Chaos Theory and Epilepsy

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Recently, interest has turned to the mathematical concept of chaos as an explanation for a variety of complex processes in nature. Chaotic systems, among other characteristics, can produce what appears to be random output. Another property of chaotic systems is that they may exhibit abrupt intermittent transitions between highly ordered and disordered states. Because of this property, it is hypothesized that epilepsy may be an example of chaos. In this review, some of our basic concepts of nonlinear dynamics and chaos are illustrated. Mathematical techniques developed to study the properties of nonlinear dynamical systems are outlined. Finally, the results of applying these techniques to the study of human epilepsy are discussed. The application of these powerful and novel mathematical techniques to analysis of the electroencephalogram has provided now insights into the epileptogenic process and may have considerable utility in the diagnosis and treatment of epilepsy. The Neuroscientist 2:118-126, 1996

KEY WORDS Epilepsy, Electroencephalogram, Chaos, Nonlinear dynamics

Epilepsy is a group of disorders characterized by recurrent paroxysmal electrical discharges of the cerebral cortex that result in intermittent disturbances of brain function. The bulk of research into human epilepsy has emphasized the description and categorization of the clinical and electroencephalographic features of seizures, defining clinical features of various epileptic syndromes, and correlating clinical and electroencephalographic features with anatomical lesions of the brain or with genetic disorders. However, this research has not addressed the essential feature of epilepsy, which is the fact that seizures come and go over time - that seizures occur intermittently. The intermittency of seizures is difficult to explain according to the concepts of linear dynamics because in linear systems sudden transitions in state occur only in response to external input. In human epilepsy, however, external triggers have been observed only in relatively rare syndromes, such as photoconvulsive epilepsy, or in reflex epilepsies, such as reading epilepsy. For the vast majority of epilepsies, specific environmental triggers have not been identified. In contrast to linear systems, nonlinear systems can exhibit a state of intermittency without any external trigger. Therefore, a promising avenue for research into epileptogenesis is within the domain of nonlinear systems.

Nonlinear Systems and Epilepsy

Intermittency is a dynamical phenomenon (see Box 1 for Glossary). The study of dynamics requires a mathematical approach. Given the complexity of the brain and our incomplete knowledge of it, the quantative analysis and mathematical modeling of normal and abnormal brain functions are formidable tasks. Intuitively, one might assume that complex systems, such as the brain, am governed by many variables which, in turn, would require mathematical models of high dimension (many variables), which may not be practical. On the other hand, simpler, deterministic nonlinear models of low dimension (few variables) can produce highly complex and even seemingly random behavior, such as that observed in complex systems existing in nature (1-9). For example, Figure 1 depicts a complicated signal generated by a low-dimensional nonlinear system (Box 2), which seeks to model global changes of the atmosphere using only three variables (10). It is conceivable that the epileptogenic brain may behave as a nonlinear system in which specific global activities are amenable to mathematical modeling.

Nonlinear systems can be modeled by sets of differential or difference equations where changes over time are functions of one or more variables taken to powers different from one. An example is the logistic difference equation where each subsequent value of the variable *x* is a function of the square of the previous value:

$$X_{n+1} = \alpha \cdot X_n \cdot (1 - X_n)$$

where α is the control parameter and n represents discrete steps in time. An interesting property of the logistic equation, as well as of many nonlinear deterministic systems, is that for certain values of the control parameters the system behaves chaotically - such a deterministic system (see Glossary) can generate output that looks random. The formal mathematical definition of chaos is beyond the scope of this article. However, certain properties of chaotic systems can be described qualitatively. For example, chaotic systems exhibit strong dependence on initial conditions. In the can of the logistic equation, small differences in the initial value x_1, will result in big differences in the subsequent values x_n over time. This strong dependence on initial conditions means that predicting the long-term behavior of chaotic systems is difficult. Another important property of chaotic systems is the ability to show self-organization - to evolve toward ordered temporal and spatial patterns (11). The transition from chaotic to ordered behavior, or the reverse, can occur as an abrupt phase transition with a minute change in the control parameters. As we shall see subsequently, abrupt phase transitions and self-organizing behavior have been demonstrated in electroencephalographs (EEGs) from the epileptogenic foci in humans.

Historically, the mathematical models used to explore brain function have been applied to individual neurons or to relatively small networks of neurons. In the case of human epileptogenesis, our understanding of the underlying neuronal mechanisms and circuitry is insufficient It is premature, therefore, to formulate mathematical models on which to base a conclusive dynamical analysis. Mathematical modeling of simpler neuronal systems, however, has succeeded. For example, Freeman and colleagues (12, 13) have developed mathematical models for EEG signals generated by the olfactory system in rabbits. These models exhibit most of the important dynamical features observed in the EEG from extracellular microelectrode recordings in the rabbit olfactory bulb, including transitions to states reminiscent of epileptic seizures. These investigators have suggested that the learning and recognition of novel odors, as well as the recall of familiar odors, can be explained through the chaotic dynamics of the olfactory cortex's electrical activity. Another group, Traub and colleagues (14, 15), have developed nonlinear models for CA1 and CA3 hippocampal neurons. Their model incorporates many of the known anatomical and physiological features of the rat hippocampus and reproduces many of the observed phenomena in electrical recordings from the rat hippocampus. The degree to which this nonlinear model can simulate faithfully the full range of the dynamical features of the hippocampus remains to be determined.

An alternative to mathematical modeling, based an known properties of a system's components and their connections, is to obtain empirical measures of the behavior of the system as a whole over time. This macroscopic approach is particularly useful for biological systems, such as the brain, where exact knowledge of the system is lacking. Analysis along these lines can provide insight into the global dynamical properties of the system. After such information is extracted, it may be possible to derive useful empirical models. The recent application of this approach to the analysis of EEG recordings in epileptic patients has provided exciting discoveries regarding epileptogenesis. These observations will be summarized in this review.

Methods for Nonlinear Dynamical Analysis - Application to the EEG

The EEG can be conceptualized as a series of numerical values (voltages) over time. Such a series is called a "time series." The standard methods for time series analysis (e.g., power analysis, linear orthogonal transforms, and parametric linear modeling) not only fail to detect the critical features of a time series generated by an autonomous (no external input) nonlinear system, but may falsely suggest that most of the series is random noise (16). In recent years, the methods developed for the dynamical analysis of complex series have been applied to the investigation of signals produced by red biological systems, such as the EEG.

The statistical properties of the EEG depend on both time and space (17). The characteristics of the EEG, such a the existence of limit cycles (α activity), instances of bursting behavior (during light sleep), jump phenomena (hysteresis), amplitude-dependent frequencies (the smaller the amplitude, the higher the EEG frequency), and frequency harmonics (e.g., under photic driving conditions), are among the long catalog of typical properties that nonlinear systems can exhibit (18). Several researchers have provided evidence that the EEG is a nonlinear signal with deterministic and, perhaps, chaotic properties (12, 13, 19-25). Other groups have pointed out characteristic dynamical properties of EEG corresponding to specific normal and pathological states, such as mental tasks, sleep, dementia, and coma (see [26] for a review).

Figure 1: Output of the Lorenz system of equations Box 2) with control parameters δ = 16.0, r = 45.92, and b = 4.0. Values for Y (vertical axis) are plotted as a function of time (horizontal axis). The resulting time series is chaotic. This figure illustrates that a simple, low-dimensional nonlinear system can generate a complex and chaotic signal.

A well-established technique for visualizing the dynamical behavior of a multidimensional system is to generate a phase space portrait of the system. A phase space portrait is created by treating each time-dependent variable of the system as a component of a vector in the phase space. Each vector represents an instantaneous state of the system. These time-dependent vectors are plotted sequentially in the phase space to represent the evolution of the state of the system over time. For many systems, this graphic display creates an object confined over time to a subregion of the phase space. Such subregions of the phase space are called "attractors." The geometrical properties of attractors provide information about the global state of the system.

One of the problems in analyzing muitidimensional systems in nature is knowing which observable (variable of the system that can be measured) to analyze. Experimental constraints may limit the number of observables that can be obtained. It turns out that when the behavior over time of the variables of the system is related, which is always the case when a system exists, the analysis of a single observable can provide information about all of the related variables of the system. In principle, through the method of delays (Box 3) described by Packard et al. (27) and Takens (28), the sampling of a single variable of a system over time can reproduce the attractors of a system in the phase space. To illustrate this point, the Lorenz attractor is depicted in Figure 2, showing that the states of the system over time are confined within a mask-like structure (the attractor) in the phase space (Fig. 2a) and that the method of delays well approximates the attractor in the phase space (Fig. 2b).

This technique for the reconstruction of the phase space from one observable can be used for more complex signals, such as the EEG. In Figure 3, a phase space portrait has been generated from an ictal EEG signal recorded from a single electrode on the temporal cortex. The characteristics of the formed epileptic attractor are typical of all of the seizures we have analyzed - trajectories are moving in and out of the main body of do attractor. In Figure 3, the excursions correspond to spikes.

The geometrical properties of the phase portrait of a system can be expressed quantitatively using measures that reflect the dynamics of the system. The complexity of an attractor is reflected by its dimension. The larger the dimension of an attractor, the more complicated it appears in the phase space. It is important to distinguish between the embedding dimension and the dimension of an attractor. The embedding dimension p - always a positive integer - is the dimension of the phase space that contains the attractor. On the other hand, the attractor dimension D may be a noninteger; it is directly related to the number of variables of the system and inversely related to the existing coupling among them. For example, with the Lorenz attractor, three variables are needed to specify each state of the system. Hence, a phase space of p = 3 is needed to embed every state of the system. The dimension D of the Lorenz attractor itself, however, is ~2.05 – less than 1 – because the three variables that define the Lorenz attractor are not independent; rather, they are nonlinearly coupled through the set of the three differential equations that define the system.

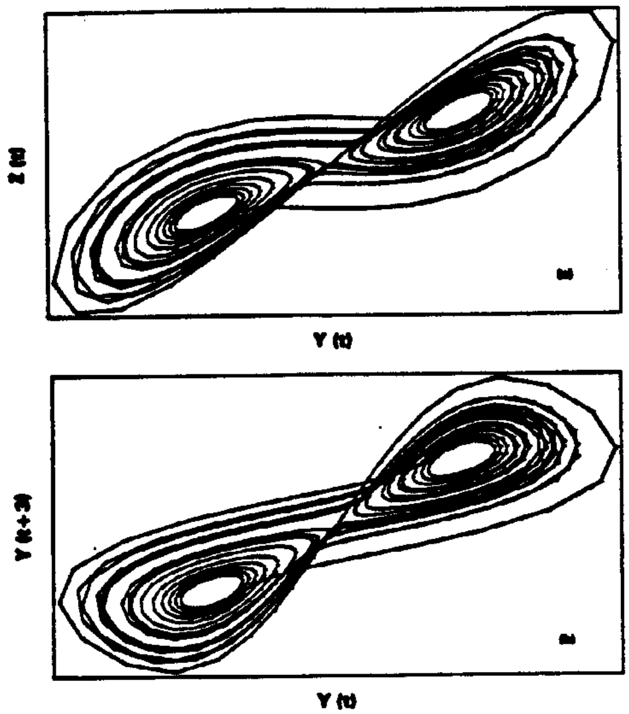

Figure 2: The states of the Lorenz system of equations in the phase space (a). The result, a chaotic attractor in the phase space, is projected onto the YZ plane. In (b), the phase space plot was generated from a single output variable Y(t), using the method of delays (Box 3). A time lag τ of 3 was used. The resulting attractor is a good approximation of the original attractor in (a). This figure illustrates the point that it is possible to approximate an attractor generated by a multidimensional system from the time series data of a single variable (observable).

According to Takens (28), the embedding dimension p should be at least equal to 2D + I for a correct embedding of an attractor in the phase space. Of the many different methods used to approximate D of an object in the phase space, each has its own practical problems (26, 29, 30). The measure used most often to approximate D is the correlation dimension v. Methods for calculating the correlation dimension from experimental data have been described (31, 32).

A chaotic attractor is an attractor where, on the average, orbits originating from nearby ictal conditions diverge exponentially fast (expansion process); they stay close together only for a short time. If these orbits belong to an attractor of finite size, they must fold back into it as time evolves (folding process). The result is a layered structure (7). The measures that quantify the chaoticity of an attractor are the Kolmogorov entropy and the Lyapunov exponents (33-35). For an attractor to be chaotic, the Kolmogorov entropy or at least one of the Lyapunov exponents should be positive. The Kolmogorov (Sinai or metric) entropy (K) measures the uncertainty about the future state of the system in the phase space, given information about its previous states (positions) in the phase space. The Lyspunov exponents (Ls) measure the average rate of expansion and folding that occurs along different local directions within an attractor in the phase space. If the phase space is of p dimensions, we can estimate theoretically up to p Lyapunov exponents. Methods for calculating these dynamical measures from experimental data have been published (36-39). The estimation of the largest Lyapunov exponent (L_{max}) in a chaotic system has been shown to be more reliable and reproducible than the estimation of the remaining exponents (29, 40).

Another useful set of dynamical measures are the time dependence indices (8_j), developed by Savit and Green (41, 42). Time dependence indices measure, on the average, the dependencies between the components of the vectors in the phase space. When the method of time delays is used, these dependencies are translated into dependencies between values of the original signal at successive points in time, separated by a time lag, *r*. If the phase space is of p dimensions, we can estimate theoretically up to p-1 dependence indices. Applications of these methods are discussed by Wu et al. (43), Iasemidis et al. (44), and Savit and Green (41, 42).

Dynamical Studies In Epilepsy

Dynamical analysis of EEG recordings from patients with epilepsy has provided novel perspectives regarding epileptogenesis. Recent studies have provided evidence that epileptic seizures represent a nonlinear chaotic process. The first evidence for chaos in human epilepsy was provided by Babloyanz and Destexhe (45). They found that the EEG signal during a petit mal epileptic seizure could be characterized by low-dimensional chaos, in that the attractor appeared to have a low fractal dimension (between 2 and 3) and a positive Lyapunov exponent. Our group's studies of partial seizures of temporal lobe origin (46) demonstrated the presence of limit cycles in the seizure discharges recorded from subdural electrodes overlying the epileptogenic focus. The limit cycles are characteristic of nonlinear systems. We also found evidence for low-dimensional chaos in partial seizure discharges of mesial temporal origin using an embedding dimension p of 7 (low-dimensional attractors with a fractal dimension between 2 and 3, and a positive maximum Lyapunov exponent of about 2 bits/sec) (47, 48). Chaotic attractors are usually of fractal dimension and contain at least one positive Lyapunov exponent. Frank am co-workers (49) reported evidence for chaotic dynamics in an EEG during a mixed generalized seizure.

Some authors have found only weak nonlinearities in the EEG and have postulated that its dynamical properties may be explained by the theory of linear stochastic processes (50-52). In EEGs recorded from patients with temporal lobe epilepsy, however, we have found evidence for nonlinearities that could not be explained by linear deterministic or stochastic dynamics (Casdagli et al., manuscript in preparation). In this work preictal, (before seizures), ictal (during seizures), and postictal (immediately after seizures) EEG signals were recorded from bilaterally placed subdural and depth electrodes in a patient with medically refractory complex partial seizures of mesial temporal origin. The most striking nonlinearities were observed in the signals generated by the epileptogenic focus and in the signals recorded from anatomical regions that generated interictal spikes. Further evidence that nonlinear deterministic processes underlie the occurrence of seizures was obtained by analyzing the time intervals between individual seizures, using the 8_j measures (44). Taken together, these studies suggest that seizures are generated by deterministic nonlinear chaotic systems; thus, the occurrence of epileptic seizures may represent the intermittent phase transitions characteristic of such systems.

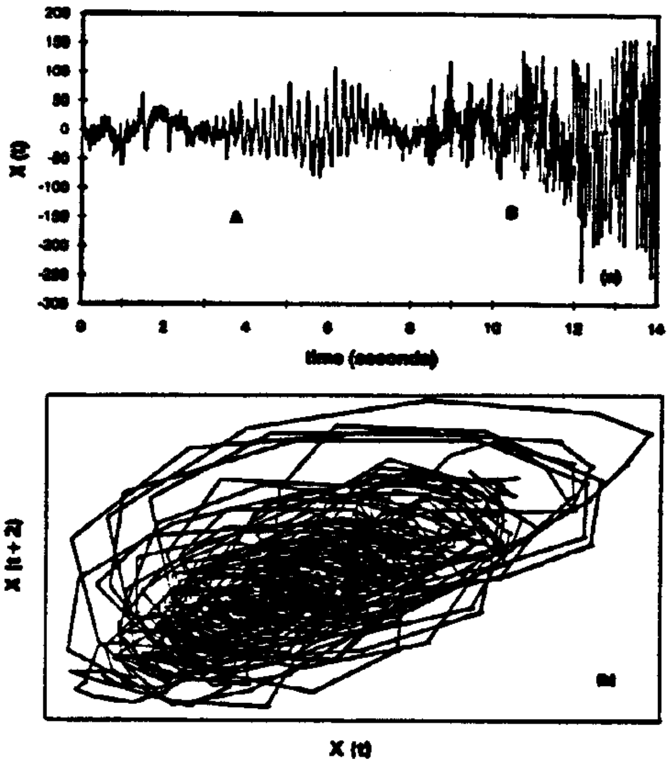

Figure 3: The plot shown in (a) is a 14-second epoch of EEG at the onset of a seizure originating from the left temporal cortex. X(t) (voltage in microvolts) is plotted against time (seconds). Projected onto two dimensions, (b) is a phase space representation of the portion between A and B of the ictal shown in (a).

Our group went on to demonstrate that in temporal lobe epilepsy, the dynamical properties of the preictal, ictal, and postictal states are distinctly different and can be defined quantitatively. This result was derived by as analyzing EEG recordings from subdural and depth electrodes. As an example, the maximum Lyapunov exponent over time profiles for one seizure in one patient as shown in Figure 4. The important observation, subsequently confirmed in other patients, is that the chaoticity of the signal (reflected by the value of L_{max}) was highest during the postictal state, lowest during the seizure discharge, and intermediate in the preictal state. Also, in all of the cases studied, the characteristic drop in the value of the L_{max} exponent at the time of the seizure's onset occurred first at electrode sites located where the seizure discharge originated. Thus, from a dynamical perspective, the onset of a seizure represents a spatiotemporal transition from a complex to a less complex (more ordered) state. It is likely that the more ordered ictal EEG signal reflects the synchronized rhythmic firing pattern of neurons participating in the seizure discharge.

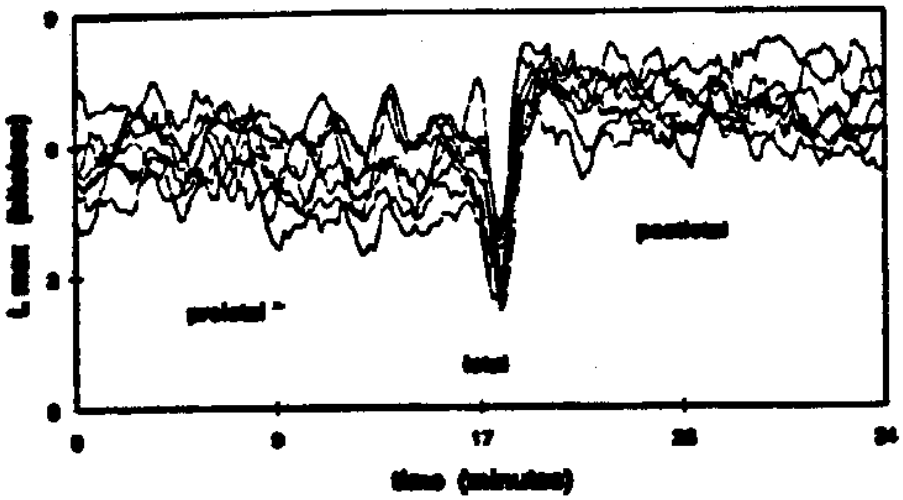

Figure 4: This figure depicts values for L_{max} (vertical axis) versus time (horizontal axis) derived from EEG signals recorded from eight different subdural and depth electrodes placed bilaterally. This segment of the recording began ~17 minutes before the onset of the seizure and continues for ~15 minutes after the seizure. Each line represents L_{max} values from a single electrode site. Note that for each site, L_{max} values are lowest during the seizure, highest during the immediate postictal period, and intermediate in the preictal period. Also note that at the beginning of the seizure, there is a sudden drop in L_{max} values for all electrodes. This plot demonstrates some of the characteristic dynamical differences among preictal, ictal, and postictal states.

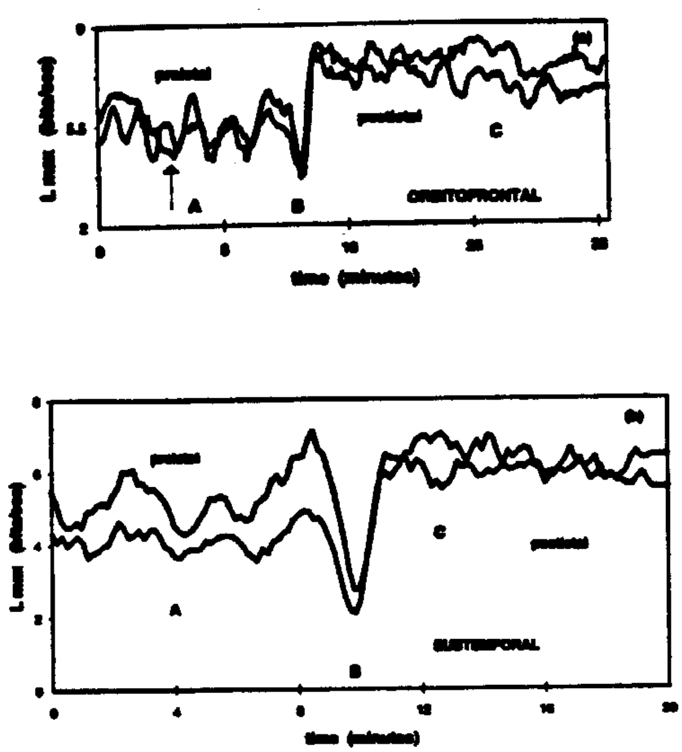

Figure 5: In (a) L_{max} values versus time are plotted for signals recorded from left (black line) and right (blue line) orbitofrontal electrode sites. The recording was obtained in a patient with seizures of left mesial temporal origin. The plot begins ~12 minutes before the onset of the seizure (point B). At point B, there is a characteristic ictal drop in L_{max} at both electrode sites. Before the seizure, there are intermittent small drops in L_{max} at both sites. In this case, entrainment of L_{max} for the two electrode sites has begun 8 minutes before the seizure (point A). Postictally, the sites are disentrained with respect to L_{max} values and phases. In (b), L_{max} versus time plots were derived from EEG signals

recorded from bilaterally placed subtemporal electrode sites in the same patient. Preictal phase locking of the L_{max} *oscillations is already evident 10 minutes before the seizure. Episodic preictal drops also are present in these plots. Postictally,* L_{max} *oscillations in the two electrode sites are out of phase. Episodic drops in* L_{max} *and phase locking of* L_{max} *are characteristic features of the preictal state in invasive EEG recordings from patients with temporal lobe epilepsy.*

How the phase transition from the preictal state to the ictal state occurs has recently been explored. Traditionally, the investigation of physiological disturbances in epileptic patients has relied upon the visual inspection of the electrographic trace and analysis via the traditional techniques of signal processing, such as Fourier analysis and coherence measures (17). The detection of potentially epileptogenic foci from the EEG of epileptic patients has depended upon the recognition of characteristic transient waveforms, such as spikes and sharp waves, in the interictal or ictal periods (53-55). Research along these conventional hues of analysis has unsuccessfully sought to detect precursors of the epileptic seizure (56, 54). Such approaches have generated descriptive information regarding interictal and ictal epileptogenic physiological phenomena, but they were not able to explain why seizures occur.

Perhaps the most exciting discovery to emerge from dynamical analysis of the EEG in temporal lobe epilepsy is that seizures are preceded by dynamical changes in the EEG signal occurring several minutes before the seizure. By analyzing the L_{max} values over time for signals recorded from subdural electrodes placed over the epileptogenic temporal lobe and regions of ipsilateral frontal and parietal cortex, our group discovered that beginning several minutes before seizure onset, regions of the anterior temporal cortex and, later, regions more distant from the focus become phase locked with respect to their content of chaos. This observation indicated that, several minutes before a seizure, large regions of the cortex became dynamically entrained (58-60). The same entrainment process was demonstrated subsequently in recordings from hippocampal depth electrodes (61). This phenomenon could not be detected by visual inspection of the original EEG signal or by other more traditional methods of signal processing. Examples of preictal entrainment are illustrated in Figures 5 and 6. The long-term nature of the process (order of minutes) indicates that it may be possible to predict the onset of a seizure in time to intervene with abortive therapy.

Another important finding is that, in the preictal states, the dynamical properties of the EEG recorded from the epileptogenic hippocampus differ from those of the signal recorded from the contralateral hippocampus. Preliminary studies in a few of our patients suggest that this difference may hold true throughout much of the interictal period. We found that the epileptogenic hippocampus exhibited a more ordered and less complex behavior interictally and preictally than the more normal hippocampus did (62). These findings are illustrated in Figure 7, which compares the Lyapunov profiles obtained from the epileptogenic and the more normal contralateral hippocampus, and in Figure 8, which compares δ_j profiles between the two hemispheres, demonstrating that the time dependency structure of the EEG signal obtained from the epileptogenic hippocampus differs strikingly from that recorded from the normal hippocampus. Thus, in the preictal period, the dynamical state of the epileptogenic hippocampus is distinctly different from that of the more normal contralateral hippocampus. We speculate that this altered dynamical state renders the epileptogenic hippocampus more susceptible to an abrupt phase transition to the ictal state. We further hypothesize that the conditions of spatiotemporal dynamical entrainment described above facilitate this transition.

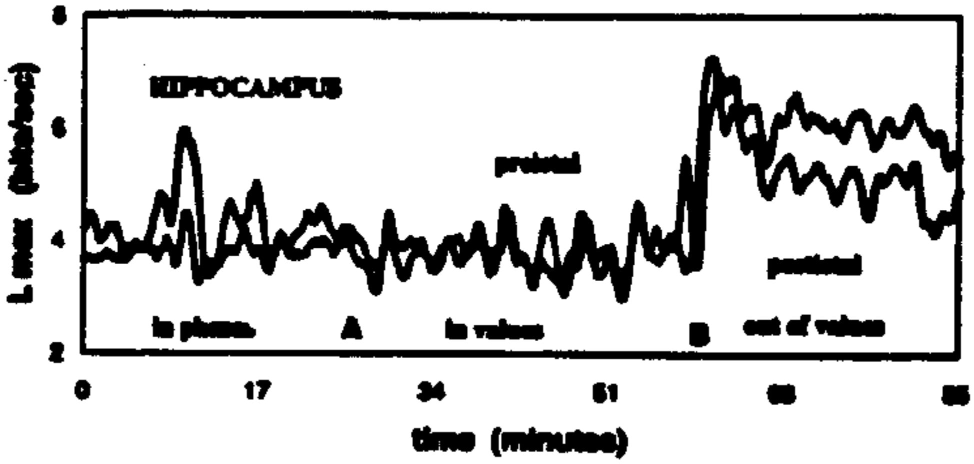

Figure 6: L_{max} versus time plots, obtained from EEG signals recorded from the left anterior hippocampus (blue line) and the epileptogenic right anterior temporal hippocampus (black line), are shown for a period beginning ~60 minutes before the seizure's onset (point B). Note that oscillations of L_{max} for the two electrode sites are approximately in phase but have different mean values until ~35 minutes before the seizure (point A). Subsequently, the two L_{max} oscillations have similar mean values (entrainment noted as in values). This preictal entrainment appears to represent a transition from the interictal to the ictal state. Note that in the immediate postictal period (noted as out of values), the mean value of L_{max} for the epileptogenic electrode site is substantially lower than that of the more normal contralateral hippocampus.

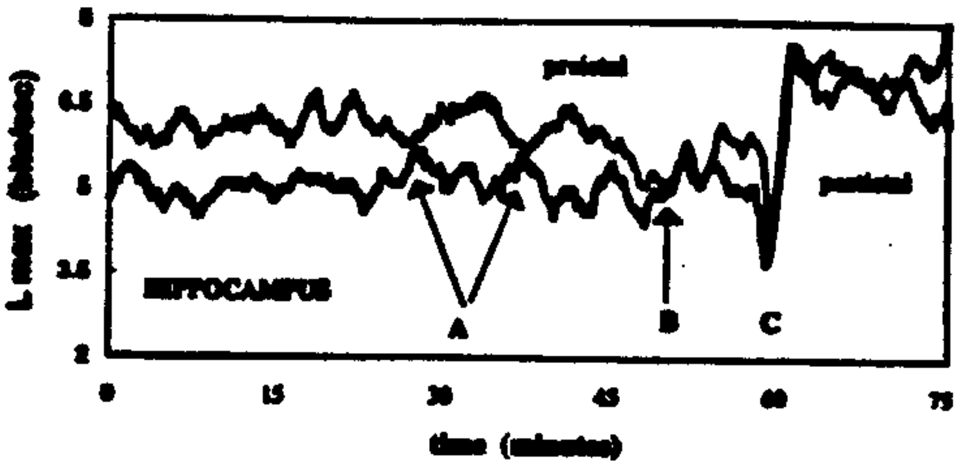

Figure 7: L_{max} versus time profiles for signals recorded from the epileptogenic left hippocampus (black line) and a homologous electrode site in the more normal right hippocampus (blue line) are compared for a period of ~1 hour before the seizure. The typical ictal drop in L_{max} occurs at both electrode sites (point C). Preictally, oscillations in L_{max} are out of phase (e.g., points A) until ~10 minutes (point B) before the seizure. After point B, L_{max} oscillations for the two electrodes are phase locked, and the mean values are more similar for each electrode site. Note that for the entire 1 hour preictal period, L_{max} is consistently lower in the signal recorded from the epileptogenic hippocampus. Postictally, L_{max} profiles for the two sites are out of phase. The lower preictal values of L_{max} obtained from signals generated by the epileptogenic hippocampus have been observed in almost all cases examined thus far.

Conclusions and Prospects

The quantitative measures developed for the study of complex nonlinear systems hold promise for advancing our understanding of the dynamical processes underlying the occurrence of epileptic seizures. These techniques, which have the advantage of not depending on any models of normal or epileptic brain function can detect information that is inaccessible by more traditional linear and spectral methods of signal analysis. The cumulative evidence, based on the recent application of these powerful mathematical techniques, supports the conclusion that the EEG is generated by mechanisms that obey nonlinear deterministic laws. There is strong evidence that these processes are chaotic. Further elucidation of these dynamical processes of epileptogenic brain function will be necessary before realistic mathematical models become possible. Then, such nonlinear models could be employed to address questions involving the basis for the intermittency of epileptic seizures.

The observation that the signals from epileptogenic regions have different dynamics from nonepileptogenic regions, even during the interictal state, may be of more immediate practical utility for localization of seizure foci. Currently, clinicians rely primarily on ictal recordings for diagnostic evaluation and for presurgical localization of the seizure onset zone The sampling of a sufficient number of seizures requires recordings over many days. If the seizure focus can be identified through its interictal dynamical properties, however, the diagnostic and presurgical recording time may be reduced dramatically and the epileptogenic focus may be localized more reliably.

Finally, we have discovered that the evolution of a seizure involves not just two states -- interictal and ictal -- but also a preictal transitional state that dynamically differs from the other two. This finding has both scientific and clinical implications. One can anticipate that a more detailed and refined understanding of this dynamical phenomenon could shed light on fundamental questions, including why seizures begin when and where they do. As a result, it may be possible in the future to detect the preictal state with implanted devices that could then prevent the impending seizure through physiological or pharmacological interventions. This seizure detection, intervention, and prevention would be an example of controlling chaos. The control of chaotic systems is an exciting new field of study (63). Evidence that such interventions may be possible in epilepsy has been provided recently by in vitro experiments in the hippocampal slice preparation by Schiff and colleagues (64). These investigators demonstrated that chaotic dynamics in hippocampal slice preparations exist and can be controlled by low voltage electrical stimuli administered at properly timed intervals.

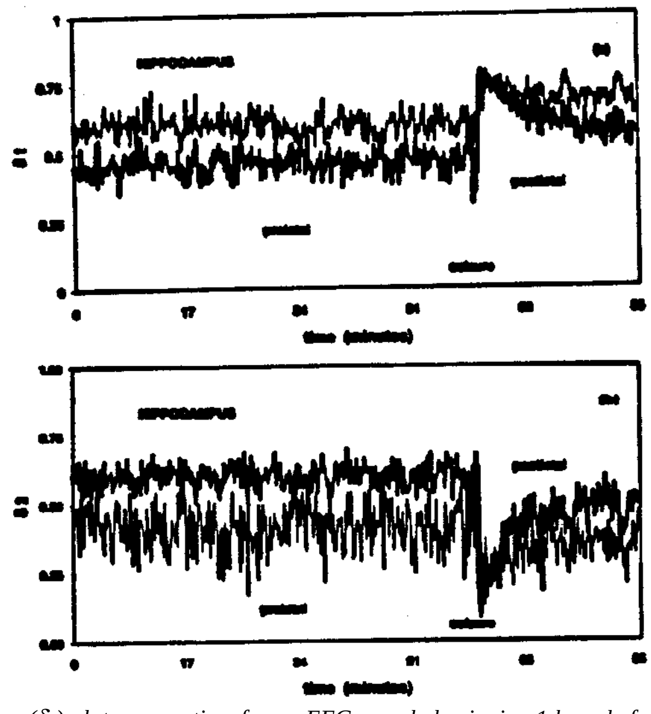

Figure 8: Time dependency (δ_1) plots versus time for an EEG sample beginning 1 hour before a seizure are plotted for signals recorded from the left (epileptogenic) hippocampus (black line) and the more normal contralateral hippocampus (blue line); (a) illustrates typical profiles for δ_1 (first lag dependency). In the preictal period, δ_1 values are consistently lower for EEG signals generated by the epileptogenic hippocampus. During the seizure, δ_1 values drop for both electrode sites. Immediately after the seizure, δ_1 values for both electrodes are higher than preictal or ictal values. The plot in (b) depicts δ_2 versus time for the same EEG sample used in (a). The δ_2 values are consistently higher for preictal and postictal signals generated by the epileptogenic hippocampus. Together with the plots in Figure 7, these plots illustrate the finding that in temporal lobe epilepsy of unilateral mesial temporal origin, dynamical properties of the epileptogenic hippocampus differ quantitatively from those of the more normal contralateral hippocampus during the preictal and postictal states.

Our overall working hypotheses are that dynamical characteristics of electrical signals generated by the epileptogenic hippocampus differ from those generated by similar but healthy regions (e.g., the contralateral hippocampus), that these signals can carry dynamical signatures of an impending epileptic seizure, and that the characteristics of these signals can be quantified using nonlinear dynamical techniques. A reasonable model, based upon studies to date, is that: 1) because of the pathological changes in the neuronal makeup and damage to the neuronal connections within the hippocampus, this region of the brain is susceptible to spontaneous phase transitions to more ordered states, and 2) the epileptogenic hippocampus initiates or participates in a seizure if and only if conditions of a long-term (order of several minutes) spatiotemporal dynamical entrainment of a critical mass of interconnected regions of temporal and frontal cortex are met. Research directed toward further characterization of the process of transition between the interictal and ictal states might lead to better understanding of epileptogenesis.

Box 1: Glossary

Dynamical: Refers to changes in the state of a system over time.
Deterministic System: A system in which future states can be predicted if one knows the initial conditions and mathematical rules (equations) that govern its behavior over time.
Stochastic System: A system for which future states can be determined only probabilistically, even if one knows the initial conditions and the equations that govern its behavior over time.
Nonlinear System: A system in which the states change over time in accordance with differential or difference equations that involve one or more variables taken to a power >1. Such systems, under certain conditions, exhibit sensitivity to initial conditions, self-organizing behavior, and intermittency.
Chaos: Dynamical state of a deterministic nonlinear system that looks stochastic. By definition, in a chaotic state, at least one positive Lyapunov exponent exists.
Phase Space: Representation of the states of a system in a geometrical space (also called “state space”) as they evolve with time.
Attractors: Regions within the phase space to which the states of the system evolve and remain confined until the structure of the system itself changes or an external input is imposed.
Dimension: A numerical value related to the number of “axes” required to construct the phase space (embedding dimension) or related to the number of variables required to span an attractor within the phase space (dimension of the attractor). When the dimension of the attractor is not an integer it is called “fractal.”
Lyapunov Exponent: A numerical value that describes the average rate at which the trajectories of adjacent states in the phase space diverge or converge over time. An indicator of how chaotic a system is.
Kolmogorov Entropy: A numerical value indicating the uncertainty of predicting the state of a system at a subsequent point in time. A global indicator of how chaotic a system is.
Time Dependence: A quantity that indicates the strength of the relationship between a point in a time series and prior points in the series.
Intermittency: The tendency for a given pattern of behavior (state) to come and go over time.

Box 2: Lorenz System

$$\dot{x} = \delta \cdot (y - x)$$

$$\dot{y} = x \cdot (r - z) - y$$

$$\dot{z} = x \cdot y - b \cdot z$$

The Lorenz System is a model for air convection caused by heating and cooling in the atmosphere (7). This simple, nonlinear system generates chaotic output for certain values of the control parameters (δ, r, and b). Figure 1 illustrates the complex time series generated by this system for δ = 16.0, r = 45.92, and b = 4.0. Figure 2 illustrates the phase space representation of the signal. In the phase space, an attractor (called the “Lorenz” attractor) is formed, and all future states of the system are confined within it (10).

Box 3: Method of Delays

The method of delays is one way of representing states in the phase space. In this representation, the dynamical state at each point in time is represented by a vector X(t) in the phase space. The components of the vector are generated by taking successive points of the original time series, x(t), separated by a final time delay, τ:

$$X(t) = [x(t), x(t - \tau), \ldots, x(t - (p - 1) \cdot \tau)]$$

Where x(t) is the original time series, X(t) is the state-vector in the phase space at time t, and p is the embedding dimension of the reconstructed phase space. Information can be extracted only about variables of the system that are coupled with the observable x(t). Information about a variable that is not coupled through a system's equations with x(t) may be obtained by increasing the number of observables.

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