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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

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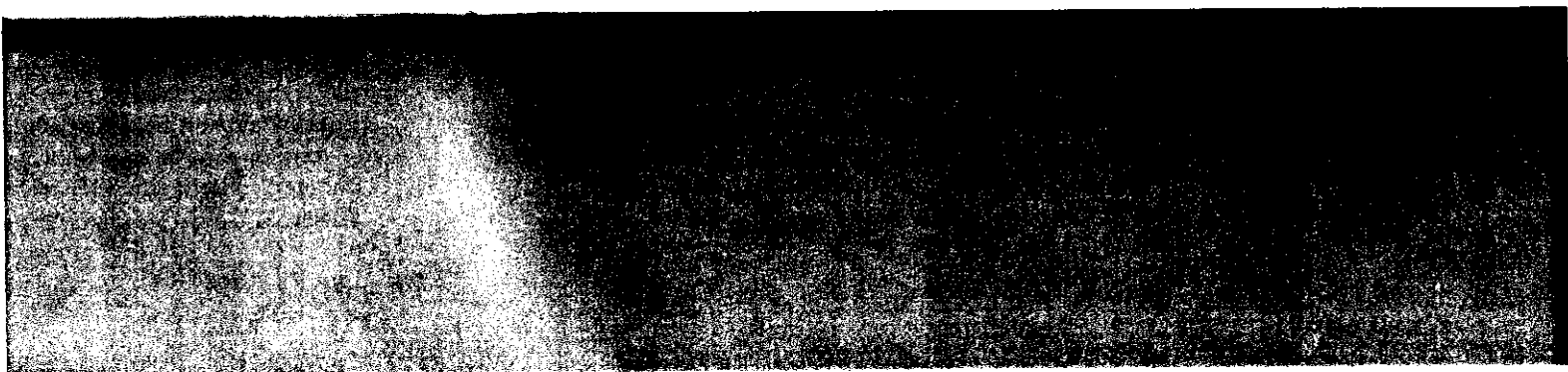vior relationships in a manner
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correlations which may be demonstrated between poorly understood brain potential measures and psychological constructs which are difficult to subject to operational definition and experimental manipulation seem to advance 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 : behavior. Thus, an alternative spontaneous brain activity with behavioral sequences is clearly r behaving organism.

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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 neuro-electric potentials.
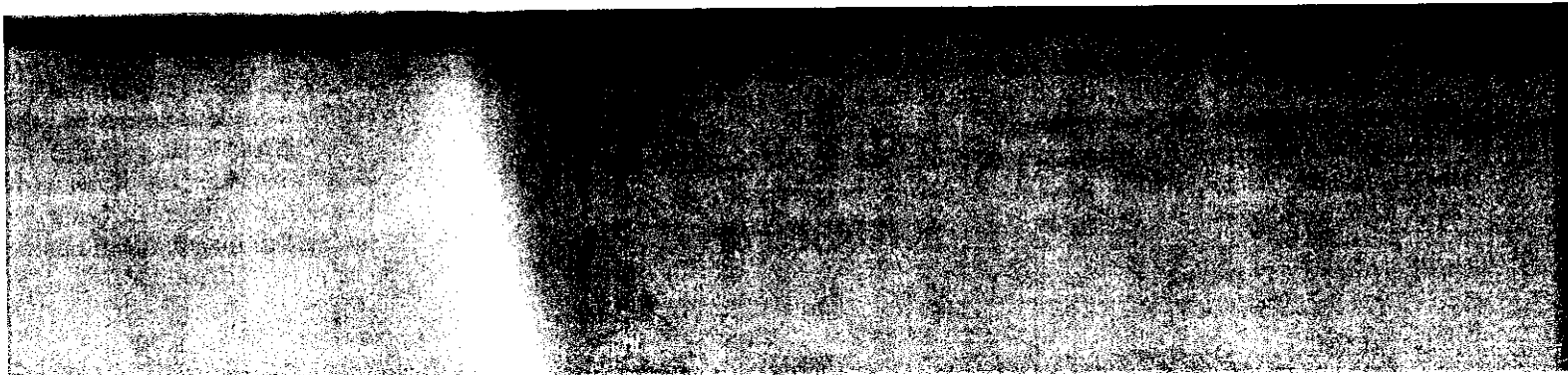
One can hardly wonder that, faced with these manifold obstacles, many have doubted the value of neurobehavioral studies employing scalp-recorded brain potentials. Nevertheless, the creative application of available knowledge and techniques can permit us to at least partially realize the possibilities 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)

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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

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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

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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
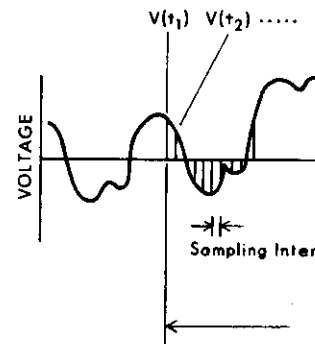

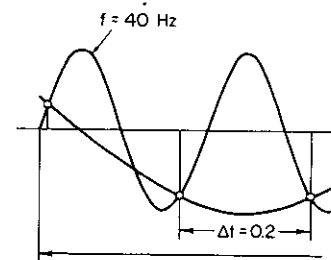FIG. 4-1. Discrete sampling of a continuc surements, $V(t_1) \cdots V(t_m)$. The ensemble by $(m - 1)$.

FIG. 4-2. "Aliasing" of a 40-Hz waveform rate (50 Hz) less than twice the frequency

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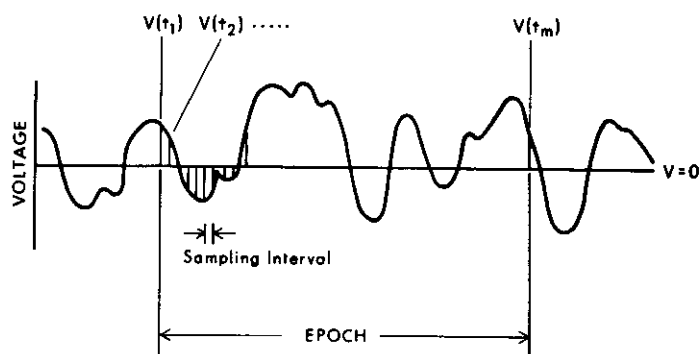e some maximum total number

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 $(m - 1)$.
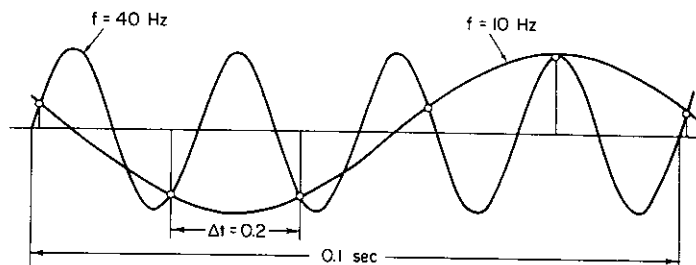

FIG. 4-2. "Aliasing" of a 40-Hz waveform as a 10-Hz fluctuation, due to the use of a sampling rate (50 Hz) less than twice the frequency of the true signal.

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: $V_k(t_1, t_2, ..., t_m)$, 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

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

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

The ensemble variance is

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

also evaluated at each sample point across ensembles.

The ensemble autocovariance is

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

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 $\overline{E}(t)$. 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 statistical 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 EE intervention of uncontrolled var tions, changes in the state of the In addition to rigorous control c it is always advisable to directly It is also a sound practice to view descriptive, and to employ them f defining the population from whi

The temporal stability of ense by the concepts of stationarity ar in the literature requires an explic tial data. A time-varying random tical purposes, if its first and sec covariance), computed across ens average voltage, its variability ab are stable across the epoch. Ergo time invariance, which permits a the statistics of all possible ensem of sufficient length to accurately The proper epoch will depend m data. In general the epoch will ha of the slowest frequency present to be satisfied. This is not necessa may be adequately represented process is random and the N is su

Let us now consider the applic tential data. First, it is apparent stationary since its mean value, l ensemble epoch. In the case of Δ by definition in the first instance, EEG. The mean voltage of the E stance ensured by the use of a.c amplification is used, which has interest in steady potential shifts, a potential bias will ordinarily be presence of very low frequency several important problems. Fir: activity is not of cerebral origin, electrode polarization, eye and o be relatively large in amplitude cranial origin. Since analog-to-window, the presence of signific

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volve either the background EEG, $G(t)$, or the ERP, $E(t)$, through the
intervention of uncontrolled variables. In electrophysiological investiga-
tions, 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 poten-
tial data. A time-varying random variable is said to be stationary, for prac-
tical purposes, if its first and second moments (mean, variance, and auto-
covariance), 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 po-
tential data. First, it is apparent that the ERP, $E(t)$, is neither ergodic nor
stationary since its mean value, $\overline{E}(t)$, 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 circum-
stance 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 intra-
cranial 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-
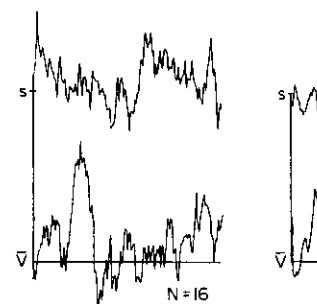

FIG. 4-3. Ensemble average ($\bar{V}$) and star for N of 16, 64, and 256. Amplitude cali

tion from the mean and is expr than as a squared voltage.

When the N is rather small, across the epoch. These fluctuati which, due to the rectification p frequencies present in the origi mean value of s computed acros of the population standard dev data by comparing the mean s f N is increased, the ensemble s a This reduction in the variability tional to the square root of N. II the mean component, the stan $(N)^{1/2}$, providing the variance is that for small samples, s flucti across the ensemble epoch, so cific time points in the ensemble mark. Generally, it will be desi fluctuations in s within the epoc priate N can be selected by not and applying the $(N)^{1/2}$ rule.

In the experimental situatio assumed to show no long-term characteristics, i.e., to represen case, however, as exemplified b from wakefulness to sleep and a circumstances the EEG statisti disclosed by examination of t

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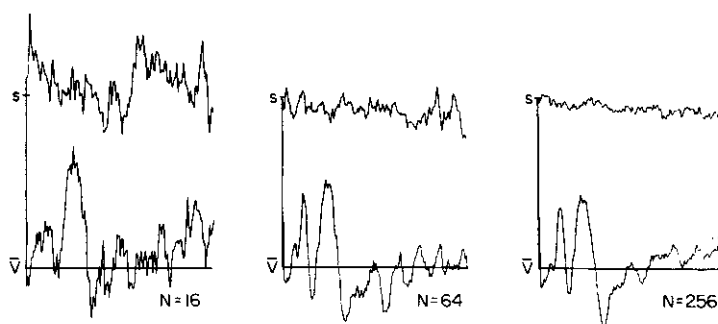ure represents the average devia-

FIG. 4-3. Ensemble average ($\overline{V}$) 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-

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A final instance in which a s) strated is the decrease in varian rhythm. This stimulus-generated many subjects who have a promi to the fact that the assumption of $G(t)$ is not always warranted.

D. Estimation of the Mean ERP (

Since the expected values (popt $\Delta E(t)$ and $G(t)$, are considered tc vides an estimate of the mean $\bar{V}^2(t)$, a measure of the accuracy ol which limit the number of ensen variance of $V(t)$ result in the usu: errors will be jointly determine(components. Theoretical consid(orem, confirmed by empirical ex us to consider statistics obtainee representing random samples of normal probability distribution i statistics, the precision of estima readily estimated by standard te(aging for extracting the mean E: is based upon the fact that the expressed as their variance, is ensembles, N, constituting the e point that the terminology emplc distinguish the ensemble standa of the ensemble averages. The lat deviation divided by $(N)^{1/2}$, is be is obtained either by dividing th or by computing the standard de\ the values obtained by these mei the population statistics over tir error computed from the ensemi the ERP waveform not seen in individual ensembles. This resu

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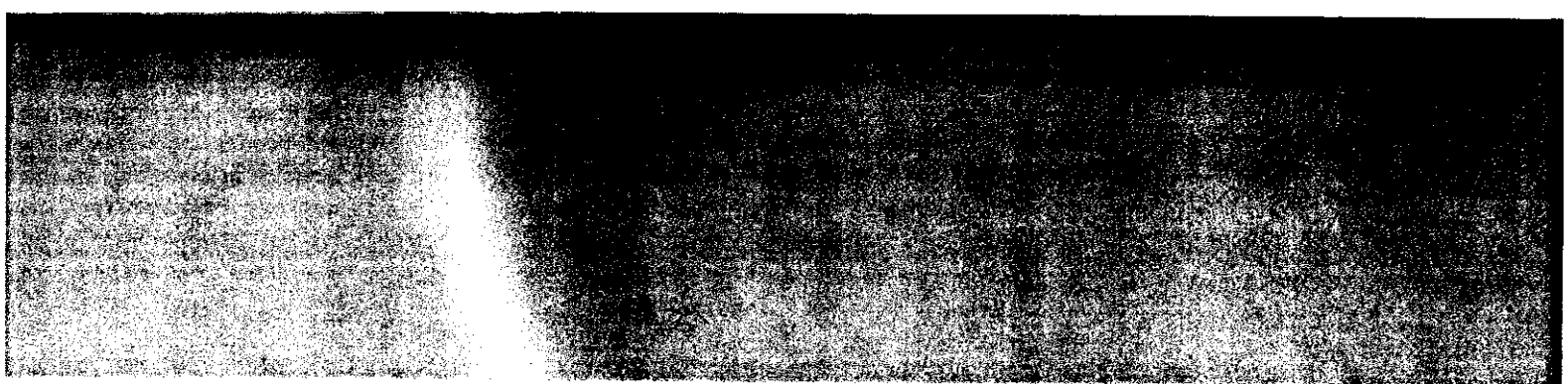in which a systematic nonstation-
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A final instance in which a systematic nonstationarity can be demonstrated is the decrease in variance associated with blocking of the alpha rhythm. This stimulus-generated change in $G(t)$ follows a light flash in 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, $\bar{V}(t)$, provides an estimate of the mean ERP component, $\bar{E}(t)$, and the variance, $\bar{V}^2(t)$, 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.

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nposition 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 $10\mu V$. Dividing this value by $(N)^{1/2}$, 8, we obtain an estimated standard error of $1.25\ \mu V$, 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 $\pm 3.25\ \mu V$ 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,
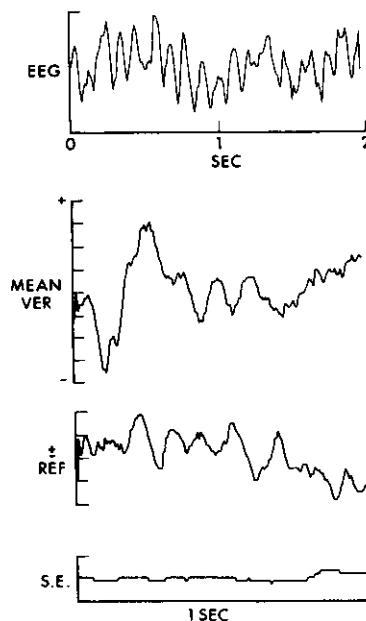
HERBERT G. VAUGHAN, JR.

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.

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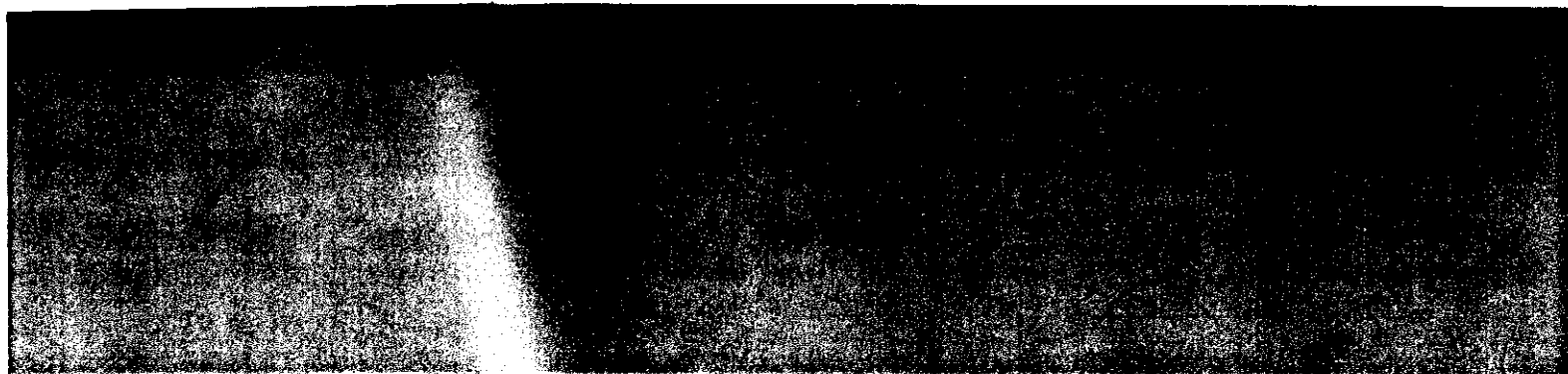: 50 μV. Mean VER, ± reference and S.E.:

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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 ± 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 ± 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 ± 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

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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
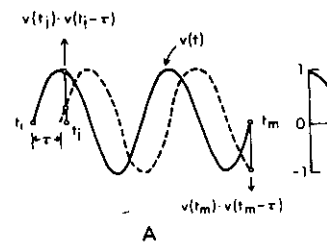
FIG. 4-5. (A) Illustrates the computatic ance. (B) The autocovariance of a sinι taining predominant rhythms at 10 and :

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F. Special Problems in ERP An

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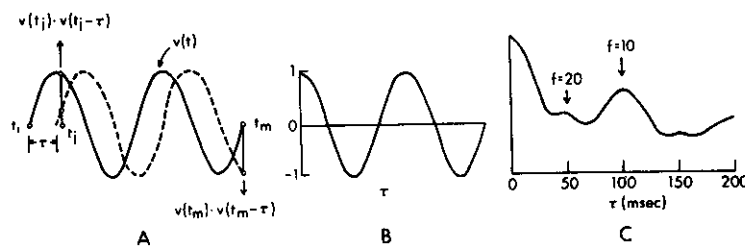
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FIG. 4-5. (A) Illustrates the computation of lagged cross products to obtain the autocovariance. (B) The autocovariance of a sinusoid. (C) Autocorrelogram of an EEG sample containing predominant rhythms at 10 and 20 Hz.

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 ± 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-

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2. EVALUATION OF DIFFERENCES IN

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ｓpects of ERP analysis.

ｔ PSYCHOPHYSICAL THRESHOLD

ｅctive physiologic index of hearing
ｎsiderable 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, $\bar{V}(t)$, 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 wa· able, the use of simple correlatioı as well as of questionable reliabil:

3. RESOLUTION OF ERP COMPONE

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Another approach to resoluti by Donchin (1966, 1969) emplo This procedure is sufficiently el: fication to ensure rather limited (1966) to illustrate the method, primarily reflect shifts in latencı conditions. Thus, what was inı turned out to be a rather distoı original data. The principal cc

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-

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B. A Method for Predicting Sca:

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Scalp-Recorded Potentials

e of the scalp represent the sum of
ber of cellular sources which vary
y a particular electrode. Any useful
s must take into consideration the
nd orientation of the intracranial
ly associated with the ERP will be
mportant to know the contribution
e potentials generated within each
e, as has been the common practice
cordings mainly depict activity from
the recording electrodes. When a
neurons are activated together, a
conduction of extracellular currents
erators. The possibility that several
contributing to the scalp-recorded
Since geometrically distinct intra-

cranial sources will generate somewhat different scalp potential distribu-
tions, 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 dis-
tribution 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 con-
forms 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 intra-
cranial 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
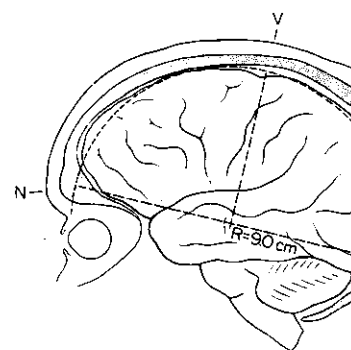

FIG. 4-6. Representation of the head in sag mation to a spherical configuration. The r inion) and intracranial structures are based ations in dimensions are to be expected.

in a steady state can be justified. Thi and Heppner (1967), who conclude applied with reasonable accuracy considering. The main uncertainty the assumption that the impedanc resistive. The presence of a signifi in the phase of the waveforms at th cranial potentials. However, most pedance is negligible within the ra although detailed measurements d sence of a significant capacitive in ingly, the potential distribution, is mates of these values are availabl Although the resistivity measurem pecially for the skull, the range of variations can be computed. It is kn structures differs somewhat, and it a fiber direction within the white ma geneous nor an isotropic medium a simple volume conduction model. can be neglected when dealing witl tions on the scalp surface. Only w are being considered will these effe selection of appropriate scalp and man adult is discussed by Rush have followed.

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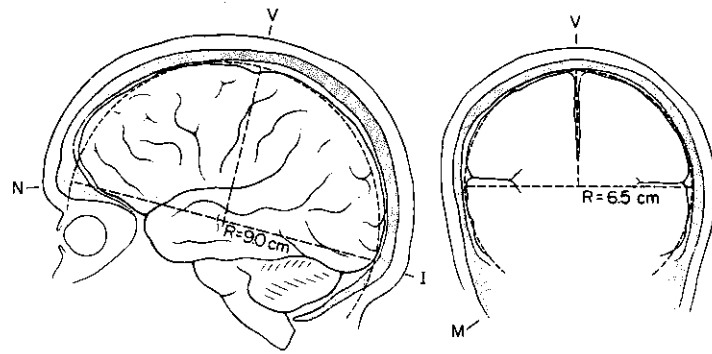itribution comparable to that existing

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

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bution of changes in membrane
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The geometry of the cortex can
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Case B (Fig. 4-7B) represents
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E. Representation of Specific Int

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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.
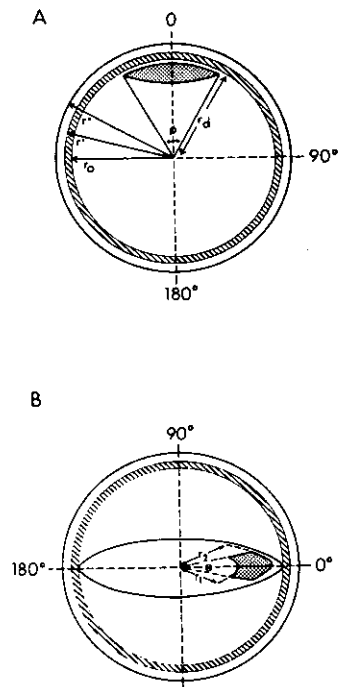
FIG. 4-7. Diagrams of simplified dipole layer source configurations. (A) A circular cap at a radial distance r_d, subtending a solid angle ϕ. The radii corresponding to brain (r_o), skull (r'), and scalp (r'') are also indicated. (B) The portion of a sector bounded by two radii (r_1, r_2), subtending 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 somatosensory, visual, and auditory corte somatosensory projections are considered are represented by a case A model. The au form to case B. Striate cortex presents a c configurations.
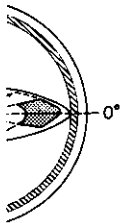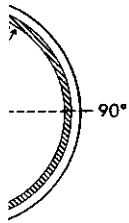
3. VISUAL CORTEX

The primary visual projection a of the sensory projection area, a test of the model. The central re the surface of the occipital pole, a cal axis and about twice that hor retina projects to cortex lying wit fissure according to a recognized infolded visual areas can be mod cruciate arrangement.

Additions and refinements of th due to other source configuration elaborate hypotheses or by partic the quantitative estimates obtaine

F. Computations from the Model

1. CASES A AND B COMPARED—U

In Fig. 4-9 the potential distrib dipole of unit strength are displa

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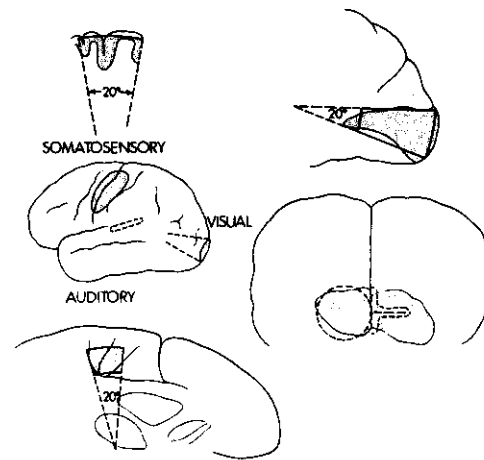ided by two arcs at three quarters
the sphere (Geschwind & Levitsky,

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

HERBERT G. VAUGHAN, JR.

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

maximum potential amplitude at
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3. EFFECTS OF GENERATOR SIZE

The maximum amplitudes of
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In case B the annular sector exter
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G. Application of the Model to E

In order to evaluate the source
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be paid to selection of an appropr
spacing, and proper identificatio

1. REFERENCE ELECTRODE PLACE

A valid potential distribution
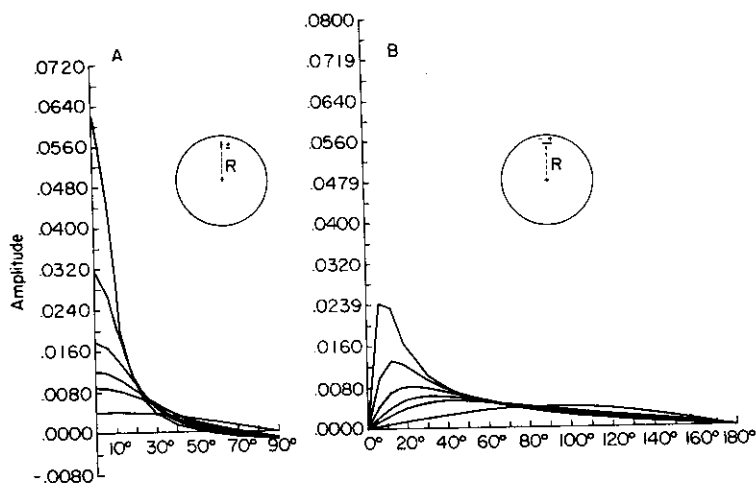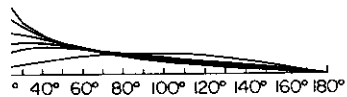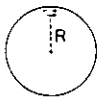be inactive with respect to the E

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.

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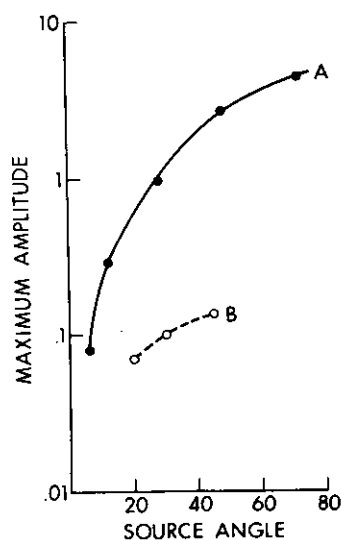
FIG. 4-10. Relative maximum amplitudes of the surface fields generated by case A and B generators of different sizes. The case A generators are circular caps located 2 mm beneath the surface of the inner sphere to simulate cortical sources. The case B generators extend from 50 to 97.5% of the distance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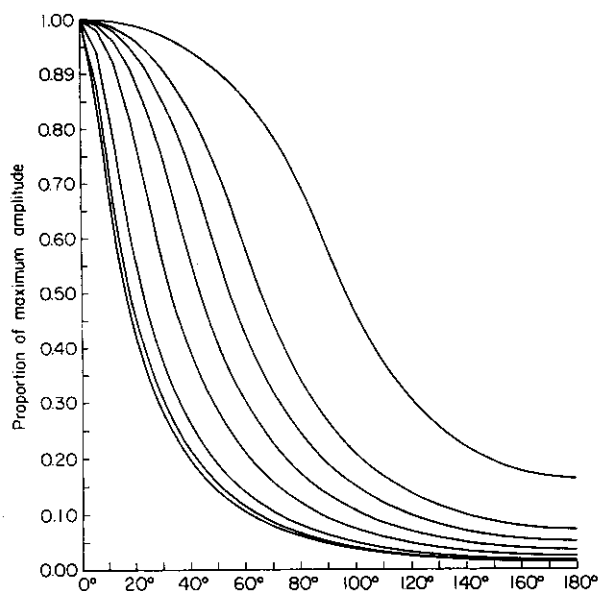

FIG. 4-11. Field distributions for case A generators scaled to a common maximum amplitude. These distributions may be compared against empirical potential distributions to estimate the angular extent of a surface cortical source. Curves represent sources of 6, 12, 24, 48, 72, 96, 120, and 180°.
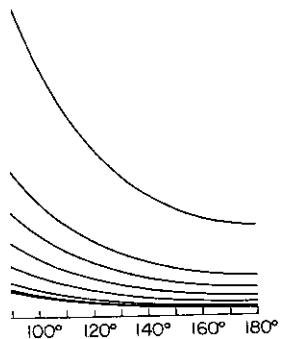
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extraneous electrical activity which
requirement is often difficult to mee
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common to both electrodes of the
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may also be incompletely rejected.
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activity from the temporal lobes,
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out the EKG, and finally an "avera
the active one are linked through
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is rather inconvenient and is not in
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2. ELECTRODE ARRAYS

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G. 4-10. Relative maximum amitudes of the surface fields genered by case A and B generators of fferent sizes. The case A generors are circular caps located 2 m beneath the surface of the ner sphere to simulate cortical urces. The case B generators exnd from 50 to 97.5% of the disnce from the center of the sphere ppropriate for simulating the esial striate cortex).
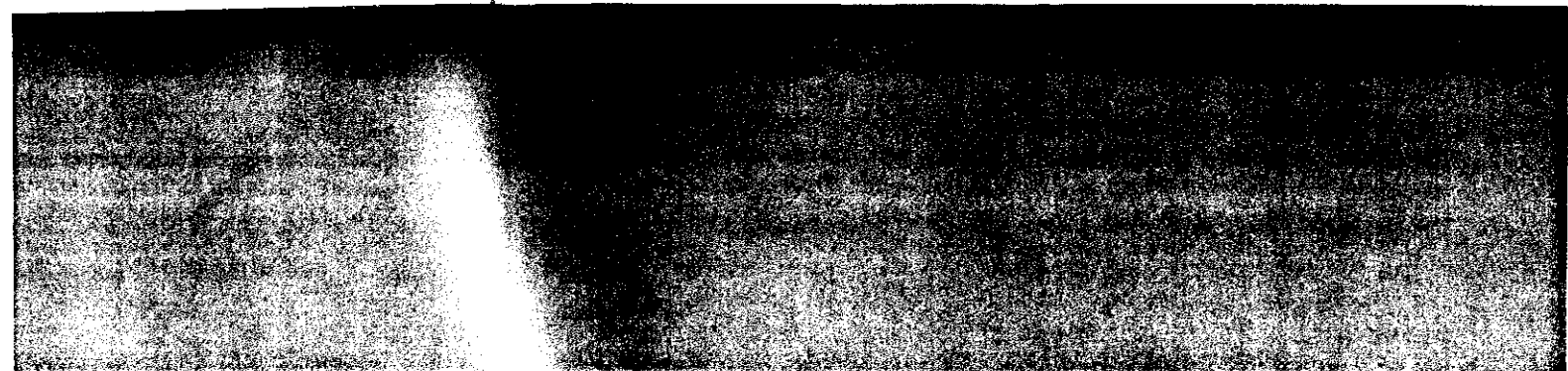
100° 120° 140° 160° 180°

s scaled to a common maximum amplitude. irical potential distributions to estimate the represent sources of 6, 12, 24, 48, 72, 96, 120,

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
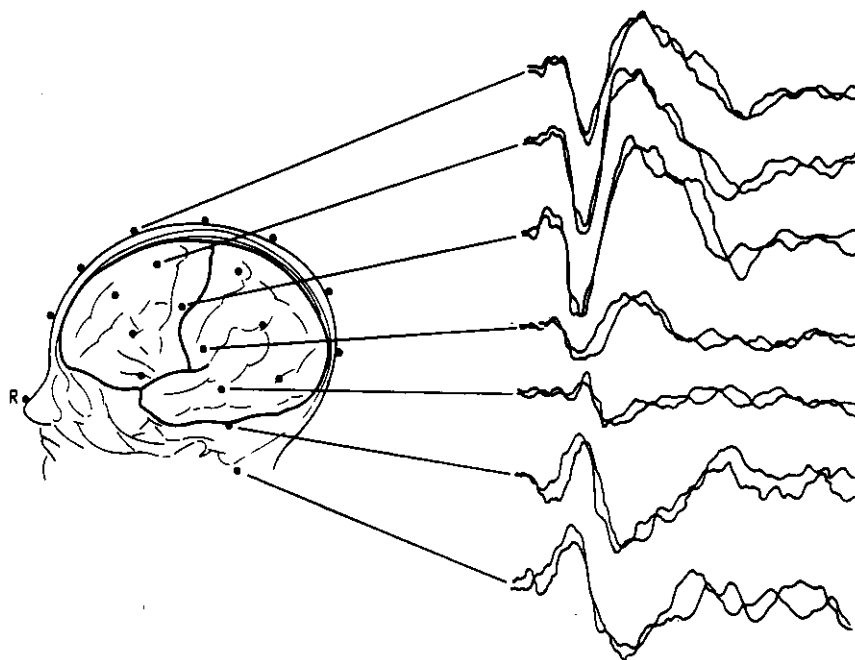
Fig. 4-12. (A) Set of auditory evoked respo Electrode placements for mapping are indi plot of major negative-positive deflection.
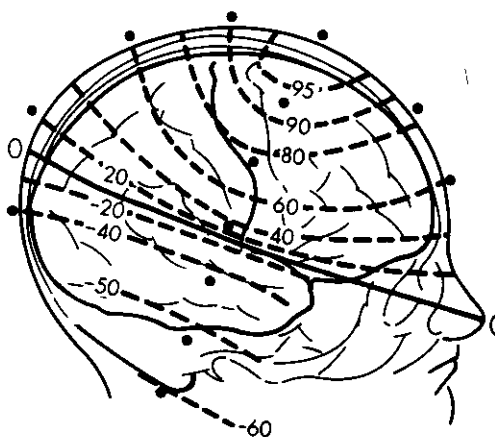
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FIG. 4-12. (A) Set of auditory evoked responses along a coronal line from vertex to mastoid. Electrode placements for mapping are indicated. Reference on tip of nose. (B) Isopotential plot of major negative-positive deflection.
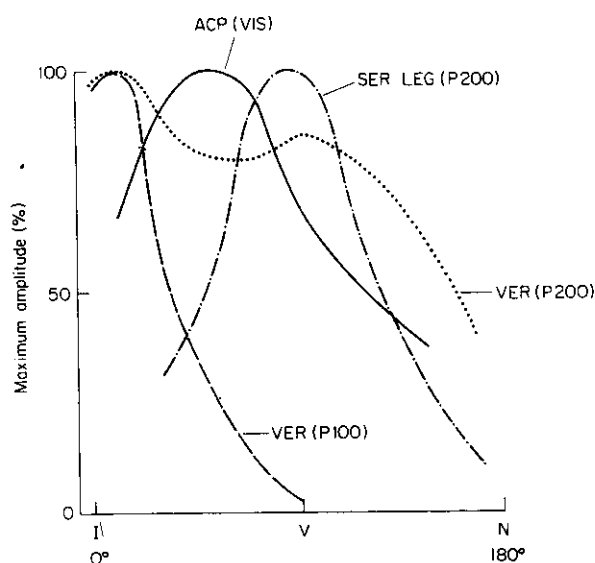
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FIG. 4-13. Amplitude distributions of ERP along a sagittal line. VER (P100): visual evoked response component peaking near 100 msec. VER (P200): visual evoked response component peaking near 200 msec. Note saddle-shaped distribution indicating the 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-
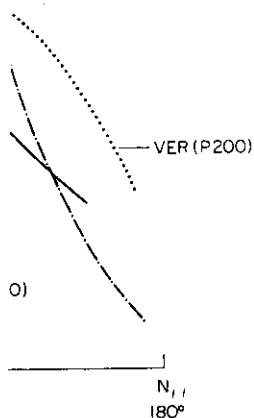
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tributions have been appropriately positioned, the theoretical curves can be summed, which should produce a match with the empirical distribution. In the case of the sensory evoked potentials and the motor potentials, specific hypotheses could be made 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, repre-sented 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 anal-ysis 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 illus-trates the usefulness of a quantitative theoretical model to assist in the selection of an appropriate reference placement. The noncephalic sterno-vertebral 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 direc-tion 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 poten-tials, 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 record-ings 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 re-sponse 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 pre-striate 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,

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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

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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.

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