# Non-Linear Dynamical Analysis of Multichannel EEG: Clinical Applications in Dementia and Parkinson's Disease

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Abstract: The irregular, aperiodic character of the EEG is usually explained by a stochastic model. In this view the EEG is linearly filtered noise. According to chaos theory such irregular signals can also result from low dimensional deterministic chaos. In this case the underlying dynamics is nonlinear, and has only few effective degrees of freedom. In contrast, stochastic models are less efficient, because they require in principle infinite degrees of freedom. Chaotic dynamics in the EEG can be studied by calculating the correlation dimension (D2). Although it has become clear that D2 calculations alone cannot prove chaos, the D2 has potential value as an EEG diagnostic. In this study we investigated whether D2 could be used to discriminate EEGs from normal controls, demented patients and Parkinson patients. We have analyzed epochs (20 channels; 2.5 s) from 52 EEGs (20 controls; 15 patients with dementia; 17 patients with Parkinson's disease). Controls had a mean D2 of 6.5 (0.9); demented patients of 4.4 (1.5), and Parkinson patients of 5.3 (0.9). Both groups were significantly different from controls ($p < 0.001$). There was a significant positive correlation between D2 and relative power in the beta band ($r = 0.81$) and a significant negative correlation between D2 and power in the delta ($r = -0.60$) and theta band ($r = -0.37$). These results suggest the possible usefulness of multichannel D2 estimations in a clinical setting.

Key words: Chaos; Nonlinear dynamics; Correlation dimension; EEG; Dementia; Parkinson's disease.

## Introduction

The tacit assumption underlying the use of Fourier based methods for EEG analysis is that the EEG results from a large number of random processes. In this view the EEG is considered to be filtered noise. Recent developments in the mathematics of nonlinear dynamical systems ("chaos theory") have suggested an alternative model. This approach tries to analyze the relationship between cortical dynamics and the EEG in terms of deterministic instead of random processes (Jansen 1991). A primary motivation for the alternative approach is that low dimensional chaos, if it can be proven, actually is a far more simple (and therefore better, if we use Occam's razor) explanation for the irregularity of the EEG than the filtered noise model (Theiler 1990). Chaotic dynamics with a small number of effective degrees of freedom opens the way for reverse modelling, that is deriving equations describing the dynamics of a system from a series of measurements on the system (Crutchfield and McNamara 1987). For readers unfamiliar with chaos theory, a short explanation is given in an appendix to this paper. Valuable information can also be found in a number of earlier papers in this journal (Lutzenberger et al. 1992; Rapp et al. 1989) and in a number of reviews such as: Farmer et al. (1983); Eckmann and Ruelle (1985); Theiler (1990); Denton and Diamond (1991); Grassberger et al. (1991); Jansen (1991) and Pritchard and Duke (1992).

Several methods have been described to study chaotic dynamics. From a series of measurements of only one variable of the system an approximation of the attractor can be reconstructed (Takens 1981). If a number of simultaneous series of measurements is available, the attractor can be reconstructed with so called spatial embedding (Destexhe et al. 1988; Dvorák 1990; Wackermann et al. 1993). According to Eckmann and Ruelle (1985) spatial embedding should be used whenever possible. Grassberger and Procaccia (1983) described a powerful algorithm to estimate the dimension (correlation dimension or D2) of the reconstructed attractor. Non-integer values for D2 suggest a strange attractor and chaotic dynamics. It should be stressed that in principle it is impossible to distinguish between chaos and random processes with Fourier analysis alone, because the

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spectrum will be broadband in both cases. Wolf et al. (1988) described an algorithm to estimate the largest Lyapunov exponent from an attractor. The Lyapunov exponent is a measure for the divergence rate of nearby points on the attractor. A positive largest Lyapunov exponent indicates sensitive dependence on initial conditions and is a powerful argument for chaotic dynamics.

Many authors have attempted to use these techniques to investigate whether or not the EEG shows evidence of low dimensional deterministic chaos. Babloyantz et al. (1985) were probably the first to estimate the correlation dimension of the human scalp recorded EEG. They found an attractor with dimension 4.05 during sleep stage 4. In a later study a chaotic attractor with dimension 2.05 and a positive Lyapunov exponent were found during a petit mal seizure (Babloyantz and Destexhe 1986). Positive Lyapunov exponents were identified during the waking / eyes closed state, sleep stage 4 and during Creutzfeldt Jakob coma (Gallez and Babloyantz 1991). Rapp et al. (1985) reported low D2 values calculated from single unit recordings in monkey cortex. Detailed EEG recordings from the bulbus olfactorius in the rabbit indicate chaotic dynamics which is intimately related to sensory information processing (Skarda and Freeman 1987; Skinner et al. 1992; Freeman 1991). Nan and Jinghua (1988) studied three subjects during a resting condition (awake / eyes closed) and during mental arithmetic. In the one left handed subject, D2 increased at the right centro-temporal lead during mental arithmetic; in the two right handed subjects, D2 increased at the left centro-temporal lead.

Rapp et al. (1989) investigated five subjects during rest and mental activity. Prior to calculating the D2 they used single value decomposition as a noise reducing technique. In this study D2 also increased during mental activity, and was highest in the most demanding task. In a larger study correlation dimensions were calculated from 15 electrodes in 31 subjects during a variety of tasks (Lutzenberger et al. 1992). D2 values were higher during mental imaging than during perceptual processing. In this study a comparison was made with Fourier analysis. D2 estimations contained information that was not available from Fourier analysis. Röschke et al. (1993) estimated the Lyapunov exponent in 15 subjects during the four sleep stages, and found a systematic decrease going from stage I to stage IV sleep.

Initially, saturation of D2 versus embedding dimension, and non-integer values of the D2 were considered by many authors as sufficient evidence for low dimensional chaos (see for instance Babloyantz 1985, and many of the other studies cited above). Demonstration of a positive largest Lyapunov exponent was also considered to prove chaotic dynamics. However, calculation of measures such as D2 from relatively short epochs of noise contaminated EEG data are hampered by serious difficulties which can undermine their usefulness in proving chaotic dynamics. For instance, it has been shown that short epochs of filtered noise can mimic low dimensional chaotic attractors (Rapp et al. 1993). Filtered noise can also give rise to a positive largest Lyapunov exponent (Theiler et al. 1992). Alternative techniques have been developed to test for the presence of determinism in short, noise contaminated time series.

A very general and thorough approach has been developed by Theiler et al. (1992). Experimental time series are compared with a series of test signals, which share some important property (for instance the power spectrum) with the original signal but are otherwise random. A statistic (for instance D2, but in principle any measure can be used) is calculated from the time series and the test signals. The values of the statistic from the original time series can now be expressed as a z-score (deviation from the mean values of the statistic for the test signals expressed in number of standard deviations). With this approach, the likelihood that the original time series is in fact different from filtered noise can be specified exactly. Theiler et al. (1992) found evidence for determinism (but not for low dimensional chaos) in 1 out of 2 investigated EEG time series. Glass et al. (1993) examined real EEG signals en EEG signals from artificial neural nets using the surrogate data method of Theiler and an alternative method developed by the authors. With both methods evidence for determinism was only found in the artificial EEG, but not in the real EEG data. Using a simplified version of Theiler's method (with only one random test signal) Pijn et al. (1991) found evidence for low dimensional deterministic chaos in rat EEG only during an epileptic seizure, but not during other states. These studies suggest that claims for low dimensional chaos in the EEG based only on D2 or Lyapunov exponent calculations should be viewed with extreme skepticism. The question whether in general the EEG should be modelled as deterministic chaos or filtered noise cannot be answered on the basis of the presently available evidence; the answer will have to come from future studies using the rigorous control methods as suggested by Theiler et al. (1992) and Glass et al. (1993).

However, even though D2 calculations by themselves cannot prove chaotic dynamics, D2 could still have some value as an interesting EEG diagnostic. In the first place, a significant amount of data reduction is achieved, in particular when spatial embedding is used. Secondly, the relationship of D2 values and different brain states is of potential interest. Low values of D2 are generally associated with deep sleep or pathology (coma, Creutzfeldt Jakob, epilepsy). Intermediate values are found during the awake / eyes closed state and the highest values are associated with mental activity. This

suggest D2 estimations could be useful in a clinical setting, but so far there have been only few reports of D2 in neurological disease.

In this study we examined the potential clinical usefulness of D2 estimations using the multichannel approach as suggested by Dvorák (1990). We calculated the global D2 from EEGs of control subjects, demented patients and Parkinson patients. Dementia is known to be associated with EEG changes (Maurer and Dierks 1992; Soininen and Riekkinen 1992; Schreiter-Gasser et al. 1993). In the early stages of the disease, EEG changes can be mild or absent. Several attempts have been made to increase the sensitivity of the EEG in early dementia, such as topographic mapping (Maurer and Dierks 1992), and specific analysis of the response to photostimulation (Drake et al. 1989; Politoff et al. 1992). Similar considerations apply to Parkinson's disease. Although uncomplicated Parkinson's disease is not associated with EEG changes, demented Parkinson patients do show EEG changes (Neufeld et al. 1988; Soikkeli et al. 1991). If the multichannel D2 contains information that is not available from visual analysis or Fourier analysis of the EEG, it could potentially contribute to diagnosis in Parkinson's disease and dementia. As a first step however, it is necessary to investigate whether there are group differences in D2 for demented and Parkinson patients compared with controls. This was the main object of this study.

## Methods

### Study protocol

EEGs were selected as follows. From each digital EEG recorded in the department since 1988 (Cadwell Spectrum RDC 32 digital EEG apparatus) an amount of data have been stored in a database. With this database 15 randomly selected EEGs of patients with the clinical diagnosis of dementia, and 17 randomly selected EEGs of patients with Parkinson's disease were retrieved from the archive on optical disks. The EEGs of the control group were selected as follows. Starting from a random point in the EEG archive consecutive EEGs were judged according to the following criteria: 1. age of patient over 50 years; 2. no diagnosis of dementia or Parkinson's disease; 3. normal EEG on visual inspection (falling in category 1 or 2; see below for definition of the categories). This procedure was continued until 20 EEGs fulfilling the criteria had been found.

Each EEG was inspected visually and scored according to a 4 point scale (1 = normal; 2 = low voltage fast activity; 3 = mild diffuse slowing; 4 = severe diffuse slowing). Category 1 and 2 were considered to be normal; category 3 and 4 abnormal. From each EEG one representative artifact-free epoch of 2.5 seconds was chosen (20 channels; average reference; low pass 70 Hz, time constant 1 second, sample frequency 200 Hz, 8 bit amplitude representation) and copied as an ASCII file to a personal computer (Tandon 386 MCS slc/50 ) for further analysis (calculation of D2 and FFT).

Clinical files from all patients (controls, demented and Parkinson patients) were retrieved. Diagnosis was checked against the clinical file. In the case of dementia, NINCDS/ADRDA (National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and related Disorders Association) criteria for "possible Alzheimer disease" had to be fulfilled (this was the case in all 15 patients). Age, sex and disease duration were recorded. In 7 demented patients MMSE (Mini Mental State examination) scores could be retrieved.

### Software

Analysis of the EEG epochs, in particular calculation of the power spectra and estimation of the correlation dimension was done using software developed at our department. The program was written in Borland Pascal with Objects 7.0. Spectral analysis was done with a FFT algorithm. With 512 samples per epoch and a sample frequency of 200 Hz maximum resolution of the spectrum was 0.39 Hz. The spectrum was analyzed from 1.5 to 50 Hz. Relative power was calculated for 4 frequency bands: delta (1.56 - 3.9Hz); theta (4.29 - 7.82 Hz); alpha (8.19 - 12.48 Hz) and beta(12.87 - 49.84). For statistical analysis, relative power in each band was averaged over all 20 electrodes.

### Calculation of multichannel D2

The multichannel D2 is calculated from an EEG epoch consisting of 20 channels with 512 samples per channel (sample frequency 200Hz; 8 bit data path). From these data a series of vectors x(i), i= {1..512} is constructed. The coordinates of the vectors are the sample values of the 20 channels at one of the 512 discrete time points. The EEG epoch is thus represented as a series of 512 points (vectors) in a 20 dimensional phase space, each "axis" corresponding with one of the original 20 EEG channels. This series of points constitutes a geometrical shape, which, if certain conditions are met, is an approximation of the systems attractor.

The dimension of the reconstructed attractor is calculated as follows. One of the vector points is taken as a reference. Around this reference point a 20 dimensional sphere with radius r is drawn. Next, the fraction (between 0 and 1) of vector points that fall within the sphere with radius r is calculated. This is the number of points that lie closer to the reference point than a distance r divided by the total number of points. The same proce-

Table I. Result of visual classification of EEGs. EEG classes: 1: normal; 2: low voltage fast EEG; 3: mild diffuse slowing; 4: severe diffuse slowing. (Chi square = 51.34; $p < 0.001$).

| EEG Class | Controls | Dementia | Parkinson | Total |
|---|---|---|---|---|
| 1 | 4 | 3 | 9 | 16 |
| 2 | 16 | 0 | 0 | 16 |
| 3 | 0 | 7 | 8 | 15 |
| 4 | 0 | 5 | 0 | 5 |
| Total | 20 | 15 | 17 | 52 |

dure is repeated for all of the points on the attractor, and for a range of values for r. Thus, for each value of r, an average value for the fraction of points lying closer together than r can be calculated. This fraction is called the correlation integral Cr. The formula for Cr is:

$$Cr(r) = 2/N^2 \sum_{i=1,\, j=i+1}^{N} H(r - |x(i) - x(j)|)$$

Here N is the number of vectors, and H denotes the Heaviside function, which is 1 if the distance between the two vectors is smaller than r, and 0 if the distance between the two vectors is larger than r. A very important characteristic of the correlation integral is that for relatively small values of r, and a sufficient number of points N the following relation holds:

$$Cr \propto r^{D2}$$

where D2 is the correlation dimension. Taking logarithms shows that, for a certain range of values of r, the slope of log(Cr) versus log(r) is equal to D2.

$$LOG(Cr) \propto D2 * LOG(r)$$

In order to calculate D2, the first derivative of the log(Cr) versus log(r) curve is plotted. This is in fact a plot of D2 against log(r). If, for a certain range of r, a plateau is present in this curve, we take D2 to be the value of this plateau. Each D2 / log(r) curve was inspected visually, and reasonable upper and lower bounds for r were chosen on the basis of this visual inspection. To estimate the height of the plateau, we calculated the number of crossings of the D2 / log(r) curve (within the reasonable range of values for r) with straight lines plotted at increasing value of D2. This procedure was repeated for a range for values for D2 (from 1.5 to 15, increment 0.01). The value of D2 for which the maximum number of crossings between the line and the curve was found, was taken as an estimate of D2. On visual inspection the estimates of D2 thus obtained corresponded very well with the largest plateau present in the D2 versus log(r) curve.

### Statistics

Storage of data and statistical procedures were done using the statistical package Systat (version 5.01 for Windows). Group differences were tested with a two tailed t-test for independent samples or with an ANCOVA with age as a covariable. Cross tabs were evaluated with the Chi square test. Correlations were tested with the Pearson correlation coefficient, and with a multiple linear regression.

## Results

EEGs of 52 subjects were studied. Of these 20 belonged to the control group (mean age 62.1 year, s.d. 10.4; 14 females, 6 males); 15 to the demented group (mean age 80.8 year, s.d. 9.0; 9 females, 6 males), and 17 to the Parkinson group (mean age 77.0 year, s.d. 5.9; 8 females, 9 males). Mean disease duration (s.d.) was 1.45 (0.72) year in the demented group, and 4.7 (4.0) year in the Parkinson group. In view of the age differences between the control group and the demented and Parkinson groups, age was used as a covariable in all statistical tests on neurophysiological differences between controls and patients. Disease duration was shorter in the demented group than in the Parkinson group, but reliable information could not always be retrieved from the clinical records.

Results of the visual classification of the EEGs are shown in table I. Per definition, EEGs of the controls fall in class 1 or 2; however there is a relative preponderance of low voltage fast EEGs. In the demented group, 3 EEGs were considered to be normal on visual inspection. Most EEGs were classified as "mild or severe slowing". In the Parkinson group, 9 EEGs were normal on visual inspection, and 8 showed mild diffuse slowing. In both patient groups none of the EEGs was classified as class 2 (low voltage fast activity). For statistical analysis, results for EEG classes 1 and 2 (normal) and 3 and 4 (abnormal) were clustered. There were significantly more abnormal EEGs in the demented group than in the control group (Fisher exact test, two tailed, $p < 0.001$). There were also more abnormal EEGs in the Parkinson group compared to controls (Fisher exact test, two tailed, $p < 0.001$).

For analysis of the FFT results relative power in each of the four main frequency bands was averaged over all electrodes. Results are shown in table II. Again, there is a preponderance of relative power in the beta band in the control group. Group differences were tested with an ANCOVA, with age as covariable. Demented patients had more power in the delta ($F(1,32) = 10.285$; $p < 0.003$) and theta bands ($F(1,32) = 12.099$; $p < 0.001$), and less

Table II. Mean relative power (%) in the four frequency bands, averaged over alle 20 electrode sites. Standard deviation in brackets. ANCOVA (analysis of covariance, with age as covariable): *significant difference from controls; $p < 0.05$; ** $p < 0.005$; #significant difference between dementia and Parkinson's disease; $p < 0.05$; ## $p < 0.005$.

| | Controls | Dementia | Parkinson |
|---|---|---|---|
| Delta | 21.1 (8.0) | 40.5 (21.8) ** | 22.8 (9.2) ## |
| Theta | 13.0 (3.0) | 32.4 (13.9) ** | 28.7 (16.3) ** |
| Alpha | 26.5 (14.7) | 13.8 (9.8) | 28.7 (16.3) ## |
| Beta | 39.4 (12.4) | 13.4 (10.2) ** | 19.8 (10.3) ** |

Table III. Correlation coefficients. Data are shown for all subjects in who a D2 could be calculated (N= 47). *: $p < 0.05$; **: $p < 0.005$.

| | Age | D2 | Delta | Theta | Alpha | Beta |
|---|---|---|---|---|---|---|
| Age | 1 | | | | | |
| D2 | -0.395** | 1 | | | | |
| Delta | 0.226 | -0.597** | 1 | | | |
| Theta | 0.437** | -0.371* | 0.046 | 1 | | |
| Alpha | -0.125 | 0.172 | -0.619** | -0.426** | 1 | |
| Beta | -0.534** | 0.811** | -0.476** | -0.476** | 0.06 | 1 |

power in the beta band ($F(1,32) = 24.281$; $p < 0.001$) compared with controls. Parkinson patients had more power in the theta band ($F(1,34) = 15.088$; $p < 0.001$), and less power in the beta band ($F(1,34) = 16.594$; $p < 0.001$) compared with controls. In comparison with demented patients, Parkinson patients had less power in the delta band ($F(1,29) = 9.420$; $p < 0.005$ ) and more power in the alpha band ($F(1,32) = 10.705$; $p < 0.003$).

In a few cases (2 controls, 1 demented patient and 2 Parkinson patients) the D2 / log(r) curve did not show a clear scaling region, mostly due to excess muscle artifact. In these cases no reliable D2 could be calculated. Results of the multichannel D2 calculation are shown in figure 1. Mean D2 (s.d. in brackets) in the control group was 6.54 (0.9), in the demented group 4.45 (1.5), and in the Parkinson group 5.28 (0.9). Compared with controls, D2 was significantly lower in the demented group ($F(1,30) = 14.368$; $p < 0.001$) and in the Parkinson group ($F(1,31)= 9.410$; $p < 0.004$). Although D2 is somewhat higher in the Parkinson group than in the demented group, this difference was not significant ($F(1,26) = 3.206$; $p < 0.085$). Examples of individual curves for a control subject, a demented subject and a Parkinson patient are shown in figure 2, 3 and 4.

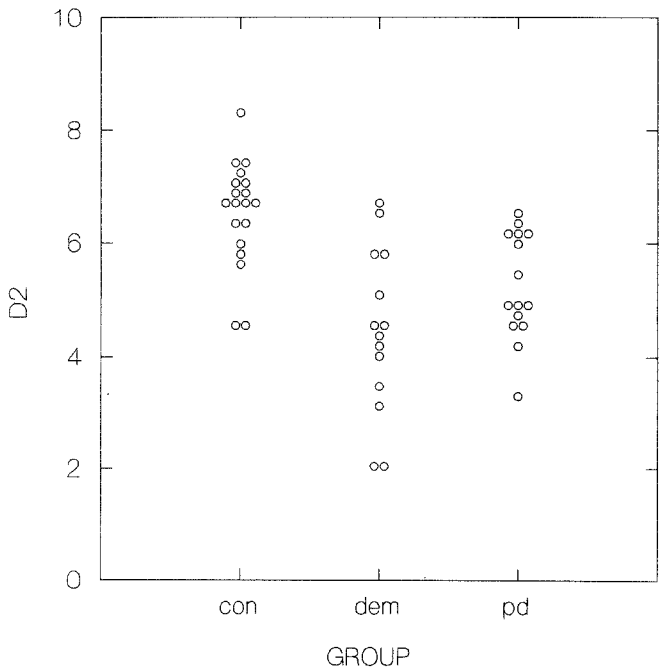


Figure 1. Plot showing the individual D2 values for controls (N=20), demented patients (N=15) and Parkinson patients (N=17).

Correlations between age, D2 and relative power in the four frequency bands are shown in table III. Higher age is significantly correlated with lower D2 values, less power in the beta band and more power in the delta band. Higher D2 values are correlated with less power in the delta and the theta bands, and with more power in the beta band. Multiple linear regressions were done with D2 as dependent variable, and total power in the four frequency bands as independent measures and age as a covariable. After this correction for age effects, there is still a significant negative correlation between D2 and power in the delta band (standard coefficient = -0.535; $p < 0.001$), and a significant positive correlation between D2 and power in the beta band (standard coefficient = 0.840; $p < 0.001$).

Mean D2 values (s.d. in brackets) for the visual classification groups were for class 1: 5.73 (0.96); class 2: 6.75 (0.85); class 3: 4.82 (0.91) and class 4: 3.35 (1.36). D2 values are highest for class 2, and decrease going from class 1 to 3 and 4. There is a significant global effect of EEG class on D2 ($F(3,44) = 19.509$; $p < 0.001$). Post hoc analysis (Bonferroni adjustment) showed significant differences in D2 between class 1 and 2 ($p < 0.037$); class 1 and 4 ($p < 0.001$); class 2 and 3 ($p < 0.001$); class 2 and 4 ($p < 0.001$) and class 3 and 4 ($p < 0.030$).

## Discussion

This study demonstrated a decrease of multichannel D2 in demented and Parkinson patients. Low values of

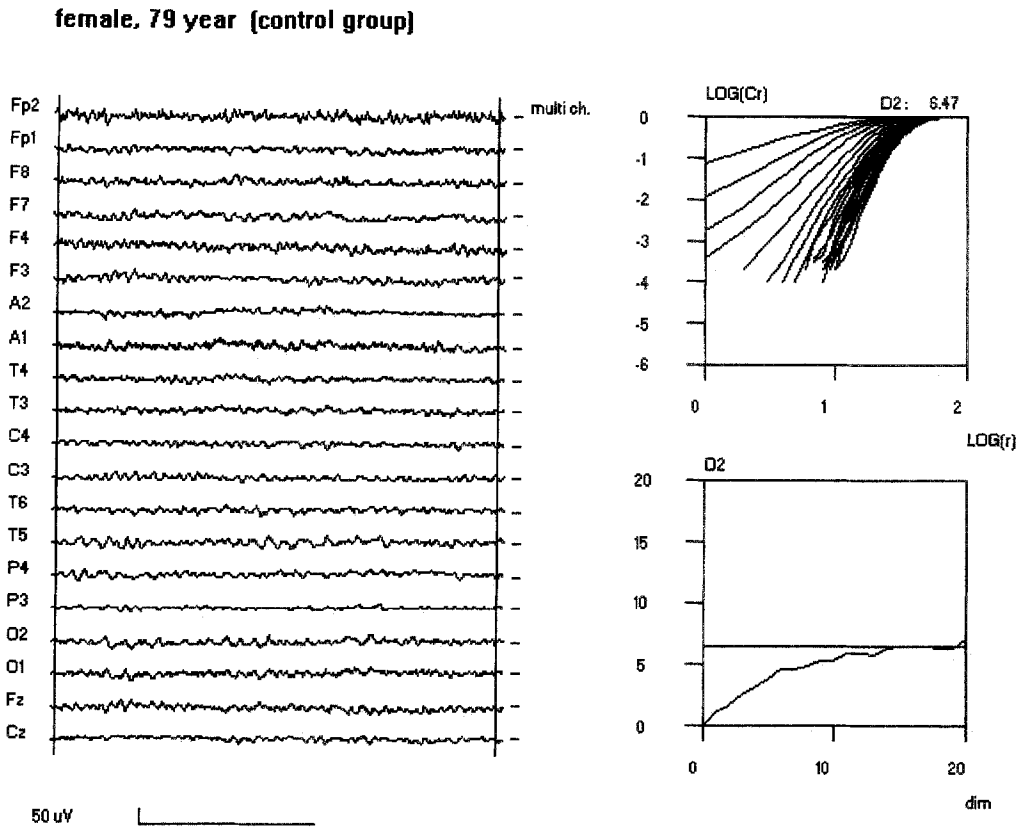


Figure 2. Subject from the control group. The left part shows the EEG epoch (2.5 seconds; average reference). The graph in the upper right shows the Log(Cr) / Log(r) curve for increasing spatial embedding from 1 to 20 channels. The straight part of the curve converges to a limit. The curve in the lower right shows D2 as a function of spatial embedding (number of channels used in the reconstruction of the attractor). D2 converges to a limit.

D2 were associated with increased relative power in the delta and theta bands, and less power in the beta band. D2 values of EEG fragments also correlated with a classification based upon visual analysis. However, D2 analysis could not discriminate between demented and Parkinson patients as well as Fourier analysis. Spectral analysis showed a more severe slowing of the EEG in demented than in Parkinson patients. There was a trend for lower D2 values in the demented group compared with controls, but this was not significant.

Our demonstration of generalized slowing of the EEG in demented and Parkinson patients corresponds with the findings of other authors (Maurer and Dierks 1992; Soininen and Riekkinen 1992; Schreiter-Gasser et al. 1993). Despite the relatively short disease duration in the demented group, the degree of EEG slowing suggests rather severe disease. The most likely explanation for the intermediate slowing found in the Parkinson group is that at least some of them were suffering from (early) dementia. Due to the retrospective nature of the study, no definite conclusions can be drawn on the exact number of demented Parkinson patients.

D2 values in the control group are only slightly higher than D2 values found in the "awake / eyes closed" state by Destexhe et al. (1988) and Dvorák (1990). The slightly higher D2 values in our study could be related to preponderance of beta activity in the EEGs of controls (higher D2 values correlated significantly with more power in the beta band). Our control subjects were also much older than those studied by Destexhe et al. (1988) and Dvorák (1990). Changes in D2 in Alzheimer's disease were also reported by Pritchard et al. (1991). In this study there was no difference in D2 of the eyes closed / resting condition between controls and Alzheimer patients. However, in the control group D2 increased on eye opening, whereas D2 remained the same in the Alzheimer group. There are no prior studies on D2 in Parkinson's disease. The present results confirm the general impression so far, that brain pathology is usually associated with a decrease, and not with an increase in D2 values.

The retrospective nature of the present study poses some limitations on its clinical aspects. Although all medical records were studied extensively, and the

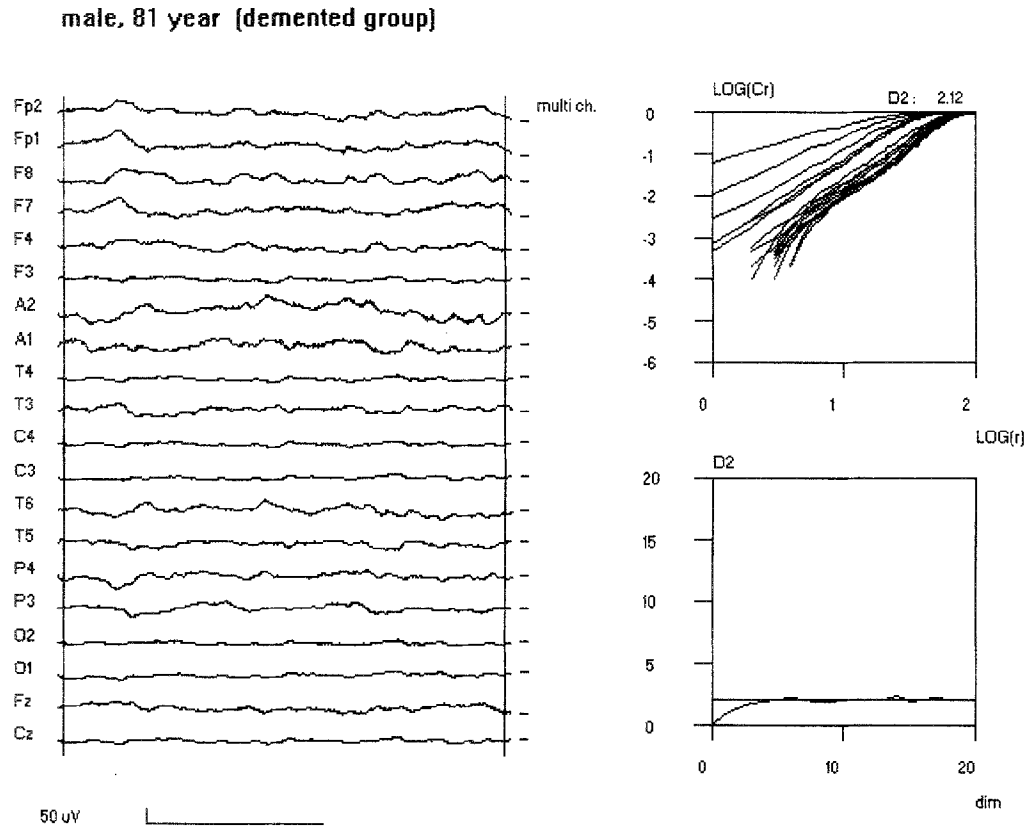


Figure 3. Subject from the demented group. The left part shows the EEG epoch (2.5 seconds; average reference). The graph in the upper right shows the Log(Cr) / Log(r) curve for increasing spatial embedding from 1 to 20 channels. The straight part of the curve converges to a limit. The curve in the lower right shows D2 as a function of spatial embedding (number of channels used in the reconstruction of the attractor). D2 converges to a limit.

primary diagnosis of dementia or Parkinson's disease could be confirmed in all, it proved to be difficult to obtain reliable information on disease severity at the moment of EEG recording in all cases. Finding a reliable control group posed special problems. Our protocol resulted in a relatively large control group, which was however younger than both patient groups. Letting the younger controls out in order to obtain the same mean age in the control group proved impossible because this resulted in a control group of only a few subjects. The only solution for the problem right now is to use age as a covariable in all statistical tests, as has been done in this study. Another problem with the control group is that these subjects, although they do not suffer from dementia or Parkinson's disease, do have neurological signs and symptoms. Neurological disease could result in a lower D2 in the controls. Despite this bias, significant differences between controls, demented patients and Parkinson patients could still be found, which strengthens our main finding.

Two problems were encountered with the multichannel D2 calculation procedure. The first problem is that the calculations are very time consuming. This was the main reason for limiting the analysis to one single epoch per EEG. Future implementation of algorithms such as described by Theiler (1987) and Grassberger (1990) could substantially reduce the required calculation time. The second problem is that some amount of subjective judgement enters into the procedure. The "reasonable range" of values for r in the D2 / log(r) curve was derived from a visual inspection of the curve. We have also experimented with automatic algorithms to find lower and upper limits of r, but so far the results have been less reliable. On visual analysis, a reliable plateau could not be identified in 5 of the 52 cases (equally divided over the 3 groups). This was almost always due to excess muscle artifact in more than 2 channels.

The present study shows that Fourier analysis is better able to discriminate between demented and Parkinson patients than the correlation dimension. At this stage, FFT is still superior for clinical purposes, because its calculation is straightforward and fast, and it is slightly more specific than D2. On the other hand one should realize that Fourier analysis has more or less matured,

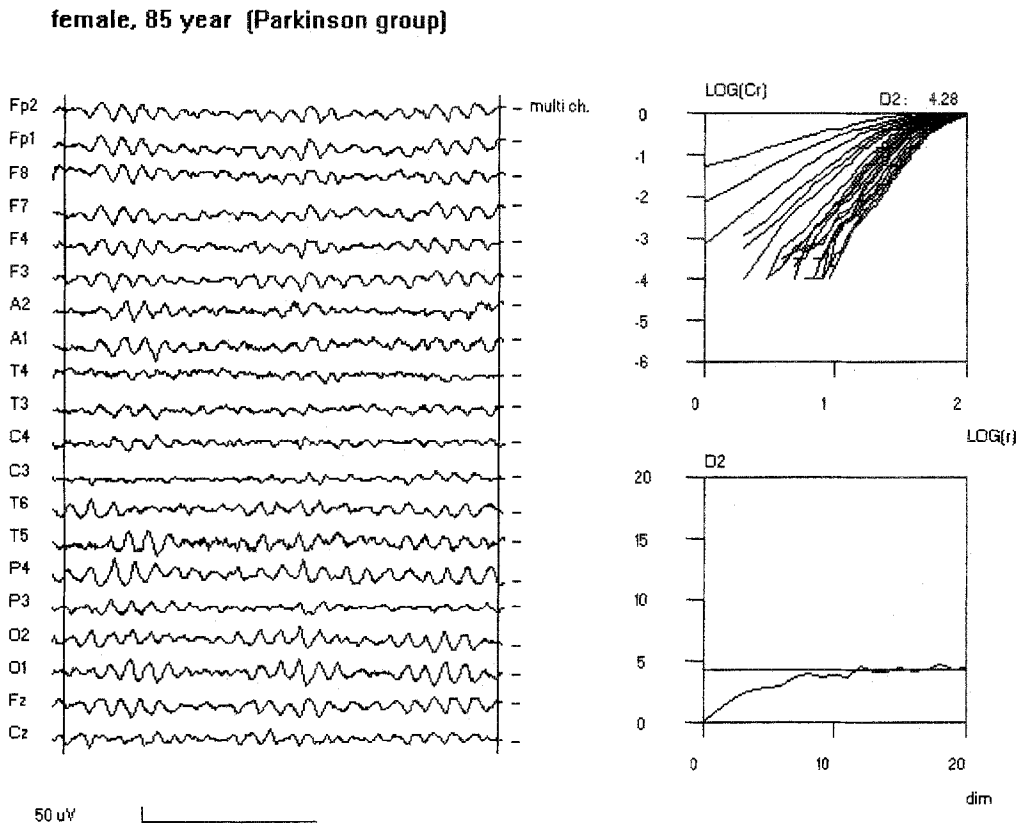


Figure 4. Subject from the Parkinson group. The left part shows the EEG epoch (2.5 seconds; average reference). The graph in the upper right shows the Log(Cr) / Log(r) curve for increasing spatial embedding from 1 to 20 channels. The straight part of the curve converges to a limit. The curve in the lower right shows D2 as a function of spatial embedding (number of channels used in the reconstruction of the attractor). D2 converges to a limit.

and significant improvements are not very likely. Nonlinear EEG analysis on the other hand is still in its infancy, and major progress is more likely to occur. Nonlinear EEG measures such as D2 contain information that can never be derived from the power spectrum. This is shown very clearly by Theiler et al. (1992): one and the same power spectrum can result from filtered noise or low dimensional chaos. Given this fact that, on analytical grounds, the FFT and nonlinear analysis provide different information, it could be that a combined use of these techniques will prove to be the best strategy in a clinical setting.

At this stage it is only possible to give a tentative explanation why D2 is lowered in dementia and Parkinson's disease. As stated in the introduction, low non-integer values of D2 by themselves cannot be taken as evidence for low dimensional chaos, although they are fully consistent with it. Nevertheless, this study has shown that the D2 can be used as a single number "statistic" that characterizes clinically relevant aspects of the EEG. In our view, D2 is a measure of EEG complexity, and as such is closely related to the phenomenon of desynchronisation. Low D2 values in the patient groups suggest decreased complexity and increased synchronization of the cortical dynamics. We demonstrated the relationship between EEG desynchronization (which is a measure of cortical activation) and EEG complexity in an earlier study (Stam et al. 1993). Loss of dynamical complexity seems to be a general finding in different kinds of brain pathology (similar results were reported in epilepsy and Creutfeldt Jakob disease). It seems likely that the causes of lower complexity will be different in these various diseases. Mathematical analysis suggests that most nonlinear dynamical systems are governed by one or more so called "control parameters". These are variables that describe general characteristics of the system, such as the strength of interactions between the elements. Increasing the value of such a control parameter leads to a stepwise (discrete) increment in the dimension of the systems attractor (Eckmann and Ruelle 1985). This suggests at least one possible mechanism for lower D2 values in brain disease.

Cholinergic fibres from the nucleus basalis of Meynert

are known to project to large parts of the neocortex and to exert a strong excitatory influence on cortical neurons (Steriade et al. 1990). In terms of cortical dynamics the general level of activity in the ascending cholinergic system seems to be a good candidate for a "control parameter". Under physiological circumstances, increased activity of the ascending cholinergic system would lead to a (possibly discrete) increase of D2. This corresponds with the known increase of D2 going from deep sleep to the awake state. Under pathological circumstances, abnormal low activity in the ascending cholinergic system could lead to abnormal low D2 values, even in the awake state. In Alzheimer's disease, one of the most important neuropathological findings is the loss of ascending cholinergic neurons of the nucleus basalis (Whitehouse et al. 1981). Similar findings have also been reported in Parkinsonian patients with dementia (Whitehouse et al. 1983). Our hypothesis is that the lower D2 values in dementia and Parkinson's disease reflect, at least partially, a loss of "dynamical complexity" in the cortex due to diminished activity in the activating cholinergic system.

The results of the present study suggest the potential usefulness of EEG analysis with techniques from nonlinear dynamics, even when the presence of chaos cannot be rigorously proved. Future studies will have to confirm and expand the present findings, for instance to measure D2 in a prospective study in dementia and Parkinson's disease, which will allow more accurate disease criteria and study of the relationship between measures of disease severity and D2. Correlations between neuropsychological measurements and D2 will be particularly interesting. As a next step, it will be useful to measure D2 not only under the standard "awake / eyes closed" condition, but also under other well defined conditions (awake / eyes open; during mental arithmetic). Measurement of the influence of cholinergic drugs on D2 in Alzheimer's disease could provide a good test of our hypothesis.

## Appendix: A Short Introduction in Chaos Theory

Chaos theory can be defined as the study of unstable aperiodic behaviour in nonlinear deterministic dynamical systems (Kellert 1993). A nonlinear deterministic dynamical system consists of elements which have nonlinear influences on each other. The system is dynamical if its state changes over time. If the state of a dynamical system at a certain time point can be described by M variables, this state can be represented by a point (vector) in a M dimensional "phase space". The time evolution consists of a series of such points which form a trajectory in phase space. In the limit of infinite time the trajectory will only fill a subspace of the system's phase space. This subspace is called the system's "attractor". An attractor is a geometrical representation of the long term dynamics of a system. Attractors can be characterized by their dimensions. An attractor dimension of 0 (point attractor) corresponds to a static system: there is no change over time. An attractor dimension of 1 corresponds with a periodic system. In such a system a finite number of states is repeated indefinitely. Attractor dimensions of 2 and higher (provided they are whole "integer" numbers) correspond with quasi periodic systems. The attractor dimension indicates the number of independent frequencies. In a fully random system the attractor dimension is equal to M. Such a system cannot be described by differential equations and would show a broadband ("white") frequency spectrum.

The main discovery of chaos theory is that there exists a third type of dynamics, which is different from (quasi) periodic and from random dynamics. This third type is called "chaotic dynamics" and is characterized by sensitive dependence on initial conditions and "strange attractors". Sensitive dependence on initial conditions means that even if two states of the system are only infinitesimally different, after a short time these differences will become very large. This characteristic corresponds to the unstable character of chaotic dynamics, and makes long term predictions impossible in principle (such long term predictions would require measurement of some initial conditions with infinite precision). Strange attractors are attractors with non-integer ("broken") dimensions. Such geometrical shapes are called fractals. Fractals are extremely complex structures which show scale independent self similarity. Chaotic dynamics differs from (quasi) periodic dynamics in showing sensitive dependence on initial conditions, and in being unpredictable and far more complex. Measurements from chaotic systems usually appear quite random and Fourier analysis shows broad spectra. On the other hand, chaos is different from random processes in that it is fully deterministic and has a (very complex) structure.

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