Electroencephalogram signal characterization of tinnitus patients based on sample entropy algorithm and wavelet transform

JianBiao Mai1,2,a, XinZui Wang1,b*, ZhaoBo Li1, HaiYin Jia1, Hui Fu2
1JJI HUA LABORATORY, Foshan, Guangdong, 528200, China
2School of Electromechanical Engineering, Guangdong University of Technology, Guangzhou, Guangdong, 510006, China
aemail:765923801@qq.com
*bCorresponding author’s e-mail: wangxz@jihualab.com

Abstract. Tinnitus is a disembodied, abnormal sound hallucination in the ear or skull, such as buzzing or hissing, in the absence of an external sound source. Tinnitus is a subjective sensation with no objective observable signs, and its causes are extremely complex. This paper explores the differences in sample entropy of EEG signals between tinnitus patients and normal subjects at different electrodes, using the non-parametric test Kruskal-Wallis test to find areas where there are significant differences between the different lateral tinnitus groups and the control group. Thirty tinnitus patients and 10 healthy controls were used to participate in the scalp EEG signal acquisition. The wavelet transform was first chosen to obtain the activity of each frequency band of the EEG, and then the electrophysiological differences between the two experimental groups were investigated by comparing the sample entropy of the EEG of the tinnitus patients with that of the healthy controls. The results reflect significant differences (p<0.05) in tinnitus patients at FT7, T7, C5, C6, TP7 and CP5 electrodes, mainly in the Delta band. These results compare the abnormalities of sample entropy in the resting state of patients with tinnitus on different sides of the ear with those of controls from an electrophysiological perspective, and are expected to be used as a potential characteristic indicator to distinguish normal people from tinnitus patients for the auxiliary diagnosis of tinnitus and to provide physicians with an aid in diagnosing depressed patients.

1. Introduction
Tinnitus has a high prevalence and low cure rate and its treatment is a global challenge. Worldwide, 12% - 13% of the general population suffers from tinnitus[1]. Due to its complex pathogenesis, there is no clear way to diagnose and cure tinnitus, so research into its treatment is still urgent. In this study, patients with heterolateral tinnitus and healthy controls were selected for approximately 10 min of resting EEG data. Electroencephalography (EEG) is a method of recording brain activity using electrophysiological indicators. During brain activity, postsynaptic potentials occurring simultaneously in a large number of neurons in the brain are summed to form a general reflection of the electrophysiological activity of brain nerve cells on the surface of the cerebral cortex or scalp. Commonly used methods for time-frequency domain analysis are FFT[2] (fast Fourier transform), AAR[3] (adaptive auto-regressive), AR[4] (auto-regressive), wavelet transform, etc. FFT, AAR and AR are only suitable for the analysis of smooth signals and have significant limitations for non-smooth
EEG signals. The wavelet transform\cite{5} is a typical time-frequency analysis method with multi-resolution properties and good resolution in both time and frequency domains, suitable for non-smooth signal processing. Using wavelet packet decomposition to divide the EEG signal into five bands as Delta (0.5-3.5 Hz), Theta (4-7.5 Hz), Alpha (8-12 Hz), Beta (13-30 Hz), Gamma (30.5-44 Hz).

EEG as a typical non-linear time series\cite{6}. The stability and sensitivity of traditional linear analysis is difficult to achieve satisfactory results\cite{7}. Non-linear analysis methods are gradually being applied to EEG analysis, with "entropy" being a typical measure of complexity and involving a variety of computational methods, each with its own characteristics. For example, it has been shown that approximate entropy can be used as a feature of EEG signals to distinguish between different states of brain activity\cite{8}. Sample entropy is a metric parameter to describe the complexity of a time series proposed by Richman et al. in 2000\cite{9}. Compared with approximate entropy, sample entropy has better accuracy and robustness, and the computation time of sample entropy algorithm is almost half than approximate entropy algorithm, and it is insensitive to lost data\cite{10}. Jia-Cheng Zhu et al. propose that Beta-band sample entropy can be used as a feature to classify depressed patients\cite{11}. The sample entropy is more suitable as an EEG feature than the approximate entropy. In previous studies, feature extraction as well as analysis of tinnitus patients has been less frequently carried out.

The main contributions of this paper are discussed as follows.

- To present an intelligent approach for for extracting resting state tinnitus features.
- To calculate resting-state tinnitus brainwave features using the 10-level wavelet packet decomposition and sample entropy algorithm.
- Significant difference between tinnitus patients and control group tested by non-parametric test.

The organization of the entire is designed in the following manner: Section 2 describes in detail the acquisition of EEG signals and the pre-processing methods. Moreover, Section 3 shows the principles of EEG signal analysis and the methods. The entire results and discussions are shown in Section 4. Section 5 provides a summary.

2. Materials and methods

2.1. Participants

The data for this study were provided by the partner hospitals. Data inclusion criteria\cite{12} for the tinnitus and healthy control groups were as follow: (1) All participants ranged in age from 18 to 65, they are both right-handed. (2) All participants were free of Central nervous system disease, mental illness and were not in anxiety and depression state (self-rating anxiety scale score and self-rating depression scale score, SAS and SDS < 50). (3) All participants had normal intelligence that matches their age. (4) Binaural pure tone threshold average (PTA) of less than 25dB for all tinnitus patients. The exclusion criteria for the tinnitus group were as follows: (1) Diagnosed progressive neurological disease, history of drug and alcohol abuse. (2) tinnitus duration < 3 months. (3) Those who have been treated for tinnitus. All participants are required to sign an informed consent form.

2.2. EEG pre-processing

The resting EEG raw data included tinnitus and control groups, with the tinnitus group being a binaural tinnitus group, a left tinnitus group and a right tinnitus group. MATLAB for R2014a and the EEGLAB for v13.0.0 toolbox were utilized. The raw data for each subject were loaded into EEGLAB. Pre-processing steps were as follows: (1) Load the electrode coordinates file, corresponding to the electrode coordinates of the electrode caps. (2) Browse through the full data and delete the section of abnormal signals with large fluctuations. (3) Removal of electrodes unrelated to the central brain, such as those around the eyes and those located at the root of the nose (CB1, CB2, FP1, FPZ FP2, AF3, AF4). (4) Remove 50 Hz industrial frequency interference by filtering 49.5 to 50.5 Hz using filtered depression filtering. Band-pass filtering from 0.5 to 80 Hz to remove signal-to-noise interference. (5) Re-referencing with reference electrodes at both ears (M1M2). (6) Linear interpolation replacement of bad electrodes. (7) Removal of independent components associated with artifacts using independent
component analysis (ICA). (8) Segmentation of data (into two-second segments). (9) Referring to previous studies, electrode data were derived for ten channels around the binaural area (FT7, FT8, T7, C5, C6, T8, TP7, CP5, CP6, TP8).

Figure 1. Distribution of 64 conductive poles.

3. Signal analysis

3.1. Wavelet packet transform

The wavelet transform is a multi-scale signal analysis method with the ability to characterise the local features of a signal in both the time and frequency domains, making it well suited to analysing the transient and time-frequency characteristics of non-stationary signals. The continuous wavelet transform of the signal \( f(t) \) is defined as:

\[
W(a, b) = \frac{1}{\sqrt{a}} \int f(t) \varphi \left( \frac{t-b}{a} \right) dt
\]  

(1)

\( W(a, b) \) is the wavelet transform coefficient, ‘a’ is the scaling or scale factor, ‘b’ is the translation factor, \( \varphi \) is the wavelet function, and ‘t’ is time. The binary discrete wavelet transform is defined as:

\[
C_{j,k} = \int f(t) \varphi_{j,k}(t) dt
\]  

(2)

\( \varphi_{j,k}(t) = 2^{-j/2} \varphi(2^{-j}t - k) \)  

(3)

The Mallat decomposition algorithm for the wavelet packet transform can be implemented by means of a filter bank circuit. Wavelet packets decompose EEG signals into different frequency bands at arbitrary time-frequency resolution and project the time-frequency components of the signal onto different orthogonal wavelet packet spaces. The single-channel EEG signal is set to scale space V0, and the process of dividing it into 3 levels of space is considered as Figure 2.
3.2. Sample entropy

Sample entropy is an improved measure of time series complexity based on approximate entropy, and is represented in this paper by SampEn (m, r, N), where ‘N’ denotes the length of the series, ‘r’ denotes the measure of "similarity", and ‘m’ denotes the number of dimensions. The calculation process is as follows:

1. Reconstruction of single-channel EEG signal sequences in a specific order to form a set of m-dimensional vectors:
   \[ X(i) = [u(i), u(i + 1), \ldots, u(i + m - 1)] \quad (4) \]
   for \( 1 \leq i \leq N - m + 1 \), count the number of vectors that meet the following conditions,
   \[ B_i^m(r) = \left( \text{number of } X(j) \text{ such that } d[X(i), X(j)] \leq r / (N - m), i \neq j \right) \quad (5) \]

   \( d[X, X^*] \) defined as \( d[X, X^*] = \max|u(a) - u^*(a)|, X \neq X^* \).

   \( u(a) \) is an element of the vector \( X \) and \( d \) denotes the distance between the vector \( X(i) \) and \( X(j) \), determined by the maximum difference of the corresponding elements, with \( j \) taking values in the range \([1, N-m+1], j \neq i \).

2. Find the average of \( B_i^m(r) \) over all values of \( i \), noted as \( B_i^m(r) \),
   \[ B^m(r) = (N - m + 1)^{-1} \sum_{i=1}^{N-m+1} B_i^m(r) \quad (6) \]

3. Let \( k = m + 1 \) and repeat steps (2)-(3) to obtain \( A_i^k(r) = (N - k + 1)^{-1} \sum_{i=1}^{N-k+1} A_i^k(r) \),
   \[ A_i^k(r) = \left( \text{number of } X(j) \text{ such that } d[X(i), X(j)] \leq r / (N - k), i \neq j \right) \quad (7) \]

4. The sample entropy (SampEn) is defined as
   \[ \text{SampEn} = \lim_{N \to \infty} \{-\ln[A^k(r)/B^m(r)]\} \quad (8) \]

   In practical computational applications, \( N \) cannot be \( \infty \), so when \( N \) takes a finite value, the sample entropy is estimated as:
   \[ \text{SampEn} = -\ln[A^k(r)/B^m(r)] \quad (9) \]

   where ‘ln’ denotes the natural logarithm, it can be found that the value of the sample entropy is related to the choice of parameters \( m, r, N \). According to the literature[13], I chose a parameter value of \( N = X_i(t), m = 2, r = 0.2 \text{SD} \), according to which the entropy value of the sample calculated has more reasonable statistical characteristics.

3.3. Statistical analysis

This experiment was statistically scored using MATLAB 2014a. The sample entropy of the EEG did not conform to a normal distribution and could not be directly tested for significant differences using a
t-test. The condition of normal distribution can be ignored using a non-parametric test. The component factors are group (binaural tinnitus group/right tinnitus group/left tinnitus group/normal group) statistics are considered significantly different if the p-value is less than 0.05. Statistical results with a p-value less than 0.01 are considered to be highly significant differences. The value of sample entropy reflects the randomness of the EEG signal [14]. A higher sample entropy represents less regularity and more randomness in neurodynamics [15].

4. Results & Discussion

4.1. Analysis of the difference in entropy results between the sample of patients with binaural tinnitus and the healthy group

Sample entropy values at FT7, FT8, T7, C5, C6, T8, TP7, CP5, CP6 and TP8 electrodes were analysed separately for comparison between 10 binaural tinnitus patients and 10 healthy volunteers. The results showed that the sample entropy values in the Delta band in the TP7 electrode were significantly different from those in the normal group (P<0.05) and in the Delta band in the CP5 electrode were significantly different from those in the normal group (P<0.05) in patients with binaural tinnitus, both of whom had significantly greater sample entropy values than normal. The entropy of the theta band in the C5 electrode was significantly different from that of the normal group (P<0.05). The entropy of the alpha band in the C6 electrode was significantly different from that of the normal group (P<0.05). As shown in Table 1.

| Channels | Delta | Theta | Alpha | Beta | Gamma |
|----------|-------|-------|-------|------|-------|
| FT7      | 0.2914| 0.6652| 0.1762| 0.0742| 0.1850|
| FT8      | 0.6652| 0.6263| 0.1762| 0.4488| 0.5518|
| T7       | 0.4989| 0.6456| 0.3720| 0.6652| 0.8287|
| C5       | 0.0787| 0.0231*| 0.4819| 0.2448| 0.7455|
| C6       | 0.8287| 0.2235| 0.0200*| 0.6263| 0.9569|
| T8       | 0.8077| 0.6849| 0.2793| 0.9353| 0.8711|
| TP7      | 0.0398*| 0.1298| 0.5885| 0.2914| 0.6652|
| CP5      | 0.0265*| 0.1595| 0.1595| 0.1595| 0.4017|
| CP6      | 0.6849| 0.3302| 0.2793| 0.4652| 0.7251|
| TP8      | 0.4171| 0.6456| 0.5700| 0.6073| 0.7455|

4.2. Analysis of the difference in entropy results between the sample of patients with right ear tinnitus and the healthy group

Sample entropy values at FT7, FT8, T7, C5, C6, T8, TP7, CP5, CP6 and TP8 electrodes were analysed separately for comparison between 10 binaural tinnitus patients and 10 healthy volunteers. The results showed that the sample entropy values in the Alpha band in the FT7 electrode were significantly different from those in the normal group (P<0.05). The sample entropy values in the Alpha band in the C6 electrode were significantly different from those in the normal group (P<0.05). The sample entropy values in the Gamma band in the FT7 electrode were highly significantly different from those in the normal group (P<0.01). As shown in Table 2.
4.3. Analysis of the difference in entropy results between the sample of patients with left ear tinnitus and the healthy group

Sample entropy values at FT7, FT8, T7, C5, C6, T8, TP7, CP5, CP6 and TP8 electrodes were analysed separately for comparison between 10 binaural tinnitus patients and 10 healthy volunteers. The results showed that the sample entropy values in the Delta band in the FT7 electrode were highly significantly different from those in the normal group (P<0.01). The sample entropy values in the Delta band in the T7 electrode were significantly different from those in the normal group (P<0.05). The sample entropy values in the Delta band in the C5 electrode were highly significantly different from those in the normal group (P<0.01). As shown in Table 3.

Table 3. Absolute power t-test results of left tinnitus group and control group.

| Channels | Delta  | Theta  | Alpha  | Beta  | Gamma |
|----------|--------|--------|--------|-------|-------|
| FT7      | 0.0068*| 0.5885 | 0.3577 | 0.4171| 0.8287|
| FT8      | 0.1441 | 0.1298 | 0.9353 | 0.9784| 0.0620|
| T7       | 0.0149*| 0.4652 | 0.2914 | 0.8498| 0.5338|
| C5       | 0.0053*| 0.1046 | 0.1368 | 0.7455| 0.5338|
| C6       | 0.6073 | 0.3438 | 0.9784 | 0.6263| 0.9353|
| T8       | 0.7049 | 0.4989 | 0.4171 | 0.4171| 0.2674|
| TP7      | 0.0787 | 0.5518 | 0.2559 | 0.7455| 0.3577|
| CP5      | 0.0884 | 0.0699 | 0.1368 | 0.8924| 0.8924|
| CP6      | 0.3867 | 0.9353 | 0.3169 | 0.1298| 0.7251|
| TP8      | 0.8711 | 0.9784 | 0.5162 | 0.4819| 0.3577|

4.4. Discussion

This study shows that the electrodes and frequency bands where the EEG activity appears abnormal in the resting state of tinnitus on different sides of the ear are different, and the analysis is carried out with a sample entropy value. The larger the sample entropy value, the less regular the neurodynamics proves to be and the greater the randomness. The electrodes that showed the most significant
differences were FT7, C5 and C6, while no significant differences were found for other electrodes such as FT8, T8, CP6 and TP8. The results in this paper found a higher chance of chaos in the Delta band, as noted in the literature [16], with reduced frequencies in the alpha band in the tinnitus population compared to the control group.

The study still has some shortcomings and the sample size is insufficient to perform a large scale sample entropy calculation. The next study will expand the sample size. What’s more, there are no special restrictions or matches for age or gender. And there was no detailed questioning and control of the medication taken by the tinnitus patients before the experiment. Future studies should be more rigorous in terms of the quality and condition of tinnitus patients and healthy volunteers.

5. Conclusion
This study used resting-state EEG to investigate abnormal differences in entropy in resting-state samples from patients with heterolateral tinnitus. The results of the study showed that there were more frequency bands with highly significant differences between patients with tinnitus in the left ear and controls, and the differences were greater, followed by tinnitus in the right ear. Binaural tinnitus patients had significantly different sample entropy values in C5, C6, TP7 and CP5 electrode from the normal group, especially in the Delta frequency band (0.5-3.5 Hz). Patients with tinnitus in the right ear had significantly different sample entropy values in the FT7 and C6 electrode compared to the normal group. Patients with tinnitus in the left ear had significantly different sample entropy values in the Delta frequency band (0.5-3.5 Hz). Overall, where significant differences were exhibited, the Delta band anomalies were more frequent.

These results compare the sample entropy abnormalities of patients with tinnitus on different sides of the ear with those of normal controls from an electroneurophysiological perspective. It is expected to provide a criterion for future clinical diagnosis of tinnitus and quantitative evaluation of tinnitus treatment, providing a more detailed and precise treatment plan for patients with tinnitus on different sides of the ear and improving treatment efficiency.

For future research on the EEG signals of tinnitus patients, the EEG signals can be carefully divided, decomposed into Delta1, Delta2, Beta1, Beta2, Beta3 frequency bands. Extracting features such as Approximate entropy(APEN), Fuzzy entropy(FuzzyEn), Reyni’s entropy(RE), Wavelet entropy, etc., increasing the number of samples for training, and using classifiers such as Support vector machines(SVM), K-nearest neighbour classifier(KNN), Radial basis function(RBF) to classify tinnitus patients and healthy subjects to improve accuracy and provide a feasible solution for clinical confirmation of diagnosis.

Acknowledgments
This work was supported by the Jihua Laboratory of China [grant numbers X201221XD200 and X190341TD190]; the National Key Research and Development Program of China [grant number 2019YFC0121300 and 2019YFC0121303].

References
[1] ZHANG Shuo-Ying, ZHANG Tian-Hong. Research progress in tinnitus-related treatment[J]. Medical Review, 2019, 25(15):3071-3075+3080.
[2] POLAT K, NES S. Artificial immune recognition system with fuzzy resource allocation mechanism classifier, principal component analysis and FFT method based new hybrid automated identification system for classification of EEG signals [J]. Expert System with Applications, 2008, 34(3):2039-2048.
[3] PFURSTCHELLER G, NEUPER C. Motor imagery and direct brain-computer communication[J]. Proceedings of the IEEE, 2001, 89(7): 1123-1134.
[4] Xu Baoguo, Song Aiguo. Feature extraction and classification of single-motion imagery EEG [J]. Journal of Southeast University: Natural Science Edition, 2007, 37 (4): 629-633.
[5] Xu Baoguo, Song Aiguo, Fei Shumin. Feature extraction and classification methods for EEG signals in online brain-computer interfaces[J]. Journal of Electronics, 2011, 39(05): 1025-1030.

[6] Chen Yongjun, Zeng Min, Yao Dezhong. Nonlinear kinetic analysis of multichannel EEG signal time series [J]. Journal of Epilepsy and Neurophysiology, 2001, 10(1): 28-31.

[7] TENG Jing, WANG Yulai, YAO Bin, et al. Application of EEG nonlinear analysis in medical research [J]. Chinese Rehabilitation Theory and Practice, 2007, 13(8): 748-750.

[8] Cai C, Ren J, Guo S, et al. Approximate entropy analysis on the electroencephalogram signal evoked by mental tasks[C]// Electrical & Electronics Engineering. IEEE, 2012: 52-54.

[9] Richman J S, Moorman J R. Physiological time-series analysis using approximate entropy and sample entropy [J]. American Journal of Physiology Heart & Circulatory Physiology, 2000, 278(6): H2039-H2049.

[10] Li Li, Cao Rui, Xiang Jie. A comparative study of the approximate entropy and sample entropy characteristics of EEG data [J]. Computer Engineering and Design, 2014, 35(03): 1021-1026.

[11] Zhu JiaCheng, Li YingJan, Cao Dan, Tang YingYing. A study on the abnormal entropy of positive emotion processing EEG samples in depressed patients [J]. Signal Processing, 2018, 34(08): 943-951.

[12] Wei Cao et al. Microstate in resting state: an EEG indicator of tinnitus [J]. Acta Otolaryngologica, 2020, 140(7): 564-569.

[13] Pincus S M, Goldberger A L. Physiological Time-Series Analysis: What Does Regularity Quantify [J]. American Journal of Physiology, 1994, 266(2): 1643-1656.

[14] Song Y, Zhang J. Discriminating preictal and interictal brain states in intracranial EEG by sample entropy and extreme learning machine [J]. Journal of Neuroscience Methods, 2016, 257: 45-54.

[15] Yum M K, Jung K Y, Kang H C, et al. Effect of a ketogenic diet on EEG: Analysis of sample entropy [J]. Seizure the Journal of the British Epilepsy Association, 2008, 17(6): 561-566.

[16] Schlee W, Schecklmann M, Lehner A, et al. Reduced Variability of Auditory Alpha Activity in Chronic Tinnitus [J]. Neural Plasticity, 2014, 2014(1): 436146.