Nonlinearity in All-night Sleep EEG Recorded with Foramen Ovale Electrodes in a Patient with Temporal Lobe Epilepsy

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Abstract

Objective: It is investigated to which extent measures of nonlinearity derived from surrogate data analysis are capable to quantify the changes of epileptic activity related to varying vigilance levels.

Methods: Surface and intracranial EEG from foramen ovale (FO-)electrodes was recorded from a patient with temporal lobe epilepsy under presurgical evaluation over one night. Different measures of nonlinearity were estimated for non-overlapping 30-s segments for selected channels from surface and intracranial EEG. Additionally spectral measures were calculated. Sleep stages were scored according to Rechtschaffen/Kales and epileptic transients were counted and classified by visual inspection.

Results: In the intracranial recordings stronger nonlinearity was found ipsilateral to the epileptogenic focus, more pronounced in NREM sleep, weaker in REM sleep. The dynamics within the NREM episodes varied with the different nonlinearity measures. Some nonlinearity measures showed variations with the sleep cycle also in the intracranial recordings contralateral to the epileptic focus and in the surface EEG. It is shown that the nonlinearity is correlated with short-term fluctuations of the delta power.
The higher frequency of occurrence of clinical relevant epileptic spikes in the first NREM episode was not clearly reflected in the nonlinearity measures.

Conclusions: It was confirmed that epileptic activity renders the EEG nonlinear. However, it was shown that the sleep dynamics itself also effects the nonlinearity measures. Therefore, at the present stage it is not possible to establish a unique connection between the studied nonlinearity measures and specific types of epileptic activity in sleep EEG recordings.

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1 Introduction

In several recent studies it was reported that interictal EEG of epileptic patients showed signatures of nonlinearity (Casdagli et al., 1996, 1997; Jing and Takigawa, 2000; Andrzejak et al., 2001b,a). These results were achieved using the method of surrogate data analysis. Nonlinearity detected by this method is only negatively defined as some temporal correlation deviating from linear correlation, without suggesting any positive characteristics, such as deterministic chaos. In particular, there is no clear distinction between nonlinearity and nonstationarity, because the null hypothesis of the surrogate data analysis incorporates both. To overcome this problem Andrzejak et al. (2001a) tested their data for some kind of "weak stationarity", i.e. stationarity of variance and center frequency, before applying the surrogate data test. However, as the authors admit themselves, their procedure could not guarantee that the rejection of the null hypothesis is not due to nonstationarity.
In a recent study by Olbrich et al. (2003) this problem was investigated for surface sleep EEG from healthy persons. It was found that almost all occurring nonlinear signatures can be explained by nonstationarity of the linear properties on time scales longer than a few seconds. The amount of nonstationarity was found to depend on the sleep stage. In order to control for this dependency we also monitored the fluctuations of the linear properties in the present analysis.
In the studies of Casdagli et al. (1996) and Andrzejak et al. (2001b) the rejection of the null hypothesis was basically considered as a qualitative feature of epileptic EEG both ictal and interictal. But already in these studies the analysis involved quantitative measures, which were found to be maximal near the epileptogenic zone (Andrzejak et al., 2001b). In the present paper we investigated, whether quantitative measures of "nonlinearity" can be used as a measure of epileptic activity in interictal EEG recordings. Our study also accounts for the fact that interictal epileptic activity is strongly influenced by the vigilance states thus going beyond previous studies. Moreover, several investigations of sleep EEG of healthy subjects revealed weak nonlinearity in certain sleep stages (Fell et al., 1996; Pereda et al., 1998; Shen et al., 2003). Therefore we analyzed interictal EEG from a whole night. This enables us to investigate, whether the reported nonlinearity is specific to the epileptic activity and how it is influenced by changes in the vigilance level. In order to be

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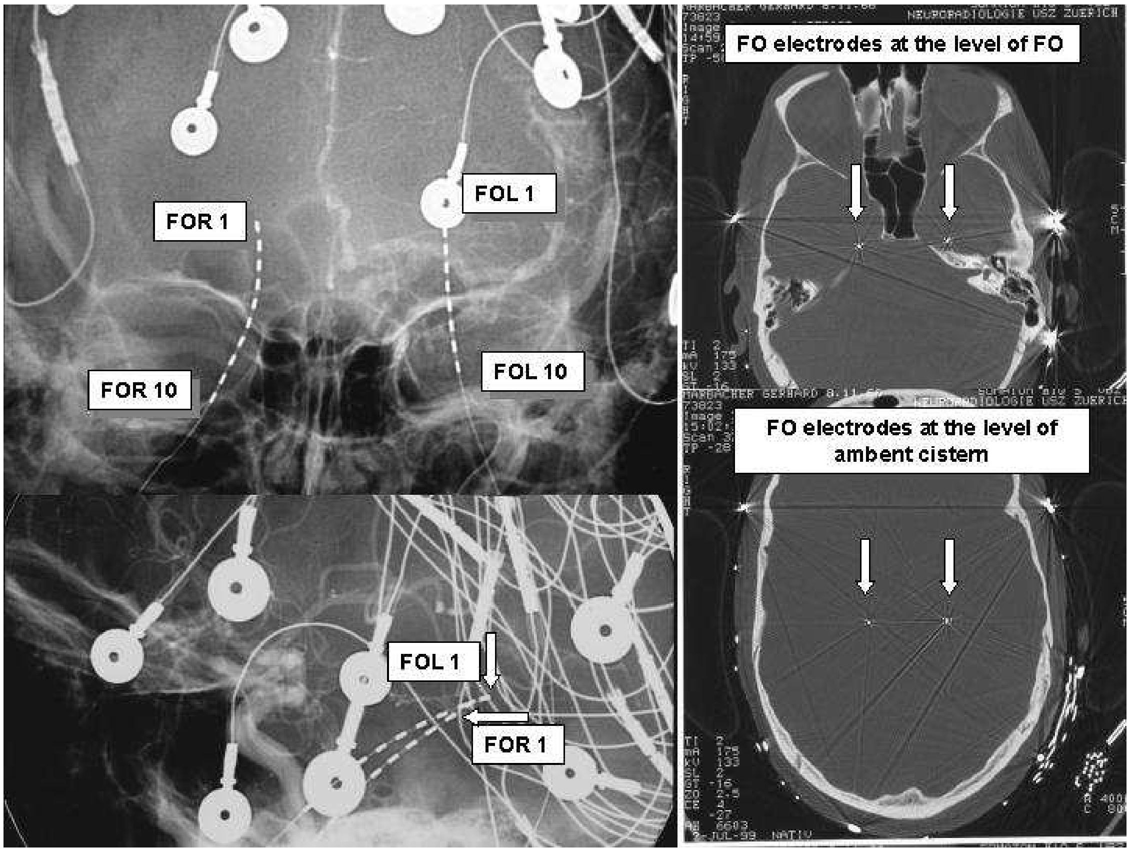

Fig. 1. Position of the implanted FO electrodes.

able to study also the detailed relationship between the epileptic activity and the nonlinearity measures we needed an independent measure for the epileptic activity. This was provided by visual scoring of epileptic transients.

2 Materials and Methods

2.1 Patient and EEG

The EEG data were recorded under presurgical evaluation from a patient (32 year-old, male) who was diagnosed as mesial temporal lobe epilepsy(MTLE) (Wieser et al., 1993), using the standard 10/20 system scalp EEG and FO electrodes inserted on both sides (FO-EEGs), with simultaneous video-monitoring of the behavior. The whole video-EEG data consisted of about 6 hours in the night when the patient was asleep, although some short awake periods were included. The recordings started about 15 min after sleep onset. The EEG data did not include any seizures or subclinical discharges, although at the end of the analyzed data a simple partial seizure was recorded.

After analog high-pass and low-pass filtering the data were recorded, digitally filtered (low pass -3 db at 70 Hz and high pass -3db at) and finally stored with a sampling rate of 200 Hz. The FO electrodes had 10 contacts of 2mm each in length and a intercontact distance of 2 mm. For the position of the electrodes see Fig. 1. FO-EEG was recorded with bipolar lead that connects contacts next to each other. For further analysis, FOL7-9 (7th contact referenced to 9th on the left FO electrode) and FOR4-6 (4th to 6th on the right) channels were selected as representatives of epileptic and non-epileptic sides, with the reason that the former showed epileptiform transients with highest amplitude during great part of the record, and the latter was located in an almost symmetrical position to the former.

2.2 Conventional sleep staging

Conventional sleep staging was done by means of C3-M2 bipolar lead, which looked not affected by epileptic activities. Because of absence of special electrodes for monitoring eye movement and muscle tonus, the judgment of rapid-eye-movement (REM) sleep was done by scalp EEG findings in which eye movements were detected by the frontal polar electrodes (FP1-M2), together with watching the behavior of the patient in video display. An EMG signal was measured by T3-M2 derivation.

2.3 Counting of spikes and steep transients

Spikes and epileptiform transients were counted visually using all FO-channels by one of the authors (H.G.W.). The scored transients were divided in four classes:

(1) clinically relevant spikes
(2) steep epileptiform transients of questionable significance
(3) state dependent transient
(4) M-waves (Freemon and Walter, 1970)

For the further analysis we calculated the numbers of spikes in the non-overlapping 30-s segments used for the spectral and nonlinearity analysis.

2.4 Nonlinearity analysis

The analysis for detecting nonlinearity was performed on non-overlapping 30-s segments from the channels FOL7-9, FOR4-6 and C3-M2 by the method of surrogate data analysis. We used the iterated amplitude adjusted Fourier transformed (IAAFT) surrogates. These are data sets which reproduce the correlation function and the amplitude distribution of the original data, but are random otherwise. They are generated by an iterative procedure based on randomizing the phases of the Fourier transformed data. For details see Schreiber and Schmitz (2000). We used surrogates with the exactly reproduced amplitude distribution function and approximately reproduced power spectrum.
Four different nonlinear test statistics were employed: the correlation integral C2(r) and the correlation dimension D2(r) (Grassberger and Procaccia, 1983) using time delay embedding with an embedding dimension $m = 6$, time delay $d = 12$ and a Theiler correction $w = 20$. The result was quantified by the "number of sigmas"

$$S_Q = \frac{\langle Q^{\mathrm{surr}} \rangle - Q}{\sigma_Q} \tag{1}$$

The S values for C2 or D2 were averaged on small scales (S) $-1.5 < \ln r/\sigma < -1$ and on large scales (L) $0 < \ln r/\sigma < 0.5$ and will be denoted by S_{CL}, S_{CS}, S_{DL} and S_{DS} respectively in the following, σ denoting the standard deviation of the data in the segment.

2.5 Spectral analysis

We estimated the power spectral density (PSD) using the maximum entropy method based on autoregressive modeling. An AR(12)-model was computed on 1-s EEG segments. The power in a frequency range [$\mathrm{f}_{\mathrm{min}}$, $\mathrm{f}_{\mathrm{max}}$] was estimated by

$$P = \sum_{f_{\mathrm{min}} \le f \le f_{\mathrm{max}}} P(f) \cdot \Delta f \ . \tag{2}$$

for the the following frequency bands: delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), sigma (12-16 Hz), beta (16-30 Hz) and gamma (30-100 Hz). For 30-s segments the mean of its logarithm, $\langle \ln P_i \rangle$, and its standard deviation $\Delta \ln P_i$ was computed.
To quantify the nonstationarity of the spectral properties of the segments we

used the difference between the standard deviations $\Delta \ln P_i$ and the standard deviations of the estimates of P_i due to statistical fluctuations

$$\delta \ln P_i = \Delta \ln P_i - \Delta_{stat} \ln P_i \tag{3}$$

The statistical fluctuations were estimated by applying the same algorithm on 1-s segments of the IAAFT surrogates described in 2.4 [1] If there is $\delta \ln P_i > 0$ for one or more frequency bands in a significant way the null hypothesis of the surrogate data analysis can not be true and has to be rejected. Therefore these measures allow to quantify the non-linearity, i.e. rejection of the null hypothesis, due to nonstationarity of the spectral properties of the signal in contrast to a stationary nonlinearity as it can be observed in the classical chaotic systems such as the Lorentz or the the Rössler system (see e.g. Ott, 1993).

2.6 Correlation analysis

We used the Spearman rank-order correlation coefficient r_s (Press et al., 1992) to quantify the relationship between two different characteristics. The significance p for a r_s-value is the probability of observing the r_s-value under the null-hypothesis that the different measured characteristics are not correlated. This null-hypothesis will be rejected, if p for a r_s-value is smaller than 0.05.

3 Results

3.1 Conventional sleep stage scoring

By conventional sleep staging, 5 NREM episodes were clearly identified, although none of them included slow wave sleep (SWS; stages 3 and 4) for a significant duration because of the lack of slow waves with sufficiently large amplitudes. The first part of the first NREM episode was not included in the data because of external inferring factors. Moreover, ca. 2 min after the end of the analyzed data set a subclinical discharge occured during transition from

[1] The rationale behind this approach is the fact that the IAAFT surrogates have the same spectral density for whole segment and are stationary. A possible problem of this method could be that the spectral density of the IAAFT surrogates is estimated an unwindowed FFT algorithm. We found that this can be result in a higher spectral power in the high frequency bands in the surrogates compared to the original data if the spectral density is estimated by using autoregressive modeling.

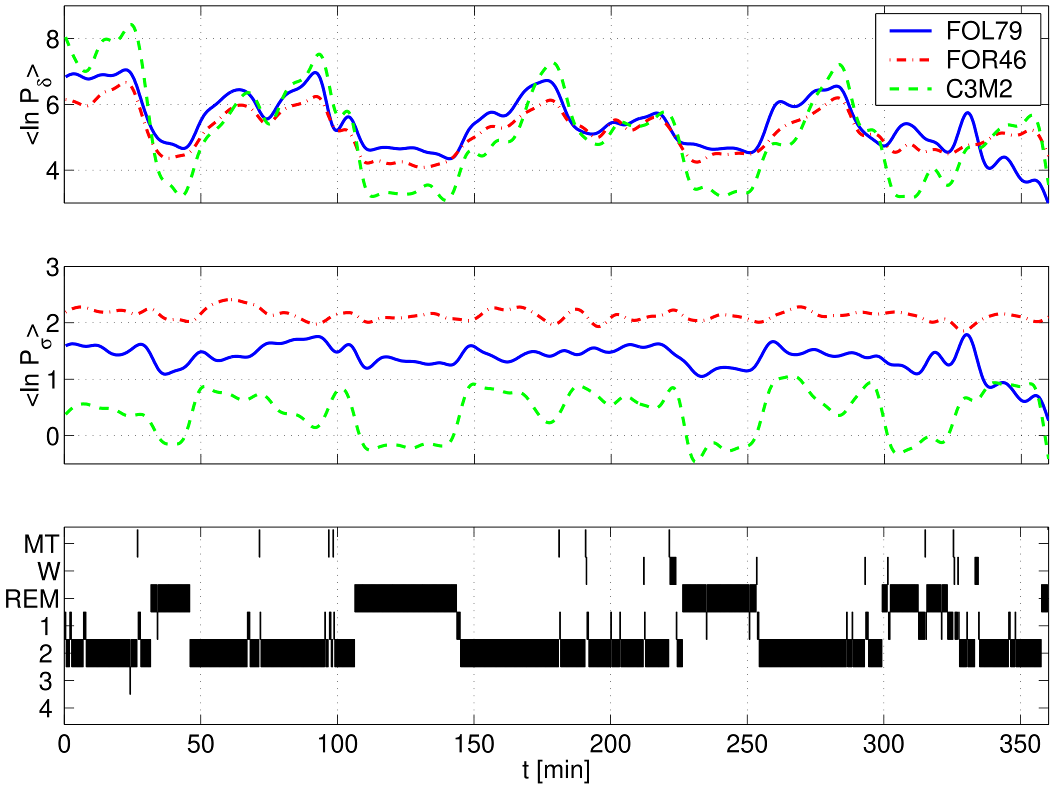

Fig. 2. Upper panel: Mean log Delta power estimated from surface EEG (C3M2 - solid line), FO-EEG from the contralateral side (FOR4-FOR5 - dashed line) and from the ipsilateral side (FOL7-FOL9 - dashed dotted line. Middle panel: Mean log sigma power. The curves in both panels were smoothed by a 4th order low-pass Butterworth filter with cutoff frequency 0.0017 Hz. Lower panel: sleep stages. W awake, MT movement time, R REM sleep, 1-4 NREM sleep stages 1-4.

REM to NREM sleep.
However, the sleep structure is rather regular and not strongly fragmented.

3.2 Spectral analysis

	REM	NREM	REM+NREM	REM	NREM	REM+NREM
C3M2-FOL79	0.115	0.700**	0.7439**	0.068	0.138*	0.353
C3M2-FOR46	0.161	0.799**	0.889**	0.149	0.136*	0.194*
FOL79-FOR46	0.279*	0.841**	0.826**	-0.033	0.042	0.099

Table 1
Rank correlation coefficients between mean log delta power of the different channels (columns 2-4) and for the fluctuations (columns 5-7). (* $p < 10^{-2}$,** $p < 10^{-8}$).

The time course of delta power (Fig. 2, upper panel) of scalp EEG showed basically smooth increase and decrease corresponding to the occurrence of

each of NREMS episodes in conventional sleep EEG. Generally the slope of decrease was steeper than that of increase, as previously reported on healthy subjects (Aeschbach and Borbély, 1993). Delta power of scalp EEG showed one or more drops for a short period during NREMS episodes, which was also observed in healthy persons (see e.g. Merica et al. (1997) for a discussion). The time course of delta power of FO-EEG on both the epileptic and non-epileptic side were very similar to that of scalp EEG except for the last NREM cycle preceding the seizure, the correlation coefficients are shown in Table 1. This finding is concordant with a previous report by Dijk and Wieser (1990).
Fig. 2 shows also the mean sigma power, which is in the case of surface EEG a measure of spindle activity. The typical negative correlation between the mean sigma and delta power (Aeschbach and Borbély, 1993) during NREM sleep can be seen clearly in the surface EEG but not for the FO-EEG. The maxima in the mean delta power are accompanied by minima in the sigma power.
The fluctuations of the delta power (upper panel in Figure 3) show a different picture than the mean. We found strong fluctuations both on the surface and on the epileptic side with maxima at the beginning and the end of the NREMS epochs and also after the drops of delta power within the NREMS epochs. The fluctuations in the surface EEG can be related to transients as K-complexes or short trains of delta waves, while the fluctuations in FOL79 can be ascribed to the wave part of spike-wave complexes and other pathological transients assigned mainly to class 3. Although the smoothed curves from Fig. 3 might suggest that both quantities are correlated the analysis of the raw data revealed almost no correlations between the two during NREM sleep.
The other panels of Fig 3 shows the significant fluctuations of the alpha power, $\delta \ln P_\alpha$ and the gamma power, $\delta \ln P_\gamma$. For all three power bands they are strongest for FOL79 followed by C3M2 and FOR46. Only for FOR46 they are so small that one can expect to find at least some segments where an assumption of "weak stationarity" might be justified. In general we see that the null hypothesis of a stationary linear process for the 30-s segments from the channels FOL79 and C3M2 has to be rejected already because of the fluctuations of the linear properties. These fluctuations might be generated by epileptic transients but can be also produced by other processes, such as sleep spindles and K-complexes in the surface EEG.

3.3 Spike counting

Fig. 4 shows that both clinically relevant spikes (class 1) and unspecific sharp transients occurred most frequently in the first NREM and at the beginning of the second NREM sleep epoch and showed no obvious modulation during the remaining NREM sleep epochs. In contrast the state dependent transients

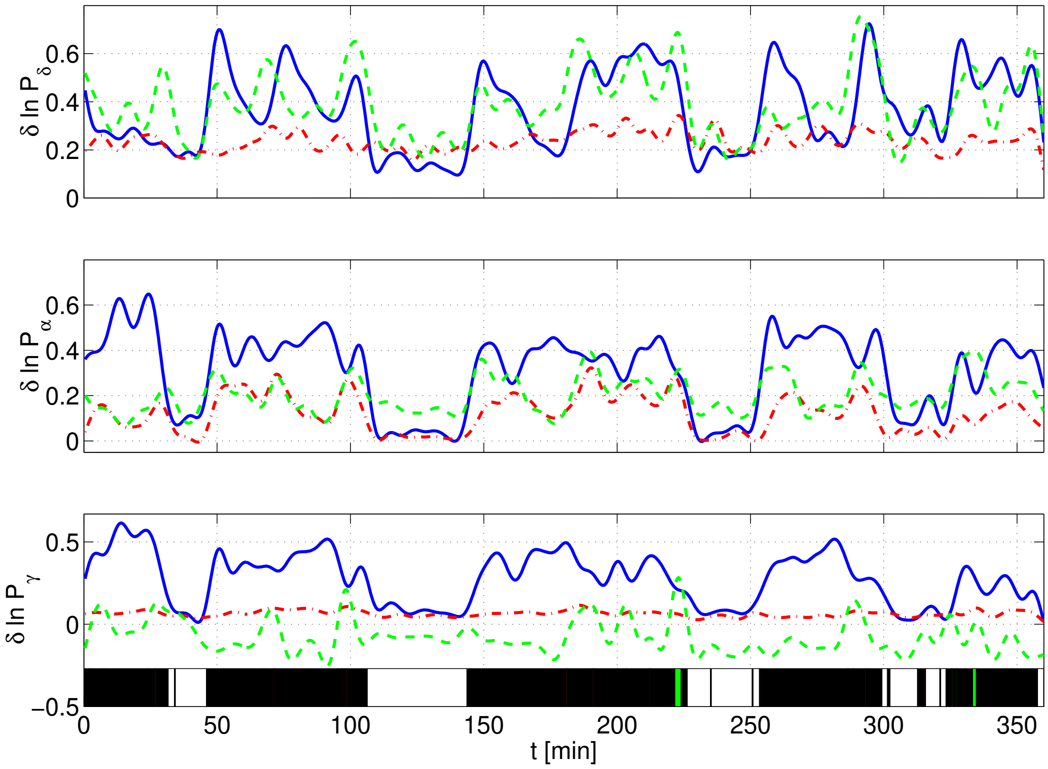

Fig. 3. Upper panel: Significant part of the fluctuations of the logarithm of the delta power for the three channels. Middle panel: same for theta power. Lower panel: same for gamma power. The bar shows the epochs of REM sleep (white) and NREM sleep (black). All curves are smoothed similar to Fig. 2.

(class 3) occurred most frequently at the beginning of the NREM sleep epochs and exhibit also two maxima during the third NREM sleep epoch. There are only weak correlations between the occurrence of spikes of class 1 and 2 (0.199) and between class 3 and 4 (0.197) and no significant correlations for other pairs.

3.4 Nonlinear analysis

The time course of the correlation dimension (D2) of FO-EEGs showed the properties already known from previous studies: It is strongly anticorrelated to the delta power of the corresponding channel (Shen et al., 2003). D2 of the epileptic side was consistently lower than in the non-epileptic side throughout the night, except for fluctuations Weber et al. (1998). This behavior did not depend on the details of the dimension estimations. In Fig. 5 the results are shown for D2 on small length scales (DS).
The four studied nonlinearity measures exhibited remarkably different behavior in the time course of the night. The largest difference was found be-

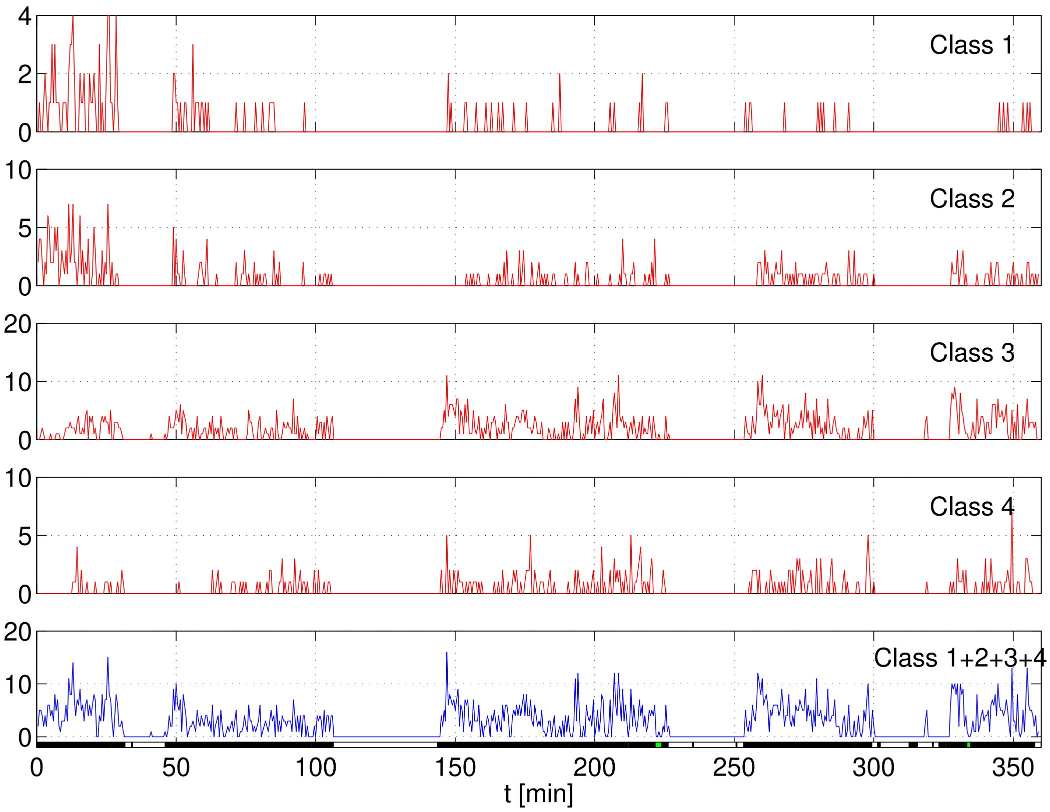

Fig. 4. Time course of spike occurrences (number of events per 30-s segment) during the night for the different classes.

tween S_{CL} and S_{DS}, for which the smoothed time courses are shown in Fig. 5, while S_{CS} and S_{DL} showed similar behavior somewhere between the two other measures. S_{CL} shows a pronounced difference between REM and NREM in all three channels, i.e. in the surface EEG as well as in FO-EEG on both sides. Most pronounced nonlinearity is found in FOL79, followed by C3M2 and fewest in FOR46. In contrary, S_{DS} shows a large amount of nonlinearity only in FOL79 with maximal values related to the maximal values of delta power and almost no difference between NREMS and REMS in FOR46 and C3M2.

However, all nonlinearity measures from the same channel are correlated to each other significantly during NREM sleep, with a maximal correlation between S_{CS} and S_{DL} (0.912, 0.938 and 0.964 for FOL79, FOR46 and C3M2, respectively) and minimal correlation between S_{CL} and S_{DS} (0.351, 0.441 and 0.527). Nonlinearity measures from different channels show no such correlations. That means that the processes producing nonlinear signatures in the different channels are independent.

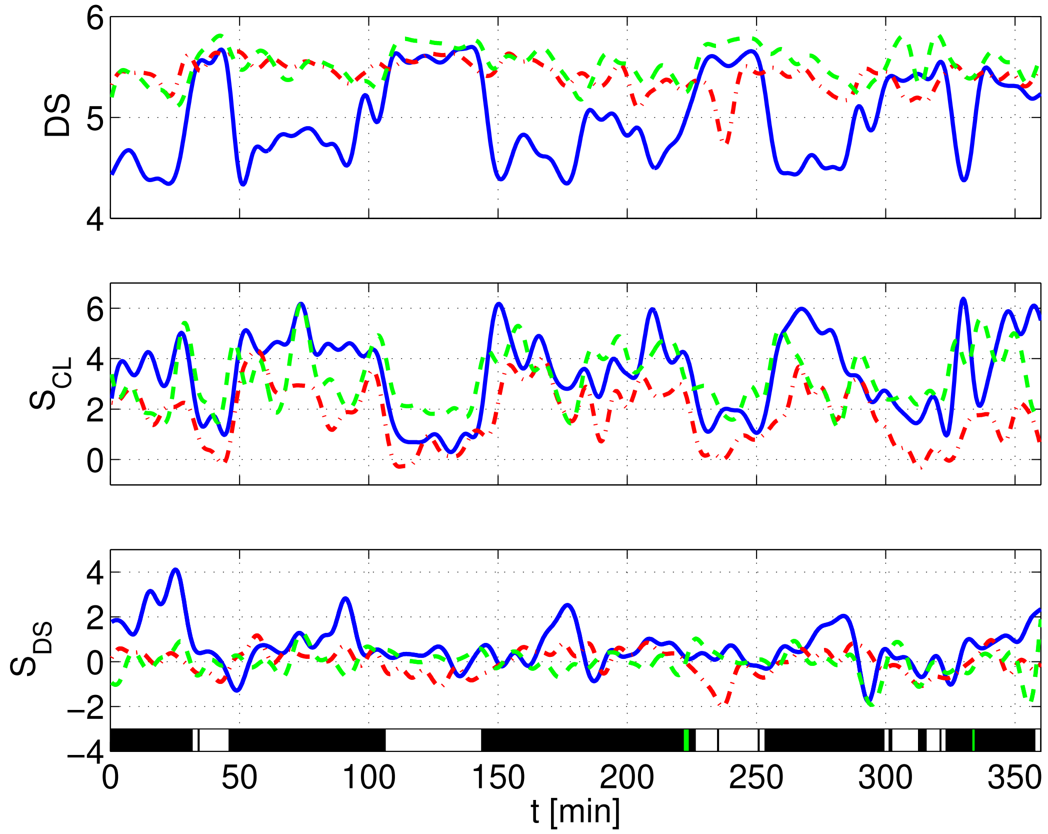

Fig. 5. All night time course of the correlation dimension on short length scales (DS, upper panel), nonlinearity measure based on the correlation sum on large length scales (S_{CL} - middle panel) and the nonlinearity measure based on the correlation dimension on small length scales (S_{DS} - lower panel) for FOL79 (solid line), FOR46 (dashed dotted) and C3M2 (dashed). The bar shows the epochs of REM sleep (white) and NREM sleep (black). All curves are smoothed similar to Fig. 2.

3.5 Correlation analysis between different measures

To study the relationship between the visually detected epileptic transients, the nonlinearity measures and the spectral properties of the signal we computed rank correlations between the different measures for 30-s segments. The analysis was restricted to segments classified as artefact free NREM sleep, because most studied quantities showed strong differences between REM and NREM sleep and this difference would dominate the correlations estimated over the whole data set.

First we studied the relationship between the sleep dynamics and the occurrence of epileptic transients and the nonlinearity measures, respectively. The sleep dynamics is quantified using mean delta power. Additionally we looked for correlations with mean sigma power, a measure for sleep spindle activity.

	C3M2 $\langle \ln P_\delta \rangle$	C3M2 $\langle \ln P_\sigma \rangle$
Class 1	0.209*	-0.069
Class 2	0.190*	0.001
Class 3	-0.104	0.186*
Class 4	0.036	0.018
Class 1+2	0.212*	-0.003
Class 3+4	-0.078	0.162*
1+2+3+4 (all)	0.084	0.108
FOL79 S_{CL}	-0.054	0.155*
FOL79 S_{CS}	0.263**	-0.086
FOL79 S_{DL}	0.206**	-0.028
FOL79 S_{DS}	0.404**	-0.252*

Table 2
Correlations between surface delta power and sigma power, respectively, spike numbers and nonlinearity measures estimated from FO-EEG on the epileptic side (* $p < 0.01$,** $p < 10^{-8}$).

The results are shown in table 2. Weak correlations were found between epileptic transients of class 1 and 2 and mean delta power, while class 3 transients were correlated weakly with the mean sigma power.
The studied nonlinearity measures showed very different behavior too. While S_{CL} is weakly correlated to the mean sigma power, S_{CS},S_{DL} and, most strongly, S_{DS} are correlated with the mean delta power.

Nonlinearity	Class 1	Class 2	Class 3	Class 4	1+2	3+4	1+2+3+4 (all)
S_{CL}	0.055**	0.169*	0.270	0.281	0.169*	0.339	0.374
S_{CS}	0.111**	0.207*	0.235*	0.308	0.204*	0.320	0.410
S_{DL}	0.080**	0.206*	0.259*	0.257*	0.197*	0.322	0.403
S_{DS}	0.162*	0.214*	0.174*	0.262	0.225*	0.249*	0.355

Table 3
Correlations between the nonlinearity measures and the visual counted epileptic transients. ** $p > 0.01$, * $p > 10^{-8}$

We found no significant correlations between the numbers of clinical relevant epileptic spikes per segment (class 1) and three of the four nonlinearity measures (Table 3). Weak correlations were found only in S_{DS}. Much stronger correlations were found for the state dependent transients (class 3) and mu-waves (class 4). However, strongest correlations were found between the nonlinearity measures and the summed numbers of all types of transients per segment.
It is interesting to compare these correlations with the correlations between

Spikes	spectral measure	r
Class 1	$\delta \ln P_\gamma$	0.488
Class 2	$\delta \ln P_\gamma$	0.494
Class 3	$\delta \ln P_\theta$	0.365
Class 4	$\delta \ln P_\alpha$	0.311
Class 1+2	$\delta \ln P_\gamma$	0.643
Class 3+4	$\delta \ln P_\theta$	0.422
1+2+3+4 (all)	$\delta \ln P_\alpha$	0.592

Table 4
Spectral measures with maximal correlations to spike numbers. All correlations r are highly significant ($p < 10^{-8}$).

the spike numbers and spectral measures. Table 4 shows the spectral measures showing the maximal correlations to the spike numbers.
Strongest correlations are not found for the mean power in a frequency band but for the fluctuations. This is not surprising, because these fluctuations lead to a rejection of the null hypothesis of the surrogate data test due to nonstationarity (see also 2.5. Transients of class 1 and 2 are containing always spikes, leading to maximal correlations with the fluctuations of the highest frequency band.
In general the correlations are somewhat stronger than the correlations found with the nonlinearity measures.
Finally, we studied also the correlations between the spectral measures and

Nonlinearity	FOL79	r	FOR46	r	C3M2	
S_{CL}	$\delta \ln P_\theta$	0.352	$\delta \ln P_\theta$	0.382	$\ln P_\theta$	0.330
S_{CS}	$\delta \ln P_\alpha$	0.397	$\delta \ln P_\theta$	0.396	$\ln P_\sigma$	0.270
S_{DL}	$\delta \ln P_\alpha$	0.301	$\delta \ln P_\theta$	0.387 #	$\ln P_\sigma$	0.240
S_{DS}	$\delta \ln P_\sigma$	0.424	$\delta \ln P_\theta$	0.254	$\delta \ln P_\alpha$	0.161#

Table 5
Spectral measures with maximal correlations to nonlinearity measures from the same channel. All correlations r are highly significant $p < 10^{-8}$, except for # with $p < 10^{-2}$.

the nonlinearity measures. Again, it is not possible to show the complete set, so Table 5 shows the spectral measures which exhibited maximal correlations to the nonlinearity measures. Unlike table 4 we included also the channels FOR46 and C3M2, because significant fluctuations of the spectral power should lead to a rejection of the null hypothesis in any case. The observed moderate correlations show that indeed the nonlinearity quantified by the nonlinearity measures can be partially related to the fluctuations of the spectral measures, i.e. the nonstationarity of the linear properties of the signal.

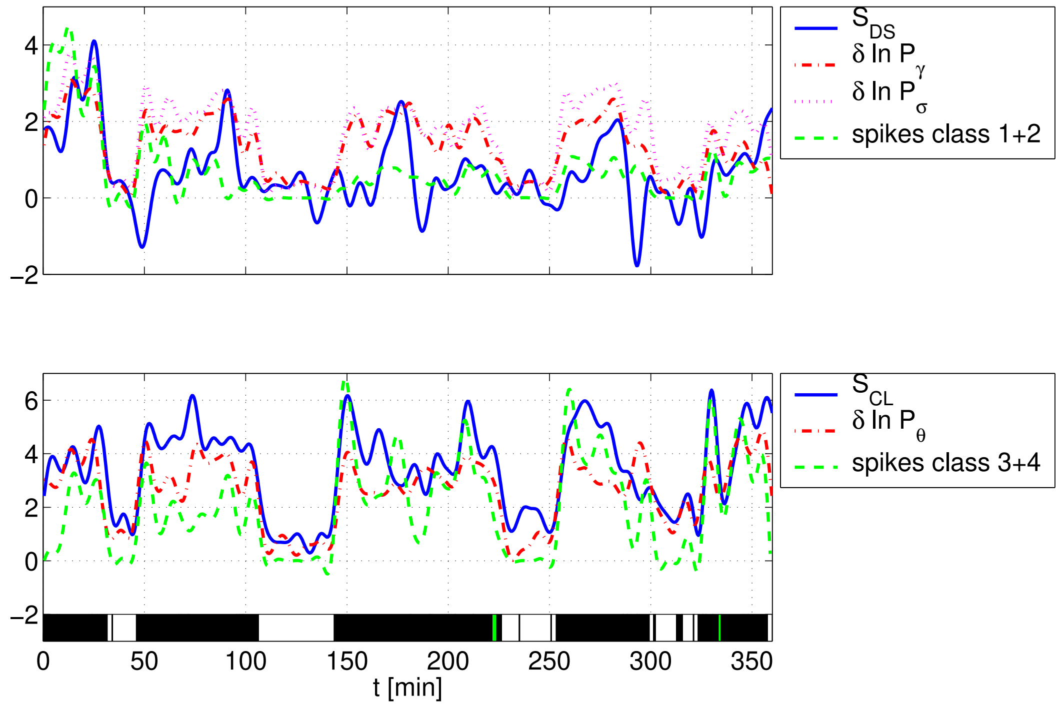

Fig. 6. Comparison between spike counts, selected nonlinearity measures and significant fluctuations of spectral bands from channel FOL79.

Contrary to our expectations the correlations in FOR46 and FOL79 are in the same order of magnitude although the epileptic transients, which obviously generate such fluctuations are more pronounced and frequent in FOL79. From this follows that there must be additional processes leading to the fluctuations of the spectral measures.

4 Discussion and Conclusions

It is well known that generally sleep synchronization promotes epileptic activities. Therefore epileptic synchronization (sometimes called "hyper-synchronization") and sleep-related synchronization are supposed to share some common mechanism. Although research on interactions between epilepsy and sleep has a history that is almost as long as that of modern epileptology, still various specific points remain controversial (Mendéz and Radtke, 2001, for an overview see). Although some differences were found among epileptic syndromes as to in which sleep stage epileptiform transients appear most often (F. Ferrillo and Nobili, 2000), there is a general consensus that in adult patients with partial epilepsies, especially temporal lobe epilepsy (TLE), epileptiform transients appear much more often in non-rapid-eye-movement (NREM) sleep than in rapid-eye-movement (REM) sleep Lieb et al. (1980); Billiard et al. (1987); Montplaisir et al. (1987); Wieser (1991). This is in agreement with our findings. The visual spike counts showed clearly this difference because almost no spikes were detected during REM sleep. The REM-NREM differences found in the nonlinearity measures, however, cannot exclusively explained by epileptic activity, because S_{CL} showed also a pronounced REM-NREM difference for both intracranial recordings contralateral to the epileptic focus and the surface EEG.

This finding can be related to a general problem of the approach used in the present and related former studies (Casdagli et al., 1996, 1997; Jing and Takigawa, 2000; Andrzejak et al., 2001b,a): Because the nonlinearity measures were estimated on segments longer than 1 second, they cannot distinguish between non-linearity due to nonstationarity of linear properties, measured by the $\delta \ln P_i$ and nonlinearities due to the waveform of epileptic transients, i.e. nonlinearity measured for a stationary train of epileptic waveforms. Interictal epileptic transients influence the nonlinearity measures in both ways, which could lead to the idea, that this could even enhance the usefulness of this measures for the quantification of epileptic activity. However, the analysis of the spectral fluctuations showed that the EEG in general is far from stationary on a 30-s time scale. For the surface EEG this nonstationarity can be related to K-complexes, sleep spindles and delta bursts, in the FO-EEG on the nonepileptic side the sources of the observed fluctuations are less known. However, as one can see in Fig. 3 these fluctuations are also, even though only weakly, correlated to the sleep process.

Keeping this in mind our results allow the following conclusions: Epileptic activity leads to increasing nonlinearity as it is measured by surrogate data analysis. The quantitative results, however, depend strongly on the used nonlinear test statistic. At the moment we are not able to establish a direct connection between one of the measures and certain classes of epileptic transients, although some weak correlations were found. Moreover the nonlinearity measures respond not only to processes which are directly connected with the visual counted transients, but also to other processes, for instance such processes which are leading to nonstationarity of the spectral measures without epileptic activity. In order to develop measures, which can be used to quantify epileptic activity directly or even to distinguish different types of such activity we see two promising approaches: First the measures of nonlinearity could be evaluated on shorter time scales, i.e. on 1-s segments, which requires further development of the surrogate data techniques. Second one can try to refine the description of different types of dynamics by combining several suitable selected measures, e.g. measures of nonlinearity and spectral measures.

Regarding the distribution of epileptic activity during the NREM sleep our results allow no definite conclusions. There are, however, indications for a distinction between two types of processes and quantities, resp.: a) spikes class 1+2, $\delta \ln P_\gamma$ in FOL79, $S_D S$, $< \ln P_\delta >$ and

b) spikes class 3+4, S_{CL}, $\delta \ln P_\theta$ in FOL79 and $< \ln P_\sigma >$, i.e. spindle activity. For confirming the clinical relevance, however, systematic studies using a large population are needed. Nevertheless, we believe that this single case study should definitely serve deeper understanding of nonlinearity in EEG, especially in relation to sleep-related and epileptic synchronization.

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