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Time-Frequency Distribution Analysis for Electroencephalogram Signals of Patients With Schizophrenia and Normal Participants

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Abstract

Background: Psychiatrists diagnose schizophrenia based on clinical symptoms such as disordered thinking, delusions, hallucinations, and severe distortion of daily functions. However, some of these symptoms are common with other mental illnesses such as bipolar mood disorder. Therefore, quantitative assessment of schizophrenia by analyzing a physiological-based data such as the electroencephalogram (EEG) signal is of interest. In this study, we analyze the spectrum and time-frequency distribution (TFD) of EEG signals to understand how schizophrenia affects these signals.

Methods: In this regard, EEG signals of 20 patients with schizophrenia and 20 age-matched participants (control group) were investigated. Several features including spectral flux, spectral flatness, spectral entropy, time-frequency (TF)-flux, TF-flatness, and TF-entropy were extracted from the EEG signals.

Results: Spectral flux (1.5388 ± 0.0038 and 1.5497 ± 0.0058 for the control and case groups, respectively, $P=0.0000$), spectral entropy (0.8526 ± 0.0386 and 0.9018 ± 0.0428 for the control and case groups, respectively, $P=0.0004$), spectral roll-off (0.3896 ± 0.0434 and 0.4245 ± 0.0410 for the control and case groups, respectively, $P=0.0129$), spectral flatness (0.1401 ± 0.0063 and 0.1467 ± 0.0077 for the control and case groups, respectively, $P=0.0055$), TF-flux (1.2675 ± 0.1806 and 1.5284 ± 0.2057 for the control and case groups, respectively, $P=0.0001$) and TF-flatness (0.9980 ± 0.0000 and 0.9981 ± 0.0000 for the control and case groups, respectively, $P=0.0000$) values in patients with schizophrenia were significantly greater than the control group in most EEG channels. This prominent irregularity may be caused by decreasing the synchronization of neurons in the frontal lobe.

Conclusion: Spectral and time frequency distribution analysis of EEG signals can be used as quantitative indexes for neurodynamic investigation in schizophrenia.

Keywords: EEG signal classification, Spectral, Time-frequency distribution

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Introduction

Schizophrenia is a mental disorder that seriously affects the brain mechanism in a way that these patients hear and see unreal things. These patients lose touch with reality in some occasions, and if these patients are left untreated, the symptoms of schizophrenia can be persistent and disabling. However, if a proper treatment is delivered in a timely and coordinated manner, it can help patients engage in school or work activities, be independent, and have personal relationships.[1] Cortical data processing is seriously damaged in these patients which significantly affects the cognitive tasks.[2,3]

Electroencephalogram (EEG) signal is the spatio-temporal integration of neurons' activation, which can be captured by scalp electrodes. It is logical to expect an exclusive deterioration in the EEG signals for each specific brain disease. Experiments and observations on the EEG signals of different neurological and psychiatric diseases confirms this.[4-6] Quantitative EEG analysis could be used as a standard tool for early diagnosis of these abnormalities.[7-10]

To reveal the EEG content, feature extraction is an essential step to convert EEG samples within successive widows into representative feature vectors to enable classifying healthy subjects from a specific patient group. Several research studies analyzed quantitative EEG signals to assess neural activations of the brain during cognitive tasks.[11-13] In this regard, different features such as energy

of EEG signals within different frequency bands, Shannon entropy, power spectrum, and autoregressive coefficients have been proposed as discriminative features.[14-17] Ciprian et al[18] developed a machine learning algorithm (MLA) based on closed eyes resting-state EEG datasets for distinguishing patients schizophrenia from healthy controls. They showed MLA could achieve a total accuracy of 96.92% which implies that the symbolic transfer entropy feature may be a promising tool for clinical diagnosis of schizophrenia.

Sun et al[19] showed that the fuzzy entropy EEG feature was more significant than fast Fourier transform coefficients in classification of patients with schizophrenia from normal individuals. Kim et al[20] claimed that EEG microstate features have reasonable accuracy in the classification of patients with schizophrenia from normal individuals. Prabhakar et al[21] used several EEG features such as detrend fluctuation method, Hurst exponent, and recurrence quantification analysis and they achieved an acceptable classification accuracy for participants with schizophrenia. Sabeti et al[22] reported a classification accuracy of 86% and 90% by linear discriminant analysis and Adaboost classifiers in differentiation of patients with schizophrenia from normal ones based on both linear and nonlinear EEG features. Kutepov et al[23] revealed that schizophrenia could be better characterized by the largest Lyapunov exponents which increased the classification accuracy using larger number of significant channels.

Synchronized oscillatory activity of temporal and frontal neurons is defined as an effective feature in diagnosing of normal cognition and perception. Research findings emphasize that in patients with schizophrenia, there is an obvious distortion of synchronized brain circuit activity.[24,25] Thus, using informative EEG characteristics of asynchronization may help in the diagnosis of patients with schizophrenia. Since the relation between patients with schizophrenia and their EEG time-frequency characterizations is not well-investigated, we aimed to analyze both spectrum and time-frequency distribution (TFD) of EEG signals to understand how schizophrenia disorder affects the brain electrical activity.

Methods and Materials

Data Description

Twenty patients with schizophrenia (gender: male, age: 20-53 years) and 20 age-matched individuals (control group, gender: male, age: 18-55 years) were enrolled in the center for clinical research in neuropsychiatry, Perth, Western Australia in 2007. DSM-IV[1] and ICD-10[26] criteria were used to diagnose and confirm schizophrenia or schizophrenic spectrum disorders in the affected group who were selected by browsing psychiatric hospital admissions. Patients with known organic neurological disease or history of substance addiction and significant language difficulties were excluded from the study. The participants in the control group were gathered by having advertisements in Red Cross blood donor agency or local newspapers. Control participants with any history of psychotic disorder either in themselves or in their first-degree relatives were excluded. All participants with schizophrenia continued their prescribed neuroleptic therapy during this study.

A 24-channel Synamps neuroscan system with signal gain of 75 K was used for recording EEG signals. The length of recorded EEG signals for each person was two minutes. The subjects sat on a comfortable chair in upright seated position with open eyes. In addition to 20 routine EEG electrodes (Fpz, Fz, Cz, Pz, C3, T3, C4, T4, Fp1, Fp2, F3, F4, F7, F8, P3, P4, T5, T6, O1, and O2), bilateral mastoids, plus vertical and horizontal electrooculograms (VEOG and HEOG) were recorded with sampling frequency of 200 Hz. Eye-blink and muscle contracture artifacts were eliminated using suitable techniques.[27] A band pass filter at 0.75 to 45 Hz was applied to reduce the very low frequency noise and power line frequency, respectively. Figure 1 shows Cz channel signal of a normal person and a patient with schizophrenia.

Suggested Features

A short description of the main state-of-the-art features used for EEG characterization in the frequency and time-frequency domain is mentioned below.

Spectral Flux

Spectral flux[28] defines the spectral change between two successive frames as:

$$FL(i,i-1)=\sum_{k=1}^{f_L}\left(NX_i(k)-NX_{i-1}(k)\right)^2 \quad (1)$$

where $NX_i(k)=\frac{X_i(k)}{\sum_{l=1}^{f_L}X_l(k)}$ is the kth normalized discrete Fourier transform (DFT) coefficient at the i^{th} frame, and f_L shows defined frequency band that is set to 100 Hz.

Spectral Entropy

The irregularity of the signal spectrum[29] is calculated by spectral entropy. In the i^{th} frame, it is defined as:

$$En=-\sum_{k=1}^{f_L}P_i(k).logP_i(k) \quad (2)$$

where $P_i(k)$ is the power density over a known frequency band, and is normalized as $\sum P_i(k)=1$.

Spectral Centroid and Spread

Spectral centroid and spread are two common measures for determining spectral position and shape. Spectral centroid represents the gravity center of the spectrum. In

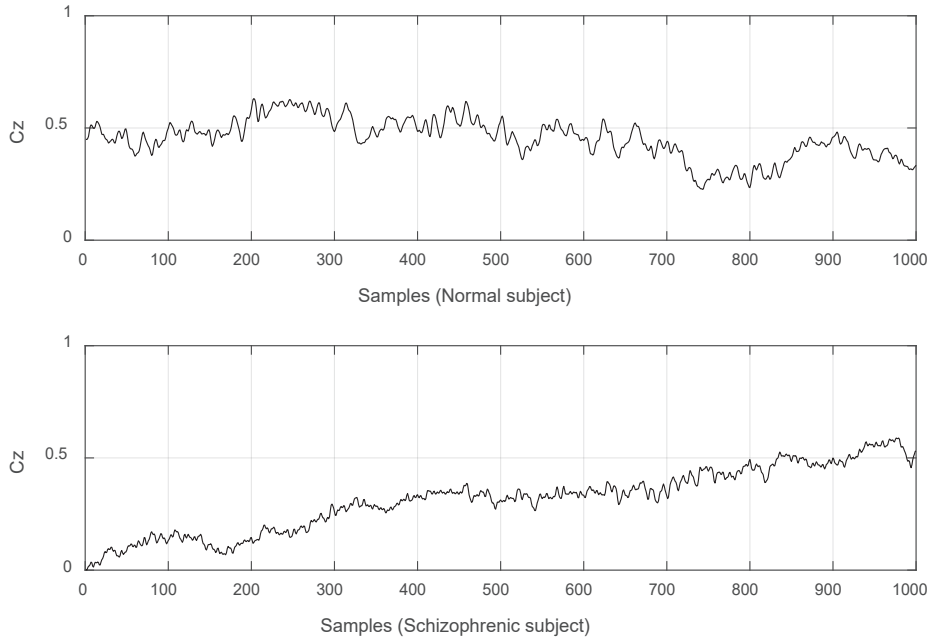


Figure 1. Cz Channel Signal of a Normal Person and a Patient With Schizophrenia.

i^{th} frame, its value is defined as:

$$C_i = \frac{\sum_{k=1}^{f_L} kX_i(k)}{\sum_{k=1}^{f_L} X_i(k)} \quad (3)$$

where $X_i(k)$ is the k^{th} DFT coefficient at i^{th} frame. Additionally, the second central moment of the spectrum (spectral spread) is calculated as the deviation of the spectrum from spectral centroid at i^{th} frame is calculated as:

$$S_i = \sqrt{\frac{\sum_{k=1}^{f_L} (k - C_i)^2 X_i(k)}{\sum_{k=1}^{f_L} X_i(k)}} \quad (4)$$

where C_i is the spectral centroid of i^{th} frame.

Spectral Rolloff

Spectral rolloff is computed as the frequency lies below a specified percentage of total spectral energy (e.g. 85%) and as a measure of spectral shape skewness at i^{th} frame is defined as:

$$\sum_{k=1}^{R_t} X_i(k) = 0.85 \sum_{k=1}^{f_L} X_i(k) \quad (5)$$

where $X_i(k)$ is the kth DFT coefficient at i^{th} frame.

Spectral Flatness

A high spectral flatness shows a similar amount of power in all frequency bands of the spectrum (such as white noise) and the spectrum graph will be relatively smooth and flat. A low spectral flatness represents a spiky pattern for spectral power. Spectral flatness at the i^{th} frame is calculated as:

$$Flt = \frac{\exp\left(\frac{1}{N}\sum_{k=1}^{f_L} lnX_i(k)\right)}{\frac{1}{N}\sum_{k=1}^{f_L} X_i(k)} \quad (6)$$

where $X_i(k)$ is the k^{th} DFT coefficient at the i^{th} frame.

Time-Frequency Flux

Analyzing a signal in the time-frequency plane may have more advantages than considering it in separate domains of time and frequency.[30,31] TFD specifies the energy distribution of a signal over the two-dimensional time-frequency space. After estimating TFD, first measure in this domain named TF-flux extends the spectral flux by calculating the rate of signal energy change along frequency and time axis together.[32,33] TF flux is defined as

$$TF_{Fl} = \sum_{n=1}^{N}\sum_{k=1}^{N} \rho[n+l, k+m] - \rho[n,k]$$

where ρ[n, k] shows TFD, l and m are predetermined values depend on the rate of signal energy change in the time-frequency plane (Here, these parameters are set to $l=1$ and $m=1$).

Time-Frequency Flatness

The TF-flatness is defined as a ratio of the geometric mean of a TFD divided by its arithmetic mean

$$TF_{Flt} = N^2 \frac{\prod_{n=1}^{N}\prod_{k=1}^{N} \rho[n,k]}{\sum_{n=1}^{N}\sum_{k=1}^{N} \rho[n,k]} \quad (8)$$

where $\rho[n, k]$ shows TFD.

Time-Frequency Entropy

The TF-entropy estimates the randomness in the distribution of signal energy in the time–frequency domain. It is calculated as:

$$TF_{En} = -\frac{1}{2} log_2 \sum_{n=1}^{N}\sum_{k=1}^{N}\left(\frac{\rho[n,k]}{\sum_n\sum_k \rho[n,k]}\right)^3 \quad (9)$$

where $\rho[n, k]$ shows TFD.

Statistical Analysis

In this study, Student's *t* test was applied to compare the means of the two mentioned groups. It is often used in hypothesis testing to determine whether a schizophrenia disorder actually has an effect on the population of interest or the two groups are different from each other. Here, $P<0.05$ is considered as statistically significant.

Results

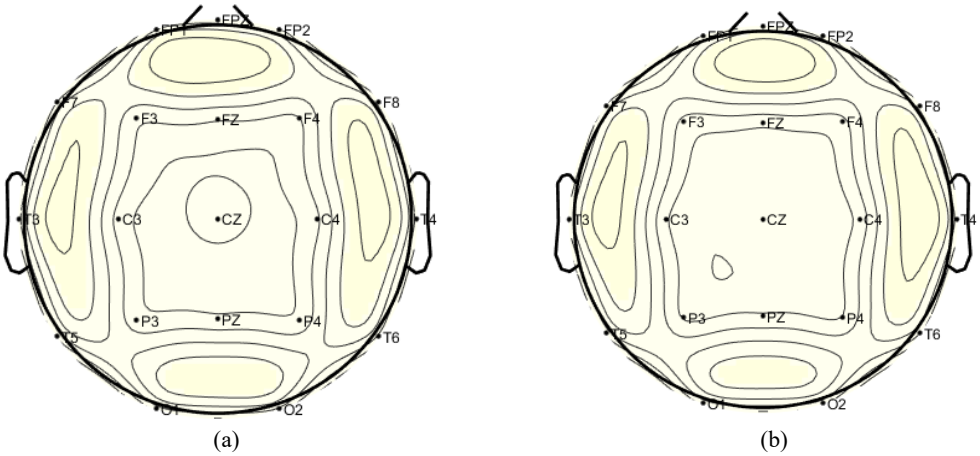
In the first stage, different measures for EEG signals of 20 patients with schizophrenia and 20 control participants were calculated. EEG signals practically consist of a non-stationary time series,[34] hence time series are divided into 2.56-second (512 samples) frames and their dynamics are assumed to be approximately stationary within each frame. The first measure, spectral flux was reported to be 1.5388 ± 0.0038 for the control group which is slightly lower than the case group (1.5497 ± 0.0058). Figure 2 presents the topographic image for spectral flux averaged over the case and control groups. Differences of spectral flux values between the two groups are significant in most channels ($P=0.0000$, Table 1).

The second measure, spectral entropy is higher in patients with schizophrenia compared with the control group (0.9018 ± 0.0428 and 0.8526 ± 0.0386, respectively). There was a significant difference in most channels between spectral entropy of the two groups ($P=0.0004$), with higher amounts in patients with schizophrenia (Figure 3 and Table 2). In both groups, the spectral entropy in frontal areas had lower values compared with other areas of the brain.

Topographic images of spectral centroid for each group are presented in Figure 4, and numerical values of this parameter over different channels are shown in Table 3. There was no significant difference ($P=0.4620$) between the two groups in spectral centroid (it was estimated to be 0.1180 ± 0.0022 and 0.1185 ± 0.0022 for control and case groups, respectively). In both groups, lower values of spectral centroid are obtained in frontal channels.

Table 1. The Mean ± SD of Spectral Flux

	Control Group	Schizophrenic Group	*P* Value
Fpz	1.5348 ± 0.0361	1.5371 ± 0.0399	0.5138
Fz	0.5414 ± 0.0320	1.5562 ± 0.0344	0.0000
Cz	0.5434 ± 0.0292	1.5538 ± 0.0399	0.0015
Pz	0.5468 ± 0.0313	1.5521 ± 0.0342	0.0851
C3	0.5414 ± 0.0289	1.5592 ± 0.0383	0.0000
T3	0.5417 ± 0.0358	1.5411 ± 0.0325	0.8335
C4	0.5382 ± 0.0275	1.5565 ± 0.0337	0.0000
T4	0.5363 ± 0.0317	1.5458 ± 0.0376	0.0040
Fp1	0.5329 ± 0.0348	1.5572 ± 0.0428	0.0000
Fp2	0.5357 ± 0.0353	1.5460 ± 0.0405	0.0040
F3	0.5377 ± 0.0334	1.5509 ± 0.0340	0.0000
F4	0.5420 ± 0.0355	1.5551 ± 0.0329	0.0001
F7	0.5388 ± 0.0490	1.5418 ± 0.0410	0.4828
F8	0.5298 ± 0.0403	1.5468 ± 0.0436	0.0000
P3	0.5414 ± 0.0291	1.5495 ± 0.0309	0.0040
P4	0.5399 ± 0.0295	1.5499 ± 0.0294	0.0003
T5	0.5371 ± 0.0286	1.5475 ± 0.0308	0.0002
T6	0.5375 ± 0.0300	1.5503 ± 0.0304	0.0000
O1	0.5403 ± 0.0310	1.5475 ± 0.0277	0.0092
O2	0.5386 ± 0.0312	1.5497 ± 0.0259	0.0000
Total	1.5388 ± 0.0038	1.5497 ± 0.0058	0.0000 ($P<0.05$)



(a) (b)

Figure 2. Topographic Image of Spectral Flux for (a) Control Group, (b) Schizophrenic (Case) Group.

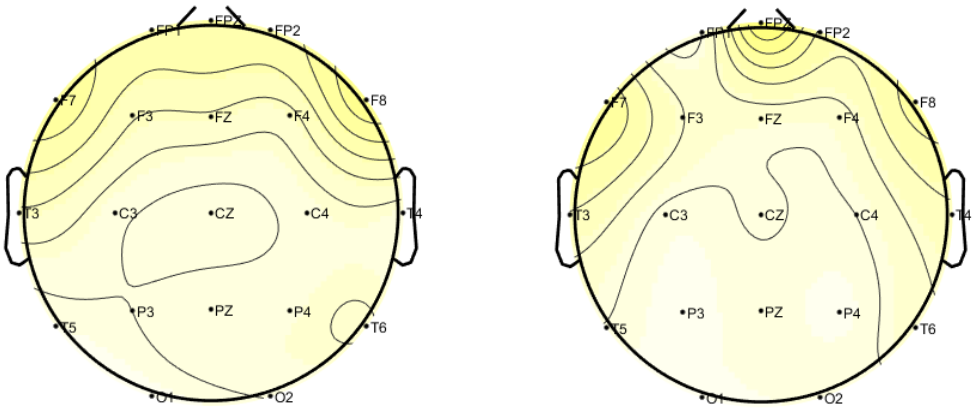


Figure 3. Topographic IMAGE for Spectral Entropy for (a) Control Group, (b) Schizophrenic (Case) Group.

Table 2. The Mean ± SD of Spectral Entropy

	Control Group	Schizophrenic Group	*P* Value
Fpz	0.8036 ± 0.1636	0.7880 ± 0.2016	0.3656
Fz	0.8518 ± 0.1635	0.9155 ± 0.0892	0.0000
Cz	0.8876 ± 0.0957	0.8952 ± 0.1212	0.4575
Pz	0.8897 ± 0.0926	0.9109 ± 0.0992	0.0187
C3	0.8854 ± 0.0937	0.9374 ± 0.0824	0.0000
T3	0.8698 ± 0.1519	0.8742 ± 0.1162	0.7322
C4	0.8770 ± 0.1152	0.9351 ± 0.0780	0.0000
T4	0.8658 ± 0.1286	0.8943 ± 0.1271	0.0175
Fp1	0.8362 ± 0.1608	0.9433 ± 0.1119	0.0000
Fp2	0.8246 ± 0.1479	0.8760 ± 0.1187	0.0001
F3	0.8493 ± 0.1415	0.8932 ± 0.1656	0.0025
F4	0.8477 ± 0.1450	0.9252 ± 0.0958	0.0000
F7	0.7903 ± 0.1293	0.8208 ± 0.1343	0.0138
F8	0.7377 ± 0.1625	0.8439 ± 0.1282	0.0000
P3	0.8753 ± 0.1017	0.9217 ± 0.0746	0.0000
P4	0.8581 ± 0.1575	0.9290 ± 0.0666	0.0000
T5	0.8734 ± 0.1206	0.9177 ± 0.0980	0.0000
T6	0.8640 ± 0.1545	0.9329 ± 0.0778	0.0000
O1	0.8880 ± 0.1157	0.9347 ± 0.0879	0.0000
O2	0.8769 ± 0.1222	0.9465 ± 0.0737	0.0000
Total	0.8526 ± 0.0386	0.9018 ± 0.0428	0.0004 ($P<0.05$)

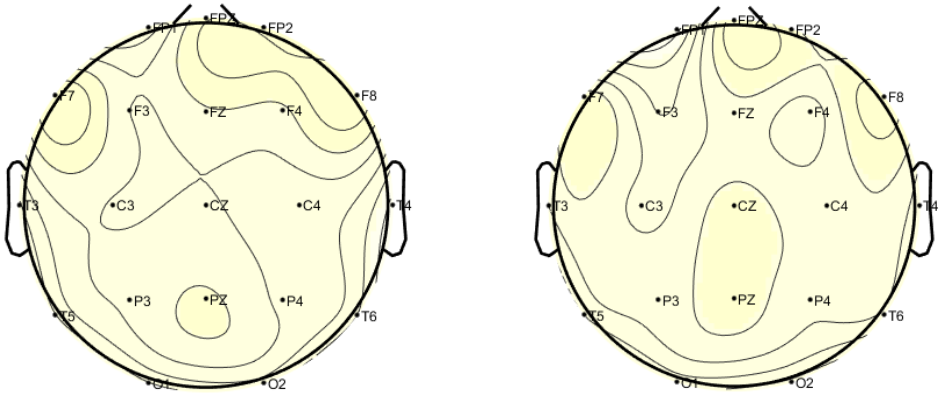
Table 3. The Mean ± SD of Spectral Centroid

	Control Group	Schizophrenic Group	*P* Value
Fpz	0.1162 ± 0.0087	0.1162 ± 0.0098	0.9409
Fz	0.1172 ± 0.0082	0.1173 ± 0.0113	0.9174
Cz	0.1175 ± 0.0084	0.1162 ± 0.0100	0.1423
Pz	0.1158 ± 0.0083	0.1174 ± 0.0105	0.0781
C3	0.1176 ± 0.0085	0.1188 ± 0.0117	0.2152
T3	0.1220 ± 0.0131	0.1173 ± 0.0095	0.0000
C4	0.1192 ± 0.0094	0.1188 ± 0.0119	0.7093
T4	0.1216 ± 0.0105	0.1201 ± 0.0109	0.1202
Fp1	0.1207 ± 0.0115	0.1240 ± 0.0119	0.0029
Fp2	0.1170 ± 0.0092	0.1177 ± 0.0109	0.4588
F3	0.1181 ± 0.0089	0.1187 ± 0.0111	0.5309
F4	0.1176 ± 0.0094	0.1195 ± 0.0118	0.0653
F7	0.1137 ± 0.0092	0.1157 ± 0.0121	0.0430
F8	0.1146 ± 0.0083	0.1146 ± 0.0102	0.9826
P3	0.1166 ± 0.0079	0.1180 ± 0.0105	0.1209
P4	0.1173 ± 0.0091	0.1181 ± 0.0105	0.3464
T5	0.1187 ± 0.0087	0.1194 ± 0.0103	0.4051
T6	0.1201 ± 0.0094	0.1193 ± 0.0096	0.3512
O1	0.1192 ± 0.0097	0.1211 ± 0.0114	0.0610
O2	0.1193 ± 0.0102	0.1221 ± 0.0107	0.0040
Total	0.1180 ± 0.0022	0.1185 ± 0.0022	0.4620 ($P>0.05$)

Figure 5 shows the topographic images of spectral rolloff for the two groups. The calculated parameter over different channels and statistical evaluation is shown in Table 4. For this modality, there was a significant difference between the two groups in most channels ($P=0.0129$), with higher values of spectral rolloff for patients with schizophrenia (0.3896 ± 0.0434 for the control group and 0.4245 ± 0.0410 for the case group). Similar to spectral entropy and centroid, our results show specific differences in most channels.

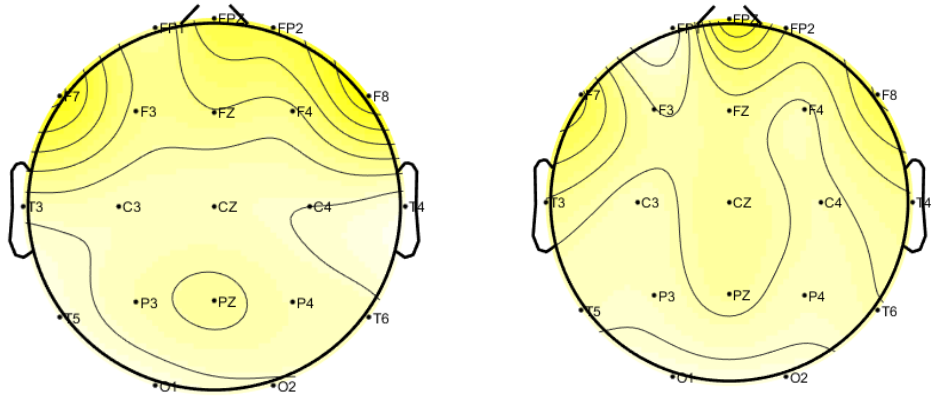
The spectral flatness was apparently lower in the control and case groups (0.1401 ± 0.0063 and 0.1467 ± 0.0077, respectively). Topographic images and numerical values of spectral flatness for the two groups are shown in Figure 6 and Table 5, respectively, showing a significant difference between the two groups ($P=0.0055$), with lower values in frontal and temporal channels.

The TFD-flux was estimated to be1.2675 ± 0.1806 for the control group, but in the case group, it gained a much higher value of 1.5260 ± 0.2083. Figure 7 shows the topographic images of TF-flux for the two groups. Calculated parameter over different channels and statistical



(a) (b)

Figure 4. Topographic Image for Spectral Centroid for (a) Control Group, (b) Schizophrenic (Case) Group.



(a) (b)

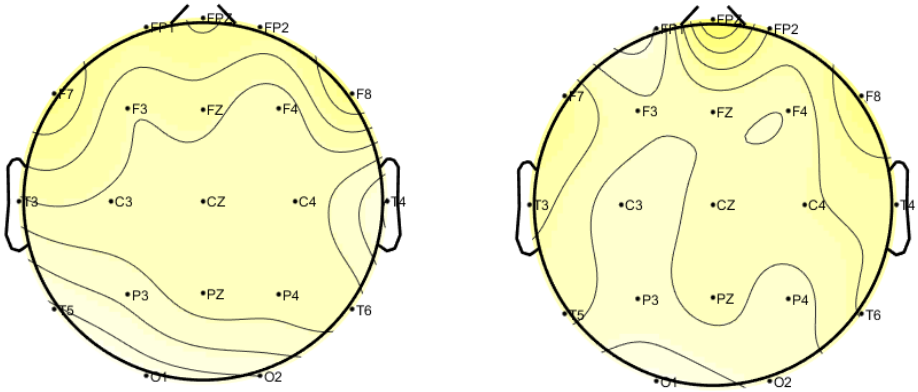
Figure 5. Topographic Image for Spectral Rolloff for (a) Control Group, (b) Schizophrenic (Case) Group.

Table 4. The Mean ± SD of Spectral Rolloff

	Control Group	Schizophrenic Group	*P* Value
Fpz	0.3411 ± 0.1690	0.3373 ± 0.1656	0.8056
Fz	0.3786 ± 0.1381	0.4094 ± 0.0967	0.0061
Cz	0.4040 ± 0.1083	0.3933 ± 0.1135	0.3033
Pz	0.3852 ± 0.0888	0.4081 ± 0.0983	0.0092
C3	0.4131 ± 0.1093	0.4496 ± 0.1040	0.0003
T3	0.4427 ± 0.1696	0.4048 ± 0.1225	0.0065
C4	0.4191 ± 0.1269	0.4441 ± 0.0997	0.0198
T4	0.4383 ± 0.1563	0.4435 ± 0.1398	0.7073
Fp1	0.4168 ± 0.1582	0.4934 ± 0.1221	0.0000
Fp2	0.3636 ± 0.1609	0.4129 ± 0.1385	0.0005
F3	0.3925 ± 0.1482	0.4208 ± 0.1408	0.0366
F4	0.3783 ± 0.1399	0.4473 ± 0.1059	0.0000
F7	0.3110 ± 0.1355	0.3480 ± 0.1488	0.0056
F8	0.2653 ± 0.1649	0.3653 ± 0.1407	0.0000
P3	0.3851 ± 0.0984	0.4301 ± 0.0906	0.0000
P4	0.3852 ± 0.1319	0.4303 ± 0.0937	0.0000
T5	0.4144 ± 0.1195	0.4497 ± 0.1087	0.0011
T6	0.4125 ± 0.1518	0.4550 ± 0.0873	0.0003
O1	0.4243 ± 0.1223	0.4681 ± 0.1164	0.0001
O2	0.4203 ± 0.1264	0.4780 ± 0.1040	0.0000
Total	0.3896 ± 0.0434	0.4245 ± 0.0410	0.0129 ($P<0.05$)

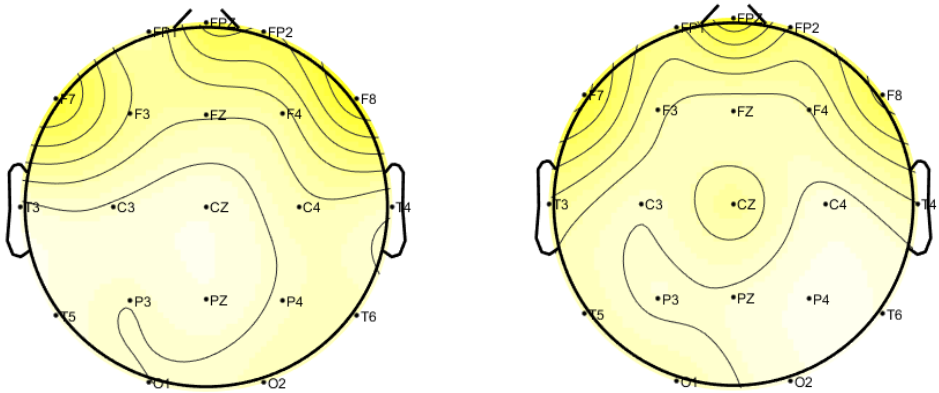
Table 5. The Mean ± SD of Spectral Flatness

	Control Group	Schizophrenic Group	*P* Value
Fpz	0.1345 ± 0.0676	0.1287 ± 0.0689	0.3642
Fz	0.1414 ± 0.0684	0.1447 ± 0.0657	0.6010
Cz	0.1368 ± 0.0666	0.1401 ± 0.0643	0.5969
Pz	0.1419 ± 0.0613	0.1467 ± 0.0684	0.4334
C3	0.1358 ± 0.0636	0.1547 ± 0.0623	0.0014
T3	0.1426 ± 0.0714	0.1433 ± 0.0643	0.9163
C4	0.1400 ± 0.0690	0.1507 ± 0.0644	0.0859
T4	0.1474 ± 0.0644	0.1518 ± 0.0677	0.4823
Fp1	0.1402 ± 0.0727	0.1597 ± 0.0771	0.0056
Fp2	0.1408 ± 0.0704	0.1420 ± 0.0649	0.8446
F3	0.1421 ± 0.0656	0.1418 ± 0.0674	0.9599
F4	0.1425 ± 0.0667	0.1533 ± 0.0684	0.0890
F7	0.1292 ± 0.0677	0.1349 ± 0.0656	0.3582
F8	0.1244 ± 0.0609	0.1385 ± 0.0682	0.0206
P3	0.1342 ± 0.0604	0.1491 ± 0.0639	0.0108
P4	0.1397 ± 0.0688	0.1462 ± 0.0664	0.3087
T5	0.1448 ± 0.0674	0.1484 ± 0.0706	0.5783
T6	0.1465 ± 0.0615	0.1481 ± 0.0679	0.7934
O1	0.1493 ± 0.0669	0.1559 ± 0.0736	0.3140
O2	0.1487 ± 0.0648	0.1549 ± 0.0694	0.3214
Total	0.1401 ± 0.0063	0.1467 ± 0.0077	0.0055 ($P<0.05$)



(a) (b)

Figure 6. Topographic Image for Spectral Flatness for (a) Control Group, (b) Schizophrenic (Case) Group.



(a) (b)

Figure 7. Topographic Image for TFD Flux for (a) Control Group, (b) Schizophrenic (Case) Group.

evaluation is presented in Table 6, showing a significant difference between the two groups ($P=0.0001$), with higher values of TF-flux for patients with schizophrenia. Our results showed that the frontal channels had lower values compared with the other channels.

The TFD-flatness was 0.9980 ± 0.0000 and 0.9981 ± 0.0000 for the control and case groups, respectively. Topographic images and numerical values of TF-flatness for the two groups are shown in Figure 8 and Table 7, respectively. Our results showed lower TF-flatness for the control group compared with patients with schizophrenia. There was significant difference between TF-flatness of the two groups in most channels ($P=0.0000$).

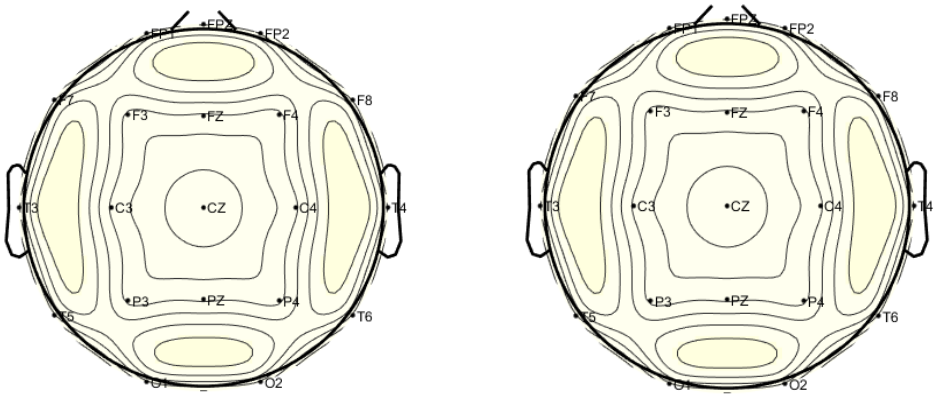
The TFD-entropy was slightly lower in the control group compared with the case group (16.23 ± 0.07 and 16.29 ± 0.13, respectively). Figure 9 shows the topographic images of TF-entropy for the two groups. The calculated values over different channels and statistical evaluation are presented in Table 8. For this parameter, there was no significant difference between the two groups ($P=0.1540$) with a higher value in the case group.

Table 6. The Mean ± SD of TF-Flux

	Control Group	Schizophrenic Group	*P* Value
Fpz	0.9861 ± 0.5586	1.0797 ± 0.5575	0.0699
Fz	1.2784 ± 0.5698	1.6162 ± 0.5761	0.0000
Cz	1.4412 ± 0.5851	1.4907 ± 0.6141	0.3711
Pz	1.4420 ± 0.5515	1.6675 ± 0.5759	0.0000
C3	1.3917 ± 0.5944	1.6455 ± 0.5384	0.0000
T3	1.4013 ± 0.7626	1.4635 ± 0.6044	0.3287
C4	1.3163 ± 0.5571	1.7167 ± 0.4256	0.0000
T4	1.3600 ± 0.6479	1.6002 ± 0.6690	0.0001
Fp1	1.2676 ± 0.6534	1.3985 ± 0.4538	0.0123
Fp2	1.0266 ± 0.4976	1.4002 ± 0.5962	0.0000
F3	1.2028 ± 0.5993	1.4945 ± 0.6064	0.0000
F4	1.2297 ± 0.5735	1.5706 ± 0.5424	0.0000
F7	0.9266 ± 0.4906	1.1044 ± 0.5656	0.0003
F8	0.8407 ± 0.4893	1.1917 ± 0.5752	0.0000
P3	1.3838 ± 0.5640	1.7003 ± 0.5167	0.0000
P4	1.3651 ± 0.5886	1.7916 ± 0.5397	0.0000
T5	1.4363 ± 0.6823	1.5668 ± 0.5290	0.0213
T6	1.3328 ± 0.6020	1.7332 ± 0.5966	0.0000
O1	1.3818 ± 0.5900	1.6199 ± 0.6226	0.0000
O2	1.3387 ± 0.6360	1.7162 ± 0.6219	0.0000
Total	1.2675 ± 0.1806	1.5284 ± 0.2057	0.0001 ($P<0.05$)

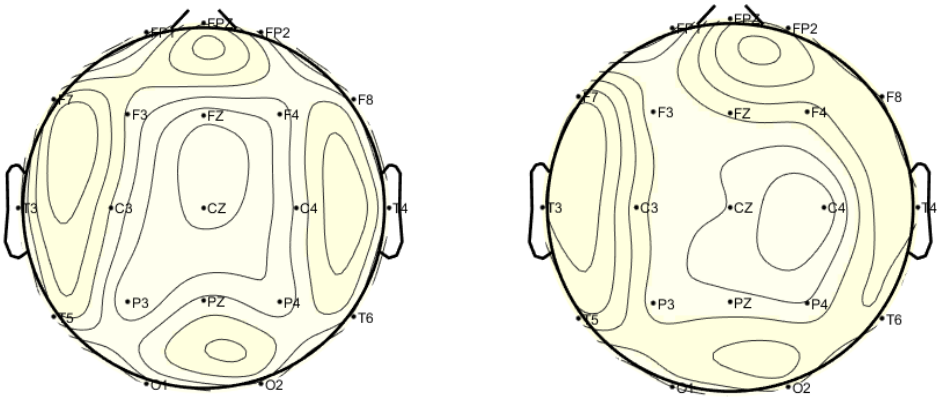
Discussion

We found that most spectral and TF features for the



(a) (b)

Figure 8. Topographic Image for TFD Flatness for (a) Control Group, (b) Schizophrenic (Case) Group.



(a) (b)

Figure 9. Topographic Image for TFD Entropy for (a) Control Group, (b) Schizophrenic (Case) Group.

Table 7. The Mean ± SD of TF-Flatness

	Control Group	Schizophrenic Group	*P* Value
Fpz	0.9979 ± 0.0003	0.9979 ± 0.0004	0.7072
Fz	0.9980 ± 0.0004	0.9981 ± 0.0003	0.0001
Cz	0.9980 ± 0.0003	0.9981 ± 0.0003	0.1909
Pz	0.9980 ± 0.0003	0.9981 ± 0.0003	0.0125
C3	0.9980 ± 0.0003	0.9981 ± 0.0003	0.0349
T3	0.9980 ± 0.0003	0.9980 ± 0.0003	0.6113
C4	0.9980 ± 0.0003	0.9981 ± 0.0003	0.0005
T4	0.9979 ± 0.0003	0.9980 ± 0.0003	0.0039
Fp1	0.9979 ± 0.0004	0.9982 ± 0.0004	0.0000
Fp2	0.9979 ± 0.0003	0.9980 ± 0.0003	0.0335
F3	0.9980 ± 0.0003	0.9981 ± 0.0004	0.0007
F4	0.9980 ± 0.0003	0.9981 ± 0.0003	0.0002
F7	0.9979 ± 0.0003	0.9980 ± 0.0004	0.0783
F8	0.9979 ± 0.0004	0.9980 ± 0.0003	0.0001
P3	0.9980 ± 0.0003	0.9981 ± 0.0003	0.0101
P4	0.9980 ± 0.0004	0.9981 ± 0.0003	0.0000
T5	0.9980 ± 0.0003	0.9981 ± 0.0003	0.0062
T6	0.9980 ± 0.0003	0.9981 ± 0.0003	0.0000
O1	0.9980 ± 0.0003	0.9981 ± 0.0003	0.0001
O2	0.9980 ± 0.0004	0.9981 ± 0.0003	0.0000
Total	0.9980 ± 0.0000	0.9981 ± 0.0000	0.0000 ($P<0.05$)

Table 8. The Mean ± SD of TF-Entropy

	Control Group	Schizophrenic Group	*P* Value
Fpz	16.09 ± 1.15	16.20 ± 1.15	0.3143
Fz	16.31 ± 1.19	16.27 ± 1.14	0.7233
Cz	16.35 ± 1.23	16.40 ± 1.28	0.7104
Pz	16.20 ± 1.11	16.35 ± 1.13	0.1395
C3	16.15 ± 1.14	16.26 ± 1.05	0.2914
T3	16.24 ± 1.24	16.07 ± 1.15	0.1192
C4	16.20 ± 1.12	16.39 ± 1.21	0.0776
T4	16.25 ± 1.30	16.22 ± 1.10	0.8063
Fp1	16.30 ± 1.27	16.48 ± 1.30	0.1234
Fp2	16.22 ± 1.24	16.14 ± 1.20	0.4456
F3	16.16 ± 1.14	16.32 ± 1.09	0.1168
F4	16.24 ± 1.15	16.28 ± 1.12	0.7296
F7	16.10 ± 1.29	16.12 ± 1.25	0.8542
F8	16.25 ± 1.36	16.18 ± 1.18	0.5396
P3	16.33 ± 1.22	16.34 ± 1.30	0.9160
P4	16.26 ± 1.19	16.40 ± 1.25	0.1931
T5	16.18 ± 1.15	16.18 ± 1.03	0.9984
T6	16.24 ± 1.12	16.30 ± 1.11	0.5627
O1	16.32 ± 1.30	16.30 ± 1.11	0.8666
O2	16.23 ± 1.20	16.25 ± 1.05	0.8676
Total	16.23 ± 0.07	16.27 ± 0.10	0.1540 ($P>0.05$)

case group were greater than the control group in all EEG channels which is in line with some other previous studies. Kutepov et al[23] showed that Lyapunov exponent of the control group was lower compared with patients with schizophrenia. In another study, Koukkou et al[35] reported different correlation complexity of EEG signals between the schizophrenic and control groups. They concluded that the complexity of the time series was significantly higher in patients with schizophrenia compared with the control group. They suggested the higher spatial complexity of the functional mechanisms of the brain in patients with schizophrenia could be a reflection of worsened organization of thinking.

Our results show that spectral and TF feature values decreased on the frontal cortex of patients with schizophrenia. According to some previous studies,[36-38] most patients with schizophrenia exhibit structural, functional, and metabolic abnormalities on their frontal lobe. Magnetic resonance imaging shows functional and structural changes in volume, white matter, gray matter, and functional activity of this lobe, but the underlying mechanisms of these findings are not yet completely understood. Additionally, our findings over the topographic images showed that there were differences between the two groups especially in central and parietal channels that is in line with a previous study,[39] showing that the brain connectivity in patients with schizophrenia increased non-synchronously compared with the control groups, especially in parieto-temporal and occipital regions.

Some limitations of this study should be considered. First, a relatively small sample has been studied. Second, all patients with schizophrenia were under antipsychotic treatment, therefore, the presence of drug effects could not be completely excluded. Future studies in a larger population of patients are needed in order to exclude these limitations. As a future work, we decide to analyze and compare the mentioned features in different frequency band (delta, theta, alpha, beta, and gamma).

Conclusion

The analysis of spectral methods for EEG signals of patients with schizophrenia showed abnormal patterns compared with healthy patients. The achieved results support the bad connection hypothesis in schizophrenia. From a methodological view, this study suggests that analysis of spectral and TF distribution of EEG signals could become an efficient tool for studying the neurobiological basis of psychiatric disorders. The suggested features could classify the two groups with a high degree of reliability.

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Conflict of Interest Disclosures

The authors declare that they have no conflict of interests.

Ethical Statement

Not applicable.

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