ELSEVIER

Electroencephalography and clinical Neurophysiology 106 (1998) 220–228

Non-linear dynamical analysis of the EEG in Alzheimer's disease with optimal embedding dimension

Jaeseung Jeong[a,*], Soo Yong Kim[a], Seol-Heui Han[b]

[a]*Department of Physics, Korea Advanced Institute of Science and Technology, Taejon, South Korea 305–701*
[b]*Department of Neurology, Chungbuk National University Hospital, Chungbuk, South Korea 361–711*

Accepted for publication: 6 July 1997

Abstract

We used non-linear analysis to investigate the dynamical properties underlying the EEG in patients with Alzheimer's disease. We calculated the correlation dimension D2 and the first positive Lyapunov exponent L1. We employed a new method, which was proposed by Kennel et al., to calculate the non-linear invariant measures. That method determined the proper minimum embedding dimension by looking at the behavior of nearest neighbors under a change in the embedding dimension d from d to $d + 1$. We demonstrated that for limited noisy data, our algorithm was strikingly faster and more accurate than previous ones. Also, we found that, in almost all channels, patients with Alzheimer's disease had significantly lower D2 and L1 values than those for age-approximated healthy controls. These results suggest that brains afflicted by Alzheimer's disease show behaviors which are less chaotic than those of normal healthy brains. In this paper, we show that non-linear analysis can provide a fruitful tool for detecting relative changes, which cannot be detected by conventional linear analysis, in the complexity of brain dynamics. We propose that non-linear dynamical analyses of the EEGs from patients with Alzheimer's disease will be a diagnostic modality in the appropriate clinical setting. © 1998 Elsevier Science Ireland Ltd.

Keywords: Alzheimer's disease; Quantitative EEG; Chaos; Lyapunov exponent; Correlation dimension

1. Introduction

The human electroencephalogram (EEG) is a complex and aperiodic time series which is a sum over a very large number of neuronal membrane potentials. In the latter half of the 1980s, scientific research focused on whether the EEG is a simple noise or a deterministic chaotic signal. Babloyantz et al. (1985) first reported that the EEG data from the human brain during the sleep cycle had chaotic attractors for sleep stages II and IV. Much research with non-linear methods revealed that the EEG is generated by a chaotic neural process of low dimension (Rapp et al., 1985; Babloyantz, 1988; Röschke and Basar, 1988; Soong and Stuart, 1989). According to these reports, the EEG has a finite non-integer correlation dimension and a positive Lyapunov exponent. Furthermore, the distinct states of brain activity had different chaotic dynamics quantified by non-linear invariant measures such as correlation dimensions and Lyapunov exponents (Babloyantz and Destexhe, 1987; Babloyantz, 1988; Röschke and Aldenhoff, 1991; Fell et al., 1993).

However, there is also some evidence that the EEG is not a chaotic signal of low dimension. Osborne and Provenzale (1989) demonstrated that 1/f-like linear stochastic systems, so-called colored noise, also resulted in a finite correlation dimension. Their results indicate that the sole observation of a finite correlation dimension from an analysis of the EEG is not sufficient to infer the presence of a strange attractor in brain dynamics. Theiler et al. (1992) investigated surrogate-data tests that attempted to distinguish linear stochastic systems from systems having non-linear dynamics. They showed that the EEG was non-linear; however, it was not produced by low-dimensional chaos. Rapp et al. (1993) showed that filtered noise could mimic low-dimensional chaotic attractors as the EEG data did. Pritchard et al. (1995) applied surrogate-data testing to a normal resting human EEG to detect the presence of non-linearity and

* Corresponding author. Tel.: +82 42 8692569;
e-mail: jsjeong@sensor.kaist.ac.kr

PII S0013-4694(97)00079-5

low-dimensional chaos. Their results also indicated that the normal resting human EEG was non-linear, but did not represent low-dimensional chaos.

Whether the EEG is, therefore, generated by a low-dimensional chaotic system or a linear stochastic system is still controversial. Regardless of what the true dynamics of the EEG is, non-linear analysis of the EEG to make D2 and/or L1 estimates have proven to be very useful in making relative comparisons of different physiological states (Rapp, 1993). Many investigations with non-linear methods have revealed possible medical applications for non-linear analysis and have given rise to the possibility that the underlying mechanisms of the brain function may be explained by non-linear dynamics (Babloyantz and Destexhe, 1986, 1987; Frank et al., 1990; Pritchard et al., 1991, 1993, 1994; Stam et al., 1994, 1995, 1996; Besthorn et al., 1995; Fell et al., 1995).

It has been reported that the chaotic behavior of the human EEG during sleep changed as the sleep stage changed (Röschke and Aldenhoff, 1991; Fell et al., 1993). Especially, the fact that brain dynamics in the rapid-eye-movement (REM) sleep state is more chaotic than that in other sleep states suggests that chaos plays an important role in information processing in the brain because according to some measures, as much brain activity exists in the REM sleep state as in the awake state. In animal studies, REM sleep was found to be a characteristic of highly developed brains; the more complex the brain was, the more REM sleep there was (Bloom and Lazerson, 1988).

For the above reasons, we used non-linear methods to investigate the dynamical properties underlying the EEGs from patients with Alzheimer's disease (AD) and we compared the chaotic brain dynamics in patients with Alzheimer's disease with those in the normal controls. There have been several previous studies on non-linear EEG analyses of Alzheimer's patients. Pritchard et al. (Pritchard et al., 1991, 1993) estimated the dimensional complexity of topographic EEG data (resting, eyes closed, and eyes open) by using the Takens–Ellner method on 3 subject groups: normal young, normal elderly, and elderly probable Alzheimer's patients. Pritchard et al. (1994) attempted to classify Alzheimer's disease subjects versus controls by using spectral-band and non-linear EEG measures and by using a neural-net classification procedure to improve the performance level. They found that the addition of non-linear EEG measures improved the classification accuracy of the subjects as either AD patients or controls. Stam et al. (1995) calculated the D2, the L1, and the K_1 (Kolmogorov entropy) of the original EEG epochs and the surrogate (phase-randomized) data in 9 control subjects, 9 demented patients, and 13 Parkinson patients by using the spatial embedding method. They found evidence for non-linearity in normal and abnormal EEGs during the awake and/or the eyes-closed states.

Some problems exist, however, in applying non-linear methods to experimental data. Classical algorithms for calculating non-linear invariant measures from the experimental EEG data require a very large number of computations in the embedding process (Grassberger and Procaccia, 1983). The amount of data required for meaningful results is beyond the experimental possibilities for physiological data (Smith, 1988; Eckmann and Ruelle, 1992). In this paper, we use a new algorithm, which was proposed by Kennel et al. (1992), to estimate the non-linear invariant measures efficiently for finite noisy data. This algorithm is strikingly faster and more accurate than other algorithms. We also use some modifications of the Grassberger-Procaccia algorithm (GPA) to calculate the correlation dimensions to obtain reliable results for finite noisy data.

In Section 2, we explain our new algorithm for determining the proper embedding dimension and for compensating for both noise contamination and edge effects. The correlation dimension and the Lyapunov exponents are also defined and discussed. Section 3 briefly presents the procedure for recording data. Section 4 shows the differences in the values of the correlation dimension and the first positive Lyapunov exponent between patients with Alzheimer's disease and the normal controls. In Section 5, we discuss our results with respect to both the role of chaos in the brain function and the possibility of modeling the brain by non-linear dynamics. Our conclusions are given in Section 6. The procedure for reconstructing brain dynamics from an EEG and for analyzing the EEG by non-linear methods is given in Appendix A.

2. Algorithm

We applied a reconstruction procedure to each EEG segment. For the time delay T, we used the first local minimum of the average mutual information between the set of measurements $v(t)$ and $v(t + 1)$. Mutual information measures the general dependence of two variables. Therefore, it provides a better criterion for the choice of T than the autocorrelation function, which only measures the linear dependence (Fraser and Swinney, 1986).

Classical algorithms for calculating the non-linear invariant measures, such as the correlation dimension and the Lyapunov exponent for time signals, require a very large number of computations. We calculate a non-linear invariant measure by increasing the embedding dimension until the value of the invariant measure is saturated. The value is independent of the embedding dimension d for $d \geq d_{\min}$ (i.e., after the geometry is unfolded), where $d_{\min}$ is the minimum embedding dimension. However, working in a dimension larger than the minimum embedding dimension leads to excessive computations. It also enhances the problem of contamination by roundoff or instrumental error because such noise will populate and dominate the additional $d - d_{\min}$ dimensions of the embedding space in which no dynamics is operating. In our new algorithm, we calculate the correlation dimension D2 and the first positive Lyapunov exponent L1 in the minimum embedding dimension.

We determine the minimum embedding dimension by

using the calculation method, presented by Kennel et al. (1992), which is based on the idea that in the passage from dimension d to dimension $d + 1$, one can differentiate between points on the orbit that are 'true' neighbors and those on the orbit which are 'false' neighbors. A false neighbor is a point in the data set that is a neighbor solely because we are viewing the orbit (the attractor) in too small an embedding space ($d < d_{min}$) When we have achieved a large enough embedding space ($d \geq d_{min}$), all neighbors of every orbit point in the multivariate phase space will be true neighbors. We define the embedding rate as the ratio of the true neighbors to the neighbors in the embedding dimension. Fig. 1 shows a typical example of the embedding rate as a function of the embedding dimension for 16 384 EEG data points at T_4 in a patient with Alzheimer's disease. The proper minimum embedding dimension was selected as 11 in this case. Next, we can estimate the invariant measures by calculating them only in the minimum embedding dimension, which is different from the conventional method (Grassberger and Procaccia, 1983). Fig. 2 shows a comparison of the new method for calculating D2 with the old method. Both estimate the D2 of the EEG at T_4 in a patient with Alzheimer's disease. The calculation of D2 is done once in the determined minimum embedding dimension in the new method whereas several calculations of D2 are needed, using different embedding dimensions, in the old method. This shows the increased efficiency and accuracy of the new method relative to the old one.

We evaluate the correlation dimension D2 of the attractors from the EEG by using the GPA (Grassberger and Procaccia, 1983). In order to calculate D2, one computes the correlation integral function

$$C(r) = \frac{1}{N^2} \sum_{i,\ j=1;\ i \neq j}^{N} \theta(r - |\boldsymbol{x}_i - \boldsymbol{x}_j|) \quad (1)$$

where θ is the Heaviside function, $\theta(x) = 0$ if $x < 0$, and $\theta(x) = 1$ if $x > 0$. $C(r)$ measures the spatial correlation of the points on the attractor obtained from the time series data. For small r, it is known that $C(r)$ behaves according to a power law:

$$C(r) \propto r^{D_2} \quad (2)$$

The value of D2 for the attractor is, therefore, given by the slope of the log $C(r)$ versus log r curve:

$$D_2 = \frac{d\log C(r)}{d\log r} \quad (3)$$

The graph of log $C(r)$ versus log r has a linear region called the scaling region. The GPA assumes that most of the information about the dimension is contained in the scaling region (Babloyantz et al., 1985).

A finite sequence of EEG data exhibits an anomalous structure in the correlation integral by overcontributing early terms from the start in the correlation integral. We used a slight modification, proposed by Theiler (1986), of the GPA to prevent the anomalous structure in the correlation integral:

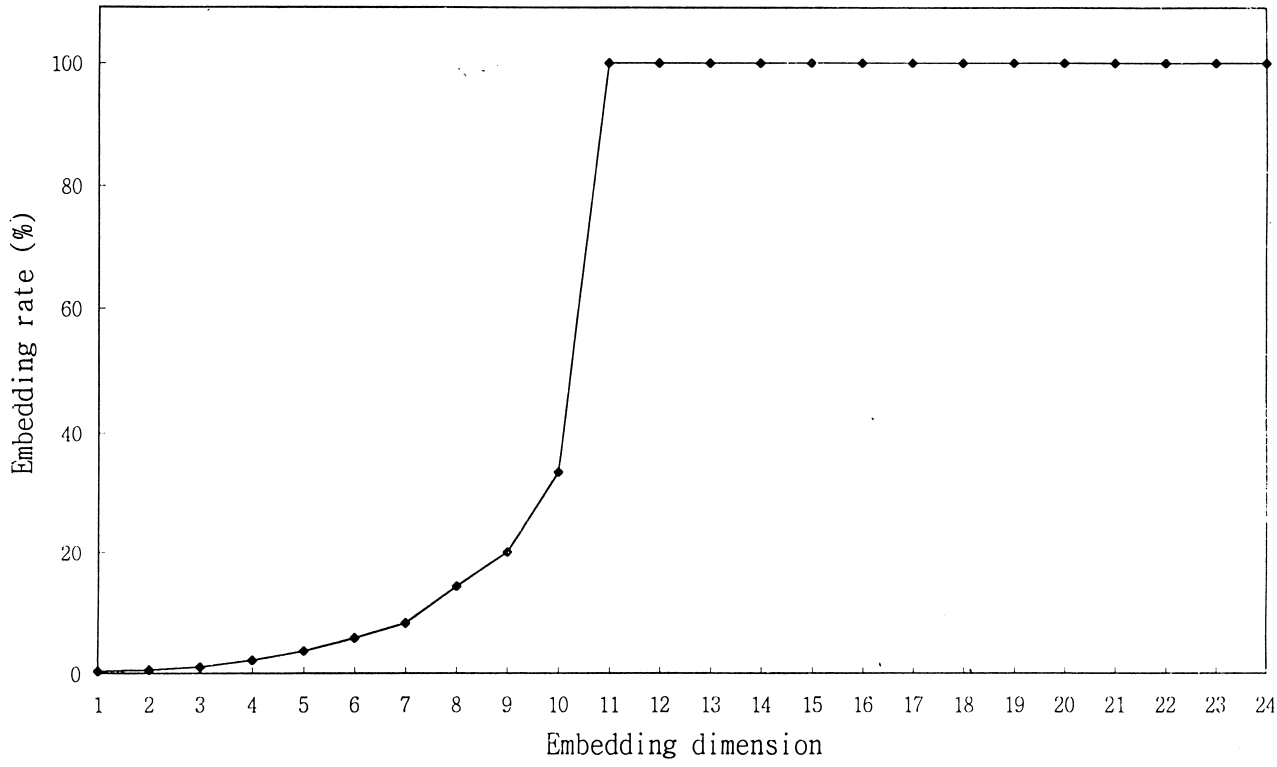

Fig. 1. The embedding rate as a function of embedding dimension for 16 384 EEG data points at T_4 in a patient with Alzheimer's disease. The proper minimum embedding dimension for calculating the invariant measures was selected as 11 in this case.

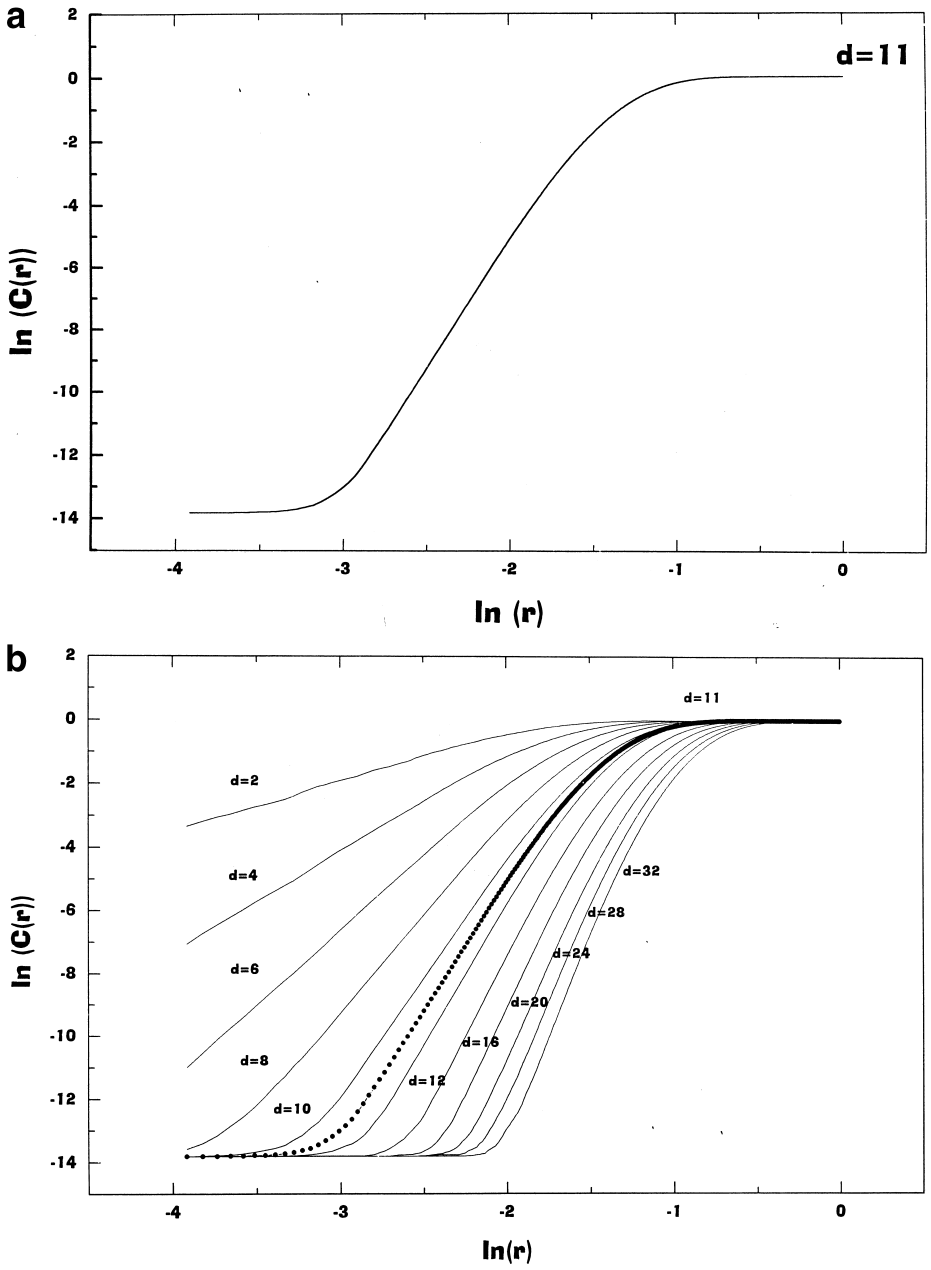

Fig. 2. Comparison of the (a) new method for calculating the D2 with the (b) old method. The two methods estimate the D2 of the EEG at T_4 in a patient with Alzheimer's disease.

$$C(r,N,W)=\frac{2}{N^2}\sum_{n=W}^{N}\sum_{i=1}^{N-n}\theta(r-|\boldsymbol{x}_{i+n}-\boldsymbol{x}_i|) \quad (4)$$

In our study, W is determined by the first local minimum of the mutual information, i.e., by the delay time T.

When we analyze the real data, the scaling region is very often observed to oscillate around some straight line. These oscillations may be either intrinsic sample oscillations caused by the lacunarity of the attractor or finite sample oscillations caused by the limited amount of data (the edge effect). We used a modification, proposed by Dvořak and Klaschka (1990), of the GPA to compensate for the edge effect.

We calculate the first positive Lyapunov exponent L1 by applying a modified version of the Wolf algorithm (Wolf et al., 1985) and by following a proposal by Frank et al. (1990). Essentially, the Wolf algorithm computes the initial vector distance *di* of two nearby points and evolves its length at a certain propagation time. If the vector length *df* between the two points becomes too large, a new reference point is chosen with properties minimizing the replacement length and the orientation change. Now, the two points are evolved again and so on. After *m* propagation steps, the first positive Lyapunov exponent results from the sum over the logarithm of the ratios of the vector distances divided by the total evolving time:

$$L_1 = \frac{1}{m}\sum_{i=1}^{m}\frac{\ln\frac{df_1}{di_i}}{\mathrm{EVOLV}\cdot dt\cdot \ln 2}(\mathrm{bits/s}) \quad (5)$$

where *dt*, *di*, and *df* are the sampling interval, and the initial and the final separations between the points in the fiducial trajectory and in the nearest-neighbor trajectory separated in time by i^{th} EVOLV step, respectively (Wolf et al., 1985).

By using the weight function proposed by Frank et al. (1990), we improve the L1 estimate by widening the search to allow replacements to be well-aligned points lying further apart but still within the region of linear dynamics:

$$W(r,\theta) = \left(\alpha + \beta\left(\frac{b-r}{b-a}\right)^{\gamma}\right)\cdot\cos\theta \quad (6)$$

where *b* and *a* are distances over which the dynamics is assumed to be linear and to be noise-dominated, respectively, *r* is the radial separation between the candidate and the evolved benchmarks, and θ is the angular separation between the evolved displacement and the candidate replacement vectors. The numeric parameters α, β, and γ control the relative importance of the proximity to the alignment priority.

As suggested by Principe and Lo (1991), we use the information contained in the power spectrum of the signal segment for the proper evolving time EVOLV. We select the *l*/*e* spectral frequency - the frequency that divides the power spectrum in the ratio of *l*/*e* as the frequency to be used to obtain the number of points for the EVOLV step. Realistic values for the average additive noise levels can be extracted from the curves of the correlation integral function which are used to calculate the correlation dimension. Intermediate knees in the correlation integral are related with noise contamination. The value of *r* for which the knee starts to appear can be used as an estimate of the noise scale. The criteria to establish the maximum scale are derived from the upper boundary of the scaling region in the correlation function (Principe and Lo, 1991).

3. Materials

We studied 12 patients (8 females and 4 males; age = 68.72 ± 5.11 years, mean ± SD) fulfilling the criteria of probable AD as defined by the National Institute of Neurological and Communicative Disorders and by the Stroke-Alzheimer's Disease and Related Disorders Association work group (McKhann et al., 1984) and 12 age- and sex-matched healthy cognitively normal controls (8 females and 4 males; age = 66.78 ± 4.25 years, mean ± SD). The local ethics committee approved the study. All subjects and all caregivers of the demented patients gave informed consent for participation in this study. The patients underwent the following examinations: general physical and clinical neurological examination (MMSE-K) (Kwon and Park, 1986) originated by Folstein et al. (1985); assessments of depressive signs by using the Hamilton scale (Hamilton, 1960); extensive batteries of laboratory tests to exclude secondary causes of dementia: magnetic resonance imaging (MRI) and/or computed tomography (CT) of the brain; and single photon emission computed tomography (SPECT) of the brain. The AD subjects had been free of psychotropic medication for at least 1 week before the EEG recording. The AD subjects had an MMSE score under 12 (mean MMSE = 9.2 ± 3.51), indicating a severe degree of dementia. They had a score of less than 4 on the modified ischemic scale (Rosen et al., 1980). The average age at onset of dementia was about 64.93 ± 3.11 years, and the average length of the illness was about 46 ± 7.32 months. The controls were administered the MMSE once and had a mean score of 27.1 ± 0.67. The controls underwent the same protocol, except for the SPECT scan and the assessment based on the Hamilton scale.

The EEGs were recorded from the 15 scalp loci of the international 10–20 system. The EEGs from the T_5 channel were not recorded because of a hardware problem. With the subjects in a relaxed state with closed eyes, 32.768 s of data (16,384 data points) were recorded and digitized by a 12-bit analog-digital converter in an IBM PC. Recordings were made under the eyes-closed condition in order to obtain as many stationary EEG data as possible. The sampling frequency was 500 Hz. Potentials from 15 channels (F_7, T_3, Fp_1, F_3, C_3, P_3, O_1 F_8, T_4, T_6, Fp_2, F_4, C_4, P_4 and O_2) against 'linked earlobes' were amplified on a Nihon Kohden EEG-4421K using a time constant of 0.1 s. All data were digitally filtered in order to remove the residual EMG activity at 1–35 Hz. Each EEG record was judged by inspection to be free from electrooculographic and movement artifacts and to contain minimal electromyographic (EMG) activity.

4. Data and results

The first step in our analysis was to construct phase space using the delay coordinates proposed by Takens (1981). We used the time delays calculated by the method of mutual information to reconstruct the attractor. The values of D2 were calculated by a slightly modified version of the GPA. Time delays of 34–50 ms and embedding dimensions of 11–18 were used for the AD patients, and time delays of 28–34 ms and embedding dimensions of 11–19 were used for the normal controls. The slope of the correlation integral curve in the scaling region was estimated by a least-squares fitting method (Fig. 3). The average values of D2 and the standard deviations for both the Alzheimer's patients and the normal controls, for the 15 channels identified above, are summarized in Table 1. It can be seen that Alzheimer's patients have significantly lower values of D2 than the normal controls (two-tailed *t* test, $P < 0.001$), except in the F_7 and the O_1 channels ($0.05 < 0.1$). The EEGs of the patients at channel F_8 have lower values of D2 than the normal

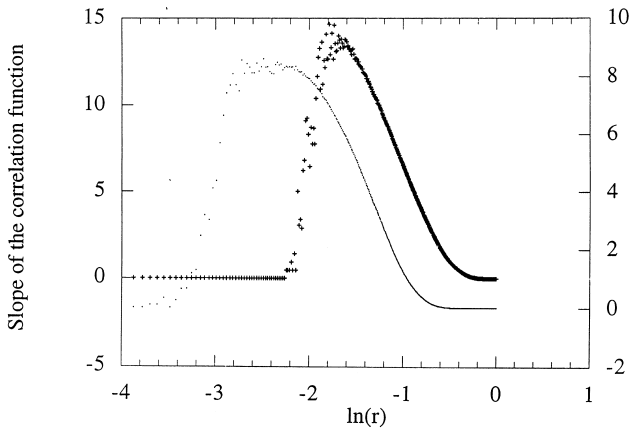

Fig. 3. Comparison of the slope estimate at the minimum embedding dimension of 11 with Dvořak and Theiler's correction for an EEG at T_4 in a patient with Alzheimer's disease with a higher embedding dimension of 32 as obtained by the classical GPA for the same data. The former has a larger scaling region.

controls ($P < 0.05$), the differences between the values being about 1.0–1.6 units.

Another non-linear invariant measure, the first positive Lyapunov exponent L1 was calculated for all subjects in all channels. The EVOLV was selected by using the *l*/*e* spectral frequency and was about 200 ms. The calculation of L1 naturally depended on the time over which the trajectory was evaluated. After 200 propagation steps, the values converged in an interval of ±0.9% around the final value of L1.

The average values of L1 and the standard deviations for the patients with Alzheimer's disease and for the normal controls in all channels are summarized in Table 2. The average values of L1 of the EEGs are higher for the normal controls than for the patients with Alzheimer's disease (F_7, T_3, Fp_1, P_3, F_8, T_4, T_6, Fp_2, C_4, P_4, $P < 0.001$; F_3, C_3, F_4, $P < 0.01$), just as the D2s are. The EEGs of the AD patients at channels O_1 and O_2 are not statistically different from those of the normal controls (O_1, $0.05 < 0.1$; O_2, $0.2 < P$). The differences between the values of the L1 at the F_7, T_3, Fp_1, P_3, F_8, T_4, T_6, Fp_2, C_4, and P_4 channels are very significant, about 1.0–1.8 units. The results for L1 are consistent with those for D2, except F_7 and O_2 channels.

Table 1

The average values of the D2 of the EEGs for all the subjects in all channels with their standard deviations

Lead position	Subjects	
	Alzheimer's disease	Normal controls
F_7	8.90 ± 0.35	9.14 ± 0.43
F_3	8.92 ± 0.58	10.07 ± 0.67
F_4	8.71 ± 0.42	9.67 ± 0.39
F_8	8.27 ± 0.55	8.81 ± 0.42
Fp_1	8.41 ± 0.52	9.58 ± 0 48
Fp_2	8.03 ± 0.43	9.24 ± 0.43
C_3	9.06 ± 0.55	9.96 ± 0.32
C_4	8.62 ± 0.63	9.84 ± 0.55
T_3	8.40 ± 0.38	9.75 ± 0.31
T_4	8.25 ± 0.35	9.37 ± 0.46
T_6	8.09 ± 0.39	9.53 ± 0.47
P_3	9.01 ± 0.52	9.93 ± 0.37
P_4	8.63 ± 0.48	9.68 ± 0.26
O_1	8.16 ± 0.33	8.23 ± 0.41
O_2	8.15 ± 0.39	8.79 ± 0.43

Table 2

The average values of the L1 of the EEGs for all the subjects in all channels

Lead position	Subjects	
	Alzheimer's disease (bits/s ± SD)	Normal controls (bits/s ± SD)
F_7	7.13 ± 0.38	7.74 ± 0.32
F_3	6.85 ± 0.56	7.52 ± 0.31
F_4	7.15 ± 0.49	7.75 ± 0.34
F_8	6.88 ± 0.32	7.51 ± 0.42
Fp_1	7.16 ± 0.45	7.95 ± 0 51
Fp_2	7.37 ± 0.39	8.07 ± 0.43
C_3	7.59 ± 0.46	8.16 ± 0.49
C_4	7.15 ± 0.31	8.02 ± 0.36
T_3	6.61 ± 0.22	8.27 ± 0.43
T_4	6.82 ± 0.28	8.24 ± 0.43
T_6	6.46 ± 0.46	7.85 ± 0.33
P_3	7.25 ± 0.40	7.98 ± 0.37
P_4	7.56 ± 0.44	8.41 ± 0.12
O_1	6.90 ± 0.46	7.18 ± 0.28
O_2	7.11 ± 0.34	7.13 ± 0.24

An analysis of variance (ANOVA) with GROUP as an independent factor and CHANNEL as a repeated-measure factor yields significant main effects for the factor GROUP for D2 ($F = 6.88$, df = 1, 330; $P < 0.001$) and L1 ($F = 6.62$, df = 1, 330; $P < 0.001$) and for the factor CHANNEL for D2 ($F = 1.89$, df = 14, 330; $P < 0.05$) and L1 ($F = 1.93$, df = 14, 330; $P < 0.05$). No interaction for GROUP × CHANNEL was found for D2 ($F = 1.38$, df = 14, 330; $P > 0.05$) and L1 ($F = 1.31$, df = 14, 330; $P > 0.05$). The results clearly show that for each subject, but different channels, the values of D2 and L1 do not vary within broad ranges. However, in Alzheimer-disease state, many channels have more stable lower values than other lead positions do, which means that patients with Alzheimer's disease have less chaotic brain dynamics globally. The similar behavior of D2 and L1, depending on the brain state, is an absolutely non-trivial outcome. The results for L1 are crucial evidence that chaos plays an important role in brain functions, a conclusion which cannot be made from correlation-dimension calculations alone.

5. Discussion

In EEG analyses, the number of data points was not large enough to obtain reliable results. The data length required

for meaningful results was beyond the experimental possibilities for physiological data. Our study was done with a larger number of data points (16 384 data points) than other previous experiments. We also used slight modifications of the algorithms for limited noisy data.

We now consider the efficiencies of our algorithm for the embedding procedure and for calculating the non-linear parameters. First, it is much faster than classical algorithms which calculate non-linear invariant measures for several embedding dimensions. In our algorithm, it takes a few minutes to evaluate the minimum embedding dimension with a personal computer (Pentium), whereas it takes about 1 h to calculate D2 at an embedding dimension. Therefore, it is strikingly faster to calculate a non-linear invariant measure in only one minimum embedding dimension after determining that minimum embedding dimension than to calculate it in several embedding dimensions. Second, our algorithm is more accurate than classical ones. In the case of D2 the classical GPA has many kinks and apparently shrinks the scaling region, while our method preserves the dimensional measurement in a wider region, as Fig. 3 shows. We found that the knee was reduced, and the measurement of the dynamics was still preserved. The new algorithm is less affected by noise than are other conventional methods. In our method, the slight modifications of the GPA contribute to the accuracy of D2.

Our results are compatible with the more general hypothesis that a loss of complexity appears when biological systems become functionally impaired (Ravelli and Antolini, 1992; Fell et al., 1993). The clear distinction on the basis of dimensionality suggests a reduction of the degrees of freedom in conjunction with a change from the normal to the Alzheimer disease state. The reduction of the dimensionality might be an expression of strongly coupled oscillators or the inactivation of previously active networks (Röschke and Aldenhoff, 1991) or a loss of dynamical brain responsivity to the environmental. According to Pritchard et al. (1991), eyes-open dimensional complexity did not differ from eyes-closed dimensional complexity in Alzheimer's patients whereas eyes-open dimensional complexity was markedly higher than eyes-closed dimensional complexity in the normal young group; a similar, but somewhat weaker, pattern was seen in the normal elderly group. From this, it can be inferred that Alzheimer's disease may be associated with a loss of dynamical brain responsivity to the environmental rather than a global loss of dimension. We infer from our results that brains injured by the development of Alzheimer's disease show a decreased chaotic electrophysiological behavior.

An important question is how to interpret L1 from dynamical system theory in terms of information processing. Since L1 describes the divergence of trajectories starting at nearby initial states, the question of how L1 corresponds to the flexibility of information processing is very important (Fell et al., 1995). In this context, flexibility is understood as the facility of the central nervous system to reach different states of information processing from similar initial states (Röschke and Aldenhoff, 1991). This means that, in comparison with a normal brain, the brain which has been injured by Alzheimer's disease and which has a smaller L1 would show a drop in its flexibility of information processing.

Besthorn et al. (1995) estimated the correlation dimensions of the EEGs in patients with Alzheimer's disease and in normal controls. Their results have more stable and larger differences between patients with Alzheimer's disease and normal controls than ours do. This disagreement may be due to differences in the courses of the disease, the numbers of subjects, the races, etc. They mentioned in their paper that a reduced D2 may be associated with an increase in the proportion of lower- frequency component in the EEGs from patients with Alzheimer's disease.

We suggest the application of several methods from non-linear analysis, although still in a fundamental stage of development, for diagnosis of Alzheimer's disease. Absolute values for the non-linear parameters can not be estimated, in spite of all efforts, because the brain is not a uniquely defined physical system. However, it is truly remarkable that we could still use non-linear analysis to differentiate brain states, such as a normal and an AD state, that present sufficiently different characteristics. A reasonable interpretation should be based on statistically significant differences of the parameters. Moreover, extension of the analysis to a large population leads to a large variance due to the variability in the progress of the disease. Consequently, the analysis should be made with care.

6. Conclusion

We applied an optimal embedding method to the analyses of EEGs from patients with Alzheimer's disease. Our investigations showed that the optimal embedding method is faster and more accurate than the conventional embedding procedure and that it may be useful for estimating the non-linear invariant measures necessary to diagnose Alzheimer's disease in the clinical point of view. We expect that non-linear analysis will give us a deeper understanding of the brain function in ways which are not possible by conventional power spectral analysis.

Acknowledgements

This research was supported by the G7-project from the Ministry of Science and Technology, the Biotech 2000 project, and the '96 Chungbuk National University Hospital Research Fund. We thank Dr. Dae-jin Kim, Dr. Jung-ho Chae, and Mr. J. Lee at St. Mary's Hospital in Taejon for experimental help during this study. The authors are also thankful for the fruitful comments of the unknown referees.

Appendix A Theoretical concepts

The brain may be considered as a dissipative dynamical system. A dynamical *n*th-order system is defined by a set of *n* first-order differential equations. The states of the system can be represented by points in an *n*-dimensional space, where the coordinates are simply the values of the state variables x_1, x_2, x_3, ..., x_n. The phase space is the set of all possible states that can be reached by the system. In general, a phase space is identified with a topological manifold. The sequence of such states over the time scale defines a curve in the phase space called a trajectory. In dissipative systems, as time increases, the trajectories converge to a low-dimensional indecomposable subset called an attractor (Eckmann and Ruelle, 1985).

In experiments, one cannot always measure all the components of the vector giving the state of the system. Therefore, we have to reconstruct brain dynamics from a one-dimensional EEG by using delay coordinates and the Takens' embedding theorem. Takens showed that an attractor, which is topologically equivalent to the original data set, can be reconstructed from a dynamical system of *n* variables x_1, x_2, x_3, ..., x_n by using the so-called delay coordinates $y(t) = [x_j(t), x_j(t + T), ..., x_j(t + (d - 1)T)]$ from a single time series x_j and by performing an embedding procedure, where *d* is the embedding dimension. The purpose of time-delay embedding is to unfold the projection back to a multivariate state space that is a representation of the original system (Takens, 1981; Eckmann and Ruelle, 1985).

Attractors of dynamical systems can be characterized by their correlation dimensions. The correlation dimension D2 is a metric property of the attractor that estimates the degree of freedom of the EEG signal in our study. It determines the number of independent variables which are necessary to describe the dynamics of the central nervous system. In other words, it is a measure of complexity. While periodic and quasiperiodic systems have integer dimensions, systems of deterministic chaos have non-integer dimensions (fractals). In the latter cases, the attractor is called a strange attractor. Strange attractors are identified with deterministic chaos, which means that the different states of the system, which are initially arbitrarily close, will become macroscopically separated after sufficiently long times (Fell et al., 1993).

Lyapunov exponents estimate the mean exponential divergence or convergence of nearby trajectories of the attractor. Lyapunov exponents are usually ordered in a descending fashion from L1 (the highest value) to Ln (the 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 that of a fixed point). It is the one corresponding to the forward direction of the flow. For dissipative dynamic systems, the sum of all Lyapunov exponents is less than zero. A system possessing at least one positive Lyapunov exponent is chaotic. This fact reflects the sensitive dependence on the initial conditions (Fell et al., 1993).

References

Babloyantz, A. Chaotic dynamics in brain activity. In: E. Basar (Ed.), Dynamics of Sensory and Cognitive Processing by the Brain. Springer, Berlin, 1988, pp. 196–202.

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

Babloyantz, A. and Destexhe, A. The Creutzfeld-Jacob disease in the hierarchy of chaotic attractor. In: M. Markus, S. Muller and G. Nicolis (Eds.), From Chemical to Biological Organization. Springer, Berlin, 1987, pp. 307–316.

Babloyantz, A., Salazar, J.M. and Nicolis, C. Evidence of chaotic dynamics of brain activity during the sleep cycle. Phys. Lett., 1985, IIIA: 152–156.

Besthorn, C., Sattel, H., Geiger-Kabisch, C., Zerfass, R. and Forstl, H. Parameters of EEG dimensional complexity in Alzheimer's disease. Electroenceph. clin. Neurophysiol., 1995, 95: 84–89.

Bloom, F.E. and Lazerson, A. Brain, Mind and Behavior. Freeman, New York, 1988, pp. 185–190.

Dvořak, I. and Klaschka, J. Modification of the Grassberger-Procaccia algorithm for estimating the correlation exponent of chaotic systems with high embedding dimension. Phys. Lett. A, 1990, 145 (5): 225–231.

Eckmann, J.P. and Ruelle, D. Ergodic theory of chaos and strange attractors. Rev. Mod. Phys., 1985, 57 (3, Part I): 617–656.

Eckmann, J.P. and Ruelle, D. Fundamental limitations for estimating dimensions and Lyapunov exponents in dynamical systems. Physica D, 1992, 56: 185–187.

Fell, J., Röschke, J. and Beckmann, P. The calculation of the first positive Lyapunov exponent in sleep EEG data. Electroenceph. clin. Neurophysiol., 1993, 86: 348–357.

Fell, J., Röschke, J. and Beckmann, P. Non-linear analysis of sleep EEG data in schizophrenia: calculation of the principal Lyapunov exponent. Psychiatr. Res., 1995, 56: 257–269.

Folstein, M.F., Folstein, S.E. and McHugh, P.R. 'Mini-Mental State': a practical method for grading the cognitive state of patients for the clinician. J. Psychiatr. Res., 1985, 12: 189–198.

Frank, G.W., Lookman, T., Nerenberg, M.A.H. and Essex, C. Chaotic time series analysis of epileptic seizures. Physica D, 1990, 46: 427–438.

Fraser, A.M. and Swinney, H.L. Independent coordinates for strange attractors from mutual information. Phys. Rev. A, 1986, 33 (2): 1134–1140.

Grassberger, P. and Procaccia, I. Measuring the strangeness of strange attractors. Physica D, 1983, 9: 189–208.

Hamilton, M. A rating scale for depression. J. Neurol. Neurosurg. Psychiatr., 1960, 23: 56–62.

Kennel, M.B., Brown, R. and Abarbanel, H.D.I. Determining embedding dimension for phase-space reconstruction using a geometrical construction. Phys. Rev. A, 1992, 45: 3403–3411.

Kwon, Y.C. and Park, J.-H. Korean version of mini-mental state examination (MMSE-K). Part I: development of the test for the elderly. J. Korean Neuropsychiatr. Assoc., 1986, 28: 125–135.

McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D. and Stadlan, E.M. Clinical diagnosis of Alzheimer's disease. Report of the NINDS-ADRDA work group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. Neurology, 1984, 34: 939–944.

Osborne, A.R. and Provenzale, A. Finite correlation dimension for stochastic systems with power-law spectra. Physica D, 1989, 35: 357–381.

Principe, J.C. and Lo, P.C. Towards the determination of the largest Lyapunov exponent of EEG segments. In: D.W. Duke and W.S. Pritchard (Eds.), Proceedings of the Conference on Measuring Chaos in the Human Brain. World Scientific, Singapore, 1991, pp. 156–166.

Pritchard, W.S., Duke, D.W. and Coburn, K.L. Altered EEG dynamical responsivity associated with normal aging and probable Alzheimer's disease. Dementia, 1991, 2: 102–105.

Pritchard, W.S., Duke, D.W., Coburn, K.L., Moore, N.C. and Tucker, K.A. Altered EEG dynamical responsivity associated with Alzheimer's disease: replication and extension. In: B.H. Jansen and M.E. Brandt (Eds.), Proceedings of the Second Annual Conference on Nonlinear Dynamical Analysis of the EEG. World Scientific, Singapore, 1993, pp. 165–168.

Pritchard, W.S., Duke, D.W., Coburn, K.L., Moore, N.C., Tucker, K.A., Jann, M.W. and Hostetler, R.M. EEG-based, neural-net predictive classification of Alzheimer's disease versus control subjects is augmented by non-linear EEG measures. Electroenceph. clin. Neurophysiol., 1994, 91: 118–130.

Pritchard, W.S., Duke, D.W. and Krieble, K.K. Dimensional analysis of resting human EEG. II: Surrogate data testing indicates nonlinearity but not low-dimensional chaos. Psychophysiology, 1995, 32: 486–491.

Rapp, P.E. Chaos in the neurosciences: cautionary tales from the frontier. Biologist, 1993, 40: 89–94.

Rapp, P.E., Zimmerman, I.D., Albano, A.M., deGuzman, G.C., Greenbaun, N.N. and Bashore, T.R. Experimental studies of chaotic neural behavior: cellular activity and electroencephalographic signals. In: H.G. Othmer (Ed.), Nonlinear Oscillations in Biology and Chemistry, Lecture Notes in Biomathematics. Springer-Verlag, Berlin, 1985, pp. 175–205.

Rapp, P.E., Albano, A.M., Schmah, T.I. and Farwell, L.A. Filtered noise can mimic low-dimensional chaotic attractors. Phys. Rev. E, 1993, 47: 2289–2297.

Ravelli, F. and Antolini, R. Complex dynamics underlying the human electroencephalogram. Biol. Cybern., 1992, 67: 57–65.

Rosen, W.G., Terry, R.D., Flud, P.A., Katzman, R. and Beck, A. Pathological verification of ischemic score in differentiation of dementias. Ann. Neurol., 1980, 17: 486–488.

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

Röschke, J. and Basar, E. The EEG is not a simple noise: strange attractors in intracranial structures. In: E. Baaar (Ed.), Dynamics of Sensory and Cognitive Processing by the Brain. Springer, Berlin, 1988, pp. 203–216.

Smith, L.A. Intrinsic limits on dimension calculation. Phys. Lett. A, 1988, 133 (6): 283–288.

Soong, A.C.K. and Stuart, C.I.J.M. Evidence of chaotic dynamics underlying the human alpha-rhythm electroencephalogram. Biol. Cybern., 1989, 62: 55–62.

Stam, C.J., Tavy, D.L.J., Jelles, B., Achtereekte, H.A.M., Slaets, J.P.J. and Keunen, R.W.M. Nonlinear dynamical analysis of multi-channel EEG data: clinical applications in dementia and Parkinson's disease. Brain Topogr., 1994, 7: 141–150.

Stam, C.J., Jelles, B., Achtereekte, H.A.M., Rombouts, S.A.R.B., Slaets, J.P.J. and Keunen, R.W.M. Investigation of EEG nonlinearity in dementia and Parkinson's disease. Electroenceph. clin. Neurophysiol., 1995, 95: 309–317.

Stam, C.J., Jelles, B., Achtereekte, H.A.M. and Birgelen, J.H. van and Slaets, J.P.J. Diagnostic usefulness of linear and nonlinear quantitative EEG analysis in Alzheimer's disease. Clin. Electroencephalogr., 1996, 27: 69–77.

Takens, F. Detecting strange attractors in turbulence in dynamical systems and turbulence. Lecture Notes in Mathematics, 898. Springer, Berlin, 1981, pp. 366–381.

Theiler, J. Spurious dimension from correlation algorithm applied to limited time-series data. Phys. Rev. A, 1986, 34 (3): 2427–2432.

Theiler, J., Eubank, S., Longtin, A., Galdrikian, B. and Farmer, J.D. Testing for nonlinearity in times series: the method of surrogate data. Physica D, 1992, 58: 77–94.

Wolf, A., Swift, J.B., Swinney, H.L. and Vastano, J.A. Deterministic Lyapunov exponents from a time series. Physica D, 1985, 16: 285–317.