tubes are connected to flexible fine-gauge polyethylene tubing carrying the coolant. A heater wire supplied by d.c. current keeps the shaft at brain temperature, and microthermocouples on the shaft and the tip of the probe monitor the temperature of each. The electrodes for electrical recording or stimulation are plugged in to a matching plug and cable carrying the potentials to the EEG amplifiers and the stimulating current to the animal.

In one experiment (Peck & Lindsley, 1972) cats were trained behaviorally to discriminate a single flash of light from a pair of flashes separated by an interstimulus interval (ISI) of 200 msec or less. The problem was to reduce the ISI to a value where the discrimination could no longer be made and to record from the optic nerve or tract, lateral geniculate nucleus, and visual cortex and attempt to determine where in the visual system this limit to perceptual resolution occurred. The ISIs for two-flash thresholds in humans, depending upon stimulus parameters, usually range from 50 to 80 msec and the behavioral two-flash thresholds for the cat were found to be comparable. At all levels of the visual pathways two flashes at an ISI of 20 msec produced an average evoked potential which closely resembled that of a single flash. Obviously, if the nearly identical responses to a pair of flashes and a single flash reflect accurately the underlying impulse discharges or messages being conveyed to a central "discriminator," their essential identity would leave nothing to discriminate which seems to have been the case with flash pairs having short ISIs.

In another experiment, similar implantations were made in *Macaca nemestrina* monkeys. The purpose of this experiment was to duplicate a backward or retroactive perceptual masking study carried out in humans by Donchin, Wicke & Lindsley (1963) where the only electrophysiological response recorded was the average evoked response from the scalp over the visual association areas. The monkeys in this experiment had electrodes (skull screws) directly on the dura over primary visual area 17 (see Fig. 15A), but also electrodes in the optic tract for monitoring retinal ganglion cell responses and in the lateral geniculate body.

The monkeys were trained to discriminate a triangle from a square and gradually the time of the stimulus presentation was reduced to 10 msec with performance at the 95–100% correct level. After overtraining at this level, a 20-μsec photoflash masking stimulus was introduced at ISIs of 450 msec which did not interfere with the discrimination of the square

from the triangle presented in the first test flash. Only when the interstimulus interval had been reduced to 20 msec did performance drop to chance level and it was at a point approaching this level that it was of special interest to examine the electrical responses recorded along the visual pathways. As it turned out (see Fehmi, Adkins, & Lindsley, 1969), most, but not all, of the masking effect occurred in the retina. An important aspect of this kind of experiment resides in the programming. The monkey had to learn to press a lever to initiate a trial, after which there was a 300-msec delay before the 10-msec test flash occurred. This allowed the monkey to fix his gaze on the two display panels before him. If he pressed the panel with a square on it (see Fig. 15B), he received a banana pellet reward. Then there was a 15-sec time-out, after which he could press the lever for another trial.

This discrimination task, but without the masking stimulus, is now being used to study the EEG changes, especially the average evoked potentials, which occur with the learning of a new discrimination after the whole program has been learned. A program for analyzing the results with a PDP-12 computer has been written and the changes which occur in the visual cortex, lateral geniculate nucleus, and the pulvinar of the posterolateral association nuclear group of the thalamus are proving very interesting indeed.

These animal experiments show how it is possible to examine perceptual discrimination and learning processes simultaneously by behavioral and electrophysiological methods. The EEG, average evoked potentials, and the CNV are all aspects of the electrical signs of underlying activity in terms of which it is hoped that a better understanding of perceptual and learning processes will come about.

Another type of animal experiment in which the EEG and deep brain recordings played a very significant role was concerned with the effects of long-term sensory (light) deprivation (Lindsley, Wendt, Lindsley, Fox, Howell, & Adey, 1964). Monkeys were kept from infancy in isolation in a light-tight and soundproofed box for 2–3 years. Except for 1 hr of unpatterned diffuse light each day to prevent retinal degeneration, the monkeys were deprived of light for a prolonged period of time. The daily light period was shifted so that circadian rhythms were disrupted. Bodily activity was recorded and it was found that the activity cycles anchored themselves to the light periods, shifting accordingly as the light periods varied from time to time. The EEGs recorded near the end of the light deprivation period of 2 years or more showed a remarkable change. Whereas normally the spontaneous rhythms (alpha) of the EEG in man and monkey block to the onset of light, these monkeys showed a reverse pattern with waves and rhythms present during light stimulation and blocking when the light was turned off (see Fig. 1-16). Spontaneous activity after long-term deprivation was monitored by infrared television and recorded on film. Bizarre forms

of behavior in the isolation box occurred, with animals biting and slapping their limbs, moving ceaselessly about the sides of the cage, and exhibiting ritualistic movements while eating. Their behavior suggested sensory hunger and disorientation in time and space. These bizarre behavioral manifestations seemed to correspond to the abnormal and paradoxical EEG reactions of blocking of alpha rhythms to darkness instead of light. A further interesting fact was the intensity and persistence of their drive to satisfy their sensory hunger for light. When allowed to bar press for 1 sec of light per press and in this way fulfill their diffuse light requirement, they continued to press at near maximum rates (in excess of 2000 to 3000 presses per hour) for 16 weeks, whereas control animals with 22 hr of light deprivation per day during the testing period only pressed for light at rates averaging 100 per hour, even after 9 weeks of deprivation.

Figure 1-17 illustrates the layout of an experimental arrangement for testing an hypothesis which relates to the alpha wave of the EEG as an excitability cycle. Lansing (1957), working in my laboratory, used a reaction time paradigm to test the hypothesis I had proposed earlier (Lindsley, 1952) and developed further later (Lindsley, 1961). Briefly, Lansing found that there was a time segment of the 100-msec alpha wave cycle when a light flash which triggered a simple reaction time response in the subject would result in the shortest reaction times, whereas at other periods in the cycle reaction times were longer. This fit the notion that impulses (in this case from the light flash) reaching the cortex at a favorable time in the alpha cycle would get through without delay, whereas at other times the delay in passage due to decreased excitability would cause reaction times to be longer. It was well known that reaction times do vary widely when they are tested serially, so that Lansing's finding seemed to provide partially confirming evidence for the hypothesis as to why reaction times vary. Lansing, Schwartz, and Lindsley (1959) followed with an experiment that showed reaction time could be maintained consistently at a low level (as has been known from the time of Wilhelm Wundt) if an auditory stimulus serving as a forewarning signal preceded the light flash by at least 300 msec, which is just sufficient time to desynchronize the alpha rhythm. Lindsley (1961) had interpreted desynchronization of the alpha rhythm to mean that several subaggregates of neurons or neural circuits could beat with their own microalpha rhythm but maintain their excitability periods at different times and afford alternative pathways for the processing of incoming information. This would cause a shorter delay time because of the almost continuous availability of an optimal excitability cycle in one group or another.

A measure of success with the two reaction time experiments in relation to the excitability cycle concept led us to try another experiment. This is the one illustrated by Fig. 1-17. EEGs were recorded from the subject while he fixated a central point on the screen before him where rear projection flashed tachistoscopically two letters to be perceived. A glow modulator

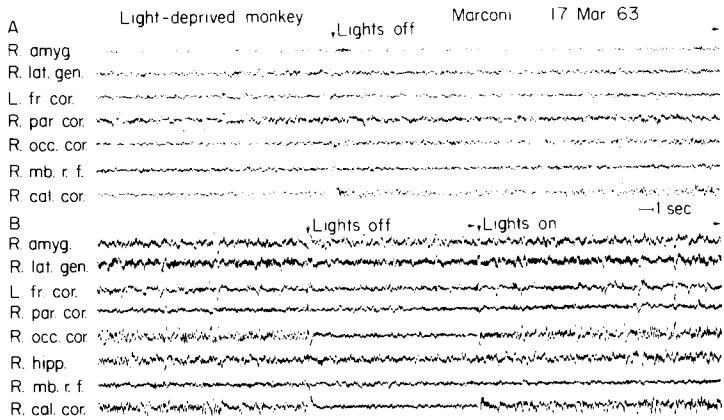


FIG. 1-16. Electrograms from various cortical and subcortical sites in a monkey isolated and light-deprived for a period of almost 3 years except for 1 hr of diffuse, unpatterned light per day. Monkey manifested bizarre behavior and signs of sensory "hunger." His brain electrograms showed paradoxical reactions to light stimulation, with alpha waves appearing cortically and theta waves in the hippocampus when the light was turned on; these waves disappeared when the light was turned off. Such reactions are the opposite of those for a normal nonlight-deprived monkey. Electrical recordings are from occipital, parietal, frontal, and calcarine cortex, midbrain reticular formation, lateral geniculate body, and the amygdala. (From Lindsley *et al.*, 1964.)

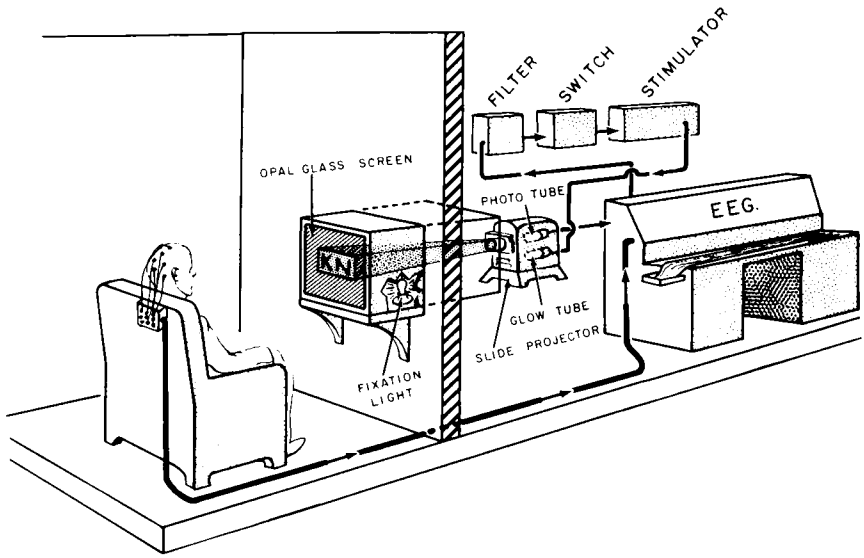


FIG. 1-17. Schematic representation of an experiment in which a brief tachistoscopic presentation is to be perceived, either during alpha abundance, during alpha blockade, or at various phases of the alpha wave excitability cycle. Stimulus patterns are projected on opal glass screen by glow modulator tube. A phototube records the flash on the EEG and it can be related to the phase of the alpha wave cycle. (From Lindsley, unpublished data.)

tube controlled the intensity and duration of the light pulse which flashed the letters on the screen. An alpha wave triggering device, something like a Schmitt trigger, permitted the timing of the flash in relation to a preceding alpha wave peak. Unfortunately, the data did not bear out the hypothesis this time and the experiment was abandoned in favor of other projects. The idea behind it was that the letters should be perceived at one and only one phase of the alpha wave cycle, but it did not work. I still have a feeling that the experiment should be repeated with the better facilities we now have for timing and triggering the test flash at even shorter durations.

Figure 1-18 shows an EEG record which portrays a slightly different version of the experiment. In this case the buzzer served to desynchronize the ongoing alpha rhythm and during the blocked period of the alpha rhythm the light flash presented the letters "KN." The subject's response is shown on the voice recording line. The object of this experiment, like the Lansing, Schwartz, and Lindsley (1959) reaction time experiment mentioned above, was to contrast the relative ease and speed of information processing during a period of desynchronized alpha rhythm with that when the test flash was presented during the full-blown alpha pattern.

3. Attention and Vigilance and Selective Attention Experiments with the EEG

Figure 1-19 shows the subject's apparatus employed in two attention and vigilance experiments. The subject is lying on a cot with his face in a viewing hood and looking at a 5 × 7 inch opal glass viewing screen. A television camera watches his face and especially his eyes to ensure that he remains awake, with eyes open and fixed on the screen. His task is simple, just to observe regularly appearing moderately bright flashes produced on the screen by a photoflash lamp at the rate of 1 every 3 sec. Interspersed aperiodically are several slightly dimmer flashes. The subject is instructed to press a key whenever he detects a dim flash. The dim flashes are inserted to keep the subject alert and vigilant, and also to provide a measure of his attentiveness and vigilance. This experiment by Haider, Spong, and Lindsley (1964) demonstrated that average evoked potentials recorded from the right occipital cortex and from the vertex during each 5-min period of a 1½ hr session, were larger by a significant amount during 5-min periods when the subject detected and responded to all ten interspersed signal stimuli than they were during other 5-min periods in which half or less of the signals were noted, even though the subject was awake. Furthermore, during the experiment there was an increase in response times to dim signals and a corresponding decrease in the size of the evoked potentials to the nonsignal stimuli. Thus as vigilance over the entire period waned so also did the amplitude of the evoked response.

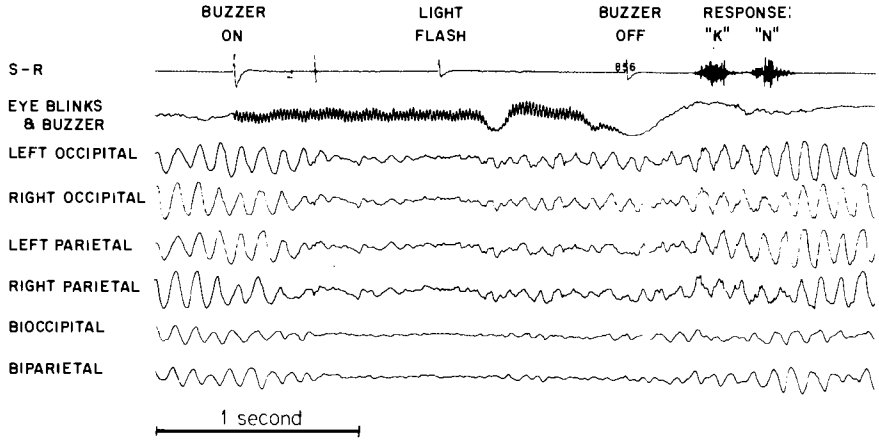


FIG. 1-18. Alpha waves recorded from various cortical areas during discrimination and report of letter pairs. Buzzer causes alpha blockade; light flash presents stimulus during alpha desynchronized period, and subject's voice response is recorded. After buzzer is turned off alpha waves return. (From Lindsley, unpublished data.)

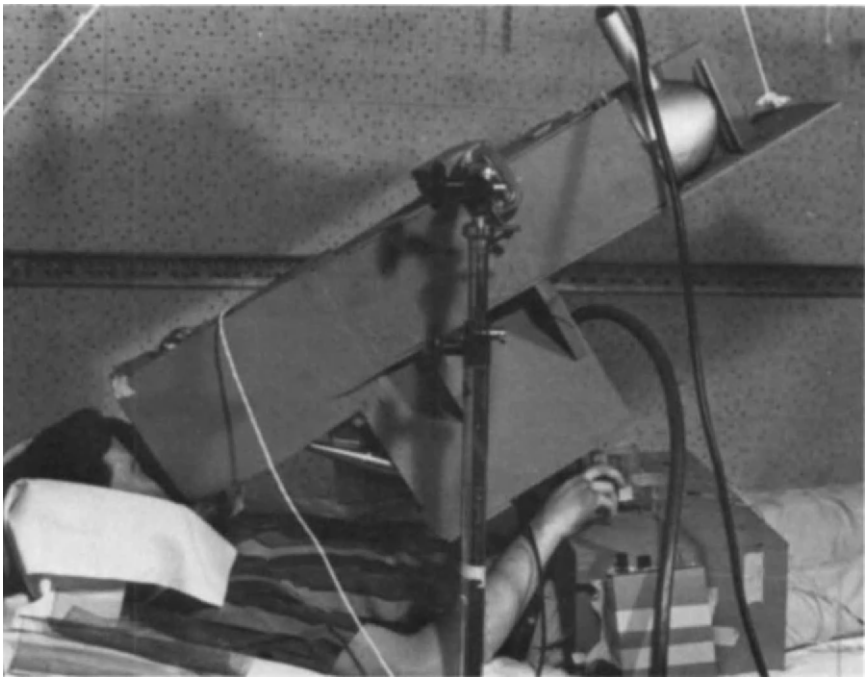


FIG. 1-19. Vigilance and attention experiment. Subject reclining and looking into viewing hood to fixation point on opal glass viewing plate. Photoflash at end of tube provides visual stimuli which alternate with clicks presented via insert earphones. Subject presses key when he detects a dim flash or a weak click. A television camera in the base of the viewing hood monitors eyes and face. (From Spong, P., Haider, M., & Lindsley, D. B. Selective attentiveness and cortical evoked responses to visual and auditory stimuli. *Science*, 1965, **148**, 395–397. Copyright © 1965 by the American Association for the Advancement of Science.)

The second experiment by Spong, Haider, and Lindsley (1965) was an attempt to study selective attention. The subject received regularly alternating flashes of light and auditory clicks presented 1 sec apart. When he was instructed to attend to flashes and respond to any dim interspersed flashes and ignore clicks, the amplitude of the average evoked responses to nonsignal flashes increased markedly. Similarly, when he was instructed to pay attention to clicks and ignore flashes, the responses to the clicks were enhanced. Thus, directed attention to a particular task seemed to enhance the brain response in the mode of the sense selectively attended to. This result was challenged by Näätänen (1967), who was a visitor from the University of Helsinki doing his thesis in my laboratory.

Näätänen's past experience in measuring reaction times with a randomly variable foreperiod led him to believe that regularly and rhythmically occurring stimuli such as we had used in the alternation of clicks and flashes would allow the brain (arousal and alerting mechanisms) to prepare for each flash (or click) when that was the sense mode attended to (task-relevant stimuli) as opposed to the other sense mode not attended to (irrelevant stimuli), with the result that the arousal level would be slightly enhanced for those particular stimuli. To remedy this situation he designed three clever experiments, all variants of the Spong, Haider and Lindsley (1965) selective attention experiment.

Experiment 3 was essentially a replication of our experiment using one sense mode instead of two. The result was the same, enhancement of evoked response to relevant (selectively attended) stimuli. The second experiment used flashes and clicks but varied randomly the intervals between them. The result was no enhancement of relevant *versus* irrelevant stimuli. Experiment 1 used a reaction time forewarning paradigm with a first or warning flash followed in 1–3 sec by a second flash to which the subject was to respond as quickly as possible by pressing a reaction time key. Clicks throughout were "irrelevant" stimuli but part of them fell within the forewarning period ("inside" clicks) and part fell outside during the interval between pairs of flashes ("outside" clicks). This experiment showed that "inside" clicks, during the preparatory interval for the visual task, were enhanced relative to "outside" clicks, thus presumably confirming what Näätänen had assumed, namely, some kind of arousal or alerting effect, which he has interpreted as a negative potential shift similar to the CNV. I do not think it is quite as simple and straightforward as that, but undoubtedly more work will have to be done in order to further clarify the issue.

Näätänen, and others, have made considerable capital of his results, which have been viewed as disproving the relationship between magnitude of evoked potentials and selective attention, but I do not believe this is

entirely justified on the basis of his results or those of others. It is my opinion that attention, among other things, is an organizing process and that unless one can organize on a temporal basis, as well perhaps as on a spatial one, he cannot attend consistently and efficiently. If you deny a person the possibility of organizing successive tasks regularly and rhythmically (for example, in the juggling of three or more balls) you make the task impossibly difficult for him, for he is no longer able to mobilize his selective attention mechanism in order to make discrete and selective samples of the ongoing events and integrate them with a response mechanism. In any case, part of the selective attention mechanism must be dependent upon basic arousal as represented in the reticular activating system, and part of it must be related to thalamocortical extensions of that system, either via midline thalamoorbitocortical systems of cortical regulation and control, or by more closely linked sensory association systems as represented in the posterolateral association nuclei of the thalamus. Several experiments in progress with cats and monkeys bear upon these issues, and some with human subjects employing the EEG and average evoked potentials do also. When we understand better some of these mechanisms of thalamocortical relationships we will undoubtedly be in a better position to pursue the matter of attention and information processing.

Figure 1-20 shows the portion of our apparatus (optical bench, selsyns for rotating stimuli into position, filters, etc.) which extends into the subject room. This is similar to the apparatus adapted by Näätänen for his experiments. The side of the box has been removed to show its contents. Näätänen, with electrodes on his head for recording EEG and average evoked potentials, is shown with his head positioned in the head-holder and chin rest, with a microphone before him. His right eye is aligned with an artificial pupil so that he can see a dim red fixation cross where flash stimuli will appear. The input stimulus control in this Maxwellian view situation is excellent. Miniature insert earphones are in place for click stimuli. His finger rests on a response key. The other end of the apparatus and the equipment for controlled stimulation and the recording and analyzing of EEG and evoked responses are shown in Fig. 1-21, which represents a reasonably modern and up-to-date laboratory.

Briefly, this laboratory contains several items of equipment for generating and controlling the stimulus parameters and sequences (Tektronix pulse and waveform generators, Massey-Dickenson control modules, Grass physiological stimulators, etc. as well as a punched paper tape reader for scheduling experimental events). On the recording side there is an eight-channel Grass Model 6 EEG, an Ampex FR-1300, seven-channel FM tape recorder for handling EEG data analysis off-line, a Computer of Average

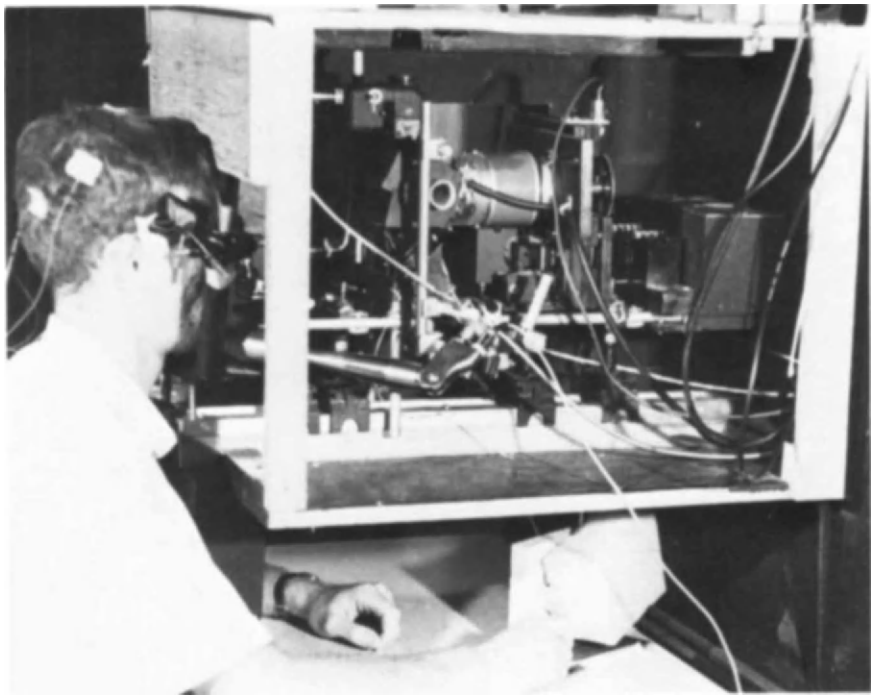


FIG. 1-20. Apparatus for presenting well-controlled visual stimuli in Maxwellian view. The side has been removed to expose interior. Risto Näätänen as his own subject sits with head positioned on chin bar and in head holder. His finger is on the response key. He has insert earphones for click stimuli. Bright and dim flashes and strong and weak clicks can be presented. All stimuli are programmed from the experimental control room. See text.

FIG. 1-21. A modern EEG and perceptual laboratory, equipped for EEG, average evoked potential, and CNV recording. 1. Tektronix 502 oscilloscope; 2. Tektronix Polaroid camera; 3. Grass Kymograph camera; 4. Grass physiological stimulators; 5. Tektronix power supply, waveform and pulse generators; 6. Moseley X-Y plotter; 7. Massey-Dickinson control and programming equipment; 8. Power supply; 9. Hewlett-Packard counter; 10. Tapereader; 11. Oscilloscope monitors; 12. Mnemotron computer of average transient (CAT) and accessories; 13. Preset controller and tape coder; 14. Ampex FR-1300 7-channel FM tape recorder; 15. Grass Model 6 8-channel EEG.

Transients (Mnemotron) for averaging evoked potentials, and an $X-Y$ plotter for graphing the results. There are monitoring scopes and other auxiliary equipment to meet specialized needs. In recent years a DEC PDP-12 computer has been added, which replaces some of the foregoing equipment and adds much greater potential in terms of flexibility and speed of analysis of data and in addition provides facilities for programming the experiment according to various specifications. For each of these items there are several alternative suppliers from which to choose.

In choosing equipment, naturally it is important to understand as much as one can about the principles involved to ensure that the equipment will do the job properly. It is also important to understand what the nature of the phenomena are that one wishes to record and what constraints and limitations that puts on the type of equipment that one should employ. Earlier comment was made about physiological responses, whether slow or fast and having different time courses. One must choose equipment with appropriate time constants for amplifying and recording these phenomena faithfully, but even given appropriate equipment it is important to select the right parameters, for there are often numerous special features such as filters, time constants, etc., which are adjustable. Thus one must know something about what is in the "black boxes," as well as many special technical details about shielded rooms, electrodes, subject conditions, amplifiers and their characteristics, recording systems and their characteristics and limitations, etc. Section V of this chapter presents many of these important technical matters together with some of the theory involved.

V. Recording of the EEG

A. Instrumentation

Systems used to record EEGs usually have two functionally distinct parts: the amplifier, used to increase the voltage of the input signal, and the output device, used to display the amplified signal. Often both are contained within a single integrated unit, as in the case of clinical electroencephalographs. The circuits, components, and other electronic aspects of EEG amplifier-output systems have been explored in many excellent books, such as those of Cooper, Osselton & Shaw (1969), Geddes and Baker (1968), Hill and Parr (1963), Offner (1967), and Stacy (1960). In this section, we will consider these more or less as "black boxes" with several control knobs, and direct our attention toward the functional characteristics of such systems.

1. Amplifier Systems

An EEG amplifier must be able to pick up very small electrical signals from a high impedance source, and amplify them without distortion over a frequency range of from near d.c. (0 Hz) to 100 Hz or more, by a factor of perhaps 1 million or more. Further, it must do all of this under conditions where sources of electrical interference frequently have a magnitude of 100 to 1000 times that of the EEG signal itself. All this places rather stringent demands on the amplifier and requires the use of relatively complex circuitry.

a. Types of Amplifiers. The two most common types of EEG amplifiers are "capacitively coupled" and "chopper" amplifiers. Capacitively coupled amplifiers are so called because successive stages of amplification are interconnected with capacitors. This design factor limits their low frequency response capability and gives rise to their being generally called a.c. amplifiers. Chopper amplifiers use a rapidly alternating switch (a chopper) to modulate the input signal at a high frequency (relative to that of the EEG—usually about 400 Hz). This higher frequency signal is then amplified using capacitively coupled stages of amplification, and then demodulated at the output stage by an equivalent chopper system. The modulation of the input signal by the chopper allows all low frequency components to be recorded, and even steady-state levels, which is why these are often called d.c. amplifiers. Major characteristics of each type of amplifier are summarized in Table 1-3.

b. Input Impedance, Interference, Differential Amplifiers and CMR. These four aspects of EEG amplifiers are closely intertwined with one another. The input impedance of the EEG amplifier must be at least 100 to 1000 times greater than the output impedance of the EEG signal itself, which, for scalp electrodes, means a minimum input impedance of 1–5 MΩ is required (for a method of measuring the input impedance of amplifiers, see Saunders, 1958). The high input impedance minimizes the "loading" of the EEG signal by the amplifier, and allows it to be picked up without significant attenuation. The nature of this interface, however, also allows interference signals, which might be present in the environment, to be picked up without significant attenuation. The most efficient method of preventing these interference signals from being amplified, obviously, is to not allow them to be picked up by the amplifier in the first place. Methods which may be employed to eliminate interference signals from the environment will be discussed later, in Section V,B,1. But even these procedures are not perfect, and often a considerable residual amount of interference is present at the time of recording.

TABLE 1-3

COMPARISON OF FEATURES IN CAPACITIVELY COUPLED AND CHOPPER TYPE EEG AMPLIFIERS

	Capacitively coupled	Chopper
Low frequency response	Limited to about 0.1 Hz	0 Hz (d.c.)
High frequency response	Several kHz	In theory, limited by chopper to less than ½ the chopper frequency; in practice high frequency response will have appreciable attenuation at 1/10 chopper frequency.
Noise	Minimized by selection of low noise components. Greater frequency response range allows noise of higher frequency to be seen	Lower frequency noise minimized by modulating the input signal to higher frequency range where amplifier stability is greater, and by component selection. Higher frequency noise greatly limited by frequency response of amplifier; some noise may be present at subharmonic of chopper frequency
Input impedance	Approximately 1–5 MΩ with 2–4 MΩ to ground	Approximately 1–5 MΩ completely isolated from ground
Interaction with other amplifiers	None	Can have chopper interaction if same electrode leads are used in two different amplifiers
Common-mode rejection	Limited by inequalities in electrode impedance	Essentially independent of electrode impedance

Other procedures must be relied upon to attenuate interference signals which remain superimposed on the EEG as it enters the amplifier. It is for this reason that most, if not all, EEG amplifiers have differential inputs, i.e., the amplifier has two independent inputs, both of which are relatively well, if not completely, isolated from ground. The differential amplifier amplifies the difference between voltage potentials at two different points (electrode sites on the scalp, cortex, etc.) neither of which usually is at ground potential. These amplifiers are able to "reject" or cancel voltages which, at any given moment are identical at the two inputs; this is referred to as common mode rejection (CMR).

Most interference potentials appear as in-phase signals at the amplifier inputs, and, within certain limits, they are rejected, while the difference in

brain-generated potential between the two electrode sites is amplified and appears as the EEG. Most EEG amplifiers have the capability of a CMR ratio of 5000 to 1 or higher, which means that under ideal conditions, if one is recording a 100-μV signal, an in-phase interference signal would have to be 500 mV before it appears equally large in the recording. In actual use, the CMR ratio of nonchopper EEG amplifiers depends on the equality of the electrode contact resistance, or more exactly, the electrode contact impedance at the frequency of the interference signal at the two electrode sites. Poor electrode contact or unbalanced first stage tubes may considerably lower CMR from its maximum specified value. When properly employed, CMR can serve to reduce interference potentials to a considerable extent, even under the worst recording conditions.

c. Frequency Response and Phase Shifts. The frequency response of most EEG amplifiers is variable, with independent switch settings for the upper and lower extremes. The lower frequency limit is determined by the cutoff frequency of the high-pass filter (also called time-constant setting); the upper frequency limit is determined by the cutoff frequency of the low-pass filter. Between these two frequencies is a band of frequencies which are "passed" by the filter networks, and are amplified.

High- and low-pass filters do not precipitously cut off all frequencies below and above their respective cutoff values. Instead, attenuation begins gradually from a point somewhere near the middle of the "pass" region, where the output amplitude is maximal, to the cutoff frequency itself where the output amplitude is reduced to some fixed percentage of the maximum. Different manufacturers have chosen to use different levels of relative amplitude to determine the cutoff frequency values of their amplifiers; so while actual filter switch settings may be identical for two amplifiers made by different manufacturers, their actual frequency response capability may be quite different. Relative amplitude values commonly used for cutoff points are: 80% (2-dB voltage attenuation), 70.7% response (3-dB voltage attenuation), and 50% response (6-dB voltage attenuation).

With further change in the frequency of the amplified signal away from the "pass" region, the amount of attenuation increases, until the rate at which it "rolls off" reaches an asymptotic value. This asymptotic rate is often expressed as the voltage attenuation in decibels per octave. A commonly used rolloff for both high- and low-pass filters in EEG amplifiers is 6 dB per octave (50% decrease in amplitude every time the frequency of the input signal is doubled). In addition, many EEG amplifiers have a "notch" filter designed to discriminate maximally against one single frequency, namely, the power line frequency (60 Hz), while passing frequencies both lower and higher than this value. Here too, there is no precipitous drop in amplitude at the notch frequency, but instead there is a gradual

attenuation of amplitude of frequencies on either side of the notch peak, but at a somewhat faster rolloff than occurs with either low- or high-pass filters.

Coupled with their ability to selectively attenuate frequencies of the amplified signal, all of these filters produce a change in the temporal or phase relationship between the input and output of the signal at all frequencies which have been so attenuated. That is, the peaks and troughs of a frequency near the middle of the pass region of the amplifier will have, when amplified, an exact temporal correspondence at both the input and output. However, the peaks and troughs of an input signal whose frequency is near the extremes of the amplifier pass region will be shifted in time at the output as compared to the input. The amount of this induced phase shift is a function of how much the amplitude of the signal at this frequency has been diminished by the filter network—the greater the diminuition, the greater the shift. These phase shifts may not be particularly important when the EEG is being recorded with an ink-writer at a slow paper speed, as they would generally be too small to be observed. However, there are situations in which even the smallest differences in time may be of large significance, as, e.g., in evoked potentials, where phase shifts introduced by amplifying the EEG with too narrow a bandpass will produce differences in the relative latency of high and low frequency components.

Geddes (1951) discussed a method of simultaneously measuring the frequency and phase shift characteristics of amplifiers using a waveform composed of sine waves and square wave pulses. Geddes and Baker (1968, Chapter 14) and Oliver (1966) have discussed measurement of frequency response characteristics of amplifiers using voltage step functions. Saunders and Jell (1959) discussed a procedure for measuring the phase response of EEG amplifiers using sinusoidal input voltages.

d. DYNAMIC RANGE. Orthogonal to the frequency response characteristic of amplifiers are their voltage response characteristics. It may be assumed that the output of an EEG amplifier in good working order is a linear function of the input signal voltage, but there is a limit to the range over which the input signal can vary and still be faithfully reproduced at the amplifier output. The upper limit of this range is determined by the maximum input signal that can be applied (at a given gain setting) yielding a distortion-free[1] output. The lower limit of this range is determined by

[1] A "distortion-free" output, in the absolute sense, is never obtained by any amplifier system. By "distortion-free" it is meant that any distortion in the amplified signal is no greater than that specified by the manufacturer. As the input signal is increased, a point will be reached when the output of the amplifier shows obvious distortion; these may be the clipping of peaks, intrusion of harmonics where none were present in the original signal, etc. An input signal amplitude at some value below this will represent the maximum signal that can be amplified while yielding a distortion-free output.

the smallest input signal that can be applied (for the same gain setting) and still be resolved in the amplifier output. The ratio of these maximum and minimum values is the *dynamic range* of the amplifier, and an EEG amplifier should be expected to have a dynamic range of 100 to 1 or better. In other words, if the gain of the amplifier is set so that an input signal of 10 μV can just be seen reliably in the amplifier output, the amplifier should, at this same setting be able to amplify a 1000-μV signal without introducing distortion. When greater amplification is required, a point will be reached where the noise in the amplifier system will limit the smallest input signal which can be resolved. For example, if the system noise of an EEG amplifier with a dynamic range of 100 to 1 is about 5 μV, and the gain is increased in an attempt to resolve a 1-μV signal, i.e., set so that the maximum signal that can be amplified without distortion is 100 μV, the dynamic range of the amplifier would no longer be 100 to 1. The 1-μV input signal would be "buried" in the 5-μV noise level of the amplifier, and the effective dynamic range would be reduced to no higher than 20 to 1 (100 to 5).

2. Output and Recording Media

a. Types of Output Devices. Methods used in recording the EEG fall into two broad classifications: graphic writeout, and magnetic tape recording. Graphic writeouts include all methods by which an EEG is made to appear as a permanent trace on some form of paper. The most common are inkwriter tracings and photographic recordings of the image of a beam or spot of light. Magnetic tape recording is most often by "direct" mode or by frequency modulation (FM) recording processes. Digital magnetic tape recording is a procedure which has certain advantages (e.g., Brown & Kado, 1965), but will not be discussed here because its relatively high cost puts it beyond the means of many, if not most, individual investigators, and because the digitization of many EEG records is done from analog tape recordings. In the latter case, the limiting features of the digitally stored data, in all probability, would be determined by the analog, rather than the digital, recording procedures and devices.

All methods of data storage involve moving a writeout medium (paper, magnetic tape) past a recording device (moving pen, electromagnet with varying electromagnetic flux). Graphic writeouts can be obtained from pens which apply ink to paper either by capillary action or by squirting, or by pens which heat or scratch specially treated paper. Light can be made to produce a photographic writeout either by electromechanical oscillation of mirrors reflecting a beam of light (light beam oscillograph), or by electrostatic deflection of a beam of electrons over a phosphor-coated surface (oscilloscope). The graphic writeout in all cases is a permanent record of the voltage oscillations that may be viewed without the aid of any further

specialized equipment. Tape-recorded data, however, require not only a tape recorder (in reproduce mode) but also some device, such as an oscilloscope, to make the electrical signal visible each time it is desired to view the recording.

The principal advantage of tape-recorded data is that it may be electronically processed any number of times, as by computer for signal averaging or frequency analysis, and at different speeds or amplifications. Equivalent analysis of graphically stored data is virtually precluded except "on line" as the data is originally collected. This is not to imply that any one method of data storage is unequivocably the "best" for all situations, as the purposes for which the EEG is being recorded will determine the best method of data storage.

b. Frequency Response. For graphic writeouts, frequency response is limited principally by mechanical inertia in the recording device, but other factors such as chart-to-pen friction, the sensitivity of oscillograph film or paper to the image of light, and even the frequency response of the amplifier system, may also be involved. Most graphic writeout devices have a low frequency response capability of 0 Hz (d.c.) and a high frequency response capability of about 100–150 Hz for ink-writers and several kilohertz for light beam oscillographs. For CRT photography, the high frequency limit is usually determined by the amplifiers, or the sensitivity of the film to light. The frequency response range of tape-recorded data is a function of the mode of recording and the speed with which the tape moves across the recording heads. Increasing the speed of tape movement produces a linear increase in the high frequency response for both modes, but does not appreciably alter the low frequency response characteristic (0 Hz for FM recording, 50–100 Hz for direct recording). At any given tape speed, however, the high frequency response capability of direct mode recording is considerably higher than that of the FM mode. At a tape speed of $1\frac{7}{8}$ inches per second, the upper frequency response for FM mode is about 0.6–0.7 kHz for most recorders, while that for direct mode recording is between 6–8 kHz.

As in the case of amplifiers, wherever the frequency response of a system changes, the phase relationship between input and output may also be expected to change. The frequency and phase changes introduced by any output device would summate with those changes introduced by the amplifier itself, and hence, these characteristics must be determined for the system as a whole.

Another factor, related to the frequency response, to be taken into consideration with graphic writeout devices is the frequency resolution of the output. While the actual frequency response capability of graphic writeout

devices is little affected by a change in chart speed, the ability of an observer to resolve the frequencies displayed in the output may be significantly altered. At slow chart speeds high frequencies may become smeared together, producing a thick trace in which individual high frequency oscillations cannot be resolved. Once recorded, there is no way to "stretch" these records, and the information contained at these high frequencies would be irretrievably lost. The chart speed selected, then, should be one that allows resolution of the highest frequencies which are of interest.

c. DYNAMIC RANGE. The electromechanical action itself is the principal factor limiting the dynamic range of graphic writeout systems. In CRT photography and tape recording, the dynamic range is usually determined by the system electronics. A 1-inch ink-writer pen deflection will allow a maximum dynamic range of about 30 to 1; a 2-inch pen deflection may allow a dynamic range as high as 60 to 1. For light beam oscillographs and CRT photography, the dynamic range may be as high as 100 to 1 or more. The dynamic range of tape-recorded data increases somewhat with increases in tape speed, and for FM is about 60–100 to 1, but only about 30–40 to 1 for direct mode recording.[2]

The lower limits of the amplitude response in graphic writeout systems depends on the amount of voltage necessary to overcome pen-to-chart friction, the thickness of the ink line or the sharpness of the image of the focused spot of light, as well as electronic noise from the amplifiers. For tape-recorded data, the lower limit is determined by the noise characteristics of the magnetic tape, and by the system electronics.

For all kinds of output systems, variations in the relative movement of the recording medium past the recording device is an additional source of noise (called "flutter" in tape-recording terminology). Often this will introduce a noise component at a frequency related to that of the power lines, but flutter may also occur at other frequencies as a result of any imbalance in rotating components. While not usually a problem with graphic writeouts, as this noise is usually too small to be resolved, it can be a major concern in tape recorders, and in CRT photography (due to nonlinearities in the sweep). Flutter in these cases is best overcome by good equipment design by the manufacturer; however, with FM tape recording, there is usually an optional "flutter compensation" channel which will electronically compensate for this source of noise.

The upper amplitude limit of graphic writeout is usually determined by

[2] Direct mode recording is also used in audio applications, in which dynamic range may be 100–1000 to 1. This relatively high value is achieved by preemphasis of the input signal which makes allowance for the differential sensitivity of the human ear to sounds over the audio spectrum. Direct mode, for instrumentation purposes, records the input signal with equal emphasis over the entire frequency band, which results in a loss in dynamic range.

the physical limit of the movement of the pen or spot of light. For FM mode tape recording, the upper limit is determined by the electronics (the maximum range over which the carrier frequency can be modulated), but for direct mode, the upper limit is determined by magnetic saturation phenomena in the recording tape.

It has been implicitly assumed that amplifiers amplify input voltages linearly over the limits of their dynamic range, and in general, this is true to an accuracy of 1% or better for EEG amplifiers in good working order. However, this may not always be true for output devices. For example, an ink-writer with a 2-inch pen deflection may respond linearly only over the central 60% of its travel, and have increasingly nonlinear response characteristics beyond this range. Similar phenomena may occur in many kinds of output devices; and the extent to which a linear display is possible within its response limits should be determined for each output device in use.

In general, the procedures involved in the measurement of the frequency, phase, and amplitude characteristics of output devices are similar to those used with amplifiers. In particular, Saunders (1957) has described a technique for measuring the phase response of pen galvanometers, and Athey (1966) has covered in considerable detail many aspects and measurement procedures used in magnetic tape recording.

3. Electrodes

An electrode is a conductive substance placed in contact with the brain, or some part of its electrically conductive environment, in order to lead a small amount of current to an amplifier-output system. The interface it makes with the subject is critical to the entire procedure of obtaining an EEG, and has relatively complex functional characteristics. A useful model of these characteristics may be constructed in terms of an "equivalent circuit" of electronic components (e.g., Cooper, 1963; Weinman & Mahler, 1964), and procedures designed to improve the functional characteristics of the interface may then be framed in the context of a change in the values of one or more of these equivalent circuit components. An ideal electrode interface would have an equivalent circuit of a wire allowing free passage of all brain-generated current present at the interface regardless of frequency and direction. In actual practice, the equivalent circuit is more complex, and the component values depend principally on three factors: (1) the material in the electrolyte, (2) the material in the electrode, and (3) the density of current passing through the junction.

In recording the EEG, there is little or no choice as regards the electrolyte. When recording with scalp electrodes, the electrolyte used (i.e., electrode paste or jelly) must not cause undue irritation to, and should be consistent

with the chemical makeup of the skin. The "active" ingredient in most electrolytes is a chloride salt, usually sodium or calcium, with the former being less irritating. When recording with an indwelling electrode, whether subdermal or subcortical, the biochemical environment in which the electrode is placed forms the electrolyte.

There is a somewhat greater range of alternatives for the electrode material, but these must obviously be selected for optimum use with the electrolyte. Among the metals which have been commonly used are silver, platinum, gold, and many varieties of stainless steel. For scalp electrodes, selection of electrode material may be made almost exclusively on the basis of electrical properties of the metals, and there is general agreement that chlorided silver (silver-silver chloride) is the material of choice (e.g., Cooper, 1963; Geddes & Baker, 1967). Silver-silver chloride forms a very stable, noise-free junction with the commonly used electrolytes, and in principle has a time constant which is infinite, for all practical purposes, allowing "d.c." EEG waves to be recorded without distortion. In practice, the chloriding of silver electrodes for use in recording "a.c." EEG activity (e.g., 0.5 Hz and higher) is relatively straightforward (but see Geddes, Baker & Moore, 1969). However, the situation is more complex when electrodes are to be used to record d.c. activity (see Cooper, 1963, and references cited therein). For this latter purpose, one might consider the purchase of electrodes made of a compressed mixture of silver and silver-chloride powder, available from several manufacturers, which are of rugged construction, and which have excellent d.c. recording characteristics.

Because of the relatively large surface area of the interface when recording with most scalp EEG electrodes, the levels of current density involved will be small enough so as to have relatively little effect on the electrical characteristics of the interface if the input impedance of the amplifier is higher than about 4–6 MΩ (Geddes, Baker, & Moore, 1968).

There is an additional consideration when using scalp electrodes; this concerns prevention of any disturbance of the steady potentials which are set up at the electrode interface. When an electrode comes into contact with an electrolyte, there is an immediate exchange of ions which takes place between the electrode and electrolyte. Initially, the rate of exchange is relatively high, but after a period of time, it will stabilize at a rate dependent upon the material in the electrode and electrolyte. At this point there will be a gradient in potential at the electrode–electrolyte interface. Similarly, another gradient in potential will be created at the interface between the electrolyte and the underlying skin. The gradient in potential involved in these regions is often two to three orders of magnitude greater than that of the EEG itself, but their presence does not normally interfere with the recording of the EEG unless they are disturbed in some way.

Obviously, physical movement of the electrode along the surface of the skin will alter the relative position of material at these interfaces, and disrupt the electrochemical stability. This disruption will cause voltage transients (artifacts) as these interfaces seek to restabilize in their new environment. Attaching the electrodes to the skin firmly, as by means of adhesive collars, thick electrode paste, or collodion, will prevent gross slipping and sliding at the electrode interface. It will still be possible for physical movement of electrode and electrolyte to occur, which though very small, would be large enough to produce voltage transients. The electrode–electrolyte interface may be made relatively impervious to such movements if the electrode contacts the skin only through an electrolyte bridge, thus giving a mechanical "cushion" to the critical area of the interface where the potential gradient exists (Cooper *et al.*, 1969, p. 19; Geddes & Baker, 1968, p. 217ff.; Weltman, Klagsbrun, Ukkestad, & Ettelson, 1968, p. 15ff.). This is usually accomplished by recessing the electrode metal into a cup of nonconducting, inert material, such as a plastic, by about $\frac{1}{16}$ to $\frac{1}{8}$ inch.

The potential gradient between electrolyte and the underlying skin is formed across the outer skin layers of the epidermis. The magnitude of this potential gradient will be partially dependent upon how well standard electrode application procedures have been followed (i.e., scrubbing with alcohol or acetone to dissolve skin oils so as to penetrate the outer horny layer of the epidermis, and rubbing in the electrolyte so that its liquid may penetrate through to the inner epidermal layers), but can never be eliminated entirely. If the skin area over which an electrode has been placed is not allowed to stretch or move, the potential gradient will usually become, and remain, quite stable. If however, the skin does stretch or move, the resistance of the epidermis can change, disrupting the steady-state conditions of the potential gradient, and causing large voltage transients until a new steady-state condition is reached. These artifacts due to skin stretching may be minimized if the epidermal layers are pierced through down to the dermis by lightly pricking the skin with a sterile needle, or using the skin drilling technique of Shackel (1959).

The selection of electrode material for indwelling electrodes cannot be based solely on the electrical characteristics of the metals. Here another factor, the toxicity to the tissue in which it is implanted, becomes extremely important, and usually precludes the use of certain materials. A case in point is silver (e.g., McFadden, 1969). Among the other commonly used inert substances, none could be considered the best for all, or most all, recording conditions. The electrical characteristics of these metals fall short of the ideal of silver-silver chloride. Typically the greatest problem is one of a relatively short time constant, subjecting the EEG to high-pass

filtering even before it reaches the amplifier. Another frequently occurring problem is that the gradient potentials established at the electrode interface are not always stable, even in the absence of physical movement; this results in a relatively high background noise level. Both of these problems may be particularly evident in the case of stainless steel electrodes.

It is with indwelling electrodes, where the actual area of contact may be only a fraction of a square millimeter, that current density can play an appreciable role in determining the values of the equivalent circuit components of the electrode interface. The smaller the current density at the electrode interface, the more uniform will be the impedance of the interface over a range of frequencies for a given set of electrodes. If it is required that the electrode surface area be very small, the only way to reduce current density is to increase the input impedance of the amplifier. In the extreme case of microelectrodes, the input impedance must be very high (the order of $10^{11}\ \Omega$ or higher) in order to record a satisfactory signal. Data which may be used as a guide in estimating the minimum acceptable input impedance under a number of different conditions have been presented by Geddes *et al.* (1967, 1968).

4. Grounding

The use of most EEG amplifiers requires that they, as well as other associated equipment, be connected to ground—i.e., an electrical connection which actually makes a low-resistance contact with earth. In making such a connection, it is important to minimize the voltage drop between the grounded instrument and earth itself, which means using heavy wire whose overall length to ground is as short as possible. There are three types of ground connection that are possible to use in the laboratory. First, there is the grounding conductor of the standard two-pole, three-wire outlet found in most present-day wiring applications. ("Poles" refers to the number of current-carrying conductors, "wires" refers to the total number of wires in the application.) The grounding, or green-colored, conductor of the power line is identified by the U-shaped slot in the outlet. In some wiring of older vintage, two-pole, two-wire outlets are used, and at times the grounded conductor, or white wire, indicated by the larger of the two slots in the outlet, may provide a satisfactory ground with regard to equipment noise. However, safety considerations, both for the subject and the experimenter, absolutely preclude the use of the grounded conductor as a ground connection because this conductor is one of two which carry current. With this wiring system, the metal box in which the outlet is situated is usually connected to ground (but check to be sure) via the metal conduits in which the conductors are encased, and may prove serviceable. Second, grounds may be provided from water pipes, with cold water pipes preferred

over hot, as they usually have a shorter path to ground, and usually do not have thermal insulation which may also insulate the pipe from ground. Other kinds of pipe connections, such as drainage, gas, air pressure outlets, etc., are generally unsatisfactory, as they may have bushings which insulate them from ground. Third, one may decide to make his own connection to ground and about this more will be said later.

Much, if not all EEG equipment made today has three-wire power cords, which automatically connect the chassis to ground when plugged into the power outlet. If the grounding conductor of the power line is satisfactory in use with this and other equipment, then the grounding procedure is considerably simplified. But, because the grounding conductor contains ground currents from other equipment, which may be sufficient to create interference, and because the grounding conductor may be several millivolts or even volts off ground, often its use is not satisfactory. Before using the ground conductor of the power line, it should be checked to be sure that no potential exists on it with respect to a good "earthy" ground—both when the power line is not in use, and when all equipment to be used is plugged in and operating—and that its resistance to such an "earthy" ground is very small—of the order of 0.1 Ω or less. If grounding conductors are used from several different outlets, they should be checked to be sure that no potential difference, and negligible resistance, exists between each.

If the power line ground proves unsatisfactory, the automatic connection of the equipment to this ground via the power plug must be disabled before another ground connection is used. Three-wire to two-wire adapters may be used for this purpose, with the grounding lead wire on the adapter connected to the newly selected ground. The orientation of the power plug and socket should be respected when using such an adapter, so that the prong of the power cable originally destined for the grounded conductor of the power line, without use of the adapter, does, in fact make connection to the grounded conductor through the adapter. If several pieces of equipment are to be grounded, thick (say, 12 gauge or less) wires from each, as well as from the room shielding (if any) should lead to a conveniently located terminal strip which is then connected to the ground by soldering, or through the use of a grounding clamp. The connection to the ground should be located so that the chance of any corrosion of this joint will be minimized.

In making a connection to ground itself, the basic principle is to put a fair quantity of metal with high conductivity into a relatively damp location in the ground. Further, this metal should not interact with the ground in such a way as to create electrical current or gradually increase its contact resistance with the ground itself. For this purpose, copper is the metal of choice. The ground terminal can be made by driving 6–10 ft of solid

copper or copper-coated steel rod into the ground, or by digging trenches several feet long and several feet deep in which solid copper rod is buried. This grounding rod is then soldered or brazed to a thick buss bar (say 0 gauge or thicker) which is then led to the laboratory via the most direct path possible, where it then connects to a grounding terminal strip for distribution to the various pieces of apparatus.

B. Artifacts

1. Nonsubject-Generated Interference

a. Electromagnetic Fields. The most common source of interference encountered in the recording of EEGs are electromagnetic fields surrounding conductors carrying alternating current. These electromagnetic fields are of two types: induction fields, most often a problem around 60 Hz electric power lines, and radiation fields, which may come from a variety of sources, including sparking contacts in switches and motors, diathermy machines, and radio-TV transmitters. Either kind of field is capable of severely compromising the fidelity of an EEG recording, if it is of sufficient strength. If the interference is of low enough frequency to fall within the response range of the amplifier, it will be amplified and recorded along with the EEG. With higher frequencies, large signals may cause saturation in the preamplifier before being filtered out in later stages, thus causing distortion in the EEG, or preventing it from being recorded at all.

b. Mechanisms of Interference. The induction fields are composed of two components: an electric and a magnetic field. The relative strengths of these two components vary greatly under different conditions, and while each is capable of inducing interference, they do so in different ways. The electric component of an electromagnetic induction field will actually induce a voltage potential on nearby objects. It has long been known that an object charged with static electricity, when brought near a second uncharged object, will induce an electric charge of opposite polarity on the second object where the two are in closest proximity. Now if this potential on the charged object is made to alternate, like that of an a.c. power line carrying no current, then the charge induced on the second object will also alternate, although with opposite polarity. The more complete the electrical isolation of the second object from the voltage reference for the charged object (usually ground in most cases), the more nearly will the potential induced on the second object equal that on the first. In effect, the two objects act as the plates of a capacitor, with the intervening space (air) serving as a dielectric, and they are said to be "capacitively coupled."

The strength of the magnetic component in an electromagnetic induction field depends on the amount of current flowing through a conductor—the more current, the stronger the field. If the flow of current is made to alternate, the poles of the magnetic induction field will also alternate, causing an expanding and collapsing magnetic induction field in the surrounding area. If a conductor is within the changing magnetic induction field, the relative motion between conductor and magnetic lines of force will cause a voltage to be induced in the conductor, in much the same fashion as conductors moving through a stationary magnetic field produce electricity in generators. Major sources of magnetic induction field interference are motors and transformers; the magnetic induction fields surrounding a.c. power lines themselves are largely (although not completely) neutralized because the two wires carry equal and opposite current flows, and produce canceling magnetic fields.

In a conductor carrying alternating current only at power line frequencies, there is very little energy in the radiation field. The power in the radiation field, however, increases with the square of the frequency, other things being equal, and with relatively high frequencies, e.g., above 10 kHz, it may have sufficient power to be important as a source of interference. If a radiation field, moving through space, encounters a conductor, a small amount of the signal energy is abstracted from the passing field, which, in turn, produces a voltage in the conductor. While a radiation field also contains both electric and magnetic components, it is possible to consider the voltage to have been induced in the wire by either component (not by both), because in a radiation field, these are two different ways of viewing the same energy (see, e.g., Skilling, 1948, Chapter XII).

The conductor in which the voltage is induced by the radiation field may be an intended one, e.g., the antenna of a radio or TV receiver or may be any wire associated with an EEG recording, such as the electrode leads. But such direct reception is not the only means whereby a radiation field may introduce interference in an EEG recording. Radiation fields may first induce voltage in other wires, such as telephone and power lines, which then conduct them directly to a point closer to the EEG amplifiers, where they are then picked up by reradiation. Voltage induced in the power lines by radiation fields may also introduce interference without reradiation by entering directly into the power supply of the EEG amplifier, or of other equipment.

The amount of energy in both induction and radiation fields is an inverse function of distance, but with the former decreasing more rapidly than the latter. Increasing the distance between the field source and the recording site, therefore, is the simplest method of reducing any resulting interference. However, since sufficient distance may not always be at hand, and

as much equipment requires the use of a major interference source—the power lines—other means of reducing interference must be employed. These fall into three groups: Those involved in (1) minimizing the available energy in the electromagnetic field that can be picked up as interference, (2) minimizing the energy in the electromagnetic field that is actually picked up, and (3) minimizing interference to the EEG record once electromagnetic field energy has been picked up.

c. MINIMIZING AVAILABLE ELECTROMAGNETIC FIELD ENERGY. *i. Shielding Principles.* The basic principle in shielding against electric and magnetic components of both induction and radiation fields is similar, and usually consists of interposing metal between the source of interference, and the EEG subject. However, the mechanisms by which shielding is effective against each component are different.

Electric induction fields. In shielding against electric induction fields, we take advantage of the fact, first demonstrated by Faraday, that the locus of an electric charge on a conductor is entirely on its outer surface—i.e., the net electric field inside a charged conductor is zero. Thus by enclosing the subject entirely within a conducting metal shield, the shield will become charged, while the subject will remain in an equipotential environment. The shield should be grounded, and only at one point, to minimize the magnitude of any potentials induced on the shield, and, if the subject himself is grounded, to prevent any currents induced into him by the shield from running up and down his grounding wire.

The most important property of the metal to be used as a shield against electric induction fields is that of its electrical conductivity (the efficiency with which it is able to conduct electric current)—the better the conductivity, in both the shield material and in all joints, the more efficient the shield. The metal may be quite thin, but its effectiveness as a shield is greatest if it contains no perforations. The extent to which holes in the metal reduce its shielding properties depends on the open space-to-metal ratio, but in practice, fine wire mesh screening has proven satisfactory under most conditions. The shield's effectiveness may be increased by an order of magnitude or more by using a second shield entirely within the first, separated by one or more inches, and completely insulated from one another except at one point, where both are joined and grounded. Ideally this point should be a corner where three sides of the shield join, because the density of electrical charge induced on a conductor is not uniform over its surface, but is greatest at places of greatest curvature, such as a corner of a rectangular metal box. Such a point is the most efficient place from which to lead any induced potentials to ground.

Magnetic induction fields. Shielding against magnetic induction fields depends upon the frequency at which the magnetic field alternates. For

low frequencies within the audio spectrum, shielding is accomplished by diverting and concentrating the magnetic lines of force of the induction field within a metal shield of high magnetic permeability (the extent to which the density of magnetic flux may be increased by a given substance relative to that of air). But, unfortunately, unless the field is very weak, thick heavy shielding material is necessary, and here it is often more efficient to simply increase the distance between the source and the subject. Sometimes simply changing the orientation of the source will completely eliminate the interference, as magnetic induction fields are usually not of uniform strength in all directions.

As frequency is increased into the radio spectrum, permeability of metals falls off appreciably, and they progressively fail to divert the lines of force in a magnetic induction field. But with this change in frequency, there is an increase in the effectiveness of another shielding mechanism—induced eddy currents in the shielding material. As these eddy currents increase in strength, they develop their own magnetic fields which oppose and begin to cancel the original induction field. Here again, the most important property of the shielding material is its electrical conductivity, and, in addition, its thickness. It is not necessary to ground the shield if it is only to be used against magnetic induction fields, but it is important that all joints have minimum resistance both for the diverted magnetic field at low frequencies, and for the induced eddy currents at higher frequencies.

Radiation fields. Shielding against radiation fields is accomplished in much the same way as against the magnetic component of an induction field: by utilizing induced opposing eddy currents. The voltage induced into a conductor by a radiation field is the same, and likewise, the procedures for shielding against it are the same, whether it is considered to have been induced by the electric or the magnetic component. As with eddy currents set up by high frequency magnetic induction fields, the effectiveness of the shielding material depends on its electrical conductivity. But in contrast, the shielding effectiveness does not depend to any large extent on its thickness, because such high frequency radiation fields cannot penetrate very deeply into a conductor. It is most important that seams and joints have a continuous metal-to-metal contact, including those around doors and windows, because at these high frequencies, even relatively small holes can "leak" a significant amount of radiation. A further complication is that the shielded room will have a cavity resonance frequency at which a standing wave pattern can exist completely within the room, and which then behaves as a tuned circuit. At this frequency, and its harmonics, even a small amount of energy leaked into the room can set up an intense field within the room. Fortunately, in many cases, the cavity resonance will be at frequencies at which there is little or no radiation field energy (e.g., no radio transmitter using that wavelength), and it will cause no problem.

A double shield, as described for use against electric induction fields, may also be used to increase the attenuation of energy in radiation fields.

Radiation fields are a member of the same electromagnetic spectrum which includes visible light, and, like light, radiation fields may also be reflected as they pass from one conducting medium to another (e.g., as it passes from air into the metal of a shielded room). The amount of reflection is inversely proportional to the frequency of the radiation field, but also depends on the size of the reflector relative to that of the wavelength. In practice, however, the reflection of radiation fields is usually small enough so that its effect is neglected in the design of shielded rooms, and therefore provides an additional safety factor when the shield is in use.

ii. Construction of a Shielded Room. In deciding what material is to be used as shielding, consideration should be given to the nature of the interference to be shielded against, as well as the cost of the shielding material. Thompson and Yarbrough (1967) have suggested that greatest consideration be given to interference arising from the 60-Hz power line for several reasons: (1) Energy in induction fields at higher frequencies is usually negligible, (2) energy in radio-TV radiation fields is usually so small that almost any metal would suffice as an effective shield, and (3) radiation energy from other sources, such as sparking contacts, is best controlled at the source. At power line frequencies, they indicate that the magnetic permeability of the shielding material is at least as important as its conductivity, and while the conductivity of metals most commonly used in shielding varies over a range of less than 10 to 1, the range of magnetic permeability of these same metals varies by more than 200 to 1.

Of the metals they considered, low carbon steel had relatively high magnetic permeability, fairly good conductivity, and very low cost, and could be considered to be a "best buy" in shielding materials. Others which have proven satisfactory in use are copper fly screening, copper foil-lined Kraft paper, galvanized-after-woven screening (hardware cloth), and metal-lined (copper, steel, iron) plywood.

The construction of the shielded room need not be very elaborate. Besides the fact that there must be excellent bonding between all joints, almost any method may be used to support the shielding material. Accurate construction is necessary to assure that faulty connections do not occur, that the shield is grounded at only one point, and that there is no possibility of corrosion of the shielding material. The shielding material should be protected from damage from people and objects within the room, especially the floor. Coverings may be used on the floors, walls, and ceiling to protect the shield, for sound attenuation, and for decoration. These should not be made of materials, such as vinyl or rubber, which may lead to the generation

of static electricity within the room itself. Viewing windows may also be desired, in which case the integrity of the shield may be at least partially maintained through the use of wire-mesh safety glass, with the wires connected to the shield walls. Provision should be made that the access door is in firm contact with the shield walls when closed, and it may be desirable to use spring-loaded wipers all around the door edge for this purpose. In cases where high frequency radiation fields are a problem, special wave guides may have to be placed on ventilation openings in the room. Hale (1956) and Leadbitter (1963) have discussed consideration in radiation field interference screening in more detail.

iii. Other Methods. We have referred to the importance of distance as a factor in reducing the strength of an electromagnetic field, but it deserves reemphasis. The subject and all amplifier input leads should be as far as possible from power lines and power line-operated equipment. In particular, attention should be paid to the distance from transformers, motors, cooling fans on the EEG amplifiers, and other equipment in use. The leads to stimulating equipment, such as flash tubes, should be at some distance from the amplifier input cable at all times. If lighting is used within the subject room, well-filtered direct current will produce the least interference, but the induction fields surrounding incandescent lights powered by alternating current are usually small enough that they produce negligible interference at a distance of 6–10 feet. However, fluorescent lamps should not be used, preferably not even in adjacent observation rooms, as they produce bursts of radiation fields in synchrony with the line frequency, which are a potent source of interference.

Another aspect of distance is that of the choice of location of the recording environment. The rooms where EEGs are to be recorded should be at some distance from sources of interference within the building, such as motors in elevators, and air conditioning systems, power distribution panels, and other heavy electrical machinery. Also important to consider is the location of other laboratory medical equipment such as X-ray and diathermy machines. Finally, the extent to which interference may arise from sources outside the building should be investigated, including the location of radio-TV transmitters, proximity to street traffic with possible interference from automobile and truck ignitions, etc.

Filtering may be used against radio frequency interference if it has been induced into wires. If the radio frequency energy has been induced into the power line, resulting interference may be eliminated by inserting a commercially available filter in the power line before it is used to power the amplifier, lights, or other equipment in the observation and subject rooms. Often the use of an isolation transformer will serve the same purpose.

Once radio frequency energy has been removed from the power line, its wires should be shielded over their entire length from the filter to the outlet boxes to prevent further pickup. The power cables leading to amplifiers and other equipment should be shielded over their entire length for the same reason. Power lines which enter a shielded subject room should be encased in a shield separate from that of the room, and at no point should the two shields touch.

d. MINIMIZING AMPLIFICATION OF INFILTRATED ELECTROMAGNETIC FIELD INTERFERENCE. *i. Common Mode Rejection (CMR).* We have already mentioned the mechanism of CMR when discussing amplifiers, and the rejection ratio of in-phase signals of which most EEG amplifiers are theoretically capable. In actual practice, the magnitude of CMR is usually determined by the electrode contact resistance for the two inputs: In differential amplifiers whose inputs have finite resistance to ground, CMR is inversely proportional to the difference in contact resistance between the two electrodes. However, the higher the resistance to ground of each input terminal, the smaller the change in CMR for a given difference in contact resistance. This is one of the reasons why it is stressed that electrode applications be made very carefully, with the resistance of all electrodes being as low and uniform as possible. In chopper amplifiers, where the input terminals are completely isolated from ground, CMR is determined only by the amplifier characteristics itself.

ii. Grounding the Subject. If interference once reaches the subject-electrode-electrode lead wire complex, much of it may be prevented from reaching the EEG amplifier if the subject is grounded. This is especially effective if the interference is due to electric induction fields, although it can reduce interference from other sources as well. If the subject is grounded there are two precautions that should be considered. The first is to be sure that no "ground loops" are formed. A ground loop occurs when more than one ground connection is made on an object or a group of objects which have been electrically connected to one another. In such a case, a conducting loop is formed by conducting media with the object, or by wires connecting the group of objects, and by the conductors between the two grounds. This loop may serve as a very effective antenna for electromagnetic fields of all kinds, into which potentials may be induced. For a given uniform electromagnetic field, the magnitude of potentials induced is proportional to the area of the conducting loop that is perpendicular to the direction of the field. The area in a ground loop may be very large, and hence be a source of interference potentials of appreciable size. Because of the ubiquity of electromagnetic fields from the power line, the interference from a ground loop is most likely to appear as 60-Hz activity.

The simplest way of preventing ground loops is to connect a wire to the "ground" connections of each piece of equipment to be used, including the subject, if he is to be grounded, and lead these wires to one point, such as a heavy terminal strip, where they are joined. Finally, a heavy piece of wire should lead from this terminal strip to ground. It should be remembered that most items of electronic equipment are provided with a three-prong plug which automatically connects their chassis to the power line grounding conductor. To avoid this, the automatic grounding provision must be disabled with an adapter plug, and then the ground reapplied with a wire to the terminal strip.

The second precaution is that described by Bureš, Petráň, and Zachar (1962, p. 151) in which grounding the subject may lead to artifactual recordings. In cases where the interelectrode resistance is very low, if the inputs of the differential amplifier have a finite resistance to ground, grounding the subject may cause a significant reduction in the grid-to-ground resistance in all channels. If this happens, each channel may amplify a combination of potentials from three electrode sites (the two normal electrodes going to the amplifier inputs, plus the ground electrode) rather than only two.

iii. Other Procedures. Just as a ground loop may have potentials induced in it, the electrode wires leading from subject to amplifier input form a conducting loop and may have interference potentials induced directly on them. There are three ways such interference potentials may be reduced. (1) If the interference is produced by electric induction fields or radiated fields, additional shielding over the entire length of the electrode wires may reduce the interference. The shields should all be joined together and grounded to the ground lug of the amplifier input terminal or electrode board. In addition, if the electrode leads are very long, it may help to join the shields together at the end nearest to the electrodes, as well, but without any additional grounding. This serves to reduce the impedance of the loop formed by the shields themselves, and tends to equalize any potentials which may be induced in them so that if, in spite of their being grounded, they are still able to induce potentials into the electrode leads, the CMR may better act to reject them. (2) Potentials induced into electrode lead wires from all interference sources may be reduced by twisting the wires (with or without shielding) together. This minimizes the area of the loop they form and decreases the amplitude of any potentials which might be induced. In addition, it tends to cause any potentials which are induced at one point on a wire to be canceled by an equal and opposite potential at another point on the same wire. (3) Radio frequency interference that is picked up by electrode lead wires, and cannot be eliminated by shielding procedures may be eliminated by inserting a low-pass filter in series with the electrode leads (Whit-

field, 1959, p. 133). (4) In case of magnetic induction fields, changing the orientation and/or position of the subject, electrode leads, and amplifier input terminals may reduce interference to a tolerable level, as such fields are not usually equally strong in all directions.

e. MINIMIZING THE DISPLAY OF ELECTROMAGNETIC INTERFERENCE IN THE RECORD. Should interference potentials actually enter the amplifier and be displayed in the output along with the EEG, they may sometimes be reduced by means of filters in the amplifiers. Specifically, "notch" rejection filters, tuned to maximally reject frequencies of 60 Hz, may be employed to reduce interference from the power lines. This is the least desirable of all methods of reducing such interference, as its presence often implies some other procedure has not been correctly followed (e.g., electrode application). "Notch" filters result in the least distortion of the EEG when the interference frequency is outside the band of EEG frequencies, as, e.g., is largely the case with 60-Hz "notch" filters, and human scalp-recorded EEG.

f. OTHER NONSUBJECT INTERFERENCE. Electric induction fields which cause interference in EEG recordings may be generated in more "classic" ways, i.e., by means of charges of static electricity on insulators. Many man-made fabrics and substances serve admirably as collectors of such static electricity charges. Included among possible offending objects would be clothing, floor tiles, and even the insulation on the electrode lead wires. Relative movement of the electrode lead wires with respect to any electrostatic induction field will, of course, cause potentials to be induced in the wires, along with the EEG that is being recorded. It is best to avoid such materials in floor coverings and in clothing, if possible, and to keep the relative humidity in the recording area sufficiently high so that any charges which do build up will be quickly dissipated.

Movement of electrode lead wires either as a group, or relative to one another, should be minimized by keeping them as short as possible, and supported on their way from subject to electrode lead box. Left unsupported, they may vibrate or sway with slight subject movement, such as respiration, or because of building or equipment movement. In the extreme case where subjects are freely moving, it may be necessary to have preamplifiers on the subject, or perhaps even on the electrodes themselves, to prevent this type of interference. The preamplifiers convert the high impedance, very low voltage EEG source picked up by the electrodes to a low impedance moderate-voltage source, which is much more resistant to interference. The shorter the lead length to the preamplifier, the less likely that interference will be picked up in the recording. The output of the preamplifier may then be led to further amplification and recording by conventional shielded wires, or by telemetry. Several investigators have dis-

cussed the use of such systems, including Hanley, Adey, Zweizig, and Kado (1971) and MacKay (1970).

Finally, a relatively unique form of interference may be generated through the use of "wireless" intercommunication systems. These insert a radio frequency carrier signal (usually between 100 and 300 kHz) back into the power line which is destined for other intercom units plugged into the same power line, but which may be picked up by any other equipment as well. Without filtering of the power lines, their use may cause sudden, and otherwise unexplicable episodes in the EEG, lasting for the duration of each transmission. Dobbie (1967) has reported the cause, and cure, of an unusual form of interference due to an interaction between a hospital low frequency inductive loop paging system, and a 400-Hz chopper EEG amplifier.

2. Subject-Generated Interference

a. Interference Related to Muscle Activity. Interference related to muscle activity falls into two broad classifications: The first is of high frequency (30–40 Hz and higher) which results from a spatial average of the action potentials of the muscle group(s) as they are activated. Second, low frequency interference which arises from a change in the position of a recording electrode relative to some underlying tissue, the volume-conducted field of a biopotential generator (such as that produced by the eyeball), or an electromagnetic field in the subject's environment, brought about by the muscle action itself. Common instances with human subjects involve tensing or straining of neck muscles, frowning or raising the eyebrows, gritting the teeth, squinting, wrinkling the nose, wiggling the ears, swallowing, etc. Each of these may produce a burst of high frequency activity, as well as a slow baseline shift, for the duration of the muscle action. The magnitude of these artifacts is greatest from electrodes located nearest the muscle group involved, but can produce related artifacts at some distance due to stretching of the skin. If the muscle activity occurs rhythmically in bursts, as might be the case with some forehead, or nose movements, or with respiration, the low frequency interference may appear as if it were delta activity.

Usually this type of interference is eliminated when using cooperative subjects by requesting that they refrain from these movements. At times, a tense subject will exhibit a constant background of high frequency muscle activity, which may be mistaken for beta activity and even when asked, he may be unable to completely relax his muscles. In such cases, shifting his position, or gently massaging the offending muscle group may alleviate the problem. If none of these procedures is successful, it may be necessary to decrease the cutoff frequency of the low-pass filters on the amplifiers,

as a last resort.[3] Care should be taken that the EEG activity which is actually under study is not significantly altered by decreasing the cutoff of these filters. The filter settings on all channels should be the same to minimize phase shifts between them.

The most common source of low frequency interference, without any obvious concomitant higher frequency muscle activity, is the eyeball, on which there is a standing d.c. potential of some 100 mV with the cornea being positive with respect to the retina. As the eye moves, the potential field associated with it also moves, and these changes in potential may be picked up by recording electrodes, especially those near the eyes. The amplitude of the eye movement potentials which are recorded depends on the orientation and proximity of the electrode pair, as well as the direction and magnitude of eye movement. Rapid shifts in regard from one point to another, eye blinks during which the eye briefly rolls upward, and slow drifts in eye position, will produce eye movement artifacts in the record. The first two cause short transients, and if they occur rhythmically, may resemble slow frequency EEG activity. The latter type of movement will produce slow baseline shifts, and often are slow enough that they are filtered from the record when a.c. amplifiers are used.

Rather than try to minimize such eye movement artifacts by having the subject keep his eyes still, which may cause him to be uncomfortable, it may be possible to simply note the artifacts as they appear on the record, and delete these sections from analysis. Should it be desirable to control eye movements, which may be particularly important in some experimental situations, or where they are very frequent, the subject should be provided with, and instructed to look at, a fixation mark with sufficient background illumination to prevent the wandering subjective apparent movement of the autokinetic effect.

Milnarich, Tourney, and Beckett (1957) have described another source of interference of this type produced by fillings in the teeth of dissimilar metals which generate a d.c. potential, and which may be modulated by mouth and tongue movements.

b. OTHER SOURCES. Action of the heart may cause two types of artifacts in the EEG record. The first type occurs when an electrode is placed over or near an artery, causing slight movement of the electrode with each pulse. This balistocardiographic artifact appears like a poorly shaped sawtooth wave whose amplitude is a function of the amount of electrode movement.

[3] At times, attenuating the amplitude of muscle activity by changing the low-pass filter setting may make it appear more like beta activity, especially if the attenuation is such that only the higher amplitude, lower frequency motor potentials are displayed, resulting in the appearance of bursts of betalike activity.

To eliminate this artifact, the electrode must be shifted off and away from the artery.

The second type of artifact from the heart is from the volume-conducted potential field its action sets up throughout the body. It is this potential field which allows the electrocardiogram (ECG) to be recorded. Fortunately, this field is equipotential over the scalp in most human subjects, so that it appears as an in-phase signal to the EEG amplifier input stages, and is rejected. In unipolar recording, when reference leads are placed away from the scalp, on earlobes, nose, chin, etc., the chance of picking up ECG potentials which are not exactly in phase at the recording and reference leads increases, with a subsequent increase in the likelihood of an ECG artifact. The ECG artifact usually cannot be eliminated by a small change in electrode position; rather, a change in location of the unipolar reference lead or a change to bipolar derivations may be necessary. The extent to which ECG artifacts occur in an EEG record also depends, in part, on the physical characteristics of the subject, as, for example they are more commonly found in subjects with short, thick necks.

The skin may be a source of interference in three ways: (1) The skin itself may generate potentials (Tarchanoff effect), (2) the resistance of the skin can change (e.g., the Féré effect or the galvanic skin response), and (3) sweating can occur, causing a change in the electrolyte. All three phenomena are related, and are frequently observed under conditions where the subject is undergoing some psychological or emotional stress. Sweating obviously can also occur simply because the recording is being made in a hot room. Artifacts from these skin mechanisms appear as slow baseline swings which can vary greatly in amplitude. To the extent these are due to an interaction with the potential gradient at the electrolyte–skin interface, they may be reduced by light pricking of the epidermis to allow a more complete penetration of the electrolyte down to the dermis, as was mentioned when discussing electrodes. In addition, attempts should be made to reduce the cause of these artifacts by relaxing the subject, if they are thought to be the result of emotional tension, or by decreasing the room temperature if they are thought to be the result of heat. As a last resort, a change in the high-pass filter setting may be used to attenuate the recorded amplitude of these artifacts.

3. Equipment-Generated Artifacts

Most artifacts which come from the EEG amplifier-output system are best avoided by following routine preventative maintenance and checkout procedures, usually outlined in the equipment manuals. Among other things, these might include checks for the level of background noise, fre-

quency response, CMR, amplitude linearity, noise from dirty switch or electrode input contacts, broken or frayed wires and cables, etc.

The recording system can interact with other equipment in the environment, producing artifacts which may be difficult to trace. Reference has already been made to possible interactions with intercommunication or paging systems. Another kind of interaction can occur if more than one phase of electrical power is used to simultaneously operate different pieces of equipment. The artifacts which occur can assume a waveform that may be any combination of the different phases of the line power in use. To eliminate this problem, all pieces of equipment in use at the same time which make either direct or indirect electrical contact with one another should be connected to the same phase of the electrical power.

C. Considerations for an EEG Laboratory

An EEG laboratory usually has at least two rooms, one for the subject and one for the experimenter. Each of these contains the equipment necessary for their occupants to perform their respective tasks. Frequently the subject's room will contain little more than something to hold or contain the subject (such as a chair) and an EEG amplifier input terminal board. The experimenter "room," on the other hand, may consist of several rooms which contain the EEG amplifier-output system, as well as other associated equipment such as stimulators, control devices, and various supply material. Individual preference will generally determine most of the specific features of an EEG laboratory, but the floor plans for hospital EEG laboratories, suggested by Griffin (1963), may serve as a useful source of ideas. There are, however, several general design aspects that should be considered which will be covered below, in the context of recording from human subjects; many are equally applicable to laboratory situations where recordings are obtained from animals.

One of the primary considerations in the subject's environment, although he is totally unaware of it, is the extent to which it is protected from electromagnetic fields. Much has been said about the whys and hows of electromagnetic shielding, but not about whether it may actually be needed in a given situation. The only way the need for shielding may be determined is by actually recording test EEGs under the exact conditions where they are to be obtained in the future. These recordings should be obtained in the exact desired, future location of the laboratory at different times of the day, and when intermittent sources of interference, such as near-by elevators, are operating. Frequently electromagnetic shielding can be dispensed with entirely, especially if care is given to electrode application and the placement and orientation of electrode lead wires. Except where interference

signals are relatively high, the effective CMR of most modern EEG amplifiers will be sufficient to keep interference below the amplifier noise level. Walter and Parr (1963) have suggested that a certain amount of "tame" interference from the power line is desirable as an aid in detecting electrodes with high contact resistance or broken leads, and Schwab and Chock (1953) have described a method whereby power line "interference" may be injected into the recording system to check electrode resistance while recording. Either proposal, however, would work only if the line frequency "notch" filter had not been switched into the EEG amplifier circuit.

Acoustical shielding may be desirable if the laboratory is located where ambient noise is high, or if the subject is not supposed to hear noises from experimental equipment or the experimenter's room. The amount of acoustical shielding can vary from a complete anechoic chamber, to the use of nothing more than sound absorbing acoustical tiles or drapes. Again, only a data recording session can give the exact information needed to determine what is needed. For some situations, it may be possible to mask extraneous sounds with a constant background level of white noise (sound whose spectrum is uniform in amplitude but random in phase—at least over the audio range; subjectively white noise sounds like a "hiss") delivered by loudspeaker or earphones. Any sound deadening or masking devices will usually also make it necessary to use a two-way intercommunication system between subject and experimenter.

Lighting in the subject's room should be controllable from the experimenter's room, at least to the extent of being turned on and off. It may also be desirable to use a control which allows illumination to be varied continuously between these extremes, but it should be remembered that solid-state controllers (silicon-controlled rectifiers, triacs) can be a potent source of radio frequency interference, and variable auto transformers have relatively strong induction fields surrounding them. Predicting the amount of interference which might be produced by either is difficult if not impossible, and only by trying them out can one be sure that they will be satisfactory in a given situation. In either case, their position, relative to the subject and the electrode lead input wires is an important determinant of how much interference they will actually inject into a recording. It might also be desirable to have the subject in a light-tight room, so that all illumination is completely under the experimenter's control. With the installation of any shielding against sound, light and/or other electromagnetic fields in the subject's room, a ventilation system should be considered, with, perhaps, temperature and humidity controls.

Attention should be directed toward making the whole environment experienced by the subject as relaxing as possible. Included might be room decorations lending a relaxed atmosphere such as pictures on walls, drapes,

table lamps, background music when electrodes are being applied, etc. During the period of data collection the subject's physical comfort is important, especially if he is sitting up; e.g., some form of head, chin, and back rest support is usually desirable to minimize muscle tension.

In many cases it is desirable that the subject be visible to the experimenter, but not vice versa. An observation window with the subject suitably oriented to prevent his looking out the window, or the use of a "one-way" mirror with an appropriate differential in the illumination level of subject and experimenter rooms, will allow unidirectional viewing. Alternatively, and at a greater expense, a closed circuit television monitor could be used. The requirement that the subject be visible will limit the range of illumination that may be used in the subject's room, which may pose a problem if dark adaptation of the subject is important. The use of an infrared closed circuit television system is one possible solution.

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Chapter 2

The Electroencephalogram: Human Recordings

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The electroencephalogram (EEG) is a graph of voltage plotted over time, measured from the most superficial layers of the cerebral cortex. This voltage, a measure of electrical potential between two points, may be derived from two active areas on the scalp or within the brain (bipolar recording) or from an active scalp or cerebral electrode and a relatively inactive reference point ("unipolar" recording). As a voltage/time graph, the EEG can vary in only two dimensions; frequency (waves per second) and amplitude (voltage). Similarly, these two parameters can vary in two directions: frequencies can be too fast or too slow, and amplitude too high or too low. On various permutations of these four variables the entire art of electroencephalography rests.

The story becomes somewhat more complex when definitions of normal frequencies and amplitudes are introduced, for these vary with age, with state of arousal, and in relation to the region of scalp or brain from which the tracing is derived. In general, the EEG of infancy and early childhood is slower, higher in amplitude, and shows less regional differentiation of wave forms than that of older children and adults (Fig. 2-1). In premature and very young infants, frequencies are slow and irregular, and amplitudes are also rather less than in older infants. Maturation of the EEG is a gradual process in which 4–7-Hz activity (θ) predominates early from all regions, but is best developed posteriorly and over the temporal areas with faster frequencies over the frontal lobes (Table 2-1). By midchildhood a strong 8–12-Hz rhythmic component is usually evident posteriorly, the alpha rhythm, which waxes and wanes in "spindles" with amplitudes of 20–100 μV. This activity is singularly sensitive to visual stimuli, being most prominent with eyes closed or absence of visual attention and markedly attenuated by visual fixation. It is interrupted transiently by unexpected stimuli of many modalities. Over the frontal lobes, much faster, lower voltage, less regular activity is typically recorded (β, beta, 14–30-Hz). Rhythmic frontal fast activity may be arrested by movement of or intention to move the contralateral extremities. The 4–7-Hz θ activity of 50–60 μV is prominent throughout childhood and early adult life, gradually decreasing in amount

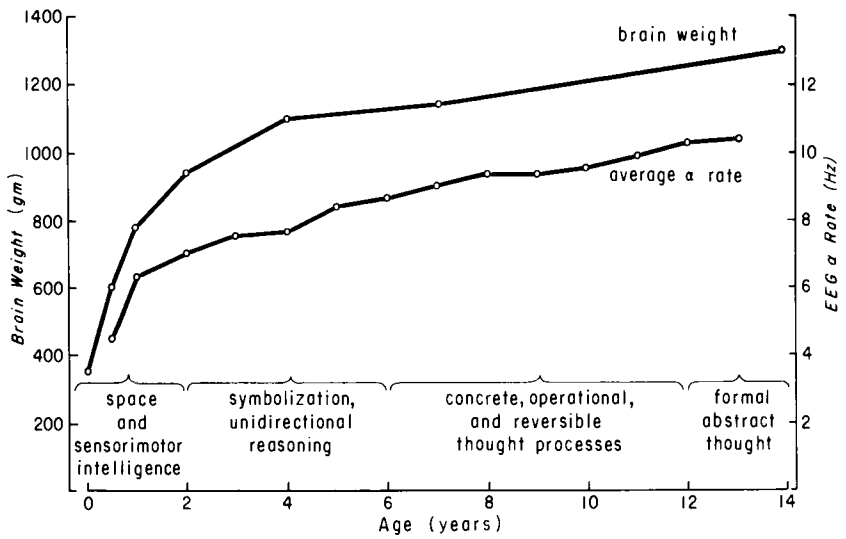

FIG. 2-1. Parallel growth of brain weight and average frequency of EEG background activity from posterior regions of the scalp. Psychological maturation milestones adapted from Piaget (1952). (From Stevens, Sachdev, & Milstein, 1968.)

TABLE 2-1

MAJOR FREQUENCY BANDS OF NORMAL EEG

Frequency (Hz)	Frequency band designation	Occurrence
½–3	Δ (delta)	Infancy Deep sleep Coma
4–7	θ (theta)	Childhood Light sleep Temporal areas through adolescence
8–13	α (alpha)	Adults, older children Parietal, occipital (> temporal) regions when eyes closed
14–30	β (beta)	Anterior scalp Arousal, excitement

to less than 25% of the total waveforms present at around age 20, and abnormal beyond the age of 30, in the waking EEG. Very slow activity, Δ, is abnormal in any waking record in adulthood, but is not infrequent in the occipital regions throughout childhood. Theta and alpha components are typically superimposed. An abundance of delta waves posteriorly in 8–12-year-olds is often interpreted as evidence of cerebral "immaturity" and is commonly prominent in children with hyperkinetic behavior disorders, but is so frequent in apparently normal children that the significance of the finding is moot. Similarly, persistence of abundant theta activity over the temporal regions in teenagers and adults has been considered evidence of delayed cerebral maturation, and is often recorded from individuals with severe behavior disorders and psychopathy (Hill, 1952).

I. Sleep

In addition to important variations of frequency and amplitude with maturation, there are dramatic changes in pattern and distribution of the EEG during relaxation, drowsiness, and sleep (Fig. 2-2). While the record of an alert, mentally occupied adult often consists of low voltage, fast frequencies from all regions of the head, closure of the eyes and mental idleness foster the appearance of posterior alpha rhythms which are quite symmetrical in most subjects. (For reasons not clear, the alpha rhythm tends to be somewhat higher over the right hemisphere than the left in young subjects,

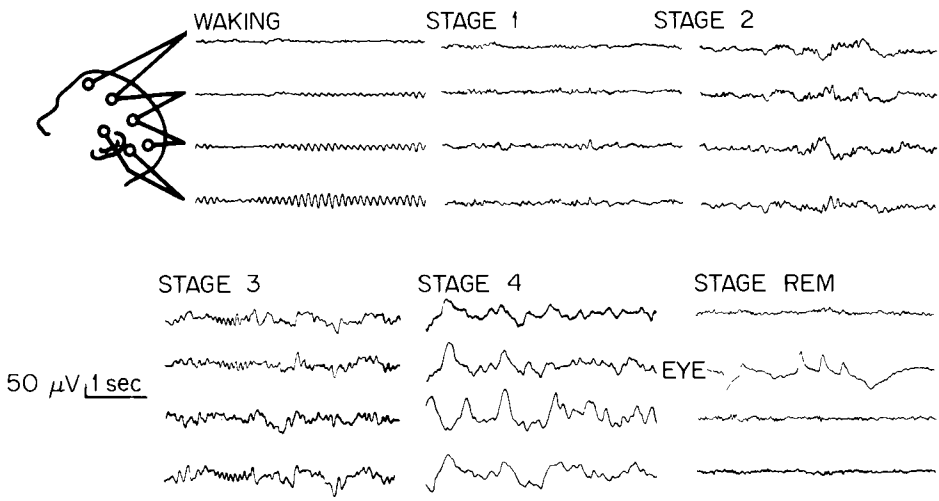

FIG. 2-2. Progressive stage of sleep: Posterior alpha in waking EEG with eyes closed; disappearance of alpha in drowsing (stage 1); appearance of anterior spindles and reversal of voltage gradient in stage 2; increasing slow activity in stage 3; Loss of 14-Hz spindles in stage 4; low voltage fast activity accompanied by jerky eye movements in stage REM.

regardless of handedness.) A minority of individuals have little or no visible alpha activity, although components in the alpha band can be detected by spectral analysis. W. Grey Walter (1953) considers these "alpha minus" individuals to be distinguished by their habitual use of visual thinking modes. As relaxation progresses to drowsiness and sleep, the posterior alpha components lose their sine-wave-like rhythmicity, slower elements are interposed both posteriorly and among the beta waves anteriorly, replacing the waking voltage and frequency gradients with a diffuse 50–60-μV, 5–7-Hz pattern (Fig. 2-2). As stage 2 sleep appears, the voltage gradient is entirely reversed from the waking state: amplitudes are now higher anteriorly, 12–14-Hz spindles appear and persist down through stage 3 sleep. Posteriorly, the theta activity of stage I grows in amplitude and diminishes in frequency with the appearance of high voltage delta waves. In deepest (stage 4) sleep, the anterior spindles are less evident and high voltage irregular 1–3-Hz activity is widespread with little regional variation. Sensory stimulation during light and medium sleep provokes a sharp wave, followed by a rhythmis spindled 12-Hz component known as the K complex. During nocturnal sleep there is periodic alternation of these various planes of slow-wave sleep, interrupted every 90–100 min by so-called *paradoxical sleep*, so named because the coincident scalp record of low voltage fast activity closely resembles that of alert vigilance. It is during this fifth stage of sleep that rapid eye movements (REMs) occur in brief bursts, muscle tone is abruptly diminished, and a number of visceral changes (cardiac acceleration, irreg-

ular respiration, penile erection) occur. Subjects awakened during paradoxical sleep report dreams four times more frequently than during slow wave sleep. Irregular bursts of spikes from pons, lateral geniculate, and occipital cortex, and rhythmic θ activity from hippocampus are recorded from subcortical electrodes during REM sleep.

II. Pathological Slow Activity

With these ontogenetic and state of arousal exceptions, waveforms which are too slow in the waking EEG usually signify a depression of function or a destructive process in subjacent brain. Pathological slowing in the EEG may be either focal or diffuse. If focal, the underlying cerebral disturbance is likely to be localized to the area over which the slow activity is maximum, shows phase reversals on bipolar recording, and maximum negativity or positivity on unipolar recording. Infarcts, tumors, contusions, abscess, hemorrhage, or other focal damage give similar EEG patterns of local slow activity (Fig. 2-3A). In general, the more acute, severe, and superficial the underlying destructive process, the slower and higher in amplitude the ab-

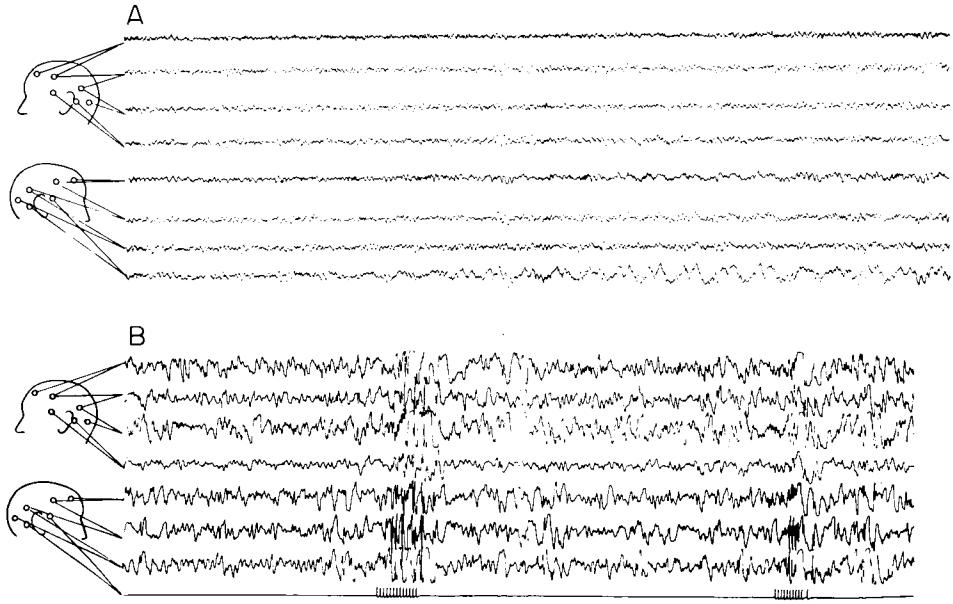

FIG. 2-3. (A) Waking EEG from 33-year-old engineer with tumor of right temporal lobe. Note slow activity localized to this region and seen faintly from frontal area of same side. (B) Diffuse paroxysmal spike activity in EEG in response to photic stimulation in 13-year-old girl with "character disorder." (From Stevens & Milstein, 1970.)

normal waveforms will be. It may be anticipated from the above that widespread disturbances, whether inflammatory, traumatic, metabolic, etc., will give rise to diffuse, nonlocalized slow activity.

III. Pathological Fast Waves

In contrast, EEG activity which is too fast may signify cerebral hyperirritability. Tense, anxious individuals often show little or no alpha activity in the EEG, the entire record being dominated by low voltage β waves. Fast activity is also prominent in delirium tremens, and with a number of sedative drugs, such as barbiturates. The phenothiazine tranquilizers, in contrast, evoke moderate slowing of the EEG, presumably due to their depressing effect on brainstem arousal systems. Although low voltage fast activity is normal in the frontal areas, two types of fast waveforms deserve special attention; the spike and the sharp wave. Spikes, defined in electroencephalography as 50–200+ μV waves with abrupt rise time and a duration of around 80 msec signal pathological hyperirritability of the brain, and probably are a summation of synchronous, simultaneous depolarizations or hyperpolarizations in the terminal ramifications of vertically oriented dendrites. Seldom recorded in the normal EEG, spikes often indicate epileptiform activity. An exception are the 14 and 6-Hz rhythmic spikes, negative in sign at the ear and positive on the scalp, which are recorded from many normal drowsy young people. When spikes are evident, sharp waves are nearly always present also, and are considered a hint of probable distant spike activity. Sharp waves are peaked potentials of 50–100 msec duration with slightly less abrupt rise time than spikes and with a similar but less definitive significance for cerebral hyperirritability. Although most commonly associated with epileptic processes, sharp waves and spikes may also be found in the EEG during certain psychiatric disturbances, particularly schizophrenia, child psychoses, acute and chronic brain syndromes (Fig. 2-3B). Slow, spike, and sharp activities often appear abruptly and with episodic augmentation of amplitude, and may be generalized, or localized over one or more scalp regions.

IV. Technique

The recording of the human EEG has become increasingly easy as technical improvements in equipment have rendered shielded rooms or electronic expertise by recording personnel quite unnecessary under most cir-

cumstances. Clinical EEG laboratories make use of multiple channel electroencephalographs, which permit simultaneous recording from 8 to 16 or more bipolar derivations from the head. The patient is attached to the recording unit by 18–24 metal or saline-pad electrodes evenly spaced over the surface of the scalp (Fig. 2-4). Despite remarkable technical advances in recording equipment, no compensation is possible in the recording apparatus for poorly applied electrodes, defective wires, or poorly relaxed patients. The best EEGs are made with patients lying in a comfortable bed or reclining chair in a room heated to 70–75 . Most laboratories in the United States make use of electrode disks constructed of silver, silver chloride, or tin affixed to the scalp with collodion under which electrolyte paste is placed in contact with the acetone-cleansed scalp. Perforated metal disks facilitate the introduction of electrolyte paste. Resistances well below 5000 Ω can be easily achieved by this technique. Bentonite paste is often used as an alternative but adheres less satisfactorily, requires adhesive tape unless the subject is totally immobilized, and occasionally causes rash—especially in infants or upon prolonged contact. Whatever the method of attachment, resistances below 10,000 Ω should be achieved between electrodes. Needle electrodes inserted into the skin of the scalp are widely used in the western part of the United States. They are faster and require little or no expertise in application on the part of the technician other than sterile precautions. Disadvantages are the discomfort in having 18–20 needles inserted in the scalp for an hour or more, high resistance (generally 15–30 kΩ), more movement artifact, and the necessity to autoclave electrodes between each use.

Electrode placements vary from laboratory to laboratory, the trend being toward adopting the International (10–20) system for electrode identification and position (Fig. 2-4). Advantages of a uniform electrode placement system are obvious in facilitating exchange of information between EEG laboratories throughout the world via publications, meetings, etc. The 10–20 system, officially endorsed by the International Congress of Electroencephalography, is fully described in the *Journal of Electroencephalography and Clinical Neurophysiology* (Jasper, 1958), but is best learned under supervision of a qualified EEG technician or electroencephalographer.

Following firm affixation of electrodes to the scalp, resistances are measured between all electrodes. A calibration signal is then sent to the pens of all channels of the EEG through a master switch. A brief recording from identical scalp areas is made on all channels to verify the equivalence of recording fidelity of each amplifier-galvonometer unit. If these preliminary procedures satisfy technical requirements, the operator proceeds to select various combinations of electrodes, typically comparing homologous derivations from the right and left sides of the head with both longitudinal and

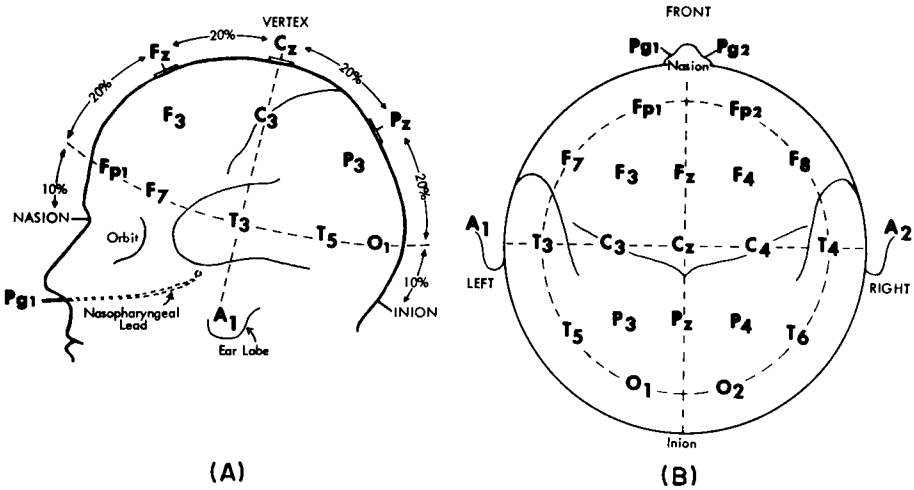

FIG. 2.4. International electrode placement system in wide use in the United States and in the majority of EEG laboratories throughout the world. Detailed instructions for application appear in Jasper (1958). For examples of typical montages (recording linkages) see Table 2-2. (From Jasper, 1958, Fig. 1.)

horizontal linkages (Table 2-2). Nasopharyngeal or sphenoidal electrodes may be introduced to record activity from the base of the brain, particularly the medial and inferior surface of the temporal lobe.

Each montage is usually run for around 3 min, the total recording of the EEG requiring 25–30 min, usually including 3 min of hyperventilation and stimulation by stroboscopic light flashes. During the routine EEG recording, the subject is required to open his eyes for 50–60 sec during the recording with each montage. This procedure facilitates detection of underlying

TABLE 2-2

SAMPLE MONTAGES FOR 8-CHANNEL EEG[a]

1	2	3	4
F_{p1}–F_3	F_7–F_3	T_3–P_3	F_{p1}–F_7
F_3–C_3	F_3–F_z	P_3–P_z	F_7–T_3
C_3–P_3	F_z–F_4	P_z–P_4	T_3–T_5
P_3–O_1	F_4–F_8	P_4–T_4	T_5–O_1
F_{p2}–F_4	T_3–C_3	T_5–O_1	F_{p2}–F_8
F_4–C_4	C_3–C_z	O_1–P_z	F_8–T_4
C_4–P_4	C_z–C_4	P_z–O_2	T_4–T_6
P_4–O_2	C_4–T_4	O_2–T_6	T_6–O_2

[a] Notation as in Fig. 2-4.

rhythms when pervasive alpha activity swamps the tracing with eyes closed, tends to suppress drowsiness, and fosters the appearance of certain epileptiform potentials at the moment of eye closure in those so predisposed. After recording from each electrode combination for 3 min or more, the subject is instructed to breathe as deeply and rapidly as he can for 3–4 minutes. This period of hyperventilation causes a marked loss of plasma carbon dioxide and results in cerebral vasoconstriction and relative ischemia. Slow, sharp and spike activity are potentiated by CO_2 depletion. The procedure is avoided in patients for whom cerebral ischemia is hazardous. Physiologic slowing of the EEG during and following hyperventilation may be very dramatic in cooperative young individuals, but can usually be readily differentiated from the pathological response of epileptic or focal pathologies. Modest decreases in the blood sugar, i.e., below 120 mg %, although within the normal range, may contribute to the prolongation of slowing following hyperventilation. Photic stimulation, although not as widely used as hyperventilation, is valuable for detecting underlying cerebral irritability. A bright strobe light is placed 10 to 12 inches from the nasion of the subject who sits or lies with eyes closed during the procedure. Flashes of light from the stroboscopic unit are usually delivered with maximum intensity at frequencies of 1 to 20 flashes per second. Each frequency may be employed for 10 sec on and 10 sec off. Most subjects will show entrainment (driving) of their posterior scalp rhythms at frequencies close to their own alpha and at faster frequencies. Other subjects may only show attenuation of background amplitudes by visual inspection. A few individuals, however, will demonstrate marked augmentation in amplitude of the EEG in response to the flash either at the frequency of the light or a subharmonic. Occasionally this exaggerated response will take the form of paroxysmal high voltage spike or spike wave discharges associated with subjective distress or even a clinical epileptic seizure (photoconvulsive response). This effect is most commonly induced with frequencies of 12–14 flashes per second in children with petit mal epilepsy, certain child psychoses and character disturbances, and in individuals recently withdrawn from sedative drugs (Fig. 2-3B). Photomyoclonic response, consisting of jerking of the muscles of the face and eyes without definitive EEG change in response to the flashing light, is also seen commonly in individuals withdrawing from sedative drugs, including alcohol.

Sleep is commonly employed as an activating procedure in the EEG laboratory for investigation of individuals, especially children too active to record satisfactorily awake, and to disclose abnormal spike activity which may not be apparent in the waking states. Particularly in the case of temporal lobe epilepsy, the sleep activation with nasopharyngeal or sphenoidal electrodes in place may provide localizing information totally lacking in the

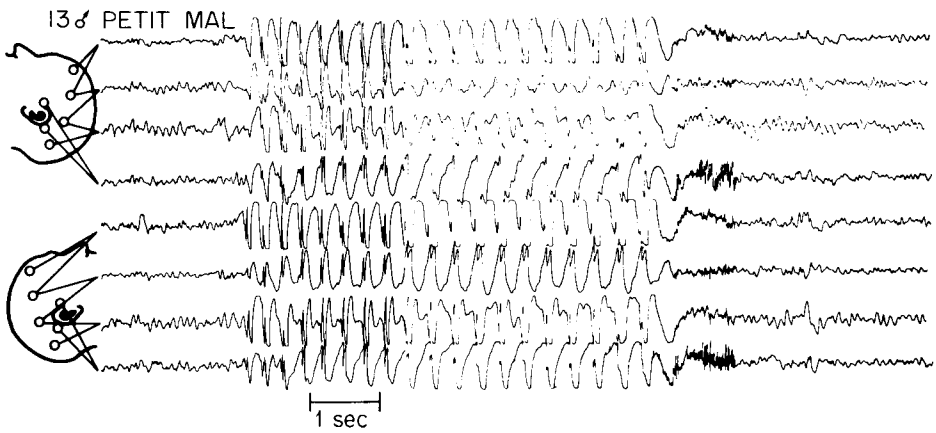

FIG. 2-5. Routine EEG on 13-year-old male with petit mal epilepsy disclosing abrupt onset of 3 Hz high amplitude (paroxysmal) spike wave discharge from all regions of the head, associated with coincident failure to respond and irregularities of respiration.

waking trace. Even between frank seizures, some 70–80% of epilepsies can be electrically confirmed using these routine techniques (Fig. 2-5).

Rarely, the clinical problem of localization will require placement of electrodes within the skull, either chronically or acutely. Recording from intracerebral electrodes reveals the extraordinary limitations of scalp electroencephalography, which at best picks up only from the superficial ½ cm or less of the brain. Placement of electrodes within the skull or brain in individuals with epilepsy often reveals well-localized high voltage spike activity of which no hint appears in the routine scalp EEG (Fig. 2-6). Similar evidence of localized spiking from deep subcortical structures in patients with schizophrenia, impulsive behavior disorders, or under influence of certain drugs has been reported from a number of laboratories (Heath, 1958; Walter, 1953; Stevens, Mark, Ervin, Pacheco, & Suematsu, 1969).

The EEG diagnosis of epilepsy or behavior disorders depends on the likelihood that derangements in cerebral electrical activity will be present in the intervals between overt symptoms, and indeed this is true for 60–70% of individuals with seizure disorders. However, it is often desirable to record the EEG during the period of clinical abnormality in order to examine the region of origin, electrical characteristics, and distribution of the pathological waveform. For this purpose, convulsants such as pentylenetetrazol (Metrazol) or bemigride (Megimide) may be administered intravenously to the patient in the EEG laboratory while recording from surface or depth electrodes. When intracerebral electrodes are in use, electrical stimulation

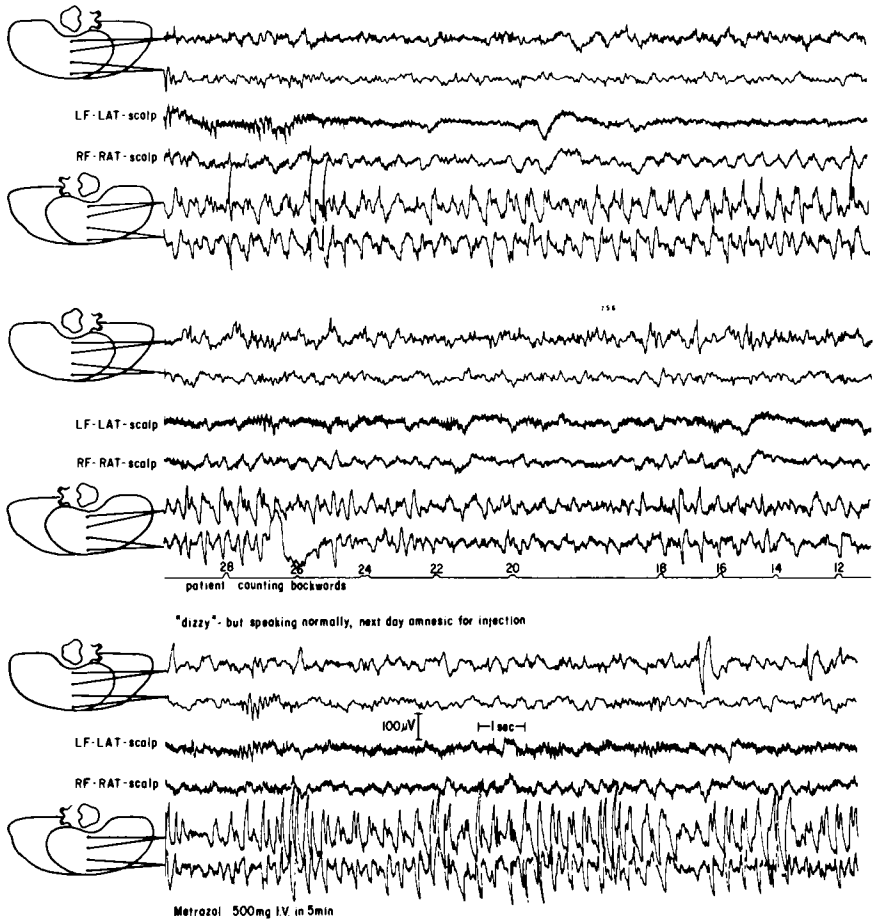

FIG. 2-6. Little change in surface EEG during continuous abnormal spike activity in the right amygdala unaccompanied by detectable clinical signs or subjective symptoms. Patient suffered from intermittent psychomotor epilepsy which was subsequently completely relieved following right temporal lobectomy. (From Stevens, 1966.)

and elicitation of clinical symptoms or afterdischarge may be utilized for localization of areas of cerebral hyperirritability (Figs. 2-6, 2-7).

For prolonged recordings of EEG during daily activity, radio telemetered transmission is a useful technique. Electrodes from the patient are attached to a small multichannel radio transmitter worn on the head or in a back pack, permitting free mobility while the EEG is continuously recorded from a multichannel matched receiver-demodulator, the antenna for which is located 50–100 ft from the patient (Fig. 2-8).

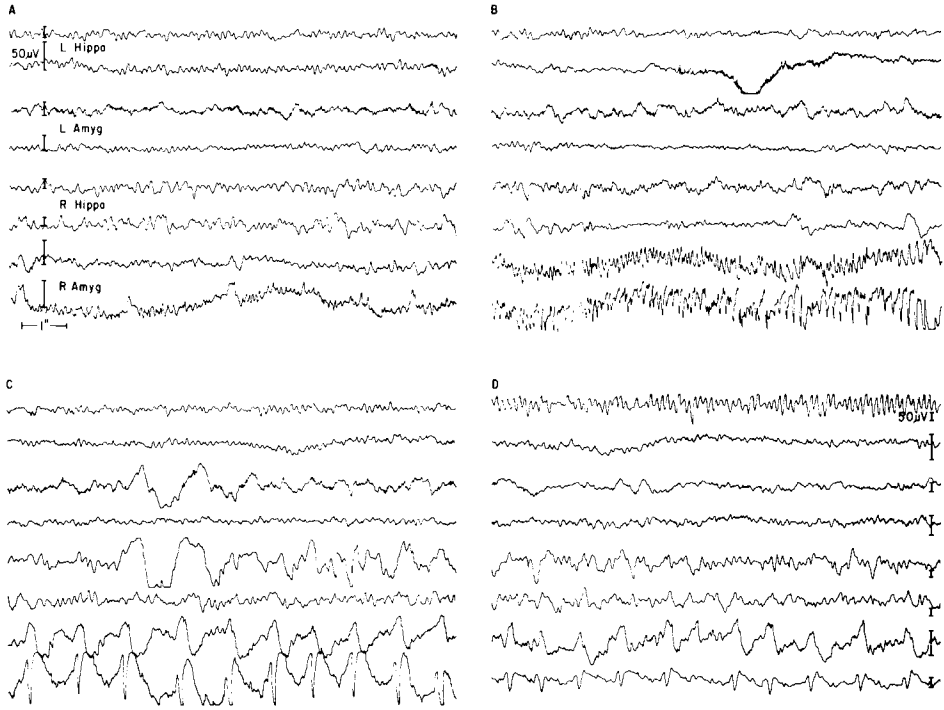
A
50μV
L Hippo
L Amyg
R Hippo
R Amyg
1"
B
C
D
50μV
1"

FIG. 2-7

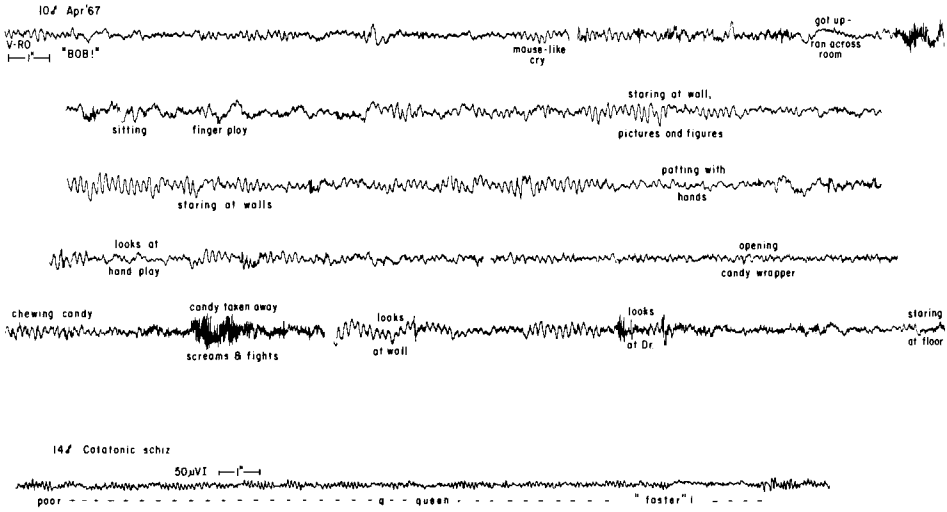
10♂ Apr'67
V-RO
"BOB!"
mouse-like cry
got up - ran across room
sitting
finger play
staring at wall, pictures and figures
staring at walls
patting with hands
looks at hand play
opening candy wrapper
chewing candy
candy taken away
screams & fights
looks at wall
looks at Dr
staring at floor
14♂ Catatonic schiz
50μV
1"
poor
queen
"faster"

FIG. 2-8

V. Experimental Uses of EEG

The EEG is widely used in clinical neurological and psychiatric medicine and is particularly useful in the diagnosis of epilepsies. In contrast to patients with tumors, strokes, or severe head injuries, in whom objective clinical or laboratory signs of brain pathology are usually available, in patients with epilepsy the EEG is often the only objective evidence of a cerebral disturbance between attacks.

Although between 5 and 15% of the general population have some abnormality in the EEG, the more severe pathologies such as pronounced spike or delta activity occur in less than 1% of healthy adults. Neither does a normal EEG exclude the possibility of organic brain dysfunction. Patients with subcortical abnormalities and/or chronic disorders such as Parkinsonism, congenital cerebral palsy, and mental retardation may have quite normal tracings despite severe and indubitable brain defect. Thus, the practice of utilizing the EEG to rule in or out the contribution of organic factors to disturbed behavior must be interpreted with caution and with appreciation of the limitations of the technique.

The EEG has been widely used in investigative work in clinical and experimental psychology in man and animals. Conditioning of EEG patterns, endogenous conditioning to spontaneous intrinsic rhythms through audio feedback of spike wave, alpha, or other EEG rhythms, relationship to maturation, intelligence, psychological test performance, psychiatric disorder, drug effect, circadian and ultradian variations, biochemical changes, environmental and psychological stress, selective brain lesions and stimulation, sleep deprivation, self-stimulation, sexual, auditory, visual, and other sensory stimulation comprise a literature increasingly bulky and often poorly digested. Interpretation of many of the findings of the mounting number of

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FIG. 2-7. Cocaine-induced "high" is associated with a paroxysmal continuous spike discharge from the electrodes chronically placed in the right amygdala of a 25-year-old male with seizure and impulse disorders. During the spike discharge, patient's performance was improved on several speed and perception tests and patient felt unusually well during the 2 hr that high voltage spikes continued to appear from the amygdala-hippocampal region. There were no changes visible in the scalp, nasopharyngeal, or sphenoidal EEG. Both the euphoria and paroxysmal EEG change were markedly diminished by pretreatment with chlorpromazine: (A) Control. (B) 8 min after cocaine, 100 mg intranasally. Patient feels exceptionally well. (C) 90 min after cocaine. Patient feels well, performance improved. (D) Pretreatment with 200 mg chlorpromazine blocks cocaine "high" and diminishes spike wave effect from amygdala. (From Stevens, Mark, Ervin, Pacheco, & Suematsu, 1969.)

FIG. 2-8. Single channel recording by telemetry from miniature transmitter worn on child's head during free behavior including a number of typical autistic automatisms, accompanied by no change in the scalp EEG from right occiput. (From Stevens & Milstein, 1970.)

EEG investigations awaits a widening of our understanding of the mechanisms responsible for generation of cerebral electrical activity.

The above remarks can serve only as an introduction to the use of the electroencephalogram in clinical and investigative work. The interested reader is referred to several references in the bibliography which include an excellent introductory volume (Kiloh, 1961), a comprehensive reference work (Hill & Parr, 1963), and an atlas in which many of the patterns discussed above are illustrated (Gibbs & Gibbs, 1950–1952).

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Chapter 3

Human Average Evoked Potentials: Procedures for Stimulating and Recording

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I. Introduction

Electrical potentials arising from the nerve cells of the human brain and recordable from the scalp can be divided conceptually into two types. The first type is a continuous series of potential oscillations which are not related in a specifiable way to sensory input. This spontaneous electrical activity is recorded as the electroencephalogram (EEG). The second type has a fixed temporal relationship to external sensory stimuli and is therefore said to be evoked by such stimuli. When potential changes evoked by repeated stimuli are averaged and plotted as a function of time after stimulus presentation, the result is termed the average evoked potential (AEP). There is abundant evidence that the AEP is indicative of the neural activity of the brain involved in the processing of sensory input. To the degree that we can learn to interpret this indicator, we should gain insight into sensory neural mechanisms operating in both the normal and pathological brain.

The first recording of evoked potentials in mammals is credited to Richard Caton who in 1875 recorded them directly from the surface of a rabbit's brain. It was 85 years later, and only about 10 years ago, that systematic analysis of the phenomenon became possible in man. The delay resulted from two factors. First, the layers of the brain case—meninges, skull, and scalp—attenuate the millivolt levels found directly at the cortical surface to microvolt levels at the scalp. It was not until 1929 that electronic amplification permitted Hans Berger to demonstrate that brain potentials could be recorded in man through the unopened skull. This discovery laid the foundation for clinical electroencephalography. However, much of the evoked activity is obscured by the larger potentials of the EEG. This adverse "signal-to-noise ratio" continued to limit human evoked potential research to components that could be distinguished in EEG traces or recorded directly from the brain during neurosurgical operations.

Systematic investigation of evoked potentials from the intact human head began to be feasible when Dawson (1951) suggested that those potentials regularly evoked by a repetitive stimulus could be discriminated from the irregularly occurring EEG potentials if all electrical activity subsequent to the stimulus was summated. The technique of summating, or averaging if summed voltage is divided by the number of repetitions, to extract systematic fluctuations from asystematic ones was used as early as the eighteenth century; Dawson's contribution was to apply the technique to human neurophysiology. Averaging enhances any activity which has a consistent temporal

relation to a recurrent event, i.e., is "time-locked" to the event, while concurrent activity inconsistently related to the event tends to cancel itself. Mathematically it can be shown that the time-locked activity (signal) summates directly as the number of repetitions whereas activity not time-locked (noise) summates only as the square root of the number of repetitions. The averaging technique, then, is a means of improving an initially adverse signal-to-noise ratio. Commercially built apparatus for averaging or summating evoked responses became available about 1960 and the bulk of research on human evoked responses dates from that time. Figure 3-1 illustrates the necessity of averaging to record the AEP. The traces in the first and third columns are examples of individual poststimulus EEG activity which contributed to the averages shown in the second and fourth columns. The 100-msec records are an expansion of the first part of the 500-msec records for better resolution. They show that small, shorter latency AEP components (1–4) are not distinguishable in the EEG record. Consistent activity begins to emerge after 16 repetitions but is still obscured by spontaneous potentials. Averaging additional repetitions progressively enhances the components. Larger amplitude later evoked activity (component 5) is inconsistently distinguishable in poststimulus EEG records. An average of 16 repetitions extracts the evoked potentials; further repetitions improve the signal-to-noise ratio.

This chapter is intended to be a practical guide to evoked response re-

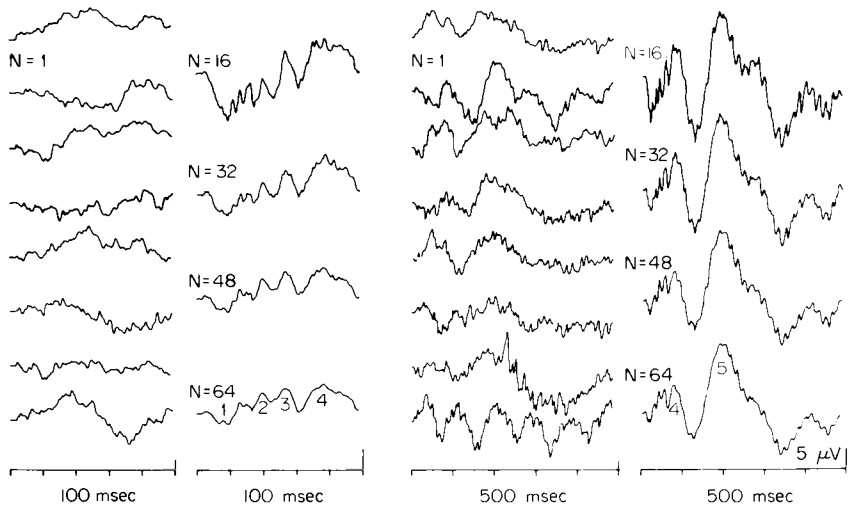


FIG. 3-1. Comparison of single poststimulus EEG records (1st and 3rd columns) and averages of increasing numbers of repetitions (2nd and 4th columns). Derivation: parietal scalp (P_3) to linked ears (A_1–A_2). In this and subsequent AEP records, positivity is upward at the scalp electrode. Stimulus: right median nerve shock delivered at start of records.

cording. There are many detailed discussions of most aspects of the technology of recording bioelectric potentials from the scalp but these are scattered throughout the engineering, chemical, physical, physiological, and psychological literature. My effort is to bring together practical information which I have found relevant. Where appropriate I have referred to commercially available equipment currently in use in my laboratory so that the beginning investigator may have some starting point for developing a recording system. In addition to the "hows" I have tried to answer the "whys" where I feel the knowledge will significantly increase the investigator's proficiency or flexibility.

When considering the characteristics of electrodes and amplifiers, it is useful to think of the AEP as being of two types: the so-called a.c. (alternating current) and d.c. (direct current) potentials. Alternating current potentials, like the EEG, fluctuate between positive and negative voltages. They can be recorded with conventional EEG electrodes and amplifiers. Direct current potentials are slow, usually aperiodic, changes which can be recorded from the scalp only by the use of specialized electrodes and amplifiers. This chapter will include recording methods for both a.c. and d.c. potentials since there is considerable communality between them. However, d.c.-evoked potentials, especially the contingent negative variation (CNV), are discussed elsewhere in this volume.

II. Electrodes

The same electrode characteristics required for a.c. AEP recording are also required for EEG recording and numerous discussions in considerable technical detail are available (e.g., Bureš, Petráň, & Zachar, 1967; Cooper, 1963; Cooper, Osselton, & Shaw, 1969; Geddes & Baker, 1968; Margerison, St. John-Loe, & Binnie, 1967; Walter & Parr, 1963). An electrode is a metallic connection between the complex physiological electrolyte of tissue and the recording circuitry. This metal-to-electrolyte junction or interface itself gives rise to potential differences between electrodes which can be quite large relative to the neuroelectric signals we wish to record. Potentials are developed because metal conductors in contact with a solution have a tendency to discharge cations into, and receive cations from, the solution. Whether the net result of this ionic transfer creates a positive or negative potential across the electrodes depends on the electrochemical activity of the metal and the cation concentration of the solution. Potential differences between electrodes are of two types: a bias potential, often incorrectly termed polarization (Edelberg, 1967), and true polarization.

A bias potential results when differences in the properties of two electrodes cause an imbalance in the net electrode-electrolyte ionic transfer. Therefore, an important characteristic of electrodes is that their surface properties be as identical as possible, in other words, they should be of the same pure metal free from surface contamination. Under such conditions, because of the reasonably homogeneous electrolyte concentration of tissues, the net ionic transfer will be approximately equal at the two electrodes and to the extent that it is equal, no potential difference will develop between them. Considerations of cost, availability in pure form, resistance to oxidation and corrosion, and harmlessness to living tissue have indicated the use of silver, gold, and platinum for electrode metals.[1] Their purity and resistance to surface contaminations minimizes the generation of bias potentials. However, electrodes of these metals are polarizable.

Polarization requires the passage of a current through an electrode pair and results from the action of electrolysis occurring between the electrodes and the tissue electrolyte solution. When a voltage is impressed, positive ions migrate to the more negative electrode and negative ions to the more positive electrode. An electromotive force (emf) in opposition to that of the impressed voltage (a back emf) is thus developed and the electrodes are said to be polarized. Polarized electrodes favor the flow of current in one direction and resist the flow in the other direction; thus they may exaggerate or diminish the recorded current. The voltage recorded will be an interaction between the true biological potentials and the back emf developing at the electrode, resulting in "capacitative" distortion of the true potentials. A detailed discussion of electrode polarization is given by Schwan (1963) who states that polarization can affect a.c. signals such as the EEG and that the effect of the a.c. signal is to modulate the polarization potential. However, the modulation will be proportional to the a.c. current density if current density is kept sufficiently small. Electrode polarization impedances through a saline solution have been measured for a pair of platinum electrodes by Schwan (1965). The resistive component was relatively constant at approximately 100 Ω at frequencies of 10–100 Hz.

The current passage required for electrode polarization can come from internal or external sources. Modern instrumentation draws negligible current and this source may be ignored for scalp AEP work. Measuring interelectrode resistance with an ohmmeter is a significant source of external polarizing voltage and should be avoided. Indeed, a simple demonstration of polarization effects is to apply an ohmmeter across polarizable electrodes

[1]Margerison *et al.* (1967) have pointed out that these noble metals are chemically inert and technically do not conduct signals as low as those of scalp-recorded potentials in the same way as other metals.

attached to the scalp. The resistance reading will gradually increase as polarization occurs; reversing the leads will produce a sharp drop and then a gradual rise in resistance (Zablow & Goldensohn, 1969). Impedance is the more accurate measurement for a.c. potential recording; electrode resistance to a d.c. signal is frequently higher than electrode impedance to an a.c. signal. An impedance meter (1)[2] avoids polarization by applying an a.c. signal across the electrodes. Polarization can be minimized by having a reasonably large electrode surface which reduces current density of d.c. voltages across the electrodes. Furthermore, with a.c. potentials, the direction of current flow is continually reversing and to the extent that the reversal is equal and opposite, polarization will not occur. R. F. Thompson, Lindsley, and Eason (1966) point out, however, that polarizable electrodes can distort a.c. potentials if the proportional current flow is significantly more of one polarity than the other.

In summary, the use of gold, silver, or platinum electrodes kept free of surface contamination minimizes bias potentials. Furthermore, they are d.c. potentials and are blocked by the common use of capacitors at the inputs of amplifiers designed for a.c. potential recording (see Section V). Such electrodes are polarizable but polarization can be minimized by using surface areas large enough to keep current density low. Polarizable electrodes behave somewhat like capacitors (Cooper, 1963; Grass, 1948). However, this has been found to have a negligible effect on the recording of biopotentials in the EEG frequency range (Zablow & Goldensohn, 1969). Since evoked potential frequencies are in the EEG range or higher, this conclusion can be generalized to AEP recording.

While bias potentials and polarization effects may not affect AEP recording using high impedance capacity-coupled amplifiers, fluctuations in these potentials will be recorded and may be indistinguishable from legitimate biopotentials. The most effective means of avoiding such fluctuations is to minimize interelectrode impedance. The resistive component of this impedance is the easier to manipulate since the capacitative component is determined essentially by electrode-tissue properties. The smaller the interelectrode resistance, the less the range of resistive change and resulting potential fluctuations; and the smaller the percentage change of the total input impedance of the circuit.

Electrodes for a.c. AEP recording are commercially available in the form of gold-plated or silver disks for surface application and thin needles of sharpened platinum alloy wire for subdermal application.[3] Examples of

[2] Numbers in parentheses refer to equipment listed in the Appendix.

[3] Jenkner (1967) has reported encouraging results for EEG recording using electrodes made of conductive silicone rubber which require no electrolyte paste or jelly, no maintenance, develop no standing potentials, and adhere very tightly to the skin, minimizing electrode movement.

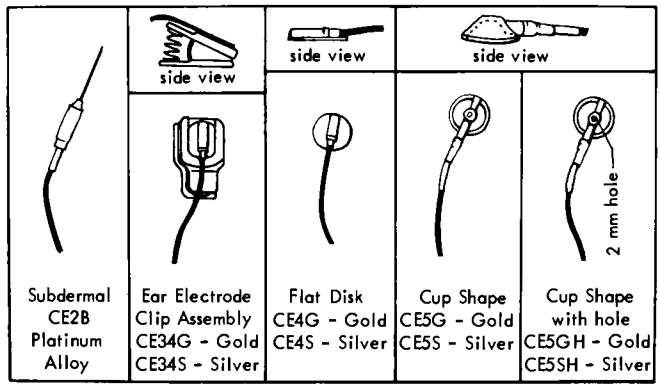


FIG. 3-2. Commonly used electrodes for a.c. AEP recording. (Courtesy Grass Instruments Co., Quincy, Mass.)

these electrodes are shown in Fig. 3-2. Silver electrodes can become tarnished by oxides and sulfides upon exposure to the atmosphere. Such contamination contributes to bias potentials. Gold, being more resistant to contamination, is preferred by many as producing fewer artifacts than silver. Disk electrodes properly applied should have impedances of 1 kΩ to 10 kΩ. Impedances below 5 kΩ are desirable; impedances over 10 kΩ require reapplication of electrodes. Subdermal (needle) electrodes may have resistances of up to ten times that of disks. Zablow and Goldensohn (1969) report that needle electrodes show much larger impedance changes with frequency in the EEG range than do surface disks. Impedance varied inversely with frequency, becoming as low as disks at 50 Hz (the highest frequency measured), rose significantly at 5 Hz, reaching approximately 0.14 MΩ at 0.5 Hz with a lagging phase shift of nearly 60 degrees. They concluded, however, that the alteration of the EEG was significant only for components below 1 Hz and only if the input impedance of the amplifier was less than 1 MΩ. They also found that needles are somewhat freer of potentials generated at the skin surface since they apparently make their best contact below these generators.

While needle electrodes are used in EEG laboratories and for AEP recording, primarily due to their speed and ease of application, their disadvantages should be kept in mind. First, since they tend to have somewhat higher interelectrode impedances, they are more susceptible to the generation of artifacts and the pickup of 60-Hz interference (see Section VII). Their use may be contraindicated for recording in unshielded areas where this kind of interference is prevalent. In such instances the use of disk electrodes with their generally lower impedances is preferable. However, we have recorded successfully in unshielded areas using needle electrodes. Second, they must be sterilized by autoclaving (see Section III). Finally, needles are not usually comfortable in nonscalp areas where reference electrodes are commonly

placed for monopolar recording (see Section IV). Silver or gold disks are therefore used for the reference and the dissimilarity of these metals to the platinum needles may generate bias potentials. For reasons already stated, this is in practice ignored for the recording of a.c. potentials.

Polarizable electrodes cannot be used for d.c. recording because of the capacitative effect of the polarization. For similar reasons, capacity-coupled amplifiers cannot be used (see Section V). Direct-current recording techniques are mandatory for CNV experiments and are desirable whenever frequencies below 1 or 2 Hz are of dominant interest. These techniques require the use of "reversible" or "nonpolarizable" electrodes. A nonpolarizable electrode is one in which the passage of current does not qualitatively change the electrode's chemical composition and if a quantitative ion exchange occurs due to the application of a voltage, the change is completely reversible upon reversing the current. Metal electrodes covered with a poorly soluble salt of the metal in a solution containing anions of the salt meet these requirements. Some form of the silver-silver chloride (Ag-AgCl) electrode is the most commonly used. All physiological electrolytes contain chlorine ions and silver chloride is insoluble but easily formed on the surface of the silver either by electrolysis with a low voltage battery (faster procedure) or by the self-chloriding method (slower procedure) of leaving electrodes electrically connected in a saline solution. Methods for chloriding silver electrodes and for their maintenance are found in Cooper (1963), Margerison *et al.* (1967), and Walter and Parr (1963). A detailed discussion of Ag-AgCl electrodes is given by Janz and Taniguchi (1953). Various kinds of Ag-AgCl electrodes are commercially available which improve over the plain chlorided disk by providing a larger surface contact area to decrease current density. For example, the nonpolarizable electrodes in use in our laboratory (Fig. 3-3) use an Ag-AgCl pellet as a transducer element with an electrolytic reservoir between the electrode face and the pellet. When the electrode is applied, electrolyte is forced into the reservoir through holes in the electrode face, forming an interface between the skin and the pellet. The pellet is a porous, compressed mixture of Ag and AgCl powder. The porosity makes a larger amount of Ag-AgCl available to the electrolyte, fostering the development of a stable half-cell voltage between pellet and electrolyte. To the extent that such stability is achieved, there is no half-cell voltage artifact to shift the recording baseline (Beckman Instruments, 1965).

In summary, commonly used electrodes for AEP recording where frequencies below 1 or 2 Hz are not of major interest are silver or gold percutaneous disks or subdermally placed needles made from sharpened fine-gauge platinum alloy wire. The choice of which to use largely depends upon the circumstances of the individual experiment or the experimenter's preference in the tradeoff between ease of application versus somewhat higher

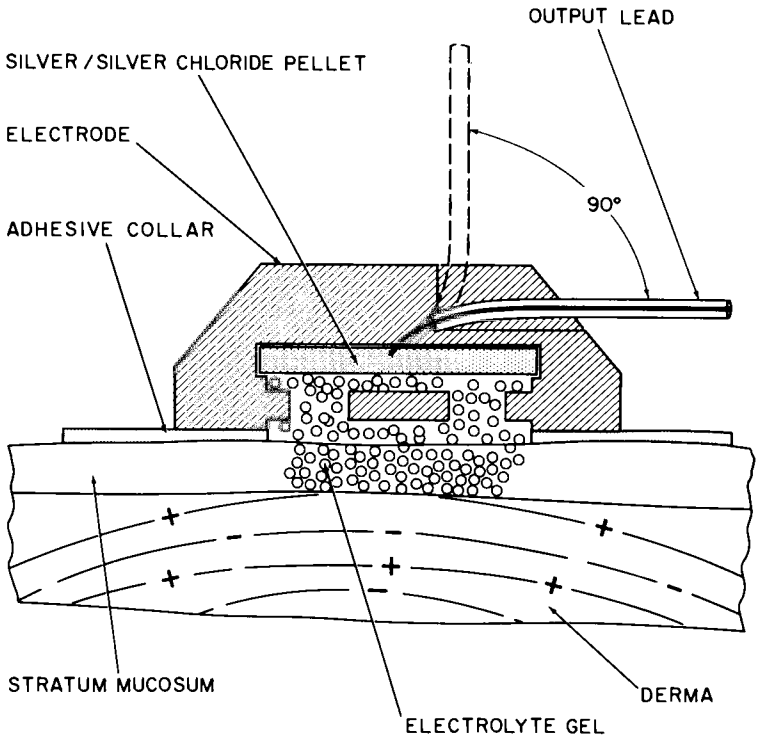


FIG. 3-3. Nonpolarizable electrode. Explanation in text. (Courtesy Beckman Instruments, Inc., Palo Alto, Calif.)

interelectrode impedance and the necessity for sterilization. Needle electrodes are not indicated for sleep experiments where the contact between head and pillow can cause painful movement of the needles. If very low frequencies or d.c. potentials such as the CNV are being investigated, nonpolarizable electrodes must be used.

III. Electrode Application and Maintenance

In terms of electrode application problems, there are two types of electrodes and two types of locations. The electrodes are surface or percutaneous (e.g., disks), and subdermal (needles). The locations are scalp and nonscalp. Scalp locations are usually hairy and the areas generally used as reference locations for "monopolar" recording are hairless. The simplest applications are needles to hairy areas and disks to hairless areas.

Between uses, needles should be examined for sharpness under an optical magnifier of 10× or more and sharpened if necessary by hand on a fine grit stone. They should be soaked in a hemosolvent and then sterilized. Conn and Neil (1959) indicated the major hazard of needle electrodes for the transmission of viral hepatitis and pointed out that "cold sterilization" techniques such as immersion in germicidal solutions or ultraviolet light do not destroy the hepatitis virus. Early versions of needle electrodes would not withstand repeated heat sterilization but modern ones will. Steam sterilization before every use is a mandatory procedure.[4] In a study reported by Grass and Hazel (1962), electrodes were contaminated with different types of organisms similar in resistance to the hepatitis virus which can be transferred only through the human blood stream. Steam sterilization at 250°F for 15 min at 15 lb pressure sterilized 100% of the organisms. Recommended methods for needle electrode sterilization are steam autoclaving for 20 min at 250–260°F at 15–20 lb pressure. In our laboratory we use a small, countertop autoclave (2). Several needles are put in a test tube with cotton at the bottom to protect the tips. The wire leads are coiled outside the tube and fastened with sterile indicator tape (3). A cotton wad is jammed into the top of the tube and the assembly is autoclaved. After autoclaving, the needles are stored in their tubes undisturbed until use.

Before insertion of a needle, the scalp is rubbed with gauze soaked in alcohol or other sterilizing solution. Pulling on a tuft of hair or pinching the skin on bald scalps adjacent to the insertion point to lift the scalp, the needle is thrust firmly under the skin nearly parallel to the surface, imbedding the needle at least 8–10 mm along its length. A dull needle hurts; pain during or subsequent to insertion of a sharp needle is unusual and mild. When it occurs, it is usually in muscular frontal or temporal areas and can usually be eliminated by relocation 1–2 mm distant. For septic reasons, to protect their sharpness, and because contamination is conducive to bias potentials, the needles should not contact hands or other objects upon removal from the sterile tube. It is important to provide stress relief for needle electrode leads to prevent their pulling out and to prevent excessive movement which can cause pain. Gathering the leads at the neck and securing them to the skin or clothing with adhesive tape is adequate. Needles are not used in areas which are normally hairless because they tend to be painful.

Disk electrodes are easier to maintain. A thorough cleaning between each use and an occasional polishing is sufficient. They should be stored in a germicidal solution. Attachment to hairless areas such as forehead, nose,

[4]Needle maintenance problems would be eliminated by the development of disposable needles. A brief report of such an electrode was made by Miller, Shettel, and Parry (1963) but to my knowledge, disposable needle electrodes are not commercially available.

earlobes, etc. is done with adhesive tape or washers. The skin is prepared by rubbing with alcohol or acetone to remove sebaceous oils and dead skin. Acetone is the more effective but may irritate sensitive skin, especially if rubbing is excessively vigorous. A superficial scraping of the skin followed by pricking the epidermis once or twice with a sterile hypodermic needle is very effective in reducing electrode impedance. To ensure good contact with the skin, disks require electrolyte cream or jelly which in excessive amounts precludes good adhesion by the tape. Experience will show the best compromise. We use cup-shaped disks, put the electrolyte in the cup, and then tape it in place.

A quick, neat, flexible method for applying disks to hairy areas is yet to be perfected. The choice of method involves compromise between ease and durability. After cleaning the area as above, we use one of the following methods. For shorter recording sessions (1–2 hr) a small mound of viscous electrode cream (4) is applied directly to the scalp after carefully parting the hair. The disk is imbedded into the cream and the edges of the depression are folded over the disk, holding it in place. As with needles, stress relief is important as disks attached in this manner are easily dislodged. The advantages of this method are ease and speed; the disadvantages are ease of dislocation, possible drying out of the cream if recording is prolonged, and moderate difficulty in removing the electrolyte paste from the hair. For long-term recording as in sleep studies, disk electrodes must be attached very securely. Collodioned electrodes properly applied will almost never pull off. Proper preparation to remove sebaceous or hair oil and scraping of the skin are especially important. The first trick is to apply just enough electrolyte to the electrode cup to make maximum contact with the skin but not so much that it squeezes out around the edge when the disk is pressed onto the scalp and interferes with the adhesion of the collodion. We find this balance easier to achieve with an electrolyte jelly (5) than with a paste. Disks are also available with holes in the cup through which electrolyte may be injected after application. The disk is pressed onto the scalp and held in place by, for example, the reverse end of a swab stick while a quick-drying, *non-flexible* collodion is dripped around its edges and the adjacent scalp and hair. A disposable syringe with blunted needle is useful to apply the collodion and a stream of air hastens drying. Pressure on the electrode can be removed when the collodion is partially dry but no stress should be applied before complete drying. The advantages of this method are durability and prevention of drying of the electrolyte. The disadvantages are longer application time and difficulty of removal, although an expert technician can apply and remove an array of collodioned electrodes in an amazingly short time. The collodion solvent is acetone which must be applied with a gauze

sponge in fairly liberal quantities and which can cause skin irritation. It is usually very difficult to remove all the collodion from the hair without shampooing.

Different laboratories favor other methods for applying electrodes. Caps or harnesses may be convenient when the same electrode locations are used repetitively. Warm paraffin is sometimes used. It is kept just above the melting point in a controlled temperature bath and applied with gauze pads or swabs. The paraffin solidifies quickly at room temperature and prevents drying out. Jacobson, Kales, Zweizig, and Kales (1965) have described an electrode attachment method for sleep research which they consider better than the collodion method.

Nonpolarizable electrodes are exclusively percutaneous disks or pellets and theoretically may be applied with any of the methods used for disk electrodes. However, the necessary lack of low frequency filtering (see Section V,D) makes d.c. records more susceptible to artifacts such as slow potential shifts generated at the electrode-electrolyte-skin interface. To combat this, we find necessary a rigid electrode-to-skin connection. This is best achieved on the scalp with collodion and on a nonhairy skin with adhesive disks furnished by the electrode manufacturer. An impedance of 3 kΩ or less at 10 Hz is also important in avoiding such artifacts. At the risk of noting the obvious, a minimum of two nonpolarizable electrodes must be used for d.c. recording. In other words, one cannot reference a nonpolarizable electrode to a polarizable one. Nonpolarizable electrodes should be allowed to stabilize after application; our tests show about 20 min to be adequate. The maintenance and storage of nonpolarizable electrodes varies with the type and it is best to follow the manufacturer's instructions.

IV. Electrode Placement

An electrical potential at a given point can only be measured with reference to a second point. Thus, two electrodes are required to record scalp potentials. As will be discussed in Section V, the characteristics of "differential" amplifiers used for AEP recording are such that the amplifier output is the *algebraic difference* of all electrical activity occurring at the two electrodes connected to its input. Therefore, the placement of *both* electrodes is of critical importance in the interpretation of AEP records.

Comparison of AEP records between laboratories, and even within laboratories, has been hampered by a lack of electrode placement standardization. The importance of this problem for electroencephalography was recognized in 1947 when the First International Congress of Electroencephalography "recommended that an attempt be made to stabilize the placement of electrodes . . . to facilitate comparison of records taken in different laboratories and to make it possible to have more satisfactory communication

of results in the literature." The result of this effort is the "10–20 electrode system" of the International Federation of Societies for Electroencephalography and Clinical Neurophysiology (Jasper, 1958) which is coming into increasing use in EEG laboratories. In contrast, many AEP laboratories pay inadequate attention to, or even resist the suggestion of electrode placement standardization (Goff, Matsumiya, Allison, & Goff, 1969). There is, however, a trend for AEP investigators to utilize the 10–20 system, or at least to specify their locations with reference to adjacent 10–20 locations.

The locations of the system, shown in Fig. 3-4, are determined as percentages (10 or 20%) of the distance between the nasion and inion in the anterior-posterior plane, and the distance between the preauricular points coronally. The relation of the locations to the Rolandic and Sylvian fissures was estimated from anatomical studies. It was found that the position of the two fissures should be within about ± 1 cm of that indicated on the diagrams, assuming careful measurement and lack of gross brain distortion due to pathology (Jasper, 1958). The steps for electrode location are well specified by Jasper (1958) and Cooper *et al.* (1969).

While standardization is desirable in the general case, the purpose of the experiment and the type of subject should be the primary consideration in choosing locations. Gibbs and Gibbs (1964) criticize the 10–20 system as being geometrical rather than electroencephalographic and not locating electrodes where they yield the maximum information. Rémond and Torres (1964) found the 10–20 system inadequate for topographical research and devised a system for closer electrode spacing. Hellström, Karlsson, and Müssbichler (1963) described the problems encountered in applying the 10–20 system to infants and smaller children. They presented a modified system using fewer electrodes with estimates of the relation of the electrodes to various parts of the brain based on X-ray films.

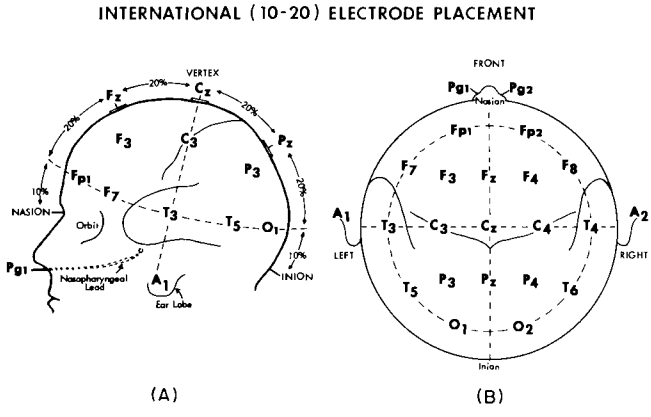
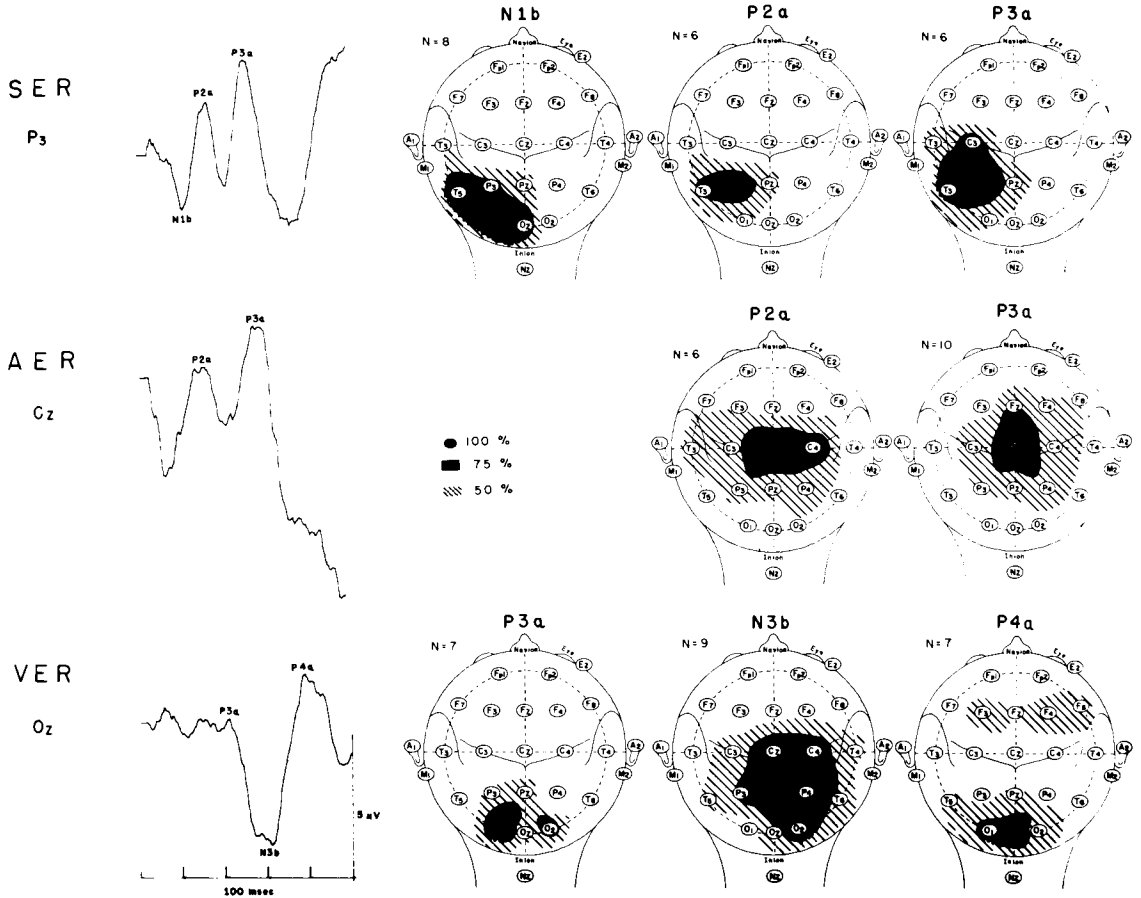


FIG. 3-4. Locations of the 10–20 electrode system. F, frontal; C, central; P, parietal; O, occipital. Odd subscripts = left side of head; Even subscripts = right side of head. Z = midline. (Diagram courtesy Grass Instruments Co., Quincy, Mass.)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P3
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N = 8
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N = 6
P3a
N = 6
P2a
N = 6
P3a
N = 10
P3a
N = 7
N3b
N = 9
P4a
N = 7
100 %
75 %
50 %

FIG. 3-5

The primary considerations in choosing electrode locations for AEP experiments are first, the sense modality being studied; second, whether one wishes to study the total duration of the response or emphasize a particular latency range, e.g., early ($\leq$80–100 msec) versus late components; and third, the minimization of contamination by "extracranial" potentials. A selection on these bases requires knowledge of the focus and distribution of response components. Topographical studies for visual evoked responses (VERs) (Bourne *et al.*, 1971; Jeffreys, 1971; Jeffreys & Axford, 1972a, b; Rémond, 1964; Rémond & Lesèvre, 1965), auditory evoked response (AER) late components (Vaughan, 1969; Vaughan & Ritter, 1970), and somatic evoked responses (SERs) (Goff, Rosner, & Allison, 1962) have been reported. Goff (1969) and Goff *et al.* (1969) compared the distributions of cranial and extracranial AEP components seen during waking for all three modalities in the same group of subjects. SER stimuli were shocks to right median nerve at the wrist, AER stimuli were clicks via an earphone presented to the right ear, and VER stimuli were white light flashes presented in Maxwellian view (see Section VI,C) to the right eye. Relevant results from their study are shown in Fig. 3-5. Early SER components N1b, P2a, and P3a are maximal in the parietal area as would be expected since it is generally accepted that at least the earliest negative-positive sequence, N1b-P2a, represents input to, and the response of the primary somatosensory receiving area of the post central gyrus. The exact maximum amplitude focus on the scalp varies with the subject. In most subjects, the P_3 or P_4 locations for right and left side stimulation respectively are sufficiently close to the maximum for SER early components. There will not be significant contamination of SERs by myogenic potentials at these locations. The focus of SER early components to stimulation of leg nerves has been shown to be at the midline (Tsumoto *et al.*, 1972; Vaughan, 1969) as would be predicted from the known topological projection to postcentral gyrus in man.

If short-latency AER components represent neural activity in the primary auditory receiving area, we might expect their focus to be over the temporal areas T_3 and T_4. However, several studies (Celesia, Broughton, Rasmussen, & Branch, 1968; Mast, 1965; Ruhm, Walker, & Flanigin, 1967) as well as our own work (Fig. 3-5), have found them to be maximal in the vertex region, that is, around C_z in the 10–20 system. Their focus remote from the primary auditory areas and their similarity to extracranial "myogenic" po-

FIG. 3-5. Topographic distribution of early components of the somatic, auditory, and visual evoked response. The prototype waveforms shown at left are recorded from the 10–20 system electrode locations indicated referred to A_1. Distributions for each component are based on averaged data for the numbers of subjects indicated. Jagged edges indicate indefinite boundaries resulting from lack of delimiting electrode locations. (Modified from Goff *et al.*, 1969.) (In reproduction, the crosshatched 100% location filled in. Thus, those locations which appear to be missing from the 75% maps are actually the 100% points.)

tentials have raised two questions about these components. The first question is whether they are of neural origin. Ruhm *et al.* (1967) recorded simultaneously from scalp and subdural electrodes at a point near the vertex. They found the waveform and latency of responses from both electrodes to be highly similar. In a second subject, scalp and direct cortical responses from approximately the T_4 position also showed considerable similarity. They compared scalp AEPs in patients with hearing loss and in one patient with inactive semicircular canal function. On the basis of similarity of response from scalp and cortex in patients with normal hearing, the absence of response at subthreshold levels in the hypacusic group, and the presence of the response in the patient with semicircular canal deficit, Ruhm *et al.* (1967) concluded that there was clear early response componentry at the vertex which was cochleoneurogenic. The second question is whether they are generated in primary cortex. Celesia and Puletti (1969) concluded that the latency, duration, and configuration of scalp potentials were not comparable to those recorded directly from the human primary auditory cortex. Recent observations by Goff, Allison, Lyons, and Fisher (in preparation) that barbiturate anesthesia suppresses early auditory components recorded from the vertex in man support the contention that they are not primary auditory components.

Early components comparable in form and latency to those observed to somatic and auditory stimulation are not seen in the VER. The earliest VER component observed by us is a small inconsistent positivity peaking around 40 msec. It is followed by a larger, consistent negativity, peaking around 60 msec, and a positivity at 80–100 msec. These components are maximal in the parieto-occipital region (Fig. 3-5).

Later AEP components in all modalities are dominated by a large-amplitude negative-positive sequence with the peak of the positivity occurring from 150 to 250 msec depending upon the sense modality stimulated, the stimulus intensity, etc. The positive peak may be followed by another positive peak at 300 msec depending on the modality, the electrode location, and the experimental conditions. This diphasic response is diffusely distributed over the scalp, that is, it can be recorded to some degree from all 10–20 system locations. It is maximum at the vertex, or C_z, region and thus is called the "vertex potential." It is evoked in highly similar form by auditory, somatic, and visual stimuli and has therefore been regarded as being modality nonspecific. Recent evidence, however, (Stohr & Goldring, 1969; Vaughan, 1969; Vaughan & Ritter, 1970) suggests that some or all of the vertex potential may actually be generated in or near the primary receiving area for the given modality. Its maxima in the vertex region could result from volume conduction.

AEP research frequently requires that a minimum number of electrodes be placed where they will maximize the responses we wish to record. For

example, the memory size and number of input channels available for most evoked response averaging devices limit the number of electrodes from which one can record simultaneously with adequate response resolution. Even with averagers having multiple input channels and generous memories, one may wish to minimize electrodes and record as a function of multiple stimulus parameters by directing responses to different parameters to different sections of memory. Optimum electrode placement requires knowledge of the focus and distribution of response components. In terms of the distributions shown in Fig. 3-5, the parietal location contralateral to the stimulus (P_3 or P_4) is within the area of at least 75% of maximum amplitude for SER early components. While the SER vertex potential is best recorded from C_z, as are the auditory and visual vertex potentials, if one were restricted to one location for the somatosensory system, P_{3-4} will serve for this component also. C_z is optimal for recording all AER components. VER component distributions show considerable variability but the occipital 10–20 locations, O_1, O_z, O_2, depending on retinal field stimulated, will record all VER components which appear to be of cranial origin. A possible exception is the vertex potential. Recent evidence suggests dual generators for the VER in this latency range, either at the occiput and the vertex (Garcia Austt & Buño, 1970; Vaughan, 1969) or in striate and extrastriate occipital cortex (Jeffreys, 1971; Jeffreys & Axford, 1972a, b). It is apparent, however, that three electrodes at P_3 or P_4, C_z, and O_1, O_z, or O_2, will record all components of auditory, visual, and somatic evoked responses. Goff *et al.* (1969) suggested these locations as standard for the respective modalities and for cross-modality comparisons. The benefit of such a standard would be that regardless of where else electrodes are placed, a minimum of one electrode would be common in different reports and comparisons of results within and between laboratories would be facilitated.

Earlier, I indicated that the placement of both electrodes was critical to the interpretation of AEP records. As the offspring of electroencephalography, AEP research has inherited much of its methodology and some of the attendant controversies. A major controversy is "bipolar" versus "monopolar" recording (Cooper, 1959; Cooper *et al.*, 1969; Gibbs & Gibbs, 1964; Goff *et al.*, 1969 and subsequent discussion; Mowery & Bennett, 1957; Osselton, 1965, 1966, 1969). If both electrodes are placed so as to record evoked activity, the result is a bipolar record representing the algebraic difference between the two electrodes. Monopolar[5] recording presumes the existence of an electrode location which is "inactive" with respect to the evoked neural potentials, but ideally, is equipotential to the "active" electrode with respect to myogenic, artifactual, and interference potentials (see

[5] "Monopolar" recording is a misnomer to the extent that it implies recording from one electrode (Storm van Leeuwen *et al.*, 1966). The term *referential* or *common reference* recording is sometimes used.

Section VII). Such a reference would cancel these unwanted signals but would not alter evoked potentials occurring at the "active" electrode. Unfortunately, unequivocal proof of the existence of such a reference is impossible. If one cannot record potentials between two locations through a differential amplifier, it can mean that both locations are truly inactive or that they are equally active and thus cancel each other. The compromise has been to use locations which seem sufficiently remote from cranial generators to avoid recording AEPs. Examples are ear, chin, and nose. Goff *et al.* (1969) presented records from these locations referenced to the earlobe contralateral to somatic, auditory, and visual stimuli. Large, probably myogenic, evoked potentials were seen at the nose. Little evoked activity was seen at the chin or between the ears, but the chin is too susceptible to muscle activity to serve as a reference in most subjects. One ear, preferably that contralateral to the stimulus (Goff *et al.*, 1969), or both ears connected together, the so-called "linked ears" (A_1-A_2 in the 10–20 system) are frequently used references. Mowery and Bennett (1957) criticized linked ear electrodes because the ear with the lower electrode resistance is predominant and because they are likely to pick up activity originating in the temporal lobe. Garnesky and Steelman (1958) suggested a method for correcting unequal ear reference resistances.

Perhaps the best way to check the indifference of a reference location is to test it against an electrode which is completely off the head. The problem here is the large EKG which contaminates the records. Stephenson and Gibbs (1951) devised a "noncephalic indifferent" method which minimizes EKG in most subjects. Electrodes are placed over the right sternoclavicular junction and the seventh cervical spine. The two electrodes are brought to a common point which serves as the reference through variable 20 kΩ resistors. The variable resistors are adjusted to balance out the EKG. Gerbrandt, Goff, and Smith (1973) checked the isopotentiality of the linked earlobes for averaged movement potentials using this noncephalic indifferent. In some subjects, neural activity occurring in the Rolandic region was also recorded from the earlobes. When the electrodes were placed on the interior surface of the upper pinna, little or no activity was seen. Lehtonen and Koivikko (1971) tested the isopotentiality of the earlobe against a noncephalic indifferent for binocular flashes, binaural clicks, and median nerve shocks. The earlobe was active in some subjects for visual stimulation but inactive for auditory and somatic stimulation. The noncephalic indifferent was active for somatic stimulation. Their results are consistent with the conclusion of Goff *et al.* (1969) that the earlobe contralateral to a unilateral stimulus is the best compromise as a common reference point to compare AEPs across modalities. Unfortunately, the noncephalic indifferent is time consuming for routine recording, the EKG cannot always be

adequately cancelled, and it does not cancel extraneous activity such as EMG from cranial musculature as well as a reference on the head. However, it can and should be used to assess activity at any intended reference for each subject under actual experimental conditions before the investigator can know the extent to which he is obtaining "monopolar" records. Some electroencephalographers favor the use of an "average" reference electrode (Cooper *et al.*, 1969; Goldman, 1950; Offner, 1950; Osselton, 1965, 1966, 1969) but it is not favored by AEP investigators.

As in the placement of the primary electrode, decisions regarding the placement of the second electrode so as to achieve bipolar or monopolar recording should ultimately depend on the purpose of the experiment. However, Goff *et al.* (1969) presented an example of differences in bipolar *versus* monopolar AEP records which varied with stimulus intensity and suggested that bipolar records are difficult to interpret in the absence of simultaneous monopolar records; that because of considerable differences in topographic distribution of various AEP components, scalp-to-scalp records may be essentially monopolar for some components and bipolar for other components of the same response; and that intersubject variability in component distribution would increase variability in bipolar records compared to monopolar records. They conclude, as have others (e.g., Davis, 1969; Gibbs & Gibbs, 1964; Vaughan, 1966; White, 1969) that *in the general case*, monopolar recording, always assuming that the "indifference" of the reference is carefully assessed, is preferable because the interpretation of records is simpler and interlaboratory comparisons of records is facilitated.

Two additional considerations favor monopolar recording: (1) As with the EEG (Knott, 1969), the polarity of an AEP component is important in interpretation of its neurogenesis. Abundant evidence from animal and human research shows that positive and negative phases of some evoked potentials are generated by separate neural events within the same cerebral structures or in different structures. Polarity in bipolar AEP records is usually meaningless without independent assessment of the contribution of each electrode from monopolar records, or unless one uses multichannel derivations from successive pairs in an electrode chain (e.g., Knott, 1969) which is frequently impractical because of limited input capacity of averaging devices. (2) In AEP recording systems where responses are stored in recoverable form, such as on analog or digital magnetic tape, simple computer subtraction of two monopolar responses provides the equivalent bipolar record. However, monopolar records cannot be derived from a bipolar record.

Arguing that monopolar recording is preferable in the general case is not to say that bipolar derivations are not valuable for specific purposes. The closer together two electrodes, the greater the cancellation of common ac-

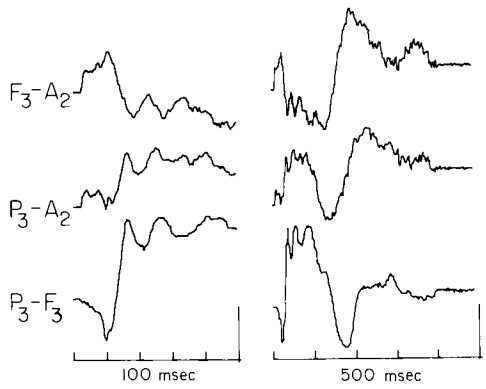

FIG. 3-6. Comparison of monopolar and bipolar records of SER early components anterior and posterior to the Rolandic sulcus. Additional explanation in text.

tivity. In the case of early AEP components with restricted distributions, it is possible to place a reference on the scalp close enough to record a larger percentage of the "noise" than from a nonscalp reference but little or none of the early evoked potential components. The effect is to significantly improve the "signal-to-noise" ratio and the resolution of small amplitude early components. A special case of improved resolution with bipolar recording results from the polarity reversal of SER early components across the Rolandic sulcus (Broughton, 1969; Broughton, Rasmussen, & Branch, 1968; Goff, Matsumiya, Goff, & Allison, in preparation). Figure 3-6 compares monopolar and bipolar records across the Rolandic sulcus for shock stimulation of right median nerve at the wrist. Early activity at P_3 is reversed at F_3 when both are referred to the contralateral ear. The diffusely distributed vertex potential with a positive peak at approximately 200 msec is similar in both recordings. The bipolar P_3–F_3 derivation summates the polarity reversal to enhance the early components; however, the vertex potential common to both locations is badly distorted compared to the monopolar records. Another application of bipolar recording is the localization of the source of an AEP component by the phase reversal technique common in electroencephalography (e.g., Vaughan & Ritter, 1970). There are, however, hazards in the interpretation of such records (Kooi, Tipton, & Marshall, 1971).

A consideration of great importance in the placement of electrodes is the possible contamination of AEP records from nonneural "myogenic" sources. Bickford (1964) first reported that potentials could be evoked in cranial musculature which mimicked in form and latency potentials considered to be of neural origin. Considerable research has subsequently been devoted to the "photomotor" (Bickford, 1964; Bickford, Jacobson, & Cody, 1964b), "sonomotor" (Bickford, Cody, Jacobson, & Lambert, 1964a; Bickford *et al.*,

1964b; Celesia *et al.*, 1968; Cody, Jacobson, Walker, & Bickford, 1964; Mast, 1965), and "somatomotor" (Calmes & Cracco, 1971; Cracco & Bickford, 1968) responses, and the extent to which they may be confused with neurogenic responses. It is established that the greatest possibility of myogenic contamination occurs under conditions of unusually high stimulus intensity and muscle tension, conditions which are normally avoided in the AEP recording situation. Nonetheless, the prudent AEP investigator should be constantly aware of this possible source of extraneous potentials in his records. Knowledge of the focus and distribution of these potentials is of practical value in the choice of electrode placements. Goff *et al.* (1969) plotted the distributions of AER, SER, and VER components which they categorized as myogenic on the basis of intersubject variability in appearance and topography.

Finally, contact nasopharyngeal electrodes (see Fig. 3-4) are coming into increasing use for EEG recording from the mesio-basal surface of the temporal lobe (e.g., Bach-y-Rita, Lion, Reynolds, & Ervin, 1969; de Jesus & Masland, 1970; Mavor & Hellen, 1964). Smith, Lell, Sidman, and Mavor (in press) recorded auditory, somatic, and visual AEPs, and Smith, Allison, and Goff (1971) attempted to record potentials to odorous stimulation using contact nasopharyngeal electrodes. Lehtinen and Bergström (1970) have reported a nasoethmoidal electrode for recording from the inferior surface of the frontal lobe.

V. Amplification

A detailed discussion of amplifier circuitry is not included in this chapter for two reasons. First, many excellent ones already exist (Cooper *et al.*, 1969; Geddes & Baker, 1968; Malmstadt, Enke, & Toren, 1963; Middlebrook, 1963; Schoenfeld, 1964; Stacy, 1960). Second, in practice one needs only to know the functional characteristics and how the various adjustments affect these characteristics in order to select an appropriate amplifier, adjust it properly, and accurately interpret AEP records.

The "differential" (discriminating, balanced, push–pull) amplifier is universally used in AEP recording. The relevant characteristics of this type of amplifier are its input impedance, sensitivity, noise level, gain and frequency response, common-mode rejection, output impedance, and d.c. level. Gain, frequency response, common-mode rejection, and d.c. level are usually adjustable.

A. Input Impedance

The input circuit of an amplifier is basically a voltmeter. It determines the current flow through a fixed resistance, i.e., the voltage between one

input and a reference point. If the reference is ground (earth), the amplifier has one, or a "single-ended" input. A differential amplifier measures the voltage between two inputs, both of which derive from electrodes placed on the subject. As with any voltmeter, it is imperative that the meter itself not alter the signal being measured. When the electrodes are connected to the amplifier, the input impedance is effectively in parallel with the impedance between the electrodes, thus creating a voltage-dividing network. If the input impedance is too low, it shunts the interelectrode impedance. Cooper *et al.* (1969) indicate that with an interelectrode impedance of 10 kΩ and an input impedance of 1 MΩ, the input signal will be reduced about 1%. The input impedance of modern differential amplifiers is in the range of 1 MΩ or more and signal reduction, if any, is slight and usually ignored. There are no adjustments for input impedance on commercial amplifiers.

B. Sensitivity

The maximum sensitivity of an amplifier is usually specified as the minimum input required to produce a specified output. The maximum sensitivity for an EEG machine, for example, is usually the minimum input (in microvolts) required to cause a full-scale deflection of the pens. In an IRIG compatible instrument, the maximum sensitivity is the input required to produce a minimum of 1 V peak to peak. IRIG is the acronym for Inter-Range Instrumentation Group who have specified a set of standards for use with guided missile telemetry and other space research applications (IRIG Telemetry Standards, 1969). The minimum sensitivity of the amplifier is usually specified in terms of the maximum voltage that can be applied to the input before the amplifier is driven beyond its linear operating range and distorts the signal (see Section V,C). Sensitivity in the microvolt range is required to record AEPs from the scalp; amplifier output ranges of ± 1–2 V are required to drive the analog-to-digital converters of most averaging devices and digital computers.

C. Noise Level and Distortion

Noise in a amplifier is any electrical activity at the output which is not a reflection of what is applied to the input. Thus it includes random voltage fluctuations inherent in resistors, tubes, and transistors, 60 Hz from inadequacies in filtering, isolation or shielding, etc. The inherent random voltage fluctuations are the only noise source which should be found in a properly constructed, properly operating amplifier. The noise level of an amplifier is specified in terms of microvolts of equivalent input. It is mea-

sured by monitoring output with the inputs shorted together. The amplitude of the output noise divided by the gain factor (see Section V,D) is the input equivalent noise level of the amplifier. Thus, if the amplifier is set to a gain of 10,000 and 50 mV of noise is seen at the output, the equivalent noise level is 5 μV. Since noise is superimposed on the signal, the amplifier noise level limits the signal that can be resolved unless averaging is used. Commercial amplifier equivalent noise levels are in the 5–10 μV range. Signal-to-noise ratios can be improved by filtering so long as the filtering does not distort the signal (see Section V,D). Noise occurring in the first stages of an amplifier is more critical since it will be amplified by the later stages. Thus first and sometimes second amplification stage tubes and transistors are selected for low noise levels. Selected replacements are usually available from the amplifier manufacturer. There is a more extensive discussion of noise in Schoenfeld (1964).

Distortion in an amplifier is any qualitative difference between the input and output signal. A tube or transistor conducts current only within certain limits which define its particular operating range. Moreover, its output is not linearly proportional to its input over the entire operating range, but rather decreases gradually at the extremes. For tubes and transistors typically used in amplifiers, a graph of plate voltage output as a function of grid voltage input is an S-shaped or sigmoid curve. There is a range symmetrical about the midpoint of this curve in which output is linearly proportional to input. This is the linear operating range. A fixed voltage is applied to the grid to hold conductivity at this midpoint. This is called the grid bias. Output voltage fluctuates around this midpoint. If a symmetrical signal such as a sine wave is applied to the grid and the signal is so large as to drive the tube beyond its linear operating range, the peaks will be attenuated, producing distortion. If a symmetrical signal is so large as to drive the tube completely beyond its operating range, the signal will be "peak-clipped," that is, the tops of the peaks will be flat. If an asymmetrical overloading signal is applied, the peaks of one polarity may be attenuated or flattened, while the other polarity peaks will still be within the linear operating range and thus undistorted. If an excessive, nonfluctuating voltage is applied to the tube, effectively biasing it beyond its operating range, no conduction will occur, and the amplifier is said to be blocked. This is seen at the output as a large, steady voltage. On an EEG machine, for example, the pen remains at maximum deflection in one or the other direction until the excessive voltage declines and the amplifier "recovers."

For most AEP recording, a.c. amplifiers are used. In such amplifiers, capacitors are used to couple the input to the first stage grid and to couple successive amplification stages. This simplifies amplifier design and usage by blocking d.c. plate voltages and very slow potential drifts which would

otherwise affect subsequent stages. This capacitative coupling causes the amplifier to pass only alternating signals. If an excessive voltage is applied to a capacity-coupled amplifier, one or more of the capacitors may become overcharged. The amplifier can no longer respond until the capacitor is at least partially discharged and this is another way in which the amplifier can be blocked. The time required for the capacitors to adequately discharge upon removal of the excessive voltage determines the "recovery time" of the amplifier. Another type of distortion is phase shift. This is a change in the phase relationship between input and output. A phase shift of 180° is a complete polarity reversal. There should be no distortion or phase shift in a properly designed amplifier operating at appropriate gain settings and within its linear frequency response.

D. Gain and Frequency Response

The terms gain and amplification are synonomous and refer to the factor by which an amplifier increases the output amplitude of an input signal. Frequency response refers to the range of frequencies (rates of voltage change) or the bandpass over which amplifier output is independent of frequency within specified limits. Gain and frequency response are the most important amplifier settings for AEP work and both should be specified in research reports. The frequency response capabilities of the typical a.c. amplifier range from a fraction of a cycle to frequencies well above those needed for AEP recording. Direct current amplifiers pass steady voltages but not frequencies much above 50–100 Hz. The most important frequency response characteristic of an amplifier to bear in mind is that the cutoff, that is, the limits of a specified bandpass, is not abrupt. In other words, if the high frequency filter setting[6] is specified at 1000 Hz, this does not mean that it amplifies all frequencies equally up to 1000 Hz but does not amplify 1001 Hz. Gain as a function of frequency at the limits of a given bandpass changes gradually; the term rolloff is used to describe this gradual decline. Another way of saying this is that the frequency response is not *flat* (equal gain for equal input as a function of frequency) within the specified limits of the upper and lower filter settings. The filter settings by convention specify that point in the frequency response curve of the particular amplifier where the gain is 50% of the maximum gain in the flat part of the bandpass. Sometimes they are specified in decibels (dB), typically the frequency at which the gain is −3 dB (70.7% of maximum). Figure 3-7 shows frequency response

[6]The reader should be aware of the following, often confusing, terminology: the high frequency filter setting is sometimes referred to as the low pass filter setting, i.e., it passes frequencies below it; the high pass filter setting determines the lower limit of the bandpass, i.e., it passes frequencies above it.

curves for an a.c. amplifier suitable for AEP recording. Reference to the frequency response curve for his particular amplifier tells the AEP investigator what filter settings are required to achieve a flat bandpass over the approximately 1–100 Hz frequency range of AEP components. It is apparent that with the amplifier specified in Fig. 3-7, flatness cannot be achieved below approximately 0.5 Hz. To record accurately voltage fluctuations below this level, a d.c. amplifier and nonpolarizable electrodes are required.

It is also important to remember that the rolloff rate varies considerably among amplifiers and that there is no fixed relationship between the specified one-half amplitude or −3 dB point and the rolloff curve. For example, comparing two amplifiers commonly used for AEP recording, at a low frequency setting of 0.3 Hz, the frequency response is flat to approximately 1.0 Hz for one amplifier and 2.5 Hz on the other; at a setting of 1.0 Hz the flat limits are 5 Hz and 10 Hz. Some manufacturers do not furnish frequency response curves but give only the half amplitude or −3 dB point settings. With these, the user must determine his own frequency response curves. In any case, the careful investigator will verify the curves for his equipment, initially to determine that new equipment is operating within specifications, subsequently on periodic checks, and if a circuit modification is made or a component replaced.

Determining a frequency response curve is not difficult. Using a variable oscillator covering the appropriate frequency range, check its output linearity over the range. This is best done on an oscilloscope.[7] If the oscillator output voltage is not flat at different frequencies, reset its output for each frequency used. Voltage divide the oscillator output to within the minimum sensitivity of the amplifier. A frequency response curve is determined by plotting the gain at the amplifier output as a function of frequency for a fixed input and fixed gain setting. A frequency response curve should be determined for typical gains and all filter settings likely to be used in the experiment. Distortion of waveform and phase shift may be checked at the same time by comparing input and output signals on a dual channel oscilloscope.

One might conclude from this discussion that the safest procedure is to record from d.c. to some high frequency setting above any possible neural response. The safest perhaps, but in practice not the best. Direct current recording, besides requiring nonpolarizable electrodes, has the disadvantage

[7]Alternating current voltmeters may be used for calibration purposes. However, one must check their frequency response and most of them are not accurate at frequencies below 10 Hz. Also, they read in root-mean-square (rms) which is 70.7% of the base-to-peak value of an a.c. signal. Thus, 1 Volt rms equals 2.8 V peak to peak. Serious calibration errors result from forgetting this fact and, for example, reading input values in rms on a meter and output values base-to-peak or peak to peak on an oscilloscope.

that several kinds of artifacts, such as slow drifts due to changing electrode impedances or very slow potentials such as from body movements due to respiration, are passed by the d.c. amplifier but blocked by the capacitative coupling of the a.c. amplifier. The slow drifts must be continuously compensated by manual adjustment of balance potentiometers, a nuisance proportional to the number of channels being used, and the artifacts generally deteriorate the signal-to-noise ratio. Opening the high frequency filters beyond what is needed permits considerably more myogenic and electronic "noise" to be recorded than is necessary, which further deteriorates the signal-to-noise ratio. The best filter settings are those which eliminate the maximum spurious potentials without altering the waveform of the AEP. The best way to determine such settings is empirically. This is especially easy if multichannel recording is available. Figure 3-8 shows the effect of different high and low frequency settings on the SER using the amplifiers whose frequency response curves are shown in Fig. 3-7. In the left three columns the low frequency setting was held constant at 0.1 Hz and the high frequency half-amplitude settings were, top to bottom, 3000, 1000, 300, and 100 Hz. For the "moderate" and "noisy" records, broad-spectrum noise was added to the EEG at the amplifier input. A filter setting of 300 Hz which reduces amplitude only about 10% at 100 Hz (see Fig. 3-7) is the best setting for this amplifier. Above that there is no significant change in AEP waveform, but noise, if present, is added and can seriously obscure the response. A setting of 100 Hz, with which the rolloff begins at about 12 Hz, distorts the response, principally by amplitude reduction of both early and late components. However, if one had a very noisy subject (third column), one might use the 100 Hz setting, keeping in mind its effect on amplitude.

In the right column of Fig. 3-8, the high frequency setting is constant at 300 Hz, and the low frequency -50% amplitude settings were, top to bottom, 0.1, 0.3, 1.0, and 3.0 Hz. The most obvious change is that the decreasing low frequency response increasingly differentiates the positive peak of the vertex response, giving it a sharper appearance. The peak-to-peak amplitude of the vertex response is attenuated only by the 3.0-Hz setting where the peak latency also decreases. As expected, then, minimum distortion is at the 0.1 Hz setting; however, if special considerations demanded, a setting of 1.0 Hz *on these amplifiers* could be used without excessive distortion.

In addition to high and low frequency settings, some amplifiers have 60-Hz "notch" filters designed to eliminate power line interference from the records. Whatever their value for EEG recording, they should be used in AEP recording only as a last resort and with the knowledge that they will distort at least some components of the AEP. Figure 3-9 shows AEPs recorded simultaneously from the same electrode derivation through the same type of amplifiers using identical high and low filter settings. The only

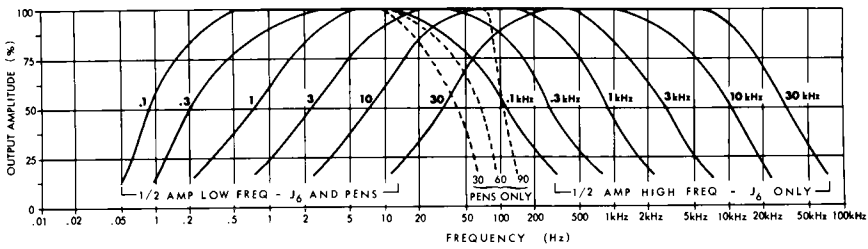

FIG. 3-7. Frequency response curves for high and low frequency filter settings for a Grass Model 7P511 EEG amplifier. Note that a filter setting indicates the point on its particular frequency response curve where the output amplitude is approximately 50% of the maximum in the flat part of the curve. (Courtesy Grass Instruments Co., Quincy, Mass.)

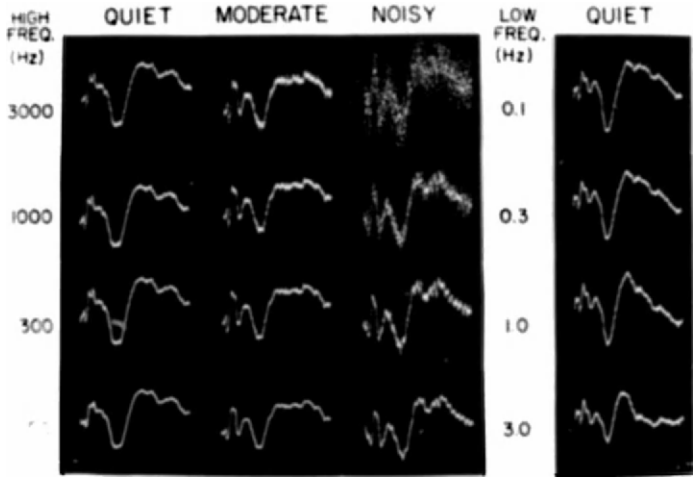

FIG. 3-8. Effects of high and low filter settings on SER to right median nerve shock recorded from P_3–A_1. Responses in each column were recorded simultaneously. Additional explanation in text.

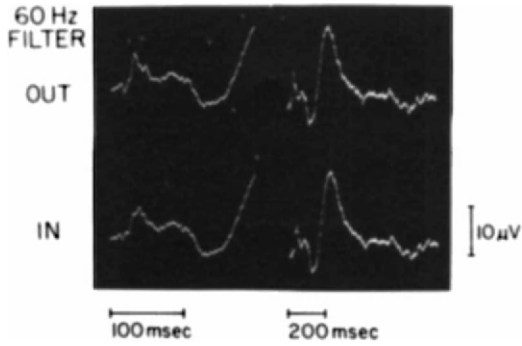

FIG. 3-9. SER recorded without (top row) and with (bottom row) 60-Hz "notch" filter. Derivation P_3–A_1; stimulus right median nerve shock.

difference between responses was that the 60-Hz filter was not used in the top and was used in the bottom records. The distortion of the early components compared in the left column is obvious; later, lower frequency components are unaffected.

The gain controls of an amplifier usually consist of a continuously variable control or a step attenuator, or preferably both. The gain is determined empirically by applying a known signal to the input, monitoring the output, and adjusting the gain controls to achieve the desired factor. It is imperative that the calibrating signal be within the flat frequency range of the amplifier when the filters are set as they will be during the experiment. If this seems like pointing out the obvious, I have known it to be overlooked. For example, a commonly used calibrator has a 1 kHz sine wave output. A commonly used differential amplifier has a high frequency filter setting of 1 kHz which was the setting to be used in the experiment. Calibration was done at this setting. But on this amplifier, 1 kHz indicated the -3 dB point. The calibration signal was thus being attenuated to 70.7% relative to lower frequencies. When gain was adjusted to 10,000 at 1 kHz, gains at lower frequencies were larger than specified. Opening the filter to the next higher setting during calibration, which brought the calibration signal into the flat gain range of the amplifier, then resetting it to 1 kHz during the experiment, solved the problem.

E. Common-Mode Rejection

In addition to the potentials resulting from neural activity, there are a variety of nonneural biological, and nonbiological potentials which occur between electrodes and between each electrode and ground. These potentials constitute "noise" with reference to potentials we wish to record. Nonneural biological potentials arise predominantly from muscle activity and eye movements. Nonbiological potentials are most commonly produced by electromagnetic or electrostatic induction from power lines (60-Hz interference) or electrical equipment (motors, relays). These artifactual potentials will be further discussed in Section VII. Fortunately, artifacts and interference signals are usually common to electrode pairs, and amplifier circuitry has been developed which discriminates against such "common-mode" or "in-phase" signals but not against signals which are out-of-phase, or "antiphase."

An historical perspective is the best way to understand the development and operation of the differential amplifier from the early, simple "push-pull" input circuit through the many subsequent improvements. According to Geddes and Baker (1968), the development was fostered by dual needs. First, there was a need for isolated inputs permitting the recording of true potential differences between independent electrode pairs. With single-ended

amplifiers having a common power supply, the "second input" was the ground reference which in effect behaved like a common electrode. The second factor was the need to improve the signal-to-noise ratio by rejecting interference, especially from power lines.

The basic input circuit of the differential amplifier is the so-called "push-pull" design. This is essentially two single-ended amplifiers connected back-to-back symmetrically with reference to ground. After one or more amplification stages, the outputs of the two parallel amplifiers are brought together and the output is the potential difference between them at the common point. If an antiphase signal is applied to the two inputs, to the extent that these inputs are equal and opposite, i.e., 180° out of phase, equal and opposite amplification will occur in the two parallel amplifiers (the "push-pull" effect) and the potential difference between them at the common point will be twice that which would have been achieved by a single amplifier alone. Any in-phase potentials in the two amplifiers, whether they occur at the input or within the amplifier itself (e.g., from a common power supply, changes in ground potentials, etc.) will be amplified equally in the same direction and there will be no potential difference between them at the common point. As a result of this circuit, the two inputs are isolated from ground in that their potential difference from ground does not affect output; only potential differences between them are amplified. Referring to the discussion of monopolar and bipolar recording in Section IV, it is because only differences in potential between two electrodes are amplified that knowledge of the evoked activity occurring at both electrodes is critical to the interpretation of AEP records.

Push-pull circuitry made practical simultaneous recording from multiple electrode pairs and provided improved signal-to-noise ratios. There were still two problems, however. First, the efficacy of the circuit in cancelling in-phase signal is a function of the equality or "balance" in the gains of the parallel amplifiers. Circuits designed to approximate this equality are called balanced amplifiers. However, complete equality is not achievable and small imbalances significantly lessen in-phase rejection. Second, push-pull rejection works only if the in-phase interference is smaller than the antiphase signal. Otherwise, interference may cause serious distortion or "block" the amplifier before adequate signal amplification is achieved. It is possible for 60-Hz interference to exceed the signal by an order of 100,000 times (Geddes & Baker, 1968). Further modifications were devised to provide negative feedback for in-phase signals while leaving antiphase signals relatively unaffected; these are called discriminating or discriminative amplifiers. However, the term differential amplifier is the inclusive term used today to describe the dual input, in-phase signal-rejecting amplifier.

The "common-mode rejection ratio" (CMRR) expresses the capability

of a differential amplifier to reject in-phase signals while amplifying antiphase signals. It is usually expressed as a ratio of the in-phase voltage to the antiphase voltage which must be applied to the input to produce the same output, or in decibels of attenuation of the in-phase signal voltage where 20 dB represents a factor of 10. Thus, a rejection ratio of 40 dB means that the common-mode signal voltage is reduced by a factor of 100 relative to the in-phase signal voltage.

Some manufacturers include a "differential balance adjustment" on their amplifiers. Instructions for setting the balance are generally provided. In general, one applies an in-phase signal, usually a 60-Hz sine wave since power lines are a maximum source of interference, to both inputs, displays the output on an oscilloscope and sets the balance adjustment for maximum cancellation. The importance of this adjustment is indicated by the fact that one commonly used amplifier has an optional balance adjustment. The CMRR without it is specified at a minimum of 1600:1 and with it, properly set, a minimum of 25,000:1. Common-mode rejection is one of the most important specifications in selecting a differential amplifier. The higher the rejection, the greater the amount of artifact and interference which can be permitted in the environment and still obtain good AEP recordings. Modern technology has produced differential amplifiers appropriate for AEP research which have CMRRs of up to 100,000:1 (100 dB).

F. Output Impedance and d.c. Level

To transfer signal voltage from one device to another, e.g., from an amplifier to a tape recorder, the output impedance of the amplifier should be low relative to the input impedance of the tape recorder. Otherwise, the input impedance of the recorder may shunt part of the amplifiers's output to ground, or in other words, load its output. If shielded cables are used to connect the devices, capacitative coupling also may shunt the signal in a high impedance cable. A low impedance output minimizes this capacitative loading. Low impedance is typically achieved by the use of a cathode follower (emitter-follower with transistors) circuit in which the potential of the cathode referenced to ground follows that of the grid. The output voltage is taken across the cathode resistor. It is necessary to compensate for the cathode bias voltage which would otherwise appear at the output. This is done by biasing the grid so that current flow through, and resulting voltage drop across, the cathode resistor is zero when there is no amplifier input. The grid bias is usually made adjustable by the use of a variable resistor. With amplifier inputs grounded, the grid bias resistor is adjusted to zero the d.c. level of the output. Most commercial instruments used in

AEP recording are designed with high impedance inputs and low impedance outputs so that interfacing between system components is usually not a problem. One must be alert to the possibility, however. It may occur, for example, if one is connecting an amplifier output to an averager and tape recorder input simultaneously. The two inputs are in parallel with the amplifier output; thus they form a voltage divider circuit to ground. Both inputs may be "high impedance" with respect to the amplifier output, but there may be an appreciable difference between them. The lower impedance instrument may load the higher impedance instrument. "Loading" can be checked quite simply by monitoring the amplifier output of a calibration signal while plugging into the inputs of one or more instruments. There should be no diminution in the signal. If there is, interfacing or "mixing" amplifiers may be required.

VI. Stimulation

A. Somatic Stimulation

The most common method of evoking a somatosensory evoked response (SER) is to activate a peripheral sensory nerve by "percutaneous electrical depolarization," otherwise known as a shock through the skin. The most commonly used nerves are the median and ulnar at the wrist and the peroneal nerve in the leg. The same silver disks used for scalp recording serve well as stimulating electrodes using the same electrolytic substances to ensure good contact. Pastes or creams are preferable to jellies because they are less likely to ooze between the electrodes, cause a shunt, and lower effective stimulus intensity. The placement of the cathode as immediately as possible over the nerve is extremely important for effective stimulation. Placement of the anode is less critical; typical placment is approximately 2 cm distal to the cathode or off to one side with respect to the nerve. If the anode is too close to the nerve, anodal hyperpolarization may occur. After rubbing the skin with acetone or alcohol-moistened gauze to reduce skin resistance, the electrodes are attached with adhesive tape or collodion. Taking as an example stimulation of median nerve at the wrist, the procedure is as follows. The median nerve lies approximately between the flexor carpi radialis and palmaris longus tendons. These tendons are easily visualized if the subject makes a fist, palmar flexes his wrist, and resists as the experimenter tries to straighten the wrist. This brings the two tendons into prominence and the cathode is located between them slightly proximal from the wrist crease. The anode can be placed about 2 cm lateral. However, we have been achiev-

ing lower, more stable thresholds using an infant limb EKG electrode on the back of the wrist for an anode. The rubber strap holding it is arranged to pass over the cathode which holds the cathode tighter against the wrist, making stimulation more effective. Electrodes can be placed over most other nerves on the basis of anatomical landmarks. For locating a given nerve for the first time, for nerves whose precise location varies in different people, or for nerves which are not associated with obvious anatomic landmarks, a small, battery-operated, portable nerve finder (6) is a useful device.

Electrode placement should be verified empirically by asking the subject where sensation is localized. This requires knowledge of the innervation of the nerve being stimulated. For example, with median nerve stimulation at moderate suprathreshold intensities, the subject should feel a "tap" at the wrist under the cathode and a tingling sensation in the thumb, first, and second fingers and the palm below these fingers. If sensation is only in the wrist, either the placement is bad or anodal current is accidentally being applied.

Stimulation is usually a monophasic square wave pulse. Most stimulators can supply a relatively constant output if stimulating electrode impedance is not too high and does not vary greatly. If these two conditions are not met, electrode impedance changes can cause significant fluctuations in effective stimulus intensity. It is generally accepted that current rather than voltage is the relevant parameter for nerve stimulation (Becker, Peacock, Heath, & Mickle, 1961). Since interelectrode impedances are not stable, devices which maintain current at a constant level (independent within limits) of electrode impedance changes have been developed.[8] These units have output capabilities up to about 10 mA at typical stimulating electrode impedances. When selecting a stimulator, one should consider that constant current maximum output varies inversely with electrode impedance. A 10 mA output is adequate for most AEP experiments but not for purposes such as determination of intensity functions or in patients with sensory deficit due to central or peripheral neuropathology. A circuit for a constant current stimulator with output capabilities of 25–30 mA has been published by Allison, Goff, and Brey (1967). In this stimulator the output is the plate current of a pentode which has the inherent property of being virtually independent of changes in load impedances. Regulation within 5% is obtained for up to 25 mA for skin impedances below approximately 20 kΩ. Skin impedance for short duration pulses is considerably less than skin resistance because of parallel capacitance (Montague & Coles, 1966) which shunts skin resistance. Allison *et al.* (1967) found interelectrode impedance to be on the order of 100 times less than resistance. Thus resistance variations will have

[8]e.g., Grass Instruments Co. Model CCU 1 constant current unit; American Electronic Laboratories, Inc. Model 106 constant current regulator; and several others.

relatively little effect in changing impedance. Schwartz, Emde, and Shagass (1964) compared SER intensity functions for a constant voltage stimulator to a constant current circuit very similar to that of Allison *et al.* (1967). They concluded that the constancy of the stimulator output was more important than whether the scale was in volts or milliamperes, and that the type of stimulator used made little difference for typical SER recording. They suggested that power might be the relevant stimulus parameter but this idea has not been tested.

The output of a shock stimulator must always be isolated from ground! The importance of this for subject safety and minimization of stimulus artifact cannot be overemphasized. Stimulus artifact occurs when stimulus current enters the amplifier. The magnitude of this current pulse is generally many times greater than the AEP signal and may block the amplifier. Amplifier recovery can take 50 msec or more and this will introduce serious distortion into the early portions of the AEP record. The problem is aggravated by response averaging since the shock artifact and any distortion it produces will be averaged along with a response. The most common "sneak paths" by which shock artifact reaches the amplifier are through a common ground, deliberate or accidental, and by means of conduction through the skin from stimulus to recording electrodes. The common ground path is defeated by isolating the stimulus source from ground. This is done by isolating the output *per se* from the main part of the stimulator, usually through an isolation transformer, or by isolating the entire stimulator as done by Allison *et al.* (1967). With either system, one must guard against accidentally compromising the isolation by, for example, using leads with grounded shielding running from the isolated output to the subject. Pulses have very high frequency components which lend themselves to capacitative shunting between leads and grounded shielding, especially with the high impedance circuit requisite for constant current stimulators. Capacitative coupling increases with lead length and to the extent that it occurs isolation from ground is compromised and shock artifact is likely.

Artifact radiation along skin can be minimized by placing a low resistance shunt to ground between the stimulating and recording electrodes, which "decouples" them. We have found that a 1-inch wide length of tinned copper, flexible "ground strap," or a strap of conductive rubber (7) liberally smeared with electrode jelly or paste, and wrapped around the limb proximal to the stimulating electrodes provides effective decoupling. The metal strap is held in place by an elastic band commonly used with EKG electrodes. The rubber strap is easier to clean and fastens with a buckle which is more convenient and facilitates tension adjustments. The straps are bound in gauze to reduce electrolyte drying and protect clothes. Grounding the subjects in this manner also reduces 60-Hz interference (see Section VII). Under conditions

where it is impractical to wrap the limb with a ground strap, an EKG plate electrode will provide reasonable artifact reduction. Proximity between stimulating and recording leads is another important factor in determining shock artifact interference.

Isolation from ground helps to protect the subject from the effects of accidental excessive shock by limiting the current path between the closely spaced electrodes. Without such isolation, should equipment malfunction combine with unintentional grounding of the subject such that the current path includes the chest area, relatively small currents could produce cardiac and respiratory arrest. The ground placed on the subject provides additional safety since it is normally placed on the limb being stimulated and thus should isolation failure combine with stimulator malfunction, it provides a path to ground which avoids the chest region. As a final safety precaution, the output of all electrical stimulators used for human research should be fused. Note that output fusing is not the same as the 110 V a.c. line fuse which commonly protects instruments from shorts. These do not necessarily protect the subject. Allison *et al.* (1967) fused their output with 10 mA fast-acting fuses which they found would "blow" when subjected to a single 1.0 msec pulse of about 25 mA.

Stimulators should be calibrated empirically through the isolation units. To maintain isolation from ground, an oscilloscope with a differential input is required. The stimulator pulse is displayed on the oscilloscope and voltage is read directly across a 1% resistor in the range of typical electrode impedance (10 kΩ) in parallel with the oscilloscope input. To calibrate a constant current device, current is calculated from Ohm's law, i.e., by dividing the voltage displayed on the oscilloscope by the value of the load resistor. Again, the load resistor should be in the same range as typical electrode impedances. A calibration curve is constructed by plotting the voltage or current values as a function of stimulator setting. These calibration curves should be checked on a regular schedule and always after replacement of any component of the stimulator system.

Determining the effective stimulus intensity, as distinguished from the physical voltage or current, for the purposes of equating intensity within and across subjects and sessions is a considerable problem with electrical somatic stimulation. Specifying intensity in "sensation levels" (a given intensity above absolute threshold) as is commonly done for auditory stimulation can be misleading. The absolute threshold will be based on cutaneous sensation immediately under the cathode and the relationship of this to depolarization of the nerve trunk is uncertain. The absolute threshold for sensation in the innervation area of the nerve would seem a better index but has not been used. Furthermore, neither of these indices is likely to be useful in a patient with sensory deficit. When using a "mixed" nerve, that

is, one with both motor and sensory fibers, the threshold for activation of the motor fibers producing a twitch in the muscles innervated by the nerve seems to be the best objective standard of intensity. Except in cases of peripheral neuropathy, it is usable in sensory deficited, aphasic, or comatose patients as well as normal subjects. Median nerve stimulation produces a palmar twitch of the thumb. Taking the thumb twitch as a standard of effective median nerve stimulation, it is easily demonstrated that changes in wrist position shift the electrode-nerve relationship and change effective intensity. The intensity which produces a twitch with a hand palm up may not if the hand is rotated palm down; similar changes occur between the dorsiflexed, unflexed, and palmar flexed wrist. For this reason, a hand rest should be used whenever possible to keep the subject's wrist in a constant, preferably slightly dorsiflexed, position. Thumb twitch threshold should be determined in this position and the subject instructed not to change the position during the session. If an arm rest is not practical, some means of maintaining a constant wrist position should be used. For most SER recording, we typically use a stimulus intensity of 3 mA above twitch threshold; in a normal subject this is usually an absolute value of 4–6 mA although values of 10 mA or better are occasionally required.

Typical durations for shock stimulation range from 100 μsec to 1 msec. The well known strength-duration relationship means that higher current levels are required at shorter durations for equally effective stimulation. Longer durations at higher current levels may increase stimulus artifact and may produce an unpleasant burning aftersensation. We use a 500 μsec duration and this is rarely painful even at 25 mA. Poor electrode contact with the skin which elevates current density per unit area may cause pain even at short durations and a relatively low current level. Reapplication of the electrode to improve skin contact should correct the problem.

This discussion has dealt mostly with electrical median nerve stimulation. It is the most frequent choice for SER research because of the ease with which one can locate the nerve, place stimulating and grounding electrodes, objectively determine the effect of stimulus intensity, and maintain a reasonably constant nerve-electrode relationship. Other stimulation sites and non-electrical stimulation have been used to evoke SERs. Responses to electrical stimulation of the finger have been compared to electrical median nerve stimulation (Calmes & Cracco, 1971; Goff *et al.*, 1962). The differences found can be attributed to lower effective intensity stimulation of the finger resulting from the activation of fewer nerve fibers. SERs to vibratory (Desmedt, Debecker & Manil, 1965; Ehrenberger, Finkenzeller, Keidel & Plattig, 1966; Franzén & Offenloch, 1969) and punctiform tactile stimulation (Meyjes, 1969; Shevrin & Rennick, 1967) have been reported. Meyjes (1969) compared the SER to an electrical stimulation of the finger, and the

blunt and sharp side of a "neurological pin" in 19 subjects. The waveforms of the three responses compared very favorably; there were slight differences in latencies, with electrical stimulation being the shortest. Meyjes also listed the disadvantages of mechanical stimulation as noise concurrent with stimulus application, inconvenience in changing the site of stimulation, and the possibility that application of large numbers of stimuli may injure the skin. To these, I would add the expectation that most electromechanical drivers would involve an inductive voltage which is a potential source of stimulus artifact.

B. Auditory Stimulation

The description, measurement, and control of the kinds of sound used to stimulate AERs are discussed by Hirsh (1966) and the parameters of auditory stimuli are discussed by Licklider (1951). It is therefore appropriate to present here only a brief overview, including certain problems peculiar to AER recording.

The most commonly used AER evoking stimulus is a click which is a very brief transient change in sound pressure. The click is usually generated by a monophasic square wave electrical pulse to an earphone. The maximum pulse duration which produces a "clean" click is about 1 msec. Clicks longer than this have a "ragged" sound or may be perceived as two clicks with a silent interval to the extent that the ear can resolve the rise and fall of the pulse. They are complex, difficult to quantify, and normally avoided for AER work. For stimuli of longer duration, pure tones, complex tones, or noise are possible sources. A pure tone is one whose sound pressure changes as a function of time have a sine waveform. They are generated by audio-frequency range oscillators. A useful instrument for generating pulses or pure tones is the voltage-controlled signal generator (8). This instrument provides sine, triangular, or square wave signals, the frequency of which may be controlled by a voltage input. It is especially useful for rapid changes to predetermined frequencies controlled manually by a fixed step voltage divider or remotely by the digital-to-analog output of a computer controlling stimulus presentation. Complex tones as such are not usually used to evoke AERs. They are sounds with a periodically repeated waveform which is a mixture of two or more sine wave components. The resulting difficulty of specification and quantification makes them less desirable than pure tones as stimuli. Noise, in the context of a stimulus, is a sound comprised of multiple, aperiodic, random-frequency components. The term white noise is sometimes used to refer to noise having a wide frequency spectrum. Electronic noise generators are commercially available, some of which (9) have an input for externally generated signals which can be "mixed" with, i.e., superimposed upon, the noise. These are useful for masking experiments.

Tones and noise are continuous signals and must be converted to discrete stimuli to evoke AERs. In other words, they must be converted to tone or noise "bursts" with onset and offset. Tone bursts have the advantage of frequency control if discriminative stimuli are desired. Tone bursts as short as 10 msec can be discriminated on the basis of frequency even though their short duration makes them sound more like a ragged click.

A major problem with tone or noise bursts is turning them on or off without generating a switching transient, that is, an onset or offset which is so rapid that it creates a click when applied to the electroacoustic transducer (earphone or loudspeaker) which converts the electrical energy to sound pressure. With any signal in which the voltage is continuously varying with no fixed temporal relationship to its connection or disconnection from the transducer, it is probable that at the instant of onset or offset, the voltage will not be zero. Thus, if an ordinary mechanical switch is used, there will be an instantaneous change in potential applied to the transducer, thus producing a click. This contaminates the stimulus if one is investigating the AER to nonclick stimuli. The transient can be avoided by turning the signal on or off gradually and instruments called electronic switches or switching amplifiers are commercially available for the purpose (10). Mechanical and photoelectric switching devices are usually cheaper but have relatively prolonged rise and fall times, that is, time from onset to full signal amplitude and maximum signal back to zero. An electronic switch can provide a rise and fall time of as little as 2.5 msec without an audible click. For short duration bursts, such rapid rise and fall times are necessary. Commercial electronic switches are available with gain controls and dual inputs wired so that when one comes on the other goes off, thus allowing rapid shifts from one signal to another. These switches are usually gated, that is, turned on and off by external triggering so that the duration of the stimulus is determined by the width of the gate pulse.

There is increasing interest in AERs evoked by speech sounds. We have recently found hemisphere-specific differences in evoked potentials between tasks which require identification of linguistic *versus* nonlinguistic acoustic parameters of the same computer-synthesized sound (Wood, Goff, & Day, 1971). Problems with noncomputer-synthesized speech sounds are lack of control over parameters and difficulty in synchronizing averaging devices.

Whatever the nature of the auditory stimulus and however it is generated, it must ultimately be converted from electrical to sound wave energy by an earphone or speaker. Speakers are used for so-called "free-field" stimulation; they are limited to binaural stimulation, and effective intensity and binaural phase relationships vary with the position of the subject's head with respect to the speaker. Earphones are therefore generally preferred. Circumaural earphones provide a significant degree of attenuation of ex-

traneous sound which is especially important when the subject is not inside a sound attenuating chamber. However, they can present problems for AER recording. First, they are usually connected by a headband and it can be difficult to place the headband or the circumaural cushion so as not to rest on a scalp electrode and cause discomfort. Second and most important, the driver units for this type of earphone typically have relatively large coils and we have found that they can introduce serious artifact into the recording in proportion to the duration of the stimulus. Bursts of tone, noise, or speech will be superimposed on the AER due to electromagnetic induction of currents in recording leads by the earphone coil. Miniature earphones of the type used in hearing aids (11) have much smaller coils and do not introduce artifact. These are inserted into the ear canal and taped in place if necessary. The discomfort of a headband or ear cushions pressing on electrodes is also eliminated. However, if circumaural sound attenuation is desirable and electrodes can be placed to avoid the headband and cushion pressure, earmuffs of the type used near jet aircraft worn over the miniature earphone provide very efficient sound attenuation.

The calibration of AER stimulating equipment varies with the type of stimulus used. A problem common to all types, however, is describing the transformation from the electrical energy of the generator to the sound pressure energy output of the transducer. First of all, impedance matching is necessary for the maximum transfer of power[9] from generator to transducer. Impedance mismatches seriously reduce power transfer and may require the interpolation of impedance matching transformers or interfacing amplifiers. Even with matched impedances there will be some power loss. As a result, measuring the voltage at the input to the transducer says little about the stimulus energy reaching the ear. As with any system, the best way to calibrate is through the entire system, transducer included. Various instruments and methods for this purpose are discussed by Licklider (1951) and Hirsh (1966). The amplitude of transient signals always presents a more difficult quantification problem than a continuous signal since their duration is usually too brief for the measuring instrument to respond and a valid reading to be taken. Clicks therefore require for calibration an impact noise analyzer (12) which samples and stores peak value, maximum instantaneous level, and time duration of impact sound. Impact noise analyzers must be used in conjunction with sound level meters of the type used to measure continuous signals (13).

Frequency of a pure tone may be checked in various ways as described by Hirsh (1966). Perhaps the easiest way is to use an events per unit time

[9]Optimal transfer of power requires impedance matching; optimal transfer of voltage requires a low impedance output to a high impedance input.

(EPUT) meter (14). An EPUT meter has several other functions and we have found it valuable as a general laboratory instrument.

Unfortunately, even these methods do not precisely quantify the sound pressure actually impinging on the ear drum, and if they did, would not take into consideration individual differences in auditory sensitivity which varies as a function of frequency, age, pathology, etc. Therefore, a commonly used practical procedure for equating auditory stimulus intensity between ears, sessions, and subjects is to specify in terms of sensation levels (SL). Sensation level is the amount of energy, specified in decibels, above the minimum energy a subject can hear, or in other words, above the subject's absolute threshold. The threshold is determined by standard psychophysical techniques, usually the method of limits, in which the intensity is gradually increased and decreased until the subject reliably reports or ceases to report hearing it. The average of one or more ascending and descending series is taken as the absolute threshold. The stimulus is then increased to typically 60–70 db above this level or in other words, 60–70 db SL. The simplest way to determine absolute thresholds and specify sensation levels is to interpolate attenuators (15) between signal generators and transducers. These attenuators sometimes also solve impedance matching problems. They usually have 10 db and 1 db step controls; thus the absolute threshold and sensation levels may be read directly from the attenuator setting, assuming it is accurate. A complete research report will still measure and specify the physical characteristics of the stimulation used.

Auditory stimulation presents no special problem with regard to the safety of the subject save one. That is guarding against the accidental presentation of excessive sound pressure levels which can produce pain and even permanent damage. For example, the oscillator output level of a 1000-Hz signal required to produce a 10-msec tone burst at 70 db SL may be very unpleasant or painful to the subject if accidentally switched in as a continuous signal. Furthermore, it may produce a (hopefully) transient hearing loss which affects the experimental results. Again, a 70-db SL click presented at a low repetition rate is not uncomfortable. If the repetition rate is accidentally raised $\times 10$, $\times 100$, or $\times 1000$, which are common step controls on some instruments, the result is most unpleasant. In general, the earphones should never be placed on the subject until all equipment is checked out and known to be working properly. If "trouble-shooting" is required during the session, the earphones should be disconnected.

C. Visual Stimulation

Several recent articles describe in extensive detail the generation, control, calibration, and specification of visual stimuli (Boynton, 1966; Riggs, 1965).

Graham (1965) presents some basic terms, methods, and data of importance to the VER investigator and Perry and Childers (1969) discuss VER stimulation variables. The reader is referred to these sources and only a few general comments are presented here.

In terms of physical control, the best way to present visual stimulation is by Maxwellian view. By this method, the light is focused to a point on the cornea causing all the light to enter the eye regardless of changes in pupillary constriction. The light beam expands beyond the focal point and stimulates a section of the retina according to the visual angle determined by the focal length of the lens. Maxwellian view system construction is discussed by LeGrand (1968) and Riggs (1965). The problems with Maxwellian view stimulation for VER work are: first, the head must be held rigid. This is typically done in non-VER experiments by a "biting board," an impression of the subject's teeth which he bites into to hold his head rigid. We quickly found, as one would expect, that the muscle potentials produced by biting made VER recording virtually impossible from any electrode over head muscles. Substituting a chin and forehead rest allows recording from some subjects. Second, regardless of the head-holder, the subject must voluntarily maintain occular fixation for the prolonged periods of repeated stimulation required for VER recording. This kind of highly motivated cooperation is usually found only in subjects with a vested interest in the success of the experiment, such as co-workers and relatives. Thus, Maxwellian view stimulation is generally not feasible for many subjects and especially not for patients.

The easiest method of VER evocation is with stroboscopic photostimulators (16) but control over the light actually entering the eye is poor. Control of pupillary dilation by drug administration or the use of an artificial pupil helps. Occular fixation is still important though less critical than with the Maxwellian view. A patterned stimulus usually evokes a better-developed evoked response. Some investigators are experimenting with the use of fiber optic "light pipes" but to my knowledge they have been used only in animals (Spehlmann & Smathers, 1968). Glow modulator tubes have the advantage that they can be triggered or modulated by a signal such as a pulse or sine wave, but their energy output is small and their spectral characteristics change with modulation. A good, practical method for general application with unsophisticated subjects and patients has been developed by Dustman and Beck (1965). A white, plastic sphere of approximately 28 inches (70 cm) in diameter is placed approximately 16 inches (40 cm) from the subject's face. It is either transilluminated or reflectively illuminated by a stroboscope. If care is taken to illuminate the sphere homogeneously, changes in effect of stimulus intensity due to changes in occular fixation are minimized as long as gross head movements, which can easily be observed by the experimenter, are not permitted.

The main artifact problems peculiar to visual stimulation are sounds associated with stroboscopic discharge and inductive currents from the discharge or trigger pulses. If possible, having the light source outside a sound-attenuating recording chamber and beaming it in through a window with double glass to preserve sound attenuation is desirable. This also eliminates heat problems in the recording chamber from light sources and power supplies. If this is not possible, the strobe light itself may require a sound-proof housing. Possible contamination from sound and electroinductive artifacts may be assessed by blocking the light and response averaging with all other conditions held constant; time-locked potentials should not be seen. Proper separation of stimulating and recording leads should eliminate inductive artifacts.

D. Odor Stimulation

Apparatus for obtaining evoked responses to odor stimulation have been reported by Finkenzeller (1966) and Allison and Goff (1967) who found the response to consist mainly of a positive wave peaking at 450–550 msec. Although initial evidence suggested that the response was olfactory, Smith, Allison, Goff, and Principato (1971) concluded that the response was mediated by trigeminal nerves.

E. Taste Stimulation

Summated cerebral evoked responses to taste solutions applied to the tongue have been reported by Funakoshi and Kawamura (1971).

F. Stimulus Repetition Rate

A consideration of great importance for AEP research is the rate at which stimuli are presented. It is well known that the response to a second or test stimulus (TS), is altered by the occurrence of a response to a preceding, or conditioning, stimulus (CS) (Allison, 1962; Bergamini & Bergamasco, 1967 and references cited therein; Davis, Mast, Yoshie & Zerlin, 1966; Gjerdingen & Tomsic, 1970; Rothman, Davis, & Hay, 1970). The alteration usually consists of a depression of the second response to a degree inversely proportional to the CS-TS interval. However, facilitation, or enhancement, of the response is reported for certain CS-TS intervals (e.g., Shagass & Schwartz, 1964). In the somatic system, Allison (1962) showed that the different components of the SER have different recovery function—in general the length of time for recovery is proportional to the component latency. The importance of interstimulus interval (ISI) for experimental results is

illustrated by Beagley and Kellogg (1970) who found radical differences in the shape of AER intensity functions using a 1.25 sec versus a 20.0 sec ISI.

A minimum of 48 to 64 stimuli must be presented to obtain a reasonable AEP and three to six AEPs are needed to estimate the reliability of the response. Experimenters are therefore legitimately concerned about response variability introduced by changes due to habituation, drowsiness, or fatigue during the resulting long session. This has led in some cases to the use of stimulus repetition rates which are well within the "recovery cycle" of AEPs. Goff (1969) pointed out that all evidence indicates that alterations in evoked responses within and between modalities occur as a function of repetition rate and that they are differential between subjects and between AEP components. Generally, the later the component, the more susceptible it is to alteration as a function of repetition rate. Estimates of time required for "complete" recovery range from 3 to 4 sec in the somatic system (Allison, 1962) to as long as 10 sec in the auditory system (Davis *et al.*, 1966). Obviously a compromise is required between excessively long recording sessions and excessive response distortion. Around 3.0 sec ISI is appropriate for most purposes. If one is interested only in early components, shorter interstimulus intervals may be appropriate. For AER clinical audiometry, Davis and Niemoeller (1968) state that an interval of 1 sec gives the maximum vertex potential voltage per minute of sampling. Perhaps the empirical approach is the best. That is, compare a response evoked at a long ISI to responses evoked at shorter intervals. The shortest interval which does not produce serious distortion in the AEP components under investigation is the appropriate one.

A final caution about stimulus repetition rate peculiar to averaging is to be sure that the repetition rate is not a multiple of the period of 60 Hz, i.e., 16.66 msec. As will be discussed in Section VII, 60-Hz interference is one of the most common problems in AEP recording. A repetition rate which is a multiple of 16.66 msec will "phase-lock" the averaging to the 60 Hz and enhance the 60 Hz as well as the AEP. It is not a common problem, but it can happen. For example, an ISI rate of 1.5 sec is close to 1.66 sec; 3 sec is close to 3.32 sec, etc. If a stimulator is set inaccurately or out of calibration, an ISI which will phase-lock to 60 Hz can occur. Instrument malfunction can also be a cause, as a recent experience in our laboratory illustrates. During recording, we were puzzled by the appearance of 60 Hz in the average when none was discernible at the averager input. Changing stimulators although maintaining the same nominal ISI cured the trouble. Figure 3-10 illustrates the difference. The upper trace is a click-evoked AER recorded with a properly functioning stimulator at an ISI of 4 sec. The bottom trace was recorded under identical conditions but with a stimulator which proved

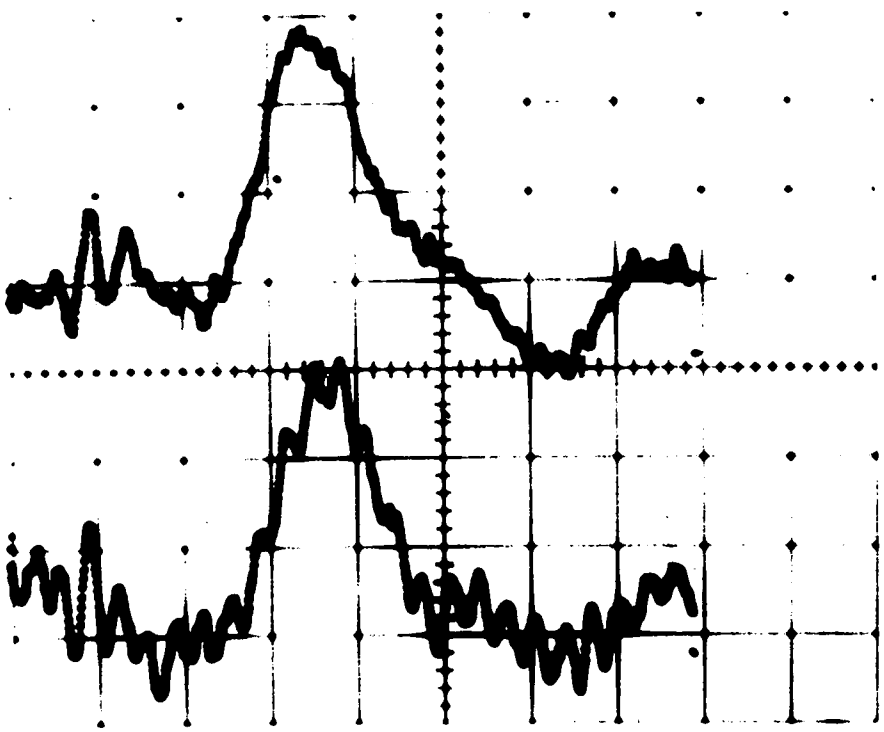

FIG. 3-10. Effect on an AEP of accidental phase-locking to 60-Hz of a nominal 4-sec interstimulus interval causing summation of the 60 Hz (bottom record) compared to recording under identical conditions but no 60-Hz phase-locking (top record).

to have 60-Hz ripple in its triggering circuit, causing the trigger to phase-lock to 60 Hz.

VII. Recording Systems, Artifacts, and Interference

The irreducible elements of an on-line AEP recording system are electrodes, amplifiers, a stimulator, an averaging device, and some shielded cable to connect them together. One can substitute a tape recorder for the averager and average responses off-line with access to a computer having appropriate input-output (IO) equipment. On the basis of experience, I consider off-line response averaging to be, in the general case, an undesirable method for AEP research because of lack of feedback of results, possible loss of data, and the fact that because we are working with "real-time"

data, off-line averaging nearly doubles the experiment time unless technically difficult tape "time compression" is achieved. However, tape recording in conjunction with on-line response averaging is desirable in permitting reanalysis of data in different ways.

Though much valuable research has been done by AEP investigators equipped with little more than a basic system, such is not optimal. A complete AEP recording laboratory might be equipped approximately as follows. A sound-attenuating, radiofrequency shielded recording chamber (17) large enough to hold a bed or at least a reclining chair has the obvious advantage of providing a reproducibly homogeneous sound and light environment. Sound-baffled ventilation is necessary, and variable illumination control is desirable, for subject comfort. It is important that the subject be seated or lying comfortably so as to keep muscle tension in the head or neck region to a minimum to avoid the myogenic artifact potentials discussed in Section IV. Provision for auditory intercommunication by which the subject is always monitored is mandatory. Closed circuit television monitoring is highly desirable, especially with patients; it frequently reveals actions by subjects such as changes in wrist position (shock stimuli); dislocation of earphones (auditory stimuli); shifts in fixation, head position, eyes closing (visual stimuli); or other idiosyncrasies, not noticeable by other monitoring, which can affect the experimental results.

Multiple recording electrodes are most conveniently connected to the amplifiers by means of a multiple jack plug-in board through an electrode selector switch panel located outside the chamber. Monitoring of the EEG is best done after the final stage of amplification just prior to input to the averager. An oscilloscope is practical for monitoring up to four recording channels simultaneously. If multiple oscilloscope inputs are not available or if more than four channels are in use, a selector switch on the oscilloscope input facilitates monitoring. Obviously, oscilloscopic monitoring provides no permanent EEG record. A better system is provided by modern EEG machines whose amplifiers have filter settings appropriate for AEP recording and IRIG compatible (see Section V,B) output jacks which permit their output to be led directly to the input of most averaging devices and tape recorders. The multichannel EEG is simultaneously graphed along with stimulus and time markers, providing a permanent record from which one may refer back to such things as the amount of muscle activity or the state of the subject when a particular response is obtained.

We have found it advantageous to provide the subject with some feedback and control over the experiment. A small, preferably battery-powered, oscilloscope upon which the subject can observe his EEG greatly assists him in reducing muscle tension. He is instructed to minimize the "width"

of the EEG trace by trial-and-error adjustment of jaw, neck, or torso position. A counter (18) indicating the number of stimuli presented is useful if the subject knows how many responses are required for a given summation. A subject with an urge to cough or sneeze, for example, can usually inhibit it if only a few stimuli remain. Subjects seem to endure experimental sessions better with this kind of feedback. Finally, a "panic button," with which the subject can interrupt the summations for some urgent need, makes him more comfortable and more relaxed. This is as easy as a switch which grounds a trigger pulse or sets a flag on a programmable computer. The "panic button" should also activate some kind of experimenter alerting device as an added safeguard for the subject. We have found that the sound attenuation of our recording chambers from the inside out is noticeably superior to the reverse. Auditory intercommunication systems sometimes fail and even if television monitoring is available, the experimenter's attention may be elsewhere.

The components of a system having been assembled and interconnected, the system should have provision for rapid calibration of system gain. The EEG amplifier gain calibrated as discussed in Section V,D is not necessarily equivalent to the gain of the entire averaging system upon which determination of AEP amplitudes is based. System gain must consider the effect on the signal of every component which affects the signal. For example, the inputs to analog-to-digital converters in most averagers and computers have input attenuators or "buffer" amplifiers. The attenuators may have several settings. The amplifiers usually have a nominal gain of unity, but will vary slightly. The most effiicient and accurate method for system calibration is to put a known signal on the input of the EEG amplifier and read the output of the final system component, usually the averager. Some experimenters go further and summate or average the calibration signal, usually a square-wave pulse.

One of the most important activities of the experimenter before and during AEP recording will be the control of artifacts. In the context of AEPs, an artifact may be considered any electrical activity in the record which does not originate in the brain. Thus the EEG is not an artifact although it is sometimes heretically referred to as "noise" by the AEP purist. Artifacts are the investigator's constant companion because they may be introduced by the subject, by minor changes in equipment configurations or interconnections, or even by changes in electrical equipment external to the laboratory. Artifacts may be roughly dichotomized into those generated by the subject and those which are independent of the subject. The dichotomy is not complete since the subject sometimes serves as an antenna which conducts artifactual signals into the system.

Subject-generated artifacts which contaminate AEP recording, with the exception of those resulting from stimulus presentation discussed in Section VI, also interfere with EEG recording and are extensively discussed in that literature frequently with excellent illustrations (e.g., Cooper *et al.*, 1969; Dunn, 1967; Fuller, 1965; Mowery, 1962; Peters, 1967; Walter & Parr, 1963). The reader should refer to these sources.

Subject-independent sources of artifacts, frequently called interference, arise from a frighteningly large number of sources. An excellent discussion of interference sources and practical steps in their location and elimination is that of Wolbarsht (1964).

The most common source of interference is 60-Hz currents introduced into the system by inductive, capacitative, or resistive coupling from a.c. power lines. Stacy (1960) estimates that this is the source of 90% of instrumentation difficulties. This interference must be eliminated or at least minimized by adequate shielding and proper grounding to the point where it can be cancelled by the common mode rejection of a differential amplifier (see Section V, C). The principles of shielding and grounding are well explained by Stacy (1960), Thompson and Yarbrough (1967), and Wolbarsht (1964). The location and elimination of 60-Hz interference is an art rather than a science and it is not unusual to cure the difficulty without knowing exactly why, which renews faith in religion and invokes the credo "if it works, leave it alone." However, the following procedures have been successful in our laboratory.

Assume that a subject has been connected to the system, we are ready to record, and the monitor shows suspicious-looking continuous periodic activity either superimposed upon or totally obscuring the EEG. This will usually be 60-Hz interference but the first step is to verify that it is. It may appear as a simple sine wave, or as a complex sine wave due to the presence of harmonics. However, the fundamental period will be one peak approximately every 17 msec. On an oscilloscope sweeping at the rate of 50 msec per major division, this is three peaks per division. If an EEG machine is the monitor, it may have a 60-Hz "notch" filter and switching the filter in will identify the signal as 60 Hz if it diminishes or eliminates it. (This filter should not be used during AEP recording, see Section V,D.) Having obtained a visual display and verified the source as 60 Hz, the next questions are whether it is peculiar to one or more channels or common to all channels, and whether it is intrinsic or extrinsic to the system, in other words, is it on the subject or apparatus side of the EEG amplifier input. This is simply tested by shorting together the amplifier inputs at the electrode board. Shorting with the switching panel or by switching from "use" to "calibrate" on an EEG machine does not test for problems in the electrode board itself

such as a loose input jack shorting to ground. If the 60 Hz is eliminated by amplifier input shorting, the system is "clean" and the trouble source is "pickup" from the recording leads on the subject. Check to see that the subject has a low resistance ground, preferably connected to the amplifier ground since grounding to some other point may cause a "ground loop" and introduce 60 Hz. Special grounding techniques for shock stimulation were discussed in Section VI, A. Otherwise, an EKG electrode on an arm or leg provides adequate grounding. Check recording electrode impedance with an impedance meter (resistance meters polarize electrodes, see Section III). An impedance of 10 kΩ or less is desirable. If the subject is in an unshielded environment, lower impedances may be required. If the 60 Hz is selective as to channel, interchange amplifiers to check for instrument malfunction. If the problem is channel but not amplifier selective, check electrode impedances, the cleanliness of the electrode plug-in pins, the soundness of the connection between pin and plug-in jack, and the integrity of the jack itself. Make sure the leads are cabled so that they follow the same path to the plug-in board. This is always important; if the path of two input leads to a differential amplifier are sufficiently separated, the phase angle of the pickup of the common source signal may differ sufficiently to compromise the common-mode rejection of the amplifier.

If the 60 Hz has appeared during the session, the ground or recording electrode electrolyte may have dried out and renewing it may be necessary. Sometimes electrolyte squirted under the recording or ground electrode by means of a syringe and blunt hypodermic needle will avoid reapplication of electrodes.

If electrodes and grounding are appropriate, and the subject is not in a shielded recording chamber, trial-and-error changes in his position with respect to 60-Hz sources such as the recording equipment itself, ceiling lights, electric cables in floor or ceiling, etc., may produce an orientation that will reduce the interference sufficiently to permit recording. If not, a shielded chamber, amplifiers with a higher common-mode rejection ratio, or moving to a different room may be required.

Even with the subject in a shielded chamber and appropriate electrode impedances and grounding, 60-Hz pickup may occur. This indicates that excessive 60 Hz is being led into the chamber. N. P. Thompson and Yarbrough (1967) discussed various ways this can occur. We have found that we can violate some of the general principles they discuss. For example, we run an a.c. line into the recording chamber for our TV camera, keeping it remote from the subject and tightly up against the metal ceiling of our chamber does not generate noticeable interference. However, any wire penetrating the shielding of the chamber is a potential source of inter-

ference. The offending source is best located by removing each possibility while constantly monitoring until the interference is eliminated. Pickup in the chamber can usually be demonstrated by the use of a "dummy subject," that is, by connecting two leads with a resistor between them to the amplifier input. We use at least 100 kΩ resistance to maximize pickup since if it is eliminated with this amount of "interelectrode impedance," we are quite sure of clean records at the lower values obtained with a real subject. The "dummy subject" is also an excellent way of checking out a new or modified recording system.

Returning to the test in which input leads were shorted together, assume that the 60-Hz interference was unaltered, indicating the problem is intrinsic to the recording system. If the 60 Hz is diminished but not eliminated by input shorting, one may have a dual problem in which case the intrinsic problem should be solved first. By far the most common source of 60-Hz interference intrinsic to the system is a "ground loop." This can occur when any of the elements of a system, including the subject, are connected to "ground" at two or more points. These points may have slightly different resistances to ground, permitting interference "pickup," resulting from the types of coupling mentioned above, to generate a potential difference between them. The circuit (loop) is completed through the ground. Because of the generally low resistances involved, the current flow may be appreciable and the resulting potentials can be amplified into the volt range by the high amplification used in AEP work.

Ideally, then, there should be only one connection to ground. This eliminates the possibility of a loop. A practical way to do this is to use "series" rather than "parallel" grounding. Series grounding means simply that the first component of the system, e.g., the recording chamber, is connected to the main ground bus, the next component, e.g., the amplifiers, is grounded to the chamber, the next component is grounded to the amplifiers, etc. Parallel grounding in which system components are connected directly to ground by individual leads should be avoided.

While simple in principle, series grounding is difficult to achieve. For example, components which are rack mounted are grounded in parallel. However, this seldom causes problems if they are connected to the a.c. power with the "high" and "low" sides comparable for each component and the racks themselves are grounded in series. The third wire safety ground provided with most instruments is a common source of ground loops. It is usually best to defeat these grounds and ground through the rack. A practical method is to supply power to all instruments in a rack through a three-wire multiple outlet box in which the ground wire has been disconnected from each outlet. Plugging them in "three-wire" keeps the "high" and "low" sides of the a.c. properly oriented for each instrument. Two

safety precautions must be observed, however: (1) Be sure that grounding through the rack is electrically equivalent to each instrument's safety ground; if not make it so. (2) Ensure that the rack itself does not become accidentally ungrounded. Soldered connections help avoid this hazard.

In any complex system, the opportunity for unrecognized ground loops is large. For example, shielded cables are not an ideal way to ground major components such as instrument racks and EEG machines. If they are disconnected for any reason, the whole component becomes ungrounded which can be dangerous. A permanent independent ground is better. Then the shielded cable should have the shielding grounded at one end only; otherwise you have dual grounds and a possible ground loop.

Assuming the interference has been determined to be 60 Hz intrinsic to the system, one must find the ground loop. Monitoring one or more amplifiers at the output of the final stage, short the amplifier inputs together and isolate the amplification-monitoring equipment completely from the rest of the system except for the normal amplifier ground. This should eliminate the interference. Then reconnect power and grounds for each system component until the interference source is revealed by reappearance of the 60 Hz. Correct the problem by improved grounding, ungrounding, a.c. plug reversal, etc., and continue step by step until the entire system is interconnected. Obviously, if assembling a new or modified system for the first time, using this procedure initially may prevent much subsequent grief. Finally, suppose that isolating shorted-input amplifiers and monitoring equipment does not eliminate the 60 Hz. We have had this happen on two occasions which illustrate the bizarre and nefarious ways ground loops can occur. We ground our recording chambers to a specially installed ground separated from all other electrical grounds in the hospital. We then ground our amplifiers to the chamber and the remaining components are grounded in series as discussed above. On two occasions our amplifier outputs showed 60 Hz interference though isolated completely from the rest of the system. Disconnecting our main ground paradoxically eliminated 60 Hz. This could only mean that our recording chamber was grounded by some means unknown to us. Checking with an ohmmeter verified a relatively high resistance path to ground. A recheck verified that our chamber was not grounded by any obvious means, including a common error of grounding through the metal conduit of the chamber lighting and ventilating system. After a considerable period of consternation, the accidental ground was discovered to be a metal channel carrying cables overhead which rested on the metal recording chamber on one end and had, for convenience, been attached on the other end to a screw holding the grill of an air conditioning cold air return which was grounded.

The second experience was even stranger. After many hours of mystifi-

cation, the sneak ground path was found to be bolts holding the vibration isolation rails of the chamber to the floor. The bolts contacted metal lathing of the ceiling below which in turn probably contacted water pipes or electrical conduits. Removal of the bolts, which were unnecessary in the first place, solved the problem.

Appendix

1. Model EZM-1 Electrode Impedance Meter, Grass Instruments Co., Quincy, Mass.
2. Speed-clave No. 777, Wilmot Castle Co., Rochester, N.Y.
3. Time Sterile Indicator Tape, Professional Tape Co., Riverside, Ill.
4. EC2 Electrode Cream, Grass Instruments Co., Quincy, Mass. Bentonite paste is used in the same application by many investigators. A formula for its mixture is in Cooper *et al.* (1969), Appendix B.
5. Cambridge Instrument Co., Inc., Ossining, N.Y.
6. Peripheral Nerve Stimulator, Model ST-4, Neurodyne Instrumentation, Napa, Calif.
7. #355 Prufex Conductive Knee Crutch Straps, American Hospital Supply, Edison, N.J.
8. Model 114, Wavetek, San Diego, Calif.
9. Model 901B, Grason-Stadler Co., West Concord, Mass.
10. Model 829E Electronic Switch, Grason-Stadler Co., West Concord, Mass.
11. Rye Industries, Mamaroneck, N.Y.; Telex, Communications Division, Minneapolis, Minn.
12. Type 1556-B Impact-Noise Analyzer, General Radio Co., West Concord, Mass.
13. Type 412 Sound Level Meter, H. H. Scott, Maynard, Mass.
14. Universal Counter-Timer, Model CF 635, Anadex Instruments, Inc., Van Nuys, Calif.
15. Model 350D Attenuator Set, Hewlett-Packard Co., Palo Alto, Calif.
16. Model PS-2 Photo Stimulator, Grass Instruments Co., Quincy, Mass.
17. Industrial Acoustics Co., New York, N.Y.
18. Type 320 Event Counter, Digilin Digital Instruments, Division of Dura-Containers, Glendale, Calif.

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Chapter 4

The Analysis of Scalp-Recorded Brain Potentials

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I. Introduction

A. The Psychological Relevance of Human Brain Potential Studies

The enormous complexity of neural transactions within the brain poses a formidable challenge to the investigator who would seek to understand some aspects of these processes by analyzing the brain potentials recorded from the human scalp. Any treatment of these neuroelectric data which aspires to more than pure description must give careful consideration to the manner in which the EEG data can best be related to appropriate psychological variables, as well as to the underlying brain mechanisms they reflect.

Psychologists who depend solely on behavioral data are restricted to inferences on the nature of information-processing mechanisms within the organism derived from patterns of stimulus and response contingencies. In the absence of data on the associated neural activity, psychological constructs have diverged quite widely from the conceptual forms which are most conducive to developing correlations between brain mechanisms and behavior.

Early efforts to link human brain potential recordings to psychological variables focused primarily upon correlations with gross changes in organismic state, or with various psychological categories. Only the well-known relationships with brain maturation, sleep stages, and organic brain pathology can be considered firmly established. Attempts to define EEG correlates of psychological constructs have not been particularly rewarding, since there has been little possibility of conceptualizing a functional relationship between the spontaneous brain activity and psychological organization. Thus, over and above the unlikely prospects for finding reliable correlations between simple measures of spontaneous EEG activity and complex constructs such as intelligence and personality, there is an intrinsic failure of these approaches to probe brain and behavior relationships in a manner which can help to elucidate the relevant physiologic mechanisms.

Recently developed methods for extracting brain potentials associated with specific sensory and motor processes have provided exciting possibilities for narrowing the gap between the psychological and physiologic domains of inquiry. It is not entirely surprising that investigators have retained much of the conceptual framework of earlier studies and continue to seek "indices" of more complex aspects of human mental processes. Yet, the modest

correlations which may be demonstrated between poorly understood brain potential measures and psychological constructs which are difficult to subject to operational definition and experimental manipulation seem to advance but little our comprehension of relationships between brain mechanisms and human behavior. It is most desirable in applying the newer methods of brain potential analysis to define a psychological framework which forms a natural context for neurobehavioral investigation.

The elementary objective variables of behavioral science are stimuli and motor responses. The founders of experimental psychology recognized that an understanding of processing mechanisms required the definition of the temporal relationship between these reference variables. Reaction time experiments formed the central paradigm for this analysis. Although the behavioral data alone cannot unambiguously delineate the underlying brain processes, use of RT methods in combination with concurrent recording of brain potentials (namely, Vaughan, Costa, Gilden, & Schimmel, 1965; Evarts, 1966; Vaughan, Costa, & Gilden, 1966; Miller & Glickstein, 1967) provides an approach to charting the course of neural events within the brain during sensorimotor sequences, both in experimental animals and in human subjects. The logical attractiveness of the RT method derives from the opportunity it provides for analyzing the concomitant variation of psychological and physiologic parameters under a wide variety of experimental conditions. Thus, despite the undoubted value of physiologic methods involving brain ablation and stimulation in elucidating certain aspects of brain-behavior relationships, even a limited understanding of the neural mechanisms will require data obtained from analyses of the concomitant variation of neural and behavioral processes. In man, there is even the possibility that some aspects of the physiologic processes which underlie conscious experience may be identified and analyzed, since the time course of various sensory experiences can be experimentally defined (e.g. Haber & Standing, 1970; Efron, 1970a, b). The basic behavioral strategy is an elaboration of the original methods of Donders (1868). These behavioral methods have recently been imaginatively extended by psychologists (e.g., Averbach & Sperling, 1961; Sternberg, 1969; Posner & Taylor, 1969), so as to provide techniques for probing by physiologic methods such neurologically obscure processes as short-term storage and memory retrieval, as well as various decision and information processing mechanisms.

B. Empirical Approaches to Event-Related Brain Mechanisms

In conceptualizing the neural mechanisms which underlie sensory, motor, and sensorimotor processes of varying complexity, we can view our task in terms of tracing a sequence of events within the brain either forward in time

from a stimulus, or backward from a motor act. In the former instance we consider the neural correlates of sensory and perceptual processes, in the latter the mechanisms which generate voluntary movement. If these processes are bounded by a stimulus and a motor response, as in the reaction time paradigm, some of the intervening neural events can be considered essential to the behavioral sequence. If the particular S–R process being studied was the only thing going on in the brain, it would presumably be possible to chart the spatial extent and temporal sequence of the associated neural processes, by recording from a sufficient number of appropriately placed electrodes. Several problems confront such a direct approach (which actually represents the classical method of sensory physiology).

1. The physiologic activity elicited by discrete stimuli and associated with motor responses is of substantial duration, measured in tenths of seconds. Thus, a motor response to a brief light flash may be initiated before evoked retinal and brain activity have subsided. This circumstance implies a substantial temporal overlap in the neural activity at successive stages of information processing, which can obscure the definition of serial functional relationships.

2. Both behavioral and physiologic evidence attest to the increasing temporal variability of neural activity, as it increases in distance from the reference event. Since the analytical method being proposed depends upon defining reliable temporal relationships of neural activity to stimuli and/or motor acts, the variable dispersion of neuroelectric potentials within a given process must be taken into consideration.

3. Since it is well known that parallel processes and feedback loops abound within the brain, even elementary processes of behavioral significance can rarely be adequately depicted as strictly serial mechanisms. This forces us to deal with the conceptually and technically difficult analysis of nonlinear systems. Among the possible approaches are the use of brain lesions to open feedback loops, in combination with simultaneous recordings at several brain sites (Vaughan & Gross, 1969). The experimental demands of such combined approaches are arduous and have yet to be satisfactorily implemented.

4. In the behaving organism the event-related process under study is by no means the only thing going on in the brain, and concurrent spontaneous brain potentials tend to obscure the relevant potentials. Early evoked potential studies in animals dealt with this problem by using general anesthesia to suppress the spontaneous rhythms. Unfortunately, this gain was achieved at the cost of eliminating the subject's capacity for emitting a behavioral response, which provides the only indication of the informational impact of a stimulus. Anesthesia (and the more recent use of paralytic agents) also

makes it impossible to directly study the physiologic correlates of motor behavior. Thus, an alternative method for reducing the interference of spontaneous brain activity with observations of events related to specified behavioral sequences is clearly needed for neurophysiologic studies in the behaving organism.

5. In man, the necessity for recording from the intact scalp, due to the inaccessibility of the brain to direct electrode probes, imposes enormous degradation of information on the location, nature, and timing of neuroelectric potentials.

One can hardly wonder that, faced with these manifold obstacles, many have doubted the value of neurobehavioral studies employing scalp-recorded brain potentials. Nevertheless, the creative application of available knowledge and techniques can permit us to at least partially realize the possibilities of human brain potential analysis for directly relating cerebral processes to psychological variables. This potentiality is, of course, quite unique in relation to complex perceptual and cognitive processes, including language. There are already indications that, properly pursued, human brain potential studies can provide some insights into the physiologic mechanisms of even the most complicated types of mental activity.

C. The Electroencephalogram and Event-Related Potentials

The foregoing considerations lead to a fundamental distinction between brain potentials which can be related to discrete stimuli or to motor acts and those which do not possess such empirically definable objective referents. The former class is composed of the event-related potentials, ERP (Vaughan, 1969) and the latter the spontaneous brain rhythms, or EEG.

We differentiate between neuroelectric phenomena which can be linked to specific, observable aspects of behavior and the manifestations of spontaneous brain activity, whose functional role is not definable in the context of present knowledge and techniques. In the language of signal theory, the distinction is made between "signals"—the ERP, and "noise"—the background EEG. Stated in another way, which partially mitigates the demotion of the EEG to the status of an obscuring nuisance, we can view the ERP as indices of neural *processes* and the background EEG as an indicator of organismic state. Certainly, the spontaneous brain activity retains a potential significance which is by no means diminished by its presently obscure physiologic and behavioral relationships.

At this time it has been possible, using the methods described in this chapter, to delineate four main types of ERP (Vaughan, 1969; Vaughan & Ritter, 1973): (1) sensory evoked potentials, (2) motor potentials, (3)

association cortex potentials, (4) steady potential shifts. The first two potentials are relatively well synchronized with their respective stimulus and motor reference events, and their intracranial sources can be localized mainly to regions in and near the primary and secondary sensory and motor cortical areas. These potentials are obligatory cortical indices of stimulus and response. In contrast, the association cortex potentials are seen only when stimuli achieve significance for the organism, either by virtue of their role as signals in a behavioral task or by their unexpected occurrence. These potentials are more variable in their time relationship to the preceding stimuli than are the sensory-evoked potentials, and they arise mainly from the parietotemporal cortex. The steady potentials comprise a less clearly defined category, due to their uncertain origins, their easy confusion with potentials generated outside of the brain, and the rather nebulous psychological associations attributed to them. These phenomena were first described in man by Köhler, Held, and O'Donnell (1952) and more recently have achieved wide interest following the description by Grey Walter and colleagues (Walter, Cooper, Aldridge, McCallum, & Winter, 1964) of the "contingent negative variation." Further information on the ERP can be found in Donchin and Lindsley (1969), and Vaughan and Ritter (1973).

D. Objectives and Methods of Scalp Potential Analysis

The preceding remarks suggest that the main thrust of human brain potential studies should be directed to the specification of physiologic correlates of behavioral processes whose temporal extent can be objectively delineated. We must seek data on the timing, magnitude, and location of the neural events which take place in the brain during a given behavioral sequence. Since scalp-recorded brain potentials provide a substantially degraded indication of intracranial neural processes, evidence on each of these variables may either be rather ambiguous or simply not available using present techniques. Accordingly, it is important to assess the limitations of scalp potential recordings as neuroelectric data, and to concentrate upon those aspects of the data which provide the most useful indices of brain activity.

Information on the timing of neural activity during the course of well-defined behavioral sequences is the least equivocal data derived from human brain potential records. If the ERP waveforms are sharply differentiated from concurrent EEG activity, the duration of some aspects of the underlying neural processes can be determined.

Inferences concerning the magnitude of neural activity are on much less secure ground. Although it is possible to derive measurements of ERP amplitude with essentially the same reliability as determinations of the

timing of its components, the interpretation of these measures is ambiguous. This uncertainty derives from the lack of specific information on the reflection of cellular neuroelectric events at the cortical surface, and thus at the scalp. Although some data on these relationships have been obtained by concurrent intracellular microelectrode and surface cortical macroelectrode recordings (Creutzfeldt, Watanabe, & Lux, 1966a, b), this work has not as yet been sufficiently extensive to permit inferences to be drawn on the nature and magnitude of intracortical neural events from surface cortical or scalp recordings. Furthermore, data already at hand make it clear that there is no simple relationship between the amplitude and polarity of scalp potential waveforms and the magnitude of the underlying neural processes. This is due, in part, to the fact that the postsynaptic potentials, which are believed to make the major contribution to scalp-recorded potentials, differ in their manifestation at the cortical surface according to their site of generation. The membrane depolarizations comprising the excitatory postsynaptic potentials appear as surface-positive events followed by a negative potential when located deep within the cortex, on or near the bodies of pyramidal neurons. When the depolarization is superficial, on the apical dendrites, it is accurately reflected by the surface potential. Since the firing of a neuron is determined by the depolarization near the initial axon segment, which is a result of the summation of EPSPs and IPSPs over the entire surface of the neuron, it can be seen that simple generalizations concerning relationships between the surface potentials and neural firing patterns are not warranted. Despite these complexities it is not at all unlikely that reliable patterns of covariation will be found when the relationships between cellular potentials and volume-conducted neuroelectric activity are more extensively studied in behaving animals. Although various pharmacologic and metabolic manipulations profoundly alter the relationship between the slow cortical activity and neural action potentials, under normal conditions of brain function a more stable correlation can be expected. For this reason it is especially important that these analyses be done in behaving animals, rather than in the grossly unnatural circumstances induced by general anesthesia and pharmacologic immobilization. Until more definite information is available, the temptation to draw simple parallels between scalp brain potential amplitude and magnitude of the underlying neural activity must be strongly resisted. It does not follow, however, that amplitude measurements of human brain potentials are meaningless. If reliable quantitative correlations can be established between appropriate psychological variables and brain potential measures, it is reasonable to suspect a relationship to some aspect of the underlying neural activity. At this point in our knowledge of human brain mechanisms, even crude indications on the timing and magnitude of neural activity associated with specific behavioral

sequences can advance our understanding of the "chronological localization" of cerebral processes. In this quest, it is crucial to have information on the intracranial sources of the scalp-recorded potentials. Although difficult to define in an unambiguous fashion from data on scalp potential distribution, techniques are available for testing simple but useful hypotheses concerning the generators of this activity.

In pursuing the objectives outlined above, the basic problems of brain potential analysis can be divided into two distinct parts: (1) the statistical analysis of brain potentials to characterize the waveform of the ERP and differentiate it from the background EEG; (2) the biophysical analysis of volume conduction within the brain and its coverings to delineate the intracranial sources of the ERP.

Taken together, these approaches permit us to begin an exploration of the gross spatiotemporal patterns of the brain activity which underlie human experience and behavior.

II. Measurement and Statistical Analysis of Scalp-Recorded Potentials

A. Representation of the EEG and ERP

In this section we will consider a sample of the potential distribution over the scalp surface recorded from a single electrode pair. It will be assumed that one electrode, the reference, is suitably placed so that the potential fluctuations sensed by it are negligible. Therefore, the potential difference, $V(t)$, between the two electrodes predominantly reflects the potential fluctuations beneath the active electrode. If both electrodes are sampling time-varying cerebral potentials (as in "bipolar" recordings), the neuroelectric data will contain indeterminate contributions from different brain regions—a circumstance which immeasurably complicates the interpretation of the neuroelectric data (see Chapter 3).

The total voltage, $V(t)$, recorded over time comprises two hypothetical potentials, the ERP, symbolized $E(t)$, and the EEG, represented by $G(t)$. In a continuous record, $E(t)$ will be nonzero only during certain restricted periods which can be related in time to the external reference events. The timing reference, t_0, for $E(t)$ may comprise either a stimulus or a discrete motor act, so the ERP may begin either before or after the reference event, or even overlap on both sides of it. For this reason, the actual timing of t_0 with respect to the beginning of a data sample will depend upon the particular experimental circumstances and the specific temporal characteristics of the ERP. Thus, it is necessary to give careful consideration to the duration and relation to t_0 of the expected ERP in determining the onset and length of the

samples selected for analysis. For obvious reasons, it is well to arrange the experimental conditions, whenever possible, to avoid possible temporal overlap of successive ERP. Many factors will enter into the decision on a specific interval between experimental trials; these should always include consideration of possible physiologic interactions among sequential processes, as well as the requirement for independent and random sampling of the ongoing brain potentials which forms an important assumption underlying the statistical analysis of the ERP.

In general the neural processes represented by an ERP cannot be considered deterministic, so that variations in magnitude and timing of the potentials related to them are to be expected. Thus the ERP, $E(t)$, can be decomposed into a mean component, $\bar{E}(t)$, and a variable term, $\Delta E(t)$. It is not desirable to make any assumptions which restrict the nature of this variability, since under specific circumstances it might be either random or partly systematic. The possible presence of systematic changes must always be kept in mind and appropriate experimental manipulations carried out to detect and characterize such changes. A well-known systematic change in sequences of sensory responses is *habituation*, whose presence would be depicted by $\Delta E(t)$.

The spontaneous EEG, represented by $G(t)$, is in most elementary treatments assumed to be a random variable independent of $E(t)$. The implications and limits of this assumption will be considered later. In order to apply the statistical formulations of signal theory to EEG analysis, simplified formal mathematical functions are ordinarily employed. Among the popular models are narrow-band Gaussian noise and sums of sinusoidal functions. It should be kept in mind that inferences drawn from such theoretical treatments will be valid only when the empirical data are adequately described by the model. It is always desirable to pursue the quantitative description of the data under consideration as far as is necessary to confirm or negate the applicability of a particular assumption or inferential technique. This caveat cannot be too strongly emphasized.

Employing the notation of the preceding discussion, we may represent the brain potential record:

$$V(t) = \bar{E}(t) + \Delta E(t) + G(t),$$

where $\bar{E}(t)$ is the mean component of the ERP, $\Delta E(t)$ its variable component, and $G(t)$ the background EEG.

B. Ensemble Statistics and Sampling Principles

The objectives of statistical brain potential analysis are: (1) to provide a suitably accurate characterization of the mean ERP, $\bar{E}(t)$; (2) to estimate the size and nature of the ERP variability, $\Delta E(t)$; and, (3) to describe the

statistical features of the background EEG, $G(t)$, to the extent required for the analysis of $E(t)$ and dictated by experimental interest in the ongoing brain activity. For practical purposes, satisfactory statistical description of these variables can be achieved by computing their first and second moments as a function of time. We will consider three statistics: the mean, the variance, and the autocovariance (autocorrelation). These measures are computed from a set of suitably chosen potential records of finite length, called ensembles. The ensemble length comprises an epoch. Each ensemble consists of a series of voltage measurements taken at successive points in time, which constitutes a discrete time-sampled description of the continuous voltage (Fig. 4-1). This sampling process can be done by making direct hand measurements at specified intervals from a continuous EEG record or, more commonly, by an instrumental analog-to-digital conversion. The sampling interval (or its reciprocal, the sampling rate) must be chosen to represent the continuous waveform with sufficient accuracy to permit satisfactory computation of the required statistics. The theoretical minimum sampling rate to permit a satisfactory representation of frequency content is at least twice the highest frequency present in the data. If samples are taken less often, spurious fluctuations at lower frequencies (called alias frequencies) show up in the sampled data (Fig. 4-2). These errors may not be too damaging in estimating the ERP, as they tend to be random with respect to the mean component, $\bar{E}(t)$, and are therefore reduced in relative size by averaging. However, characterization of the frequency composition of the ongoing EEG, using the autocovariance, may be seriously misleading since the alias frequencies are retained in these computations (see Section II,E). The frequency range (bandwidth) of the EEG and ERP can be restricted for all practical purposes to activity between 0 and 100 Hz. A minimum sampling rate of 200 Hz (sampling interval of 5 msec) will not, therefore, introduce significant aliasing errors, and will provide adequate ERP waveform resolution for most experimental purposes. Occasionally, a higher sampling rate may be employed to resolve higher frequency components for the purpose of accurate latency measurements. Since the main ERP components have a frequency content below 50 Hz, lower sampling rates can be used, providing the amplifier bandpass is set to eliminate activity at frequencies greater than half the selected rate. It is important to note that an analog-to-digital converter will sample any activity present in the record, so that high frequency activity undesired in the analysis must be eliminated by appropriate filtering prior to sampling. Knowledge of amplifier characteristics and the frequency content of the data being recorded are essential to a correct sampling procedure. Since each of the data samples must be stored in the memory of either a digital averaging device or a general purpose computer, there will be some maximum total number

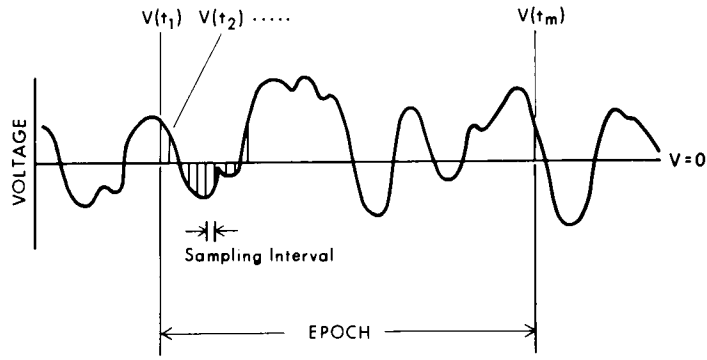


FIG. 4-1. Discrete sampling of a continuous waveform to obtain an ensemble of voltage measurements, $V(t_1) \cdots V(t_m)$. The ensemble epoch is equal to the sampling interval multiplied by $(m - 1)$.

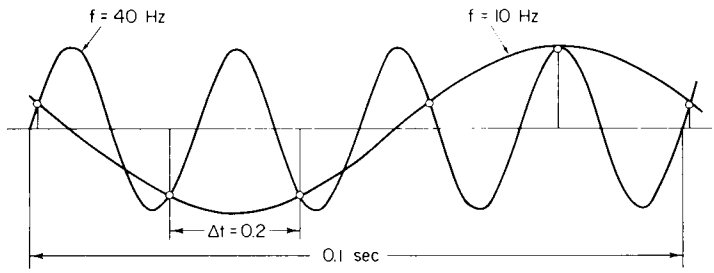


FIG. 4-2. "Aliasing" of a 40-Hz waveform as a 10-Hz fluctuation, due to the use of a sampling rate (50 Hz) less than twice the frequency of the true signal.

of samples. The permissible sampling rate will thus be jointly determined by the epoch and the number of EEG channels being simultaneously analyzed. It will, therefore, often be necessary to trade off sampling rate *versus* epoch length or number of data channels. These decisions should be made only after careful consideration of the frequency content of the data being recorded, the required accuracy of temporal resolution, and the duration of the ERP under consideration.

We now take a set of N ensembles, each of which is symbolized: $V_k(t_1, t_2, \ldots, t_m)$, where k takes on values from 1 to N, and the $V(t_m)$ represent sample voltages associated with discrete points in time.

The ensemble mean is

$$\overline{V}(t) = 1/N \sum_{k=1}^{N} V_k(t),$$

computed across the N ensembles for each of the time samples.

The ensemble variance is

$$V^2(t) = 1/N \sum_{k=1}^{N} (V_k - \bar{V})^2,$$

also evaluated at each sample point across ensembles.

The ensemble autocovariance is

$$K(t_1, t_2) = 1/N \sum_{k=1}^{N} (V_k[t_1] - \bar{V}_k[t_1]) \cdot (V_k[t_2] - \bar{V}_k[t_2]).$$

It will be noted that both the variance (the autocovariance when $t_1 = t_2$), and the autocovariance, are taken about the ensemble means, since the mean value of $V(t)$ is nonzero during $\bar{E}(t)$. In the absence of a mean component, the squaring and cross multiplication may be performed on the voltages. This permits the use of analog devices (multipliers and delay lines) to compute EEG variance and covariance. Ordinarily, however, digital computers are now employed for the statistical treatment of brain potential records.

Computation of the autocovariance, which provides a measure of the correlation between different points in the record, averaged across ensembles, is carried out for every combination of time samples. If the random process is statistically invariant across time (a property we discuss in Section II,C), the specific time values t_1 and t_2 are not significant, but rather the difference between any two points, which is symbolized τ. Thus the autocovariance can be evaluated across ensembles as a function of τ. The computation of "lagged" cross products is carried out either on a single time sample of data (which requires further assumptions about the statistical stability of the process) or upon a set of ensemble averages. As might be suspected, this statistic provides an indication concerning waveform characteristics and is especially useful in defining periodic components of the EEG. These applications will be discussed in Section II,D. We now consider the statististical stability of brain potential data, prior to discussing the practical application of ensemble statistics.

C. Stability of Ensemble Statistics

Inferences based on time samples drawn from a random process require not only an adequate number of ensembles to estimate the population statistics with the desired degree of accuracy, but also rest upon the assumption that the process is stable. We must have some assurance that no systematic changes are occurring in the brain potential data other than those associated with experimental manipulations. Such perturbations might in-

volve either the background EEG, $G(t)$, or the ERP, $E(t)$, through the intervention of uncontrolled variables. In electrophysiological investigations, changes in the state of the physiologic system are not uncommon. In addition to rigorous control of the experimental conditions, therefore, it is always advisable to directly monitor the stability of the EEG data. It is also a sound practice to view the brain potential statistics as primarily descriptive, and to employ them for inferential purposes only after carefully defining the population from which the samples are drawn.

The temporal stability of ensemble statistics is defined in signal theory by the concepts of stationarity and ergodicity. The wide use of these terms in the literature requires an explication of their applicability to brain potential data. A time-varying random variable is said to be stationary, for practical purposes, if its first and second moments (mean, variance, and autocovariance), computed across ensembles, are constant. This means that the average voltage, its variability about the mean, and its frequency content, are stable across the epoch. Ergodicity represents a more stringent form of time invariance, which permits a single ensemble to be used to characterize the statistics of all possible ensembles. It is assumed that the ensembles are of sufficient length to accurately characterize the statistics of the process. The proper epoch will depend mainly upon the frequency content of the data. In general the epoch will have to be very much longer than the period of the slowest frequency present in the data for the ergodic hypothesis to be satisfied. This is not necessarily so for stationarity, since slow activity may be adequately represented across ensembles if the sampling of the process is random and the N is sufficiently large.

Let us now consider the applicability of these concepts to the brain potential data. First, it is apparent that the ERP, $E(t)$, is neither ergodic nor stationary since its mean value, $\bar{E}(t)$, is a time-varying function across the ensemble epoch. In the case of $\Delta E(t)$, the means are stationary, being zero by definition in the first instance, and constant in the case of the background EEG. The mean voltage of the EEG is usually taken to be zero, a circumstance ensured by the use of a.c. coupled amplifiers. However, when d.c. amplification is used, which has become more common with the recent interest in steady potential shifts, a significant constant or very slowly varying potential bias will ordinarily be present in the amplified EEG data. The presence of very low frequency activity in brain potential records poses several important problems. First of all, much of the very slow potential activity is not of cerebral origin, representing fluctuations in skin potential, electrode polarization, eye and other movement artifacts, all of which may be relatively large in amplitude compared to similar frequencies of intracranial origin. Since analog-to-digital converters have a limited voltage window, the presence of significant d.c. levels or baseline wandering can

result in clipping the data, and require a reduction in gain to maintain the signal within the range of the converter. That will reduce the conversion accuracy, possibly leading to significant error in amplitude measurement. If a d.c. component is present in the ongoing EEG data, this must be eliminated before computing variance and covariance statistics. Slow fluctuations may also contribute very substantially to the total computed variance, thus reducing the apparent accuracy of an ERP estimate. Since the ERP components of interest comprise a restricted range of frequencies, it is often desirable to filter out lower and higher frequencies. Appropriate instrumental restriction of the recording bandwidth is an important method for reducing the variance of a random process. Whenever this maneuver is employed, however, it is essential to evaluate the effects of the amplifier bandpass or external filter on the amplitude and timing of the activity of interest, since substantial waveform distortion can be produced by inapt filtering. Unfortunately, the main frequency content of the EEG and the ERP are similar, so filtering can only play a limited role in differentiating the signal from background activity. Nevertheless, when detection of the ERP is more important than observing its waveform, sharp restriction of the bandpass may significantly improve the signal-to-background ratio. In general, selection of a recording bandwidth as narrow as possible, consistent with the nature of the data, will improve reliability and avoid problems associated with the analysis and interpretation of very low frequency and d.c. potentials.

The amplitude and frequency distributions of the EEG vary according to the arousal level of the subject, as well as showing substantial individual differences and variations according to age. These circumstances indicate that the variance and autocovariance of $G(t)$ will often vary according to experimental conditions, and cannot be assumed to be stationary. Information on the size of random or systematic fluctuations in variance is important for judging the reliability of estimates based on ensemble averages.

In most of the empirical data we have examined, which includes records from adults and infants taken during wakefulness and in the different EEG sleep stages, the ensemble variance approaches a stable constant value across the epoch as N is increased. These data, which were obtained from ensembles selected during visually homogeneous periods of EEG activity, meet the criterion for stationarity of variance. Furthermore, in most cases the mean variance computed across the epoch for relatively small subsamples of data turned out to be the same as the ensemble variance for samples of large N. When this is the case, the variance data are ergodic, as well as stationary. A typical set of average evoked potential data is depicted in Fig. 4-3. Instead of the variance, the root-mean-square deviation from the mean (the standard deviation, s) is shown, since this measure represents the average devia-

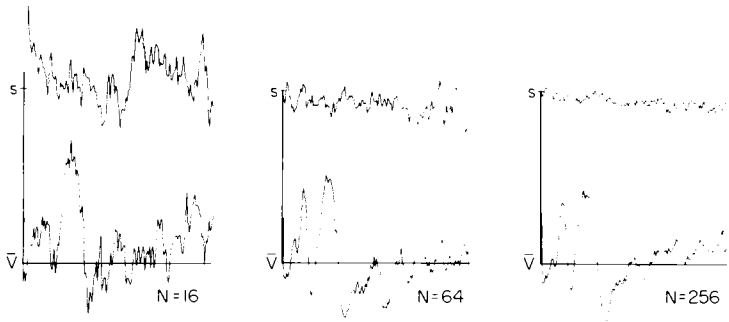


FIG. 4-3. Ensemble average ($\bar{V}$) and standard deviation (s) of a visual evoked response shown for N of 16, 64, and 256. Amplitude calibration: 15 μV to ordinate mark.

tion from the mean and is expressed in the same units as the data, rather than as a squared voltage.

When the N is rather small, e.g. 16, s shows substantial fluctuations across the epoch. These fluctuations reflect the periodic features of the data which, due to the rectification produced by squaring, appear at double the frequencies present in the original record. If the process is ergodic, the mean value of s computed across the epoch provides an accurate estimate of the population standard deviation. This can be seen to hold for these data by comparing the mean s for $N = 16$ with s for Ns of 64 and 256. As N is increased, the ensemble s approaches a constant value over the epoch. This reduction in the variability of s is systematic, being inversely proportional to the square root of N. If we consider now the probable accuracy of the mean component, the standard error of estimate also diminishes by $(N)^{1/2}$, providing the variance is ergodic. It is important to recall, however, that for small samples, s fluctuates fairly widely around its mean value across the ensemble epoch, so inferences concerning the accuracy of specific time points in the ensemble average based on the mean s can be off the mark. Generally, it will be desirable to use a sufficiently large N to reduce fluctuations in s within the epoch to 10% of their average value. The appropriate N can be selected by noting the range of s for a single small sample and applying the $(N)^{1/2}$ rule.

In the experimental situations considered so far, the EEG has been assumed to show no long-term fluctuations in its frequency and amplitude characteristics, i.e., to represent an ergodic process. This is not always the case, however, as exemplified by the changes associated with the transition from wakefulness to sleep and among the various sleep stages. Under these circumstances the EEG statistics are clearly nonergodic. This may not be disclosed by examination of the ensemble variance, however, since the

relatively infrequent shifts in the EEG statistics affect all portions of the ensemble epoch equally. A similar situation will prevail when the brain potential statistics are drifting very slowly during the recording period. This might occur, for example, during a prolonged vigilance task. The inhomogeneity of the overall record can often be detected by visual inspection if the changes in amplitude and frequency are substantial. The shift may be disclosed more clearly by changes in the mean variance of small ensemble subsets taken repeatedly over the recording period. Whenever the mean variance computed from a large ensemble N exceeds that computed from a subset of the data, lack of ergodicity can be inferred. The converse, however, is not true. A stable variance does not ensure ergodicity of the process, since the variance reflects primarily its amplitude distribution rather than frequency content. Autocovariance or spectral analysis would be required to clearly demonstrate nonstationarity primarily involving changes in frequency. It is often sufficient for practical purposes to restrict the data sampling to reasonably homogeneous stretches of EEG by continuous visual monitoring of the record. This precaution is rather important since the mean waveform, $\bar{E}(t)$, may vary as a function of the changes in state reflected in the EEG. Such variations are well known, for example, during the different sleep stages. Automated methods to accomplish this segregation will, for the reasons mentioned above, require some form of frequency analysis of the background EEG, which is often beyond the instrumental capabilities of the investigator.

We have rarely encountered situations in which a systematic nonstationarity of variance can be seen associated with the ERP waveform. The absence of a noticeable increase in variance associated with E(t) indicates that the variable component, $\Delta E(t)$, is negligible in comparison to $G(t)$. This result reflects the circumstance that $E(t)$ is almost always smaller than the background EEG, generally by a factor of from 2 to 10, and ERP variability represents but a fraction of its mean amplitude. It is rarely possible to employ a sufficiently large N to reduce the fluctuations in s within the epoch to the degree necessary to clearly detect small ERP fluctuations. This problem always has to be dealt with empirically, however, since it depends upon the specific ratio of $\Delta E(t)/\bar{E}(t)$ and the amplitude of $G(t)$, as well as the N comprising the ensemble statistics. In certain situations, as in recording the association cortex potentials, both $\Delta E(t)$ and $\bar{E}(t)$ are relatively large and the variable component may be differentiated from $G(t)$ by an increase in variance during $\bar{E}(t)$. The experimental conditions under which these potentials are recorded, however, place a sharp limit on the feasible N, so sharp characterization of $\Delta E(t)$ is not easy to achieve, even in this case. In most circumstances, the ensemble variance will reflect $G(t)$ more strongly than $\Delta E(t)$, so that great caution must be exercised in evalu-

ating apparent differences in ensemble averages associated with experimental manipulations. If the variance of $G(t)$ is taken into consideration, the mistaken attribution of waveform differences representing residual background activity to treatment effects can be avoided.

A final instance in which a systematic nonstationarity can be demonstrated is the decrease in variance associated with blocking of the alpha rhythm. This stimulus-generated change in $G(t)$ follows a light flash in many subjects who have a prominent occipital rhythm, and calls attention to the fact that the assumption of physiologic independence between $E(t)$ and $G(t)$ is not always warranted.

D. Estimation of the Mean ERP Component

Since the expected values (population means) of the variable components, $\Delta E(t)$ and $G(t)$, are considered to be zero, the ensemble average, $\overline{V}(t)$, provides an estimate of the mean ERP component, $\overline{E}(t)$, and the variance, $\overline{V}^2(t)$, a measure of the accuracy of this estimate. The practical considerations which limit the number of ensembles employed to compute the mean and variance of $V(t)$ result in the usual sampling errors. The magnitude of these errors will be jointly determined by N and the statistics of the variable components. Theoretical considerations, based upon the central limit theorem, confirmed by empirical examinations of EEG and ERP data, permit us to consider statistics obtained from averages of at least ten ensembles representing random samples of $G(t)$ to be normally distributed. Since the normal probability distribution is fully defined by its first and second-order statistics, the precision of estimates derived from ensemble averages can be readily estimated by standard techniques. The usefulness of ensemble averaging for extracting the mean ERP component from the background EEG is based upon the fact that the variability of the ensemble means, when expressed as their variance, is inversely proportional to the number of ensembles, N, constituting the ensemble average. It might be noted at this point that the terminology employed in the literature does not always clearly distinguish the ensemble standard deviation from the standard deviation of the ensemble averages. The latter measure, which is the ensemble standard deviation divided by $(N)^{1/2}$, is best designated the standard error. This value is obtained either by dividing the ensemble standard deviation, s, by $(N)^{1/2}$, or by computing the standard deviation of several ensemble means. Although the values obtained by these methods are equivalent if there is no change in the population statistics over time, it is sometimes found that the standard error computed from the ensemble means shows an increase associated with the ERP waveform not seen in the statistic computed from the total set of individual ensembles. This result is apparently due to systematic changes

in $E(t)$ over time. For this reason it may be instructive, when variations in the mean component are suspected or are of interest, to compare the two estimates of the standard error.

For the $(N)^{1/2}$-fold reduction in standard error to hold, it is essential that the background process, $G(t)$, which provides the main source of variance, be sampled randomly with respect to its periodic components. It can easily be seen that if $G(t)$ were a simple sine wave sampled at a constant phase, it would sum linearly as does $\bar{E}(t)$. If, on the other hand, alternate samples of the sine wave were 180° out of phase, $\bar{G}(t) = 0$ for an even number of samples. Any departure from random sampling of the background EEG will be associated with a deviation from the $(N)^{1/2}$ relation. Ordinarily, the EEG will be sampled randomly if the intervals between onset of successive samples are either (1) long with respect to the lowest frequencies present in the record, or (2) if the interval is varied randomly over a period as long as that of the lowest frequency in the record. It is usually more convenient to rely on a long interval between samples than to randomly vary the intervals. Since EEG frequencies are not precisely periodic, it is not too easy to set up conditions wherein the intrinsic rhythms will be phase-locked to the sampling process for any length of time. However, it is quite important to be aware of the effects associated with periodic sampling, especially at a fairly rapid rate (i.e., faster than 1/sec). The ERP may overlap in time, posing some confusion in identification of component latencies. Physiologic entrainment, or "driving" of the background activity by repetitive stimulation, can also occur in some circumstances. This may or may not represent a significant problem, but the investigator must be aware of the possibility that decreases in the intervals between samples to obtain a larger N within a fixed time period may be associated with changes in both $E(t)$ and $G(t)$ due to physiologic interactions. Perhaps less familiar is a curious type of sampling artifact introduced by taking ensembles at fixed intervals, (T). Under these circumstances the frequency $1/T$, and its harmonics, n/T, tend to be retained in the average, whereas intermediate frequencies outside of a band of width $1/NT$, where N represents the number of ensembles, are suppressed. Since frequencies intermediate to n/T are reduced by a proportion greater than $(N)^{1/2}$, this effect may be utilized to reject a particularly troublesome background rhythm. Thus, if the EEG frequency spectrum showed a sharp peak of alpha activity between 8.5 and 9.5 Hz, averaging at 500-msec intervals (2 Hz) would retain the harmonics at 2, 4, 6, 8, 10, . . . Hz and reject the dominant activity. It is important to note, however, that even rather inconspicuous periodic activity at the frequencies, n/T, will be preserved along with $\bar{E}(t)$, so that the results of periodic summing can be rather misleading unless the frequency composition of $G(t)$ has been defined.

The required accuracy in estimating the mean ERP component will be dictated by the particular experimental objectives. Thus, a substantially lower quality of waveform resolution may be acceptable for evoked response detection, as in audiometric applications, than in studies requiring precise amplitude and latency measurements. It is rather surprising that the signal-to-noise ratio of the raw data and the required accuracy of resolution have rarely been explicitly taken into account in the design of investigations of averaged brain potentials. Often, the ensemble N seems to be arbitrarily defined by custom or convenience, rather than by accuracy criteria. For this reason, many studies have reported averaged ERP data of uncertain reliability.

Many investigators of human brain potentials employ special purpose averaging computers, and cannot conveniently make direct variance computations. Instrumental limitations need not, however, seriously impede the estimation of variability to a degree of accuracy sufficient for many experimental purposes. Simple replication of ensemble averages provides the most direct, and often quite adequate, indication of reproducibility. It is often less time consuming to compute and display three averages with an averager, than to compute and display a single average and associated standard error using a general purpose laboratory computer. Unless quantitative measures of variance are required, as for formal tests of significance, the first method provides quite a satisfactory indication of the stability of the mean waveform. A reasonably good estimate of the standard error, which permits selection of an N appropriate to the desired degree of accuracy, can be derived from the raw EEG, since the major variance of the ensemble average is ordinarily contributed by $G(t)$. The method is illustrated in Fig. 4-4. The standard deviation, s, of $G(t)$ is its RMS deviation from zero, which can be roughly estimated as one half the average peak-to-peak EEG amplitude. In the data shown, this is about 10μV. Dividing this value by $(N)^{1/2}$, 8, we obtain an estimated standard error of 1.25 μV, for an N of 64, which is the same as the directly computed value. Since the ensemble means are normally distributed, there is a less than 1% chance that the true population mean, $\bar{E}(t)$, deviates from the observed mean by more than ± 3.25 μV at any point in the epoch. By increasing the N to 256, the confidence limits could be reduced by half.

It should be noted that we have been treating the time samples as if they represented independent processes. This is not so, since the values of the ensemble averages, $\bar{V}(t)$, are correlated over time when $\bar{E}(t)$ is present. In the absence of information on this temporal covariation, the assumption of independence provides a conservative estimate of accuracy. If we had more detailed information on the temporal structure of $G(t)$, however, we could improve the accuracy of our estimate of $\bar{E}(t)$. To illustrate this possibility,

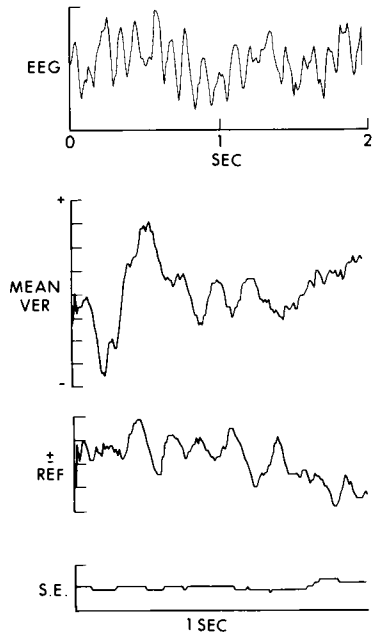


FIG. 4-4. Sample of raw EEG, average visual evoked response, ± reference and standard error of the mean. $N = 64$. Amplitude calibration EEG: 50 μV. Mean VER, ± reference and S.E.: 1.5 μV per division.

let us consider a $G(t)$ consisting of a simple sine wave of constant frequency. If this waveform is sampled randomly, it can be shown that the RMS deviation will be reduced in the ensemble average in proportion to $(N^{1/2})$ and that the residual waveform is a sinusoid of the same frequency as the original $G(t)$. If a stimulus-evoked $E(t)$ is present, its waveform may be partially obscured by the residual background activity, the size of which can be estimated as above. In this instance, however, we can precisely specify the form of the noise function over time, so given a sufficient segment of record before the onset of $E(t)$ to establish the frequency and phase of $\bar{G}(t)$, we can extrapolate its waveform through the entire record and thus define $E(t)$ with perfect accuracy. The application of this technique, where the temporal characteristics of the background (noise) function are known with sufficient accuracy to permit their extraction from the ensemble averages, is known as predictive filtering and has important applications in communications engineering. However, the temporal covariation of the EEG is rarely sufficiently predictable to apply this powerful method of signal extraction. There are certain situations where the noise rhythm is fairly regular and restricted in frequency composition in which this approach can be applied.

From an immediate practical standpoint, the distinctive temporal patterns of the EEG and ERP waveforms often permit a significant improvement in accuracy of the data by judicious smoothing. Thus, "noisy" records in which the ERP is partially obscured by muscle potentials or line frequency artifacts can often be cleaned up by taking the midpoint of their total excursion as the "true" value of the averaged waveform. This sort of correction is only justified when the residual noise is at a substantially higher frequency than the waveform of interest, or, as in the case of 60-Hz activity, represents a deterministic waveform whose distorting effect can be predicted. Sometimes the interpretation of an average ERP which contains a good deal of residual alpha activity can be improved by taking advantage of the fact that both $\bar{E}(t)$ and $\bar{G}(t)$ are smooth continuous waveforms whose individual shapes can be extrapolated for a time even when overlapping with one another. Whenever ambiguous data have been obtained, it is always preferable to modify the experimental conditions so as to improve their quality. If this is impossible, however, some useful information may be extracted from poor data by thoughtful "visual filtering." It is much better to do this than to attempt further machine statistical analysis on unreliable data in hopes of dredging out interpretable results.

A simple technique for evaluating the characteristics of residual background activity is the $\pm$ reference suggested by Schimmel (1967). This method is especially useful for investigators without access to methods for direct variance computation, as it provides information on both the amplitude and frequency content of the background activity present in an individual ensemble average. This method takes advantage of the fact that the mean component, $\bar{E}(t)$, can be removed from an ensemble average by alternately adding and subtracting successive ensembles, without affecting the statistics of the random components. As shown in Fig. 4-4, the $\pm$ reference provides an estimate of variability similar to that provided by the standard error, but it provides a clearer picture of the character of the background fluctuations. It also gives a better estimate than can be derived from the raw EEG, since extreme fluctuations have been smoothed by the averaging process. Since the $\pm$ reference provides an indication of residual background derived from the same data as the ensemble average, it is a more valid index of the variable components than averages of background activity obtained from separate data samples in which the ERP is not present.

E. Frequency Content of the EEG; Autocorrelation and Spectral Analysis

The prominent periodic features of the EEG have led investigators to various efforts to quantify it in terms of frequency content. Since any periodic waveform can be characterized as a sum of sinusoidal components differing

in frequency and amplitude, most approaches to quantitative representation of EEG frequency content have utilized some form of Fourier analysis. Early techniques employed tuned analog filters which displayed the amount of activity within a set of narrow frequency bands over the range of predominant EEG rhythms. After World War II the development of signal theory and of digital computers gave rise to alternative digital methods of frequency analysis based upon the autocorrelation function, and its Fourier transform, the power spectrum. Until fairly recently, the extensive computations required to provide reliable power spectra limited this approach to investigators with access to substantial computational resources. However, owing to the development of simplified computational methods, digital EEG frequency analysis is now within the capability of the smaller laboratory computers, as is the use of special purpose digital devices. It is likely that spectral analysis will become more extensively employed, both in the clinical and the research laboratory.

Only a superficial outline of the methods can be attempted here. The reader may consult Dern and Walsh (1963), Mason and Zimmerman (1960, Chapter 6), Blackman and Tukey (1958), and Bergland (1969) for an entry into the relevant literature. We have already defined the autocovariance (Section II,B) as an ensemble statistic which defines the average correlation between two time points in a random process. If the process is stationary, its autocovariance is independent of time so the correlations are defined soley by the difference between two times, τ. Ordinarily, it is more convenient to deal with a single stretch of record rather than an ensemble average, in computing the autocovariance, so that ergodicity is also required. The lags for which the cross products are computed across the time sample are determined by the sampling interval and range from 0 (the data multiplied by itself, which is the variance) to some maximum lag τ_m. Since in all practical applications the record is of finite length, a progressively longer portion of the record is removed from computation as the lag increases. It is usually recommended that the total lag not exceed 5–10% of the total record. Yet, in order to reflect the frequency content of the record, the lag must be sufficiently long to reflect at least one cycle of the slowest frequency present. Accurate representation will require even longer lags, and thus a proportionately longer total sample. The display of the autocovariance (autocorrelation) computed from a record of finite length is called an autocorrelogram.

To illustrate how an autocorrelogram depicts the frequency content of a periodic waveform, let us consider a simple sine wave (Fig. 4-5A). At zero lag the function is multiplied by itself and possesses its maximum value, which is often set to one, thus expressing the autocovariance in the form of a correlation coefficient. As the sine wave is shifted along its length, the value of the averaged cross products diminishes, reaching a value of -1

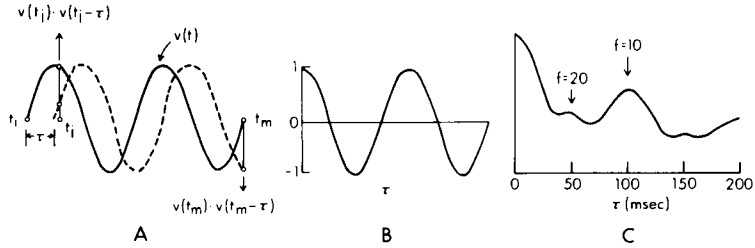


FIG. 4-5. (A) Illustrates the computation of lagged cross products to obtain the autocovariance. (B) The autocovariance of a sinusoid. (C) Autocorrelogram of an EEG sample containing predominant rhythms at 10 and 20 Hz.

when the function is 180° out of phase, and then again increasing until the sinusoid is again in phase after shifting a full period. The autocorrelation function of a sine wave is a sinusoid with the same period (Fig. 4-5B). Thus, any process which contains periodic components will reflect these as periodic fluctuations in the autocorrelogram. Unless the periodicity is perfectly regular, however, the correlation will die out as the lag increases (Fig. 4-5C).

Although the autocorrelogram can provide an indication of frequency content, its Fourier transform, the power spectral density provides a more satisfactory quantitative display. This is due to the fact that the analysis provides a measure of EEG "power" (actually squared voltage) as a function of frequency, rather than as a function of time as in the correlogram. The selection of proper methods for computation of accurate power spectra is a highly technical matter, as there are several sources of error associated with the finite sampling procedure. The investigator who adopts a particular program for spectral analysis of the EEG should ascertain that it has been specifically tailored to the nature of the data and provides sufficiently accurate estimates. In the computation of power spectra there is always a tradeoff between accuracy of estimate and the practical constraints of record length, sampling rate, and computation time.

F. Special Problems in ERP Analysis

The preceding discussion has provided a basic conceptual framework for the statistical analysis of human brain potentials, emphasizing the factors which influence the accuracy of ERP waveform resolution. We have pointed out that satisfactory assessments of reliability can be made with access only to averaging equipment, by estimating the standard error from the raw EEG or $\pm$ reference. Investigators who possess general purpose laboratory computers can obtain more precise variance measures. It must be emphasized that the variance estimates, however obtained, are more usefully employed

to define the experimental parameters required to provide data of the desired degree of accuracy, rather than as *post hoc* measures of reliability.

As general purpose computers have become more widely available to investigators of human brain potentials, there has been a natural tendency to utilize these resources for more sophisticated quantitative treatment of the data. Approaches developed in communications engineering and applied statistics for signal and multivariate analysis have been applied to EEG and ERP data by several investigators. Among the problems which are being addressed by more elaborate methods are: (1) detection of evoked potentials near threshold for "objective" audiometry, (2) evaluation of the significance of differences in ERP waveform, (3) resolution of the ERP waveform into simpler components, and (4) sorting of ERP wave shapes into classes according to predefined criteria. Each of these analytic approaches has been developed and applied in response to particular research problems, although in some instances concern with elegant methodology seems to have prevailed over experimental perspicacity. A full description and evaluation of these approaches is not feasible in a brief discussion, so only a terse outline and comment will be presented, together with some references to the original literature. Since most of these techniques are more expensive in time and resources than simple application of the statistical methods we have described, the reader will be advised to carefully evaluate the significance of the question being addressed, in relation to the expenditure of analytic effort required. Often it will be profitable to rephrase the problem or alter the experimental approaches to permit less elaborate methods of analysis. Personal experience, supported by an extensive literature, has repeatedly shown that simple experiments designed to ensure the production of reliable brain potential data generally prove more informative and reproducible than more complicated studies which require complex statistical evaluation of the data. Furthermore, analytical procedures which reduce the physiologic data to numerical form and process it without direct monitoring by the investigator deprive the investigator of his most powerful analytical tools—his eye and brain. The absence of the human observer makes it possible for artifacts to enter the analytic mill, and may preclude the discovery of unanticipated features of the data. There is no question that digital computers provide the investigator with a powerful analytic tool. But it is also a rigid and blind one, unless employed with the constant, critical, and creative attention of the investigator. With these caveats in mind, we turn to a brief consideration of some more complex aspects of ERP analysis.

1. Detection of Evoked Potentials at Psychophysical Threshold

The possibility of achieving an objective physiologic index of hearing impairment in infants has stimulated considerable work on "evoked poten-

tial audiometry." Despite early enthusiasm, it is becoming increasingly clear that ordinary visual methods for evoked potential detection near threshold are highly unreliable, being associated with a substantial proportion of "misses" and "false alarms." This situation has suggested the need for a more rigorous application of statistical signal detection methods to evaluation of the evoked potential data. Fortunately this problem seems amenable to relatively straightforward application of some of the measures already discussed. The essence of the problem is to detect a significant departure from the brain potential statistics associated with $G(t)$, following the presentation of an auditory stimulus. Thus, we may look for a nonzero value of the mean, $\overline{V}(t)$, an increase in the RMS voltage, and a change in the autocovariance. These statistics are independent of one another, so the use of more than one increases the sensitivity of the method. Since the approximate time during which the evoked response may be present is known, attention can be focused on a rather limited segment of the record, its statistics being compared with those of a prestimulus epoch. This is a situation in which additional improvement of the signal-to-noise ratio may be achieved by filtering and by periodic averaging as described earlier. The detection problem in evoked response audiometry and current approaches to quantitative statistical evaluation are discussed by Schimmel, Rapin, and Cohen (in press) who should be consulted for a fuller discussion.

2. Evaluation of Differences in ERP Waveform

Many investigations have assessed differences in ERP waveform associated with experimental treatment, diagnostic classification, site of recording, and a host of other variables. These approaches are fundamentally similar to classical EEG studies, in which the ERP data are employed as indices of differences in physiologic state. While this is not an appealing approach to human behavioral physiology, and some of the associations which have been evaluated seem rather farfetched, it must be admitted that situations arise in which the reliability of differences in ERP waveform represents an important question. Obviously, the more one knows about the physiologic significance of the waveform, the more valuable information on changes will become. Two main approaches to evaluating differences in ERP waveform have been employed: (1) use of the t test for the significance of difference between means, and (2) assessing differences in correlation of averages obtained under different conditions. Of these, the first is clearly preferable, since it provides a point-by-point estimation of the reliability of differences. The "evoked t test" provides a graphic representation of significance across the ensemble epoch. This is a useful display, since it permits one to evaluate the relationship of significant t values to the ERP waveform. Since a large number of paired time sample averages are being

evaluated, random sampling errors will produce a few significant values, e.g., 5 out of 100 at the .05 level of confidence. Also, artifactual physiologic signals, such as eye blinks and slow shifts associated with movement and skin potential changes, are frequently not sufficiently reduced by averaging owing to their relatively large size and adventitious (nonrandom) occurrence. These are commonly the cause of significant differences between two averages, a circumstance which may not be apparent unless the temporal sequence of t values across the entire epoch is evaluated. It must be noted that the successive t values are correlated owing to the essentially deterministic nature of $\bar{E}(t)$. Thus the t's will wax and wane in association with specific portions of the two ERP waveforms. Obviously, significant t values obtained prior to or after the ERP cannot be viewed as meaningful indices of ERP waveforms. We are assuming in this discussion that the variance for each ensemble average has been computed point by point across the epoch, and that the estimated standard error has been derived for each time sample from the pooled variance of the two averages obtained at each point. This is particularly important for small N, owing to the temporal fluctuation in variance across the epoch. Ordinarily it is well to insist upon a .01 confidence limit for the reliability of ERP differences, as well as requiring a systematic temporal relationship of the significant points to particular ERP features. As always, extreme caution must be exercised in the interpretation of significance. The origin of a reliable difference between averages need not be the particular variable the investigator thinks he is assessing. Nor is a "significant" difference necessarily an "important" one. Although these points are axiomatic in statistical inference, perusal of the literature suggests that they are often forgotten.

Correlational measures to evaluate ERP waveform differences have apparently been adopted because of the simplicity in representation of the relation between two waveforms as a single correlation coefficient, as well as the feasibility of using average ERP without information on the ensemble variance. A product moment correlation is computed between the sets of time-sampled voltages across the epoch of two ensemble averages. Then the correlation between two averages obtained under one condition can be compared with that obtained under another. Objections to this method can be raised. Since the adjacent voltages within the epoch are correlated, the appropriate degrees of freedom to be employed in evaluating the significance of differences are not known. They are certainly very much smaller than the number of sample pairs. This method also provides no information on which segment of the waveform contributes to any observed differences in correlation. Since residual background activity is always present in the averaged records, differences in variance contributed from this source will be indistinguishable from differences in the mean ERPs. Since specific

information on the nature of waveform differences is almost always desirable, the use of simple correlational techniques seems of very limited value as well as of questionable reliability.

3. Resolution of ERP Components

There are powerful motives for trying to dissect the various ERPs into simple component waveforms. Since a major objective of brain potential investigation is to define the physiologic origin and functional significance of the ERP components, there is a strong desire to identify portions of the observed waveform which possess distinctive properties. Since all of the ERP waveforms possess multiphasic configurations, most investigators have been satisfied to label the peaks and valleys, and to apply simple measures of latency, amplitude and, occasionally, area as a means of quantitative analysis. Early in the course of our own research we became dissatisfied with the laborious and somewhat inelegant techniques involved in ERP analysis and devised a computer technique for automatic resolution of an evoked potential into a set of Gaussian waveforms (Vaughan & Hull, 1963). A similar method has been used by Lehman and Fender (1968). This technique seemed to provide several advantages. It was objective, fitting the Gaussian components according to predefined criteria of fit. It was parsimonious, reducing a set of 400 sample points to the three parameters of the Gaussian distribution required to define each of the five or six curves required to achieve a good representation of the ERP. It was elegant and impressive, providing a dynamic display of the curve-fitting process which was a delight to behold. Unfortunately, all of this elegance was illusory. While the Gaussian component hypothesis seems a fairly reasonable one, the representation as a sum of simpler curves, although "objective," is arbitrary. The computer also makes "mistakes" in curve fitting which a human observer would not. It is easily tricked by small differences in waveform into quite different choices of components. Although the computer can be told to avoid that sort of behavior, the result is that the computer assumes the biases of the investigator and retains little of his flexibility. This is a high price to pay for objectivity.

Another approach to resolution of ERP components has been suggested by Donchin (1966, 1969) employing a principal component factor analysis. This procedure is sufficiently elaborate and obscure in its physiologic justification to ensure rather limited application. In the example used by Donchin (1966) to illustrate the method, the "components" disclosed by the analysis primarily reflect shifts in latency of the ERP under the various experimental conditions. Thus, what was intended as a resolution of ERP components turned out to be a rather distorted restatement of obvious variations in the original data. The principal components method will always seek out the

largest source of variance present in the data entering the analysis. Consideration of the actual circumstances of most ERP investigations indicates that the variance contributed by independent fluctuations of individual segments of the $E(t)$ waveform will almost always be the smallest, ordinarily being exceeded by variance due to residual $G(t)$, to overall fluctuations in $E(t)$, and to whatever differences in $E(t)$ are produced by changes in experimental conditions under which the various ensemble averages were collected. It is clear that the identification of ERP components is essentially a physiologic problem. Although it would be helpful to have some reliable procedural shortcut to the simple representation of the complex ERP waveform, we are not justified in utilizing arbitrary criteria, since the resultant "simplifications" may merely obscure the physiologically significant structure of the data. We shall return to this problem in the concluding section of the chapter.

4. Waveshape Sorting

A final problem to which sophisticated computer techniques have been applied is that posed by a desire to sort single ensembles according to their likelihood of containing one or another of two predefined mean components. This has been approached through the method of discriminant function analysis (namely, Donchin, 1969; Donchin, Callaway, & Jones, 1970).

III. Analysis of the Sources of Scalp-Recorded Potentials

A. Statement of the Problem

The potentials recorded at the surface of the scalp represent the sum of activity generated by an enormous number of cellular sources which vary in their contribution to the field sensed by a particular electrode. Any useful interpretation of human brain potentials must take into consideration the main features of the location, size, and orientation of the intracranial sources. Since neural activity temporally associated with the ERP will be present in many brain structures, it is important to know the contribution to the scalp-recorded waveform of the potentials generated within each active site. It is not sufficient to assume, as has been the common practice in electroencephalography, that scalp recordings mainly depict activity from a limited cortical area directly beneath the recording electrodes. When a substantial group of similarly oriented neurons are activated together, a potential field can be set up by volume conduction of extracellular currents at a considerable distance from the generators. The possibility that several structures in different locations may be contributing to the scalp-recorded ERP waveform cannot be overlooked. Since geometrically distinct intra-

cranial sources will generate somewhat different scalp potential distributions, the spatial configuration of the various ERP components can provide information on their disparate neural generators. It is important to know of these differences in scalp distribution even if identification of intracranial sources is not a primary objective of a particular investigation. Unless the contributions from different sources are differentiated, due to the spatial overlap of ERP components an erroneous measure of amplitude may be obtained. This is especially important in assessing the ERP associated with more complex behavioral situations, since one is often dealing with a composite waveform which includes sensory, motor, and association cortex potentials. Under these circumstances a careful analysis of the spatial distribution of the potentials is crucial.

B. A Method for Predicting Scalp Potential Distribution

We now turn to a consideration of the manner in which information on the sources of the ERP can be gained from an analysis of the scalp potential distribution. The configuration of the electric field at the scalp surface is determined jointly by (1) the distribution of charge within the brain, and (2) the geometry and impedance characteristics of the brain and its coverings. Assuming that propagation within the volume conductor formed by the cranial tissues is essentially instantaneous, the potential distribution conforms to the Laplace equation

$$\frac{d^2V}{dx^2} + \frac{d^2V}{dy^2} + \frac{d^2V}{dz^2} = 0$$

Thus, if the intracranial charge and impedance characteristics were known, the resultant scalp potential distribution could, in theory, be computed. In fact, our knowledge of the relevant variables is rather limited, and even if these were to be defined in detail the required computations would be too complicated to evaluate numerically. Nevertheless, it would be of great value to obtain even an approximate indication of the location and size of the sources of the scalp-recorded potentials, for this would enable us to draw some inferences concerning the localization and timing of brain processes associated with specific behavioral sequences.

Since a given surface field can be generated by an infinite variety of source configurations, it is not possible to uniquely define the geometry of intracranial sources from the scalp potential distribution. Unless rather stringent constraints can be placed on the possible source geometries, interpretation of the external field must remain ambiguous. Fortunately, anatomical and physiologic considerations permit a substantial simplification of the likely intracranial source configurations. Furthermore, a sufficiently simple geo-

metrical model of the head can be formulated so as to permit a numerical solution of the Laplace equation. It is possible, therefore, to compute the theoretical potential distributions at the scalp surface for the various hypothetical source geometries which conform to reasonable anatomical and physiologic assumptions. By comparing the observed with the predicted distributions, the generator configuration which best conforms to the empirical data can be identified.

In explaining the development and application of this method for identifying the sources of human brain potentials, the geometry and passive electrical properties of the brain and its coverings will be considered first, then the nature of the intracranial sources, and finally the practical inferences which can be drawn from the model.

C. The Volume Conduction Model

Geometrically, the brain approximates a sphere surrounded by concentric shells which differ in impedance, comprising the meninges, cerebrospinal fluid, skull, and scalp (Fig. 4-6). This model is inaccurate to the extent that the brain departs from a spherical configuration and its coverings are irregular in shape and thickness. Such irregularities are insignificant for the upper half of the brain, but render inferences concerning the inferior portions much less satisfactory. In the latter case complications are introduced by the marked departure of the lower parts of the brain from a spherical shape, as well as the substantial variations in impedance produced by the openings through the base of the skull. Since most recordings of interest are derived from the convexity of the scalp, these defects do not present significant difficulties for practical application of a spherical model. They do, however, demand great circumspection in interpreting the potential distributions which may be expected over the lower portion of the head. This limitation is particularly relevant to the choice of reference electrode placement, since an inactive site away from the brain is desirable. This problem will be considered in more detail following description of the method. Since there are individual differences in average diameter of the head and in thickness of the concentric layers of skull and scalp, as well as regional variations and changes in these measurements during growth, it is necessary to quantitatively evaluate the influence of each of the dimensional variations in particular circumstances.

Laplace's equation is applicable to a volume conductor when steady current flow can be assumed. Since the potential distributions with which we are concerned are time varying and reflect, not steady, but transient current flows within the medium, it is necessary to consider the extent to which the assumption of a potential distribution comparable to that existing

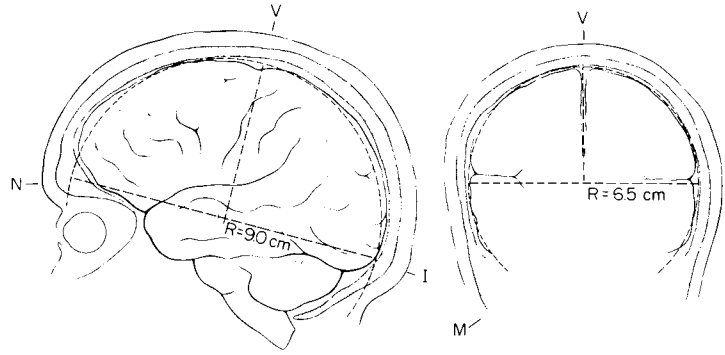


FIG. 4-6. Representation of the head in sagittal and coronal section to illustrate the approximation to a spherical configuration. The relationships between external landmarks (nasion, inion) and intracranial structures are based upon typical anatomical material. Individual variations in dimensions are to be expected.

in a steady state can be justified. This question has been evaluated by Plonsey and Heppner (1967), who concluded that the quasistationary model can be applied with reasonable accuracy to the kind of biological system we are considering. The main uncertainty and potential source of error concerns the assumption that the impedance of the brain and its covering is purely resistive. The presence of a significant capacitance would produce a shift in the phase of the waveforms at the scalp surface compared with the intracranial potentials. However, most investigators believe that capacitive impedance is negligible within the range of frequencies present in the EEG, although detailed measurements do not seem to be available. In the absence of a significant capacitive impedance, the current flow and, accordingly, the potential distribution, is defined by the tissue resistivities. Estimates of these values are available from studies in experimental animals. Although the resistivity measurements are not defined with precision, especially for the skull, the range of values can be defined and the effects of variations can be computed. It is known that resistivity of the various cerebral structures differs somewhat, and it also varies in relation to the predominant fiber direction within the white matter. Thus, the brain is neither an homogeneous nor an isotropic medium as is required for an exact application of a simple volume conduction model. These variations from the ideal model can be neglected when dealing with cortical sources and potential distributions on the scalp surface. Only when intracerebral potential distributions are being considered will these effects assume significant proportions. The selection of appropriate scalp and skull parameters for modeling the human adult is discussed by Rush and Driscoll (1968), whose values we have followed.

D. Definition of the Intracranial Generators

In order to evaluate the Laplace equation, it is necessary to specify the distribution of charge within the conductive medium. Although we know a good deal about the main neuroelectric processes at the cellular level, it is not possible to translate this information into general statements about the contributions of specific cellular processes to the external potential fields. Nevertheless, certain anatomical and physiologic considerations permit a gross delineation of the size, location, and orientation of intracerebral generators, which will permit some useful predictions concerning the distribution of scalp potentials.

The most important generalization which can be drawn concerning intracranial potential sources is derived from the principle of charge conservation and the consequent dipolar nature of bioelectric generators. Since net charge is neither created nor destroyed within the body, free charges must appear as equal numbers of negatively and positively charged ions. If the ions are randomly disposed, as in an electrolyte, no potential gradient will exist within the volume of solution. Within the brain, however, ionic charges are not randomly distributed, but are constrained by semipermeable membranes. These permit the segregation of ionic species through the expenditure of metabolic energy. The resulting distribution of charge across cell membranes produces the resting potential characteristic of living cells. The equal and opposite charges on each cell membrane represent a dipole layer, which sets up an extracellular electric field. Efforts have been made to model the potential distribution associated with some aspects of neuronal geometry (Holmes & Houchin, 1967; Rall & Shepherd, 1968). As yet, however, there has been no detailed evaluation of the extracellular fields generated by cortical neurons, as this requires more detailed information on their patterns of membrane depolarization and hyperpolarization under functional conditions than is currently available. Despite the limited data on the details of intracortical electrodynamics, the main features of the fields due to cortical activity, which will be sensed at distant electrodes, can be deduced from the characteristic configuration of dipole fields. Due to the equal and opposite charges constituting the dipole (or dipole layer), a zero potential plane will pass perpendicular to the axis of the dipole, separating zones of positive and negative potential. The field maxima are in the axis of the dipole. Thus, whenever the anatomical circumstances produce a directional preponderance of dipole orientation, a net external field will be generated. Otherwise, the positive and negative dipole charges cancel each other. In the cortex, the radial symmetry of neurons establishes an isopotential surface in the plane of the cortex, but the asymmetrical orientation of cells from surface to depth permits a net dipole to exist in this direction. The cortex

can be expected to act as a time-varying dipole layer, whose external field will reflect the magnitude and orientation of the net charge pairs. Although the detailed charge distribution will be very complex, reflecting the distribution of changes in membrane polarization, the resultant of these effects can be represented by a single equivalent dipole layer which will vary in magnitude, polarity with respect to the surface, and apparent depth within the cortex. These expectations have been amply confirmed by experimental data. Studies by Goldring and colleagues (Stohr & Goldring, 1969; Goldring, Aras, & Weber, 1970) have demonstrated in man and in experimental animals that the evoked potentials recorded from somatosensory cortex show a characteristic inversion in polarity when surface cortical recordings are compared with those taken from the subjacent white matter. A similar inversion of polarity has been shown across human auditory cortex by Celesia and Pulletti (1969), and across the motor cortex of monkeys performing a voluntary hand movement (Vaughan, Bossom, & Gross, 1970).

The geometry of the cortex can be reduced to two simple representations:

Case A (Fig. 4-7A) is a dipole layer concentric to the surface of the sphere representing the brain, which for computational simplicity is taken to be a circular "cap" subtending a solid angle, ϕ, at a distance, r_d, from the center. Case A models surface cortex when the dipole layer is 2–3 mm beneath the surface.

Case B (Fig. 4-7B) represents sulcal cortex, perpendicular to the brain surface. This is modeled as a plane surface shaped as an annular sector bounded by arcs at specified distances from the center (r_1, r_2) and by radii forming an angle, θ, with one another.

A reasonable geometrical representation of any cortical source can be achieved by a sum of these two cases, tailored to conform with the anatomy of hypothesized active areas. A further simplification is permitted by the circumstance that all sulci are bounded by cortex in geometrical opposition, so whenever the cortex on both sides of a sulcus is active, the external fields will cancel each other.

E. Representation of Specific Intracranial Sources

The simplest hypothesis concerning the generators of the evoked potentials identifies them with the primary cortical projections of the various sensory modalities. As illustrations of the model source geometries, consider the diagrams of Fig. 4-8, which provide a schematic representation of the primary somatosensory, auditory, and visual cortex. In each instance a simplified but reasonable approximation to the configuration of the particular cortical area has been constructed in accordance with gross anatomical material and cytoarchitectural maps.

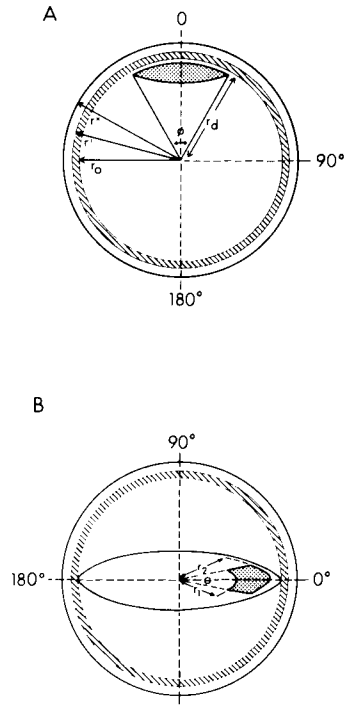


FIG. 4-7. Diagrams of simplified dipole layer source configurations. (A) A circular cap at a radial distance r_d, subtending a solid angle ϕ. The radii corresponding to brain (r_0), skull (r'), and scalp (r'') are also indicated. (B) The portion of a sector bounded by two radii (r_1, r_2), subtending a central angle θ.

1. SOMATOSENSORY CORTEX

The main somatosensory cortical projections occupy the surface and anterior bank of the postcentral gyrus according to the well-known somatotopic pattern. Musculoskeletal afferents are believed to reach the precentral motor cortex as well. In the anteroposterior dimension, the surface projections of pre- and postcentral gyri subtend about 10° each. The coronal position and extent depend upon the particular body region stimulated.

2. AUDITORY CORTEX

The primary auditory projections are buried within the sylvian fissure on the supratemporal plane. A model of this region is provided by an annular sector subtending an angle of 20°, bounded by two arcs at three quarters and half of the distance to the center of the sphere (Geschwind & Levitsky, 1968; Celesia & Puletti, 1969).

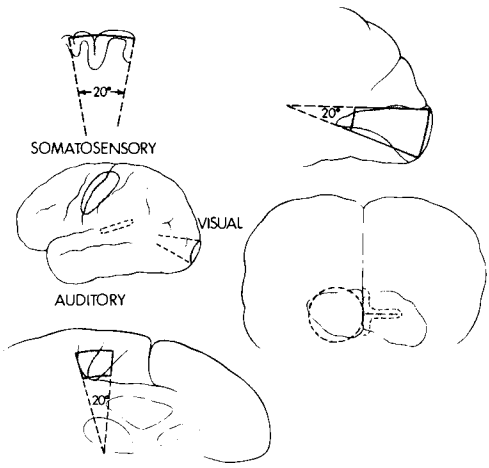


FIG. 4-8. Diagrammatic representation of idealized intracranial sources comprising primary somatosensory, visual, and auditory cortex. Projection areas are indicated by stippling. The somatosensory projections are considered to include both precentral and postcentral gyri, and are represented by a case A model. The auditory projections in the supratemporal plane conform to case B. Striate cortex presents a complex configuration requiring both case A and B configurations.

3. VISUAL CORTEX

The primary visual projection area presents the most complex anatomy of the sensory projection area, and thus provides a particularly valuable test of the model. The central retinal projections occupy a small area at the surface of the occipital pole, a region subtending about 20° in the vertical axis and about twice that horizontally (Polyak, 1957). The peripheral retina projects to cortex lying within the sagittal sulcus and the calcarine fissure according to a recognized retinotopic pattern (Holmes, 1945). The infolded visual areas can be modeled by a set of annular sectors having a cruciate arrangement.

Additions and refinements of the model can be made to evaluate the fields due to other source configurations as dictated by the need to evaluate more elaborate hypotheses or by particular empirical results. We now consider the quantitative estimates obtained from the model.

F. Computations from the Model

1. CASES A AND B COMPARED—UNIT DIPOLE

In Fig. 4-9 the potential distributions computed for a single infinitesimal dipole of unit strength are displayed for the two orientations as a function

of depth beneath the surface of the innermost sphere, representing the brain. Note the bell-shaped distribution of the radial dipole and the characteristic biphasic configuration of the tangential dipole. The outermost dipole in both cases is situated 2 mm beneath the surface to simulate an equivalent cortical dipole. In this position the radial dipole contributes two and one half times as much as the tangential dipole to the surface potential. As the dipole is moved deeper, the maximum amplitude of the surface potential diminishes sharply, with the potential for a dipole placed in the center of the sphere being one-fifteenth the amplitude of the radially oriented "cortical" dipole, and one-sixth that of the tangential dipole at the same depth. Also note the shift in the location of the potential maximum with increasing depth of the tangential dipole.

2. Effects of Changes in Parameters of the Model

Since the values of the dimensions and impedances of the brain and its coverings are approximate average measures, subject to unknown errors due to individual differences and variations within each subject, it is important to have some information on the impact of changes in these values on the potential distribution estimates. The main uncertainties are in the thickness and impedance of the skull, whose mean values have been selected to conform with the estimates by Rush and Driscoll (1968): 5 mm and 18,000 Ω-cm, respectively. Calculations indicate that a 10% alteration in the

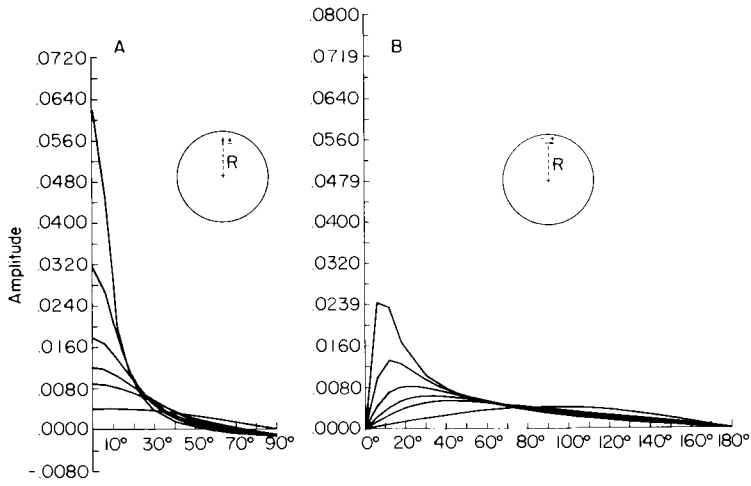


FIG. 4-9. Computed surface amplitude distributions for unit dipoles in case A and B configurations at varying angular distances from the dipole axis. The curves represent field strengths for dipoles located at the center of the sphere and 50, 62.5, 75, 87.5, and 97.5% of the distance to the surface of the inner sphere which represents the brain.

maximum potential amplitude at the scalp would be produced either by a 1.5 mm change in skull thickness or by a 6000-Ω deviation of resistivity. Thus, the model is fairly insensitive to reasonable errors or fluctuations in the skull parameters. Another possible source of error is presented by the presence of the CSF between brain and skull. This relatively low impedance medium surrounds the brain within the subarachnoid space, which is ordinarily quite thin, especially over the gyral surfaces. In subjects with brain atrophy, however, the subarachnoid space may enlarge significantly. It turns out that the effects of CSF layer thickness are quantitatively similar to increasing the skull thickness. Under normal circumstances the attenuation due to this layer can be considered to be negligible. Should it be wished to evaluate the distribution in a pathological case, the three-shell computation can be carried out using the appropriate value for CSF resistivity, or by moving the dipole the required distance deeper within the inner sphere, a maneuver which provides sufficiently accurate results and substantially reduces the required computation.

3. Effects of Generator Size

The maximum amplitudes of the distributions computed for varying source dimensions are depicted in Fig. 4-10 for the two dipole layer orientations. The dipole cap (case A) is 2 mm below the surface of the inner sphere. In case B the annular sector extends from 2 mm below the surface, halfway to the center. Note that the maxima in case B are roughly 10% of those in case A for comparable angular dimensions. This means that the contribution by sulcal cortex to the scalp potential distribution will ordinarily be relatively insignificant compared to that of surface cortex. Since the actual strength of the intracranial generators is usually not known, it is useful to scale the computed distributions for case A to a common maximum amplitude (Fig. 4-11) so as to permit convenient comparison with empirical potential distributions.

G. Application of the Model to Empirical Potential Distributions

In order to evaluate the source geometry, their theoretical field configurations must be compared with empirical ERP amplitude distributions. In order to obtain meaningful scalp potential maps, meticulous attention must be paid to selection of an appropriate reference electrode, adequate electrode spacing, and proper identification and measurement of ERP components.

1. Reference Electrode Placement

A valid potential distribution map requires that the reference electrode be inactive with respect to the ERP under study, as well as being free from

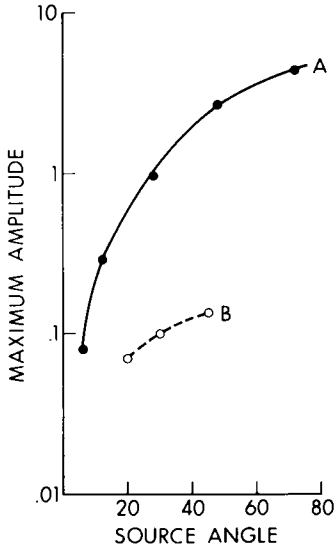


FIG. 4-10. Relative maximum amplitudes of the surface fields generated by case A and B generators of different sizes. The case A generators are circular caps located 2 mm beneath the surface of the inner sphere to simulate cortical sources. The case B generators extend from 50 to 97.5% of the distance from the center of the sphere (appropriate for simulating the mesial striate cortex).

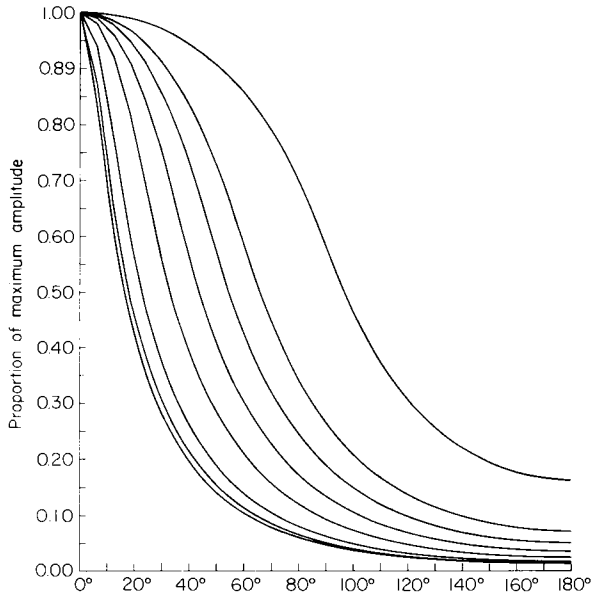


FIG. 4-11. Field distributions for case A generators scaled to a common maximum amplitude. These distributions may be compared against empirical potential distributions to estimate the angular extent of a surface cortical source. Curves represent sources of 6, 12, 24, 48, 72, 96, 120, and 180 .

extraneous electrical activity which might obscure the brain potentials. This requirement is often difficult to meet due to the nature of differential amplification. Since the brain potential fluctuations at the scalp surface are so tiny, other physiologic signals such as the EKG and electrical interference picked up by the body must be eliminated through the rejection of potentials common to both electrodes of the differential pair. Unfortunately, as the electrodes are moved further apart, the EKG is no longer identical at both electrodes and appears as a large interfering potential. Line voltage artifact may also be incompletely rejected. For this reason reference electrodes for EEG recording are ordinarily placed somewhere on the head, usually on the ear lobes or mastoid process. It is known that these placements pick up activity from the temporal lobes, so they are not entirely inactive with reference to brain activity. A number of alternatives to these placements have been tried, including tip of the nose, chin, a pair of electrodes placed on the sternum and vertebra prominens linked through a potentiometer to balance out the EKG, and finally an "average" reference in which all electrodes but the active one are linked through appropriate resistances. Each of these references has its own problems. The nose picks up electrooculographic activity, so unless ocular fixation can be maintained, the placement will contain large deviations which may obscure the activity being studied. The chin usually contains a good deal of EMG activity, but this can be eliminated in cooperative subjects with practice. The sternovertebral reference is rather inconvenient and is not inactive with respect to intracranial potential fields whose maxima are axially oriented, such as that of the auditory evoked potential. The average reference appears objectionable due to the extensive time-locked activity which it will pick up. All of these considerations dictate great care in selection of an appropriate reference. When eye movements can be eliminated, the nose may be a good choice. The linked ears are most often used due to their relative freedom from artifacts, and will be sufficiently inactive for many purposes, providing time-locked activity is not present in the temporal regions or in the postauricular muscles.

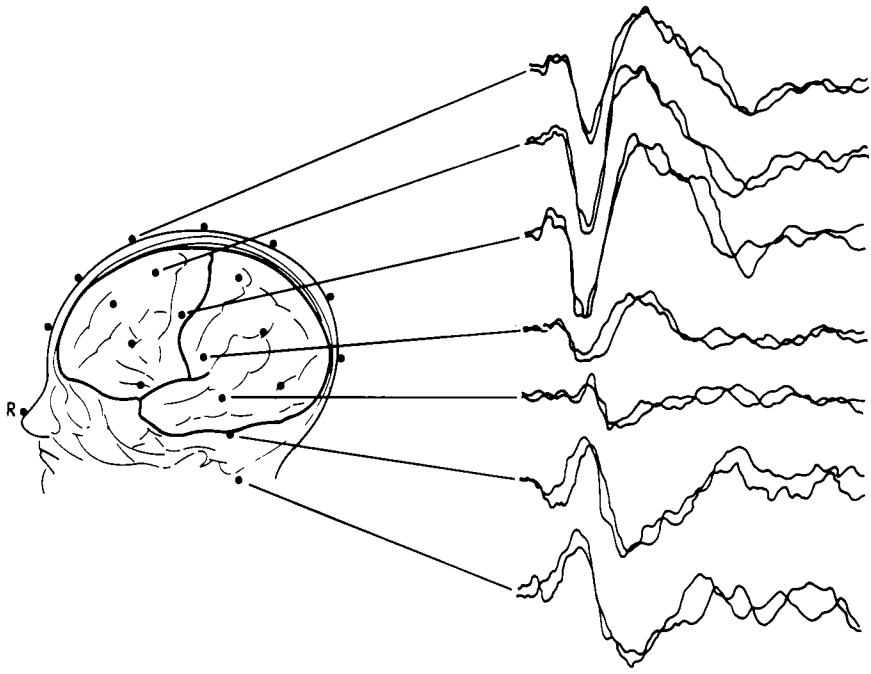
2. Electrode Arrays

In the average adult an electrode spacing of not more than 5 cm is required to provide an adequate resolution of potential gradients. For more detailed maps, even closer placements may be desirable. Ordinarily, 2.5 cm will constitute the minimum practical spacing using conventional scalp electrodes. This will be adequate separation for use in infants. Complete coverage of one side of the head, including a sagittal chain of 7 electrodes, requires about 20 electrodes. In recording from a large number of electrodes, it may be necessary to make repeated runs with subsets equal to the number of available amplifier channels. Under these circumstances, an electrode at or

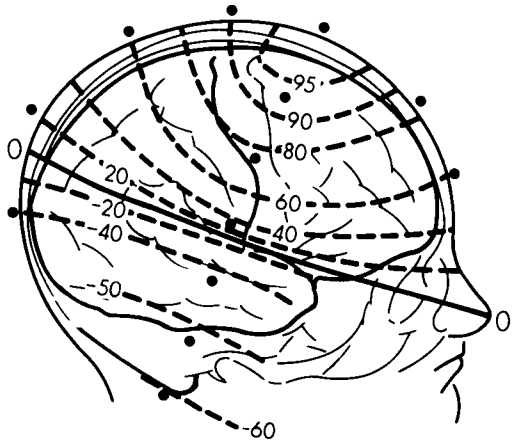
near the expected potential maximum should be included in all runs to permit the data to be scaled against the records from a common placement and thus correct for variations in amplitude which may be present in the different runs. It should be noted that the standard international EEG electrode array is not satisfactory for obtaining potential maps, as the placements are too far apart. The principle of proportionality employed in this system should be preserved, however, since this permits a ready conversion to the angular size of a cortical generator and its scalp distribution can be related to distances measured on the surface of the scalp. In the average adult a distance of 2 cm on the scalp roughly corresponds to 10° in angular dimension in the sagittal plane. Due to the smaller diameter in the coronal plane (Fig. 4-6), the distance on the scalp subtending the same central angle may be somewhat less. Appropriate corrections will have to be made to suit the head of the individual subject.

3. Identification and Measurement of ERP Components

Once a suitable set of ERP recordings which accurately depicts the scalp potential distribution has been obtained, it is necessary to reduce the time-varying waveforms into isopotential contour maps, each of which represents a component generated by a single source. Since there may be considerable spatial and temporal overlap of the various ERP components, the identification of peaks representing activity with a common intracranial origin must be made with great care. Also, the amplitude measurements must take into consideration the possible distortion produced by overlapping of components. The main criteria for identification of an homogeneous component are constant latency and a monotonic amplitude decrement from a single voltage maximum. Whenever consistent shifts in peak latency or departures from a smooth variation in amplitude can be identified, an overlap of components must be assumed to be present. Dissection of these combinations will often challenge the ingenuity and patience of the investigator. But by diligent inspection of the entire montage of ERPs, supplemented by recordings obtained from several subjects and, when necessary, by data obtained under different experimental conditions, a reliable pattern of componentry can usually be identified and amplitude measurements undertaken. Unfortunately, it is not always easy to decide what measurements are most appropriate. The initial component of the ERP waveform can be measured from the preresponse baseline. Later components are less readily measured with respect to the baseline, however, as different amounts of positive or negative bias may have been introduced by earlier components having a different distribution. In the simplest and least ambiguous cases, successive peaks of the ERP waveform will possess a similar distribution over the scalp, permitting peak-to-peak measurements to be made. Systematic maps



(A)



(B)

FIG. 4-12. (A) Set of auditory evoked responses along a coronal line from vertex to mastoid. Electrode placements for mapping are indicated. Reference on tip of nose. (B) Isopotential plot of major negative-positive deflection.

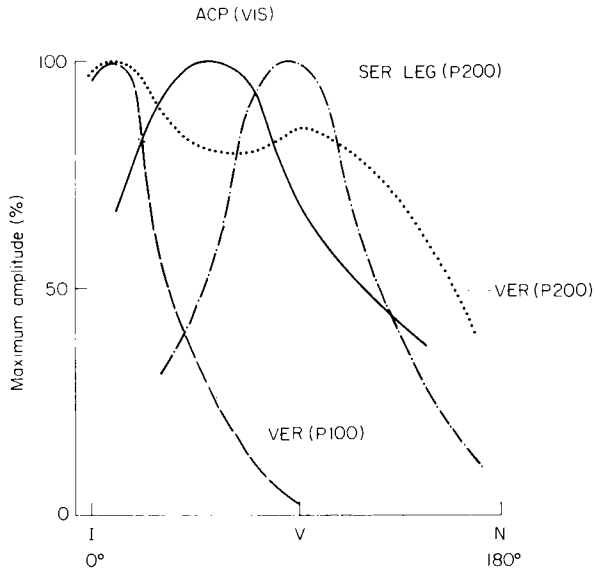


FIG. 4-13. Amplitude distributions of ERP along a sagittal line. VER (P100): visual evoked response component peaking near 100 msec. VER (P200): visual evoked response component peaking near 200 msec. Note saddle-shaped distribution indicating the presence of two distinct sources. ACP (vis): association cortex potential; positive wave peaking at about 400 msec obtained during a visual discrimination task. SER (leg): somatosensory evoked response to electrical stimulation of the common peroneal nerve.

of all major ERP components taking these interactions into careful account have not yet been obtained, so there is considerable room for further investigation in this area.

Having constructed an isopotential map, such as that depicted in Fig. 4-12, one is in a position to assess the configuration and extent of the intracranial source. It is convenient to take a series of amplitude sections along the main dimensions of the contour map, as shown for several empirical distributions in Fig. 4-13. When the distributions are bell shaped, application of the surface cortical generator model (case A) is appropriate. By comparing the shape of the empirical distribution with the family of theoretical curves corresponding to sources of varying angular extent, the appropriate generator size can be estimated.

In making this comparison, the anatomical position of the putative generators must be kept in mind. Usually there will be bilaterally symmetrical intracranial sources whose scalp distributions will sum. For this reason, the amplitude gradient furthest from the midline, or from the contribution of other possibly overlapping potentials, must be employed to correctly estimate the potential distribution. When the centers of the overlapping dis-

tributions have been appropriately positioned, the theoretical curves can be summed, which should produce a match with the empirical distribution. In the case of the sensory evoked potentials and the motor potentials, specific hypotheses could be made concerning their probable intracranial sources to be tested against the empirical data (namely, Vaughan, Costa, & Ritter, 1968; Vaughan, 1969). This technique has also been employed to estimate the location and size of the generators of the association cortex potentials, which were not predicted beforehand (Vaughan & Ritter, 1970). Potentials generated by sources perpendicular to the scalp surface, represented by the case B model, have also been studied. The two clearest examples of this configuration are provided by the primary auditory cortex and the projections of the peripheral retina to the mesial occipital cortex. An analysis of the auditory evoked potential distribution, consistent with generators in the supratemporal plane (Fig. 4-8), has been presented by Vaughan and Ritter (1970), but these conclusions have been disputed by Kooi, Tipton, and Marshall (1971). The bone of contention is the inactivity of the reference electrode employed to obtain the potential maps. This controversy illustrates the usefulness of a quantitative theoretical model to assist in the selection of an appropriate reference placement. The noncephalic sternovertebral reference employed by Kooi *et al.* to refute the inactivity of the nose reference used in the earlier study appears on the basis of computations from the dipole model to actually be the active one, since it lies in the direction of the maximum potential generated within the auditory cortex.

Intracranial recordings are of great help in supporting and extending predictions drawn from the volume conduction model. Direct observations are also necessary to establish the actual magnitude of the cortical potentials, which are known to vary substantially from area to area in recordings from chronically implanted primates (Vaughan & Gross, 1969). Ambiguities and complexities which cannot be resolved by analysis of the scalp recordings will also require direct probing of the brain for resolution.

The somatosensory evoked response has been most extensively recorded from the human cortex, and some studies have compared its amplitude with that of scalp-recorded potentials in the same subject (Giblin, 1964; Domino, Matsouka, Waltz, & Cooper, 1964, 1965; Broughton, 1969; Stohr & Goldring, 1969). These data indicate a scalp amplitude ranging from 6 to 25% that of the cortex. The larger estimates appear to be derived from recordings made with the skull open, which would tend to accentuate the scalp response. Giblin's data are most useful, as he recorded the scalp responses both before and after craniotomy. Preoperatively the scalp response was about 15% and postoperatively about 25% the size of the cortical response recorded at surgery. The cortical generator size, estimated from the model on the basis of these amplitude ratios, would range from 18°

to 50°. Giblin's preoperative ratio conforms to an angular dimension of 35°. Stimulation data (Penfield & Boldrey, 1937) indicate that the cortical hand area subtends about 20° in the anteroposterior dimension and 45° in the coronal plane (cf. Fig. 4-6). This oval source would be equivalent to a circular cap of the appropriate dimensions to account for the observed amplitude relationships. Few cortical recordings of the evoked potentials in the auditory and visual modalities are available. Celesia and Puletti (1969) have reported a particularly valuable transcortical recording of the early components of the human auditory evoked response, which permits computation of the expected scalp amplitude from the model of an auditory projection cortex. The predicted value of about 2 μV conforms to the order of magnitude usually obtained for this small initial deflection in scalp recordings.

In view of the satisfactory predictions concerning scalp-cortex amplitude relations obtained from the model, it should be possible to assess the relative amplitudes of different ERP components at the cortical surface by comparing their scalp distributions. The amplitude at the scalp is strongly influenced by generator size, so the more extensive source will produce a greater amplitude in the scalp recording if their cortical amplitudes are comparable. If the relative amplitudes of two potentials differing in distribution depart from the amplitude relation depicted in Fig. 4-10, a disparity in intracranial amplitude can be inferred. The relationship between source size and strength must always be kept in mind when interpreting changes in ERP magnitude. Probably the most ubiquitous fallacy in interpretation of ERP data derives from the assumption that amplitude changes represent a similar alteration in the intensity of underlying neural activity. In addition to the more fundamental uncertainties concerning the specific information on cellular processes which is conveyed by their volume-conducted manifestations, it will now be evident that changes in the extent of active cortex will alter the maximum amplitude recorded at the scalp. Thus, unless the potential distribution is monitored, the interpretation of amplitude changes will be ambiguous.

In order to introduce the use of the volume conduction model for the elucidation of more complex brain potential configurations, let us consider the relationship between the intracranial generators and scalp distributions of the visually evoked potentials. In Fig. 4-8 the occipital cortical areas which are presumed to represent the main generators of the visual responses are depicted. These include the primary projection (area 17) and the prestriate visual cortex (areas 18 and 19). The striate cortex presents a complex anatomical configuration, only a small portion presenting at the surface of the occipital pole and the remainder being buried within the sagittal and calcarine fissures. These relationships are represented in the model by the combination of case A and B dipole configurations diagrammed in Fig. 4-8. The specificity of the retinotopic projections onto visual cortex (Holmes,

1945) permits an especially good opportunity to test the implications of the model in relation to the size and orientation of active tissue. Since the central retina projects to the external striate cortex, a foveal stimulus will generate a bell-shaped distribution centering on the occipital pole. The initial positive components of the visual evoked response, with latencies in the order of 100 msec, have a distribution compatible with their origin in the surface part of area 17. As the area of retinal stimulation is increased, the peripheral projections to mesial striate cortex will also be activated, but these will not contribute to the scalp potential owing to their opposing geometry. Increase in the area of retinal stimulation beyond about 10° produces no change in the VER. However, when half the visual field is stimulated, or a spot of light is projected eccentrically onto the retina, the mesial cortex is asymmetrically activated and an external field conforming to case B should be elicited. This expectation has been confirmed by Biersdorf and Nakamura (1971) and in our laboratory (Vaughan, 1969). A particularly interesting instance of hemicortical stimulation has been reported by Lehman and Fender (1969) in a patient with a split optic chiasma. As is the case with stimuli limited to one side of the visual field, an inversion of response polarity typical of a case B generator was observed across the midline. In contrast to the earlier VER components which appear to be generated within striate cortex, the more widespread distribution of the later components implicates extrastriate areas as well. The relative prominence of this activity, which peaks at about 200 msec, is influenced by the nature of the visual stimuli. The presence of contours or patterns appears to be the most relevant variable. When visual stimuli achieve significance, either through their unexpected presentation or as a task-relevant signal (Ritter & Vaughan, 1969), the responses manifest very long latency components, ranging from 300 to over 500 msec. These components arise primarily from the region of the inferior parietal lobule. The striking changes in distribution of visual evoked responses with variation in the locus and area of retinal stimulation, as well as with stimulus content and significance, illustrate the need for detailed attention to the spatial characteristics of the ERP. Recordings taken from a single electrode placement or even several, without knowledge of the potential distribution to be anticipated, will not merely be incomplete but often actively misleading. Measurements of amplitude without corresponding assessment of possible changes in distribution will, as we have seen, be meaningless.

IV. Synthesis and Prospectus

The imperfect tool provided by scalp-recorded potentials for analyzing brain mechanisms requires at once a cautious interpretation and daring applica-

tion in exploring the physiologic basis of human experience and behavior. Caution is dictated by the extreme degradation of information on neural processes which these data present. From a four-dimensional panoply of intracerebral neural events, the attenuated and distorted manifestations conveyed by volume-conducted currents are reduced to a three-dimensional representation on the surface of the scalp. In the two analytical techniques we have described, a further dimensional reduction is imposed. The recording of activity from a single locus, referred to an inactive site, provides a temporal display of but one point in the potential distribution over the scalp. Employing this spatial sample, we extract through averaging an estimate of the neuroelectric signals time locked to an observable reference event. If we simultaneously obtain a sufficient number of these records, we may slice these data into a spatial representation of potential distribution at a single moment in time and achieve, with the help of a suitable analytical model, an indication of the intracranial source of that particular field configuration. In order to extract the totality of information on intracranial processes which is available in these records, a synthesis of the temporal and spatial data must be achieved. However, without some analytic focus, some simplifying principle, the mere compilation of a three-dimensional display represents but a technical *tour de force*, possibly of some aesthetic merit. There are clearly certain nodal features of the brain potential data toward which we can direct our main concern. In the time domain, we identify peaks and valleys of the potential record, which we have called "components," as if each undulation possessed some separate identity and significance. Indeed, the spatial analysis we have described depends upon the identification of salient features of the waveform which can be identified over a substantial area of the scalp. In the initial section we suggested that some aspects of the scalp potential waveform could, as "event related potentials," provide an indication of the timing and location of intracranial neural processes. The validity of such inferences ultimately depends upon evidence on the linkage between surface cortical potentials and the firing patterns of intracortical neurons in the behaving organism. It is ironic that the introduction of microelectrode techniques for recording from single neurons has led the practitioners of that art to a contemptuous attitude toward the less well-defined volume-conducted activity, at the same time that methods for chronic intracranial recording have permitted extensive study of the gross potentials in behaving animals, and the averaging technique provided us with tools for selective analysis of human brain potentials. Thus, we have been denied the extensive correlative data on relationships between neural firing patterns and gross brain potentials which are required to give more explicit physiologic meaning to the latter phenomena. The few available data give us only a tantalizing glimpse of these matters. Thus, in

the striate cortex of the monkey there is a predominant pattern of surface positivity with increased firing rate in response to a photic stimulus, and negativity with inhibition of discharge (Vaughan, 1969). By contrast, the discharge of pyramidal tract neurons associated with a voluntary hand movement (Evarts, 1966) is temporally associated with a biphasic positive-negative deflection, both in the records obtained from the cortex of monkeys (Vaughan, Bossom, & Gross, 1970) and from the human scalp (Gilden, Vaughan, & Costa, 1966) under the same experimental conditions. These data indicate that the ambiguity concerning polarity of surface response in studies carried out under less normal physiologic conditions also exists in the behaving animal, thus necessitating a detailed evaluation of the relations between gross and cellular potentials in the relevant behavioral circumstances.

Until such detailed data are available, it will be desirable to interpret the ERP amplitude measurements with great circumspection as regards magnitude of neural activity. It will neither advance our knowledge of brain mechanisms nor enhance the repute of human brain potential studies for investigators to persist in *ad hoc* speculations on neural processing based solely upon changes in ERP amplitude. We will remain on safer ground by devoting our primary attention to answering the questions of when and where. The methods briefly described in this chapter provide an approach to defining the timing and sources of ERP components. Once a component has been adequately characterized as to timing and source geometry, we may then begin to ask questions concerning its covariation with experimental variables. Without committing ourselves to specific interpretations in terms of neural processes, a change in an ERP component provides *ipso facto* evidence of a change in brain activity at a specific brain site at a particular time relative to the reference event. In elucidating the neurobehavioral significance of such changes, it will always be most useful to employ parametric techniques whenever feasible. Psychophysics and reaction time techniques provide the experimental models for these analyses. Constant attention to precise measurement and control of stimulus and response, and to the relevant anatomical and physiologic considerations, are requisite to valid results. The literature must always be critically evaluated with respect to these questions. Pressures exist to utilize the simple manifestations of human brain processes provided by scalp-recorded potentials as indices of complex psychological constructs. The possibilities for success in these ventures, though never great, will be enhanced by increasing understanding of the physiologic processes underlying the generation of the ERP, on the one hand, and attention to the precise definition of appropriate psychological constructs, on the other. Despite their undoubted heuristic value, concepts such as arousal, attention, and intelligence do not lend themselves to precise psychophysiologic analysis and interpretation (Moray,

1970; Vaughan & Ritter, 1973). In trying to fulfill its unique promise of insight into human brain processes, the analysis of scalp-recorded potentials will best be served by experimental methods which permit the observation of concomitant variations in physiologic and psychological variables.

Acknowledgments

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Chapter 5

Computer Use in Bioelectric Data Collection and Analysis

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I. Introduction

The techniques and experiments described in this volume, whether they involve evoked potentials, skin resistance, or electrooculograms, nearly always consist of the presentation of patterns of stimuli in controlled time sequences with recording of the subject's electrical and/or mechanical response. Each subject's responses are measured, often requiring elaborate computations, and the resulting numerical scores then are entered into various sorts of group statistical tests. This process, from incoming electrical signal to finished *t* test, can be accomplished with unprecedented speed, accuracy, and ease by using a single device—the *process-control computer*. This chapter will present an introduction to process-control computer use in psychophysiology, the theoretical background of signal sampling, and specific programming techniques for stimulus presentation and systems development. Signal averaging is emphasized because it can be done only by computer and because it illustrates a wide range of problems encountered in bioelectric data collection. We will not attempt to teach computer programming itself, and hope that the reader has some acquaintance with basic programming techniques and terminology. Recent books and articles by Uttal (1968), Scholz (1972), and Soucek (1972) can supply useful background material.

A. Real-Time Operation

In most large computer operations, a programmer submits a problem (usually termed a "job," with instructions entered on cards) to the computer, and after some delay (usually beyond his control) his output is returned. This procedure is satisfactory for statistical analyses that do not rely upon the program being executed at any particular moment in time. In the psychology or physiology laboratory, however, an experimenter who uses a computer is interested in recording and responding to his data as the subject generates it; thus, the computer must react to its external environment when that external environment demands it. This is called *real-time operation*. The external environment may also react to a computer produced stimulus and the computer then records the response; this, too, is an example of real-time

operation. Process-control computers are specifically designed to perform these tasks. They have commands to measure the voltage of a signal, display signals graphically, time intervals, close switches, detect whether a switch has been closed, and generate electrical signals with precision. Indeed, they can replace nearly all hardware in a standard psychophysiology laboratory. A particular advantage of real-time computer use is that the voltages and time intervals recorded are immediately available for computation, without hand measurement of polygraph records and laborious key-punching techniques.

Although each one of the many computers on the market is somewhat different from its competitors, all perform the same basic operations. Whereas the emphasis in this chapter is on practical applications of computers to bioelectric signals, a survey of the special characteristics of process control is necessary for their most efficient use.

B. On-Line Versus Off-Line Data Collection

Sampling of the data signal need not occur in *real time*, that is, while the experiment is in progress. Stimuli can be generated by electromechanical devices, and the signals then can be recorded on an analog tape recorder along with appropriate stimulus markers, and so forth, as needed. At a later time this tape can be played back to the computer system and sampled.

Although feasible, this is an approach we would hope to leave behind us along with vacuum tubes. Considering the moderate cost, high speed, and ease of operation of today's computers, the analog tape is an unnecessary step.

Data stored in digital form can be indexed, viewed on computer-driven cathode ray tube (CRT) displays, retrieved for subsequent data analysis far more conveniently, reliably, and efficiently than analog tape data. Careful consideration of sampling rates and the specific time periods actually desired for analysis can substantially reduce the volume and cost of record storage. Digital records from many subjects and conditions may be input to the computer at extremely high rates and still retain accurate records of subjects' names, dates, conditions, and other identifying information. Reanalysis of the data at a later date is thus facilitated. Of course, if one only has access to the computer at times other than when the experiment itself is running, there is no alternative to the use of an analog tape recorder. But it should be remembered that, with logic devices, paper tape readers, stimulus generators, relays, and so forth, the investigator is really building his own *single-purpose* digital computer; it is difficult to reprogram, relatively unreliable, and contains expensive single-purpose devices which limit the flexibility of the investigator's approach. The resurrection of last year's

experiment may require days of rewiring rather than a few seconds of program loading. Further, if two or more investigators share a laboratory, the changeover from one experiment to another is costly in time and often catastrophic to function.

A further question involved here is really one of on-line or off-line data analysis. With the speed of available computers, average evoked responses can easily be computed in real time, obviating the need to store data on tape for later computation of the average. However, if the investigator wishes to save single trials (that is, records of fixed length) or to sample and save a continuous record, then he must retain his data on some auxiliary storage medium due to computer memory limitations. This will be covered in Section II,C,4 under double buffering techniques.

II. Data Collection

A. Getting the Computer's Attention: Interrupts

There are two general means by which a computer can be made to react to a signal generated outside of itself. The computer can be executing a program that continuously checks a switch (for example, subject key) or voltage; then, when the appropriate condition occurs, it can leave that section of the program and branch to the proper routine. This method is straightforward, but very inefficient if a quick response is required, for the program must spend most of its time in the switch-checking loop. Of course, if only a slow response is required, it may be necessary to look at the external level relatively infrequently.

To overcome the inefficiency of this kind of looping, many real-time computers have one or more interrupts available. These work very much as the name implies. The computer can be executing a program when some event causes (through appropriate hardware) an interrupt to be set. The program currently being executed is interrupted, and control is transferred to a program section whose job it is to respond to that event. In small computers with a single interrupt, a pulse coming from an external device causes the program to branch to a specific memory location. Instructions located there first must save the location of the last executed instruction for later return to the main program, as well as retain the contents of any registers which were being used. After completion of the immediate response to the interrupt, the contents of these registers must be restored to their preinterrupt values so that interrupt routine then can branch back to the main program to resume the interrupted computation. In larger computers,

this is usually done through a dedicated memory location. The address at the entry point of the interrupt processing routine is stored in the dedicated memory slot. When the interrupt is fired, a hardware "store place and branch" is executed indirectly through the memory location. The value of the program counter at that time is stored in the entry point of the processing routine, which then functions just as a normal subroutine call would, and all registers used must be saved and then restored to their preinterrupt values.

The interrupt processing routine may function in any of several ways. It can actually execute a series of instructions for the purpose to the external event or it can merely change a word in memroy ("set a flag") to indicate that the event occurred. A clock could be read and the time of the event could be stored, or perhaps the elapsed time from some previous event could be calculated.

A system may have one or more interrupts. With only one we are somewhat limited since, if we wish to use it for more than one chore at a time, we must have some additional means of determining which of several signals may have fired it. This could be accomplished by having a signal on other input lines that would be interrogated when the interrupt fired. The most versatile system is one which has multiple interrupts, each with its own dedicated memory location so that each interrupt is directly connected to its own processing routine. With multiple interrupts it is highly desirable to have a hardware priority system to handle the problem of one interrupt occurring while another is still being processed.

B. Timing Events and Generating Intervals

In real-time operation and particularly in programs designed to perform psychological experiments, accurate timing is often a critical element. Timing of computer events may be the important feature, as in the accurate presentation of stimuli (stimulus length and interstimulus interval). Or, timing of events outside the computer may be of interest, as in measuring reaction times. In either case some means of keeping time, a clock, must be available to the computer. For an amplified discussion on the classification and use of clocks, see Markowitz and Nickerson (1968).

Borrowing from their discussion, a clock is composed of a time mark generator and a counter. A time mark generator is anything that produces a pulse, tick, or other signal at precisely spaced equal intervals. To keep time then, we merely need to keep track of the ticks by counting them.

Clocks may be classified according to whether the generator and the counter are internal or external to the computer. The most direct means of

timing is when both generator and counter are internal to the computer. The basic cycle time of the computer forms the generator. The counter is a program loop that increments a specified location, and, since we know exactly the execution time for each instruction in the loop, we have our clock, provided that neither interrupts nor "cycle stealing" (see Section II, C,4) are in progress. In general this is not a good means of time keeping since it makes very inefficient use of the computer. For timing extremely short intervals, however, this may be the easiest technique, since the execution time for the number of commands necessary to initiate other timing methods may exceed the interval itself.

A more common technique for time keeping is to have the time generator external and the counter internal to the computer. In computer systems with interrupts, time may be kept by having an external device that generates an interrupt at a fixed rate and utilizes the interrupt processing routine to count the interrupts. Since the computer is busy with the count only at the time of interrupt, this method is more efficient than the last. To time an interval (for example, to control stimulus duration) the counter value at stimulus onset is noted; then the count at which the stimulus should be turned off is computed. The program loops, checking for this computed value, perform the appropriate action. If the counter is dedicated only to this use, then the operation can be simplified by starting the count at zero at the beginning of the interval and putting the check in the counter interrupt service routine. Timing the duration of an event not under computer control is done similarly, by checking the count at the starting point and computing the difference when the event occurs. Of course, having an interrupt is not necessary; the time generator "ticks" could be counted by a program looping and testing for their occurrence.

The clock arrangement that places the least burden on the computer has both the generator and the counter external. The generator feeds directly to a hardware counter, which then can be read by the program being executed. Additional computer commands to start the counter, reset it, change the generator rate, and so forth are usually included. This arrangement is utilized just as in the previous case.

In a system with interrupts, an even better possibility exists. We preset the counter with a value and start the generator which then counts down instead of up. When zero is reached, an interrupt is fired, indicating the end of the requested interval. This is the most efficient method for generating intervals since it does not require the program to sit in a loop waiting for a specific count to come up. But to compute durations of events not under computer control, we, of course, still need the capability to use the counter as a clock.

C. Input to the Computer

Once an experimental event has occurred or the computer has stimulated the subject, we are ready to record the response. The data may be an analog signal from an electrode or a digital signal from a particular key being depressed. The analog signal must be converted into digital form at discrete intervals—that is, *sampled*—before it can be stored in the computer memory. An analog-to-digital converter actually performs the sampling operation and may function either on direct command from the computer or at a series of fixed intervals according to its own clock, the data going directly into memory. Similarly, digital information may be entered one number at a time on a direct command to read it or in a "buffered" (see Section II,C,4) fashion, with a series of numbers going at high speed directly into memory.

1. Analog-to-Digital Conversion

The analog-to-digital (A/D) converter (or simply "A to D") is the heart of the sampling system. An appropriately conditioned analog signal is applied at the input to the A/D. The absolute level of the analog signal must match the input requirements of the A/D. In order to maintain the greatest number of significant bits, the mean excursion of the analog signal should be in the middle of the input range of the A/D. In general, the absolute signal level can be controlled by adjusting the amplifier gain or introducing another adjusted gain amplifier before the A/D input. If, for example, the output of the electroencephalogram (EEG) amplitude were at a greater voltage than the A/D wanted, nothing more than a resistor voltage divider would be necessary. If an occasional high level exceeded the input range of the unit, the most desirable outcome would be a graceful saturation whereby the maximum count could be read out for any value above the limit. If this were not the case, it might be necessary to add an analog limiter circuit prior to the A/D.

a. Analog-to-Digital Conversion Techniques. A brief description of how an A/D converter works will be helpful in understanding the parameters associated with its operation. Comparison between an internally generated digital voltage and the external analog voltage forms the basic mechanism. In one technique, a staircase ramp voltage is generated by a digital counter. At the instant when the conversion is requested, a sample and hold circuit registers the analog signal value, and a trigger starts the digital counter. The digital voltage and the held analog value are fed to a voltage comparator circuit, which gives a response when the internal voltage exceeds the external voltage. The voltage at each step in the staircase is the quantification level of the A/D, and gives the value of each count in the final digital result. The

staircase commonly starts from a voltage of one-half of the first step value, and the final count readout is given as one less than the actual count; in this way, the digital value is accurate to the nearest step.

Another technique is the method of successive approximation. Here the voltage associated with each bit position is switched in or out and the comparison with the analog signal made. Since this requires only as many steps as there are bits, it is a faster method than the previous one; however, it requires more logic circuitry for its operation.

The speed of operation will determine the maximum sampling rate. If it takes a maximum of 50 μsec for the converter to count or perform the successive approximation, then the maximum rate is 20,000 samples per second. We also see the reason for the sample and hold circuit, for without it the actual time of the sample would be determined by the value of the signal.

b. ACCURACY OF CONVERSION. The quantization level is the value of a single bit or count in the digital value. This defines the resolution capability of the converter. Accuracy is to $\pm \frac{1}{2}$ the quantization. The number of bits that the counter is capable of handling determines the overall range of the device. For example, if the quantization level were .01 V and the counter were 10 bits wide, the maximum digital value at 1023 would correspond to 10.23 V. That would be for unipolar operation, where only positive signals were considered. For bipolar operation the first, most significant bit would be used to indicate the sign. The overall range would be 10.23 V, but the minimum and maximum values would be ± 5.11 V. Of course, since all computers have shift instructions, it is easy to retain only the number of bits desired for the analysis being performed. (See Section III,D,5.)

c. NUMBER OF BITS REQUIRED. The number of bits which we will need for each sample is determined by two main considerations: the characteristics of the signal and what we intend to do with the sample.

The feature of the signal we are most concerned with is its *dynamic range*. This is the ratio of the largest signal value (other than zero and counting only absolute value) to the smallest signal value of interest. This smallest value must be represented by no less than 1 bit. Since we must be able to express both of these values, this ratio determines the number of bits we will need. If both positive and negative values are considered, we must then add a sign bit also. For example, if our lowest value were .01 and our largest were 10.0, we would have a ratio of 1000:1. To express both 1 and 1000 we need at least 10 bits (recall the largest number represented by n bits is $2^n - 1$). The units involved do not matter since the value per bit is determined by the amplifier gain and the quantization level of the A/D converter.

d. MATHEMATICAL BACKGROUND OF SAMPLING. Practical considerations concerning sampling come from these main areas: (1) the signal character-

istics; (2) what information is desired about the signal; and (3) considerations about both the computer hardware and program system employed. Especially if continuous records of bioelectric potentials are to be saved in digital form, we would like to sample at the lowest possible rate so as to reduce the quantity of data to be stored. In order to choose this lowest rate, some understanding of the mathematics of signal sampling is necessary.

How few numbers can we use to represent a continuous signal and still have all the information that was present? At one extreme we see that there is no upper bound on how fast we sample, for when the sampling rate approaches infinity, we simply have the continuous case as the limit. The other extreme is the limit that we are really interested in, since if we can deal with fewer numbers without any information loss, our programming and storage problems become simpler. Actually, if the continuous signal is sampled too slowly, not only is information lost but confusion is added due to ambiguity among different frequencies. This confusion is called *aliasing*, and a time domain example is shown in Fig. 4-2, Chapter 4 of this volume, by Vaughan.

The easiest way to see the solution to determining the proper sampling rate is to view the problem in the frequency domain. Mathematically the sampling operation can be represented as the multiplication of the continuous time variant signal $v(t)$ by a pulse train $p(t)$, with pulses $1/2W$ time units apart. The function $p(t)$ has value 1 at the specified sampling points, $t = 0, 1/2W, 1/W, 3/2W, \ldots$, and is zero elsewhere (Fig. 5-1a). For the illustrated case the sampling interval is $1/2W$ sec which is a rate of $2W$ samples per second (W is a parameter having a value of one-half the sampling rate). Next we transform $p(t)$ to the frequency domain, calling its amplitude spectrum $P(f)$ in Fig. 5-1b. This special impulse signal $p(t)$ is a completely periodic signal for any multiple of the sampling rate $2W$; hence, its amplitude spectrum (Fourier transform) exists only at those values of f corresponding to the period.

Our signal is $v(t)$, which we will consider to be band limited[1]; that is, it contains no energy (information) at any frequencies above some limit. The amplitude spectrum or Fourier transform of $v(t)$ is shown as $V(f)$ in Fig. 1c. We see it to be band limited with no value above frequency f_0.

Now multiplying $v(t)$ by $p(t)$ results in the values of $v(t)$ only for $t = 0, 1/2W, 1/W, 3/2W, \ldots$, which form our sampled representation of $s(t)$. In the frequency domain this operation corresponds to convolving $V(f)$ and $P(f)$, the result of which is a copy of $V(f)$ centered around each impulse of $P(f)$. This is shown in Fig. 5-1d and e for the two cases where $f_0 < W$ and $f_0 > W$. When f_0 is less than one-half of the sampling rate, an ideal low-pass

[1] The formal definition of band-limited signals may be stated as the class of signals such that their Fourier integral has no value above some frequency.

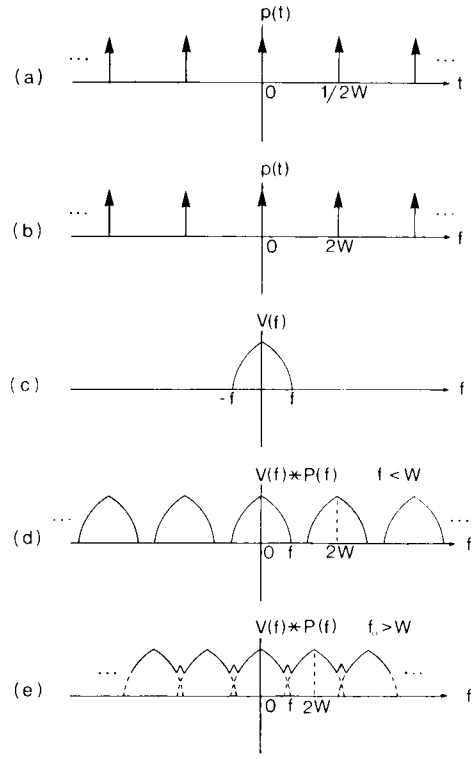

FIG. 5-1. Graphic representation of sampling effects in time and frequency domain: (a) pulse train representation of sampling rate; (b) amplitude spectrum, in the frequency domain of a; (c) amplitude spectrum of our hypothetical, band-limited signal, $v(t)$; (d) amplitude spectra resulting from sampling signal $v(t)$, that is, multiplication of $v(t)$ by $p(t)$ in time domain or convolving b with c in frequency domain; (e) same with f_0 greater than W, that is, sampling rate less than twice the highest frequency in $v(t)$.

filter that eliminated all frequencies above W would recover the original signal from the discrete samples without any distortion. For the case where f_0 is greater than W, the spectrum becomes confused due to the overlap in the region $f = W$ to $f = f_0$. This overlap is what is referred to as "aliasing," and there is no way to recover the original signal. The overlap is also called *spectrum folding* since the spectrum of the signal falls back upon itself starting at W, which is then called the *folding frequency*.

This example gives us the lower limit on sampling for complete characterization of the continuous signal. If we sample at a rate equal to twice the highest frequency present in the signal, we have a complete representation of the signal. This is sometimes referred to as the Nyquist criterion. To mathematically recover the signal from the sampled version, we need the

low-pass filter mentioned above, the frequency domain, and the time domain, representations of which are shown in Fig. 5-2. The following formula recovers the value of the signal $v(t)$ at any time t other than the sampled times (Reza, 1961):

$$v(t) = \sum_{n=+\infty}^{n=-\infty} v\left(\frac{n}{2W}\right) \frac{\sin[2\pi W(t - n/W)]}{2\pi W(t - n/W)}. \tag{1}$$

e. INTERPOLATION OF SAMPLED DATA POINTS. The previous equation can be used to retrieve the value of the signal for any point in time during the record length. If a peak in the data were present at some time other than the sampled instants, it could be located in this manner.

The series expansion must be truncated since sample values from $+\infty$ to $-\infty$ are clearly not available. In most cases an even further truncation is possible. Use of three data points on either side of the time point desired will usually provide a satisfactory estimate. The formula is then as follows:

$$v(t) = \sum_{i=j+2}^{i=j-3} v(i) \frac{\sin[2\pi W(t - i/2W)]}{2\pi W(t - i/2W)}. \tag{2}$$

The sampling rate is $2W$ as before; $v(i)$ is the *ith* sample point corresponding to a time of $i/2W$; j is the largest integer such that $j/2W < t$, where t is the time desired (j is the last sampled point before $v(t)$; see Fig. 5-3).

f. PRACTICAL CONSIDERATIONS IN SAMPLING RATE FOR ELECTROENCEPHALOGRAM SIGNALS. Electroencephalogram signals usually consist of low-frequency energy with 0–40 Hz, the major energy of interest; 60-Hz noise; and higher-frequency energy up to several hundred hertz, normally muscle artifact. Most normal EEG amplifiers have a band pass that eliminates part of this signal. In some cases this frequency response is under the experimenter's control through selectable upper- and lower-frequency limits, sometimes also designated as rise and fall time constants.

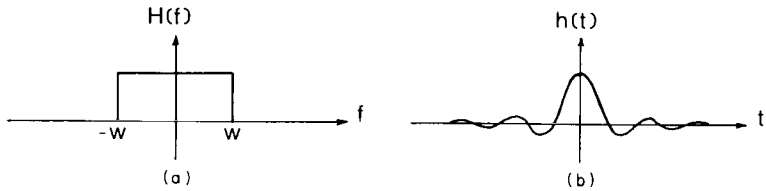

FIG. 5-2. Impulse response in frequency domain (a) and time domain (b) of an ideal low pass filter which passes with a gain of 1 everything below W Hz and completely attenuates all signals above W Hz.

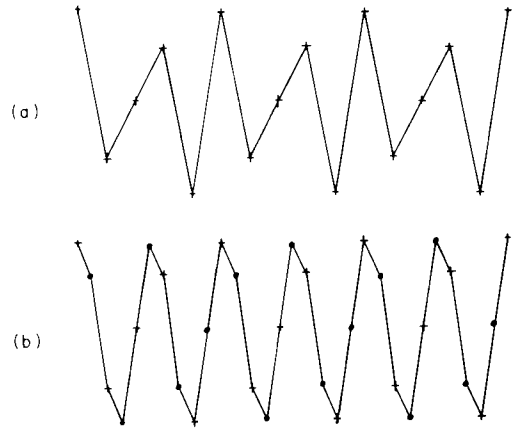

FIG. 5-3. (a) A 100-Hz sine wave sampled at 250 Hz. (b) The same sine wave with interpolated data points inserted.

The frequency limits are normally given as the half-amplitude or 3-dB points, both of which mean that a signal of that frequency would have only one-half the amplitude of a signal inside the pass band (see Goff, Fig. 3-7, Chapter 3 of this volume). An alternative way of specifying frequency response is by time constants. The rise time of an amplifier indicates how fast the circuitry will respond to a step-function input. One usual way of designating rise time is to give the length of time for the output of the amplifier to reach 63% of the input value, as shown in Fig. 5-4. The thing to remember is that the faster the rise time, the higher is the frequency response of the unit. The fall time constant refers to the length of time for the amplifier to return to zero from a steady d.c. input. Obviously, the longer the amplitude holds the value, the lower is its frequency response. The fall time constant may be specified as the time for the output to decay to 37% of the input.

Clearly, the low-frequency response does not affect the choice of sampling rate, but does influence the baseline output. This is especially important when working with the contingent negative variation and has been dis-

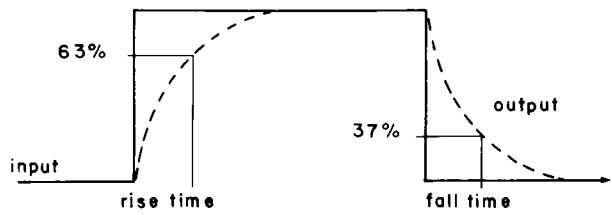

FIG. 5-4. Technique for measuring the rise and fall time of an amplifier.

cussed in the chapters which deal with that technique. However, for evoked response and EEG spectral analysis, baseline shift, whether due to amplifier drift or natural, can be an annoying problem (see pages 232–233). In these cases a half amplitude low-frequency response of .5 Hz is usually satisfactory.

The high-frequency response is the one that should determine the sampling rate (see the previous section). The type of frequency response built into EEG amplifiers is usually a smooth rolloff rather than a very sharp cutoff. For this reason, an additional low-pass filter may be inserted in between the amplifier and the sampler to avoid problems of aliasing. A side effect of extremely sharp cutoff filters is the introduction of a time delay between input and output. This is inherent in the design, since in order for the filter to "make up its mind" about passing part of the signal, it must store a portion of it. This gives us no problem, but the delay then must be taken into consideration when calculating response latencies.

Another factor in deciding upon a sampling rate is the type of measurements to be made upon the data. A common measure extracted from evoked responses is the latency from stimulus onset to some landmark (peak) of the evoked response. The sampling rate will determine how fine this measurement can be made (for example, 100 samples per second gives an interval of 10 msec between data points) without resorting to interpolation techniques. Recall from Equation (2) that we could, no matter what the rate (provided it is fast enough for no information loss), recover the exact time of a peak event. However, this is usually impractical, and measurement is made only to the nearest sample point.

In many cases the final deciding factor may be the choice of sampling rates available to the experimenter. Because of hardware design, only certain clock rates or certain multiples of a base frequency may be available. As long as one has allowed for the preceding considerations, the most convenient rate may be chosen.

2. Data Storage and Continuous Sampling

Once evoked response data are in memory, they can be added to the existing sum being used to form the average (see Section III,D). For most computers and experiments it will be possible to keep all the data in core until completion. However, if there are more different evoked responses than available memory, it may be necessary to save single trials on tape or a disk and form evoked response sums later. For the recording of single time transients we have the same situation. We must write out the data to some auxiliary storage mediums. Magnetic tape is the best choice, being the most compact, cheapest, and fastest (except for the disk). In evoked response work there are usually no timing problems if the data are written out during the interstimulus interval.

In many experimental situations we are interested in a continuous record of a signal for an extended period rather than just a short interval. This would be the case in recording a continuous EEG record for processing. If we had four channels of data, each sampled at 250 Hz, and desired a 10-sec record, this would result in 10,000 words of data. This is normally more than can be stored in core at one time. Since we are continuously sampling, there is no break during which to write the data out to tape. One technique to solve this problem is called double buffering. (See Section II,C,4.)

Essentially the input data buffer is divided into two halves. When the first half is full, these data are written out to tape, while the second half of the buffer is filling. When the second half is full, the role of input and output buffer is switched, the data input to the first half and the second half now being written out. The basic requirement here is that the time required to write the data out be less than the time to fill the half-buffer. This is usually not a problem since sampling occurs at a much slower rate than does the computer-to-tape transfer. However, tape drives usually have a certain start-up time before transfer can occur, during which the tape is brought up to the required speed for recording; this factor should be taken into consideration when the buffer length is chosen.

3. Digital Input

a. Switch Closures. Perhaps the simplest manner in which information can be input to a computer is through the use of switch closures. Many small computers have the capability to detect an external level, often via a simple instruction such as "sense external level." The instruction causes a branch to occur if the level (switch closure) is present. A simple interface utilizing resetting relays can be built so that only button presses will be necessary to communicate with the computer. Octal numbers can be transmitted by this method, either serially bitwise when only a single line is used, or in parallel when more than one level line is available. Simple experiment control can be obtained then by utilizing button presses for decisions at branch points in the program (Gips *et al.*, 1971b).

b. Digital Interfacing. After converting an analog signal to digital form, this digital value must be input to the computer just as the switch closure data.

Figure 5-5 is adapted from the analog input subsystem of the Systems Engineering Laboratory 810B computer; it demonstrates many of the possible ways that digital input can be organized.

The basic manner in which an analog signal is sampled and the digital value obtained in the computer memory is as follows. The program executes an input–output (I/O) instruction, which selects the channel and issues the

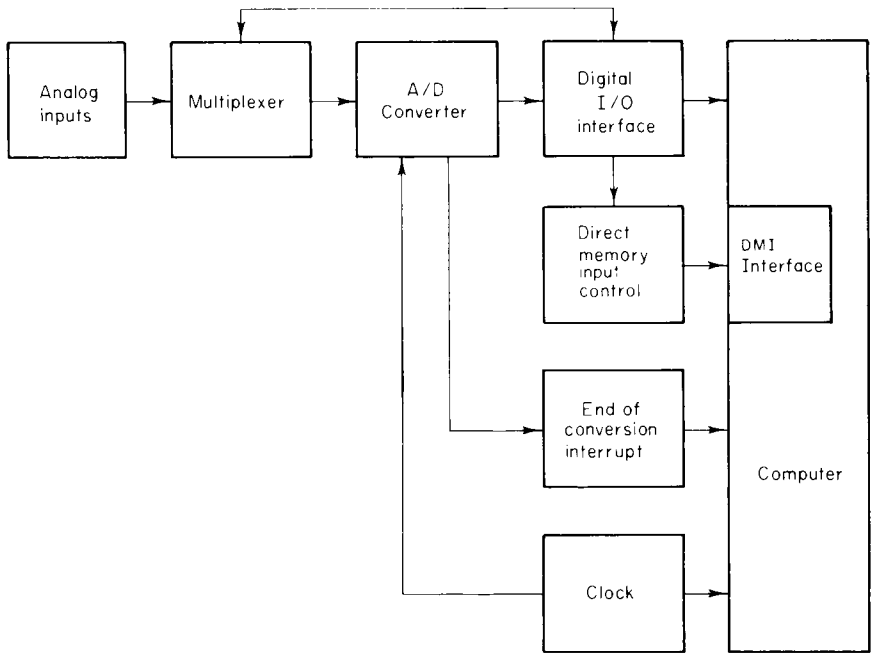

FIG. 5-5. Digital input system illustrating both direct memory and accumulator input from both analog and digital signals.

request for a conversion to be made. This command is sent to the A/D through the digital input–output (DIO) interface. The command starts the A/D conversion operation; when the conversion is complete, the end of conversion interrupt is fired. The computer responds to this interrupt by executing another I/O instruction, which brings the digital word containing the sample into memory through the DIO interface.

In this example two separate commands were necessary to get the value. This was due to the time length required for the conversion to take place. Since the computer is fast, relative to this time, it can be doing something else while waiting for the conversion to take place. Many computers would have only a single command, and the computer would wait for the conversion before going on to the next instruction.

In order to sample at a given rate it is necessary to have a means of generating a time base. In this example, the external clock is set at the desired rate. It then fires an interrupt when each sample is to be made. The interrupt processing routine then makes the sample request. In this manner the computer could be occupied with other tasks (such as averaging) since the sampling is entirely interrupt driven.

4. BUFFERED INPUT

In the manner of sampling analog data described thus far, each sample requires a certain number of instructions to be executed. Usually the time involved is not large, but it is necessary to keep careful track of the code so that sampling proceeds smoothly. Another method of bringing data into a computer exists which eliminates most of the overhead associated with I/O. The general term is *buffered I/O* but each computer system usually has its own special name. In the example of Fig. 5-5 we see an input path labeled DIRECT MEMORY INPUT (DMI). This is the method used by large computer via the DMI by setting the starting memory address of the buffer that is to receive the data and the number of words that are to be transferred in special memory locations. The DMI is then started, and executes the transfer on a "cycle stealing" basis. Whenever the input device has a word ready fer, it informs the DMI, which then interrupts the computer for one memory cycle while the word is transferred directly into core. The DMI increments the buffer address and decrements the word count. In this manner the least possible overhead is used since transfer could occur at up to the memory speed.

Analog input using the DMI would go as follows: The clock would be set at the desired sample rate, but, instead of firing an interrupt, would trigger the A/D converter directly. The A/D then, through the DIO, would inform the DMI, which was previously initiated, that a word was ready. Transfer would proceed as described. Since the rate and the number of words are known, the time when the buffer is full can be computed. Alternatively, the DMI can be connected to an "end of transfer" interrupt. Thus, in an evoked-response experiment the computer could initiate the stimulus, start the DMI to sample the EEG and then return to computation of averages, variance or even another investigator's experiment.

D. Process Control

Although, in general, process control refers to specialized input and output by computers acting in real time, we will use the term to signify the control of stimuli in the experimental situation—clicks, tones, lights, shocks, photographs, and so forth. The output methods generally available include the following: digital output, analog output via digital to analog converter, direct program control of relays, and computer displays of various kinds.

The issue that first needs to be confronted is how directly the computer will control the stimuli. As an example, consider the presentation of a tone: the computer could directly generate the analog signal of the tone or merely

switch on and off an oscillator that was set to generate the tone. In both cases an amplifier and loudspeaker are necessary. There are no hard and fast rules to be used in deciding which way to go. The basic consideration is a trade off between program complexity and how difficult it is to interface the appropriate hardware to the computer, not counting the basic consideration of most laboratories—namely, what equipment is already available? The greatest flexibility usually can be achieved by having the program do as much as possible, since only software changes need to be made to adjust the stimuli. However, the simplest solution may be to gate the oscillator through a program-controlled relay.

In either case it is assumed that the computer is the main controller. However, it is possible to have a hardware controller that presents the stimuli and fires an interrupt to the computer at the same time. In this manner the computer serves in a limited fashion and is essentially a fancy recording or summing unit that makes little use of its potential.

Also it must be remembered that almost any piece of hardware can be connected to and controlled by a computer. All that is required is sufficient ingenuity and the resources to construct the appropriate interface.

1. Programmable Switches

The simplest type of control of external hardware is that provided by opening or closing a switch. This is easily arranged with any computer; in fact many small computers have relays which are directly switched by program commands. Computer digital or analog outputs can control a relay or solid state switch via easily constructed circuitry. It must be remembered that relays require a finite amount of time to open and close and are often plagued by contact bounce problems. For this reason, fast acting relays, for example, of the mercury wetted type, are recommended. These will usually activate within 2 msec or better, which is sufficient for evoked-response work. Using these switches, simple on–off control of equipment is easily handled.

2. Analog Output

Analog output by computer is performed by a device called a *digital-to-analog converter* (D/A). It corresponds exactly to the opposite operation of an A/D. Essentially, each bit of a digital word is used to switch a voltage on or off. These voltages are summed, and the result is an analog signal that can take on any value corresponding to the discrete levels determined by the digital word. The analog level output then is held until the next request for a new value is made. By making successive requests for different values, a continuous time-varying analog signal can be generated. Many of the

same considerations that arose under sampling also apply here. Only a frequency up to one-half of the output rate can be generated. An additional problem is introduced due to the sharp transitions between discrete values. These fast transitions introduce spurious high frequencies into the output signal. This is usually overcome by smoothing and filtering the analog signal before it is actually used.

3. AUDITORY STIMULI

a. CLICKS. Clicks are easily generated by outputing a value through the D/A for a brief interval; the analog signal then is fed into an ordinary audio amplifier and speaker. The greater the value of the number output, the more intense is the click.

b. TONES. These require a continuous wave form, and if precise frequency control is not essential, they can conveniently be generated under program control. For example, a 500-Hz tone can be generated by alternately outputing 0 volts and v volts at 1000 Hz, or one value every millisecond (see Fig. 5-6a). Since the speaker cannot faithfully respond to the high-frequency components, the "tone" is really narrow band noise centered 500 Hz—quite adequate for certain evoked responses or orienting responses. A simple filter consisting of a low- and high-pass circuit in series (Fig. 5-6b) will improve the signal considerably. The values of the resistors and capacitors are chosen from

$$1/RC = 2f, \tag{3}$$

where f is the frequency to be computer generated. For example, for a 500-Hz tone, a 10-kΩ resistor and a .1-mF capacitor ($C = .1 \times 10^{-6}$ F)

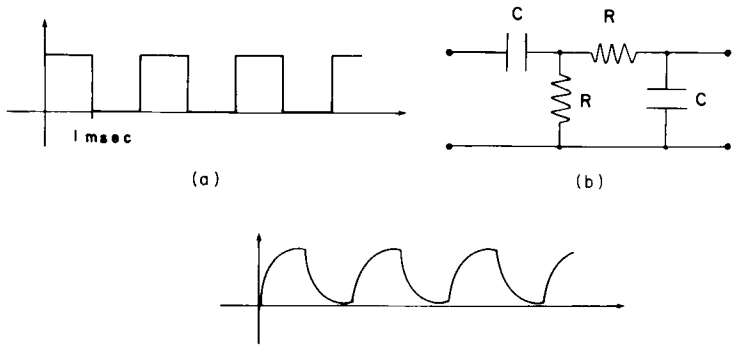

FIG. 5-6. Filtering of D/A output to produce a sine wave: (a) output of D/A converter; (b) RC circuit to filter signal with values chosen from Eq. (3); (c) filtered output.

might be used. The filtered output (Fig. 6c) will resemble a sine wave of 500 Hz. Note that this circuit will attenuate the signal lead, and the voltage must be adjusted accordingly.

If a more accurate sine wave were desired, a faster output could be used with calculated values in a table for the actual sine wave. These values can be output at varying rates to generate tone frequencies with precise center frequencies but with some small contribution from higher frequencies at multiples of the base frequency. As in analog input, many computers have the capacity for buffered D/A output; the table of values in memory can be output from the memory table directly without the program needing to keep track of the operation. Since the clock rates on these buffered output devices are usually even multiples of each other, tones not an octave apart must be generated from separate tables more than 1 cycle in length (see Lovell & Carterette, 1972; Matthews, 1969).

c. RAMP FUNCTIONS. Since the sudden onset of an auditory signal may cause a speaker to "pop" at the beginning of a tone, a ramp function can easily be generated (see Chapter 4 by Vaughan). For the 500-Hz tone, for example, the first ten values can form steps up to the maximum amplitude excursion.

d. VERBAL STIMULI. Words or animal sounds are often used in evoked response studies; precise repetition and timing of presentation are necessary (see McAdam, Chapter 6 of this volume). The analog signals can be recorded by sampling a microphone–audio amplifier output at 4000–8000 Hz and storing the signal. This signal can be stored on magnetic tape or disk and output on command through the D/A converter. The 4000-Hz rate will give approximately telephone quality voice, since it contains frequencies only up to 2000 Hz. Since large numbers of data points must be output, "double-buffering" techniques (see Section II,C,2) may be necessary. Speech also may be produced synthetically for extremely precise control of the auditory stimulus even in a small computer (Ochiai & Krones, 1972) or synthetic stimuli can be tape-recorded (for example, Wood & Goff, 1971). The development of relatively low-cost hardware speech synthesizers offers an even simpler means of producing quite intelligible verbal stimuli. They may be computer controlled to output a preset message or to actually construct the speech from stored phonemes.

4. VISUAL STIMULI

Visual stimuli require further mention since, except for CRT-type display systems, computers do not have the capability to generate such signals directly. Common types of light sources used for visual stimulation include

flash tubes, hot cathode fluorescent lamps, glow modulator tubes, light-emitting diodes, and electroluminescent panels. These devices usually are available with control circuitry that will accept logic signals directly either from the computer or an appropriate interface.

5. VISUAL DISPLAY SYSTEMS

Many computers either come with some type of CRT display or have one available as an optional peripheral device. The CRT can provide a completely silent, very precise stimulus source. With short persistence phosphors, tachistoscopic presentations can be made. The stimuli can be controlled by the subject, and thus are useful in biofeedback studies. Examples of CRT use in evoked response experiments are given by Beatty (1969), Buchsbaum (1970), and Buchsbaum and Fedio (1969).

6. ELECTRICAL STIMULATION

Since electrical stimuli usually require constant current regulation rather than merely voltage levels, digital control of a constant current stimulator may be the most convenient (for example, Emde & Shipton, 1970).

III. Data Conditioning

After the signal of interest has been sampled and collected in the computer, some general operations on the data may be required before analysis can proceed.

The data, once in core, are a discrete time series of finite record length. We will represent it as $X(i)$, where $i = 1, \ldots, N$. The array index i may be thought of as the time variable. With a constant intersample interval of T sec, the length of the record is then $(N - 1)T$ sec. One must always be on the lookout for problems arising from how the range of the index is given in various formulas, that is, it may be 1 to N, 0 to $N - 1$, or 0 to N, for which the total number of data points differ. Also whether the first data point corresponds to $t = 0$ or $t = T$ is often important. There is no reason to choose any method of representation over another, but you must understand what you have and be consistent. FORTRAN always starts the index at 1, so we have chosen that method, as shown above.

A. Mean and Trend Removal

Typical problems associated with EEG and other high gain amplifiers include a d.c. bias or offset and drift over time. This causes a shifted and moving baseline in the data recorded. It is usually desirable to have a base-

line reference of zero, keeping drift at a minimum, so that comparison over time can be made. For fixed-length records this is easily accomplished by removing the mean value and time trend from the data. The mean is removed by

$$Y(i) = X(i) - M, \qquad i = 1, \ldots, N, \tag{4}$$

where

$$M = \frac{1}{N} \sum_{i=1}^{n} X(i).$$

Considering only a linear trend, it is removed by calculating a linear regression line and then subtracting that line from the data series. Thus

$$Y(i) = X(i) - B\left(\frac{2i - N - 1}{2}\right), \tag{5}$$

where

$$B = \frac{6 \sum_{i=1}^{n} (2i - N - 1)X(i)}{(N - 1)(N)(N + 1)}$$

is convenient for small computer use (Mejia & Chang, 1970).

B. Normalization

When data are obtained utilizing amplifiers of different gain or A/D converters of different quantization, direct comparisons or measurement (dependent on amplitude) of the data can be misleading. If the calibration factors are known, then one set of data can be multiplied by the appropriate factor. However, in many cases exact calibration values are not available, so some other method of reducing the data to a common base is required. This is usually termed *normalization*, and there are several ways it can be carried out. One method is to reduce the data to a time series of zero mean value and standard deviation of one. The mean is removed as in the previous section and the data divided by the calculated standard deviation σ_x:

$$\sigma_x = \frac{1}{N}\left[\sum_{i=1}^{N} X^2(i)\right]^{1/2},$$
$$Y(i) = X(i)/\sigma_x; \qquad i = 1, \ldots, N. \tag{6}$$

This is particularly useful when integer arithmetic is to be carried out since it reduces the range of the data.

C. *Smoothing and Filtering*

Often data are contaminated with high frequencies that are not of interest or would merely confuse the analysis. These high frequencies can be eliminated, thereby smoothing the data. While a moving average is easy to compute, it distorts the frequency characteristics of the signal and may attenuate the signal amplitude. A simple digital low-pass filter can be used for this. The following is from von der Grochen (1969):

$$\begin{aligned} F(i) &= AX(i) - BF(i-1), \\ Y(i) &= F(i) - CY(i-1) - DY(i-2), \end{aligned} \tag{7}$$

where

$$A = K, \qquad B = K - 1, \qquad C = -(1 - K\cos 40^\circ),$$

$$D = (1 - K\cos 40^\circ)^2 + K^2 \sin^2 40^\circ.$$

The value of K is adjusted according to the relation $K = 2f_c/R_s$, where f_c is the desired cutoff frequency in hertz and R_s is the sampling rate in samples per second. As before, X is the input array and Y the output array. F serves only for intermediate storage, and only two variables are needed, F and G in the algorithm which follows (see Table 5-1). The initial values

TABLE 5-1

```
      DIMENSION X(N), Y(N)
C     Set initial values
      F = A*X(1)
      Y(1) = F
      G = F
      F = A*X(2) - B*G
      Y(2) = F - C*Y(1)
      G = F
C     First valid output is third value
      DO 100 I = 3,N
      F = A*X(I) - B*G
      Y(I) = F - C*Y(I - 1) - D*Y(I - 2)
      G = F
100   CONTINUE
```

are taken as zero, so that a valid output value is not obtained until the third sample. This delay is a common feature of both analog and digital filters.

D. Averaging

Whereas evoked-response averaging can be done by measuring EEG records manually (for example, Shimizu, 1966) or photographically (Dawson, 1951) or using analog devices, the most convenient, rapid, and accurate technique is the use of a special or general purpose digital computer.

1. Special-Purpose Averagers

These are special-purpose computers that include analog-to-digital converters with a permanent program to sample EEG at fixed intervals and compute the sum for each sampling interval in the averaging epoch (see Fig. 5-7). They are usually equipped with 1–4 separate A/D converters and 400–1000 memory locations for accumulating the sums. The sampling intervals may be selected by switches. The finished sums are available as a CRT display, as an analog signal for X–Y plots, and with peripheral interfaces in digital form for output on paper or magnetic tape.

2. Simple Averaging

As can be seen in Fig. 5-7, the computation to calculate the average evoked potential (AER) is very straightforward. The program flow chart shown in Fig. 5-7 is without details of process control, artifact checking, mean removal, or other computations. Only enough memory to hold the AER (and the brief program) is required since each EEG sample is added to the appropriate memory location before the next new EEG sample is obtained. Since the program is brief in comparison to a 2–4-msec sampling interval and a 500-msec epoch following the stimulus; this provides adequate resolution of AER components and samples past the last really reliable AER components at 300 msec. Sampling can begin before the stimulus to provide a prestimulus isoelectric baseline against which to measure peak amplitudes; an average of four or eight of these points can be stored conveniently in the first AER location. After calculation of the sum, division by the number of trials yields the average.

3. Backward Averaging

It is sometimes desirable to average EEG activity preceding a subject's behavioral or physiological response—for example, evoked activity preceding a key press in a reaction time trial (see Cohen, Chapter 7 of this volume). This is easily done on-line by storing each EEG sample in an

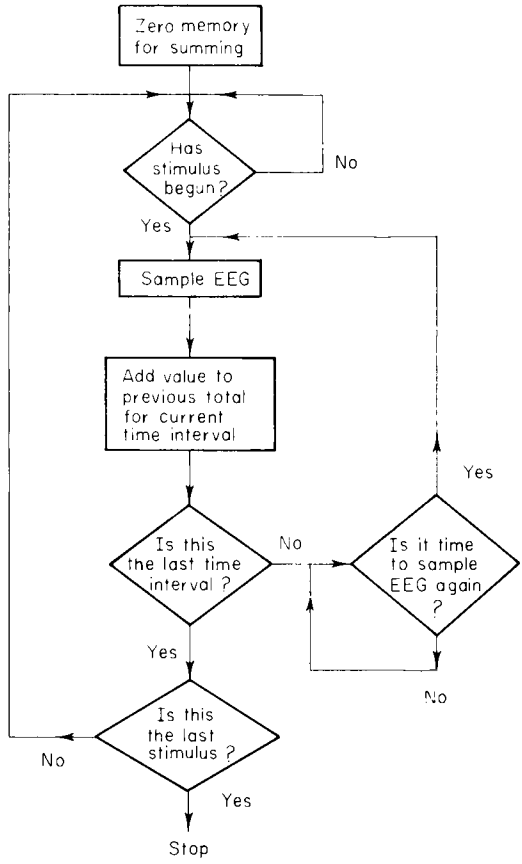

FIG. 5-7. Flow chart for simple averaging.

array. The oldest value is replaced by the newest one at each time interval until the subject has responded and the postresponse epoch is over. The time that the key press occurred and a pointer to the current memory location for EEG storage are saved, and after the trial is over, the EEG sample is added point by point to the accumulating average, the key press points being aligned. Backward averaging can also be accomplished in special-purpose averagers by tape recording EEG signals and key signals and playing the tape backward to allow the key signal to initiate the averaging procedure; this requires a forward pass to average the post-key-press activity.

4. Removing or Retaining the Mean Level

Since the AER consists primarily of components ranging from 1 to 40 Hz, the mean baseline prestimulus level of the EEG is of little interest. Peak

amplitudes can be measured from peak to trough or to an isoelectric "zero" or "baseline," usually a prestimulus point. Whereas the EEG amplifier should have held the EEG centered around zero level, small biases are common, and after summing a hundred trials, the offset from a digital value of zero may be considerable. The first 5 msec of the AER can be used as a "baseline," especially when low-pass filters which delay the EEG signal are used. This level can be subtracted from every value in the AER curve so that each AER value then can be used as an amplitude, and to allow convenient positioning of the curves on digital displays or plots. If the baseline value is subtracted from each point with each trial, the AER can be held fairly close to a mean of zero. Alternatively, it can be done at the end of the averaging process, but this procedure sometimes occasions problems with "wrap around."

5. Wrap Around and Analog-to-Digital Converter Range and Average Evoked Response Accuracy

As described earlier in this volume by Vaughan, Chapter 4, the accuracy of the AER depends partly on the signal-to-noise ratio and the number of trials averaged. It also depends on the accuracy and range of the sampling of the EEG.

An AER can be computed on the basis of only one-bit A/D conversion (Shimizu, 1966); merely recording whether EEG was positive or negative at each time interval can yield recognizable AERs. But, in practice, an 8-bit range generally needs to be used because the EEG signal mean (the d.c. level) may drift somewhat or change after a movement artifact. To keep the EEG in the range of the A/D converter, its normal excursion should occupy about 25% of the range (thus yielding 4–6 bits of change between an EEG peak and successive trough). Thus, the low-order bits contain the AER information. When successive EEG samples are summed, these must be retained in the sum. In order to retain this accuracy with integer arithmetic it is necessary to preserve most of these bits in the sum calculated. Thus, the value obtained at each time interval cannot be divided by the total number of AER trials as it is collected, or the AER will be largely lost. However, if too many bits are saved, the sum may overflow the computer word, usually 12–16 bits. For example, if the A/D converter yields 8 bits (7 bits and a sign), the largest number is 127 (177_8). As a worst case, if this highest value occurred every time, after 16 trials the sum would be 2032. If the computer had a 12-bit memory word, the largest positive signed number would be +2047; on the seventeenth AER trial, that particular time interval sum would exceed 2047 and an overflow would result. For a 12-bit machine, the addition of 1 to the number +2047 gives the result −2047[2]; the addition

[2]This is true for one's complement arithmetic; for two's complement it would be −2046.

of 127 would give the result −1919. This kind of overflow is illustrated in Fig. 5-8. Continued summing would move the AER back into middle range and remove the discontinuity. This discontinuity can be prevented in several ways:

1. *Limiting the number of AER trials.* The number of AER trials to be summed can be limited so that sums over 12 bits are not obtained. In our example, this would be a limit of 16 trials to be certain, although if the d.c. level is held close to zero, 32, or even 64 trials might be run.

2. *Reduction of the number of bits sampled by scaling.* Most computers have a command to shift all bits one or more places to the right with the low order bits being lost. This divides by the number 2 for each place shifted. Reducing the number of bits from 8 to 6 would allow 64 trials to be summed as the worst case, and would allow preservation of any prestimulus baseline for CNV work. It should be noted that this influences the accuracy of the sum very little. For example, assuming an EEG with an 8-bit range peak to peak, the loss in accuracy (one standard deviation range) through shifting 3 bits to the right in the sum of 100 random numbers will be less than 20 units, or only .2 units in the mean—a trivial amount (see Whittaker & Robinson, 1944).

3. *Removal of the mean from each trial.* The mean of the entire AER can be calculated after each trial and then subtracted from each point in raw data before addition of the raw data to the sum. This allows accumulation of an evoked-response sum, the positive and negative peaks of which are numbers separated by the maximum value of a computer word. For a 64-μV peak-to-peak EEG signal A/D converted at 1 μV per computer unit and an evoked response of 16 μV peak to peak, this allows approximately

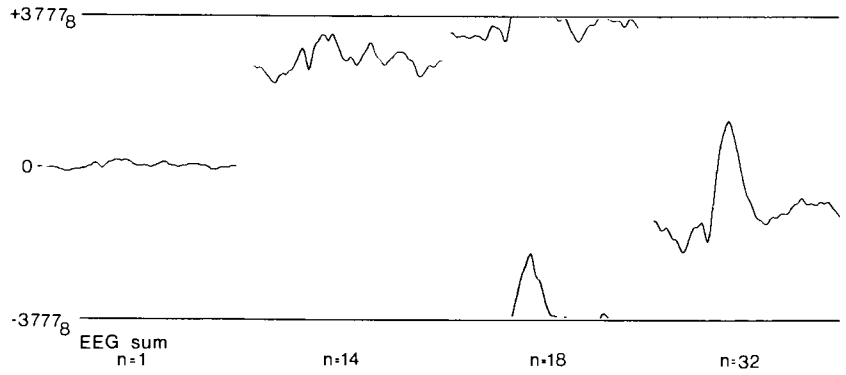

FIG. 5-8. Overflow and wrap around addition in evoked response summing.

128 trials before wrap around begins in a 12-bit word. The mean may be fairly well approximated by using a prestimulus value and subtracting it after each EEG value is sampled, and then adding the connected value to the AER sum—thus avoiding the need for a separate raw trial storage area in memory.

4. *Two-register addition.* "Double precision" or the use of two memory positions to form a double-length integer word may be used to accumulate the AER sum; after summation it may be divided by a multiple of the number of trials so that each AER point can fit as an integer number in a single memory location. This is rarely necessary, as the signal-to-noise ratio in EEG averaging makes greater than 12-bit (one part in 2000) accuracy quite adequate, and further scaling of raw values should be considered.

5. *Floating-point addition.* This is another technique that converts each integer number to a logarithm and stores the exponent and mantissa. However, since most small computers do not have specific single instructions to do this, a series of up to several hundred commands is necessary to convert the A/D sample to floating-point form and perform an addition. Further, both floating-point and double-precision data points require twice as much storage for the AER as the integer format.

6. *Removal of wrap around after summing.* Special-purpose averagers may do this by allowing the addition of a constant to the AER to bring the broken fragments together. In Fig. 5-8, addition of about 1000 to the AER where $n = 18$ would rejoin the curve. This can be done by general purpose computer as outlined in Section III,D,6 and fitted into a single integer word as long as the range of the AER does not exceed the word size. If it does, usually more than one wrap around has occurred and the unraveling becomes increasingly complex.

For some CNV studies, or averaging of output from devices where baseline level is important (for example, average evoked heart rate response from a cardiotachometer or average pupillary diameter response) the actual mean level must be calculated and it cannot be removed from each trial. In these cases, the division of raw data by scaling (Technique No. 2) is usually most convenient since such data are rarely accurate beyond 1 part in 64 (6 bits).

6. Wrap Around Removal

We will use the following example to illustrate one method of handling wrap around. Let us suppose that our evoked response sum was accumulated in a 16-bit register. The data are shifted 4 bits to the right to allow for

wrap around correction. The data are checked for a discontinuity of more than one-fourth of the maximum which would be 4096 in the remaining 12 bits. For an evoked response 125 points long stored in the array IAER the following FORTRAN statements will perform the necessary correction:

```
      DO 100 I = 1,124
      IT = IAER(I) - IAER(I + 1)
      IF (ABS(IT).LE.1000) GO TO 100
      IAER(I + 1) = IAER(I + 1) + ISIGN(4095,IT)
100   CONTINUE.
```

ISIGN is a standard FORTRAN function that applies the sign of the second argument to the absolute value of the first argument.

7. Average Evoked Response Calibration

The gain of the entire computer-amplifier system is most reliably determined by sending a known microvolt size signal into the EEG amplifier and running a program which digitizes and outputs the single trace. The calibration signal available from many EEG amplifiers is suitable. If, for example, the calibration signal is 50 μV peak to peak and the highest and lowest digital values on our 10-bit, 10-V A/D converter are +100 and −100 (recorded in response to the signal), the signal of 50 μV produced a signal 200 units high, or .5 V high. One computer unit then equals μV. The system gain thus is 10,000 times. Examining an AER produced by summing 100 trials, we find a peak value of 700 and a trough value of −300, or 1000 units. This would be an average of 1000/100 or 10 units per trial; at 1 unit per microvolt, this is an AER amplitude of 10 μV.

8. Computation of the Point-by-Point Variance for Average Evoked Response

The standard deviation for each point in the AER curve may be easily calculated as the analog signal is sampled. Each AER epoch is sampled, and the data are placed on a temporary storage array. The mean is then calculated and subtracted from each point (see Vaughan, Chapter 4 of this volume). The AER sum and sum of the squares then may be calculated. Both the mean and the sums of squares must be calculated using floating-point or double-precision arithmetic to avoid overflow. After the experiment is finished, the division of the sum of the squares at each point by the number of trials yields the variance. Alternatively, if the A/D converter outputs a number of bits equal to one-half the word length, the squared value may be divided by the total number of trials after each trial and this number summed; this would allow integer arithmetic and storage of each point in the variance

curve in only one word of computer memory. Since the A/D converter output bit length is usually less than the full computer word, there is no loss of accuracy using this technique.

9. Averaging Pure Sinusoids

One might expect a pure sinusoidal signal, such as 60-Hz artifacts, to be completely removed in the averaging process, as long as they are not time locked to the signal. However, the random phase averaging of a sinusoid yields a sinusoid of amplitude reduced approximately to 1 per number of trials averaged, not reduced to zero. This occurs because the variation in starting time of the sinusoid (phase angle) is not perfectly balanced and at the end of any series of averages only one trial will suffice to yield a perfect sine wave in the average. This problem is somewhat diminished with EEG such as the alpha wave since its frequency shifts slightly from second to second.

10. Averaging from Tape

As mentioned earlier, we would discourage the use of FM tape recordings[3] as an intermediate step in evoked response or frequency analysis unless computer time is unavailable for on-line process control and data collection. If tape is to be used for evoked response work, separate channels should be used for EEG and timing signals which mark the stimulus onset. Care should be taken to keep the tape scrupulously free of dust since spurious signal pulses may appear; it should be demounted from the tape drive at night and wrapped in a clean plastic box or bag. It is helpful to have a timing pulse with a fast rise time (<100 μsec) and a long duration (>500 msec) so that once the computer program has identified a rise in level on the signal channel it can sample again to check if the level is still present to eliminate artificial signals. Then, after the evoked potential epoch bias is finished, it can check if the signal has returned to baseline. It is helpful to display both the signal and the EEG on a digital CRT while the program runs; this provides a visual check that the signal identification is proceeding correctly. The program also should check each interstimulus interval to insure that premature spurious signals are not averaged.

11. Checking for System Function

Programming and hardware errors can combine and be difficult to check; final tests utilizing the entire system are desirable. The following are useful evoked response checkout procedures.

[3] Most ordinary AM audio tape recorders have a frequency response only down to 40 Hz so they cannot be used for EEG recording.

1. *Testing for stimulus artifacts.* Photostimulators, relays and audio equipment may broadcast electrical transients that appear in the EEG at levels too low to observe on single traces but can contribute to an average evoked response. An AER run can be made with "artificial man"—three 10K resistors tied together in a triangle with one EEG lead at each angle (Fig. 5-9). The artificial man can be placed in the position of the subject's head. The resultant AER should contain no 60-Hz or initial component. Surrounding a photostimulator or control relays with a metal shield connected to ground, or using smaller relays or solid state devices, may help to eliminate initial transcients. Using leads of short, equal length, twisted around one another, may also be useful.

2. *Testing for correct location and number of average trials.* A hand-operated push button that can produce a 10-μV, 100-msec pulse input to the EEG amplifier is useful. The button can be pushed once during an AER run after a particular stimulus condition to check if the AER to that condition appears in the correct memory location. Similarly, the output of a photocell or microphone may be averaged (with suitable signal attenuation) to check stimulus timing and physical parameters. Trials should also be counted and the total run timed to see if the programmer's conception is really being executed. Other useful EEG processing computational checking hints are given by Walter (1972).

E. Artifact Removal

In some experimental designs, head, jaw, or eye movements may be expected to be systematically related to stimulus conditions. Whereas it is better to plan the experiment to eliminate such trials, in certain circumstances it may be unavoidable. Normally, electromyographic bursts in the EEG from such sources as clenching the jaw contain high frequencies greater than 60 Hz and are quite variably time locked to the stimulus so that simple filtering eliminates them, and they do not contaminate an average appreciably. They may also cause a sudden d.c. level shift in the EEG, placing the level outside the range of the A/D converter; in an AER experiment

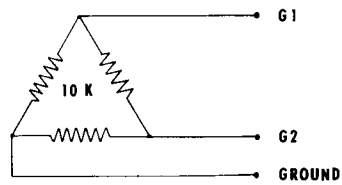

FIG. 5-9. "Artificial man" for system checkout.

a straight line then is summed, which affects the final average minimally. If desired, these artifacts may be prevented from contaminating the average by storing each EEG epoch in a temporary storage location and, at the completion of the sampling period, checking if values outside an allowable range appear. If they do not, the sample then is added to the appropriate evoked response sum; if not, the trial is repeated. It should be noted that this may be quite difficult in experiments where stimulus sequences are under study. Eye movement recordings also may be sampled and saved in a temporary store and similarly searched for artifacts. Alternatively, both EEG and eye movement epochs can be saved in digital form and after completion of the experiment visually scanned for inclusion in a final average. This is superior to recording eye movements on polygraph paper since: (1) problems may occur with matching paper and digital EEG records and (2) manual entry of trial numbers to be included or excluded must be made.

IV. Experimental Systems

The programs that carry out each of the three phases in psychophysiological research—data collection–process control, individual subject response measurement, and group statistical summary—are most efficiently written as separate programs or subroutines. But in order to move smoothly from incoming EEG to finished *t* test or from AER to CNV experimentation, each program must be planned with each of the others in mind.

A. Data Collection Process Control

When running the experiment, after a subject (or animal) enters the laboratory and has bioelectric signal transducers attached, the experimenter selects a specific experimental procedure and condition. He then runs the subject and labels the record. These functions are best managed by an operating system program. This program interrogates the experimenter as to the subject name, date, experiment, and condition, loads the specific experiment into the computer, checks the instrumentation, displays the raw incoming data for a visual check on range and centering, initiates the experimental run, outputs the data and labels it with subject and experiment information, and returns to experimenter interrogation for the next experimental run. Careful modular construction of the experimental run programs allows for rapid shifts from one experiment type to the next. Handling data output and evoked-response display through the system rather than directly within the experiment prevents duplication of output or data file protection

routines. A standard data format used for many experiments is valuable, even if it is not as compact as possible for every experiment. The value of convenient, alphabetic, and structured labeling of records cannot be overestimated.

B. Individual Subject Response Measurement

Once collected, the evoked responses, EEG single trials or other physiological data may need to be viewed by CRT, have specific records edited out, or have points of interest (for example, peaks, amplitudes; see Ax, 1967) selected visually. This is most conveniently done by using a digital CRT display of records and an adjustable cursor or light pen to identify segments of records and to select relevant points. The program can display the alphabetic identification, evoked-potential trials, and relevant measurements for rapid analysis. Once measures are obtained either visually or by computational techniques, the summary data can be entered together with the entire physiological record for access by the next stage.

C. Group Statistical Summary

Individual measurements now may be recorded or transformed to have group or condition comparisons made statistically. The summary data records need to be easily accessible in random order for convenient summary. Depending on the size of the computer, the availability of high level languages (for example, FORTRAN) and the complexity of the analysis the investigator may choose to analyze his data on his process-control computer or enter the data into a large-scale computer. A choice of output device depends primarily on data volume, frequency of use and is limited by cost.

D. Process-Control Languages

Most experiments are written in "assembly" languages—where each command corresponds to a single machine instruction. Increasingly, however, a variety of higher-level languages are being developed. These are often quite restricted in capability and specific to a single machine, but may be very useful in a laboratory where many modifications of a basic experiment are done. Evoked-response language (ERL) has been developed in our laboratory (Gips, Pfefferbaum, & Buchsbaum, 1971a), and a variety of other process-control languages have been written (see Sidowski, 1972).

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Chapter 6

The Contingent Negative Variations

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I. Introduction: The Case for Broadening Our Definitions

The term, contingent negative variation, taken in the narrow sense refers to the phenomenon first described by Walter, Cooper, Aldridge, McCallum and Winter in 1964 of a vertex negative slow wave which develops during the foreperiod while subjects are performing a fixed foreperiod reaction time task. In a broader sense, the contingent negative variation was among the very first brain electrophysiological phenomena to be reported; in the

brief summary of Richard Caton's presentation, "The electric currents of the brain," which was given to the Annual Meeting of the British Medical Association in Edinburgh in July, 1875, the following appears: "When any part of the grey matter is in a state of functional activity, its electric current usually exhibits negative variation. For example, on the areas shown by Dr. Ferrier to be related to rotation of the head and to mastication, negative variation of the current was observed to occur whenever those two acts respectively were performed." I would like to suggest that it is appropriate for us to adopt the broader meaning of contingent negative variation. To avoid unnecessary confusion, we should speak of the contingent negative variations, of which Walter's CNV is one. As of now, the other major contingent negative variation is the readiness potential (RP) first described by Kornhuber and Deecke (1965) as a negative potential arising just prior to the initiation of a voluntary motor act.

The CNV and the RP have much in common; both are negative variations which are contingent upon the performance of some response. Both have been shown to be strongly affected by manipulations of the situation which could be called "psychological." Both presumably reflect a "state of functional activity" in the cortex where they are generated. There are also marked differences between CNV and RP; CNV development is linked to the warning stimulus which is not used in the RP recording situation, and the areal distributions of the two waves differ. Since the CNV is treated in considerable detail by two other contributors to this volume (Cohen and Hillyard), I will concentrate my efforts on the RP, and upon the relationships between the two potentials.

II. Response-Related Potentials

A. History

The discoveries of the CNV and RP were virtually cotemporaneous. Walter *et al.* first reported the CNV in 1964, and Kornhuber and Deecke first reported the RP in 1965 (the latter report was received by *Pflüger's Archiv.* in 1964). Of the two phenomena, the CNV has received the greater attention. Nonetheless, it is interesting to note that considerable attention was given to the RP and to relationships between RP and CNV at the Second International Congress on the CNV, held in Vancouver in 1971. Gilden, Vaughan, and Costa (1966) were also early on the scene with a description of movement-related potentials, a discovery which they made independently of Kornhuber and Deecke.

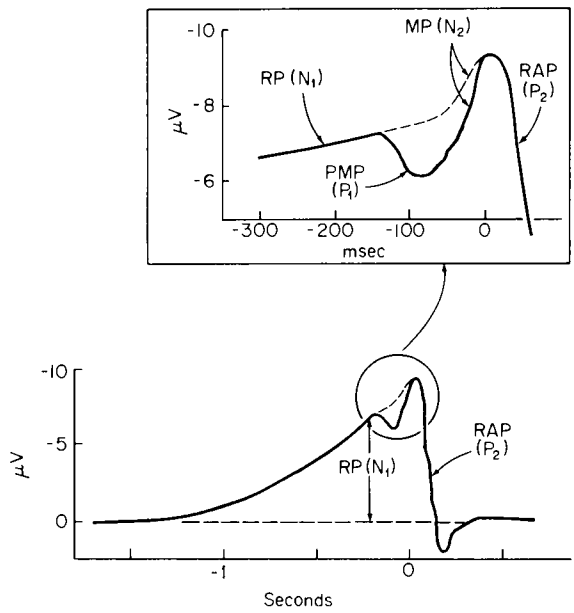

FIG. 6-1. Schematic response-related potential showing the various components as presented by Deecke *et al.* (1969), and (in parenthesis) by Vaughan *et al.* (1968). The insert shows the smaller PMP and MP components which occur just prior to the response (time zero). Abbreviations: RP, readiness potential; PMP, premotion positivity; MP, motor potential; RAP, reafferent potential.

B. Nomenclature

Figure 6-1 presents an idealized response related potential, along with the labels for its various components as they have been suggested by Deecke, Scheid, and Kornhuber (1969) and by Vaughan, Costa, and Ritter (1968). The earliest event is a slowly rising negative potential beginning up to 1500 msec prior to response initiation as measured by EMG. This is the RP, or readiness potential, and is the largest of the components. It tends to be maximal at the vertex and often to show some laterality. It may appear as a positive potential over anterior frontal sites. The RP may be followed by a premotion positivity (PMP), a very small and brief potential occurring at a latency of some 80 msec prior to the movement. Where the PMP exists, the next occurring motor potential (MP) appears as a reversal of it. When the PMP is not seen, the MP appears as a sharp, more negative-going inflection growing out of the RP. The MP occurs some 55 msec before the movement. Following the movement, there is a large positive deflection which Deecke *et al.* (1969) have called the reafferent potential (RAP), and this is followed by recovery to baseline. Like the RP, the PMP

tends to be widely distributed over the cortex. The MP however tends to be localized over the motor cortex contralateral to the responding musculature. The extent to which these various components can be delineated is heavily dependent upon the sort of movement chosen and, moreover, upon the size of sample analyzed (see Section II,D, below). All of the work which has been done to elucidate what might be called the "psychological significance" of response-related potentials has dealt with the RP.

C. Techniques

1. Recording Techniques

The faithful presentation of response-related potentials and especially of the slowest RP component requires employing stable, nonpolarizing electrodes and direct coupled amplification. In practice, some compromise of the electrode stability is always experienced, but the amount of drift should be kept below 1 μV over the period to be analyzed. Silver-silver chloride electrodes are commonly used, either in some homemade form or in one of a number of patent forms currently available. These should be firmly affixed to cleansed and abraded scalp, and care should be taken to assure that the impedances of the electrode-subject junctions are below 10 kΩ, and that the impedances do not differ from each other markedly. (Note: These impedance measures must not be done with a standard ohmeter, which impresses a relatively large voltage across the electrodes, causing them to drift badly. Some sort of a.c. energized impedance meter should be used.)

Practical considerations also often dictate some compromise of the requirement that the amplification system have an infinite time constant. In any case, the time constant of the amplification system (including also the tape recorder and the response averager) should be at least several seconds. (Note: The time constants shown on the face panels of most amplifiers are nominal at best. A test should be run, using a square-wave input, to determine the actual time constant of the system. Even when direct-coupled amplifiers are used, this test should be run and it should encompass the entire system from amplifier input through response averager output and including any intervening data storage gear such as a magnetic tape recorder.)

2. Electrode Locations

Response-related potentials are commonly sampled over the frontal lobes since most experiments seek to link them to motor activity. Vaughan *et al.* (1968) have provided very systematic data concerning the distribution

of these potentials, especially across the motor strip, for various movements. The general conclusion which may be drawn from their data is that if the movement is well lateralized (say elevation of the foot or of the hand), then the motor potentials tend to be maximum contralateral to the responding musculature and over sites topographically representing the responding musculature. If, on the other hand, the movement involves midline musculature (say, pressing the tongue against the upper incisors), then the motor potential tends to be bimodal, with symmetrical peaks, though again over areas projecting to the responding musculature.

Deecke *et al.* (1969) report maximal localization only for the MP component, with more general distribution of the RP and PMP. Their localization of the MP component is in line with that reported by Vaughan *et al.* For the RP and PMP, they report maximal responses at the vertex, although the RP does show a small but significant asymmetry in favor of the contralateral hemisphere.

There are a number of schemes for describing electrode locations. Clearly the most popular is the so-called International 10–20 system (Jasper, 1958) which is widely used in both clinical and experimental EEG. Often, however, it is necessary to place electrodes at sites other than those specified in the 10–20 system. For purposes of presentation of methods, it is useful to specify these ad hoc sites either in terms of the 10–20 system (e.g., a point midway between C_z and C_4) or in terms of prominent bony landmarks (e.g., 2 cm above the inion on the midline). While other methods of electrode location are available, and while they may indeed be better methods, specification of electrode sites in the terms outlined above is still to be preferred if only because it uses common and precise terminology.

3. Data Processing

To analyze response-related potentials it is necessary to be able to look backward in time. Unlike the CNV situation where there is a warning stimulus which can serve to synchronize the analysis device and which precedes the electrical event of interest, to look at an RP one must synchronize the analysis with an event—the response—which follows it in time. There are a number of instrument solutions to this problem. The one which is used most widely is to record the electrical data on magnetic tape and to then reproduce the data playing the tape in the reverse direction. (Most instrument-grade tape recorders allow this to be done.) When this method is used, the data analysis is, of course, done offline. While this is a disadvantage in terms of the time involved, it is often a necessary procedure in any case because trials need to be edited to be free of artifact. Also, it is often part of the experimental design to group responses into

bins on the basis of properties of them which cannot be immediately assessed, e.g., the most forceful responses as compared to the weakest.

Many instrumental tape recorders have separate and independent record and reproduce heads. If one can tap the output of the reproduce head during recording, it is possible to analyze response-related potentials on-line. There is always some length of tape between record and reproduce heads, and by utilizing this feature along with the appropriate choice of tape speed, it is possible to sample activity which occurred some few seconds prior to the response from the reproduce head output. In this application response occurrence is used to start the analysis sweep of the response averager. Since it is almost always necessary to edit the electrical activity to screen out trials where eye- or extraneous-movement induced potentials occur, this on-line procedure is ordinarily only useful to get a rough picture of what the data will look like.

If a general purpose computer is available for data analysis, data may be "boxcarred," a process wherein the data are cycled through storage with the earlier events dropping out to be replaced by later ones in the manner of a sliding time window centered on the possible time of response occurrence. With response occurrence, the process is stopped, post response data is collected, and the entire sample is subjected to whatever further analysis may seem appropriate. It is also possible, using a general purpose computer, to edit trials according to whatever predetermined criteria might be programmed into the system.

The usual analysis procedure applied to these data is "averaging." The data are summed over a number of trials so that events which are systematically, i.e., nonrandomly, related to the response are extracted from the background which is not systematically related to that response.

4. Measurement and Quantification

The procedures which can be applied to quantitative description of response-related potentials are usually dictated by the level of precision of timing of the response and by the number of responses sampled. In nearly all cases, the RP component is apparent as a slow departure from baseline beginning up to 1500 msec prior to the response. Unless one uses very precise timing of stereotyped and well-practiced movements and a large sample over one hundred responses, the later PMP and MP components cannot be adequately defined. The most usual means of quantifying the RP is to take some short terminal interval prior to the response and which ends prior to the response, and to measure the average amplitude of the deflection during this interval against the baseline occurring some few seconds prior to the response. It is necessary to choose an interval which

will not be contaminated by movement, hence the reason for ending the measurement interval prior—by 100–200 msec—to the response. The length of this unanalyzed interval is directly related to the lack of precision with which the occurrence of the onset of the movement is indexed. In many situations this event is indexed by the subject closing a switch, an act which is certainly preceded by some movement. Where an EMG monitor is used to index the onset of movement, and especially where the movement is a simple and stereotyped one, response occurrence can be very precisely determined, and a lead interval is not necessary. In most psychology (as opposed to physiology) experiments, a considerable lead is mandated. While it is possible to measure the amplitude of the response-related potential at a single point in time, when one considers the usual small number of responses sampled and the resulting amount of "noise" still left in the record, it is best to hedge this measurement by taking an average over a small 100–300 msec interval.

More involved methods of measuring response-related potentials have not as yet been reported. It may be that in some instances it would be appropriate to measure at a number of intervals during the potentials, to take a measure of area, or, beyond these relatively simple operations, to assess auto- and cross-correlation functions or the variability of the potentials. Some of these decisions can be taken (or are dictated) in the design phase of an experiment, but the usual practice is to examine ("eyeball") the data once it is collected and to then settle on an appropriate scheme for measuring it.

D. Behavioral Correlates of Response-Related Potentials

1. Simple Movements

The study of response-related potentials preceding simple, well-practiced movements has yielded considerable information regarding both the individual components of those potentials and the areal distribution of them. A good model of these experiments is provided by Deecke *et al.* (1969), who had subjects perform "quick voluntary palmar flexions of the right index finger" and other similar movements and collected data from a wide variety of sites while subjects performed these responses at self-paced rates up to 400 times. Care was also taken to instruct the subjects about the necessity of immobility of other muscles, and especially of the eyes, which were focused on a fixation point during the 4 sec prior to a movement and the 4 sec following it. The use of these methodologies allowed definition of the components of response-related potentials outlined above in Section II,B.

In their studies of these potentials, Gilden *et al.* (1966) and Vaughan *et al.* (1968) report components which are consistent with those reported by Deecke *et al.*, with the exception of the PMP which is apparently the smallest, least consistent and most elusive of the potentials. The Vaughan *et al.* study is noteworthy as an extremely thorough and careful approach to the areal distribution of these potentials using a variety of movements. They are able to conclude that the motor potential is distributed topographically in line with the accepted homuncular arrangement along the motor strip. This is indeed strong converging evidence that this negative variation indexes a "state of functional activity" in the underlying cortex.

Becker, Iwase, Hoehne, and Kornhuber (1971) have studied response-related potentials preceding eye movement. They report that the RP is largest at the vertex (agreeing with Deecke *et al.*) but that the potential is asymmetrical over precentral areas, with the larger potential being recorded ipsilateral to the direction of a lateral movement. They report further that there is an absence of an MP component preceding saccadic eye movement, a finding which they feel is consistent with unit studies of the frontal eye fields where units fire only with or after the initiation of an eye movement. It is interesting to note that Evarts (1968) has recorded changes in unit firing rates from pyramidal tract neurons which lead the initiation of movement.

2. Complex Acts

The readiness potential has begun to receive considerable attention as a useful approach to the neural substrates of complex behaviors. In a very dramatic study, Walter (1967) has shown that one may generate slow negative potentials at will, and that these potentials may be used with appropriate sensing devices, to manipulate the environment (turn on light, present CNV trials, etc.). While this phenomenon has not yet gone much beyond the parlor game stage, its implications are far reaching and it serves well to point out the generality of these slow waves.

A number of studies have illustrated the close relationship between the RP and the CNV. McAdam and Seales (1969), seeking a parallel through a tie with "attention/motivation/expectancy," report larger RPs when subjects were instructed that their self-paced responses, if given "at the right time or in the right way" would result in a monetary reward (in fact subjects were rewarded randomly), than if the RPs were taken during a "baseline," unrewarded condition.

Hillyard (1969) has reported that the CNV is larger prior to correct signal detections than prior to incorrect detections. McAdam and Rubin (1971) find a similar relationship holds for the RP; it is larger when it pre-

cedes correct and subjectively certain perceptions of a stimulus than when it precedes subject-presented stimuli which are not accurately perceived.

Jarvilehto and Fruhstorfer (1970) have concluded, on the basis of data gathered prior to voluntary movements and in a discrimination task, that the CNV is a centro-frontal potential which is a combination of a central dominant RP as a correlate of general readiness to perform a response, and a frontal dominant potential which is a correlate of subjective uncertainty.

Rubin and McAdam (1972) using a combined CNV-RP paradigm to study brain correlates of retrieval report significant differences in activity recorded over the left temporal lobe as a function of subjective certainty or uncertainty about a stimulus word's having been on a previously studied list. No differences between electrical activity accompanying these two classes of responses were seen over frontal or central areas.

McAdam and Whitaker (1971a) reported a focal maximum in RP over the left inferior frontal regions (Broca's area) prior to the articulation of a polysyllabic word. Ertl and Schafer (1967) and Schafer (1967) reported on their attempts to use a similar technique. Using RC coupled amplification, a voice trigger to synchronize the average potential analyzer, single or asymmetrical recording leads, and a task which involved repeated utterances of the same letter, number or word, they felt they were able to demonstrate reliable, nonrandom potentials occurring prior to the utterance. In a later report (Ertl & Schafer, 1969) they report the result of doing these experiments with parallel recording of lip EMG, and because of a striking commonality in the two records, state: "Our earlier findings in which time locked cortical activity preceding speech was identified are therefore equivocal." It is noteworthy that they also state: "The prediction that specific changes in the electrical activity of the human brain must precede speech remains unchanged."

In addition to pointing out the potential usefulness of recording these potentials to elucidate the neurological underpinnings of complex behavior in normal humans, the McAdam and Whitaker study, and the reaction to it, present a useful model of some of the technical difficulties entailed in doing this research. We incorporated a number of additions and refinements to the approach used by Ertl and Schafer (albeit unwittingly, for we were not aware of their work until just after ours had been published) and were able to show reliable prearticulation readiness potentials, left greater than right and with a focus over the left inferior frontal cortex during a task involving word production. In our study we used d.c. recording techniques, a breath trigger which reliably picked off the most stable element of the articulations the subjects were producing, symmetrical recording leads over precentral and inferior frontal cortical areas, and a task which

required that subjects, during any given series, produce self-generated and self-paced polysyllabic words beginning with a single phoneme. In pilot work, we had found each of these manipulations to be crucial to obtaining reliable, language production-related readiness potentials. Our report was criticized by Morrell and Huntington (1971) on the basis that it did not represent the first electroencephalographic localization of language production function in the normal brain as we had said, on the basis that our recordings might have been contaminated by EMG or movement artifact, and on the basis that they had failed to replicate our findings. In our reply (McAdam & Whitaker, 1971b), we answered the first point by noting that while Ertl and Schafer had shown potentials related to language production, there was no element of localization in their reports. In dealing with the question of possible movement or EMG artifact, attention was directed at the fact that our trigger was a much more reliable and earlier occurring one than had been used by Ertl and Schafer, and that EMG events in this situation were, first, more stable, and second, of much shorter latency. In any case, there is no reason to believe that there would be a systematic lateralization of EMG potentials which would lead to a left inferior frontal maximal focus. With respect to their failure to replicate our earlier findings, it was noted that their situation apparently differed greatly from ours, and that they had erred in many of the same ways as we had in considerable unsuccessful pilot work on the phenomenon.

III. Psychological Significance of the Contingent Negative Variations: A Brief Editorial

The study of slow potential correlates of behavior is, after 90-odd years, clearly out of its infancy. I would be rash, however, if I said it was mature. Adolescent is perhaps the term which best describes the current state of its development; the broad outlines are there, the voice has deepened, and it is a force to be reckoned with. Two international congresses have been devoted to it and rare is the meeting concerned with some aspect of biopsychology which does not contain some papers or a symposium on it; this volume has three chapters devoted in one way or another to it. Still, we have some way to go and, without disciplining our efforts, that way will be chaotic. I would suggest that the sort of discipline needed falls into two areas. First, we need to attend very carefully to what our subjects are experiencing *subjectively* in our experiments. Second, we must eschew a religious devotion to ill-defined and mushy psychological constructs.

Careful attention has routinely been given to our methodology; the characteristics of our amplifiers, the locations of our electrodes, the criteria of measurement, the stimuli and the responses—these things are carefully spelled out. However, as graduates of animal laboratories, most of us have ignored our subjects, and their opinions about what is going on. This latter factor is of primary importance when one is studying complex higher processes. As a case in point: Rubin and McAdam (1972) found that slow potentials did not vary as a function of the objective accuracy of memory retrieval processes. The important factor was the subjects' evaluations of their certainty about the behavioral responses they made. Other cases are also relevant to this point, including the original report of the CNV by Walter *et al.* (1964) where subject attitudes and predictions about the occurrence of the second stimulus contributed significantly to the development of trends in the CNV.

In the early stages of investigation of contingent negative variations, and even today, there has been a tendency for each group of investigators to adopt and to key on some psychological construct as being of singular importance in determining the development of these potentials. Among the candidates we find "expectancy" from the Bristol group (e.g., Walter *et al.*, 1964), "conation" from the Texas group (e.g., Low, Borda, Frost, & Kellaway, 1966), "motivation" from the Iowa group (e.g., Irwin, Knott, McAdam & Rebert, 1966), and "attention" from the Boston group (e.g., Tecce & Scheff, 1969). While the heuristic value of these beliefs is very high, and while their usefulness as a sort of intuitive shorthand cannot be denied; I submit that this exhausts their list of good qualities; all else is detrimental to the growth of our knowledge. The solution to the problem is, I believe, an observable one. If we will speak about stimuli, responses (including subjective ones), and contingencies, we will be using terms which are precise and which are readily understood by all. And the chips will fall where they should.

The story, when complete, will be a complicated one. We would do well as we work toward its completion to bear in mind the following thought from Walter (1969): "When you are dealing with a complex problem or a system which is open to a number of interpretations, people are nearly always right in what they assert and wrong in what they deny."

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Chapter 7

Cerebral Psychophysiology: The Contingent Negative Variation

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I. Introduction

Traditional psychophysiology until a decade ago was concerned with response measures of peripheral physiological activity of the autonomic nervous system. Although interest in brain functions was often inferred, there was no way of looking at human brain activity which could relate to

psychological states or events. The normal electroencephalogram (EEG) reveals that the intrinsic brain rhythm is its most outstanding feature, but the alpha rhythm was found to be of little significance from the viewpoint of psychology. A new phenomenon of evoked brain activity, revealed by computer analysis, provides a better handle for research in psychophysiology.

The province of psychophysiology is the study of physiological responses which accompany psychological or behavioral states or events. The field of psychophysiology has been reviewed by Darrow (1965) in the first article in the founding of the *Journal of Psychophysiology*. It is a presentation of the state and interests of the field at that time, at the threshold of the discovery of the contingent negative variation (CNV) which is the subject matter of the present chapter. Other chapters of this volume present the field of physiological psychology as it exists today, including recent developments of psychophysiology, with its concern for human brain, autonomic nervous system, and behavioral interrelationships. Psychophysiology has become at least one of the bases for the study of psychosomatic medicine and the study of psychological factors in the understanding of the onset, treatment, and course of many diseases.

The discovery of the CNV has again focused the attention of many physiological and experimental psychologists on the electroencephalograph, but now coupled with a computer, as a means of studying relevant intervening brain variables which are both objective and valid indicators of change in the internal state of the nervous system. This followed many years of disinterest due to false leads based on studies of intrinsic brain rhythms and their conditionability. It is beyond the scope of this paper to review the work on alpha rhythm, its blocking and conditioning and investigations of biofeedback training. The focus here is evoked brain activity, which must be looked at despite the interference of intrinsic brain activity of much higher amplitude. This is accomplished by careful experimental and technical methods and computer analysis, all of which will be reviewed.

II. Discovery and Significance of the CNV

The CNV was discovered by W. Grey Walter and his colleagues (1964) in Bristol, England, while they were working on averaged cerebral evoked potentials to light flashes and clicks. The Bristol group was then concerned with the cerebral interaction effects between paired clicks and flashes with different time delays between the two stimuli in normal subjects. By chance, they had the combination of three ingredients to make the discovery, plus the keen insight for scientific observation and thoughtful analysis. The CNV, like so many other scientific discoveries, was an accident.

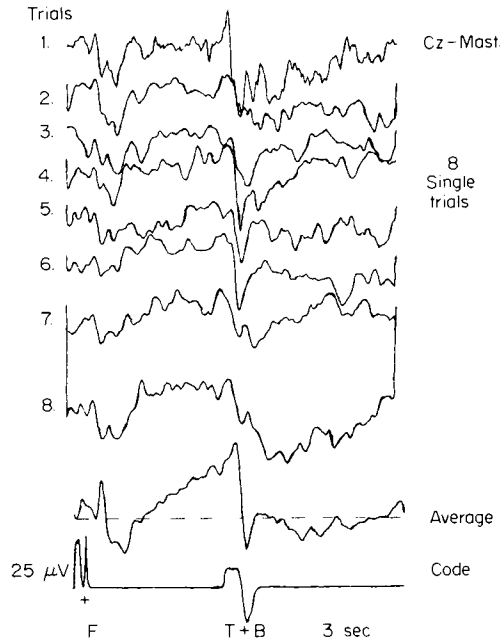

FIG. 7-1. CNV development in raw EEG traces. The brain activity recorded from the vertex to mastoid leads is shown in eight single trials, in order from the first one at the top. The bottom trace is the average of the above trials and the code line shows a flash, tone, and average button press (down deflection). A calibration signal is shown at the extreme left of the code line, just before the sharp flash pulse. Negative is always an upward deflection of the pen.

The experimenters asked the subject to press a pushbutton to the second stimulus; they were tape recording and averaging cerebral potentials to study evoked responses (ER) and were trying out (for casual interest) the d.c. capabilities of the new Beckman type "T" EEG recorder with stable silver-chloride electrodes. With those necessary conditions, in addition to the brain responses to the signals, they saw a slow negative wave begin to appear regularly between the two stimuli. Walter called it the "contingent negative variation," purely as a descriptive term, since it is contingent on a stimulus-response sequence, is negative in electrical sign and is a variation of d.c. level from the neutral baseline. He called S_1 the conditional stimulus, S_2 the imperative stimulus and the motor response the imperative response, in accord with grammatical terms. Figure 7-1 shows the CNV in a few sequences in a raw EEG record recorded in my laboratory. In only about one third of normal subjects can it be readily seen in raw records against the background activity which includes alpha and theta rhythms, other slow potentials, physiological and electrical artifacts, and electrode drift. It is

usually studied by means of averaging, either by a special purpose computer, such as the computer of average transients (CAT) or similar averaging devices, or a general purpose small laboratory computer, such as the LINC-8 or PDP-12 or other comparable computers.

The effect of averaging is to increase the signal-to-noise ratio by $(N)^{1/2}/1$ in the general case of random noise. So if 10 traces are averaged, the signal is enhanced over three times. In order to increase the signal-to-noise ratio (S/N) tenfold, then 100 traces would have to be averaged, and 400 traces are necessary to double that resolution, that is, to enhance the S/N to 20 times the value of a single trial. Since the CNV changes with repetition, increasing with conditioning trials in the early stages and decreasing with inattention, boredom, or fatigue, a compromise must be reached in the number of trials per averaging epoch. We find that from 6 to 32 trials is the practical range that people work with, and we have settled on either 8 or 16 trials as our standard. That results in a S/N enhancement of 2.8 or four, which are reasonable figures for most practical purposes. Figure 7-2 shows the CNV as a brain conditional response to a flash, also to a tone, then to a flash and tone, the next to flash, tone and button press, the condition which finally elicits the CNV. It obeys the general principles of conditional reflexes in the Pavlovian sense; it extinguishes with omission of the second signal and is restored fully only after a few trials following the restoration of the signal. Walter *et al.* (1964) also showed that the amplitude of the signal is directly related to the reinforcement ratio. For most individuals it is at peak amplitude with 100% reinforcement and it may drop to about one-fourth of its value or disappear entirely with about 50% reinforcement. Since the early confirmation of the discovery was made by Low, Borda, Frost, and Kellaway (1966), Rebert, McAdam, Knott and Irwin, (1967), and Cohen, Offner, and Blatt (1965), there has been a virtual explosion of interest in this area of research, culminating in the second international meeting about the CNV held in the summer of 1971 at the University of British Columbia.

III. Technology and Methodology

The techniques required for working with the CNV are generally what are needed for reliably measuring low level slow potential changes recorded on the scalp from human brain activity. Relatively nonpolarizable electrodes are needed to assure stability, and they must be securely attached to the skin to avoid "popping," or sudden changes in polarization, which look like a spike, or a monopolar slow wave on the record. We find that standard Grass or Beckman silver disk EEG electrodes are suitable if carefully chlorided in the laboratory in accordance with the instructions supplied with the elec-

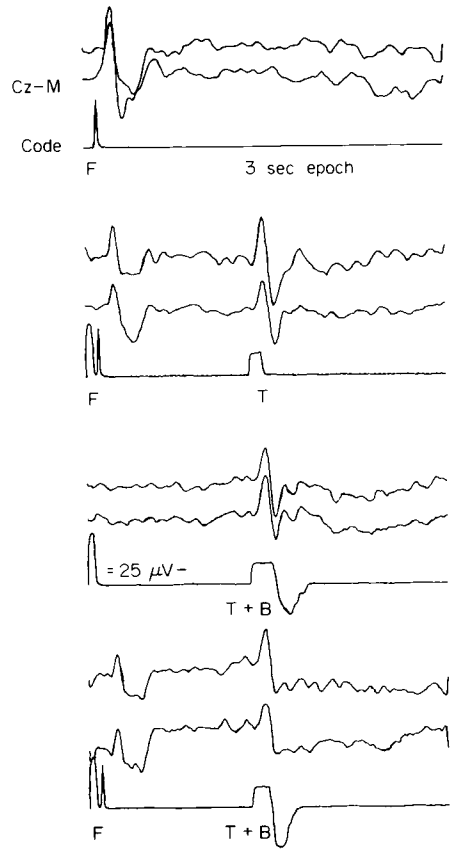

FIG. 7-2. The CNV as a conditional response. Two averages of eight trials are shown for each of the different stimulus conditions to indicate the reliability of the responses. The subject is a normal 23-year-old man. The code line shows a 25 μV calibrated signal, a sharp flash (F), a tone (T), and a pushbutton response (B). The motor reaction is shown by a downward deflection, which stops the tone. The CNV in the last trace is larger than the one above, which is the average of the first eight trials.

trodes. Six leads are chlorided at once; they are shorted together as the anode and a silver wire is submerged in the solution as a cathode. Five grams of sodium chloride is dissolved in 100 ml of distilled water as the electrolytic solution, or alternatively a 5% normal solution of hydrochloric acid is used to supply the chloride ions. We prefer the electrodes supplied with center holes, or we first drill the holes of the size to fit a small syringe needle. The new leads should be cleaned by soaking them in a strong hydrochloric acid solution in order to strip the grease or oil film left from manufacture, and they should be chlorided in the dark, by connecting them to a 1½ V dry

cell through a 220-Ω resistor in series. It takes about ½ hr or more for the electroplating of the silver chloride coating on the outer layers of the silver disks. Bubbles of hydrogen gas form on the cathode during the active process. The slower the action, the more even is the chloride coating. At first the coating has a light powdery appearance, but it turns a rich dark brownish purple on exposure to light, much like the developmental process of film. The leads tend to get more stable after a few times of use, and aging is helpful, although after a few months, due to deposition of impurities or scratching, they must be rechlorided.

We attach the electrodes to the skin with collodion as the glue which makes a moisture tight seal, and holds the lead tightly in place. When the session is finished the seal is easily dissolved with acetone. The skin is first briskly rubbed with ether to clean the oil and moisture from the surface and to rub off the outer layers of epidermis. The electrodes are held on the skin, over parted hair, glue applied all around the edges with a plastic bottle nipple, and then dried with a jet of compressed air. The electrolytic jelly is inserted under the electrode by an injection syringe with a dull needle through the hole in the center of the electrode. The skin is then rubbed around with the flat tip of the needle to further lower resistance. The impedance is usually reduced to 3000 to 5000 Ω by this method. It should be measured only by an a.c. impedance meter and it should be equalized among all the pairs of recording electrodes to minimize drift. Other, more stable kinds of plastic electrodes with silver chloride powder or sponge are commercially available and have advantages of no metal contact with the skin. The general subject of skin electrodes has been well treated by Edelberg (1967), and his analysis certainly applies to this situation.

Once the electrodes are attached to the skin, it is imperative that d.c. currents are not passed through them, or polarity equalization will be spoiled and their stability ruined for the time of the recording. For example, resistance should not be tested with the d.c. meter which is built into some electroencephalographs, and the centering control cannot be used in certain types of amplifiers which pass a bucking current through the leads to equalize the inputs to the two sides of the preamplifiers.

The low-pass filter or time constant characteristic of the amplifiers is also an important consideration. Use of a short time constant causes distortion and phase shifts through the resistor-capacitor coupling. Ideally, for the purpose of fidelity use of a straight through or direct-coupled amplifier would be recommended. However, they present one difficulty in that the slow electrode polarization drifts and large slow changes in skin potential, which, at the high gains necessary to record EEG, will overwhelm the signal and drive the amplifiers beyond their limits of recording. A suitable compromise is to record with an 8-sec time constant through a stable d.c. amplifier as used by Walter; it is easy to short across the capacitors for the shortest

time constant in the Offner-Beckman preamplifier. This leaves an 8-sec time constant in the amplifier circuit; that is the procedure in my laboratory. This is sufficient to record waves of ½ to 1 sec duration with almost no distortion, and to retain a fairly stable baseline, despite the slow polarization shifts of the electrodes or skin. Surwillo (1971) reviewed amplifier problems and condemns the use of chopper amplifiers, however.

The number of channels and the head positions which are selected depends upon the purpose of the recording. The CNV has a distinctive and individual distribution on the scalp and a record from only one position is not sufficient to reveal this, and, therefore, conveys only limited information. The necessity of guarding against possible physiological artifacts also requires multichannel recording. The availability of channels and the difficulty of computing the average results determines the upper limits of recording. Anywhere from four as a lower limit up to 16 as a practical upper limit are useful, with about eight channels being customary in adequate research. As the CNV comes into use as a clinical diagnostic method, it is desirable to look at hemispherical asymmetries with at least eight channels. In our laboratory, we monitor eye movements, a stimulus channel, left and right frontal, central, and parietal channels referred to linked mastoids for standard clinical purposes, but of course more channels are desirable. The CNV is usually maximal in amplitude at the C_z or vertex lead, so the vertex is always recorded as the standard for amplitude measurement.

Monopolar recording is the most usual with leads referred to a common reference at gains of about 5 to 8 mm per 50 μV. In our laboratory, all of the 16 channels of the EEG machine are fed into a PDP-12 computer for on-line analysis. They may also be recorded on an analog instrumental tape recorder for off-line analysis by the computer. Obviously, the output values of the EEG machine and the inputs to the tape recorder and the computer must be matched; we accept ± 1 V peak to peak as the limiting value.

The computer accepts the physiological analog input signals, converts them for digital computation and stores them on LINC tape. The outputs are displayed on the scope, graphed on an $X-Y$ plotter, printed on the teleprinter, punched on paper tape, or recorded on magnetic tape. The stimuli presented to the subjects are controlled by the computer and the subject's motor responses are sensed also by the computer.

IV. Parameters of the CNV

Customarily we analyze EEG records by describing the basic frequencies of repetitive waveforms, such as alpha rhythms, noting transient abnormalities, such as spikes, and judging the asymmetry of records from the two

hemispheres. In analyzing the cerebral evoked potentials, we are further concerned with identifying their component waves, measuring their peak amplitudes and latencies from the occurrence of the stimulus to the peak of the response component. The measurement of CNV is analogous to the measurement of evoked potentials. We must first detect the presence of the waveform at a suitable signal level against the background noise level. Fortunately, unless there is a lot of delta slow activity in the record, the CNV is not hard to find since we know where to look. It may be hard to decide whether it is genuine or perhaps due to artifacts, such as eye, head, or tongue movements. Its absence cannot be concluded if the baseline record is unstable, or if much delta activity is present. Figure 7-3 shows a typical CNV and some of the possible measurements. For every parameter, a standard deviation could be computed from a digital analysis of individual responses, since by and large the parameters are found to be normally distributed. A baseline is drawn through the record at the beginning of the trace before stimulation and at the end, if the negativity has returned to neutral. It may be useful to filter out the fast components, which can be done on our computer. The integral of the waveform may also be taken with the points of deflection representing places for the measurement of latencies.

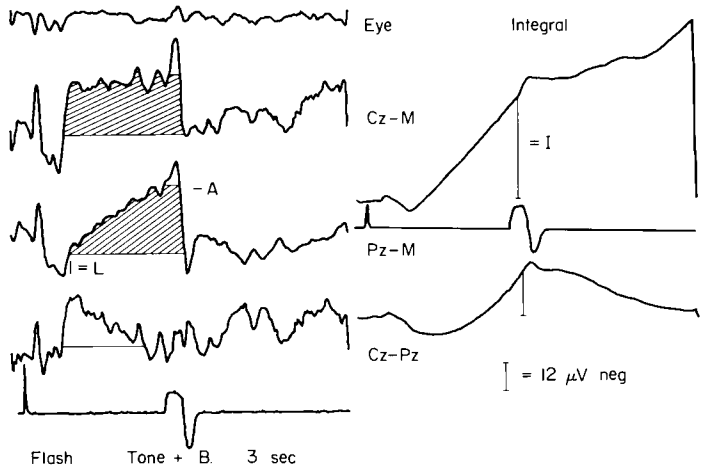

FIG. 7-3. Measurement of the CNV. CNV and eye movement recorded during eight flash, tone, and button press trials in experienced subject. Top tracing recorded at ½ gain from bipolar leads from above the eye to below the eye. Averages of the monopolar vertex and parietal leads are next and the bottom trace is the bipolar derivation of vertex to parietal lead computed from the two traces above it. The integral of the vertex and parietal leads is shown on the right side. The shaded portions of the curves show the area of the CNV. Measurement of latency to onset is marked L, and the peak amplitude is marked A. It is about 30 μV at the vertex and parietal leads, but the integral or area at the vertex is almost twice that at the parietal lead.

If the stimuli are always presented with the same time delays, then the integral becomes the measure for the area under the curve, essentially a different amplitude measure.

The maximal amplitude is measured as the peak of the smoothed curve before the response to S_2. Because of the difference in waveforms among subjects, the latency to peak is not a very useful measure, but the latency to onset is. This is often masked by ER components to the conditional stimulus, and is more clearly seen in the integral curve. The shape of the CNV is usually ramplike, or may be square with a rapid rise time, or it may be a decelerating curve on the leading edge. It is usually terminated by a fall of potential with the response to the imperative stimulus. The end or the resolution of the CNV may be measured as a latency from S_2 to the return to baseline. Occurrence of positive waves following the CNV should be noted, and sometimes an afternegativity following the CNV is seen, especially in young children (Cohen, 1973).

Comparisons between the sides of the head or other positions may involve cross-correlation, phase or time shifts, and amplitude decrements, particularly on the side of brain lesions. Vaughan (Cohen, 1969, p. 196) made the suggestion that back averaging from the motor response should be the method employed, rather than averaging from the beginning of the epoch. We have found however, that it makes no practical difference in the peak amplitude measure or the integral of the CNV, limited between the two stimuli, with the usual variation in reaction time. It can affect the resolution time, or the return to the baseline if the reaction times vary considerably, that is, more than 200 msec.

V. Physiological Significance of the CNV

The physiology and psychological determiners of the CNV are not yet well understood. The initial concept of Grey Walter *et al.* (1964) is that it acts as a primer for cortical excitability, which discharges in the motor response terminating the CNV. Due to recording of patients with intracerebral electrodes in subcortical white matter, he was able to localize the response in cerebral cortical gray matter. The white matter tends to go positive or neutral to a surface reference lead, while subdural electrodes are twice as negative as scalp electrodes. He attributes the response to the outer layers of the cerebral cortical dendritic feltwork. It probably represents the synchronized negativity of dendritic potentials as large populations of neurons become partially depolarized, therefore increasing their excitability and reducing their threshold for neuronal firing and enhancing informational flow.

Rebert (1973) found similar negative activity in the caudate nucleus of the

thalamus and the lateral hypothalamus while recording surface CNV waveforms in monkeys. The role of other subcortical centers is under investigation. The production of the wave seems to be cortical, but it may also relate to such systems as the diffuse thalamic-cortical pathways and the action of the reticular formation in stimulating cortical excitability. There is no doubt that very diffuse and widespread higher brain centers are involved because of the widespread distribution over the surface, but the subcortical brain centers involved with the diffuse activating mechanisms must also play an important role as in any integrated behavioral activity of complex living organisms.

It has long been known that stimulation of the midline reticular formation in the midbrain results in slow negative potentials on the cortex (Arduini, 1958) and Rebert also found negative slow activity in that area during CNV recording in one monkey.

Since Cohen and Walter (1966) demonstrated that a motor response is not a necessary concomitant of the CNV, but that a perceptual response to S_2 is sufficient, both Walter and Cohen conceive of the psychological parameter of expectancy as the single most descriptive concept. This led to the partial adoption of the term "expectancy wave" as an alternate term to the CNV, and it is still used by some people, since it translates so well in other languages. Expectancy of making a motor response of a perceptual or ideational event of interest also implies a sufficient motivational level. The concept of cortical priming is not restricted to preparation for a motor act, but it also includes a preparatory set for a perceptual event.

We must consider the CNV in relation to the "readiness potential" first described by Kornhuber and Deecke (1965) and confirmed by Gilden, Vaughan, and Costa (1966). Vaughan (1969) has attempted to explain the CNV as a motor readiness potential, but that cannot be true as long as no overt motor response can be observed to occur terminating a CNV. The readiness potential is an extremely interesting response and certainly relates to the CNV, but it may be considered as a special case of the CNV rather than the CNV be subsumed under motor potential. In this case, the conditional stimulus is operant, an internal idea with its emitted brain event, the readiness potential. We can detect it because the subject provides us with a trigger signal. McAdam and Witaker (1971) found that a readiness potential also precedes speech and is of higher amplitude in the left frontal region, over the speech center. In his study, the voice key is used as a trigger for back-averaging, but the muscle artifacts make the wave form unclear. The difficulty in studying strictly spontaneous CNVs with no overt response is that we don't have a time-locked signal against which to back-average. Walter's group (personal communication) have just developed a computer program to recognize a CNV or ER by a running cross-correlation tech-

nique between a template based on the average response of the subject and a continuous EEG record. During continuous time shifting over a whole record, when the isolated brain event coincides with the template, a high correlation is seen. Spontaneous subjective occurrences can be singled out for further computation. This is the first promising application of computer analyses to accomplish something other than averaging as a method of analysis of CNV-like waveforms.

Cohen (1969) showed similar CNVs to an imperative stimulus for recognition or to a motor response which terminates the stimulus, but the same subjects were not compared. His study (Cohen, 1973) of the CNV derived from the same subjects tested under comparable conditions, using perceptual expectancy of words or pictures and a motor reaction to terminate a tone, yielded largely similar CNVs. Donchin and Smith (1970) tested subjects under four conditions at the same session. All received a conditional click, followed 1 sec later by a visual presentation of one of two figures. Subjects were instructed (1) to press a button to both figures, (2) to one, but not the other, (3) to guess which figure would appear, or (4) to do differential mental arithmetic following the S_2. CNVs appeared appropriately and similarly in all conditions, although there were significant differences in the late positive wave, P_{300} as described by Sutton, Braren, Zubin and John (1965), which relates to informational content of a stimulus. There is no further doubt in this author's mind that a motor response is not necessary for a CNV, but it is a convenient way of eliciting it in most subjects. It also provides an observable behavioral response which may provide useful data for clinical considerations.

The notion of cortical priming is supported by other data showing negative correlations between CNV and the reaction time. Many studies have shown that the average reaction time tends to be shorter following large CNVs and longer following low amplitude CNVs as first reported by Walter *et al.* (1964; Walter, 1968; Hillyard & Galambos, 1967; Waszak & Obrist, 1967; Tecce, 1971). Cohen (1973) also found a significant difference between the CNV amplitudes accompanying fastest and slowest reaction times for the same subjects.

Increased cerebral excitability may also be assumed by the characteristics of brain ERs to stimuli presented during the interval between S_1 and S_2. During conditions in which the CNV was produced, such interspersed stimuli produced higher amplitudes on the scalp than when no CNV was present (McAdam, 1969). This was also seen by Timsit, Koninckx, Dargent, Fontaine, and Dongier (1969) during a study of schizophrenic patients. Walter (personal communication) electrically stimulated subcortical leads, and the brain ER measured by subdural electrodes was enhanced during the experimental situation producing the CNV. All of the above studies

indicate larger CNVs during increased attention or arousal levels, but no causal relationship of the CNV and cerebral arousal level may be implied.

VI. Psychological Factors in the CNV

As the CNV relates to greater efficiency of motor responses does it relate to efficiency of perceptual responses as well? This was answered in the affirmative by testing the accuracy of recognition of visual stimuli presented as S_2 at near threshold values (Cohen, 1973). A greater percentage of both pictorial and verbal stimuli were recognized correctly when a high amplitude CNV preceded the stimulus than a low amplitude CNV. In this case, perhaps, CNV relates to the mobilization of attention, a factor suggested by Tecce (1970). This hypothesis may also account for the finding that when S_2 is near threshold, the CNV tends to be of higher amplitude than when it is in the high intensity range, although the evoked response tends to relate slightly positively to stimulus intensity (Low, Coats, Rettig, & McSherry, 1967). Other positive correlations in the study were between stimulus intensity and respiration rate and GSR reactivity, while the reaction time was negatively correlated but not at a significant level.

Knott and Irwin (1968) explored the effects of anxiety on the CNV with negative results. They hypothesized that high anxiety subjects were operating at a chronically high level of cerebral negativity, in fact leaving no room for an increase in the CNV over the baseline. Knott's later research explored the interactions of stress, manifest anxiety level, and the sex of the subjects (Knott & Peters, 1973). Men and women behaved differently in a complex interaction with stress, anxious women showing a decrease in CNV, while men were more stable. It is true that anxiety patients generally have lower than normal CNV amplitudes, but this may be due to diverted attention to postulated internal as well as external distracting stimuli. Low and McSherry (1968) have shown that the CNV in the usual S_1-S_2-R paradigm does not peak at a physiological limit, since interposing an additional task between S_1 and S_2 results in a further elevation of the CNV, so that the two independent responses are about additive.

The matter of attention can only be inferred from the effects of distraction. Tecce and Sheff (1969) found that the CNV was reduced in most subjects when distracting stimuli were interposed in the S_1-S_2 interval. Walters group (McCallum, 1969) found the same effect, but observed that the CNV regains its former amplitude in two or three sets of trials during distraction in normal individuals, but not in anxious or psychotic patients. They use this sign of distractability in clinical diagnostic practice, finding it to be a reliable incicator. Another finding is in the testing of so-called hyperkinetic or dis-

tractable children; they have greatly reduced CNVs in a situation with auditory tones and noises superimposed on an otherwise quiet room at random short intervals, ranging from about 2 per sec to 1 per 5 sec. Any change in the experimental parameters during conditional practice sessions tends to reduce the CNV until the subject readjusts to the new condition. This holds for changes in temporal relations, type of stimuli, the nature of the imperative response, etc.

The CNV may be elicited in response to a purely imaginary stimulus. The subject produces CNVs to an imaginary order, "Think NOW," when S_2 should occur. His brain response to the idea of the S_2 terminates the CNV, just as if he pressed a button in response to it (Cohen, 1969). This fact was used by Walter to operate an electrical switch by sensing the rise in the CNV to a critical negative voltage (the 'wish switch'). This turned on the projector TV mechanism, so that the person received a picture, merely by "willing" that he see it. In a recent experiment an initial click would be followed by a visual arrow; if the response occurred at the right time the arrow pointed up, and it pointed down if it was too early or too late. An up arrow was 'right' and a down arrow meant 'wrong.' After a few conditional trials, the pushbutton control was discontinued and the S_2 omitted, but the subject continued operating the arrow display by controlling his CNV resolution phase to return it to the baseline. He tended to retain good CNVs and got more correct than if he were pushing a button to S_2 (Walter, personal communication).

The effects of embarrassment, worry, bad news, other tasks, and other competing situations for the attention of the subject, all have been found to reduce the CNV. While urging the subject to concentrate on the stimuli, telling him he's doing well, encouraging him to do better, and persuading him to make fast reactions all facilitate the expression of the CNV.

The average CNV amplitude in the Bristol laboratory is 20 μV, ranges from 10 to 50 μV in normal subjects, and has a standard deviation of $\pm 4\,\mu$V (Walter, 1968). Cohen (1969) agrees closely, with an average of 21.4 μV at the vertex and the same standard deviation in a similar experimental paradigm. The waveform and amplitude is stable with repeated measures and the reliability coefficient for 34 subjects tested on different days is .80. The form and distribution of the CNV over the scalp is an individual matter without known psychological correlates. The distribution of amplitudes of CNVs of 60 adult subjects recorded in the 21 standard electrode positions is given by Cohen (1969). The average midline amplitudes from frontal pole to occipital leads are: 12.1, 18.7, 21.4, 16.6, and 9.3 μV at the FP_z, F_z, C_z, P_z, and O_z positions, respectively. Often the CNV develops earlier in the frontal areas, and sweeps posteriorly, with about 100 msec delay between its rise in the frontal region and the same phase in the parietal

position. Low observed the same earlier rise in the frontal regions of an eye-enucleated rhesus monkey (Cohen, 1969, p. 167).

VII. Relationship to Possible Artifacts

The main physiological variable which contaminates the CNV is eye movement, since the eye field is the largest generator of electrical potential in the head. Because of the corneal-retinal gradient of several hundred microvolts positive, vertical downward eye movements inject a large negative shift in the scalp electrodes, largest in the frontal area, diminishing toward the vertex and becoming negligible in the posterior head regions. Hillyard and Galambos (1970) determined that in 10 normal subjects about 25% of the CNV at the vertex could be accounted for by eye movements. Since the eyes roll upward when the lids are closed, any stimulus demanding attention or concentration results in a downward movement of the eyes to a more forward-looking position and an electrically negative shift is recorded at the scalp, returning to the assumed baseline with relaxation of the eye muscles. Because of that fact, we record the CNV with eyes open and with instructions to maintain eye position by fixation on a target. This virtually eliminates significant eye movements during the stimulus-response intervals in cooperative subjects, but to be sure, the computer rejects trials in which eye movements occur. Recording from linked mastoid leads as a reference, virtually eliminates the horizontal eye movements as a source of artifacts.

Eye blinks remain a major source of contamination with eyes open or closed and trials in which they occur should be eliminated from the averages by a computer program or by eye in an off-line data averaging system.

Walter (1967) described a method for attenuating the vertical eye movement component from scalp recording, by including a component of the eye blink recorded from a superorbital electrode in the reference lead. The superorbital lead is connected to the linked mastoid lead (reference) through a variable potentiometer which is adjusted to balance the resistance, so that the potential from the eye movement at the vertex exactly equals the potential at the reference and thus is cancelled out. The difficulty is that it can correct only one lead such as the vertex, but in so doing it injects a voltage from the eye artifact into the reference and increases the blink artifact in all of the other leads. It would be too much trouble to correct each lead separately. The implied linearity between the angle of the eye movement and the amplitude of the voltage seems in fact to be true according to Hillyard's data.

There is no substitute for close observation of the subject to detect possible other artifactual contributions to the CNV, such as head movements or body movements when making the imperative motor response. This is especially true when the CNV is used for clinical purposes, and when good cooperation or control is lacking on the part of the patient. In some subjects, there is a relationship between CNV and autonomic response variables, but as the autonomic responses habituate readily to the stimulus repetitions, the CNV develops, and then tends to stabilize at a high level of function. Walter (1966) reports that as the CNV develops there tends to be a stabilization of heart rate, respiratory rate, and GSR variability, that is, a general stabilization of autonomic functions. This was not found to be the case in various psychopathic populations and in children in which the autonomic lability tends to be either flattened or exaggerated. All of the researchers who report monitoring the CNV and GSR simultaneously have reported no causal relationship since there is a different time course in the waves (Low *et al.*, 1966) and the GSR or CNV may appear independently with change in conditions (Cohen, 1969). Heart rate changes may occur simultaneously with CNV production, but the beat-to-beat variation requires a long interval of at least 3 or 4 sec between stimuli in order to produce reliable data, a longer interval than most CNV studies use. Larger CNV amplitudes were found to occur with either heart acceleration or deceleration (Connor & Lang, 1969). The most comprehensive work on relationship to heart rate is by Lacey and Lacey (1970, 1973) who found heart rate deceleration during the anticipatory interval before S_2, but no systematic relationship to GSR was evident.

We have seen no systematic relationship between CNV and other EEG measures with this exception, that functional or neurological impairments which tend to produce EEG abnormalities also tend to produce low level or absent CNV. In normal individuals, we could see no relationship between EEG rhythmical activity or evoked potentials. There is a tendency for alpha rhythm to block during intervals which produce the CNV, but this is a variable effect and many individuals produce more alpha during the interval after many conditioning trials. Since we usually record with eyes open, the alpha activity tends to be reduced in our records.

There is no consistent relationship between the amplitude of the ER to visual or auditory stimuli and the CNV. The only exception reported to this is that the amplitude of the P_{300} component (Sutton, *et al.*, 1965) under some circumstances may be associated with the CNV. This component has been identified with the "informational" aspects of the stimulus, and if the stimulus conveying information, such as "right" or "wrong" is delayed, a CNV appears in the fore period and the P_{300} is larger. Nevertheless, as

shown by Donchin and Smith (1970), and Tueting and Sutton (1973) the two responses may be dissociated. Even when the CNV and P_{300} were found to vary together, the magnitude is not of the same order.

The CNV may be seen in cases where spontaneous epileptiform activity is seen in the EEG record, but often the slow wave abnormalities increase the brain noise level to such an extent that the CNV is obliterated (Winter, 1967). The S/N ratio formulation holds for random noise, and an increase in noise level at the frequency of signals that one is trying to detect necessities a much greater number of trials. Zappoli, Papini, and Cabras (1969) recorded CNV from 12 epileptic patients during the time of spontaneous discharges and found it difficult to evaluate, since after the brain discharges, motor responses were delayed or disrupted. Three of the focal temporal lobe patients showed occasional "transitory suppression or considerable disorganization of the CNV." The effect was clearest in the hemisphere which did not show the spike abnormality. Much work remains to be done to elucidate the relationships between intrinsic and evoked brain electrical activity and the CNV. Some may be found, but so far none have been demonstrated, and no other cerebral or physiological activity can be found to account for the CNV.

VIII. Clinical Applications

The CNV has been found to enrich the possibilities of the EEG for diagnostic and prognostic purposes, for studies of cerebral lesions, developmental and psychiatric disorders. Since its discovery and exploration was mainly by clinical electrophysiologists, its clinical implications were keenly investigated and the clinical applications are rapidly expanding. The general methodology is to establish expected norms and variability from average data within normal populations and then to test known diagnostic categories to detect the amount and nature of impairment of the CNV. In our laboratory, we primarily measure the presence, amplitude latency, and symmetry of the distribution of the wave on both sides of the head.

The CNV is used in the "routine" investigation of many patients at the Burden Institute. McCallum *et al.* (1970) reported on 60 patients with suspected organic lesions, such as head trauma, cerebral vascular accidents (CVA), tumors, hematomas, and a few cases of Parkinson's disease. Reduced CNVs are often found in such patients, particularly at the site of the lesions, so that asymmetries are reported. Figure 7-4 shows the asymmetry of the CNV and ER seen in a patient who had a CVA and was recorded in my laboratory. We have seen about 30 patients with hemispherical lesions and we confirm the findings from Bristol, that the CNV is reduced, mostly

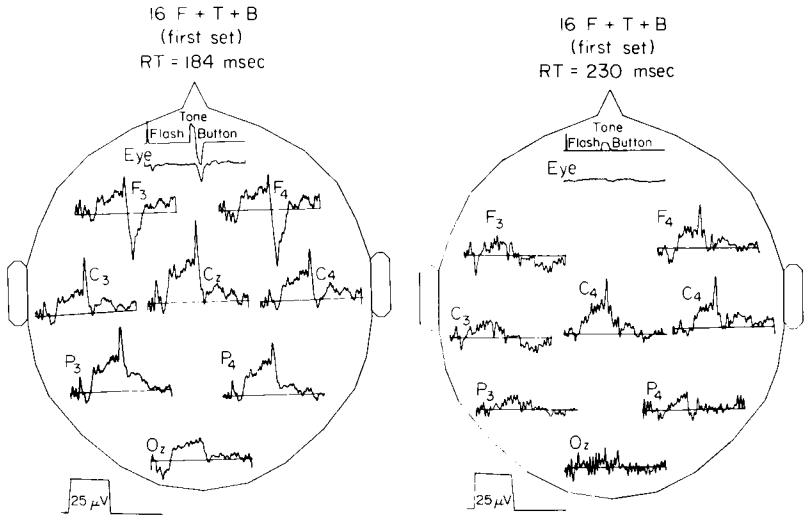

FIG. 7-4. Laterality of CNV in normal subject and patient with left CVA. The top trace is a bipolar eye movement channel, and the left and right central leads referred to the linked mastoids are shown in a patient recovering from a stroke in the left hemisphere and in a normal control subject, 63 years of age. The code line shows a 25 μV calibrated pulse, the flash, tone, and button sequences. The area of the CNV is reduced in the patient with a left hemispheric lesion. It often disappears entirely in such patients.

on the side of the lesion. We find a relationship between the presence of the CNV and progress of recovery of function, especially that of speech with left hemispherical lesions. We also have seen reduction of the CNV in patients with Parkinson's disease.

We have also studied the development of the CNV in children (Cohen, 1969) and applied it to the evaluation of children with learning disabilities. We found that about one half of such children have below normal development of the CNV, and that the children with most severe learning impairments tend not to have a CNV at all.

Psychiatric disorders have been widely studied by Walter's group in England, Dongier's group in Belgium, Small and Small, and our own laboratory in the United States. In general, severe neurotic and psychotic patients have reduced CNVs, except for compulsive patients and mildly manic patients who might show an exaggerated CNV amplitude. The basic relationships of the CNV to pathological states were first described by Walter (1966). The CNV develops slowly and irregularly in acute anxiety states, rarely reaching the average amplitude of normal subjects. It extinguishes rapidly in deconditioning trials with no imperative stimulus and reappears slowly, if at all, in reconditioning trials. "Once lost, confidence

is never restored" (Walter, 1966, p. 19). In normal individuals, the CNV rapidly disappears after a few extinction trials, and it is usually diminished by decreasing the probability of reinforcement. It returns however, as reinforcement is reinstated, sometimes at even a higher level. The subject's brain responses are appropriate to the stimulus situation and they are modified in accordance with changes in the situation. But the patients' responses are moderated inappropriately or exaggeratedly by changes in the experimental situation. Autonomic responses tend to increase rather than stabilize during the course of an experimental session in patients, whereas they usually stabilize in normal subjects.

Obsessive and compulsive patients tend to maintain a long latency slow negativity after the response is made, so that the slow resolution of the CNV is the most characteristic feature, although it may develop rapidly in acquisition trials. This effect may last over hundreds of trials; there is often less decrement with partial reinforcement and the CNV is resistant to extinction with deconditioning trials.

Psychopathic or sociopathic patients seem to develop only very low voltage CNVs or none at all. Schizoid individuals are noted for the trial-to-trial variability of the CNV, producing low amplitude waves on the average. Walter's group (McCallum & Abraham, 1973) found that the CNV is a good objective indicator of change in psychopathological states. They have monitored the improvement of dozens of patients who have been treated with electropolarizing currents, making small multifocal lesions in superorbital white matter. They mainly suffered from chronic acute anxiety and suicidal compulsions. CNVs were lacking or minimal in many patients before treatment and they became more normal as the patient's symptoms improved. The presence of the CNV became the most accurate prognostic indicator for the enduring effects of treatment.

It is difficult to gain the cooperation of psychotic patients for electrical recording during behavioral studies when they must sit very still in a laboratory setting. Therefore study of severe psychiatric disorders may be limited (Straumanis, Shagass, & Overton, 1969). However, Small and Small (1971) were able to obtain good data on schizophrenic and manic and depressed patients. They found very small or no CNVs in all of the psychotic patients, and normal CNVs in normal control subjects. Since their interstimulus interval was only ½ sec, lower amplitudes were recorded.

Timset *et al.* (1969) reported a prolonged CNV as typical of schizophrenic patients. That is, the resolution phase to baseline return took more than 2 sec. Their last report (Dongier *et al.*, 1973) on 144 patients showed prolonged CNVs in 98% of those with early schizophrenia. They also observed a similar negative wave following a single stimulus-response sequence, in which no conditional stimulus or CNV occurs. A probe stimulus, such as a

flash, presented during the prolonged negative phase evoked cerebral responses with reduced amplitude in psychotic subjects, whereas in normal subjects, when the probe stimulus is presented during the negativity of the CNV, higher amplitude responses are elicited.

As part of the ongoing psychopathological studies of Walter's group, McCallum and Abraham (1973) found CNVs in fresh schizophrenic patients, but the amplitudes were lower than in the normal control group. Patients who exhibited Schneider's "first rank" symptoms had lower amplitude CNVs and were more affected by distraction than schizophrenics without "first rank" symptoms. The latter group did not differ significantly from the normal group.

Small, Milstein, and Small (1973) actually reported "contingent *positive* variations" in certain clinical conditions when CNVs were to be expected. These were seen in acutely ill schizophrenic and manic patients and those receiving electroshock therapy. Tecce (1971) reviewed the applications of the CNV to the study of individual differences and psychiatric diagnosis.

IX. Summary

The discovery of the CNV opened a new field of cerebral psychophysiology which relates behavioral events to a whole range of slow wave electrophysiological events. These include the readiness and motor potentials, slow late components of cerebral evoked responses, slow positive waves and spontaneous slow baseline shifts in addition to the CNV. Long time-constant recording amplifiers, electronic tape storage with analog to digital conversion capabilities, laboratory computer facilities, careful techniques and imaginative experimental methodology, are necessary ingredients to explore these areas of cerebral potentials elicited by behavioral or even subjective events. The methodological difficulties make studies of young children and patients with psychopathology challenging to study, but the results have been so rich and significant as to amply reward the challenge. The whole class of evoked potential phenomena, including the CNV, represents a significant breakthrough in the objective study of brain processes relating to psychological activity and states.

Normal response parameters in a fairly standard S_1-S_2-R paradigm are well known. The spatial distribution of the CNV and its development in children has been described. The understanding of the CNV as a conditional brain event relating to expectancy makes its study applicable to many clinical psychological and neurophysiological problems which underlie disorders of high-level interaction of brain function such as attention, motivation, perception, and learning. All of the studies relating CNV to per-

formance parameters indicate that it is related to efficiency of function. Impaired functions due to psychopathology or brain disease often are accompanied by deficiencies in the CNV. A brain lesion usually reduces the CNV and ER on the damaged side.

More research is necessary to elucidate the physiological mechanisms, psychological correlates and clinical applications of the slow evoked brain potentials, but the promise of reaching explanatory mechanisms is exciting. It is still less than 10 years since the discovery of the CNV, and the next decade is likely to produce an even greater output of scientific and applied knowledge. We are engaging in research which may also result in making the CNV a standard clinical tool for the neuropsychological investigation of patients for whom the standard EEG has been a disappointing method.

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Chapter 8

Methodological Issues in CNV Research

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The term contingent negative variation (CNV) denotes a class of negative slow potential shifts of cortical origin, lasting of the order of seconds, which develop on the scalp in conjunction with certain sensory, motor, and

cognitive activities. The CNV is most clearly demonstrable during the anticipation of a signal for a motor act, yet it also accompanies purely sensory-perceptual tasks (Faidherbe & Deliege, 1968; Cohen, 1969; Hillyard, 1969b; Jarvilehto & Fruhstorfer, 1970; Picton, Hillyard, Galambos, & Schiff, 1971) and covaries with traditional measures of attention, motivation, arousal, expectancy, and preparatory set. Defining the psychological specificity of the CNV and the role it plays in the organization and execution of behavior have thus become challenging topics for research. This chapter deals with some of the specialized methodological problems that arise in the course of investigating the psychological concomitants of the CNV.

I. Recording Techniques

A. Electrodes

A convenient and reliable type of nonpolarizable electrode for recording CNVs is the commercially available Ag-AgCl pellet enclosed in a plastic housing. Pairs of these electrodes can be kept shorted together and ready for immediate daily usage with minimal preparation. Chlorided silver wire electrodes are cheaper and equally effective, but require more frequent cleaning and rechloriding.

Before applying the electrodes, the skin must be thoroughly cleansed of oil and dead epidermis (e.g., with acetone). Secure contact between electrode, conductive paste, and scalp is essential to prevent extensive drifting of the d.c. baseline. This baseline potential can be reduced in magnitude and greatly stabilized by puncturing the skin under each electrode with a sterile needle, thereby attenuating electrodermal variations (Picton & Hillyard, 1972).

Since a newly applied electrode pair will generally drift for several minutes as the interfaces attain electrochemical equilibrium, it is advisable to wait 10–15 min before beginning to record. Levels of drifting up to 15–20 μV per minute do not seem to interfere with recording the CNV. A badly drifting electrode can usually be corrected by removing it, cleaning the area, and reapplying it more securely. Occasionally, however, a steady or irregular baseline drift may begin in the course of an experiment and is not remedied by simply resecuring the electrode. It is not clear whether such drifting results from subtle changes at the interfaces or from naturally occurring bioelectric potential shifts related to the state of the subject (Section II,D). In any case, measured CNV amplitudes can be corrected to compensate for steady drifting of the baseline.

The number and location of electrodes will vary with the aims of a particular experiment, but a minimum array should include the following

placements: (1) a row of three or four electrodes along the midline from occipital to frontal scalp (including the "standard" vertex C_z), in order to measure the anterior-posterior gradient of the CNV (Section III,D), with earlobe or mastoid process (M) as the reference site; (2) the vertical electro-oculogram (V. EOG); and (3) the galvanic skin potential from palm or neck-mastoid, in subjects having unstable d.c. baselines (Section II,C). Additional electrodes can provide more information about the CNV's scalp distribution or possible artifacts (Section II,D).

B. Amplifiers

The advantages of using d.c. amplification in CNV research outweigh the minor inconveniences involved. Recording with the bandpass flat down to d.c. yields a wholly undistorted CNV waveform, even when a sustained "plateau" voltage precedes the expected stimulus. The alternative a.c. recording with long time constant will not only attenuate the CNV as a function of its waveform but will distort a monophasic negative wave into a negative-positive ensemble. Since the interaction between the CNV and the positive wave that follows it is of current theoretical importance (Section IV), it is important that both phenomena remain undistorted by the recording system. A d.c. recording also offers the opportunity to measure the resting baseline potential upon which the CNV is superimposed and the slow baseline fluctuations which may have a frequency of 0.1/sec or slower (Section II,C).

C. Tape Recording and Computer Analysis

It is advantageous to record all electrophysiological data on FM magnetic tape and computer analyze it off-line. This permits the elimination of those trials on which muscle, eye movement, or drift artifacts occurred, based upon inspection of the primary records. In lieu of tape recording, a general purpose computer may be programmed to throw out trials which violate specific standards of artifactual contamination or to adjust the CNV amplitudes to factor out the artifact (Section II). Rouseau, Bostem, and Dongier (1968) recommend making cumulative $X-Y$ plots of CNVs on successive trials and identifying as artifacts any deviations in the smooth growth of the average.

An off-line analysis also allows flexibility in choosing the number of CNVs to be included in each computer average. It is desirable to summate over as few trials as possible, so as to relate the CNV to discrete psychological states and to obtain more data for resting of reliability. This goal must be compromised against the need for achieving a reasonable signal-to-noise

ratio, which varies considerably as a function of CNV and EEG amplitudes. Summation of 4–10 trials is usually necessary, although in some subjects (e.g., Fig. 8-2B) the CNV is discernable on single trials. Measurement of CNVs on single trials in relation to short-term behavioral measures has only been attempted in one study, by McCallum and Papakostopoulous (1972). They observed significant correlations between CNV, quantified on each trial as the negative area over several hundred milliseconds prior to the response, and RT in nearly one third of their subjects within runs of only 24 trials. Given the great EEG variability in nonaveraged data, their finding of reliable correlations indicates that this method should receive more widespread usage. With tape-recorded data, CNVs can also be computer averaged *post hoc* in different cross-cutting ways, on the basis of stimulus situations, response variables, time intervals, EEG, or other physiological variables, etc.

The CNV parameters typically chosen for quantification are peak voltage, total area, or mean voltage within a time interval, all relative to the d.c. baseline existing before the warning stimulus. However, in view of the less than perfect correlations of these parameters with behavioral events (Section III), supplemental measures should be explored to improve the CNV as an index of psychological processes. The slope of the CNV in the proximity of behavioral or stimulus events, its rise and fall time, and its frequency characteristics can easily be quantified. Different measures of the d.c. baseline should also be tried out, such as the slope of the steady "drift" over several seconds prior to each trial, the posttrial baseline level, or peaks of the accompanying evoked potentials.

II. Slow Potential Artifacts in CNV Recordings

Recordings taken from the human scalp with long time constant or d.c. methods are vulnerable to slow potential artifacts that are filtered in normal EEG recordings. The most serious and well-documented contamination of the CNV results from slow rotation of the ocular dipoles, often in synchrony with the behavioral task (Sections A and B). Numerous other polarized membranes, however, may at times generate slow potential shifts at the scalp; the more important of these are identified in Sections C and D.

A. Ocular Potentials

1. Eye Movements

Within each eyeball is a standing potential of several millivolts, the corneo-retinal dipole, oriented with the cornea positive in relation to the posterior

end of the eye. The electric fields of these dipoles are distributed across the entire scalp, to the extent that eye rotations can engender potential shifts at the vertex larger in amplitude than the CNV. Changes in these field configurations caused by vertical eye movements as small as one degree of arc are easily recorded between a pair of electrodes placed above and below one eye (the vertical electro-oculogram [V.EOG]). As shown in Fig. 8-1, a voluntary downward eye movement of about 10 degrees (with subject's eyes closed) produces a d.c. potential shift of some 120 μV in the V.EOG, with the upper orbit shifting negatively due to elevation of the posterior end of the dipole. A negative potential shift of smaller amplitude is induced concurrently at the vertex (referred to linked mastoids). An equivalent upward eye movement produces potential shifts of similar magnitudes and opposite in polarity.

During CNV experiments, large involuntary eye movements are commonly synchronized with the preparatory interval, especially when the eyes are closed (Low, Borda, Frost, & Kellaway, 1966). A typical pattern of eye movements accompanying a S_1-S_2-lever pressing task is illustrated in Fig. 8-2. A downward eye rotation preceded each motor response with a time course disturbingly similar to that of the CNV. The linear dependence of CNV amplitudes upon the size of these EOG deflections is depicted in Fig. 8-3 for two subjects in the same experiment. Each plotted CNV value was the computer average over 12 trials which were stratified according to the size of the concurrent EOG deflection. The functions in Fig. 8-3 suggest that artifact was added to the CNV in proportion to the size of the EOG shift. Accordingly, when the eyes were open and immobilized by visual fixation (Fig. 8-2B), smaller, artifact-free CNVs occurred in conjunction with a stable EOG. Similarly high correlations between CNV and V.EOG amplitudes have been reported by Straumanis, Shagass, and Overton (1969) and Wasman, Morehead, Lee, and Rowland (1970). Lateral eye movements are negligible in most subjects.

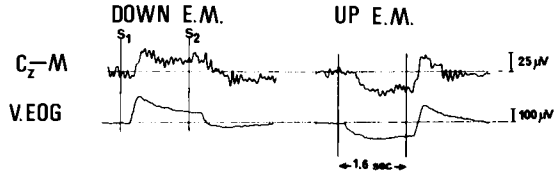

FIG. 8-1. Simultaneous averaged potential shifts induced in vertex-mastoid (C_z-M) and V.EOG channels by downward (left) and upward (right) voluntary eye movements (E.M.). The indicated E.M. (of about 10 degrees) was made in response to S1 (click), with a return E.M. made after S2 (tone). Recordings were d.c., with upward deflections signifying negativity in C_z and upper orbital leads. The magnitudes of these shifts, measured over 0.3 sec before S2 relative to the pre-S1 baseline were: Down E.M., C_z-M = -22.8 μV, V.EOG = -119 μV; Up E.M., C_z-M = 24.8 μV, V.EOG = 132 μV.

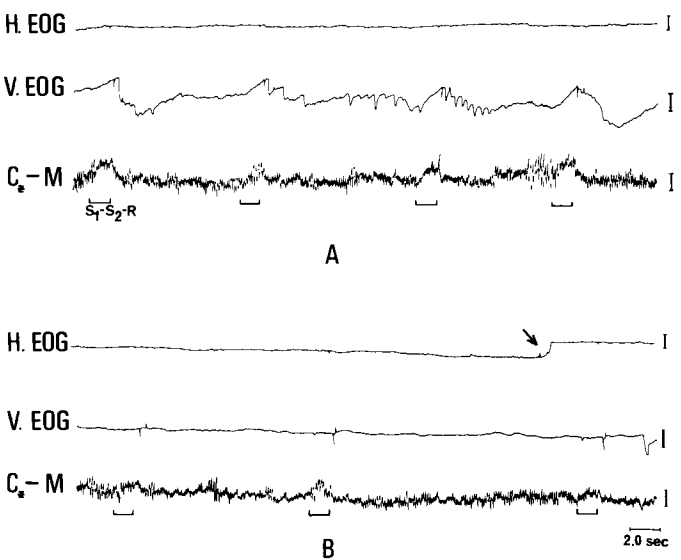

FIG. 8-2. Primary polygraph tracings of EEG and electro-ocular potentials during a click (S_1)-tone (S_2)-lever pressing task. Vertical eye movements (in V.EOG) are compared when subject's eyes were closed (A) *versus* eyes open and fixated on a point (B). Arrow indicates where experimenter adjusted the baseline. Spikes in V.EOG are response markers. Calibrations: H.EOG (recorded between right and left external canthi) = 100 μV; V.EOG = 100 μV; C_z-M = 50 μV.

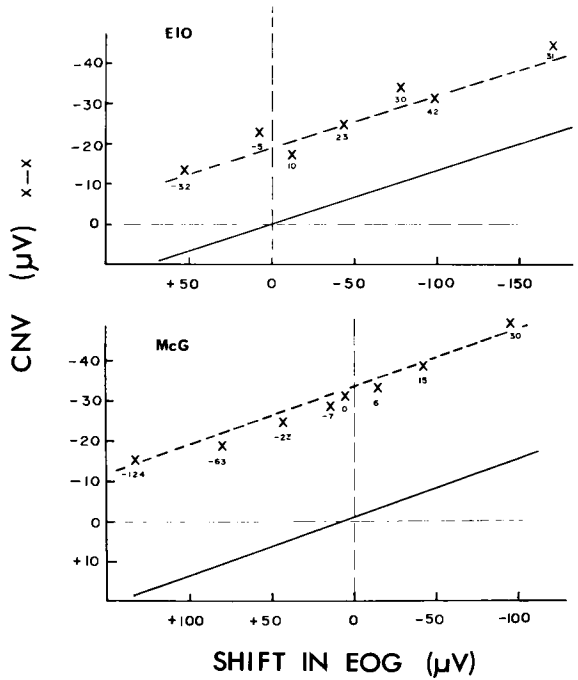

FIG. 8-3. Linear growth of CNV (dashed line) as a function of increasing EOG deflections (upper orbit negativity) in two subjects. CNVs obtained from a half-hour lever-pressing session were grouped together on the basis of the EOG deflection and computer averaged in blocks of 12. The solid line is the "calibration" function which estimates artifact amplitude at the vertex from the EOG deflection. The number adjacent to each cross is the percentage of averaged CNV that is ocular artifact.

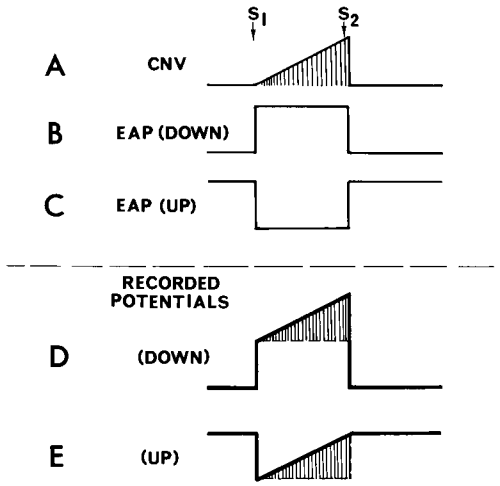

FIG. 8-4

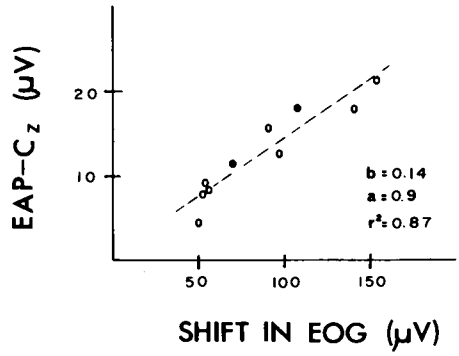

FIG. 8-5

FIG. 8-4. Idealized waveforms of the recorded vertex potential shifts, broken down into their additive components, produced by mirror image downward (D) and upward (E) voluntary eye rotations made at S_1. The recorded shift at D is the sum of a vertex-negative eye movement artifact (EAP) (B) and a CNV (A) rising before the oculomotor response to S_2. The shift labeled E is the sum of a vertex positive EAP (C) and the CNV (A). Thus, by subtracting one of the recorded potentials from the other, a remainder of twice the EAP is obtained. (Reproduced from Hillyard & Galambos, 1970, Figure 2.)

FIG. 8-5. One subject's "calibration" function. Each point is derived from a set of equal and opposite voluntary eye movements (as in Figs. 8-1 and 8-4) made with eyes closed (solid circles) or with voluntary shifts of gaze between fixation targets (open circles). Target separation was 5 degrees for the smallest EOG shifts and 15 degrees for the largest. Dashed line is the least squares line of best fit with a slope $b = 0.14$, an intercept $a = 0.9$, and linear regression coefficient $r^2 = 0.87$. "EAP," eye artifact potential.

The quantitative amount of artifact induced in the CNV by eye movements can be estimated by constructing the "calibration" function that relates the size of the EOG deflection to the concurrent artifact at the vertex. This can be accomplished by making a series of voluntary, mirror-image eye movements (Fig. 8-1); the total vertex potential shifts so produced must then be subdivided into two additive components—the ocular artifact and the CNV preceding the oculomotor response to S_2 (Fig. 8-4). Algebraic subtraction of the averaged potential shift during upward eye movement from that caused by downward eye movement eliminates the CNV and yields a remainder that is twice the artifact (Hillyard & Galambos 1970). Applying this additive model to the data shown in Fig. 8-1, an EOG shift of

125 μV is calculated to produce a vertex-artifact of 23.8 μV. The artifact-to-EOG shift ratio is 0.19.

By repeating these eye movements over a wide range of angular displacements, a complete function is defined by the paired artifact-EOG shift values. These functions are typically linear (Fig. 8-5) and indicate how much artifact must be subtracted from CNVs per unit of EOG shift. The functions are similar whether constructed by making eye movements with eyes closed or by making voluntary shifts of gaze between two targets.

By applying such artifact "calibration" curves to CNVs recorded during a S_1-S_2-lever pressing task with eyes closed, CNVs were found to be typically comprised of 10–50% ocular artifact (mean = 23%) (Hillyard & Galambos, 1970). The validity of these estimates of artifact was supported in two ways. First, the constructed artifact versus EOG functions (Fig. 8-3, solid lines) accurately predicted the growth of the CNV (dashed lines) with increasing EOG deflections. Second, the mean CNV amplitude recorded under eyes-fixated conditions was equal to that obtained with the eyes closed and free to move, after correction of the CNVs for the additive artifact.

2. Lid Movements

While good approximations of the ocular artifact magnitude could be achieved by the calibrated V.EOG method, there are some unresolved problems which may limit its precision and applicability. Foremost among these is that the artifact *versus* EOG functions may not remain fixed when the eyes are open, because the positioning of the eyelids can change the corneo-retinal field configuration. Displacement of the eyelids across the stationary eyeball produces large d.c. potential shifts in the V.EOG with field spread into the C_z-M channel. In Fig. 8-6 are shown potential shifts caused by voluntary "squinting" (primarily a downward movement of the upper lid) while the eye was stabilized to within $\pm$ ½ degree by fixating a point with a ½ degree afterimage upon the retina. In the inverse experiment, relaxation of the squint caused shifts of opposite polarity. Presumably, these potential changes represent distortion of the standing corneo-retinal fields due to "shorting" of the dipole by the lid. Simply grasping the upper lid and pulling it down over the eye also produces a large d.c. shift in the V. EOG (upper orbit positive); this is probably a partial basis of the well-known eye blink artifact.

Employing again the additive CNV + artifact model to the data from Fig. 8-6, an artifact of 12.9 μV is calculated to coexist with an EOG shift of 180 μV. The ratio of vertex artifact to EOG shift is much smaller (.07) during the squint than during a voluntary eye movement (.19, Fig. 8-1). In other words, a given amount of EOG shift will be accompanied by a different amount of artifact when caused by lid displacement rather than by eye

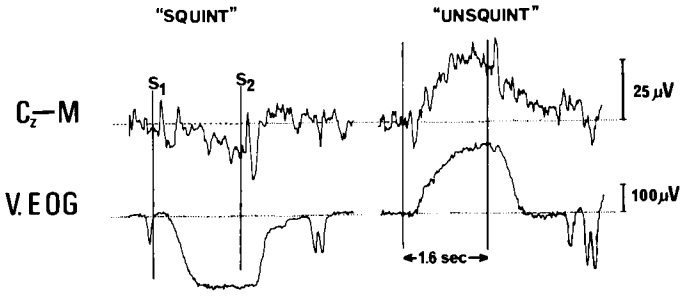

FIG. 8-6. Concurrent potential shifts induced in C_z-M and V.EOG channels by voluntary squinting at S_1 and a relaxation of squint made at S_2 (left), and by the reverse procedure (right) wherein squint was maintained except during the S_1-S_2 interval. Orbital electrodes were mechanically fixed during squinting to prevent their shifting. Same subject and polarities as in Fig. 8-1.

movement. Since it is difficult to discern what combinations of lid and eye movements underlie each EOG shift, the EOG may not be a reliable predictor of artifact amplitudes when the eyes are open. The exact artifact-to-EOG relationship is probably a complex function of relative eye and lid positions, which would be laborious to define for each subject. Nonetheless, as Fig. 8-5 indicates, the artifact-to-V.EOG ratios were not substantially different when derived under eyes open versus closed conditions; therefore, the biasing of the calibration function by lid positioning may not always be large.

A further complication is that upward shifts of gaze with the eyes open produce V.EOG deflections that are invariably 10–30% smaller (absolutely) than the mirror image downward shift of gaze between the same targets. Overton and Shagass (1969) have suggested that this substantial discrepancy results from an asymmetry of eyelid displacement between up and down eye movements. Until these questions are resolved, the functions interrelating eye position, V.EOG, and scalp artifact cannot be assumed to be invariant under all circumstances.

B. Summary of Techniques for Eliminating Ocular Artifacts

None of the techniques developed so far for controlling ocular artifacts in CNV recordings is fully satisfactory, and the strengths and weaknesses of each are evaluated below.

1. SUBTRACTION OF THE ARTIFACT, BASED ON THE "CALIBRATED" EOG

This method, described in detail above, has several drawbacks in practical usage. It is time-consuming to establish the entire artifact-to-EOG function and then to subtract the appropriate artifact from each averaged CNV. There is also the possibility that the artifact-to-EOG relationship

established by voluntary eye movements may not be precisely correct for EOG deflections resulting from lid movements, squints, or eye movements having different eye closure. Finally, if EOG deflections are computer averaged before the artifact is estimated, it is required that the calibration function be approximately linear, to ensure that the mean artifact maintains proportionality to the mean EOG shift. The linearity assumption seems to be fulfilled, at least for small and medium eye movements (Fig. 8-5).

Despite these qualifications, available evidence (Section II,A) indicates that this procedure yields a reasonable approximation of the scalp artifact under some experimental conditions and may find use with subjects such as children or patients for whom there is no way to restrict eye movements.

2. Potentiometric Subtraction of the Artifact

If one terminal of a 25 K potentiometer is attached to an electrode above the eyes and the other terminal placed on the mastoid, the center tap can be adjusted to lead off any proportion of the potential developed near the eye. The center tap can then serve as the reference for the vertex-recorded CNV, after it is balanced to make the eye movement artifact appearing in the tap and at the vertex identical (McCallum & Walter, 1968).

This method is very convenient, but otherwise suffers from the same drawbacks as method 1. When the potentiometer is adjusted to eliminate lid movement artifacts, it may not cancel out eye rotation artifacts having a different artifact-to-EOG ratio. The method's validity further depends upon a strict linear relationship between the EOG shift above the eye and the artifact at the vertex. There is no guarantee that linearity will hold true for all kinds and sizes of EOG deflections. In conclusion, this method only approximates the true correction of the ocular artifact; its validity would be improved by rejection of trials having large or anomalous EOG deviations.

3. Equating Experimental Conditions with Regard to EOG Deflections

This method involves quantification and comparison of EOG deflections observed under different experimental conditions. If the EOG deflections do not differ significantly, it is assumed that comparisons among CNVs are not confounded with differential amounts of artifact (Tecce & Sheff, 1969). The validity of this method is subject to the same considerations as methods (1) and (2): possible instability of the artifact-to-EOG ratio and the assumption of linearity if computer-averaged EOGs are equated.

4. Recording Montage Insensitive to Ocular Artifacts

CNVs recorded from the vertex referred against a temporal site are reported to be relatively uncontaminated by ocular potentials during a S_1-S_2-

respond task (Straumanis *et al.*, 1969). This insensitivity to artifact probably results from the electrodes lying along an equipotential line of the displaced ocular field.

A major disadvantage of this "bipolar" recording is that CNVs are attenuated by about 60% in relation to the standard mastoid reference, necessitating more computer averaging to obtain a comparable signal-to-noise ratio. Moreover, mappings of eye movement artifacts on the scalp (Overton & Shagass, 1969) indicate that a significant amount of artifact could enter a vertex-temporal channel if large eye movements occur. Twenty-degree vertical eye movements were found to induce artifacts of about 7–11 μV in the vertex-temporal channel—about the same amplitude as CNVs recorded there. It is likely that even smaller eye movements could at times contribute significant contamination. Monitoring of EOG would seem a necessary adjunct to this technique.

5. Visual Fixation and Elimination of Trials with EOG Deviation

Most adult subjects have little difficulty fixating their gaze for long periods during CNV tasks, if opportunity exists for blinking in the intertrial intervals. In this way EOG deflections can be kept below about 10 μV on most trials and those having larger shifts can be excluded from further analysis. This method seems least subject to systematic error and is recommended for general usage whenever subjects are capable of such fixation.

Residual EOG shifts below 10 μV could produce at most some 2 μV of artifact in the vertex-mastoid channel which may be neglected for most purposes. Even this small artifact, however, could be compensated by one of the above-described procedures. Peters, Knott, Miller, Van Veen, and Cohen (1970) have improved upon this method by recording from supra- and infraorbital leads separately against a mastoid reference. In this way, potentials caused by vertical eye movements, approximately equal and out of phase in the two leads, may be distinguished from the possible spread of large CNVs into the superior orbital electrode. Furthermore, this method might serve to identify lid movement potentials if they elicited differential potential shifts in upper and lower orbital electrodes.

C. Large Baseline Shifts Related to "Arousal"

During an occasional recording session, high amplitude (100–300 μV) vertex-negative slow potential shifts are observed following the motor response to S_2 (Fig. 8-7). These deflections have a characteristic shape, beginning about the time of the response and peaking some 2½ to 3½ sec later, having a total duration of 5–7 sec. The largest of these waves may be followed by a positive afterwave of similar duration.

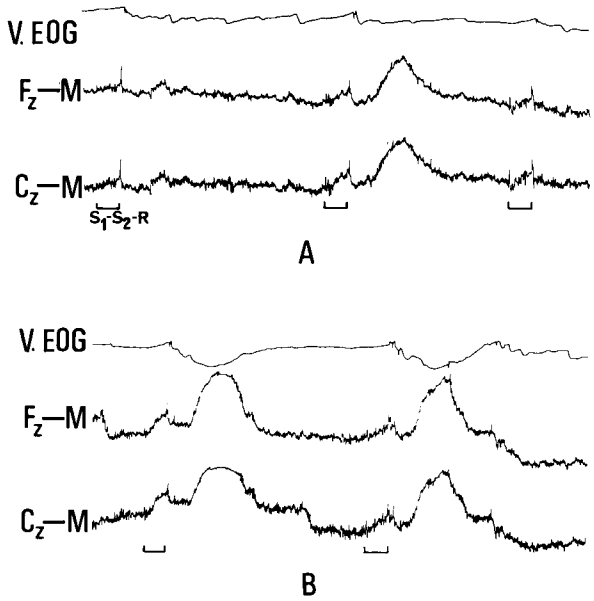

FIG. 8-7. Primary EEG and EOG records during a S_1-S_2-lever pressing task from a subject who displayed large phasic potential shifts after some responses. A and B depict different time segments in a half-hour session. Time base: S_1-S_2 interval = 1.3 sec. Calibrations: V.EOG = 100 μV; C_z-M and F_z-M = 50 μV. Negativity upward in C_z, F_z, and supraorbital leads.

The conditions governing the appearance of these potentials are not completely understood. They occur only in some recording sessions and then only on certain trials (Fig. 8-7A), in association with an unstable d.c. baseline. Karrer, Fabregat, Czaja, Kohn, and Ptashne (1971) report finding such waves in over half their subjects as they become drowsy and link them to an "arousal from drowsiness" provoked by the task. These workers also have observed, less commonly, a positive baseline shift following the motor response, which they attribute to a relaxation of effort in alert subjects. Timsit, Koninckx, Dargent, Fontaine, and Dongier (1970) have reported that a similar negative afterpotential (though somewhat smaller) bears an astoundingly good correlation with the mental status of patients.

These slow "arousal waves" are similar in latency, time course, and conditions of evocation to the galvanic skin phenomena seen during CNV tasks (Low *et al.*, 1966). Karrer *et al.* reported that the waves were not altered either by chemical manipulations which influenced palmar skin potentials or by skin drilling beneath the electrodes and concluded that the skin was not their source. In support of this conclusion, Sano, Miyake and Mayangi (1967) have obtained similar surface-negative potential shifts following various arousal manipulations from epidural electrodes.

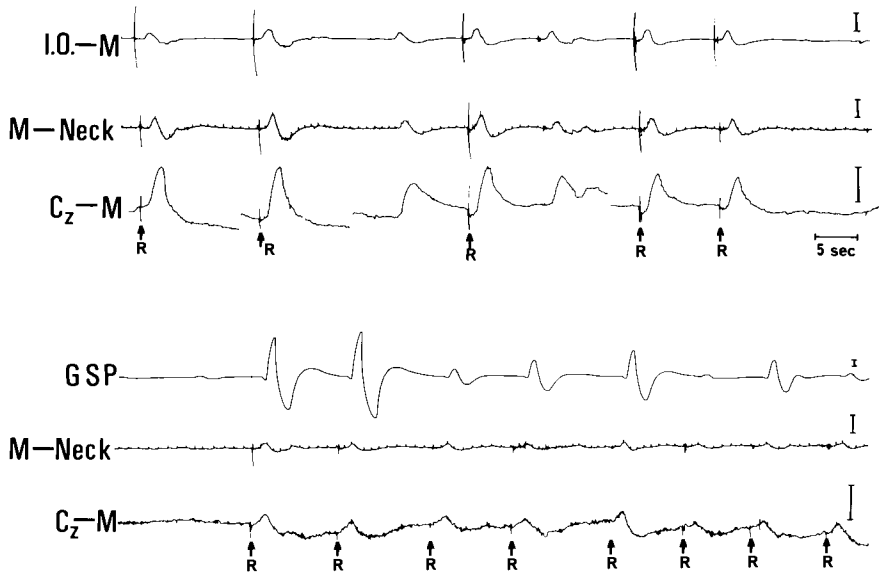

FIG. 8-8. Upper tracings: concurrent recordings of potentials developed in infraorbital-mastoid (I.O.-M, T.C. = 0.45 sec), mastoid-midline neck (M-Neck, T.C. = 0.45 sec), and C_z-M (d.c.) channels during a lever pressing task. Arrows indicate subject's lever presses. Note large waves in all channels following each response. Breaks in C_z-M tracing are readjustments of d.c. baseline by experimenter. Polarity convention: upward deflection signifies negativity in first-named lead of pair. Lower tracings: continuation of lever pressing task, with I.O.-M channel replaced by the palmar galvanic skin potential (GSP, T.C. = 0.45 sec). Calibrations: 100 μV.

In unpublished studies of six subjects having these large waves, I observed a rather high concurrence between the waves recorded simultaneously from different sites on the scalp and in the palmar galvanic skin potentials (GSP). A typical example is presented in Fig. 8-8, showing the conjoint occurrence of "arousal waves" in vertex-mastoid, mastoid-neck, mastoid-orbit, and palmar GSP. The onset of the palmar wave was delayed by about 1 sec in relation to the others. While the correlation among the waves in different channels was not large with respect to their amplitudes, in very few instances was a wave in the C_z-M channel not followed by some deflection in the GSP (Hillyard, 1968). These results suggest that at least some of the scalp-recorded arousal waves are closely associated with an autonomic activation pattern which includes the galvanic skin potentials.

Picton and Hillyard (1972) have recently obtained direct evidence that the preponderance of these potential shifts is, in fact, of electrodermal origin. Scratching the skin under the mastoid "reference" electrode with a sterile needle until blood appeared almost completely abolished these "vertex-negative" potential shifts, indicating that they actually represent mastoid-positive skin phenomena. We plotted the distribution of these phasic shifts upon the

head and found them to be maximal on the skin surrounding the ear (including the mastoid) and on the posterior neck below the inion, and minimal on the ear itself and on the central scalp. Since biochemical manipulations of Karrer *et al.* (1971) were performed on the relatively inactive scalp electrode sites, no alteration of the waves would be expected (Picton & Hillyard, 1972).

Since these huge waves can seriously contaminate the latter portion of the CNV on some trials (Fig. 8-7B), the time constant of CNV recordings should be large enough to detect whether or not they are present. These slow artifacts could cause serious misinterpretations of CNV data if, as reported (Karrer *et al.*, 1971), they occur mainly on those trials which "surprise" the subject.

D. Other Possible Sources of Artifact

1. Sensory-Evoked Slow Potential Shifts

Tone bursts or lights of several seconds' duration can evoke sustained potential shifts of 10–50 μV on the scalp (Kohler, Held, & O'Connell, 1952; Hillyard, 1969a). Animal research has localized these shifts primarily within the specific sensory projection cortices (Lickey & Fox, 1966). If continuous auditory or visual stimuli are introduced in a CNV paradigm, the danger exists that variations in these highly unstable sensory-evoked shifts could be confused with changes in the CNV.

2. Skin and Sweat Glands

Galvanic skin potentials on the scalp accompanying the "scalp tingling" of autonomic arousal may approach the order of millivolts, according to Sano *et al.* (1967). While the latency and time course of skin potentials can be clearly distinguished from those of the CNV, there may be occasions where conditioned skin potential shifts may infiltrate the latter phases of the CNV (Picton & Hillyard, 1972) (Section II,C).

3. Vasculature and Blood–Brain Barrier

In conjunction with neuronal activity are regional variations of pCO_2, pH, and blood flow within the brain which are linked to large d.c. shifts at the cortical surface (for reviews, see O'Leary & Goldring, 1964; Hillyard & Dargent, 1969). Ionic changes in different brain compartments may influence the CNV not only as a slow additive artifact (with a rise time as fast as 1–5 sec) but also by direct physiological interaction.

4. Shifts of the Absolute Baseline d.c. Level

The total d.c. "offset" potential may amount to many millivolts and represents a complex summation of potentials developed across the recording interfaces and across innumerable biological membranes. Some authors report that the standing potential is highly stable, even during arousing stimulation and mental activity (Sano *et al.*, 1967), while others find that the fronto-occipital standing potential changes by millivolts in conjunction with a host of psychological variables (Cowen, 1968). The scalp-mastoid baseline voltage may be substantially reduced by puncturing the skin, however, indicating that a large component of this potential is generated extracranially. A neglected research problem is to determine the interaction of the CNV with changes in the absolute baseline.

5. Movement of the Electrode–Scalp Interface

Changes in the electrode contacts may alter their electrochemical equilibrium and create potential shifts. Very often, spontaneous movement of the subject is accompanied by a large slow potential shift lasting several seconds, although these could in part represent "arousal waves" (Section II,C).

6. Tongue Movements

Finally, Klass and Bickford (1960) have collected data showing that shifts in tongue position can induce nonneglible d.c. artifacts on the scalp. An example of large "glossokinetic" artifacts appearing in a C_z-M recording during voluntary tongue movements is shown in Fig. 8-9. According to Klass and Bickford, a d.c. negativity at the vertex is produced when the negatively charged tip of the tongue comes in contact with the roof of the mouth.

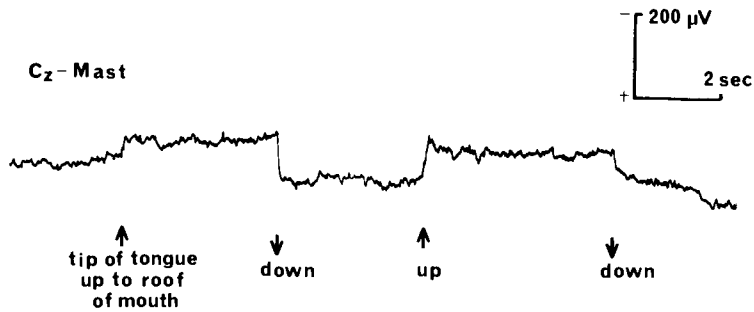

FIG. 8-9. Direct current potential shifts produced in a vertex-mastoid channel as a function of tongue position. Data obtained by Dr. T. W. Picton.

III. Correlations of CNV with Behavior

The correlation between the faster EEG rhythms and behavioral dimensions is notoriously evanescent, although promising new attempts are being made to extract complex EEG parameters that are predictive of performance (e.g., Adey, 1970). The psychological specificity of the CNV is equally problematical, although, unlike the EEG, the CNV correlates indiscriminately with a broad range of behavioral activities. The situations in which CNVs develop may be classified into four distinctive types: (1) sensory discrimination (selective attention), (2) preparation for motor response, (3) anticipation of reinforcement (positive or negative), and (4) timed cognitive performance. In an effort to abstract some common denominator from these tasks, the CNV has been identified with such "global" unitary processes as activation, attentiveness, concentration, expectancy, drive, arousal, and effort (for review, see Cohen, 1969).

Although the CNV accompanies a wide realm of behavioral acts, seldom does it display a strong and consistent correlation with specific behavioral parameters. Consider, for example, the well-known, inverse association between large CNVs and fast reaction times (RTs) in the S_1-S_2-respond task. It is amply evident that statistically significant reciprocal changes in CNV and RT can be produced by manipulating such variables as learning, intensity and duration of S_2, distraction, incentive, S_1-S_2 interval, and fatigue (see Hillyard, 1969a; Peters *et al.*, 1970), but these correlations are generally small, inconsistent, and subject to dissociation. Moreover, it does not follow that the altered RT was a direct consequence of the change in CNV, since each could have been induced independently by the manipulation. Some experimental manipulations have, in fact, created dissociations of RT from CNV amplitude; these include distraction (Tecce & Scheff, 1969), extended practice (Donald, 1968; McCallum, 1969), reducing the probability of S_2 (Hillyard & Galambos, 1967), and varying the S_1-S_2 interval (McAdam, Knott & Rebert, 1969). Under constant conditions and with order effects controlled, CNV amplitudes were not found to account for an appreciable amount of the variability in RT, except in a few subjects (Besrest & Requin, 1969; Hillyard, 1969a; Wilkinson & Haines, 1970; Rebert & Tecce, 1973). Finally, Naitoh, Johnson, and Lubin (1971) found that near total absence of CNV following sleep loss did not necessarily retard RTs.

The correlation of CNV with other performance measures (e.g., sensory acuity: Hillyard, 1969b; Wilkinson & Haines, 1970; Hillyard, Squires, Bauer, & Lindsay, 1971) is similarly loose, although at times statistically significant. This raises the question of whether the CNV plays an active

functional role in the genesis of behavior or is rather an epiphenomenon which reflects a very general property of brain activity. For example, Castelluci and Goldring (1970) have linked certain cortical d.c. shifts to the extracellular potassium ion concentration, which would increase with the total cellular activity in a brain region rather than with the differentiated neuroelectric patterns presumed to underly specific behaviors. It is up to future research to establish whether the CNV bears a fixed, necessary relationship with *any* dimension of behavior and to determine its specificity. Some of the methodological and interpretative problems which may obscure the actual nature of CNV-behavior interrelationships are discussed in the following section.

A. Intertrial Interval and the d.c. Baseline

Knott and Irwin (1967) have suggested that the CNV might be the shifting of a tonic d.c. baseline potential that can vary in resting level and "saturates" at some maximal ceiling level. This hypothesis was designed to account for an unexpected reduction in CNV that accompanied heightening of the subjects' arousal. The sustained arousal allegedly raised the negativity of the baseline potential nearer to its ceiling so that the CNV saturated earlier.

Measurement of this hypothetical baseline level has not yet become feasible, but its possible existence poses problems in relating the CNV to behavior. If behavioral performance is actually determined by the total d.c. negativity (baseline + CNV), the phasic CNV will be dissociated from performance to the extent that spontaneous or systematic baseline fluctuations occur. Alterations of the baseline level might also generate U-shaped functions relating the CNV to processes like arousal (Tecce, 1971), if arousal raises both the baseline and the CNV amplitude, but with different thresholds.

The baseline voltage may depend in part upon the duration of the intertrial interval. Low (1969) reported that CNVs were larger when positive drifting of the baseline preceded S1 and suggested that larger intertrial intervals may permit a more complete return to baseline between trials. In an experiment with brief intertrial intervals (2–4 sec) CNVs were found to be small and poorly predictive of performance (Hillyard *et al.*, 1971); it was postulated that "relaxation" of the baseline between trials had been prevented. Activation of the subject during intertrial intervals (by stimulation, motor activity, etc.) might also alter the baseline level and hence the subsequent CNV. For these reasons it would seem prudent to use longer intertrial intervals, control for variations in these intervals, and to confine the subject's anticipation and activity to the S_1-S_2 interval.

B. Effects of Learning and Fatigue

The magnitude of the CNV depends not only upon the nature of the expected event or response, but also upon the strength of learning of the S_1-S_2 contingency and the timing of stimuli. In some instances, the relation of CNV to performance may in part be confounded with the stage of learning of the task. An experimentally naive subject, for example, will invariably display a strong inverse correlation between CNV and RT as he learns a S_1-S_2-respond task. Yet the CNV could be acquired independently of the rapid responses and may not govern them, making the correlation a spurious consequence of their mutual acquisition curves (Hillyard, 1969a).[1] With extensive practice in the S_1-S_2-respond task, on the other hand, RTs can be sustained at fast levels while CNVs actually decline (Donald, 1968; McCallum, 1969). This dissociation may be attributed to the learning of "automatic" precisely timed responses that do not require as much CNV.

After training in a CNV task, motor (or perceptual) performance may become more skilled, accurate, and precisely timed while requiring less effort. Since response effort seems to be one of the few reliable determinants of the CNV (Low & McSherry, 1968; Waszak & Obrist, 1969; Hillyard & Galambos, 1970; McAdams & Seales, 1969), CNVs may decline with practice while performance improves. These considerations make it doubtful that learning effects can be eliminated from most CNV experiments, but the following steps may help to minimize any dissociations: (1) vary the S_1-S_2 interval over a small range to prevent anticipatory responding based on learning of the interval; (2) take behavioral measures after full acquisition of the CNV and asymptotic performance; (3) make comparisons among trials close together in the experimental sequence.

Fatigue may also result in artificially high correlations between CNV and performance measures. Wilkinson and Haines (1970) found that in the course of a lengthy vigilance-RT task CNVs progressively declined as RTs became slower and perceptual accuracy fell. The reciprocal CNV-RT correlation evaporated, however, when the effect of simple passage of time was statistically controlled. Fatigue and other long-term changes in the state of the subject may be controlled statistically (Hillyard, 1968) or by steps (2) and (3) above.

C. Use of Averaged Data

When CNVs are computer averaged in sequential blocks of 6–12 trials, the usual practice, only the average values of CNV and behavioral parameters are available for comparison. Computer averaging may therefore

[1] CNV and fast RT may be acquired via different mechanisms; for example, CNVs might grow simply with conditioning of the S_1-S_2 contingency, while RTs might be shortened by precise learning of the S_1-S_2 interval and making more effective motor patterns.

obfuscate the actual shape of the function that relates the CNV to behavior (if such exists). If, for example, CNVs are diminished in a subject only on the infrequent trials with the longest RTs, this fact may be embedded within the noise of the averaged CNV and pass undetected. A second type of distortion arising from the sequential averaging of CNVs derives from the temporal "jitter" of the behavioral event with respect to the averaging epoch. Increased variability of response latencies could reduce the peak values of the averaged CNV through temporal dispersion, even though the CNV amplitude at the time of each response was constant (see Hillyard, 1969c).

These problems would ideally be overcome by quantifying CNVs on single trials, which is feasible in certain subjects having high CNV-to-noise ratios. Alternatively, CNVs can be computer averaged on the basis of categories of behavioral performance (RT, response intensity, perceptual accuracy, etc.) and with time-locking to the subject's response rather than to the signals. By averaging CNVs according to more refined categories of performance and according to other measures of the subject's state (EEG, autonomic variables), some of the indeterminacy in the CNV-behavior "transduction" may be reduced.

D. Multiple CNVs?

There is increasing evidence from spatial distribution studies that multiple types of CNVs exist, each associated with a different cortical region and psychological process (Cant & Bickford, 1967; Cohen, 1969; Borda, 1970; Jarvilehto & Fruhstorfer, 1970). This is not surprising, in light of the anatomically and functionally discrete slow potential shifts found in animals during motor activity, sensory input, reinforcement, arousal, conditioning, etc. (for reviews see Rowland, 1968; Hillyard & Dargent, 1969). The multiple CNV hypothesis could help to explain both the ubiquity of the CNV in diverse sensorimotor acts and its loose correspondence with specific behaviors. If more than one CNV were activated on a given task, a scalp electrode would record their composite, portions of which could be unrelated to the behavioral measures under investigation. This possibility, and that of more complex interactions among CNVs, should be tested by always recording the entire scalp distribution of the CNV. In this way the multiple CNV hypothesis might be distinguished from the alternative of a single anatomical-functional entity having little psychological specificity.

IV. The CNV in Evoked Potential Research

Sensory signals which convey "task-relevant" information or require a perceptual judgment generally elicit larger averaged evoked potentials (AEPs) upon the human scalp than do neutral stimuli (e.g., Sutton, 1969).

Experiments demonstrating this principle often have the same structure as a CNV task, with an anticipated stimulus requiring a motor response, decision, or perceptual assessment. Had investigators utilized long time-constant recordings, in many cases the AEPs would have been found superimposed upon a CNV.

In Fig. 8-10 are shown CNVs accompanying an auditory discrimination task, patterned after a classical study of evoked potential enhancement during sensory decision (Davis, 1964). The subject's task was to judge whether tone pip "2," randomly varied in intensity by ± 3 dB, was louder or softer than the fixed standard (tone pip "1") and to report his decision when a "response light" was lit. Leaving aside the details of this experiment,[2] the growth of the CNV between tone pips "1" and "2" raises the question of whether Davis' major finding—an enhancement of the amplitude of the AEP to the second tone—was in part a consequence of the CNV.

Näätänen (1970) answered this question affirmatively and hypothesized that the CNV, representing cortical activation, causes enhancement of any AEP superimposed upon it. Several experiments, however, were inconsistent with the suggestion that the CNV is a nonspecific magnifier of AEPs: the AEP to neutral, irrelevent signals was found not to be enhanced in amplitude by the presence of CNV (Donald, 1968; Ellis, 1969; McAdam, 1969), and enlargement of the AEP to a task-relevant signal was found to be dissociable from the preparatory CNV amplitude (e.g., Donald & Goff, 1971; Tueting & Sutton, 1973).

It has also been proposed that an abrupt termination of the CNV upon presentation of an anticipated task-relevant stimulus may constitute a portion of the late positive component of the AEP (Karlin, 1970; Donchin & Smith, 1970). Recent experiments using d.c. recordings, however, indicate that the late positive AEP is enlarged by the receipt of task-relevant information to a much greater extent than could be achieved by the simple cutoff of the antecedent CNV (Donald & Goff, 1971; Hillyard *et al.*, 1971). Thus, while the CNV and late positive AEP appear to be separate and dissociable physiological events, under certain circumstances [e.g. when a motor response is made to an expected signal (Donchin & Smith, 1970)] the AEP is probably contaminated by summation with the positive terminal phase of the CNV.

Observations that spontaneous, trial-to-trial fluctuations in CNV amplitude may be positively correlated with the size of the late positive AEP to component evoked by an anticipated task-relevant event (Hillyard, 1969b; Donald & Goff, 1971) are suggestive of a direct functional interaction be-

[2] The hypothesis that instigated this experiment—that CNV amplitude might serve to predict the correctness of the sensory decisions—was not substantiated.

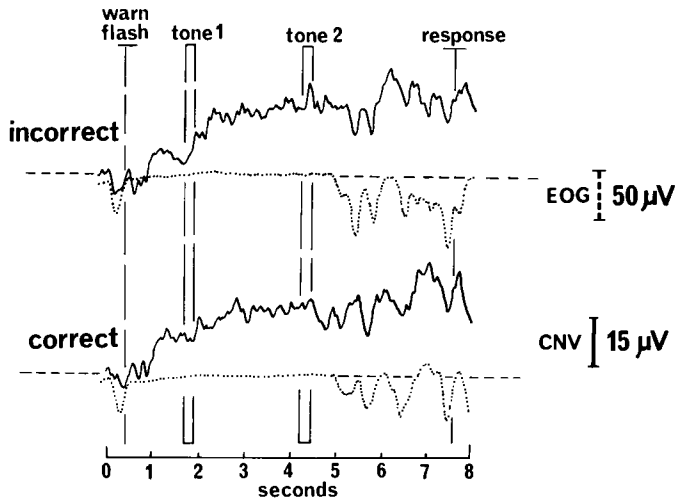

FIG. 8-10. CNVs (vertex-mastoid) during an auditory intensity discrimination. CNVs were computer averaged over 12 trials according to whether subject's intensity judgment was correct or incorrect. Deflections in the vertical EOG were negligible.

tween the two types of waves. In a signal detection task, CNVs preceding correctly detected signals were slightly larger on the average (by a few microvolts) than before undetected signals, while the AEPs were some 5–20 μV larger after the detected signals (Hillyard, 1969b; Hillyard *et al.*, 1971). This suggested that the CNV can provide a rough index of a cortical process that facilitates sensory processing. Since a signal evokes a larger late positive AEP to the degree that its task relevance and informational or motivational content is accurately appreciated, a CNV which correlates with accuracy of processing will also correlate with the late positive wave. By implication, d.c. recording should receive more general usage in AEP experiments, in order to discover how much AEP lability can be attributed to the CNV.

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The references given here are classified approximately in terms of the categories of techniques given in the volume. The first category is human EEG recording techniques and the second includes human evoked potentials and CNV. Methods related more to recording of cellular processes and to analytic recording of brain activity in animals are given in the bibliography at the end of Part A, whereas methods related to recording of receptor and effector activity are given in the bibliography at the end of Part C.

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