LONG-RANGE TEMPORAL CORRELATIONS IN EPILEPTOGENIC AND NON-EPILEPTOGENIC HUMAN HIPPOCAMPUS

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Abstract—Epileptogenic human hippocampus generates spontaneous energy fluctuations with a wide range of amplitude and temporal variation, which are often assumed to be entirely random. However, the temporal dynamics of these fluctuations are poorly understood, and the question of whether they exhibit persistent long-range temporal correlations (LRTC) remains unanswered. In this paper we use detrended fluctuation analysis (DFA) to show that the energy fluctuations in human hippocampus show LRTC with power-law scaling, and that these correlations differ between epileptogenic and non-epileptogenic hippocampus. The analysis shows that the energy fluctuations exhibit slower decay of the correlations in the epileptogenic hippocampus compared with the non-epileptogenic hippocampus. The DFA-derived scaling exponents demonstrate that there are LRTC of energy fluctuations in human hippocampus, and that the temporal persistence of energy fluctuations is characterized by a bias for large (small) energy fluctuations to be followed by large (small) energy fluctuations. Furthermore, we find that in the period of time leading up to seizures there is no change in the scaling exponents that characterize the LRTC of energy fluctuations. The fact that the LRTC of energy fluctuations do not change as seizures approach provides evidence that the local neuronal network dynamics do not change in the period before seizures, and that seizures in mesial temporal lobe epilepsy may be triggered by an influence that is external to the hippocampus. The presence of LRTC with power-law scaling does not imply a specific mechanism, but the finding that temporal correlations decay more slowly in epileptogenic hippocampus provides electrophysiologic evidence that the underlying neural dynamics are different within the epileptogenic hippocampus compared with contralateral hippocampus. We briefly discuss possible neurobiological mechanisms for LRTC of the energy fluctuations in hippocampus. © 2004 IBRO. Published by Elsevier Ltd. All rights reserved.

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Since the earliest recordings of the human electroencephalogram (EEG) (Berger, 1929) the origin and interpretation of EEG oscillations have remained active areas of basic and clinical research (Llinas, 1988; Steriade et al., 1990, 1993; Connors and Amitai, 1997; Herculano-Houzel et al., 1999). Motivated by the finding that EEG oscillations of different frequencies are manifestations of the network dynamics underlying functional brain states, the focus of most clinical and basic research has been on correlating specific EEG oscillation frequencies or frequency bands with specific states, for example, the 8–13 Hz posterior dominant rhythm with quiet wakefulness (Niedermeyer, 1987). Unfortunately, most quantitative methods for studying the temporal dynamics of the EEG, such as spectral analysis (Niedermeyer, 1987) and nonlinear dynamics (Palus, 1996; Stam et al., 1999), require the EEG signal to be stationary, that is, that the signal mean, variance and higher moments do not change with time. While human EEG signals can remain stationary for up to minutes at a time, stationarity often fluctuates over seconds (Cranstoun et al., 2002), limiting the usefulness of these methods for investigating correlations over long time scales. In previous quantitative studies of EEG, this limitation has been bypassed by consecutively analyzing relatively short segments of EEG, assuming them to be stationary, but this approach is ill suited for probing long-range temporal correlations (LRTC). For this reason, complete characterization of the temporal dynamics of EEG fluctuations, and in turn the collective neuronal oscillations responsible for EEG, has received little attention.

In recent years, new methods have been developed which make the problem of analyzing LRTC in non-stationary data tractable. Detrended fluctuation analysis (DFA) is one such method. It provides a systematic method for the analysis and characterization of LRTC embedded in non-stationary time series. Detrending the signal on multiple time scales, which has been demonstrated to eliminate spurious detection of temporal correlations that arise as an artifact of signal non-stationarity, allows the method to determine a scaling exponent that characterizes the temporal correlations in mono-fractal signals. Recently, DFA has been used to demonstrate the presence of LRTC with power-law scaling in human scalp EEG and magnetoencephalogram (MEG) recordings. In fact,
there is accumulating evidence that the dynamics of many complex natural systems have LRTC characterized by power-law scaling behavior. Examples include heart rate dynamics (Bunde et al., 2000; Peng et al., 1995), human gait (Hausdorff et al., 1997), and long-term weather patterns (Talkner and Weber, 2000).

In our work investigating epileptogenic brain and seizure generation, we have used DFA to analyze continuous EEG time series obtained from intracranial hippocampal depth electrodes placed in five consecutive patients with unilateral mesial (amygdalohippocampal) temporal lobe epilepsy undergoing pre-surgical evaluation for epilepsy surgery. These patients provide a unique opportunity to obtain high-fidelity hippocampal field recordings (intracranial EEG) directly from focal regions of epileptogenic and non-epileptogenic human brain. Since all patients in this study had seizures originating from one hippocampus, we are able to compare the neural networks responsible for seizure generation to contralateral, non-seizure generating networks.

**EXPERIMENTAL PROCEDURES**

**Study design**

We studied patients admitted consecutively to the Emory University Epilepsy Monitoring Unit (Atlanta, GA, USA) for presurgical evaluation with intracranial depth and subdural strip electrodes (subdural strips in one patient) for medically intractable temporal lobe epilepsy. We identified five patients who were determined to have exclusively unilateral mesial temporal lobe seizure onsets. Each patient underwent long-term continuous video and intracranial-EEG monitoring as part of their evaluation for epilepsy surgery. This study was conducted with the approval of the Human Research Committee of Emory University and the written consent of each patient. Patients were implanted with intracranial depth and subdural electrodes (Fig. 1) as dictated by pre-surgical noninvasive studies, including scalp-EEG recordings of seizures, magnetic resonance imaging (MRI), and in some cases functional imaging (single photon computed tomography and positron emission tomography), according to standard procedures for presurgical evaluation. Electrodes were placed using standard stereotactic methods, and post-operative MRI confirmed all electrode placements, and none needed repositioning. Each patient’s entire continu-

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**Fig. 1.** MRI with electrodes. Sagittal MRI scan of a patient implanted with intracranial EEG electrodes. Note the electrodes are smaller than they appear on the scan.

**Fig. 2.** Fifty seconds of unprocessed EEG from the seizure onset zone of patient 1. Channels 1, 2 and 3 are the three anterior-most contacts from the left temporal depth electrode (LT1, LT2, LT3 in Fig. 1) and channels 4, 5 and 6 are the three anterior-most contacts of the right temporal lobe depth electrode. The seizure onset is marked with the ellipse and involves the two anterior contacts of the right temporal depth electrode (channels 4 and 5). For further analysis channels 4 and 5 were used as the seizure onset zone and the contralateral contacts 1, 2 and 3 were used to represent non-epileptogenic brain.
ous intracranial EEG and video were archived as described below. Two expert EEG readers (B.L. and G.W.) marked each patient’s record for seizures (Fig. 2). For each patient, we selected the first five seizures out of wakefulness for which the record extended at least 20 min before and after the seizure. All patients had at least five seizures available for study except patient 4 (three seizures).

Two EEG records were created for each seizure: a pre-seizure record comprising 20 min immediately preceding seizure onset and a seizure/post-seizure record containing 20 min immediately following seizure onset. In addition to the seizure records, five 20-min sleep records and five 20-min waking records were randomly selected from the periods between seizures for each patient, each no closer than 2 h from either the onset or termination of the nearest seizure.

Data collection and storage

Continuous intracranial EEG and video were collected and stored on videotape using the Nicolet BMS-5000 (Nicolet Biomedical, Madison, WI, USA), a digital, 64-channel, 12 bit epilepsy monitoring system. Referentially recorded EEG was digitized at 200 Hz from tape, band-pass filtered from 0.1–100 Hz and archived to CD-ROM for later processing. Bipolar electrode montages were used to eliminate common mode artifact and a digital 60 Hz notch filter was employed to eliminate line noise. Data were processed using custom routines implemented in MATLAB (The Mathworks, Natick, MA, USA). Hospital stays varied from 3 to 27 days, yielding roughly 1.5 gigabytes/day of raw intracranial-EEG data available for processing.

Determination of seizures and seizure onset zone

The entire video-EEG record of each patient was reviewed and all clinical and sub-clinical seizures were marked. The seizure onset zone, as defined by the electrode contact(s) showing the earliest evidence of seizure onset, was identified for each patient (Fig. 2). All patients had unilateral mesial temporal lobe epilepsy, with seizures originating from only one temporal lobe and with the earliest onset within the amygdala–hippocampal structure in the anterior mesial temporal lobe. In all the patients studied the seizure onset zone could be localized to one or two intra-hippocampal depth electrode contacts, corresponding to a region spanning 2–3 cm in the anterior mesial temporal lobe in the amygdala–hippocampus (contacts LT1, LT2, LT3 in Fig. 1).

Determination of behavioral state

Due to the increased risk of infection in concurrent scalp and intracranial recordings, we could not obtain the scalp recordings necessary for conventional sleep staging. Here we use a method similar to that described by Gross and Golman (1999) for staging sleep from intracranial depth electrodes. Continuous videos of the patient’s entire monitoring stay were viewed in their entirety to determine the patient’s behavioral state (sleep, wake, or indeterminate) and identify clinical seizures. Only behavior clearly recognized as wakefulness or sleep was recorded as such, otherwise the segment was labeled indeterminate. Intracranial EEG was then quantitatively analyzed to achieve finer resolution of sleep–wake cycles into slow-wave sleep, wakefulness, and indeterminate periods. Periods of slow-wave sleep were characterized by predominantly synchrony, widely distributed high amplitude delta frequency (0–4 Hz) activity and behavior consistent with sleep on simultaneous video recordings. To be selected as a sleep record, greater than 75% of the EEG record had to be consistent with slow-wave sleep. Slow-wave sleep and unequivocal awake records were randomly selected for analysis.

EEG energy fluctuations in hippocampus

To investigate the energy fluctuations in human hippocampus we create an average energy time series from the depth electrode recorded EEG (Fig. 3a). Let \( \{V\} \) represent the discrete time series of potential difference between two contiguous depth electrode contacts, where the potential at discrete time \( t_i \) is represented as \( V[t] \). The average energy time series (Fig. 3B) is obtained by averaging over a 0.25 s window (\( M=50 \) data points) using a 0.045 s window overlap (\( D=9 \) points):

\[
E[k] = \frac{1}{M} \sum_{i=1}^{M} V^2[i] \quad \text{for } k=1,2,\ldots
\]

The 0.25 s window captures the relevant energy fluctuations in the hippocampus. The bipolar recordings are used to eliminate common mode artifacts and the background activity from structures outside the mesial temporal lobes.

LRTC and DFA

For a discrete time series \( \{E_i\} \) generated by a stationary stochastic process the autocorrelation function is \( C(t_j) = \langle E_i E_{i+j} \rangle \), where \( t_j \) is the time difference between two measurements separated by \( i \) discrete time steps and \( \langle \ldots \rangle \) denotes the ensemble average. For time series without LRTC \( C(t_j) \) decays rapidly to zero. When the decay of temporal correlations exhibits its power-law scaling, \( C(t_j) \propto t^{-\beta} \) for large \( i \) and \( 0<\beta<1 \), \( C(t_j) \) is said to exhibit LTC because the slow logarithmic decay. For stationary time series standard spectral analysis methods can be used to determine \( \beta \), the exponent characterizing the decay of correlations. Biological signals, however, are often non-stationary with slowly varying trends that can lead to the spurious detection of LRTC.

DFA is a scaling analysis method that can be used to detect LRTC in noisy non-stationary signals. The fundamental idea is to determine how the average root-mean-square (r.m.s.) fluctuation, \( F_\tau \), of the integrated time series of interest varies as a function of the time scale. Using DFA to calculate the average r.m.s. fluctuations it can be shown that when LRTC are present \( F_\tau \propto \tau^\alpha \), where \( \alpha=(2-\beta)/2 \) (Rangarajan and Ding, 2000).

To apply DFA, in analogy with the analysis of a random walk, first the “integrated displacement” of the time series is calculated (Fig. 3C) as described by Peng et al.:

\[
Y[k] = \sum_{i=1}^{N} (E[i] - \bar{E})
\]

where \( E[i] \) is the energy at discrete time \( i \) and \( \bar{E} \) is the average for the entire time series of length \( N \). Next the entire time series (2) of length \( N \) is divided into \( N/M \) non-overlapping windows (overlapping windows could be used as well) each of length \( l \) (Fig. 3C). In each window the “local trend” is calculated using a least-squares fit to the data (2) in that window. The \( y \)-coordinate of the local trend in the particular window is denoted by \( Y[k] \), which can be used to calculate the detrended integrated time series (Fig. 3D). The r.m.s. fluctuation of the detrended time series is given by

\[
F_\tau = \frac{1}{N} \sum_{k=1}^{N} \left( Y[k] - Y[k] \right)^2
\]

for window size \( \tau \). To determine the functional relation between \( F_\tau \) and \( \tau \) the computation is performed over a range of time scales (window sizes), where \( \tau \) ranges from 1 s to 500 s (Fig. 3E). Signals with LRTC and power-law scaling yield a linear relation on a log-log plot, i.e. \( \log(F_\tau) = \alpha \log(\tau) \), and the scaling exponent \( \alpha \) can be obtained by linear regression analysis (Fig. 3E).
Simulated time series (Fig. 3) with specific LRTC characteristics, i.e. particular values of $\alpha$, are easily generated and can serve as a test of the analysis method and help to elucidate the manifestations of different scaling behavior. To generate a time series with defined LRTC and a particular scaling constant we first generate a zero mean white Gaussian noise process, $\{\xi_k\}$, $k = 0, 1, \ldots, N$, with variance $\sigma^2$. The coefficients of the Fourier transform of $\{\xi_k\}$ are multiplied by the appropriate scaling factor, $(k/N)^{-\alpha/2}$, and then the inverse transform back to the time domain will yield a time series with the specified scaling behavior with variability around the mean spectrum provided by the white noise process.

The scaling exponent provides a quantitative measure of temporal correlations that exist in the time series. When the signal is completely uncorrelated (Gaussian or non-Gaussian probability distributions), the calculation of the scaling exponent yields $\alpha = 0.5$. When applied to a signal with LRTC and power-law scaling DFA will generate scaling exponents with either $0 < \alpha < 0.5$ or $0.5 < \alpha < 1$. When $0.5 < \alpha < 1$ the data are correlated such that large energy fluctuations are likely to be followed by large energy fluctuations and small energy fluctuations are likely to be followed by small energy fluctuations. When $0 < \alpha < 0.5$ the time series has LRTC, but the correlations are “anti-correlated” such that large fluctuations are likely to be followed by small fluctuations and small fluctuations are likely to be followed by large fluctuations. When $\alpha = 1$ the LRTC become independent of time with infinite range. As the scaling exponent increases from $\alpha = 0.5$ toward
α = 1, the temporal correlations in the time series are more persistent (decay more slowly with time). When α > 1, however, the correlations no longer exhibit power-law scaling and decay more rapidly.

Statistical tests used to determine average scaling exponents and their significance

DFA (Figs. 3 and 4) was used to calculate a separate scaling exponent for each of the bipolar recorded 20-min time series (Fig. 5). In each of the four behavioral states (wake, sleep, pre-seizure, and seizure/post-seizure) five independent 20-min records were analyzed using DFA to determine scaling exponents which were then averaged to obtain an average scaling exponent for a given behavioral state for each bipolar recorded time series.

To compare epileptogenic to non-epileptogenic hippocampus the depth electrode recordings contralateral to the seizure onset zone were identified. Because it is not possible to place intracranial electrodes with perfect symmetry between the two hemispheres, we could not be assured that the EEG activities from ipsiunumeric contralateral electrodes were recording from exact homologous hippocampal regions. The depth electrodes were placed using stereotactic methods, which are generally accurate to approximately 0.25 cm. However, with electrode spacing of 1.0 cm and even small errors associated with placement we do not expect the contralateral ipsiunumeric electrodes to give the exact equivalent anatomical position of the seizure onset zone in the contralateral hippocampus. For this reason, comparison of epileptogenic and the contralateral non-epileptogenic hippocampus uses the average scaling exponents from the seizure-onset zone and the contralateral anterior most electrodes (electrode contacts 1, 2, and 3 in Fig. 1).

Comparison between behavioral states and brain region (epileptogenic or non-epileptogenic) were performed using the Student’s t-test. A statistically significant difference was considered present if P < 0.05. As a control, simulation data with known scaling constants and random shuffling the EEG time series data created surrogate signals to test the sensitivity of the analysis to detect changes in scaling constants.

RESULTS

Time series with LRTC and defined scaling exponents were simulated (Fig. 3) and DFA applied to determine the scaling constants (Fig. 4). Because the simulated data are from a known stationary process standard spectral methods can be used to determine the LRTC and associated power-law scaling exponents. To clarify the ability of DFA to accurately detect differences in LRTC we applied DFA and standard spectral analysis to simulated time series with a range of known scaling constants (Fig. 4). Over the range of scaling constants of interest the DFA derived scaling exponents showed excellent agreement with standard spectral analysis.

The EEG energy fluctuations in human hippocampus all demonstrated robust power-law scaling for all patients and behavioral states studied. All scaling exponents, α, fell...
between 0.58 and 1.0 demonstrating that energy fluctuations in both epileptogenic and non-epileptogenic hippocampus have persistent LRTC with power-law scaling with large (small)-energy fluctuations preferentially followed by large (small)-energy fluctuations. The scaling exponents of all five patients in sleep, wake, pre-seizure and seizure/post-seizure periods are presented in Table 1.

When the EEG records were randomly shuffled, destroying any temporal correlations in the records and producing a white noise power spectrum, the average of all the scaling exponents was $\alpha = 0.54 \pm 0.01$, which is close to the expected value ($\alpha = 0.5$) for uncorrelated data. It has been shown that the approach of $\alpha \rightarrow 0.5$ (uncorrelated data) can be very slow. In all patients studied, robust power-law scaling behavior was present over a range of times scales from approximately 2.5 to 200 s. While the temporal correlations may persist even beyond this time scale, the variability of the r.m.s. fluctuation, $F_{\tau}^{l}$, increases with window size, and correlations beyond this time window would require longer data records.

In order to probe differences in the network dynamics of epileptogenic and non-epileptogenic brain, we compared the scaling exponents from the seizure onset zone and the contralateral hippocampus. Non-epileptogenic hippocampus, contralateral to the seizure onset zone (and without evidence of pathology on MRI) showed evidence of long-term temporal correlations ($0.60 < \alpha < 0.69$), but with scaling exponents that were significantly smaller than those in epileptogenic hippocampus ($0.68 < \alpha < 0.88$; Table 1). This finding was present for all five patients, and statistically significant ($P < 0.05$) for four of the five patients studied (Table 1). This effect, a larger scaling exponent within the seizure onset zone compared with the non-epileptogenic hippocampus, was also present as a trend in the sleep records, but was statistically significant in only two patients.

Previous studies of intracranial EEG in epileptogenic hippocampus using other measures have found changes in the EEG dynamics up to hours before a seizure begins. To investigate the possibility of a change in the long-range scaling behavior prior to the onset of seizures we compared the pre-seizure and baseline wake records. While evidence for power-law scaling of temporal correlations persisted, we did not detect a significant difference in the scaling exponents in the pre-seizure period compared with baselines in either epileptogenic or non-epileptogenic hippocampus, indicating there is no significant change in the long-range correlation of energy fluctuations as a seizure approaches.

In the seizure/post-seizure records the scaling exponents in the epileptogenic and non-epileptogenic brain were significantly different in only one patient (Table 1). Interestingly, the exponents approached $\alpha = 1.0$, showing evidence for more persistent LRTC between energy fluctuations in the post-seizure period. We should note that in all patients studied the unilateral onset seizures spread to involve both temporal lobes, and that post-seizure EEG activity in both temporal lobes showed prominent quasi-periodic epileptiform discharges.

### DISCUSSION

Using DFA we show that the energy fluctuations in human hippocampus exhibit LRTC with power-law behavior. The analysis of human hippocampal network energy fluctuations shows persistent long-range correlations over time scales ranging from seconds to minutes that were consistent across the five patients studied. The presence of power-law scaling in the temporal correlations of hippocampal energy fluctuations, i.e. $F_{\tau}^{l} \sim \tau^{-\alpha}$, with $0.5 < \alpha < 1.0$, demonstrates that the fluctuations are not modulated at a characteristic time scale, but that the energy fluctuations occur as a part of a self-similar cascade of events that have a fractal structure. The presence of power-law scaling with $0.5 < \alpha < 1.0$ shows that there are persistent temporal correlations where high (low)-energy fluctuations tend to cluster together in time, as seen in other complex systems exhibiting power-law scaling behavior (Peng et al., 1995).

Previous studies have reported scaling behavior in scalp recorded EEG (Linkenkaer-Hansen et al., 2001). The existence of a crossover in the scaling behavior of scalp EEG voltage fluctuations, with two different scaling regimes characterized by different scaling constants, has been reported (Ferree and Hwa, 2003). However, the du-
ration of the records, 10 s, used to determine the results are much shorter than what we have found to be reliable for determination of LRTC scaling behavior. The presence of LRTC in non-epileptogenic regions in individuals with epilepsy does not necessarily imply LRTC in normal brain, since the hippocampus contralateral to the seizure onset zone often demonstrates pathologic EEG findings, even when seizures do not originate from that area. Nonetheless, the scaling exponents calculated here from intracranial hippocampal EEG are grossly similar to scaling exponents found in scalp recorded EEG from normal subjects (i.e. \( \alpha \approx 0.7 \); Linkenkaer-Hansen et al., 2001), and provide additional support that LRTC with power-law scaling is a fundamental feature of human brain activity.

**Scaling of temporal correlations in the epileptogenic hippocampus**

There is a significant difference in the LRTC in epileptogenic (seizure generating) compared with non-epileptogenic hippocampus. This result was present in all patients studied, and statistically significant in four of the five patients. The difference persisted in the sleep records of three patients, and remained statistically significant in two patients. While this result does not implicate a specific underlying mechanism, it could be that the mechanism responsible for persistent correlations in the post-seizure state (\( \alpha \approx 1.0 \)) is responsible for changes seen in the epileptogenic hippocampus interictally. A recent study shows that epileptiform bursts in hippocampal slice, which are morphologically similar to post-ictal epileptiform discharges, were the result of increased neuronal synchrony. It may be that a pathologic increase in neuronal network synchrony is the mechanism responsible for the more persistent temporal correlations in the epileptogenic hippocampal network. The proof of this conjecture, however, will have to wait a more complete understanding of the neural network dynamics in epileptogenic and normal hippocampus.

**Similarity of dynamics in pre-ictal and baseline records**

In contrast to previous studies using nonlinear and linear time series analysis methods we did not find evidence for a pre-seizure state. The lack of a change in LRTC as seizures approached may reflect the relatively long records (20 min in the present study) required to obtain statistically accurate measures of LRTC. The selection criteria for baselines records was different in our study, with baselines restricted to be more than 4 h from seizures as compared with 4 h in one previous study (Litt et al., 2001). However, when we compared the LRTC in baselines that were greater than 4 h removed from seizures we did not find a statistically significant difference. It has been suggested that DFA allows the separation of the intrinsic dynamics of a complex multicomponent system, which are assumed to underlie long-range correlations, from external driving forces operating with characteristic frequencies (Peng et al., 1995). The absence of a change in the LRTC as seizures approach may indicate that seizures begin, or are triggered by events outside the local network. That is, an external signal drives susceptible hippocampal tissue to seizure without changing the underlying intrinsic neuronal network dynamics. Validation of this idea is likely to require careful exploration in vivo in spontaneously seizing animal models of temporal lobe epilepsy, as the extent of electrode implantation in humans during evaluation for epilepsy surgery is limited by clinical necessity and ethical considerations.

**Possible mechanisms underlying long-term temporal correlations**

Why do energy fluctuations in human hippocampus have LRTC with power-law scaling? This remains an open question, but simulations demonstrate (Feder, 1988) that the introduction of a biased probability distribution of event occurrence, whereby large (small) fluctuations preferentially tend to follow large (small) fluctuations, can produce LRTC with scaling exponents \( 0.5 < \alpha < 1.0 \). The energy fluctuations measured by hippocampal depth electrodes represent collective synchronous activity of a population of neurons that have both local interactions and more distant interactions via synaptic connections (Lopes da Silva, 1991). Thus, it is possible that the LRTC of energy fluctuations are manifestation of a number of mechanisms, and exactly how these correlations arise, and why they are more persistent within the epileptogenic hippocampus remains unclear. We can speculate about some interesting possible neurobiological mechanisms that might lead to a bias in the probability distribution of energy fluctuations: 1) The local electrochemical environment created by glia cells could produce a relative depolarization and increased synchronized bursting of neurons with memory effects. 2) The strength of synaptic interaction between neurons might be increased by large population events (synchronized firing of neurons) which would in turn make subsequent large population events more probable.

Lastly, studies from a wide variety of complex systems have demonstrated the presence of LRTC with power-law scaling (Sornette, 1994; Sornette, 2001; Bak et al., 1987, 1988) and it is now clear that this does not point to a unique network mechanism. This point has recently received considerable interest (Sornette, 1994, 2001) and a number of possible physical mechanisms have been suggested. Nonetheless, perhaps the most commonly cited mechanism for LRTC and power-law behavior in complex systems is self-organized criticality (Bak et al., 1987, 1988), which describes how complex systems made up of local interacting subunits can self-organize via local interactions to a state exhibiting long-range spatio-temporal correlations (Chen and Bak, 1989; Mantegna and Stanley, 2000). Self-organized criticality has recently been suggested as a possible mechanism for the presence of LRTC in scalp EEG and MEG (Linkenkaer-Hansen et al., 2001), and scaling behavior in epileptogenic hippocampus (Worrell et al., 2002). This speculation is tempered by the evidence that there are other possible explanations for temporal correlations with power-law scaling (Sornette, 1994, 2001), and that the proof of a critical state ultimately requires...
demonstration that the fluctuations scale with the size of the system (Bak et al., 1988; Sornette, 2001), which may be difficult to realize experimentally. However, detailed realistic models might provide an excellent test of these concepts, and we anticipate that our findings in human brain will stimulate interest for modeling.

CONCLUSION

In this paper we have demonstrated that the energy fluctuations in both epileptogenic and non-epileptogenic human hippocampus exhibit LRTC with power-law scaling. While LRTC in the temporal dynamics of energy fluctuations human hippocampus does not implicate a unique mechanism, the results for the first time give evidence of more persistent temporal correlations in the seizure onset zone of epileptogenic hippocampus.

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