Epileptic Focus Location: Spectral Analysis Method

Abstract. *A spectral analysis technique for locating the site of an epileptic focus in the cat brain with the use of multielectrode data, obtained during a generalized seizure, is described. The data, indicating widespread appearance of epileptic activity, does not lend itself to conclusive analysis by conventional means. Three channels of data are examined at a time. One channel is said to drive the other channels if the first channel explains or accounts for the linear relation between the other two over a frequency interval corresponding to the interval of greatest energy concentration. The method of analysis involves computation of the coherence and partial coherence between data from all electrode pairs.*

An epileptic focus (*1*) was located by spectral analysis of data taken during the ictal (seizure) phase of an epileptic cat in whose brain electrodes were permanently implanted. In the analysis, the self and cross spectral energies and the spectral coherencies at each frequency of the observed (assumed stationary), multidimensional, data set (time series) were computed (*2*). The focus is defined to be at one of the electrode recording sites. The technique used is quite general and may be used wherever electrophysiological waveforms are examined to determine whether any one of the observed anatomical recording sites can be interpreted as "driving" the other anatomical sites.

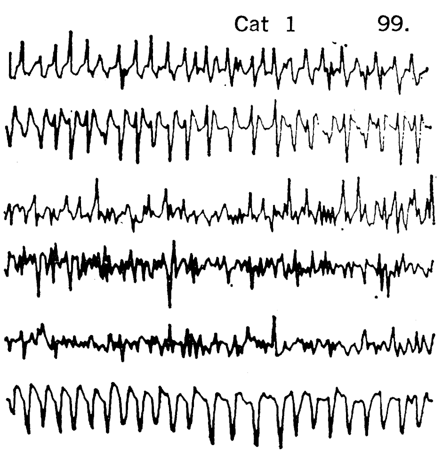

Fig. 1. Eight seconds of simultaneous data taken from a cat, during an epileptic seizure, from (top to bottom) the septal area, piriform cortex, mesencephalic reticular formation, putamen, nucleus lateralis posterior of the thalamus, and motor cortex.

Epileptic seizures in the cat were induced by a daily 5-second electrical stimulation in the piriform cortex (*3*). The stimulation apparently produced no lesion. After several weeks of such stimulation, epileptic spike and wave activity was observed in response to each stimulation. Ultimately, the response to the electrical stimulation developed into a full clonic-tonic seizure. Recordings of six simultaneous channels of activity taken from bipolar electrodes implanted into sites deep in the brain were taken daily of normal, ictal, and postictal activity. During the ictal phase, data from the septal area, piriform cortex, mesencephalic reticular formation, putamen, nucleus lateralis posterior of the thalamus, and the motor cortex were simultaneously recorded. Computations on these data were performed later. Figure 1 illustrates data from an 8-second data record of the electrical activity at the sites during a seizure. The records are quite complex, and there is no obvious visual clue that might identify the driving channel.

Three channels of these data were simultaneously examined to determine whether one channel could be identified as driving the other two. The time series are assumed to be random (unpredictable) processes. In a random time series, the energy at any frequency is a random variable. Spectral coherence versus frequency, that is, the square of the correlation coefficient between the energies of two different time series at one frequency, is conventionally computed (*2*) to determine the dependence or independence of the two time series at a frequency. We compute both spectral coherence and partial spectral coherence (*2*) (that is, the coherence remaining between two time series after the influence of a third time series is removed from each of the first two) for each of the three possible pairs of three different data channels to determine whether one channel drives the other two.

For example, Fig. 2 illustrates the coherence at each frequency between the piriform cortex and motor cortex (solid line) and the partial coherence at each frequency (dotted line) between the piriform cortex and the motor cortex, taking into account the electrical activity in the septal area.

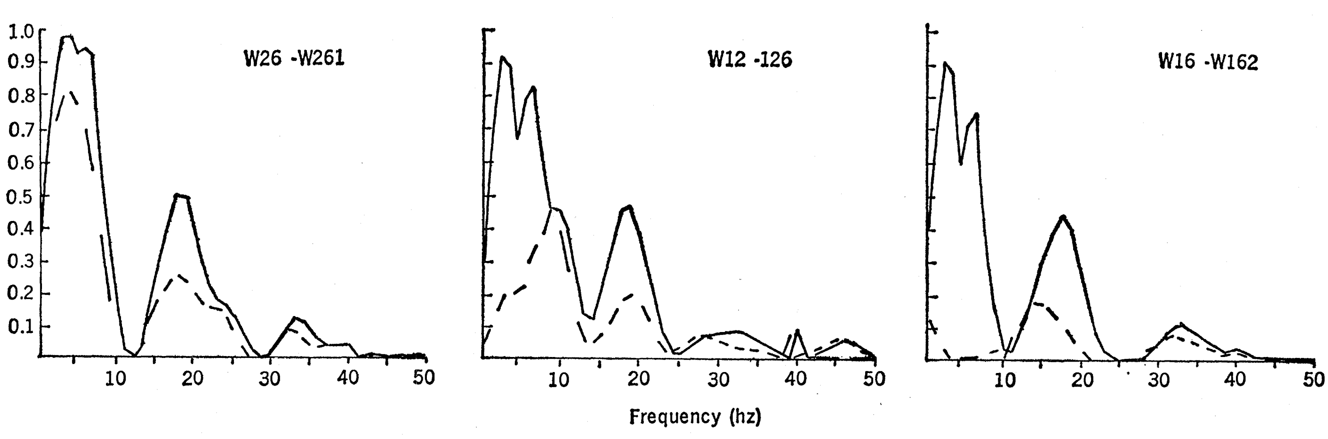

Fig. 2 (left). Spectral coherence, piriform cortex–motor cortex (solid line). Partial spectral coherence, piriform cortex–motor cortex with septal area taken into account (dotted line). Fig. 3 (center). Spectral coherence, septal area–piriform cortex (solid line). Partial spectral coherence, septal area–piriform cortex, with motor cortex data taken into account (dotted line). Fig. 4 (right). Spectral coherence, septal area–motor cortex (solid line). Partial spectral coherence, septal area–motor cortex, with piriform cortex data taken into account (dotted line).

There is conspicuous coherence between the piriform cortex and the motor cortex in both cases. This evidence suggests that the electrical activity of the piriform cortex and the motor cortex are interdependent in some way that is independent of the influence of the motor cortex. Similarly, Fig. 3 indicates that there is significant coherence (interdependence) between the piriform cortex and the septal area, which is independent of the electrical activity of the motor cortex.

There is also significant coherence between the septal area and motor cortex (Fig. 4); however, between 4 to 10 hz, the partial coherence between these sites when the piriform cortex data is taken into account, is approximately zero. Therefore, essentially all of the coherent energy in both the septal area and the motor cortex in the interval between 4 to 10 hz (the concentration of energy is greatest for the six data channels in this interval) is a result of the energy imparted to it by that in the piriform cortex. From Fig. 2 to 4, we conclude that the piriform cortex supplies the energy or "drives" the activity in the septal area and the motor cortex.

Systematic examination of pairwise coherence and partial coherence in each of the 20 distinct triples of data sets taken from the six simultaneous recordings leads to the conclusion that the piriform cortex exclusively was also diriving the putamen, the reticular formation, and the nucleus lateralis posterior of the thalamus. In this sense, we say that we have identified the piriform cortex as the driving site of the epileptic focus.

The foregoing results were obtained on day 19 of the daily repetition of the piriform electrical stimulation. This was when the direct "driving" reached a maximum. Later, as the cat developed generalized tonic-clonic behavioral convulsions, the coherences diminished, suggesting that the various separate areas of the brain developed a degree of autonomous epileptic activity that did not depend on the piriform for direct driving.

The spectral computations were performed by the autoregressive representation method of spectral analysis (*4*). The spectral coherence and partial spectral coherence in Figs. 2 to 4 were computed with 89 degrees of freedom and have a maximum standard deviation of .094 at each point of zero coherence and considerably less variation for increasing values of coherence (*5*). Evidence of the validity and statistical stability of the results was obtained by observing apparently similar computational results from records that were adjacent, overlapping, and of longer duration (16 seconds, 160 degrees of freedom, maximum standard deviation .023).

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References and Notes

1. In a large number of cases it is useful to consider epileptic seizures as being driven or synchronized by the electrical activity of an anatomically distinct region in the brain. This region is commonly referred to as the epileptic focus. F. Morrell, *Arch. Neurol.* **1**, 141 (1959).
2. G. M. Jenkins and D. G. Watts, *Spectral Analysis and its Applications* (Holden-Day, San Francisco, 1968). An earlier effort to apply partial coherency analysis to electroencephalogram data appears in D. O. Walter and W. R. Adey, *I.E.E.E. Inst. Elec. Electron Eng. Trans. Bio-Med Eng.* **12**, 8 (1965).
3. G. V. Goddard, D. C. McIntyre, C. K. Leech, *Exp. Neurol.* **25**, 295 (1969); G. V. Goddard, *Nature* **214**, 1020 (1967).
4. The (multidimensional) autoregressive, time series representation is a parametric formula that best expresses, in a least-squares sense, the observed data set as a linear combination of its own past history plus an additional, unpredictable, uncorrelated vector. Spectral density, coherence, and transfer functions between data sets can be computed as attributes of the autoregressive representation formula. E. Parzen, in *Multiple Time Series Modelling in Multivariate Analysis II*, P. R. Krishnaish, Ed. (Academic Press, New York, 1969), pp. 389–406; H. Akaike, *Ann. Inst. Statist. Math.*, in press; W. Gersch, *Math. Biosci.*, in press.
5. The analysis was performed on an 8-second record of data sampled every 10 msec. The number of degrees of freedom n for the autoregressive representation spectral analysis is $n = N/p$, where p is in the order of the autoregressive fit to the observed data and N is the number of observed data points (*4*). For the results of Figs. 2 to 4, $N = 800$, $p = 9$, so that $n = 89$. The standard deviation of the coherence estimate was computed from D. E. Amos and L. H. Koopmans, *Tables of the Distribution of the Coefficient of Coherence for Stationary Bivariate Gaussian Processes* (Sandia Corp. Monograph SCR-483, Albuquerque, N.M., 1963), for a coherence value of zero. Since the poorest estimate of sampling coherence occurs at zero coherence this is a conservative estimate. The same numerical results and justifications hold for the partial coherence estimate. The tables are computed with the assumption that the time series are jointly Gaussian. V. A. Benningus [*I.E.E.E. Inst. Elec. Electron Eng. Trans. Audio Electroacoust.* **AU-17**, 198 (1969)] demonstrated that this assumption is not critical.
6. The experiments were performed while we were visiting fellows in the laboratory of Dr. F. Morrell, Stanford University Medical School, Division of Neurology. All of the computations were performed at and supported by the ACME facility of the Stanford University Medical School. W.G. (on leave from Purdue University, School of Aeronautics, Astronautics, and Engineering Sciences, Center of Applied Stochastics, Lafayette, Ind.) was supported by NIH special training and research fellowship 1F 10NB 1686-C1A at Stanford University, Division of Neurology. G.V.G. was supported by a traveling fellowship from the Ontario Mental Health Foundation.

20 March 1970; revised 22 June 1970

Drinking and Eating Elicited by Cortical Spreading Depression

Abstract. *Single waves of unilateral and bilateral cortical spreading depression were administered to rats by electrophoretic injection of potassium ions into the occipital cortices. Aggressive and stereotyped eating, drinking, and exploratory behavior were elicited by unilateral and bilateral spreading depression. Onset of the elicited behaviors varied among rats from 4 to 8 minutes after injection of the ions. Direct activation of, or rebound from, inhibition of subcortical motivational mechanisms may be responsible for the effects.*

Functional decortication by spreading depression has been commonly found to attenuate or inhibit the performance of various behaviors including feeding and drinking (*1*). We now report an additional opposite effect—namely, that single waves of cortical spreading depression (CSD) induced in one or both hemispheres can, after the inhibitory effect is over, elicit drinking, eating, grooming, and exploratory behavior.

Hooded male rats, about 3 months old, were prepared for electrophoretic injection of K^+ ions into the cortex and for recording of slow potential changes in both hemispheres. For injection of K^+ ions, refillable glass cannulas were implanted over each hemisphere with the tip placed about 1 mm below the occipital surface. The cannulas contained 25 percent KCl solution, a coiled silver wire, and a mandrel attached to a sealing screw. About 2 μg of K^+ ions were injected into the cortex by passing 1-ma anodal current for 10 seconds between the silver wire and an indifferent silver-wire electrode attached to the back of the skull. The injected amount of K^+ triggered a single wave of spreading depression. To monitor the slow potential changes