NONINVASIVE DETECTION OF DEEP BRAIN SPIKING PATHOLOGY: IMPLICATIONS FOR EVALUATING THE VIOLENT OFFENDER[1]

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INTRODUCTION

The correlation of abnormal deep brain electrical spiking activity with violent behavior has been demonstrated in non-human primate studies by employing invasive methods which involve the surgical implantation of electrodes and subsequent analysis of the electrical activity recorded from the implanted deep brain structures. In light of these results, a significant advancement in the diagnosis of abnormal brain activity, especially that deep brain activity associated with persons exhibiting uncontrolled violent behavior, would be achieved by the development of detection methods that are noninvasive and therefore applicable in ordinary clinical EEG settings. This would not only provide evidence of a possible underlying organic basis for the uncontrolled acts of violence committed by the violent offender, but could also contribute an important objective method for evaluating treatment effectiveness.

Our EEG research on noninvasive detection was stimulated primarily by the initial finding of complex patterns of consistent waveshape in scalp EEG which were time-locked to spikes recorded from electrodes implanted in deep brain structures of rhesus monkeys. These studies have also shown that such scalp correlates of deep spiking can be detected even in

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severe EEG noise backgrounds by the application of digital filters appropriately designed to minimize the effects of unwanted EEG background activity, or by special application of cepstral methods in cases where digital filters for pattern recognition are not suitable because the pattern to be detected is not known a priori. The analytical methods used are described in Saltzberg, 1975, 1976-a, 1976-b; Saltzberg, Lustick, & Heath, 1971; and Saltzberg, Lustick, & Heath, Note 1.

DETECTION METHODS

The digital filtering procedures developed for detecting scalp correlates of deep spiking were based on an analysis of monkey and human scalp EEG data obtained from research projects where simultaneous recordings from deep brain structures were available. Using the deep spike as the trigger for averaging scalp EEG activity, it was observed that transient slow wave activity frequently appeared in scalp activity at the same time that a spike occurred at depth. The waveshape of this transient activity was usually distorted by the presence of noise; therefore averaging procedures were used to achieve a better estimate of the transient waveshape. The power spectral density of the scalp EEG background activity was also estimated in order to appropriately weight the spectral components in the transient waveshape obtained by averaging. The digital filter derived from the spectral estimates of both the transient waveshape and the noise was employed as a detector which looks at scalp activity and reports on the presence or non-presence of transient patterns which match the characteristics of the digital filter. It is interesting to note that this coincidence of deep spiking and transient EEG slowing implies that pathological sharp spiking activity at depth produces slow wave activity at the surface. This is consistent with clinical EEG criteria which consider focal slow activity to be an abnormal indication.

The procedure for evaluating candidate digital filters was based on the number of spikes detected in normal subjects as compared to the number of spikes detected in the recording of mentally-ill subjects.[2] In the initial evaluation a comparison was made of the incidence of spikes in normals and in violent subjects, based on a Poisson model for random spiking. In this model the number of spikes detected over a given length of recording is compared with the expected number derived from data on normals. The normal control is used to

[2] *The number of spikes detected is a function of detection threshold, as described in Saltzberg, et al., 1971.*

test the hypothesis that a given record represents the EEG of a normal subject under the assumption that spikes in normal subjects are uniformly randomly distributed. The methods of analysis underlying these evaluation procedures depend on the performance characteristics of the digital filter as a detector, as well as on the statistical model for evaluating the significance of the number of spikes detected. These methods are described in the next section.

COMPUTER IMPLEMENTATION

By virtue of our computer configuration, Fourier series methods (rather than matrix inversion methods) were used to implement the design and evaluation of the digital filter. The Fourier methods for the design of the optimum filter proceed as follows:

1. Obtain (a) the complex Fourier series of the candidate transient pattern and, (b) the power spectral density of the signal plus noise; that is, the background EEG signal.

2. Divide the conjugate complex Fourier series of the transient pattern by the power spectral density of the signal plus noise.

3. Take the inverse transform of the Fourier series obtained in Step 2 which gives a discretely sampled time function that is the desired template or matched filter.

In addition to performing the above operations, the computer in our laboratory is also capable of performing running convolution. This allows continuous digital filtering of the scalp EEG to rapidly evaluate the performance characteristics of a candidate digital filter as a detector of abnormal transient activity. These digital filtering techniques applied to the detection of EEG transient patterns are described in Saltzberg, et al., 1971, and Saltzberg, et al., Note 1.

The above analytical procedures refer to the detection of spike induced events, but it is necessary to assign some significance to the number of events detected in terms of background activity and artifacts that produce false spike indications. The major difficulty which presents itself in physiological signal studies of this type arises from the fact that any given signal characteristic such as a spike can and usually does appear due to random background effects. The problem then becomes one of determining whether the appearance of this signal characteristic is due to background effects or to some inherent quality of the EEG being analyzed. The analysis and evaluation rationale are straightforward if it is assumed that the time interval between spike indications is random and uniformly distributed due to background activity in the normal EEG. With the foregoing assumptions, the analysis proceeds as follows:

let $p_n(t)$ = probability of exactly n spikes occurring in time t due to EEG background activity in normal subjects and,

$p_n(t+\Delta t)$ = probability of exactly n spikes occurring in time $t+\Delta t$ due to EEG background activity in normal subjects and,

λ = average rate at which spikes occur in EEGs of normal or control subjects;

then $$p_n(t+\Delta t) = p_n(t)(1-\lambda\Delta t) + p_{n-1}(t)\lambda\Delta t \ . \tag{1}$$

Equation (1) states (a) that the probability of exactly n spikes occurring over $t+\Delta t$ is equal to the probability that n spikes occur over time t and none in Δt, plus the probability that exactly $(n-1)$ spikes occur over time t and exactly one in Δt and that the time increment Δt is so small that (b) the probability of two or more spikes occurring during Δt is zero, and (c) that the probability of one spike occurring in Δt is $\lambda\Delta t$. Rearranging terms in Equation (1), and passing to the limit as $\Delta t \to 0$ gives:

$$\frac{dp_n(t)}{dt} + \lambda p_n(t) = \lambda p_{n-1}(t) \ . \tag{2}$$

The solution of this difference-differential equation is the Poisson probability density:

$$p_n(t) = \frac{(\lambda t)^n}{n!} e^{-\lambda t} \ . \tag{3}$$

The average or expected number of spike occurrences, $\bar{n}$, during time t is given by:

$$\bar{n} = \lambda t \ .$$

The variance of spike occurrences is also equal to λt, so:

$$\sigma_n^2 = \bar{n} \ .$$

If the actual number of spikes detected in an EEG record of length t is N, then to test significance we need to determine the likelihood that N or more spikes could occur in a normal EEG record. This is given by the cumulative distribution:

$$P_N(t) = \sum_{n=N}^{\infty} \frac{(\lambda t)^n}{n!} e^{-\lambda t}$$

$$= 1 - \sum_{n=0}^{N-1} \frac{(\lambda t)^n}{n!} e^{-\lambda t} \quad . \qquad (4)$$

If N is large compared to $\bar{n}(=\lambda t)$, then the likelihood computed from Equation (4) is small. If this likelihood is sufficiently small, then we reject the hypothesis that an EEG record containing N spikes in a time t is a normal record.

For several values of spike-count expectation, the level of significance associated with this hypothesis for a record with N spike indications can be obtained from plots of the cumulative distribution shown in Figure 1. For example, if the expected number of spikes over a given length of a normal record is 6, then the plot shows that the probability of 18 spikes occurring in a normal record is 0.0001. Therefore, the hypothesis that an EEG in which 18 spikes are detected represents a normal subject is rejected at the 0.0001 level. The detection of 12 spikes would allow rejection of the hypothesis at the 0.02 level.

It should be pointed out that such statistical modeling of multiple detections over long EEG records is essential because of the false signals, artifacts, and the many uncontrollable sources of physiological interference that plague the evaluation of EEGs. These statistical procedures follow and supplement the digital filtering procedures used in designing the detector, as outlined in the previous sections and described in our publications.

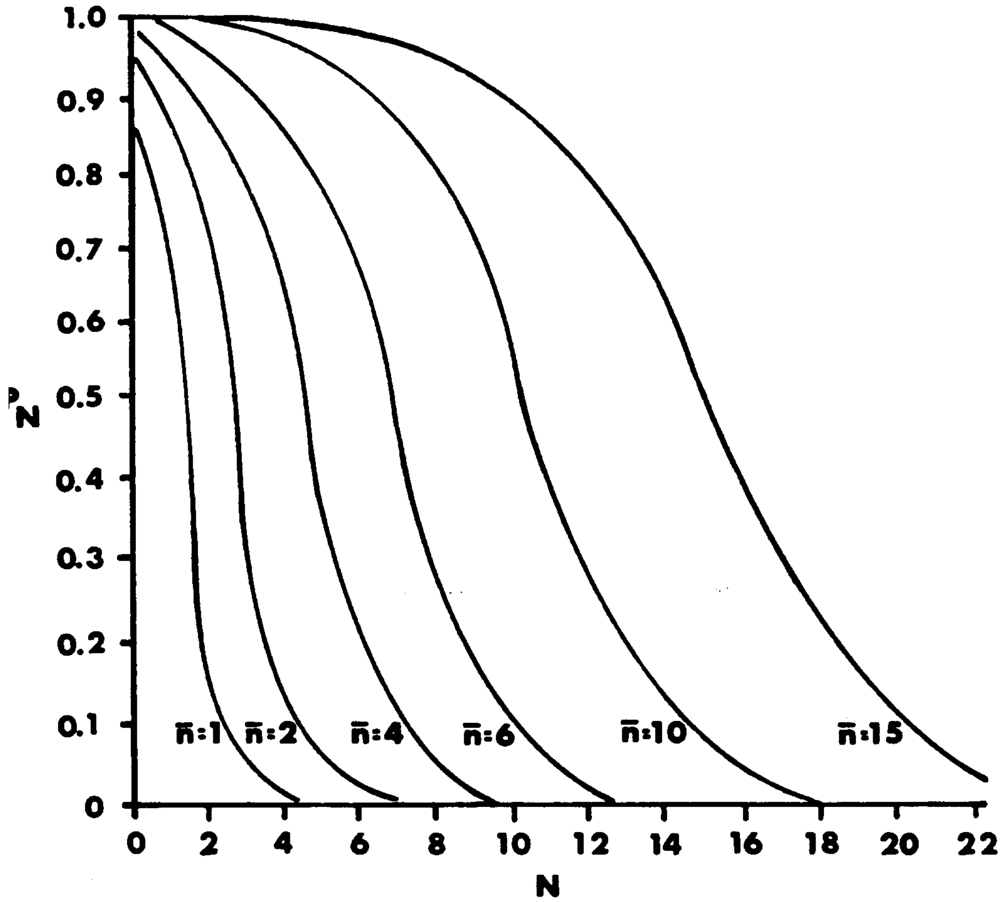

FIGURE 1. Probability criterion for the significance of N spike indications given $\bar{n}$ (Poisson Model). N = the actual number of spike indications in a given EEG recording, P_N = the probability of N or more spike indications, and $\bar{n}$ = the expected number of spike indications in a normal or control record of the same length.

SCALP DETECTION OF DEEP SPIKES IN HUMANS

We have analyzed several archival magnetic tape recordings which were made available to our computer laboratory. These tape recordings of human subjects represented an unique opportunity to test the digital filtering concepts developed in animal studies. As part of a larger investigation of the biological basis of mental illness, magnetic tape recordings with both surface EEG and deep brain data from two patients became available for analysis. The data from one of the patients was ideal for testing the concept of using the average scalp EEG activity time-locked to the deep spikes as a basic template for the design of a digital filter detector. The application of digital filtering to scalp spike detection was developed on an independent project after the data on this program was collected but, fortuitously, both scalp EEG and deep brain electrical activity were recorded simultaneously on the same magnetic tape in the larger project. This made possible the design of a digital filter based on deep spiking activity in a human. The filter design derived from this data was used to analyze the filter's performance as a detector of spike-correlated events in the scalp EEGs of the two implanted patients and in the scalp EEGs of age- and sex-matched normal controls.

The analysis of these tapes gave results that are highly encouraging because of the clear-cut differences between the number of detections in the patients versus controls and between the two sides of the head in the patient whose deep spiking activity was unilateral. In the patient who exhibited bilateral deep brain spiking activity, the digital filter detector indicated approximately the same number of spike counts on both sides of the head. Thus, a digital filter which was designed using the EEG data from one patient gave consistent results when applied to another patient. (It was not possible to design a digital filter using the second patient's EEG recordings because the scalp EEG activity was not recorded on tape simultaneously with the deep electrical activity.)

Deep recording channels were available on magnetic tape from both right and left brain hemispheres for patient P_1. Deep electrical spiking activity was exhibited only in left-side recordings with the most prominent spiking recorded from the left anterior septum (LAS). Therefore, the spikes in this deep recording channel were used as triggers for computing time-locked scalp EEG averages. Average potentials of similar shape were obtained from the two bipolar left-side scalp leads F7/T3 and T3/T5. Both symmetrical right-side leads (F8/T4 and T4/T6) did not produce an average time-locked potential above that obtained by using a random trigger. The average potential (shown in Figure 2) obtained from 200 time-locked scalp responses in channel F7/T3 provided the basis for the digital filter design used in this analysis of the scalp EEGs. The actual shape of the digital filter is shown in Figure 3, which represents the average time-locked potential of 1.5 seconds duration following the spike trigger, with appropriate waveform smoothing to minimize EEG background effects. This digital filter (Figure 3) acted as the matching template in performing an analysis of the ongoing surface EEG activity of the symmetrical EEG channels available for the two patients and on identical channels for the two sex- and age-matched controls.

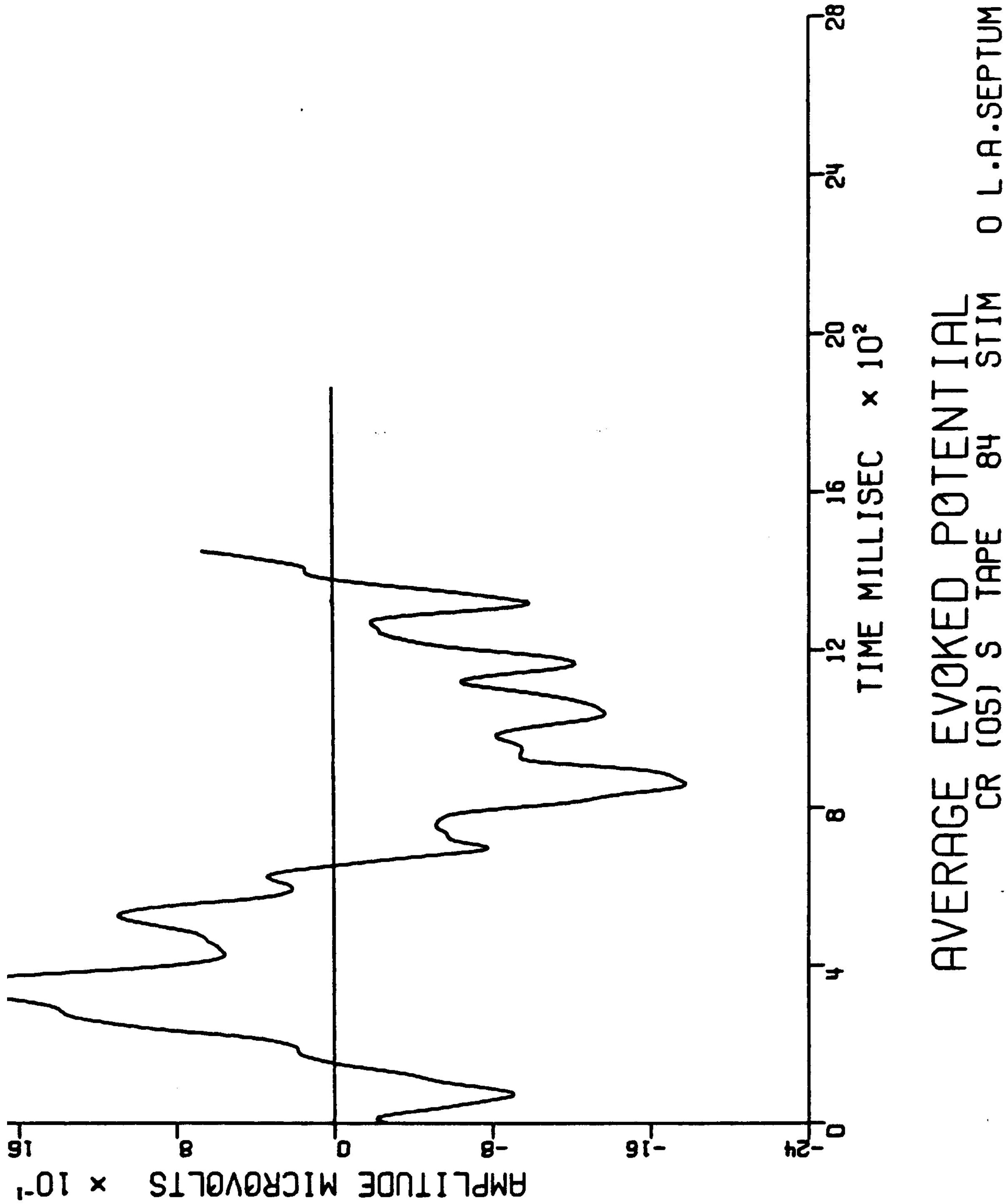

FIGURE 2. Average Evoked Potential.

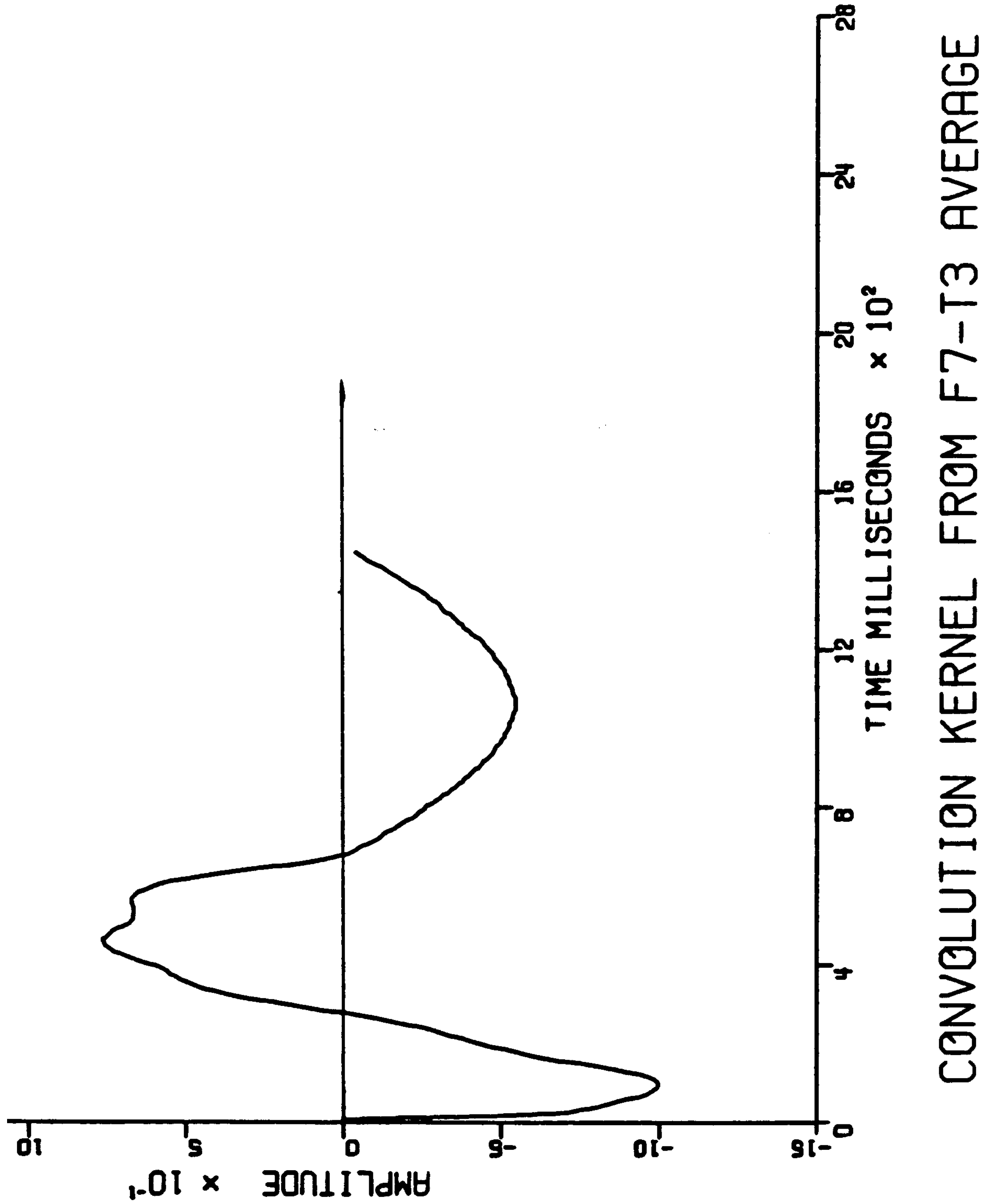

FIGURE 3. Digital Filter Template - Smoothed AEP.

The results are summarized in Table 1 and are based on a detection threshold at the output of the digital filter of two times its RMS output.

TABLE 1. Number of Events in 20 Minutes which Meets 2/1 Detection Criterion[a]

	Recording Site	
Subject	*F7/T3 Left-side EEG*	*F8/T4 Right-side EEG*
Patient P_1 with deep left spiking only	<u>216</u>	148
Patient P_2 with deep bilateral spiking	<u>190</u>	<u>212</u>
Normal Control C_1	128	132
Normal Control C_2	128	144

[a]*It should be noted that in the three scalp EEG channels in which one would expect a high incidence of spike-correlated events to occur (see underlined values in above table), a mean number of 206 detections was obtained with a standard deviation of 11; whereas in the five scalp channels in which one would expect a lower incidence of spike-correlated events, a mean number of 136 detections was obtained with a standard deviation of eight.*

DETECTION OF RECURRENT PATTERNS OF UNKNOWN WAVESHAPE

An alternate approach to the noninvasive detection problem is required when the recurring transient pattern is of unknown waveshape. Since averaging methods for visualizing a recurrent waveshape in noisy EEG require that the averaging process be synchronized by the deep spike event (which can be detected only by invasive methods), the waveshape of the recurrent transient is frequently unknown. Under these conditions, the methodology for detecting the presence of a recurrent complex transient in scalp recorded brain electrical activity is based on the application of deconvolution procedures as described

A recurrent transient waveform in the EEG can be represented as follows:

$$(1) \quad E(t) = \sum_{k=0}^{n} A_k X(t-\tau_k) + N(t)$$

Alternately, *(1)* may be written as a convolution product:

$$(2) \quad E(t) = X(t) * \sum_{k=0}^{n} A_k \delta(t-\tau_k) + N(t)$$

where * designates convolution, and

$X(t)$ = intermittent pattern; i.e., waveshape of recurrent transient

$N(t)$ = EEG background activity

$\delta(t-\tau_k)$ = Dirac delta function at τ_k.

The deconvolution of the convolution factors in equation *(2)* is accomplished in several steps. First, the Fourier transform of *(2)* gives the algebraic product of the individual Fourier transforms of the intermittent pattern and the set of delta functions. This suggests the use of cepstral analysis which involves computation of the logarithm of the Fourier transform as a second step and, as a third step, computation of the inverse Fourier transform of this result to produce a function called the cepstrum. The properties of the cepstrum will reveal the presence of a repetitive pattern in the EEG by virtue of spikes which will appear in the cepstrum when two or more recurrences of the pattern are embedded in the EEG epoch analyzed.

If the waveform characteristics are of interest, then this methodology can also be used to determine the shape of the transient pattern. This is accomplished by smoothing the cepstrum to eliminate the spikes, and then reversing all the transformations used to produce the cepstrum. However, this is a difficult computational problem and it is possible to circumvent these procedures if one is not interested in ascertaining the shape of the pattern, but simply in detecting whether a recurrent pattern is contained within the time epoch analyzed. If at least two patterns are captured in the data epoch, then analysis shows that the power spectral density (PSD) will contain ripples which are attributable to the presence of the recurring pattern. The assumption underlying the utility of this approach is that the background EEG, in the absence of a repeated transient pattern, will possess a smooth

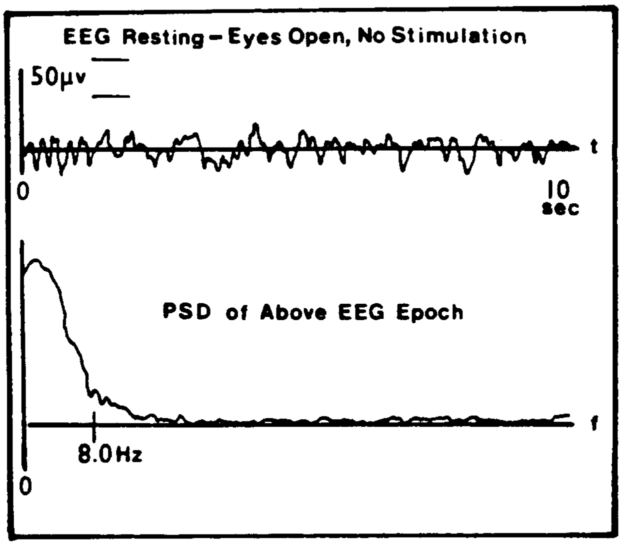

FIGURE 4. EEG Resting - eyes open, no stimulation.

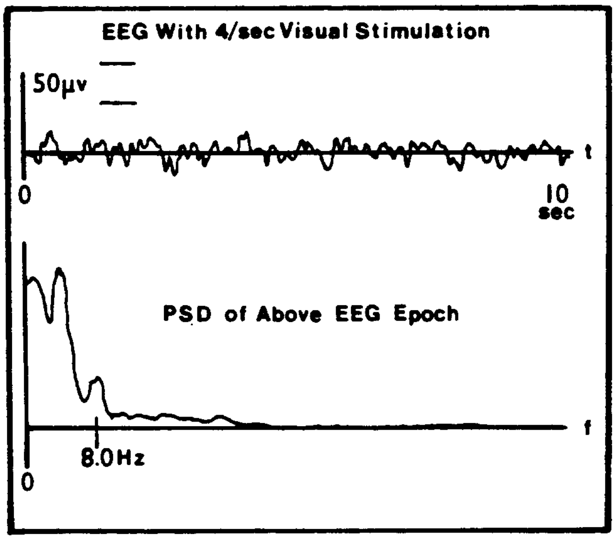

FIGURE 5. EEG with 4/sec visual stimulation.

or unrippled PSD. Figures 4 and 5 demonstrate that this assumption holds for the EEG data recorded under "eyes open" conditions from occipital leads during an experiment in which transients were introduced into the background EEG by intermittent visual stimulation. The figures show that the PSD for the no-stimulus condition is smooth (Figure 4) while the PSD for the stimulus condition exhibits ripples (Figure 5) whose peaks are separated by the reciprocal of the stimulus interval.

In summary, the above results demonstrate that PSD analysis of sufficient frequency resolution to resolve ripples may provide a tool for evaluating the violent offender. More generally, the analytical methods described in this manuscript provide a basis for investigating the clinical implications of weak recurrent transients which are embedded in EEG background and therefore usually not discernible by visual inspection of the EEG time series.

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