Nonlinear analysis of the EEG of schizophrenics with optimal embedding dimension

Jaeseung Jeong [a,*], Dai-Jin Kim [b], Jeong-Ho Chae [b], Soo Yong Kim [a], Hyo-Jin Ko [b], In-Ho Paik [b]

[a] *Department of Physics, Korea Advanced Institute of Science and Technology, Taejon 305-701, South Korea*
[b] *Department of Psychiatry, College of Medicine, The Catholic University of Korea, Seoul, South Korea*

Abstract

We estimated the correlation dimensions of EEGs in patients with schizophrenia to investigate the dynamical properties underlying the EEG. We employed a new method, proposed by Kennel et al. (Kennel MB, Brown R, Abarbanel HDI. Determining embedding dimension for phase-space reconstruction using a geometrical construction. Phys Rev A 1992;45:3403–11), to calculate the correlation dimension $D2$. That method determined the proper minimum embedding dimension by looking at the behaviour of nearest neighbours 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. We estimated the $D2$ of EEGs from 16 channels in patients with schizophrenia according to DSM-IV whereas previous studies, which estimated chaoticity of EEG in schizophrenia, recorded EEG only in a limited number of channels. Schizophrenic patients had a lower correlation dimension in the left inferior frontal and anterior temporal regions compared with controls. Our finding of decreased left frontal and temporal chaotic activity in schizophrenics is in line with the findings of a hypofrontality and hypotemporality reported in previous clinical studies such as EEG, blood flow, brain MRI and positron emission tomography studies in schizophrenia. This result suggests that chaos analysis may be a useful tool in analysing EEG data to explore the brain mechanism of schizophrenia. © 1999 IPEM. Published by Elsevier Science Ltd. All rights reserved.

Keywords: Schizophrenia; Chaos; EEG; Nonlinear dynamics; Correlation dimension

1. Introduction

Schizophrenia is a devastating psychiatric disease, whose broad clinical picture ranges from "negative" deficit symptoms including pervasive blunting of affect, thought, and socialization, to "positive" symptoms such as florid hallucinations and delusions. Its worldwide prevalence is approximately 1%, and even with the most up-to-date treatment the majority of patients suffer from chronic deterioration [1]. A detailed understanding of the neuronal mechanism associated with schizophrenia remains an elusive goal, not only because the human brain is an extremely complex organ, but also because it is relatively inaccessible to investigate during life.

During the past two decades, refinements of imaging techniques have provided access to the function and structure of the living brain. EEG, the spontaneous electrical activity detected at scalp electrodes, provides an indication of neuronal activity. Unfortunately, the spatial variation of scalp electrical potentials gives a very diffuse image of the location of underlying neuronal events [2]. Schizophrenia research has developed into a main field of power spectral analysis over the past 20 years, generating results which are not always clear-cut [3]. Although various electroencephalogram (EEG) abnormalities in schizophrenia have been reported, it is generally agreed that no pathognomic or characteristic EEG pattern is apparent on visual inspection [3]. This may be caused by the forcing of such a heterogeneous disorder as schizophrenia into group statistics, neglecting different subtypes and activity of a schizophrenic process. Schizophrenics demonstrate EEG and other abnormali-

* Corresponding author. Tel.: + 82 42-869-2569; fax: + 82 42-869-2510; e-mail: jsjeong@sensor.kaist.ac.kr

ties suggestive of bilateral or left frontal dysfunction or hypoarousal. One stable finding is the increased beta power of EEG [3,4]. The increased beta activity may also appear significantly on the left side, especially on the frontal area [5]. Gattaz et al. [6] also showed increased activities for fast alpha and beta bands in first onset, neuroleptic naive schizophrenics. The other stable finding is the increased slow-wave abnormalities on the left side, especially on the left anterior temporal area [6,7]. The amount of delta activity on the left anterior temporal area separates the schizophrenics from controls [6].

Recent progress in the theory of nonlinear dynamics has provided new methods for time-series analysis. In the latter half of the 1980s, scientific research focused on whether the EEG is a simple noise or a deterministic chaotic signal. Babloyantz and Salazar [8] 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 nonlinear methods revealed that the EEG is generated by a chaotic neural process of low dimension [9–12]. 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 nonlinear invariant measures such as correlation dimensions and Lyapunov exponents [11,13–16].

To the contrary, there is some evidence that EEG is not a chaotic signal of low dimension [17–19]. Osborne and Provenzale [17] demonstrated that $1/f$-like linear stochastic systems, so-called coloured noise, also result in a finite correlation dimension. Using the surrogate data methods, Theiler et al. [18] showed that the EEG is not produced by low dimensional chaos. Pritchard et al. [19] also applied the surrogate-data testing to a normal resting human EEG and showed that the normal resting human EEG was nonlinear 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 are, nonlinear 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 [20]. Many investigations with nonlinear methods have revealed possible medical applications for nonlinear analysis and have given rise to the possibility that the underlying mechanisms of the brain function may be explained by nonlinear dynamics [13,21–30]. Pathological conditions such as epileptic seizures, coma and dementia showed decreased chaotic activities in the EEG, whereas normal attentional states tended to show increased chaotic activities by the estimating the correlation dimension [22,29,31–33].

There are only a few studies about the nonlinear analysis of the EEG in schizophrenia. Previous studies estimated the nonlinear invariant measures of the EEG in schizophrenia at limited electrodes [34,35]. We tried to record the EEG from 16 channels in patients with schizophrenia in order to investigate the whole pattern of chaotic dynamics in the brain by the estimation of correlation dimension. Our result is somewhat different from previous results of nonlinear analysis of the EEG in schizophrenics, which is discussed in the later section.

Some problems exist, however, in applying nonlinear methods to experimental data. Classical algorithms for calculating nonlinear invariant measures from the experimental EEG data require a very large number of computations in the embedding process [36]. The amount of data required for meaningful results is beyond the experimental possibilities for physiological data [37,38]. In this paper, we use a new algorithm, which was proposed by Kennel et al. [39], to estimate the nonlinear invariant measures efficiently for finite noisy data. This algorithm is strikingly faster and more accurate than other algorithms [40–42]. 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 the procedure for reconstructing brain dynamics from an EEG and for analysing the EEG by nonlinear methods and our new algorithm for determining the proper embedding dimension and for compensating for both noise contamination and edge effects. The correlation dimension is 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 between the schizophrenic patients 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 modelling the brain by nonlinear dynamics. Our conclusions are given in Section 6.

2. Theory and algorithm

The brain may be considered as a dissipative dynamical system. A dynamical nth-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 undecomposable subset called an attractor [42].

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 $x_1, x_2, x_3,\ldots, x_n$ by using the so-called delay coordinates $y(t) = [x_j(t), x_j(t + T),\ldots, x_j(t + (d - 1)T)]$ 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 [42,43].

Attractors of dynamical systems can be characterised by nonlinear measures such as the correlation dimension. 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 noninteger 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 [16].

In the nonlinear analysis, we applied a reconstruction procedure to each EEG segment at first. For the time delay T, we used the first local minimum of the average mutual information between the set of measurements $v(t)$ and $v(t + T)$. 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 [44].

Classical algorithms for calculating the nonlinear invariant measures, such as the correlation dimension and the Lyapunov exponent for time signals, require a very large number of computations. We calculate a nonlinear 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 operate. In our new algorithm, we calculate the correlation dimension $D2$ in the minimum embedding dimension.

We determine the minimum embedding dimension by using the calculation method, presented by Kennel et al. [39], 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" neighbours and those on the orbit which are "false" neighbours. A false neighbour is a point in the data set that is a neighbour 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 neighbours of every orbit point in the multivariate phase space will be true neighbours. We define the embedding rate as the ratio of the true neighbours to the neighbours in the embedding dimension. Fig. 1 shows a typical example of the embedding rate as a function of the embedding dimension for an EEG segment (16 384 data points). The proper minimum embedding dimension was selected as 11 in this case. Next, we can estimate the correlation dimensions by calculating them only in the minimum embedding dimension, which is different from the conventional method [36]. Fig. 2 shows a comparison of the new method for calculating $D2$ with the old method. 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 [36]. In order to calculate $D2$, one computes the correlation integral function

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

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:

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

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

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

The graph of log $C(r)$ versus log r has a linear region called the scaling region. The GPA assumes that most
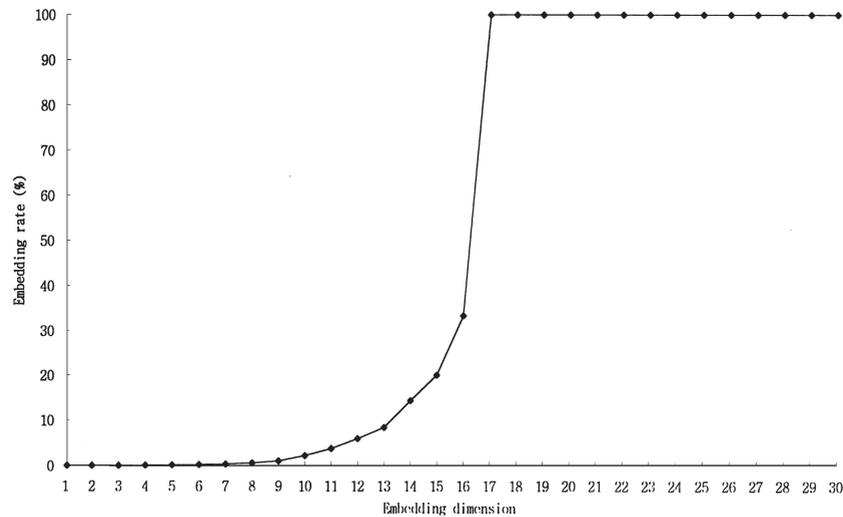
Fig. 1.   The embedding rate as a function of embedding dimension for a EEG segment (16,384 data points). The proper minimum embedding dimension for calculating the invariant measures was selected as 11 in this case.
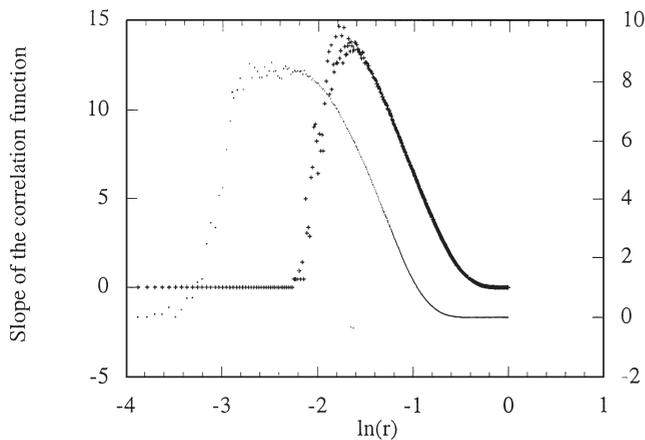

Fig. 2.   Comparison of the slope estimate at the minimum embedding dimension of 11 for an EEG at T4 in a subject with a higher embedding dimension of 32 as obtained by the classical GPA for the same data. The former has a larger scaling region.

of the information about the dimension is contained in the scaling region [8].

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 [45], of the GPA to prevent the anomalous structure in the correlation integral:

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

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

When we analyse 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 [46], of the GPA to compensate for the edge effect.

3. Materials and method

We studied 13 patients (four men, nine women; age 27.3 ± 8.5 years, mean ± SD) fulfilling DSM-IV. None of the patients had a history of neurological disorder or drug or alcohol abuse. The effects of neuroleptic drugs by cholopromazine (CPZ) equivalent doses were analysed with demographic data. The patients were under neuroleptic medication with a mean of 400.0 ± 65.8 mg CPZ-equivalent. The eight control subjects (three men and five women; age 31.1 ± 4.0 years) were healthy individuals with no history of psychiatric or neurological disease, who were selected from 11 normal volunteers. All subjects were right-handed and showed moderate amplitude (30–100 μV) on EEG background activities. We compared the schizophrenics with the age-and sex-matched controls. The EEGs were recorded from the 16 scalp loci of the international 10–20 system. With the subjects in a relaxed state with closed eyes, 32.768 s of data (16 384 data points) were recorded and digitised by a 12-bit analogue–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. Potential from 16 channels (F_7, T_3, T_5, F_{p1}, F_3, C_3, P_3, O_1, F_8, T_4, T_6, F_{p2}, 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. Whenever a decrease in vigilance was detected on the ongoing EEG, the technician instructed the patients to open his or her eyes, and a short pause was allowed if needed to minimise drowsiness. The recordings were obtained at approximately the same time of day (usually in the afternoon).

Statistical analysis was performed with SPSS (6.0 release version) and Independent Samples T tests were used to evaluate the difference between the schizophrenic patients and control groups.

4. Results

In the experiment, the schizophrenic patients consisted of four men and nine women, with a mean age of 27.3 ± 8.5 years and the control group consisted of three men and five women, with a mean age of 31.1 ± 4.016 years. There were no significant differences between the two groups by age and sex.

The values of $D2$ were calculated by a slightly modified version of the GPA. Time delays of 28–54 ms and embedding dimensions of 11–21 were used for the schizophrenic patients, and time delays of 28–44 ms and embedding dimensions of 13–19 were used for the controls. The slope of the correlation integral curve in the scaling region was estimated by a least-squares fitting method. The average values of $D2$ and the standard deviations for both the schizophrenic patients and the controls, for the 16 channels identified above, are summarized in Table 1. It can be seen that schizophrenic patients had a lower $D2$ at the left inferior frontal (F_7, $p = 0.005$) and anterior temporal electrodes (T_3, $p = 0.016$) compared with controls. It means that the chaotic activity of schizophrenia in the left frontotemporal area is lower than that in a normal brain.

5. Discussion

The recent developments in nonlinear dynamics have heralded a new understanding of many biological processes. The neurobiology of the various states of brain activity is being explored through the application of nonlinear dynamics. However, 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 nonlin-

Table 1
The average values of the $D2$ of the EEGs for all the subjects in all channels with their standard deviations (Independent Samples T tests)

Location	Schizophrenia ($N = 13$)		Control ($N = 8$)		T	P
	Mean	SD	Mean	SD		
F3	8.0323	0.733	7.9713	0.801	− 0.18	NS
F4	7.8485	0.817	8.0088	0.622	0.48	NS
F7	7.9577	0.427	8.8550	0.863	3.20	0.005
F8	8.2092	0.425	8.5000	0.506	1.66	NS
Fp1	7.9685	0.615	7.9535	1.050	− 0.40	NS
Fp2	7.7554	0.652	8.0588	0.649	1.04	NS
T3	7.6046	0.549	8.2025	0.418	2.64	0.016
T4	8.2038	0.489	8.2938	0.684	0.35	NS
T5	8.5038	0.450	8.3350	0.725	− 0.66	NS
T6	8.4015	0.387	8.5138	0.535	0.56	NS
C3	7.8400	0.466	8.1750	0.637	1.38	NS
C4	8.3808	0.460	8.3325	0.540	− 0.22	NS
P3	8.2754	0.651	8.6013	0.396	1.27	NS
P4	8.8369	0.467	8.6600	0.511	− 0.81	NS
O1	8.1623	0.655	8.2525	0.462	0.34	NS
O2	7.8469	0.860	7.7275	0.848	− 0.32	NS

NS, not significant.

ear parameters. First, it is much faster than classical algorithms which calculate nonlinear 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 nonlinear 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. The classical GPA has many kinks and apparently shrinks the scaling region, while our method preserves the dimensional measurement in a wider region [40,41]. Jeong et al. [40,41] 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 $D2$.

The hypothesis that the CNS is a nonlinear dynamical system exhibiting deterministic chaos has offered a fruitful tool to investigate the information processing in the brain. In the dynamical aspect, correlation dimension determines the number of independent variables which are necessary to describe the dynamics of the central nervous system.

There are some previous studies on chaotic dynamics of the schizophrenic brain. Elbert et al. [47] calculated the two descriptive measures (complexity and mobility) proposed by Hjorth and dimensional complexity of EEG from schizophrenic and normal subjects. They reported

that most schizophrenic patients exhibited higher frontal than central dimensional complexity values. They suggested that the simultaneous perception of the delusional and the real world by schizophrenic patients might be based on increased information-processing power expressed through higher correlation dimension, in which the frontal and the central dynamics are dissociated even in the relaxed waking state. Koukkou et al. [35] reported that the correlation dimension of the temporal–parietal EEG differed between first-episode schizophrenics and controls. It was significantly higher in first-episode schizophrenics than in controls. It is suggested that the higher dimensional complexity of functional brain mechanisms in schizophrenics versus normals is reminiscent of the loosened organization of thought, and of suggestions of certain superior abilities in the patients.

However, our studies are very different from previous studies on nonlinear analysis of the EEG in schizophrenic patients. In the first place, we estimated the nonlinear measure correlation dimension in all 16 channels, but previous studies estimated the correlation dimension $D2$ in a limited number of channels. In our result, we showed that schizophrenic patients in waking states had lower values of the correlation dimension at the left inferior frontal and anterior temporal electrodes compared with controls. This means that the chaotic activities of the left fronto-temporal regions in the schizophrenic brain are lower than those of normals. Our finding of decreased chaotic activities in the left fronto-temporal area in the schizophrenic brain is consistent with the findings of hypofrontality and hypotemporality reported in the studies on schizophrenia with linear analysis of EEG [6,5], cerebral blood flow [48–51], MRI [52] and positron emission tomography [53,54]. In the last half century an impressive number of studies have reported qualitative and quantitative EEG abnormalities in schizophrenia [3]. Diffuse slowing of EEG and the differences were often more pronounced in the left hemisphere [7]. Recent investigation using power spectral analysis further suggest slowing of brain electrical activities, especially in the frontal regions [55,56].

The temporal lobe is also implicated in schizophrenia [57]. It has been repeatedly reported that a significant minority of individuals with temporal lobe epilepsy suffer from prolonged and/or repeated instances of major psychopathology. Similarly, it has been repeatedly demonstrated in histological studies that the temporal lobes of schizophrenics are characterised by excessive focal temporal lobe neuronal damage, including gliosis as well as evidence of neural migration errors [58].

Our result reveals the hypofrontality and hypotemporality of the chaotic activity in the left hemisphere of schizophrenic patients. It means that the schizophrenic brain has decreased information processing and less flexible neural network in left fronto-temporal area. This result supports the hypothesis that the temporal and frontal areas are key structures of pathophysiology of schizophrenia.

One limitation was the fact that the antipsychotic medication was uncontrolled. In our study, the patients were taking neuroleptic medication with range of CPZ equivalent doses, 0–1000 mg. Although there was no correlation between the $D2$ and neuroleptic dosages and Itil and colleagues [4] also reported no effect of medication on EEG activities in patients with schizophrenia, our findings cannot be taken as a proof of the absence of drug effects (Table 2). We are now tempted to speculate that the presently observed patterns of $D2$ in the patients cannot be easily attributed to effects of medication, but adhere to the psychotic processes. This speculation, however, must be substantiated by future comparisons of medicated and unmedicated patients.

Absolute values for the nonlinear parameters can not be estimated in spite of all efforts because the brain is not a uniquely defined physical system. However, it is remarkable that we could still use nonlinear analysis to differentiate the brain states, such as a normal and a schizophrenic state, that present enough 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 of progress of the disease in patients. Consequently, the analysis should be made with care.

Table 2
Correlation coefficient and *p*-value between CPZ equivalent dosage and correlation dimensions of the patients with schizophrenia

Location	CPZ equivalent dosage	
	Person correlation coefficient	Significance (*p*-value)
F3	−0.496	0.085
F4	−0.054	0.862
F7	−0.023	0.940
F8	−0.140	0.648
Fp1	−0.502	0.081
Fp2	0.060	0.846
T3	−0.254	0.403
T4	0.182	0.552
T5	−0.268	0.375
T6	−0.330	0.270
C3	−0.021	0.852
C4	−0.021	0.945
P3	−0.149	0.626
P4	0.006	0.984
O1	−0.256	0.399
O2	−0.466	0.109

Correlation is significant at the 0.05 level (two-tailed).

6. Conclusion

The EEG is a dynamic measure that contains the ongoing brain activity. Recent progress in the theory of nonlinear dynamics has provided new methods to analyse the dynamical properties of EEG. However, nonlinear analysis has some problems when applied to experimental time-series data. We employed a new method which is strikingly faster and more accurate than previous ones, especially for limited noisy data.

In this paper, our result showed that schizophrenic patients in waking states had lower values of correlation dimension at the left inferior frontal and anterior temporal electrodes compared with controls. This result suggests that the left frontal and temporal areas should be key to the aetiology of schizophrenia due to lowered information processing. The implications of chaotic dynamics may shed light on our understanding of the brain and pathologic condition.

Acknowledgements

References

[1] Horn D, Ruppin E. Compensatory mechanisms in an attractor neural network model of schizophrenia. Neural Computation 1995;7:182–205.

[2] Liddle PF. Brain imaging. In: Hirsch SR, Weinberger DR, editors. Schizophrenia, 1st ed. Blackwell Science, New York, 1995:425–39.

[3] Itil TM. Qualitative and quantitative EEG findings in schizophrenia. Schizophr Bull 1977;3:61–79.

[4] Itil TM, Saletu B, Davis S. EEG findings in chronic schizophrenics based on digital computer period analysis and analog power spectra. Biol Psychiatry 1972;5:1–13.

[5] Hughes JR. A review of the usefulness of the standard EEG in psychiatry. Clinical Electroencephalogram 1996;27:35–9.

[6] Gattaz WF, Mayer S, Ziegler P, Platz M, Gasser T. Hypofrontality on topographic EEG in schizophrenia. Eur Arch Psychiatry Clin Neurosci 1992;241:328–32.

[7] Karson C, Coppola R, Daniel DG, Weinberger DR. Computerized EEG in schizophrenia. Schizophr Bull 1988;14:193–7.

[8] Babloyantz A, Salazar JM, Nicolis C. Evidence of chaotic dynamics of brian activity during the sleep cycle. Phys Lett 1985;111A:152–6.

[9] Rapp PE, Zimmerman ID, Albano AM, deGuzman GC, Greenbaun NN, Bashore TR. Experimental studies of chaotic neural behavior. Cellular activity and electroencephalographic signals. In: Othmer HG, editor. Nonlinear oscillations in biology and chemistry, Lecture notes in biomathematics. Springer-Verlag, Berlin, Heidelberg, New York, Tokyo, 1985:175–205.

[10] Röschke J, Başar E. The EEG is not a simple noise: Strange attractors in intracranial structures. In: Başar E, editor. Dynamics of sensory and cognitive processing by the brain. Springer-Verlag, Berlin, Heidelberg, New York, 1988:203–16.

[11] Babloyantz A. Chaotic dynamics in brain activity. In: Başar E, editor. Dynamics of sensory and cognitive processing by the brain. Springer-Verlag, Berlin, Heidelberg, New York, 1988:196–202.

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

[13] Babloyantz A, Destexhe A. The Creutzfeld–Jacob disease in the hierarchy of chaotic attractor. In: Markus M, Muller S, Nicolis G, editors. From chemical to biological organization. Springer-Verlag, Berlin, Heidelberg, New York, 1987:307–16.

[14] Röschke J, Aldenhoff J. The dimensionality of the human's electroencephalogram during sleep. Biol Cybern 1991;64:307–13.

[15] Röschke J, Fell J, Beckman P. The calculation of the first positive Lyapunov exponent in sleep EEG data. Electroenceph Clin Neurophysiol 1993;86:348–52.

[16] Fell J, Röschke J, Beckmann P. The calculation of the first positive Lyapunov exponent in sleep EEG data. Electroenceph Clin Neurophysiol 1993;86:348–52.

[17] Osborne AR, Provenzale A. Finite correlation dimension for stochastic systems with power-law spectra. Physica D 1989;35:357–81.

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

[19] Pritchard WS, Duke DW, Krieble KK. Dimensional analysis of resting human EEG II: Surrogate data testing indicates nonlinearity but not low-dimensional chaos. Psychophysiology 1995;32:486–91.

[20] Rapp PE. Chaos in the neurosciences : cautionary tales from the frontier. Biologist 1993;40:89–94.

[21] Babloyantz A, Destexhe A. Low-dimensional chaos in an instance of epilepsy. Proc Natl Acad Sci USA 1986;83:3513–7.

[22] Frank GW, Lookman T, Nerenberg MAH, Essex C, Lemieux J, Blume W. Chaotic time series analysis of epileptic seizures. Physica D 1990;46:427–38.

[23] Besthorn C, Sattel H, Geiger-Kabisch C, Zerfass R, Forstl H. Parameters of EEG dimensional complexity in Alzheimer's disease. Electroenceph Clin Neurophysiol 1995;95:84–9.

[24] Fell J, Röschke J, Beckmann P. Nonlinear analysis of sleep EEG data in schizophrenia: calculation of the principal Lyapunov exponent. Psychiatry Research 1995;56:257–69.

[25] Pritchard WS, Duke DW, Coburn KL. Altered EEG dynamical responsivity associated with normal aging and probable Alzheimer's disease. Dementia 1991;2:102–5.

[26] Pritchard WS, Duke DW, Coburn KL, Moore NC, Tucker KA. Altered EEG dynamical responsivity associated with Alzheimer's disease: replication and extension. In: Jansen BH, Brandt, ME, editors. Proceedings of the Second Annual Conference on Nonlinear Dynamical Analysis of the EEG. World Scientific, Singapore, 1993:165–8.

[27] Prichard WS, Duke DW, Coburn KL, Moore NC, Tucker KA, Jann MW, Hostetler RM. EEG-based-neural-net predictive classification of Alzheimer's disease versus control subjects is augmented by non-linear EEG measures. Electroenceph Clin Neurophysiol 1994;91:118–30.

[28] Stam CJ, Tavy DLJ, Jelles B, Achtereekte HAM, Slaets JPJ, Keunen RWM. Nonlinear dynamical analysis of multi-channel EEG data: clinical applications in dementia and Parkinson's disease. Brain Topography 1994;7:141–50.

[29] Stam CJ, Jelles B, Achtereekte HAM, Rombouts SARB, Slaets JPJ, Keunen RWM. Investigation of EEG nonlinearity in dementia and Parkinson's disease. Electroenceph Clin Neurophysiol 1995;95:309–17.

[30] Stam CJ, Jelles B, Achtereekte HAM, Birgelen JH, Slaets JPJ. Diagnostic usefulness of linear and nonlinear quantitative EEG

analysis in Alzheimer's disease. Clinical Electroencephalography 1996;27:69–77.

[31] Pijn JP, Van Neerven J, Noest A, Lopes Da Silva FH. Chaos or noise in EEG signals; dependence on state and brain site. Electroenceph Clin Neurophysiol 1991;79:371–81.

[32] Rapp PE, Bashore THR, Martinerie JM, Albano AM, Zimmerman ID, Mees AI. Dynamics of brain electrical activity. Brain Topography 1989;2:99–118.

[33] Lutzenberger W, Birbaumer N, Flor H, Rockstroh B, Elbert T. Dimensional analysis of the human EEG and intelligence. Neuroscience Letters 1992;143:10–14.

[34] Röschke J, Aldenhoff J. Estimation of the dimensionality of sleep—EEG data in schizophrenics. Eur Arch Psychiatry Clin Neurosci 1993;242:191–6.

[35] Koukkou M, Lehmann D, Wackermann J, Dvorak I, Henggeler B. Dimensional complexity of EEG brain mechanisms in untreated schizophrenia. Biol Psychiatry 1993;33:397–407.

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

[37] Smith LA. Intrinsic limits on dimension calculation. Phys Lett A 1988;133(6):283–8.

[38] Eckmann JP, Ruelle D. Fundamental limitations for estimating dimensions and Lyapunov exponents in dynamical systems. Physica D 1992;56:185–7.

[39] Kennel MB, Brown R, Abarbanel HDI. Determining embedding dimension for phase-space reconstruction using a geometrical construction. Phys Rev A 1992;45:3403–11.

[40] Jeong J, Joung M, Kim SY. Quantification of emotion by nonlinear analysis of the chaotic dynamics of EEGs during perception of 1/f music. Biol Cybern 1998;78:217–25.

[41] Jeong J, Kim SY, Han SH. Nonlinear analysis of chaotic dynamics underlying EEGs in patients with Alzheimer's disease. J Electroenceph and Clin Neurophys 1998;106(3):220–8.

[42] Eckmann JP, Ruelle D. Ergodic theory of chaos and strange attractors. Rev Mod Phys 1985;57(3,PartI):617–56.

[43] Takens F. Detecting strange attractors in turbulence in dynamical systems and turbulence. Lecture Notes in Mathematics 898. Springer, Berlin, 1981:366–81.

[44] Fraser AM, Swinney HL. Independent coordinates for strange attractors from mutual information. Phys Rev A 1986;33(2):1134–40.

[45] Theiler J. Spurious dimension from correlation algorithm applied to limited time-series data. Phys Rev A 1986;34(3):2427–32.

[46] Dvořak I, 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):225–31.

[47] Elbert T, Luutzenberger W, Rockstroh B, Berg P, Cohen R. Physical aspects of the EEG in schizophrenics. Biol Psychiatry 1992;32:595–606.

[48] Paulman RG, Devous MD, Gregory RR, Herman JH, Jennings L, Bonte FJ, Nasrallah HA, Raese JD. Hypofrontality and cognitive impairment in schizophrenia: dynamic single-photon tomography and neuropsychological assessment of schizophrenic brain function. Biol Psychiatry 1990;27:377–99.

[49] Ingvar DH, Franzen G. Abnormalities of cerebral blood flow distribution in patients with chronic schizophrenia. Acta Psychiat Scand 1974;50:425–62.

[50] Andreasen NC, Rezai K, Alliger R, Swayze VW, Flaum M, Kirchner P, Cohen G, O'Leary DS. Hypofrontality in neuroleptic-naive patients and in patients with chronic schizophrenia. Arch Gen Psychiatry 1992;49:943–58.

[51] Catafu AM, Parellada E, Lomena FJ, Bernardo M, Pavia J, Ros D, Setoain J, Gonzalez-Monclus E. Prefrontal and temporal blood flow in schizophrenia: Resting and activation Technetium-99m-HMPAO SPECT pattern in young neuroleptic-naive patients with acute disease. J Nucl Med 1994;35:935–41.

[52] Barta PE, Pearlson GD, Powers RE, Richards SS, Tune LE. Auditory hallucinations and smaller superior temporal gyral volume in schizophrenia. Am J Psychiatry 1990;147:1457–62.

[53] Buchsbaum MS, Ingvar DH, Kessler R, Waters RN, Cappelletti J, Van Kammen DP, King AC, Johnson JL, Manning RG, Flynn RW, Mann LS, Bunney WE, Sokoloff L. Cerebral glucography with positron tomography. Arch Gen Psychiatry 1982;39:251–9.

[54] Buchsbaum MS, DeLisi LE, Holcomb HH, Cappelletti J, King AC, Johnson J, Hazlett E, Dowling-Zimmerman S, Post RM, Morihisa J, Carpenter W, Cohen R, Pickar D, Weinberger DR, Margolin R, Kessler RM. Anteroposterior gradients in cerebral glucose use in schizophrenia and affective disorders. Arch Gen Psychiatry 1984;41:1159–66.

[55] Morihisa JM, Duffy FH, Wyatt RJ. Brain electrical activity mapping (BEAM) in schizophrenic patients. Arch Gen Psychiatry 1983;40:719–28.

[56] Morstyn R, Duffy FH, McCarley RW. Altered topography of EEG spectral content in schizophrenia. Electroenceph Clin Neurophysiol 1983;56:263–71.

[57] Crow TJ. Temporal lobe asymmetries as the key to the etiology of schizophrenia. Schizophr Bull 1990;16:433–43.

[58] Taylor DG. Advances in the neuropathology of schizophrenia. In: den Boer JA, Westenberg HGM, van Praag HM, editors. Advances in the neurobilogy of schizophrenia, 1st ed. John Wiley & Sons, New York, Berlin, 1995:111–30.