Eur Arch Psychiatry Clin Neurosci (1995) 245:27–35

ORIGINAL PAPER

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Nonlinear analysis of sleep eeg in depression: calculation of the largest lyapunov exponent

Received: 14 March 1994 / Accepted: 24 October 1994

Abstract Conventional sleep analysis according to Rechtschaffen and Kales (1968) has provided meaningful contributions to the understanding of disturbed sleep architecture in depression. However, there is no characteristic alteration of the sleep cycle, which could serve as a highly specific feature for depressive illness. Therefore, we started to investigate nonlinear properties of sleep electroencephalographic (EEG) data in order to elucidate functional alterations other than those obtained from classical sleep analysis. The application of methods from nonlinear dynamical system theory to EEG data has led to the assumption that the EEG can be treated as a deterministic chaotic process. Chaotic systems are characterized by a so-called sensitive dependence on initial conditions. This property can be quantified by calculating the system's Lyapunov exponents, which measure the exponential separation of nearby initial states in phase space. For 15 depressive inpatients (major depressive episodes according to DSM-III-R criteria) and 13 healthy controls, matched in gender, age, and education, we computed the principal Lyapunov exponents L_1 of EEG segments corresponding to sleep stages I, II, III, IV, and rapid eye movement (REM), according to Rechtschaffen and Kales, for the lead positions C_Z and P_Z. We found statistically significant decreased values of L_1 during sleep stage IV in depressives compared with a healthy control group.

Key words Sleep EEG · Lyapunov exponent · Deterministic chaos · Nonlinear dynamics · Depression

Introduction

Conventional sleep analysis according to Rechtschaffen and Kales (1968) has shown that the sleep architecture of patients suffering from depression is characterized by reduced rapid eye movement (REM) latency, increased amounts of REM sleep, reduced percentage of slow-wave sleep (SWS), reduced sleep efficiency, and an increase in REM density (for review see Reynolds and Kupfer 1987). However, none of these findings is highly specific for depression (Benca et al. 1992). Therefore, we started a new kind of analysis of sleep electroencephalographic (EEG) data by using tools from nonlinear system theory in order to detect functional alterations of the sleep EEG other than those obtained by classical analysis.

In recent years it has been demonstrated that disorders of complex physiological systems are often associated with alterations of the systems' dynamical features in terms of nonlinear dynamics (Pool 1989). The application of concepts from the theory of nonlinear dynamical systems (commonly known as chaos theory) to EEG data has led to the assumption that the EEG can be considered as a deterministic signal, rather than a stochastic process. Under selected conditions, dissipative nonlinear systems depending on at least three state variables are able to generate so-called deterministic chaos. In this case the dynamics show a sensitive dependence on initial conditions, which means that different states of a system being arbitrarily close initially will become macroscopically separated after sufficiently long times. This property can be quantified by calculating the system's Lyapunov exponents. If the principle Lyapunov exponent L_1 is positive, the system under study is called chaotic. Regardless of a description of a system's dynamics in terms of differential equations, the behavior of such chaotic systems is not predictable over longer time periods. In this sense the unpredictability of the EEG might be considered as a basic phenomenon of its chaotic character.

Up to now several research grops have reported investigations of EEG signals by calculating the corresponding correlation dimensions D_2. These values are measures for the complexity of a signal and yield a lower boundary for the degrees of freedom possessed by a system. It is the case that there are high variations between the results for the waking EEG published by different groups (for a

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summary see Basar 1990). The values for D_2 vary between 2 and 10 (Graf and Elbert 1989; Mayer-Kress and Holzfuss 1987; Pritchard and Duke 1992). Generally, for the eyes-closed condition lower dimensions are reported than for the eyes-open condition. For the sleep EEG, dimensions between 4 and 7 have been calculated (Achermann et al. 1993; Babloyantz et al. 1985; Ehlers et al. 1991; Röschke and Aldenhoff 1991). Moreover, it has been reported that significant differences exist between the correlation dimensions for the waking EEG in the case of different mental tasks (Nan and Jinghua 1988; Rapp et al. 1988; Ray et al. 1991) and different intelligence quotients (Lutzenberger et al. 1992). For epileptic (petit mal) EEG patterns a reduction of the dimensionality has been reported (Babloyantz and Destexhe 1986; Pijn et al. 1991).

Principal Lyapunov exponents provide a methodically new axis in terms of nonlinear system theory to analyze the dynamical attributes of sleep EEG data (Fell et al. 1993). These numbers estimate the mean exponential divergence or convergence of nearby trajectories in phase space. The calculation of a clearly positive principal Lyapunov exponent L_1 expressing the sensitive dependence on initial conditions gives much evidence for the hypothesis that the system under investigation is chaotic. To our knowledge there are just a few publications about the evaluation of Lyapunov exponents of EEG segments. Concerning epileptic seizures Frank and coworkers (1990) found clear evidence of chaos in only two of the epochs under study. Iasemidis and Sackellares (1991) reported on higher L_1 postically, rather than ictally or preictally. According to Krystal and Weiner (1991), the results concerning seizures during electroconvulsive therapy are similar. Principe and Lo (1991) calculated L_1 for single EEG segments during sleep stage II. They emphasized the dependence of the calculations on the choice of the input parameters of the algorithm. Gallez and Babloyantz (1991) investigated Lyapunov exponents in the case of alpha activity, sleep stage IV, and Creutzfeld-Jakob coma. They reported on at least two positive Lyapunov exponents in the situations considered.

The investigation presented here is motivated by the following question: Are there differences between the principal Lyapunov exponents during sleep stages I, II, III, IV, and REM of depressive patients compared with healthy subjects?

Methods

Theoretical aspects

The behavior of dynamical systems can be studied by investigating the properties of their attractors in phase space. A time-continuous dynamical nth order system is defined by a set of n first-order differential equations. Its states can be represented by a number of points in a n-dimensional phase space, where the coordinates are the values of the state variables $x_1, \ldots x_n$. The phase space is the set of all possible states that can be reached by a certain class of systems. Every single point of the phase space represents a defined state. As time increases the sequence of such states defines a curve in phase space called trajectory. If the trajectories converge to a lower dimensional indecomposable subset, this subset is called an attractor. Takens (1981) has proven that if a single variable x_j is measured that corresponds to a nth order system, of which the evolution tends toward an attractor, it is possible to make a reconstruction of the attractor (having the same topological properties as the original attractor) by constructing vectors as follows:

$$y(t) = [x_j(t),\ x_j(t + \tau), \ldots, x_j(t + 2n\tau)]$$

Furthermore, based on the theorem of Whitney, Takens (1981) showed that embedding into a $(2n + 1)$-dimensional phase space is sufficient.

Attractors of dynamical systems are often characterized by their correlation dimension D_2. This dimension is a metric property of the attractor that yields a lower boundary for the number of degrees of freedom a system possesses. In other words, the estimation of dimensionality quantifies the complexity of dynamical systems. Lyapunov exponents estimate the mean exponential divergence or convergence of nearby trajectories of the attractor. Mathematically, they are defined by the logarithm of the eigenvalues of a matrix, which determines the development of trajectories starting in an infinitesimal neighborhood of a reference trajectory. Lyapunov exponents are usually in descending order from L_1 (highest value) to L_n (lowest value). Here n is equal to the topological dimension of the phase space. At least one Lyapunov exponent is zero for each attractor (except of a fixed point). It is the one corresponding to te forward direction of the flow (Haken 1983). For dissipative dynamical systems the sum of all Lyapunov exponents is less than zero. A system possessing a positive principal Lyapunov exponent L_1 is chaotic. This fact express the sensitive dependence on initial conditions. For white noise the value of L_1 theoretically is infinity. Nevertheless, numerical estimations yield a maximum value of L_1 depending on data length and data resolution. This is the case, because it is impossible to find neighboring points in phase space that are infinitesimally close in the case of a time series with finite length. Because Lyapunov exponents are obtained through a long-time average, whereas the calculation of correlation dimensions relies on a metric concept, principal Lyapunov exponents are generally more resilient to noise than correlation dimensions (Wolf and Bessoir 1991). The third important parameter reflecting dynamical properties of attractors is the Kolmogorov (K)-entropy. It describes the average rate at which information about the state of a dynamical system is lost with time, which is identical with the average rate at which information is created by the signal. A chaotic attractor always has a positive K entropy, which is equal to the sum of all positive Lyapunov exponents (Pesin 1977). Hence, in simplified words the K entropy or the principal Lyapunov exponent L_1 can be used to quantify how chaotic a dynamical system is.

Mathematical procedure

We applied the reconstruction procedure as proposed by Takens (1981) to each EEG segment by embedding the signal into a 10-dimensional phase space. For the time increment τ we used the first zero crossing of the autocorrelation function, which has been shown to be a reasonable choice (Grassberger et al. 1991; Wolf and Bessoir 1991). If no zero crossing of the autocorrelation function within the first 300 samples (3 s) was found, the EEG segment concerned was left out. According to Grassberger et al. (1991), in noisy data only the largest Lyapunov exponents can be estimated well, whereas the smaller ones are not accessible. We calculated the principal Lyapunov exponent L_1 applying a modified version of the Wolf algorithm (Wolf et al. 1985) following a proposal of Frank et al. (1990). Essentially, the Wolf algorithm computes the vector distance X of two nearby points and evolves its length for a certain propagation time. If the vector length X' between the two points becomes too large, a new reference point is chosen with the properties to minimize the replacement length and the orientation change. Then the two points are evolved again, and so on (see Fig. 1). After m propagation steps the first positive Lyapunov exponent

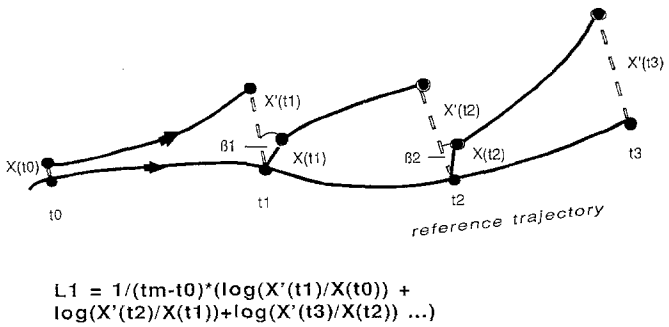

Fig. 1 Estimation of the principal Lyapunov exponent according to Wolf et al. (1985)

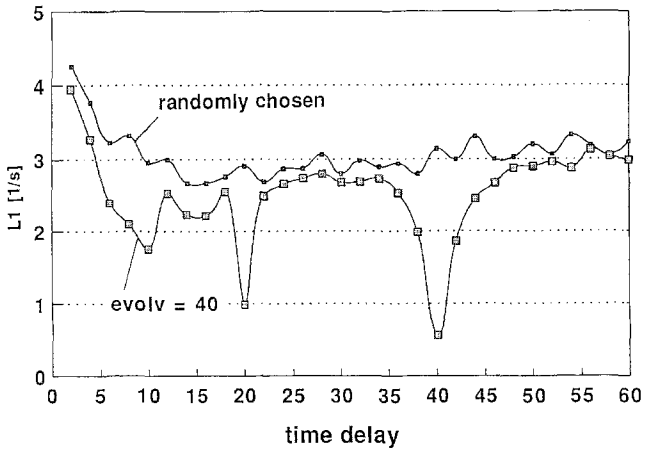

Fig. 2 Dependence of the principal Lyapunov exponent L_1 on the time delay for a single electroencephalographic (EEG) epoch (sleep stage IV) in the case of a fixed propagation time (evolving = time 40), and in the case of a randomly chosen propagation time within the interval [20; 60]

results from the sum over the logarithmic ratios of the vector distances divided through the total evolving time:

$$L_1 = [1/t_m - t_0)] \sum_{k=1}^{m} \log_2[X'(t_k)/X(t_{k-1})]$$

We implemented a displacement technique proposed by Frank et al. (1990) introducing a priority function, which depends on the replacement length r and the orientation change q:

$$p(r,q) = \{\alpha + \beta \cdot [(b-r)/(b-a)]^{\gamma}\} \cdot \cos q,$$

where $\alpha = 0.1$, $\beta = 0.9$, and $\gamma = 3.0$ (b: scalmax, a: noise level).

Frank and coworkers reported substantially improved exponent estimates in short and noisy data sets. In our experience (with sleep EEG data sets of 16,384 points = 2:44 min) the modified algorithm is much less time-consuming and converges faster to the final value. The modified algorithm was tested for the Henon map ($\lambda_1 = 0.59$/iteration), the logistic map ($\lambda_1 = 1.04$/iteration), and the Lorentz system ($\lambda_1 = 2.09$/s), and yielded results within 5% intervals around the literature values (e.g., Eckmann and Ruelle 1985; Wolf et al. 1985). For the selection of the input-parameters embedding dimension, maximum scale, and minimum scale we refer to Fell and Röschke (1994). The time-delay method introduces a certain subtle structure into the reconstructed data, which causes resonance-like phenomena in the case of an evolving time = τ, 2 τ,... (Fell and Beckmann 1994). In order to avoid these "resonances," for our calculations we chose for each evolving step the propagation time (evolving time) randomly out of the interval between 20 and 60 data points (0.2–0.6 s), corresponding to a frequency interval between 1.67 and 5 Hz. With this modification the algorithm becomes nearly independent of the time delay τ (Fig. 2). All together, we have selected the following input parameters for our calculations: minimum scale = 10 µV, maximum scale = 15% maxdist (maximal distance in phase space), evolving time E [20, 60] samples, and embedding dimension = 10. For each calculation 300 replacement steps were carried out.

Subjects and sleep EEG data

We investigated 15 unmedicated depressive inpatients (8 males and 7 females) aged between 23 and 61 years (mean age 41 ± 14 years). The patients were diagnosed according to DSM-III-R and

Table 1 Characterization of the patient's group in terms of diagnosis according to DSM-III-R criteria, the scores of different rating scales, and age and gender of controls. HAMD Hamilton depression scale; MADRS Montgomery-Asberg depression scale, BRMS Bech-Rafaelsen melancholy scale; GAS global assessment scale

Patient	Diagnosis (DSM-III-R)	Age (years)/gender		HAMD	MADRS	BRMS	GAS
		Patient	Control				
A	296.23	28/m	27/m	28	44	26	30
B	296.33	38/m	34/m	24	31	25	55
C	296.23	46/f	46/f	21	27	15	55
D	296.23	60/m	62/m	26	37	23	34
E	296.21	61/m	62/m	18	25	18	50
F	296.23	25/m	25/m	32	41	27	30
G	296.32	55/f	52/f	26	37	28	35
H	296.23	26/f	25/f	27	40	26	35
I	296.22	29/f	32/f	20	30	18	50
J	300.40	23/m	21/m	21	30	19	41
K	296.23	60/m	63/m	25	37	23	35
L	296.53	50/f	–	31	44	26	45
M	296.53	28/f	29/f	28	39	26	40
N	296.23	28/f	–	19	27	16	50
O	296.53	54/f	60/f	28	42	23	45
Mean		41	41	25	35	23	40
SD		±14	±16	±4	±6	±4	±8

Table 2 Mean values and standard deviation of conventional sleep EEG parameters of 15 unmedicated depressives (patients) and 13 healthy subjects (controls). A significant difference (two-tailed student's *t*-test) has been calculated for slow-wave sleep. TST total sleep time; SOL sleep onset latency; SEI sleep efficiency index; REM rapid eye movement; SPT sleep period time

Note: All parameters were statistically nonsignificant except SWS ($P < 0.02$)

	TST (min)	SOL (min)	SEI	REM (%SPT)	I (%SPT)	II (%SPT)	SWS (%SPT)	REM latency (min)
Patients:	393.1	29.9	0.78	20.0	7.7	40.4	14.2	75.6
SD	±99.2	±22.2	±0.21	±8.1	±4.4	±16.0	±7.6	±27.0
Controls:	405.3	31.1	0.85	17.5	7.9	42.1	21.4	86.4
SD	±49.1	±19.7	±0.08	±5.8	±4.5	±9.6	±7.4	±29.5

fulfilled the criteria of a major depressive episode. Severity of illness was characterized by Hamilton depression scale (HAMD), Montgomery-Asberg depression scale (MADRS), Bech-Rafaelsen melancholy scale (BRMS), and global assessment scale (GAS; for details see Table 1). Concerning the longitudinal diagnoses 9 Patients fulfilled the criteria of a single major depressive episode (296.2), 2 the criteria of a recurrent episode (296.3), 1 the criteria of a dysthymic disorder (300.4), and 3 the criteria of a depressive episode in bipolar disorder (296.5). The patients suffering from a recurrent depressive episode or a bipolar disorder did not receive any antidepressive or other prophylactic medication for the last 3 months. The patients suffering from a single depressive episode had never received any antidepressive medication. All patients were free from sleep-disorder diagnoses such as insomnia, restless-leg syndrome, or sleep apnea.

The control group (13 subjects) was balanced in gender, age, and education. Subjects were volunteer recruits from the university student population and the general public. All were in self-reported good health with regular sleep/wake patterns. There was no evidence of hypnotic drug abuse or above-average alcohol, caffeine, or nicotine consumption. All were free of a past history of current symptoms of psychopathology, as well as of any medical condition known to influence sleep.

Subsequent to an adaptation night to sleep laboratory conditions, the sleep EEG was registered from 11:00 p.m. until 7:00 a.m. the next day. Surface electrodes were placed on the skull (P_z, C_z, C_3, and C_4; 10–20 system) and mastoid to record electroencephalic activity, at the outer canthi on the left and right eye to record eye movements, and on the chin to record submental electromyographic activity. Interelectrode impedances were all below 5 kΩ. Visual analysis of the sleep EEG was performed according to Rechtschaffen and Kales (1968) by two independent judges. The analog EEG data (0.53 Hz high-pass filter; 50 Hz low-pass filter; 48 dB/octave) from C_Z and P_Z were digitized by a 12-bit analog digital converter, samples with a frequency of $f_s = 100$ Hz and stored on the disk of a Hewlett Packard Computer (A 900). From the sleep EEG, five artifact free time epochs ($n = 16{,}384$ data points; 2:44 min duration) were selected, each unambiguously corresponding to one of the sleep stages I, II, III, IV, and REM. The interrater agreement was 100% for the selected time periods. According to the physiological sleep profile, the representative collections of non-REM sleep stages were selected from the largest non-REM periods from the first half, the REM periods from the largest REM periods from the second half of the all-night sleep EEG.

Results

Conventional sleep architecture

Table 2 shows the results of the conventional sleep scoring procedure (according to Rechtschaffen and Kales 1968) of the patients and the control group. Except for a reduced amount (%SPT) of sleep stage IV (two-tailed *t*-test; $P < 0.02$) in the depressive group compared with the control group, no significant differences concerning the parameters total sleep time (TST), sleep onset latency (SOL), sleep efficiency index (SEI), and the percentage (%SPT) of the sleep stages I, II, III, REM, and REM latency were detectable.

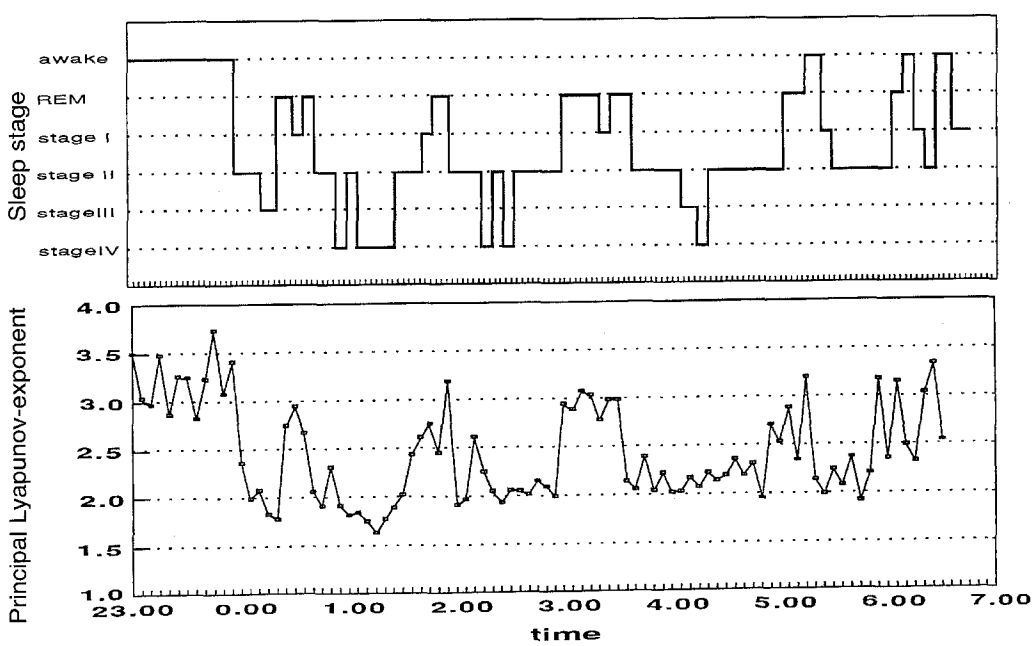

Fig. 3 Sleep structure (according to Rechtschaffen and Kales 1968) and principal Lyapunov exponents L_1 for a single healthy subject during the night

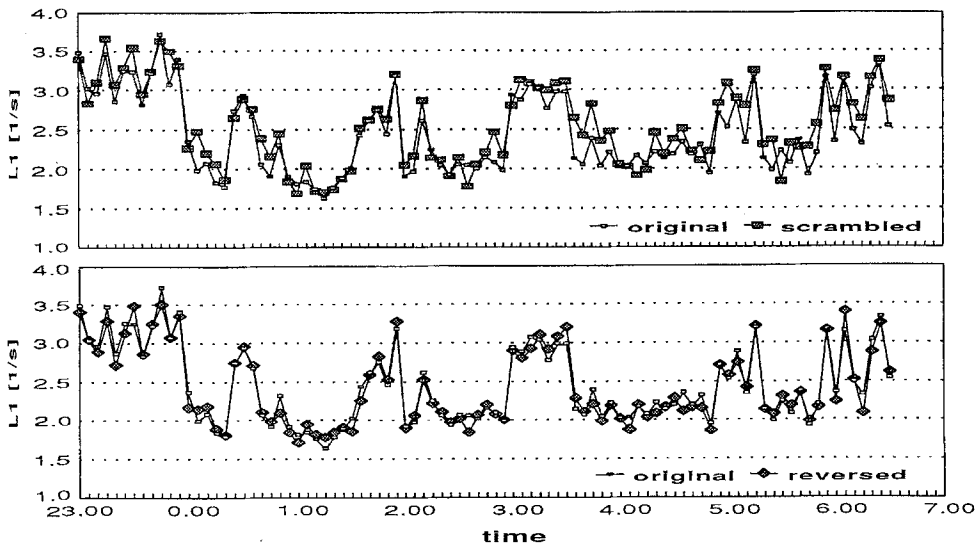

Fig. 4 Principal Lyapunov exponents L_1 for a single subject during the night compared with the results for surrogate data. *Above:* original EEG data compared with "scrambled data"; *below:* original data compared with time-reversed data (for further explanation see text)

Table 3 Individual principal Lyapunov exponents L_1 from positions C_Z and P_Z of 15 depressive inpatients and 13 controls corresponding to sleep stages

	Position C_Z					Position P_Z				
	I	II	III	IV	REM	I	II	III	IV	REM
Patients										
A	2.52	2.57	3.06	1.69	2.80	2.43	3.19	2.72	1.72	2.72
B	2.85	2.26	2.12	1.93	3.36	3.06	2.06	2.25	2.25	3.29
C	2.62	2.12	2.28	1.98	2.53	2.72	2.51	2.47	2.34	2.63
D	3.10	2.09	2.13	1.76	3.05	3.30	2.16	2.27	1.89	3.34
E	3.27	2.43	–	2.00	3.11	3.43	2.61	–	1.91	3.21
F	2.00	1.95	1.67	1.77	2.36	1.90	2.77	2.00	1.79	2.84
G	3.46	2.09	2.00	1.76	3.51	3.38	2.52	2.02	1.83	3.02
H	2.94	2.66	2.73	1.97	3.20	2.48	2.74	2.40	1.97	2.87
I	3.26	2.63	2.05	1.81	3.27	3.31	2.69	2.15	1.99	3.50
J	2.94	2.73	2.04	1.50	3.23	2.94	2.84	2.94	1.85	3.38
K	2.38	2.45	–	–	1.97	2.46	2.53	–	–	1.50
L	3.01	2.01	2.02	2.30	2.20	2.59	2.65	2.26	2.37	2.06
M	2.99	2.29	1.82	1.95	3.83	2.88	2.77	2.12	1.91	3.28
N	2.77	2.29	1.83	1.78	3.09	2.79	2.62	2.11	1.78	3.17
O	2.43	2.38	2.10	1.82	2.70	2.50	2.33	1.86	1.88	2.66
Controls										
A	2.20	2.16	2.05	1.79	2.99	2.42	2.30	2.25	1.75	2.85
B	2.92	2.85	1.90	1.83	1.93	2.02	2.67	2.04	1.96	2.00
C	2.72	2.36	2.74	2.53	3.22	2.65	2.68	2.85	2.51	3.46
D	2.90	2.33	2.71	2.30	3.07	2.84	2.25	2.75	2.60	2.96
E	2.92	2.72	2.40	2.38	3.32	30.5	2.95	2.43	2.39	3.31
F	2.73	2.33	2.00	1.83	2.13	3.03	1.88	1.97	1.81	2.35
G	2.79	2.88	2.48	2.29	2.83	3.29	2.62	2.50	2.13	3.13
H	2.70	3.49	2.51	2.02	2.52	3.00	3.17	3.25	2.21	3.18
I	3.53	2.65	1.90	2.26	3.13	3.53	2.51	2.27	2.46	2.92
J	3.20	2.04	2.23	2.00	2.40	3.44	2.46	2.13	1.82	2.93
K	2.83	2.47	2.15	2.22	2.56	2.78	2.40	2.27	2.49	2.69
M	3.43	2.13	2.45	2.19	2.69	2.74	1.88	2.14	2.14	3.13
O	2.78	1.88	2.10	1.59	2.74	2.61	2.16	2.15	1.68	2.88

Principal Lyapunov exponents L_1

Exemplarily for a single healthy subject (control subject O), we computed L_1 for consecutive sleep EEG segments (each of 2:44 duration) recorded every 5 min during the night (Fig. 3). The values for a single sleep stage show high intraindividual consistency. The mean values and standard deviations for each sleep stage are: awake: 3.16

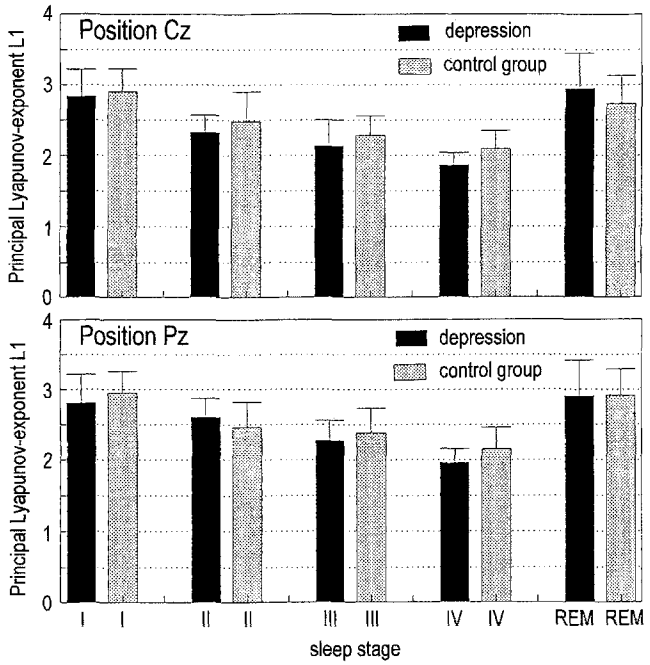

Fig. 5 Mean values and standard deviations of the principal Lyapunov exponents L_1 during different sleep stages in depression and in the control group. *Above:* lead position C_Z, *below:* position P_Z

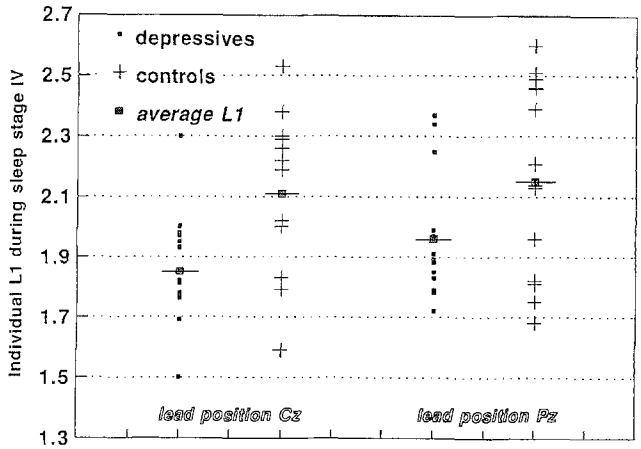

Fig. 6 Scatter gram of the individual principal Lyapunov exponents L_1 during sleep stage IV in depressives and control subjects for positions C_Z and P_Z

± 0.28; stage I: 2.52 ± 0.23; stage II: 2.12 ± 0.26; stage III: 1.92 ± 0.11; stage IV: 1.92 ± 0.15; REM: 2.81 ± 0.31.

In order to find out whether EEG signals can be distinguished from stochastic data by Lyapunov analysis, we performed two test procedures. Firstly, the EEG data were compared with colored noise data, having the same power spectra as the original data, but randomized phases of the Fourier transform. Secondly, the original data were compared with time-reversed data. Lyapunov exponents of low dimensional deterministic signals change their signs upon time reversal generally yielding to a different principal Lyapunov exponent, whereas the calculations for noise data are usually invariant under time reversal (Parlitz 1991). The result of these two test procedures for EEG epochs of a single recorded successively during the night (same data as above) are shown in Fig. 4. Compared with the variance of L_1 during the night the differences between original and surrogate data are low, meaning that EEG signals generally cannot be distinguished from stochastic data by Lyapunov analysis.

Table 3 shows the individual principal Lyapunov exponents L_1 for lead positions C_Z and P_Z of 15 depressive inpatients and 13 control subjects corresponding to the sleep stages I, II, III, IV, and REM. The mean values and standard deviations of L_1 are shown in Fig. 5. Our results show that the more the sleep moves to SWS, the lower L_1. The average L_1 for REM sleep lie close to the values for sleep stage I. Furthermore, the values of the principal Lyapunov exponent at electrode position P_Z generally are higher than at position C_Z. A global analysis of variance (ANOVA) with GROUP (depressives vs controls) and SLEEP STAGE (I, II, III, IV, and REM) as independent factors and LEAD POSITION (C_Z, P_Z) as a repeated-measure factor revealed highly significant main effects for the factors SLEEP STAGE ($F_{4,131}$ = 34.41; P = 0.0001) and LEAD POSITION ($F_{4,131}$ = 13.77; P = 0.0003). No significant main effect for the factor GROUP and no interactions of LEAD POSITION × GROUP and LEAD POSITION × STAGE were found.

Separate ANOVAs for each sleep stage with GROUP as independent factor and LEAD POSITION as a repeated-measure factor yielded a significant effect for the factor GROUP during sleep stage IV ($F_{1,25}$ = 5.24; P = 0.031). Under the assumption of a deterministic EEG dynamic, this result expresses a reduced sensitive dependence on initial condition of EEG dynamics during sleep stage IV in depression. During the stages I, II, III, and REM no statistically signifcant effects for the factor GROUP were detected.

Figure 6 shows the calculated Lyapunov exponents for both lead positions for each subject of the control and the depressive group. This scatter gram illuminates that the estimation of L_1 should not be considered as a highly specific or sensitive measure to distinguish diagnostic groups.

Discussion

The theories of deterministic chaos, dissipative systems, and self-organization have led to a new approach to understanding physiological systems. The main idea is that pathological states of complex physiological systems are reflected by alterations of the system's dynamical features in terms of nonlinear system theory. Sometimes, alterations of the dynamical properties themselves might be reasons for the system's pathological behavior. The traditional view that "healthy dynamics" exhibit simple, periodical, predictable features, whereas "ill dynamics" are irregular and unpredictable has been contradicted by investigations in recent years. Goldberger and West (1987) demonstrated that electrocardiogram (ECG) signals from patients suffering from heart diseases seem to possess less chaotic dynamics than the signals of healthy subjects.

They argue that chaos may implicate a healthy flexibility and variability, which enables physiological systems to adapt to new situations. In numerical simulations Ott et al. (1990) could show that motion on a chaotic attractor can be converted to a desired time-periodic motion or steady state by making only small time-dependent perturbations of system parameters. The principal Lyapunov exponent can be understood as an indicator for how chaotic a signal is. Iasemides and Sackellares (1991) have found that L_1 before and during epileptic seizures is lower than postictally. Krystal and Weiner (1991) reported similar results concerning seizures during electroconvulsive therapy. Skarda and Freeman (1987) postulated that behavior can best be modeled as a sequence of ordered, stable states in an evolutionary trajectory. They suppose that chaotic mechanisms enable the neural network to learn new behavior, because without such mechanisms the system could only converge to behavior it has already learned. Garfinkel (1983) suggested that the normal presence of chaos may act to prevent the organization and spread of pathological modes ("active desynchronization"), because periodic orbits within a chaotic attractor are always unstable.

Nevertheless, no unambiguous evidence has been found up to now that the human electroencephalogram is indeed a low-dimensional chaotic signal. Saturation of the correlation dimension D_2 has often been postulated as a criterion for a deterministic system. Osborne and Provoncale (1989) showed that for stochastic systems with power-law spectra, numerically a finite correlation dimension can also be calculated. As Grassberger and colleagues (1991) have pointed out, this effect is due to the finite length of the data sets, and does not contradict the fact that stochastic noise does not exhibit a finite dimension. Pijn and colleagues (1991) as well as Soong and Stuart (1989) therefore proposed to compare the dimension estimates for EEG epochs with the results for random signals possessing the same power spectra as the original data series ("scrambled data"). Pijn and coworkers (1991) stated that in some cases the EEG data appear to be distinguishable from noise. Soong and Stuart (1989) reported that the filtered alpha rhythm indeed shows a saturation behavior different from "scrambled data." Of course, the decision whether a measured signal is really chaotic or just quasiperiodic is crucial as well. All *chaotic* attractors encountered up to now depict a fractal dimension. On the contrary, the dimensionality for both periodic and quasiperiodic signals exposes an integer number. That means the maximal possible difference between the dimension of a chaotic and a (quasi) periodic system is only 0.5, and possibly may be infinitesimally small. Because of many practical restrictions, such as finite amount of data or the necessary filtering procedure, it is very impossible to judge by the performance of dimension analysis alone whether brain signals are really chaotic. For these circumstances the computation of the Lyapunov exponents serves better. Because L_1 is positive for chaotic signals, but zero for periodic or quasiperiodic signals, a clearly positive value gives strong evidence for the hypothesis that the investigated time series is neither periodic nor quasiperiodic. Recently, we could show that EEG signals can be distinguished from periodic and quasiperiodic signals, as well as from white noise, by their principal Lyapunov exponents (Fell et al. 1993). In the case of periodic and quasiperiodic signals, the principal Lyapunov exponents are approximately a factor 10^2 smaller than for the EEG signals. In order to test the colored-noise hypothesis, we compared the estimations of L_1 for sleep EEG data with the estimations for the "scrambled data" and for time-reversed series. Applying these two test procedures we could not find evidence for low-dimensional chaos. Recently, some other authors have drawn the same conclusion from applying different test procedures (e.g., Gorman 1993; Molinari and Dummermuth 1993; Palus 1993). Similarly to our evaluation Achermann and colleagues (1994) compared calculations of correlation dimensions for EEG epochs from an entire night with results for the corresponding "scrambled data." They found that the values for original and surrogate data largely change in parallel, but that the results for the surrogate data are slightly higher. In conclusion, in our opinion the ontological question concerning the dynamical nature of EEG signals is still open.

From a pragmatical point of view it is important that analytical methods of nonlinear system theory open a new system-theoretical window – besides the spectral analysis – to analyze and classify EEG signals. Nonlinear measures on principle are independent of classical measures that are based on Fourier transform. Compared with conventional spectral analysis, the information gained from a signal is reduced drastically be the application of the analytical methods of nonlinear system theory. This kind of analysis leads to a single value, which reflects a property of the whole dynamical system. The numerical results for the principal Lyapunov exponent L_1 depend on the choice of input parameters (Fell et al. 1993; Principe and Lo 1991), the data length (Wolf and Bessoir 1991), and, of course, the implemented algorithm. Consequently, the absolute values of L_1 should be considered carefully. A reasonable interpretation should be based on statistically significant differences between the values of L_1 for different mental states; respectively, between the values for a certain diagnostic group compared with healthy controls. Furthermore, one should avoid speaking of dimension or Lyapunov exponents of "EEG attractors." Attractors are conceptual objects that are defined by the indecomposable sets to which trajectories of dissipative systems asymptotically converge in phase space for times increasing toward infinity. The idea of an attractor requires the assumption that the system under study is autonomous, which means that the dynamical equations do not explicitly depend on time, or in other words, the control parameters of the system's dynamics representing influences of the environment are constant in time. Because brains are open systems, we expect that electrical brain activities can be modeled by systems of the nonautonomous rather than autonomous kind. The fact that the principle Lyapunov exponents for a single sleep stage showed high intraindividual consistency, on the other hand, suggests that during

each of the five different sleep stages, which could be called different "modes of operations," the brain can almost be regarded as an autonomous system.

Earlier investigations concerning the calculation of correlation dimensions D_2 for sleep EEG data provided that in normal healthy subjects, the deeper the sleep, the lower D_2 (Achermann et al. 1993; Babloyantz et al. 1985; Ehlers et al. 1991; Röschke and Aldenhoff 1991). In addition to the very well-established calculation of correlation dimensions, Lyapunov exponents supply a new methodical axis, in terms of nonlinear dynamics, to investigate EEG signals. It is important to be aware that correlation dimensions and Lyapunov exponents are two totally different nonlinear measures. Correlation dimensions yield a lower boundary for the degrees of freedom a signal possesses, which may be attributed to the complexity of a time series. On the other hand, principal Lyapunov exponents quantify the sensitive dependence on initial conditions, or in simplified words, how chaotic a dynamical system is. For instance, a k periodic system (K: integer), consisting of k superposed sine waves with incommensurable frequencies, possesses a dimension k, whereas the principal Lyapunov exponent is always zero.

Our results demonstrate that there are statistically significant differences between the first positive Lyapunov exponents L_1 during different sleep stages (classified according to Rechtschaffen and Kales) for both depressives and healthy controls. Essentially, the more the sleep moves to SWS, the lower L_1. The values for paradoxical sleep lie close to the values for stage I. The direct comparison between depressives and controls reveals a statistically significant decrease in L_1 during sleep stage IV in depression. In contrast, earlier results concerning the sleep EEG in schizophrenia revealed a significant increase in L_1 during REM sleep (Röschke et al. 1994). Under the view that the central nervous system (CNS) is a complex dynamical system, altered Lyapunov exponents of sleep EEG can be regarded as an expression of disturbed information processing.

At this point a more general word of caution is needed. The search for specific biological disturbances in the case of psychiatric diseases depends highly on the operational definition of these diseases. Up to now we do not have a classification (neither according to DSM-III-R nor to ICD-10, or any other system) that takes into account the biological background of psychiatric diseases. Moreover, the diagnoses themselves appear to be just constructions. Therefore, results of investigations of biological disturbances in the case of psychiatric diseases based on operationally defined systems may be regarded as a first approach to the biological aspects of psychiatric illness. On the other hand, the classification of sleep stages was based on the visual sleep-stage scoring procedure proposed by Rechtschaffen and Kales (1968), which certainly limits the advantages of methods from nonlinear dynamics or other system-theoretical approaches. With the development of computational tools for EEG analysis and segmentation, the classical sleep-scoring procedure may become obsolete. In any case, in order to allow comparison with the results of other sleep investigators, it seems reliable to still rely on the traditional scheme until a better classification procedure has been established.

Borbéley and Wirz-Justice (1982) proposed that depressive illness is correlated to a deficiency in the oscillatory system regulating SWS. More recently Beersma and van den Hoofdakker (1992) suggested that the antidepressant effects of sleep manipulations originate from a suppression of SWS intensity, rather than from a suppression of REM sleep. The apparent importance of SWS in depression has been highlighted by Kupfer and Reynolds (1989), who turned their attention away from REM sleep and REM latency, and, for instance, proposed that SWS is particularly beneficial in protecting against psychiatric disorders and pathological aging. Slow-wave sleep is supposed to be most important for the recovery of certain physiological functions. Moreover, SWS seems to be essential to the restoration of synapses mediating higher-level cognitive functioning (Horne 1993). Concerning conventional sleep analysis our results reveal a significantly reduced amount of SWS in depression, which is in accordance to the findings of other groups (Reynolds and Kupfer 1987). Altered brain dynamics, in terms of linear system theory during SWS in depression, have been reported by Borbély and coworkers (1984). They found reduced amounts of low frequency components in power spectra of depressive patients during SWS. In an earlier investigation we detected a significant decrease in the correlation dimension during the slow-wave stages III and IV in a depressive group (a subgroup of the group examined in the present study) compared with healthy controls (Röschke et al. 1994). Thus, not only the amount of SWS appears to be significantly reduced in depression, but also the quality of deep sleep in both linear and nonlinear dynamical terms seems to be impaired. On the contrary, the present study revealed neither a statistically significant reduction in REM latency nor a significant increase in the amount of REM sleep. Moreover, the quality of REM sleep in terms of nonlinear dynamics appears to be the same in depression as in normal healthy subjects. In conclusion, our results support the hypothesis that SWS plays a more crucial role in depressive illness than does REM sleep. We suppose that disturbed SWS may be an expression of the seriously impaired physical constitution in depression. Further interpretations of altered nonlinear EEG dynamics during SWS in depression would be prematures because of only scanty knowledge about the function of SWS.

Acknowledgements This work was supported by the Deutsche Forschungsgemeinschaft (Ro 809/4-1).

References

Achermann P, Hartmann R, Gunzinger A (1993) Dimensional analysis of all night sleep EEG data. APSS annual meeting, abstract 47

Achermann P, Hartmann R, Gunzinger A, Guggenbuhl W, Borbély AA (1994) All night sleep EEG and artificial stochastic control signals have similar correlation dimensions. Electroencephalogr Clin Neurophysiol 90:384–387

American Psychiatric Association (1987) Diagnostic and statistical manual of mental disorders (DSM-III-R), 3rd edn, revised. American Psychiatric Press, Washington, DC

Babloyantz A, Nicolis C, Salazar U (1985) Evidence of chaotic dynamics. Phys Lett A 111:152–156

Babloyantz A, Destexhe A (1986) Low-dimensional chaos in an instance of epilepsy. Proc Natl Acad Sci USA 83:3513–3517

Basar E (ed) (1990) Chaos in brain function. Springer, Berlin Heidelberg New York

Beersma DG, Hoofdakker RH van den (1992) Can non-REM sleep be depressogenic? J Affect Disord 24:101–108

Benca RM, Obermeyer WH, Tiested RA, Gillin JC (1992) Sleep and psychiatric disorders. A meta-analysis. Arch Gen Psychiatry 49:651–668

Borbély AA, Wirz-Justice A (1982) Sleep, sleep deprivation and depression. A hypothesis derived from a model of sleep regulation. Hum Neurobiol 1:205–210

Borbély AA, Tobler I, Loepf M, Kupfer DJ, Ulrich RF, Grochocinski V, Doman J, Matthews G (1984) All-night spectral analysis of sleep EEG in untreated depressives and normal controls. Psychiatry Res 12:27–33

Eckmann JP,Ruelle D (1985) Ergodic theory of chaos and strange attractors. Rev Mod Phys 57:617–656

Ehlers CL, Havstad JW, Garfinkel A, Kupfer DJ (1991) Nonlinear analysis of EEG sleep states. Neuropsychopharmacology 5: 167–176

Fell J, Röschke J, Beckmann P (1993) Deterministic chaos and the first positive Lyapunov-exponent: a nonlinear analysis of the human electroencephalogram during sleep. Biol Cybern 69: 139–146

Fell J, Beckmann P (1994) Resonance-like phenomena in Lyapunov-calculations from data reconstructed by the time-delay-method. Phys Lett A 190:172–176

Fell J, Röschke J (1994) Nonlinear dynamical aspects of the human sleep EEG. Intern J Neurosci 76:109–129

Frank GW, Lookman T, Nerenberg MAH, Essex C, Lemieux J, Blume W (1990) Chaotic time series analyses of epileptic seizures. Physica D 46:427–438

Gallez D, Babloyantz A (1991) Predictability of human EEG: a dynamical approach. Biol Cybern 64:381–391

Garfinkel A (1983) A mathematics for physiology. Am J Physiology 245:R455–R466

Gorman M (1993) Classification of high-dimensional chaotic dynamics using power spectra. In: Jansen B, Brandt M (eds) Nonlinear dynamical analysis of the EEG. World Scientific, Singapore, pp 3–12

Graf KE, Elbert T (1989) Dimensional analysis of the waking EEG. In: Basar E, Bullock T (eds) Brain dynamics. Progress and perspectives. Springer, Berlin Heidelberg New York, pp 174–191

Grassberger P, Schreiber T, Schaffrath C (1991) Nonlinear time sequence analysis. Int J Bifurcation Chaos 1:251–547

Goldberger AL, West BJ (1987) Applications of nonlinear dynamics to clinical cardiology. Ann NY Acad Sci 504:195

Haken H (1983) At least one Lyapunov-exponent vanishes, if the trajectory of an attractor does not contain a fixed point. Phys Lett A 94:71–72

Horne JA (1993) Human sleep, sleep loss and behavior. Br J Psychiatry 162:413–419

Iasemidis LD, Sackellares JC (1991) The evolution with time of the spatial distribution of the largest Lyapunov-exponent on the human epileptic cortex. In: Pritchard WS, Duke DW (eds) Measuring chaos in the human brain. World Scientific, Singapore, pp 49–82

Krystal AD, Weiner RD (1991) The largest Lyapunov-exponent of the EEG in ECT seizures. In: Pritchard WS, Duke DW (eds) Measuring chaos in the human brain. World Scientific, Singapore, pp 113–127

Kupfer AD, Reynolds CF (1989) Slow wave sleep as a protective factor. In: Stunkard AJ, Baum A (eds) Eating, sleeping and sex. Lawrence Erlbaum, New Jersey, pp 131–145

Lutzenberger W, Birbaumer N, Flor H, Rockstroh B, Elbert T (1992) Dimensional analysis of the human EEG and intelligence. Neurosci Lett 143:10–14

Mayer-Kress G, Holzfuss J (1987) Analysis of the human electroencephalogram with methods from nonlinear dynamics. In: Rensing L, Heiden U van der, Mackey MC (eds) Tempral disorder in human oscillatory systems. Springer, Berlin Heidelberg New York, pp 57–68

Molinari L, Dumermuth G (1993) Once more: dimension and Lyapunov exponents for the human EEG. In: Jansen B, Brandt M (eds) Nonlinear dynamical analysis of the EEG. World Scientific, Singapore, pp 140–165

Nan X, Jinghua X (1988) The fractal dimension of EEG as a physical measure of conscious human brain activation. Bull Math Biol 50:559–565

Ott E, Grebogi C, Yorke JA (1990) Controlling chaotic dynamical systems. In: Campbell K (ed) Chaos/xaoc – Soviet–American perspectives on nonlinear science. American Institute of Physics, pp 153–171

Palus M (1993) Testing for nonlinearity in the EEG. In: Jansen B, Brandt M (eds) Nonlinear dynamical analysis of the EEG. World Scientific, Singapore, pp 100–115

Parlitz U (1991) Identification of true and spurious Lyapunov exponents from time series. Int J Bifurcation Chaos 2:155–165

Pesin YB (1977) Characteristic Lyapunov-exponents and smooth ergodic theory. Russ Math Surv 32:55

Pijn JP, Van Neerven J, Noest A, Lopes da Silva FH (1991) Chaos or noise in EEG signals; dependence on state and brain site. Electroencephalogr Clin Neurophysiol 79:371–381

Pool R (1989) Is it healthy to be chaotic? Science 243:604–607

Principe JC, Lo PC (1991) Towards the determination of the largest Lyapunov-exponent of EEG segments. In: Pritchard WS, Duke DW (eds) Measuring chaos in the human brain. World Scientific, Singapore, pp 156–166

Pritchard WS, Duke DW (1992) Dimensional analysis of no-task human EEG using the Grassberger-Procaccia method. Psychophysiology 29:182–192

Rapp PE, Albano AM, Mees AI (1988) Calculation of correlation dimensions from experimental data. Progress and Problems. In: Kelso JAS, Mandell AJ, Schlesinger MF (eds) Dynamic patterns in complex systems. World Scientific, Singapore, pp 191–205

Ray WJ, Wells R, Elbert T, Lutzenberger W, Birbaumer N (1991) EEG and chaos: dimension estimation of sensory and hypnotic processes. In: Pritchard WS, Duke DW (eds) Measuring chaos in the human brain. World Scientific, Singapore, pp 199–215

Rechtschaffen A, Kales A (1968) A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Public Health Service, Washington DC, NIH publication No. 204, U. S. Government Printing Office

Reynolds CF, Kupfer DJ (1987) Sleep research in affective illness: state of the art circa 1987. Sleep 10:199–215

Röschke J, Aldenhoff JB (1991) The dimensionality of human's electroencephalogram during sleep. Biol Cybern 64:307–313

Röschke J, Mann K, Fell J (1994) Nonlinear EEG dynamics during sleep in depression and schizophrenia. Intern J Neurosci 75: 271–284

Röschke J, Fell J, Beckmann P (1994) Nonlinear analysis of sleep EEG data in schizophrenia: calculation of the principal Lyapunov-exponent. Psychiatry Res (in press)

Skarda C, Freeman W (1987) How brains make chaos in order to make sense of the world. Behav Brain Sci 10:161–195

Soong ACK, Stuart CIJM (1989) Evidence of chaotic dynamics underlying the human alpha-rhythm electroencephalogram. Biol Cybern 62:55–62

Takens F (1981) Detecting strange attractors in turbulence. Lect Notes Math 898:366–381. Springer, Berlin Heidelberg New York

Wolf A, Bessoir T (1991) Diagnosing chaos in the space circle. Physica D 50:239–258

Wolf A, Swift JB, Swinney HL, Vastano JA (1985) Determining Lyapunov exponents from a time series. Physica D 16:285–317