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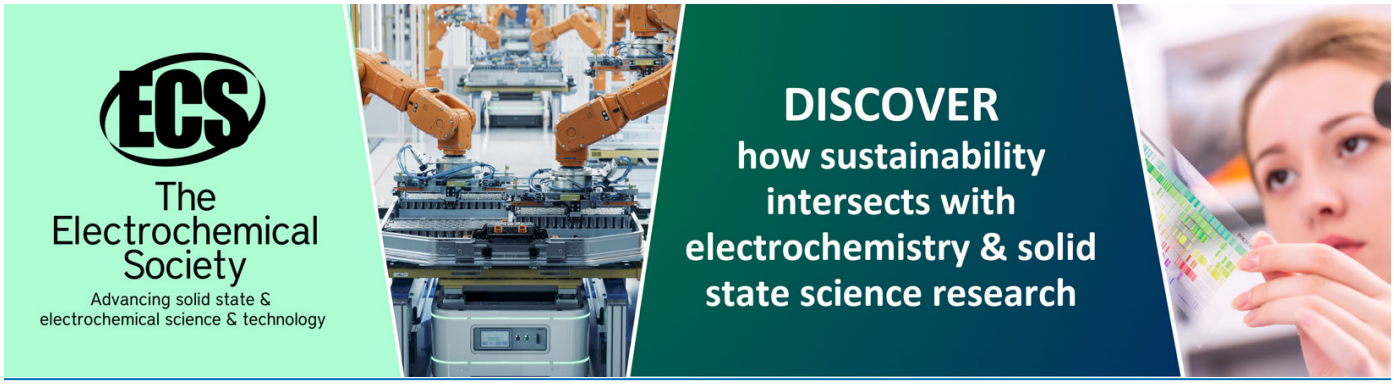

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An investigation of the specificity of features of early stages of Parkinson's disease obtained using the method of cortex electrical activity analysis based on wave trains

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Abstract. We developed a new method of signal analysis based on wavelet analysis, ROC-analysis, and non-parametric statistics for detailed investigation of the time-frequency dynamics of the electrical activity of the cerebral cortex. The idea of the method is in that the electroencephalogram (EEG) is considered as a set of wave trains (WT). WT is detected as a local maximum in the wavelet spectrogram of EEG. We consider WT as a typical component of EEG, but not as a special kind of EEG signals. The following parameters of WT are accounted: the frequency, the duration, the bandwidth, the number of WT per second, and the power spectral density (PSD). Differences between a group of the first stage Parkinson's disease patients and a group of healthy volunteers in the space of these parameters are investigated. ROC-analysis is used for this purpose. We analyzed functional dependence of AUC on the boundaries of the ranges of these parameters. Using this method, we have identified three frequency ranges, where differences between the group of the patients and the healthy volunteers were discovered. The paper describes the results of the investigation of the specificity of these features of early stages of Parkinson's disease.

1. Introduction

A lot of methods based on the analysis of Fourier spectra, wavelet analysis, autoregressive models, filtration, etc. were developed for EEG analysis [1, 2]. A decrease of the frequency in the alpha band for Parkinson's disease (PD) was demonstrated by many authors [3–10]. At the same time, EEG analysis using existing methods sometimes yields conflicting results, for example, in assessing changes in the beta rhythm power [8, 9].

Earlier, we have developed a method for analyzing the wave train electrical activity of the cerebral cortex based on wavelet analysis and ROC analysis [11]. The idea of this method of EEG analysis is in that we consider the EEG signal as a set of wave trains [12]. Unlike works devoted to the detection of electrical activity of one or two specific types, such as alpha spindles [13] and

sleep spindles [1, 2, 14–17], we analyze all kinds of wave train electrical activity in the brain in a wide frequency range. Moreover, we consider the wave train as a typical component of EEG, but not as a special kind of EEG signals. Our method of analysis is based on a statistical analysis of wavelet spectrograms, a new method for visualizing the results of the statistical analysis, and a new algorithm for detection of wave trains.

Using this method, we have identified three frequency ranges where differences were found between a group of patients with PD and a group of healthy volunteers [11, 18] in the C3 and C4 cortex areas that approximately correspond to the mu rhythm sources. The first range is 7.5–9.5 Hz (it corresponds to the mu frequency band approximately), the second range is 10.5–13.5 Hz (it corresponds to the mu band also), and the third range is 18–24 Hz (it corresponds to the beta-2 range approximately). The presence of the first and second frequency ranges possibly indicates a change in the borders of the range of the mu rhythm in patients with PD. The third frequency range is a confirmation of the regularities reported in [19]. Note that in [19], another frequency range 12–25 Hz was investigated. Therefore, the numerical characteristics of EEG given in this paper differ slightly from the numerical characteristics considered in [19]. In addition, in [19] the frequency ranges of beta-1 and beta-2 were not considered separately, but in further research, we have discovered that the characteristics of the wave trains in these sub-bands of beta differ and they should be investigated separately.

In this paper, we conduct a multichannel analysis of EEG, because it is interesting to investigate all cortex areas, but not only the C3 and C4 areas. We use the principal component analysis (PCA) method for the multi-channel analysis, which allows us to colligate data from all 17 EEG channels. Note that the principal component analysis is a useful statistical technique that represents the raw data in a lower dimensional feature space to convey maximum useful information. Many researchers use PCA for the investigation of PD disease. In some papers, the combination of PCA and other methods, for example, support vector machine (SVM), is used for the diagnosis. The authors [20] use PCA and SVM to diagnose PD on the base of a speech signal analysis; the classification accuracy of about 90% is obtained. In the paper [21], PCA is used for searching relationships between EEG data and emotional states of PD patients in comparison with healthy volunteers. In [22], the authors also investigate speech signals in patients with PD and healthy volunteers; a hybrid intelligent system is proposed which includes feature pre-processing using model-based clustering (Gaussian mixture model), feature reduction/selection using PCA, linear discriminant analysis (LDA), sequential forward selection (SFS) and sequential backward selection (SBS), and classification using three supervised classifiers such as least-square support vector machine (LS-SVM), probabilistic neural network (PNN), and general regression neural network (GRNN). The experimental results indicate that the combination of feature pre-processing, feature reduction/selection methods, and classification gives maximum classification accuracy of about 100% for the Parkinson's patient dataset. There are papers devoted to the deep brain stimulation, tremor classification, and the application of the neural networks [23], such as multiprocessor perceptron (MLP) and radial basic functional network (RBN). The results of the study [23] indicate that SVM provides about 80% accuracy of the recognition of the presence of a tremor in the patient on the base of EEG signals.

The purpose of this work is to study the specificity of the features of early PD obtained on the basis of the analysis of the wave train electrical activity of the cerebral cortex described in [11]. We check how our method works on patients with another neurodegenerative disease that is characterized by a tremor of limbs, namely, with the essential tremor (ET) disease. We discover differences in EEG when comparing patients with PD and patients with ET using the wave train analysis method. A new imaging technique based on AUC values (the area under the ROC curve [11]) and the distribution of these values on the cortex maps was used to investigate the specificity of the features of early PD.

2. Experimental Setting

The data on untreated (that is, not taking special medications earlier) patients with PD at early stages are compared with ET and healthy volunteers. Note that the group of PD patients includes patients with the left-hand tremor (14 persons) and patients with the right-hand tremor (18 persons), 32 patients in total. The number of patients with ET was 16 people. The number of healthy volunteers was 15 people. All patients and volunteers were right-handed. There were no statistically significant differences between the ages of the patients and healthy volunteers.

A standard 10x20 EEG acquisition schema was used for the data collection. A background EEG was recorded in standard conditions. The examined person sat in an armchair relaxing with arms disposing on the armrests and fingers dangling freely from the ends of armrests. The eyes were closed during the recordings. A 41-channel digital EEG system Neuron-Spectrum-5 (Neurosoft Ltd.) was used. The sampling rate was 500 Hz. The 0.5 Hz high-pass filter, the 35 Hz low-pass filter, and the 50 Hz notch filter were used. The duration of every record was about 3 minutes. The record was analyzed as is, without a selection of areas in the signal.

The values of AUC are considered for all areas of the cerebral cortex in the amount of 17 items, that is, a mapping the coefficients of components of PCA computed on AUC values is implemented over the cortex. If the AUC is close to 1, it means that the number of wave trains in the first group of subjects is greater than in the second group of subjects under consideration. If the AUC is close to 0, it means that the number of wave trains is less for the first group in comparison with the second one. The AUC values close to 0.5 correspond to the areas where differences between the groups are not detected.

3. Methods

We have calculated wave trains in the frequency interval 2–25 Hz on each cortex area in each patient with PD (the left-hand tremor patients and the right-hand tremor patients were united into a single group of 32 people), in each person in the healthy volunteers group (15 people), and in each patient with ET (16 people). For these data, the AUC values for various frequency sub-bands in the interval from 2 to 25 Hz with 0.1 Hz step were calculated.

Further, the AUC values were processed using PCA for all existed components. Figure 1 demonstrates the AUC values for the first PCA component for all patients with PD and for all patients with ET. One can see that the extreme AUC value (0.70) is in the range from 5 to 9.5 Hz, which corresponds to the theta and lower alpha frequency bands, and also in the range from 11 to 16 Hz (AUC value is 0.29), which corresponds to the upper alpha and lower beta ranges.

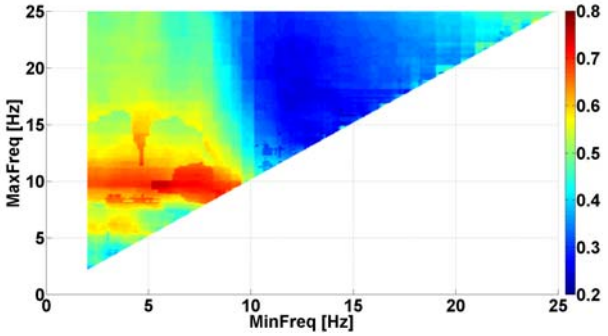

Figure 1. AUC values for the first component of PCA for the patients with PD (32) and the patients with ET (16).

The following ROC-curves correspond to the first frequency range (see Figure 2) and to the second frequency range (see Figure 3).

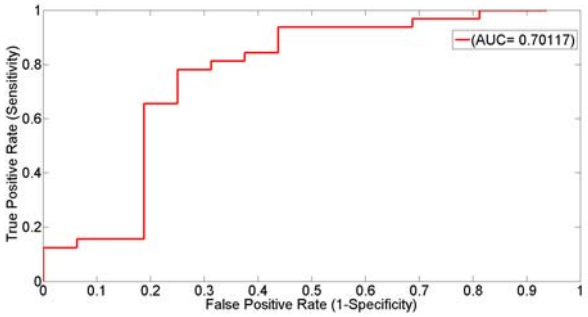

Figure 2. A ROC-curve for the first frequency range 5–9.5 Hz. The patients with PD (32) and the patients with ET (16) are compared.

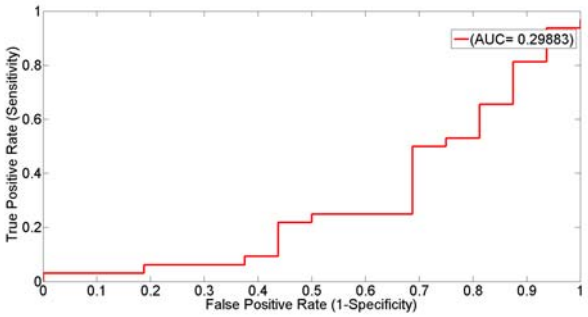

Figure 3. A ROC-curve for the second frequency range 11–16 Hz. The patients with PD (32) and the patients with ET (16) are compared.

The idea of the mapping the AUC values over the cortex is in that the coefficients of given component of PCA computed on the AUC values in given frequency band are displayed using a color map in various areas of the cerebral cortex.

Let us consider the mapping of the coefficients of the first component of PCA to the cortex areas to compare EEG signals of the patients with PD and the patients with ET. Let us consider the first frequency range, namely, 5–9.5 Hz. The most pronounced differences are observed in the occipital areas, namely, in O1 (coefficient = 0.34) and O2 (coefficient = 0.33). An interhemispheric asymmetry is not observed (see Figure 4). In the second frequency range 11–16 Hz, the most pronounced differences are observed in O1 (coefficient = 0.35) and O2 (coefficient = 0.33). An interhemispheric asymmetry is not observed also (see Figure 5). Note that the occipital areas of the cortex are a source of the alpha rhythm that is the most expressed rhythm of the cerebral cortex.

Thus, we can conclude that the developed method can distinguish the PD patients from the ET patients. Let us compare EEG of patients with PD with the healthy volunteers and then compare the patients with ET with the healthy volunteers to discover reasons for this difference.

Figure 6 demonstrates AUC values for the first component of PCA for the patients with PD and the healthy volunteers (computed in the frequency range from 2 to 25 Hz in 0.1 Hz step). One can see that an extreme AUC value (0.68) is situated in the frequency range from 5 to 9.5 Hz, which corresponds to the theta and lower alpha frequency bands, and also in the range

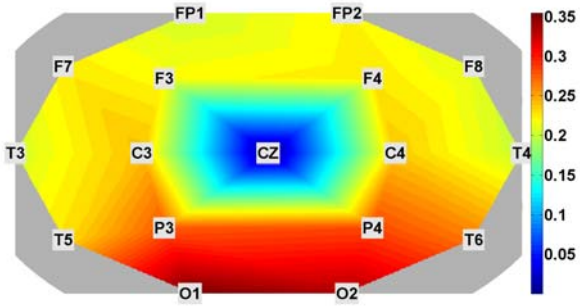

Figure 4. The cortex mapping of the coefficients of the first component of PCA. The patients with PD (32) and the patients with ET (16) are compared. The frequency band is 5–9.5 Hz. Note that the map has a blue spot in the center because the Cz electrode is the earth connection in our experimental setting.

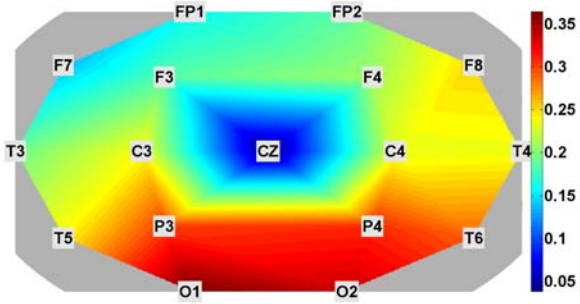

Figure 5. The cortex mapping of the coefficients of the first component of PCA. The patients with PD (32) and the patients with ET (16) are compared. The frequency band is 11–16 Hz.

from 11 to 16 Hz (AUC value is 0.33), which corresponds to the upper alpha and lower beta bands.

One can see that the discovered frequency bands do not totally coincide with ones obtained earlier in [19] for the C3 and C4 areas (namely, the first band was 7.5–9.5 Hz that corresponds approximately to the mu band, the second range was 10.5–13.5 Hz that also corresponds approximately to the mu band, and the third range was 18–24 Hz that corresponds approximately to the beta-2 band). This means that other cortex areas ensure a stronger difference between patients with PD and the healthy volunteers than the C3 and C4 areas.

Let us consider the mapping of the coefficients of the first component of PCA on the cortex areas to compare EEG signals of the patients with PD and the healthy volunteers. In the first frequency range, namely 5–9.5 Hz, one can see that the most pronounced differences are observed in the occipital areas, namely, in O1 (coefficient = 0.36) and O2 (coefficient = 0.33). The interhemispheric asymmetry is not observed (see Figure 7). Let us consider the second range, namely, 11–16 Hz. One can see that the most pronounced differences are observed in the occipital areas O1 (coefficient = 0.36) and O2 (coefficient = 0.30). The interhemispheric asymmetry is not observed also (see Figure 8).

Figure 9 demonstrates AUC values for the first PCA component for all patients with ET and the healthy volunteers (frequencies from 2 to 25 Hz in 0.1 Hz steps were considered). One can see that an extreme value of AUC (0.34) is situated in the frequency range from 5 to 9.5 Hz,

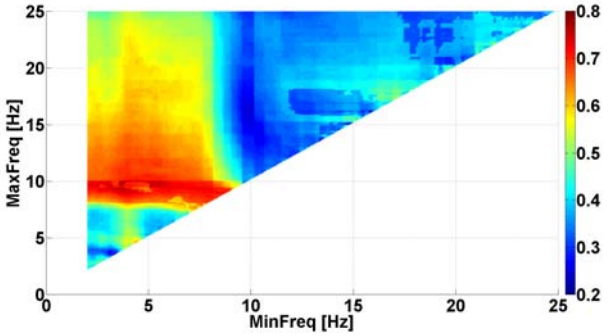

Figure 6. AUC values for the first component of PCA for the patients with PD (32) and the healthy volunteers (15).

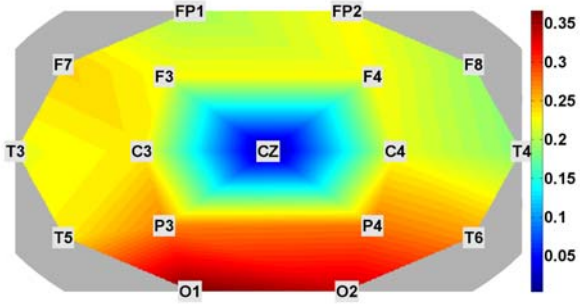

Figure 7. The cortex mapping of the coefficients of the first component of PCA. The patients with PD (32) and the healthy volunteers (15) are compared. The frequency band is 5–9.5 Hz.

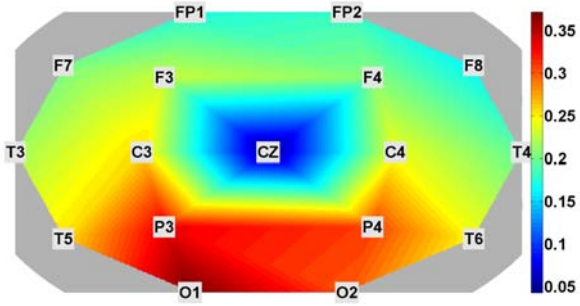

Figure 8. The cortex mapping of the coefficients of the first component of PCA. The patients with PD (32) and the healthy volunteers (15) are compared. The frequency band is 11–16 Hz.

which corresponds to the theta and lower alpha ranges, and also in the range from 11 to 25 Hz (AUC value is 0.61), which corresponds to the upper alpha and beta ranges.

Let us consider the mapping of the coefficients of the first component of PCA on the cortex areas to compare the EEG signals of the patients with ET and the healthy volunteers. Let us consider the first range, namely, 5–9.5 Hz. One can see that the most pronounced differences are observed in the occipital areas O1 (coefficient $= 0.33$) and O2 (coefficient $= 0.32$). The

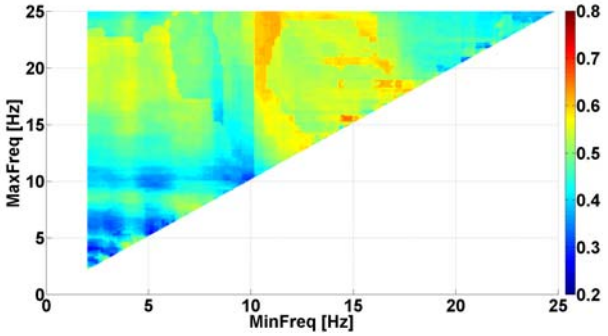

Figure 9. AUC values for the first component of PCA for the comparison of the patients with ET (16) and the healthy volunteers (15).

interhemispheric asymmetry is not observed (see Figure 10). In the second frequency range, namely, 11–25 Hz (see Figure 11), one can see that the most pronounced differences are situated in the left areas, namely, in O1 (coefficient $= 0.32$) and C3 (coefficient $= 0.31$). Note that a kind of the interhemispheric asymmetry is observed in this map (see Figure 11) that is probably a new neurophysiological regularity that is not described in the literature. Thus, the method of the analyzing the wave train electrical activity of the cerebral cortex enables to detect new neurophysiological regularities that were not detected by other methods.

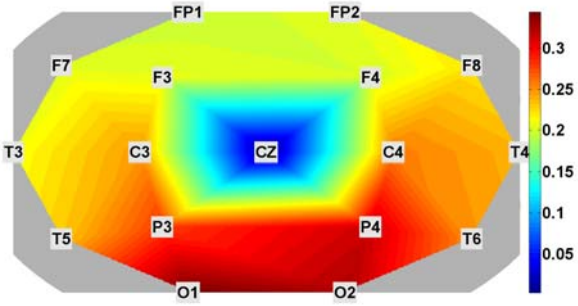

Figure 10. The cortex mapping of the coefficients of the first component of PCA. The patients with ET (16) and the healthy volunteers (15) are compared. The frequency band is 5–9.5 Hz.

4. Conclusions

The investigation of the specificity of the wave train features in the patients discovers considerable differences between the PD patients, ET patients, and healthy volunteers. We have observed differences in quantity of wave trains in the PD patients and ET patients in the following frequency bands: 5–9.5 Hz (approximately the theta and alpha frequency ranges) and 11–16 Hz (approximately the upper alpha and lower beta frequency ranges). The detailed analysis of the results indicates that both PD and ET patients differ in quantity of wave trains from the healthy volunteers, but the difference between ET patients and the healthy volunteers is less.

In [24], an increase in the power spectral density of the beta rhythm was demonstrated in animal models of the early stage of PD. Earlier an increase in the power of the beta rhythm was

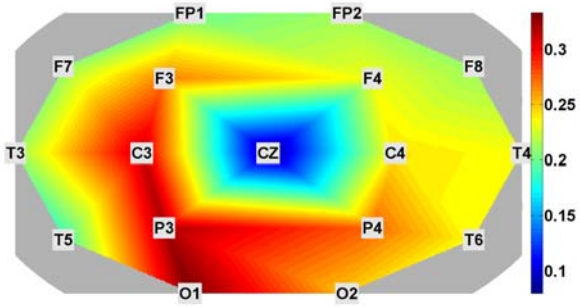

Figure 11. The cortex mapping of the coefficients of the first component of PCA. The patients with ET (16) and the healthy volunteers (15) are compared. The frequency band is 11–25 Hz.

also reported in [8]. At the same time, a decrease in the power of the beta rhythm was obtained in [9]. Our results do not resolve this contradiction, since we do not analyze the power spectral density of the beta rhythm, but only the quantity of the wave trains per second. However, our results confirm that the frequency characteristics of EEG are changed in this frequency range in patients with PD in comparison with the healthy volunteers.

The experiments with the developed method of EEG analysis based on the wave trains demonstrate that the method is prospective for looking for group statistical regularities in the early stages of Parkinson's disease and the essential tremor disease and can give a new basic knowledge about these diseases. We do not know whether revealed neurophysiological processes are compensatory ones or the early degenerative ones, however, discovered EEG features can be prospective for differentiating early stages of Parkinson's disease from the ET disease.

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