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Investigation of the noise effect on fractal dimension of EEG in schizophrenia patients using wavelet and SSA-based approaches

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ABSTRACT

Objectives: Complexity measures have been enormously used in schizophrenia patients to estimate brain dynamics. However, the conflicting results in terms of both increased and reduced complexity values have been reported in these studies depending on the patients' clinical status or symptom severity or medication and age status. The objective of this study is to investigate the nonlinear brain dynamics of chronic, medicated schizophrenia patients and healthy control subjects using Katz's fractal dimension (FD). Moreover, in order to determine noise effect on complexity of EEG data, a noise elimination method based on wavelet and singular spectrum analysis (SSA) were assessed.
Methods: Twenty-two schizophrenia patients and twenty-two age- and gender-matched control subjects underwent a resting state EEG examination with 120 s. The discrete wavelet transform (DWT) was applied for EEG decomposition. Using a SSA approach, noise was removed and EEG reconstructed by inverse wavelet transform. The brain complexity of participants was investigated and compared using Katz's FD obtained from original and preprocessed EEG data.
Results: Lower complexity values were found in schizophrenia patients. However, this difference was only statistically significant for each channel in preprocessed, noiseless EEG data. The most significant complexity differences between patients and controls were obtained in left frontal and parietal regions of the brain.
Conclusion: Our findings demonstrate that the utilizing of complexity measures with preprocessing approaches on EEG data to analyze schizophrenics' brain dynamics might be a useful and discriminative tool for diagnostic purposes. Therefore, we expect that nonlinear analysis will give us more valuable results for understanding of schizophrenics' brain.

1. Introduction

Schizophrenia is a serious and chronic psychiatric disorder diagnosed with a range of "positive symptoms" such as hallucinations, delusions and "negative symptoms" including flattened affect, cognitive impairment and disorganized speech according to the criteria of American Psychiatric Association [1]. Because of these symptoms are dynamic, brain dynamics in schizophrenia have been widely studied with a huge variety of nonlinear estimators in EEG data [2]. Nonlinear analysis of EEG reflects new information in understanding of brain activity and abnormal brain dynamics in a broad variety of pathological and physiological disorders such as Alzheimer's disease [3], dementia [4], epilepsy [5], depression [6] and coma [7]. Dimensional complexity, fractal dimension (FD), largest Lyapunov exponent (L1), correlation dimension (D2), Lempel–Ziv complexity (LZC), mutual information and approximate entropy (ApEn) are the numerous complexity measures have been used for schizophrenia patients' EEG data [8–16].

Some of the previous studies have revealed a pattern of increased complexity values especially in frontal region of schizophrenics' brain [8,17–20]. Elbert et al. study was the first experimental investigation that reported an increased dimensional complexity in the EEG of schizophrenia patients [8]. Similarly, in Koukkou et al.'s study, medication-free schizophrenia patients exhibited higher D2 values when compared to controls [9]. In contrast, a lower complexity in schizophrenia patients has been reported in some other studies [10,11,17]. According to the results of two different experiments, lower complexity values using D2 and L1 were observed in medicated schizophrenia patients [10,11]. It has been reported that complexity analysis using these earlier

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complexity measures (L1 and D2) has some drawbacks as these require a large amount of stationary and noise-free data [21]. To overcome this problem new complexity measures have been proposed for dynamical analysis of brain signals. For example, used in short data sets without any knowledge about noise and stationary conditions LZC which can be used in short data sets without any knowledge about noise and stationary conditions, had been found higher in non-medicated schizophrenics' prefrontal EEG regions than that of control subjects [13]. Similarly, medicated schizophrenia patients with high degree of positive symptoms had larger complexity values than control subjects in another LZC study [14]. Raghavendra et al. calculated FD of first-episode and medicated patient group and found lower complexity values in negative symptoms group and higher complexity values in positive symptoms group [15]. Sabeti et al. computed complexity using different entropy and FD measures in a group of medicated schizophrenia patients and they found that patients exhibited lower complexity values than controls [16].

To date, different complexity estimators have been widely used in studies on schizophrenia patients EEG data. However, a contradictory result in terms of both increased and decreased complexity has been reported in these previous studies. This enormous variability in the reports depends both on clinical status and sympathology of the patients and their medication effect. Moreover, since these complexity algorithms have different definitions for complexity such as dimensional complexity (D2 and FD), regularity (entropy) or predictability (L1), the selection of complexity estimator must be taken into account for make a correct comparison between the results of different studies [2,22,23]. While some classical estimators (D2, L1) have some limitations such as stationary, noise-free and long time series, FD has been widely used in the nonlinear analysis of time series exhibiting non-stationary and transient characteristics such as EEG [24]. As a complexity measure, FD can be calculated using two different approaches as time-domain and phase-space. While Katz, Higuchi, Petrosian FD algorithms calculate complexity of time series directly in the time domain, the D2 is a phase space calculation of complexity [25]. It has been proposed that complexity can be calculated with a faster and simpler approach than D2 technique when time domain FD algorithms are used [26,27]. In some studies, it has been reported that some of the FD estimation methods are not applicable to all types of data [28]. Therefore, in order to investigate the reliability of FD calculation with different algorithms, many studies have been carried out in EEG data [25,28–31].

In one study, it has been found that Katz's method is the most appropriate algorithm for epilepsy discrimination in EEG data [25]. In another study, the Katz algorithm has been reported as the worst discriminator for dementia patients' EEG data [29]. Katebi and coworkers accomplished FD algorithm comparison in EEG data of schizophrenia patients. They reported that while Higuchi's algorithm gives a more reliable FD estimation, Katz's algorithm is the consistent method due to its exponential transform of FD values [31]. They added that real data sets such as EEG which contain noise require a careful selection of FD algorithm type. In another study that performed over both synthetic data and real EEG waveform with epileptic seizures, the performances of different FD estimators were compared [25]. It seems from this report that all algorithms used for FD estimation are influenced by noise more or less.

The objective of the present study was to determine the noise effect on Katz algorithm based complexity value of schizophrenia patients' and controls' EEG data. To this end, discrete wavelet transform (DWT) was applied to decompose the EEG signal into sub-signals. Noise was removed by singular spectrum analysis (SSA) based methodology for each sub-band and the EEG is reconstructed by using inverse wavelet transform. The effects of denoising on EEG data were evaluated using Katz's fractal dimension. The complexity results were compared between original EEG signals and noise-cancelled signals after wavelet transform based subspace method. To the best of our knowledge, this is one of the first studies that investigate the effectiveness of noise on complexity measures to accurately characterize the brain dynamics of schizophrenia patients.

Table 1
Demographical and clinical data of the patients and controls.

	Schizophrenic patients	Control subjects
Participants	22	22
Male/female	12/10	14/8
Age	41.08 ± 6.34	37.86 ± 4.75
Age of onset of disorder	20.12 ± 5.27	–
Dominant hand	All right	All right
Positive symptoms score	16.03 ± 5.27	–
Negative symptoms score	14.55 ± 6.21	–
PANSS (total) score	62.15 ± 12.79	–

2. Materials and methods

2.1. Subjects and EEG data acquisition

Twenty-two schizophrenia patients who fulfilled the DSM-IV diagnostic criteria [32] from the Hospital[1] were included in this study. The scale for the assessment of positive and negative symptom (PANSS) was used to evaluate symptom severity of patients [33]. The patients were taking standard antipsychotic medications at the time of this study and none of them had a history of any other psychiatric and neurological disorder or alcohol abuse. The control group consisted of twenty-two age- and gender-matched healthy subjects with no history of psychiatric or neurological disorder. Table 1 shows the demographical and clinical situations of the participants.

The study was approved by the ethics committee of the hospital. Prior to EEG recording, all subjects were informed of the protocols of the study and gave their written informed consent. For the experiments, an acoustically shielded and light controlled room was used. According to the International 10–20 System, the EEG data were recorded from 6 electrodes (F3, F4, C3, C4, P3, P4) mounted on the scalp of subject who in a relaxed state with closed eyes during 2 min and were sampled at 250 Hz. 16-channel digital BIOPAC data acquisition system (Model MP150WSW, Santa Barbara, CA) was used for data acquisition and potentials from selected channels against linked earlobes were amplified on this system amplifier units.

2.2. Data analysis

2.2.1. Singular spectrum analysis

Singular spectrum analysis (SSA) which was developed in the 1980s by Broomhead and King is one of the powerful method for time series analysis in a wide variety of scientific fields such as meteorology, hydrology, climatology, economics, medicine and biomedical [34,35]. This technique can be applicable to short or long, stationary or non-stationary, deterministic or noisy data series without prior knowledge about system dynamics [35]. The aim of SSA is to decompose of the original data series into slowly varying trend components, oscillatory components and noise [36]. This technique composes of two stages including decomposition and reconstruction.

Decomposition: This stage is consisted of two sequential steps as embedding and singular value decomposition (SVD). In the embedding of the decomposition stage, the one dimensional time series is

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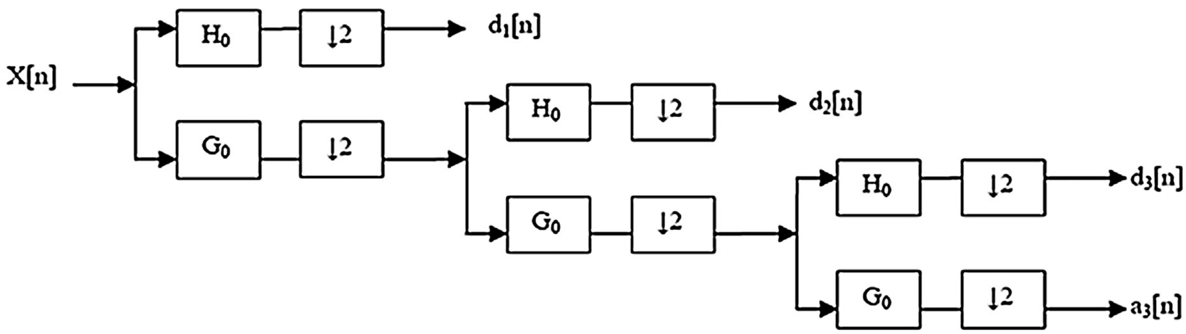

Fig. 1. Three-level wavelet decomposition tree [40].

transferred into multidimensional delayed vectors with $l\,(1 \le l \le r)$ window length or embedding as follows [37]

$$x_i = [s_{i-1}, s_i, \ldots, s_{i+l-2}]^T, \quad 1 \le i \le k \tag{1}$$

where $k = r - l + 1$ is multidimensional vector and $[\,]^T$ denotes the matrix transpose. The trajectory matrix that consists of s series can be written as

$$X = [x_1, x_2, \ldots, x_k] = \begin{bmatrix} s_0 & s_1 & s_2 & \ldots & s_{k-1} \\ s_1 & s_2 & s_3 & \cdots & s_k \\ s_2 & s_3 & s_4 & \cdots & s_{k+1} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ s_{l-1} & s_l & s_{l+1} & \cdots & s_{r-1} \end{bmatrix} \tag{2}$$

Here, the trajectory matrix X is a Hankel matrix, all elements are identical along its diagonal. Then the SVD of the trajectory matrix can be rewritten as the sum of rank-one biorthogonal elementary matrices.

$$X = X_1 + X_2 + \cdots + X_d \tag{3}$$

where $d = \text{argmax}_i\,\{\lambda_i > 0\}$.and $X_i = \sqrt{\lambda_i} e_i v_i^T$. Here, $\lambda_1, \lambda_2, \ldots, \lambda_l$ is the eigenvalues and $e_1, e_2, \ldots, e_l$ is the eigenvectors of $S = XX^T$. The ith eigentriple of the X matrix consists of principal components v_i empirical orthogonal functions e_i and λ_i singular value.

Reconstruction: Eigentriple grouping and diagonal averaging are the two substage of reconstruction procedure. In the grouping step, the index set $\{1, 2, \ldots, d\}$ is divided into m disjoint subsets as $I_1, I_2, \ldots, I_m$. After grouping the eigentriples Eq. (3) can be rewritten as

$$X = X_{I_1} + X_{I_2} + \cdots + X_{I_m} \tag{4}$$

To find an index for proper grouping, singular spectrum and weighted correlation a new element p_{ij}^w is defined as

$$p_{ij}^w = \frac{(Y^{(i)}, Y^{(j)})_w}{||Y^{(i)}||_w ||Y^{(j)}||_w} \tag{5}$$

where $(Y^{(i)}, Y^{(j)})_w = \sum_{k=1}^{N} w_k y_k^{(i)} y_k^{(j)}$ and $||\;||$ is the norm of Y series and $w_k = \min(k, l, r-k+1)$. Then by using diagonal averaging, $Y^{(i)}$ series can be calculated as

$$Y_n^{(i)} = \begin{cases} \dfrac{1}{n}\displaystyle\sum_{m=1}^{n} x_{m,(n-m+1)}^{(i)} & (1 \le n < l) \\ \dfrac{1}{l}\displaystyle\sum_{m=1}^{l} x_{m,(n-m+1)}^{(i)} & (l \le n < k) \\ \dfrac{1}{r-n+1}\displaystyle\sum_{m=n-k+2}^{r-k+1} x_{m,(n-m+1)}^{(i)} & (k \le n \le r) \end{cases} \tag{6}$$

If the $Y^{(i)}$ and $Y^{(j)}$ reconstructed series are not correlated, they are divided into two disjoint groups, it means they are separable.

2.2.2. *Wavelet transform-based signal decomposition*

As a time-frequency representation of a signal, wavelet transform has some advantages over other conventional techniques as

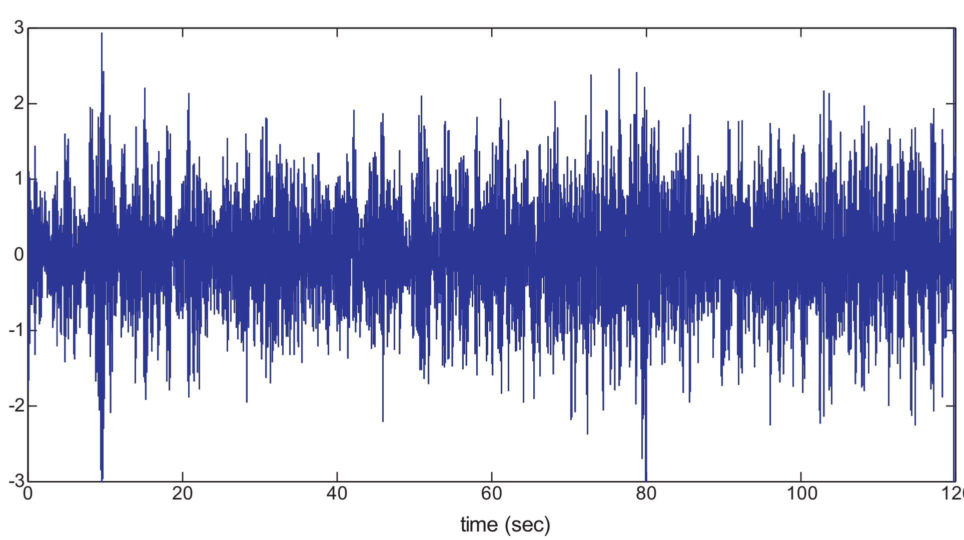

Fig. 2. A sample EEG waveform.

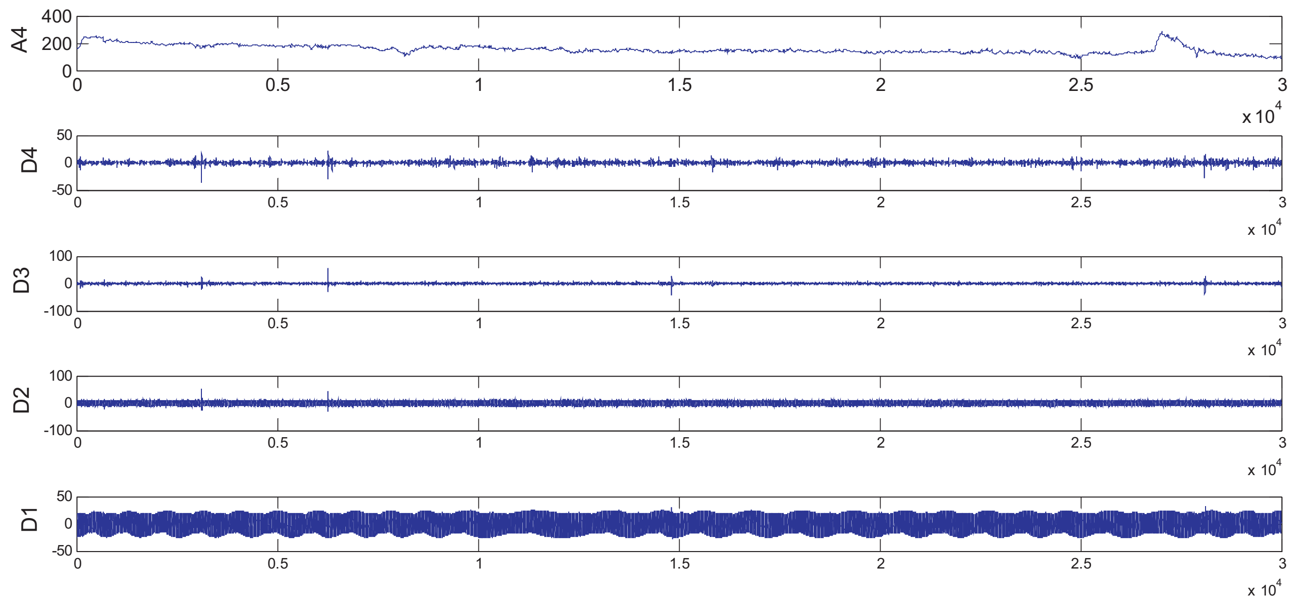

Fig. 3. Wavelet coefficients of a sample EEG data.

optimal resolution in both the time and frequency domains and lack of the requirement of stationarity of the signal [38]. Continuous wavelet, discrete wavelet and adaptive approaches are basic subgroups of the WT. Generally, it can be defined as the convolution between $x(t)$ signal and $\psi_{a,b}(t)$ wavelet function [38]

$$W_{\psi}X(a,b) = \langle x(t)|\psi_{a,b}(t)\rangle = \frac{1}{\sqrt{|a|}}\int \psi\left(\frac{t-b}{a}\right)x(t)dt \quad (7)$$

where a is a dilation (scale) parameter, b is the shift (translation) parameter and $\psi_{a,b}(t)$ are dilated and shifted versions of a unique mother wavelet function.

In the discrete wavelet transform (DWT) that uses orthogonal or biorthogonal wavelet function, wavelet decomposition can be performed by a series of high and low-pass filters followed by down-sampling [39]. Approximation and detail coefficients are obtained as the output of the low and high pass filters in this iterative decomposition process.

Therefore, DWT of a signal can be calculated with consecutive high-pass and low-pass discrete time domain signal filtering, which is shown in Fig. 1 [39]. In this figure, $x[n]$, G_0, H_0, $d[n]$ and $a[n]$ indicate the time domain signal, low-pass filter, high-pass filter, detail information and approximation information, respectively. According to this procedure, while the contracted or compressed type of the wavelet function gives the high-frequency components, the dilated form match the low-frequency components.

2.2.3. *Fractal dimension*

The term fractal refers to the shapes and objects having a self-similar form without an integer dimension value [26]. Therefore, FD represents a noninteger or fractional dimension of a geometric object. Defined as the measures of the self similarity of the signals, fractal dimension is commonly used in biomedical signals such as EEG [24,25,40,41]. It has been proven useful in quantifying the complexity of dynamical signals. There are various FD estimators such as Petrosian, Higuchi, Katz and box-counting.

The Katz's algorithm calculates FD as follows [42]

$$D = \frac{\log(L/a)}{\log(d/a)} = \frac{\log(n)}{\log(n)+\log(d/L)} \quad (8)$$

where L is the total length of the time series, a is the average number of steps in the series, $n = L/a$ is the number of steps in time series and d is the Euclidian distance between the first data of time series and the data that has maximum distance from this first point.

2.3. *Statistical analysis*

In order to investigate FD differences between schizophrenic patients and control subjects, independent sample t-test were used with SPSS (20.0 release version) program. Student's t-test was chosen due to the result of Levene's test, which was used to test whether variances among the groups were homogeneous. Under the null hypothesis "there is not a difference in FD measures between patients and control subjects", the data were normally distributed. The paired sample t-test was used to evaluate effectiveness of proposed method on each EEG channel.

3. Results

In this study, we investigated Katz's FD discrimination ability between EEG data of schizophrenia patients and control subjects. A simple EEG data is shown in Fig. 2. For preprocessing, a DWT was used to decompose each EEG channel into sub-bands (Fig. 3). This decomposition level number is chosen based on the dominant frequency components of the EEG signals. According to the results of previous studies, it has been found that daubechies wavelets of order 2 are more suitable to detect changes of EEG data [43]. Therefore, EEG data were decomposed at level 4 using Daubechies wavelet of order 2. Then noise was cancelled using the SVD-based technique for each sub-signal. Window length in this method was defined as 10 according to the mutual information technique [44]. Similarly, time delay was determined as 1 using the mutual information method as the first minimum value of the time delay graph and then the embedding dimension was calculated by Cao's method

Table 2
Eigen values and variance percentages.

Eigen value	%	Total	Eigen value	%	Total
1	47.15	47.15	6	0.608	99.26
2	46.77	93.92	7	0.366	99.63
3	2.067	95.99	8	0.361	99.98
4	2.059	98.05	9	0.003	99.99
5	0.609	98.66	10	0.0007	100

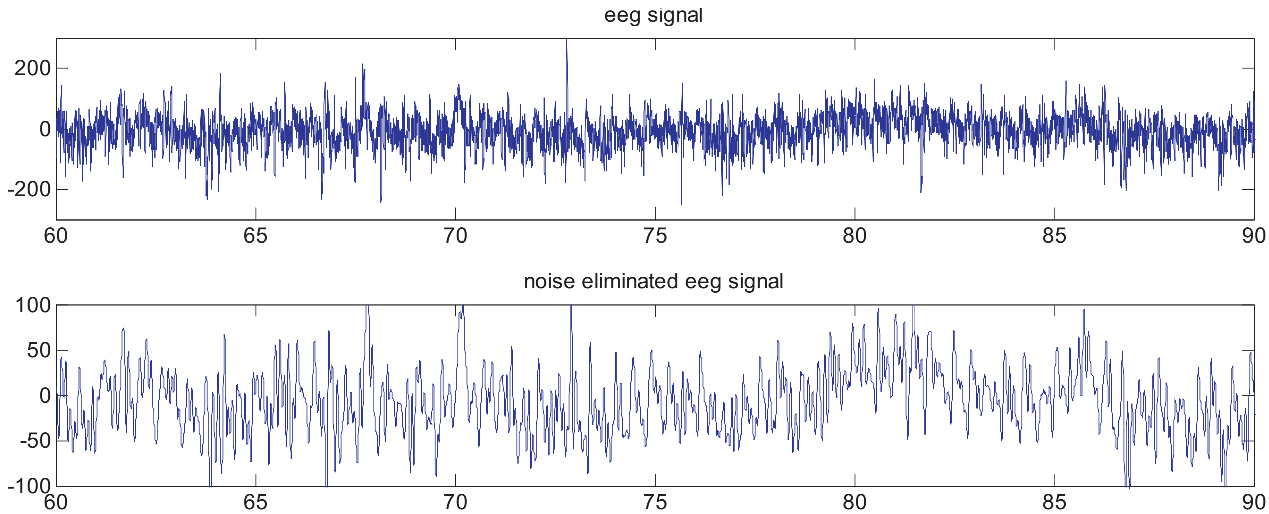

Fig. 4. A sample F3 region EEG signal with and without noise.

as 6. Eigen values and variance percentages of the SSA method in a sample EEG data are summarized in Table 2. Finally, noiseless EEG was reconstructed by using inverse wavelet transform (IWT). Fig. 4 compares the EEG signal of a patient F3 region with and without noise. While signal-to-noise values for the noisy EEG signals ranged from 1.3215 to 1.4016 for both groups, after wavelet decomposition and SSA noise cancellation the resulting SNR values ranged from 1.4409 to 1.5963. In order to clarify noise effectiveness on complexity values of EEG data between healthy and schizophrenic participants, the Katz's FD is calculated for both original and preprocessed EEG data recorded from 6 different channels (F3, F4, C3, C4, P3 and P4). For FD estimation, we investigated EEG in time window with 20 s of 120 s total data recording. Then, the mean complexity of these 6 epochs was computed for each individual EEG channel for both groups.

The FD values obtained from original EEG data of patients and controls in each channel are listed in Table 3. Here, we found that the schizophrenia patients' FD values were lower than those of the controls in all brain regions. However, the *t*-test showed that this difference was not statistically significant for each channel. The comparison between controls and patients in terms of average of the FD values in each channel is shown in Fig. 5.

Table 4 summarizes the average FD values of patients and controls in each channel obtained from noiseless EEG data. It can be noted that patients and controls have significantly different FD values from each other in all regions when EEG data were preprocessed. Lower complexity values were generated by the schizophrenia patients than by the control subjects. Fig. 6 shows the estimated complexity of schizophrenic and healthy participants. The largest differences between groups were obtained for the left frontal (F3) and right parietal (P4) lobes. For both groups, the differences in FD values obtained from original and noiseless EEG signals were further analyzed by using paired sample *t*-test. Both groups exhibited significantly lower complexity values when the original EEG data without any preprocessing step were analyzed. The comparison between average FD values obtained from

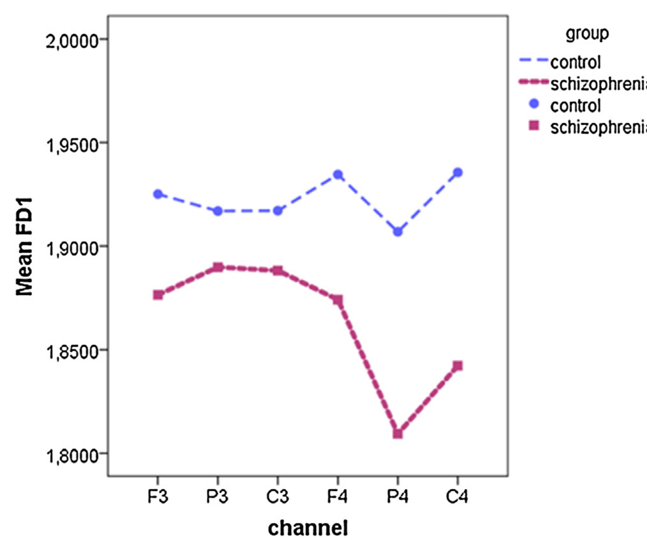

Fig. 5. Comparison between the average FD values obtained from original EEG data in each channel between patients and controls.

Table 3
Comparison of estimated Katz's FD values from original EEG data between patients and controls.

Channels	Control group	Schizophrenia group	*P* value
F3	1.9251 ± 0.25	1.8765 ± 0.17	0.451
P3	1.9169 ± 0.29	1.8898 ± 0.23	0.731
C3	1.9171 ± 0.28	1.8882 ± 0.26	0.722
F4	1.9345 ± 0.22	1.8742 ± 0.22	0.366
P4	1.9069 ± 0.20	1.8094 ± 0.22	0.131
C4	1.9356 ± 0.18	1.8423 ± 0.25	0.161

Table 4
Comparison of estimated Katz's FD values from noiseless EEG data between patients and controls.

Channels	Control group	Schizophrenia group	*P* value
F3	2.2319 ± 0.07	2.1585 ± 0.07	0.001*
P3	2.2447 ± 0.08	2.1676 ± 0.09	0.004*
C3	2.2467 ± 0.08	2.1745 ± 0.08	0.006*
F4	2.2272 ± 0.10	2.1690 ± 0.08	0.048*
P4	2.2371 ± 0.08	2.1512 ± 0.07	0.001*
C4	2.2371 ± 0.07	2.1681 ± 0.09	0.009*

* Significant difference between groups, $p < 0.05$.

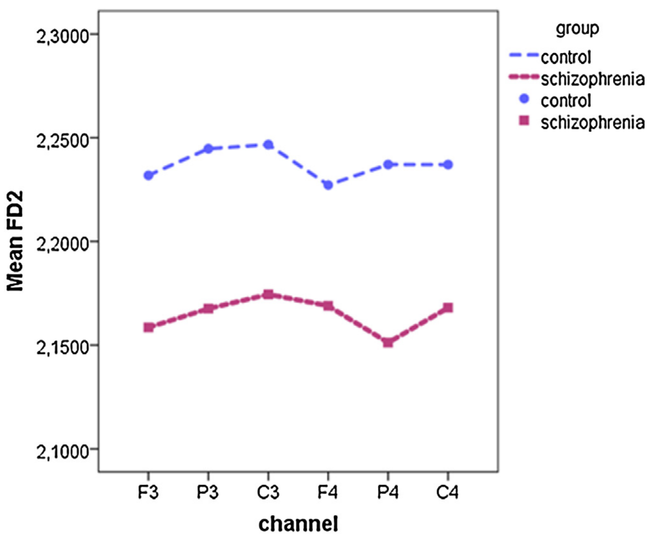

Fig. 6. Comparison between the average FD values obtained from preprocessed EEG data in each channel between patients and controls.

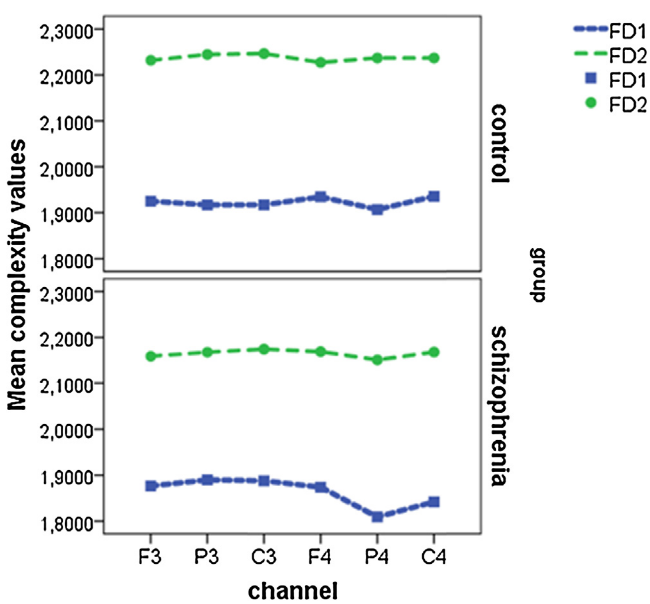

Fig. 7. Average FD values obtained from original and noiseless EEG in each group.

original and noiseless EEG data of patients and control subjects were illustrated in Fig. 7.

4. Discussion and conclusion

Over the recent years, the analysis of schizophrenics' EEG with different complexity estimators has received increased attention. The inconsistent results as decreased and increased complexity of schizophrenics in the previous studies might have been due to either demographic or clinical characteristics of patients or to the application of different complexity measures [23]. Because the most frequently used classical estimators require a huge amount of data and are proper for stationary and noise-free signals, other new complexity estimators such as FD have also been applied to EEG data of patients [21,23,45].

The importance of noise reduction in EEG data before analysis had been previously investigated in different studies with linear filtering, adaptive noise elimination and subspace based techniques such as SSA [46–49]. Although SVD methods are known as have high computational complexity, a combination of wavelet decomposition and subspace method has been proposed an effective and fast tool for noise removal from EEG signals [49]. Considering this knowledge, the purpose of present study is to investigate noise effect on complexity of EEG data of schizophrenia patients using FD analysis. To decompose 120 s EEG data into sub-bands, DWT was applied. Then, a SVD-based algorithm was used for removing of noise in each sub-band. Last, noiseless EEG data was reconstructed by IWT. Therefore, the Katz's FD was calculated and compared for both original and preprocessed EEG data between healthy and schizophrenic participants in order to clarify noise effectiveness on complexity values of EEG data.

To the best of our knowledge, this is one of the first studies to apply noise removal techniques on EEG data for complexity estimation of schizophrenics' brain. In our study, the patients' FD values obtained from original EEG data were lower than those of the controls in all brain regions. However, this difference was not statistically significant for each channel. After noise cancellation by proposed method, significantly lower complexity values were obtained by the schizophrenia patients than by the control subjects. The most significant complexity differences in preprocessed EEG data between patients and controls were found in left frontal and parietal channels of the brain. This is consistent with the frontal lobe abnormalities and structural deficits in the parietal lobe of schizophrenia patients have been reported in the previous investigations based on imaging studies [50,51]. Moreover, schizophrenia has been characterized by frontal lobe dysfunction and disordered frontal–parietal connectivity [52,53].

We conclude that the complexity of EEG based on FD was different in schizophrenia patients. The wavelet decomposition-SSA based technique has proved to be a reliable method for noise elimination in EEG data. After preprocessing based on this technique, a clear and significant discrimination was obtained between FD of schizophrenia patients and control subjects. There are some limitations in our study. First, the sample size is relatively small to divide patients into subgroups according to their sympathology. Second, our patients had been using their medications for a long time and as a representation of, the average onset of the disorder was approximately 20 years. Therefore, in future studies it will be more informative to investigate nonlinear dynamics of schizophrenics according to their medication status and age effects with more EEG channel. Besides, the proposed noise removal methodology can be compared on other complexity or entropy measures in EEG data of schizophrenia patients.

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