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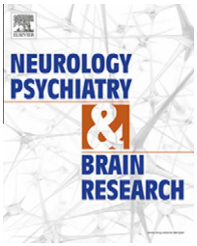

The slow and infraslow oscillations of cortical neural network

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ABSTRACT

Objective: In this study we investigated the properties of infraslow oscillations (ISOs) $\leqslant$0.05 Hz and delta frequency band in the patients during the epileptic discharges and in healthy persons who performed a variety of mental and physical tasks.

Methods: The EEG signals were recorded on the subjects who were divided into three groups. In the first group were patients with global epileptic seizures, while in the second group were patients with focal epileptic seizures. In the third group were healthy volunteers who performed different mental and physical tasks.

Results: By analyzing EEG data of epileptic patients, we showed that frequency peak exists at 1.5 Hz which is typical for general and focal epileptic seizures. In the type of general epileptic discharges the role of the slow rhythms at 0.05 Hz, was particularly pronounced and their origin was in fluctuations of cortical neural network. The properties of parameter spectral coherency of ISOs in healthy persons point to their important role in brain functioning.

Conclusions: Our results suggested that the role of ISOs could be extended, because they were detected in healthy human subjects during carrying out different tasks. Investigating the properties of parameter spectral coherency, we showed that in this case correlation between different regions of the brain was significantly modulated with ISOs.

1. Introduction

In the literature a number of works exist about the increased activity in the delta frequency band during the epileptic discharge,[1–3] but the role of slow rhythms was not sufficiently investigated, due to technical reasons. Full-band electroencephalography is a prominent method of detection of infraslow fluctuations during the execution of a somatosensory detection task. So far, there is no theory which satisfactorily explains the role of low frequencies in the functioning of the brain. Researchers at the Berkly set an interesting hypothesis that the slow frequency bands have a very important role in the functioning of the brain.[4] They have shown experimentally, that the resonant coupling between different regions of the brain was accompanied by increased activity in the delta range, which was then transmitted into higher frequency bands. All this indicates the necessity for ISOs and delta frequency bands to be further investigated. It would be too ambitious to give the answers to all questions in this paper. However, we have pointed out the similarities and differences in the properties of low frequency region, among healthy individuals who performed various mental and physical tasks and the persons who had epileptic seizures.

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2. Materials and methods

2.1. *Recording procedure and data acquisition*

The data used in this work were classified into three groups. Each group contained 50 EEG signal taken from all subjects. In the first and second group, EEG data were collected from 23 patients.[5] The duration of a time series was 1 min. During recording procedure, patients had seizures, that experienced clinical experts judged to be epileptic seizures. The sampling frequency was 256 Hz and International 10–20 system of EEG electrode positions and nomenclature was used in recording procedure. In the third group, the 64-channel EEG signals which lasted 1 min, were obtained from 23 healthy volunteers using BCI200 system[5,6] with sampling frequency of 160 Hz. Subjects in this group performed following tasks: open and close left or right fist, imagine opening and closing left or right fist, open and close both fists and both feet and finally, imagine opening and closing both fists or both feet. These tasks were carried out in every recorded time series and they were performed in consecutive order with periods of rest (~4 s) between them.

In order to remove artifacts, we applied the method of singular value decomposition of a matrix consisting of columns that represent time series with the artifacts. This method in literature known as well as Independent Component Analysis is relatively simple and efficient method of removing artifacts.[7,8] In short: a matrix containing the signals recorded in one subject (number of columns equal number of electrodes in the International 10–20 System) is decomposed by singular value decomposition into base vectors-columns. By visual inspection, all base vectors which contain ocular artefacts were discarded and the initial matrix artifacts free, was reconstructed. The whole procedure is repeated for all subjects and we formed three groups of signals for making statistical comparison of parameters power spectral density and spectral coherence of two reference signals taken from the frontal and parietal lobe.

2.2. *Data analysis*

For the purpose of detailed examination of the low frequency range (0–4 Hz), we applied an anti-aliasing low filter and resampled signals with 10 Hz. After that, we implemented Yule–Walker parametric estimation method with length of FFT of 1024 points, in order to estimate power spectral density (PSD) of signal. The Yule–Walker method is based on the autoregressive (AR) modelling in spectral analysis and can take advantage of the noise inherent in a biological system.[9] The most important feature of this method is that AR models tend to describe better spectra with certain "peaks" or data whose PSD is large at certain frequencies. This is very important in

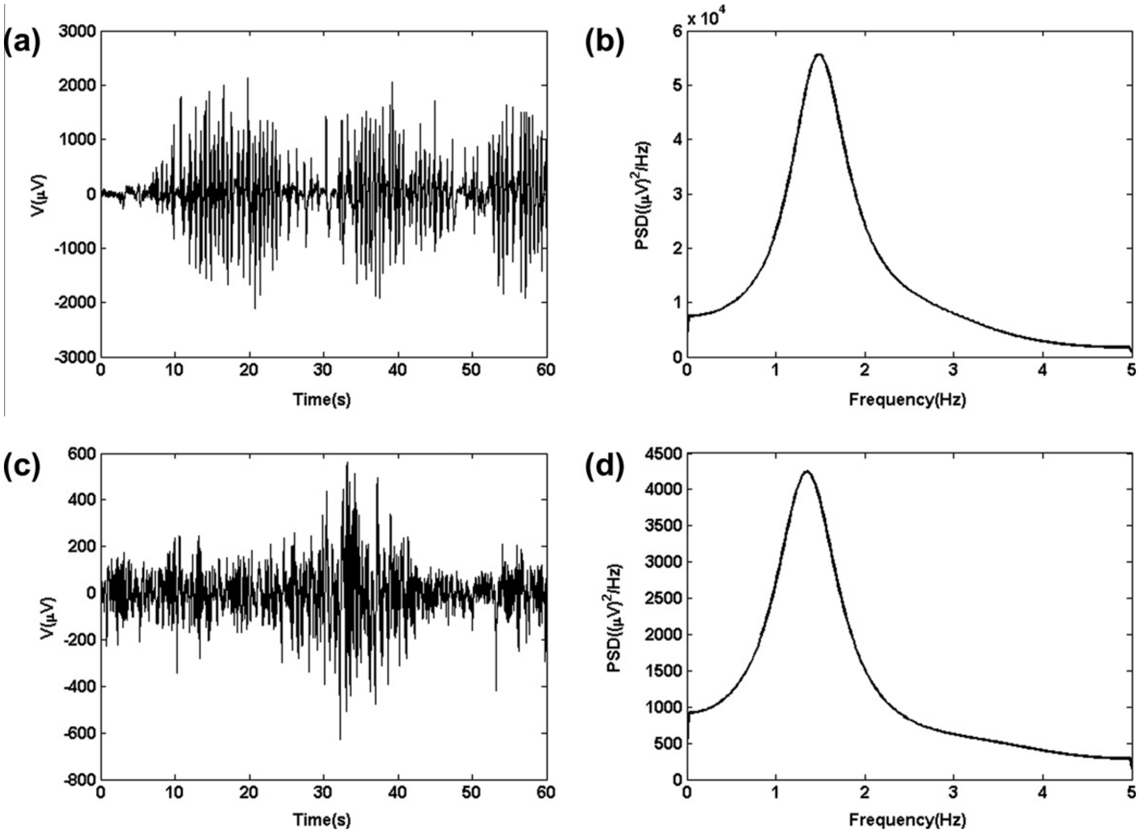

Fig. 1 – The EEG data with epileptic seizures: general (a) and focal (c). Corresponding power spectral densities (PSD) for the general (b) and focal epileptic seizures (d).

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our case, where we examined certain peak in delta frequency range during epileptic seizures. We determined correlation between the EEG signals from different regions of the brain, by calculating parameter spectral coherence $C(x, y)$, which is given in the formula:

$$C(x,y) = \frac{|P_{xy}(f)|^2}{P_x(f) \cdot P_y(f)} \quad (1)$$

where $P_{xy}(f)$ represents cross power spectral density of signals x, y and $P_x(f)$, $P_y(f)$ represent their power spectral densities. Our motivation for introducing this parameter is that the slow frequency may play an important role in the correlation between the various regions of the brain.

2.3. *Statistical analysis*

All results in this work were expressed as means ± SD and nonparametric Mann–Whitney U-test was used for statistical comparisons between groups. The standard value of $p < 0.05$ was considered significant.

3. Results

We analysed the EEG data with epileptic discharges which are recorded on frontal lobe (Fig. 1). In typical generalized epileptic attack (Fig. 1a) we observed the appearance of the characteristic peak around 1.5 Hz in the power spectrum (Fig. 1b). In addition, in Fig. 1a rhythmic activity clearly shown, with period of 20 s. This period corresponds to the frequency 1/20 s = 0.05 Hz, which indicates the important role of ISOs in generalized epileptic attacks. On the other hand, in Fig. 1c there are the characteristics of EEG of focal epileptic seizure, which was detected in the right hemisphere of the brain. As in the previous case, there was the appearance of the characteristic peak around 1.5 Hz (Fig. 1d), but without a clear expression of activity on 0.05 Hz. The signals recorded on frontal lobe in healthy volunteer who performed mental and physical tasks, are given in Fig. 2. By visual inspection of these images (Fig. 2b, d) the absence of characteristical peaks can be observed. In this case, ISOs were not clearly emphasized. All these facts, still do not indicate that the ISOs are not present in healthy individuals. To solve this problem, we determined the spectral coherence in the frequency range: 1–2 Hz of the persons who performed mentioned tasks (Figs. 3 and 4). In the first case two signals were taken from frontal lobe and in the second case from parietal lobe. Practically, in both cases, there were local maxima and minima for every 0.05 Hz (Figs. 3 and 4c), which clearly indicates that the electrical brain activity is modulated with the ISOs. However, this activity is more pronounced during the epileptic discharges.

In order to perform statistical tests, we calculated the mean value of spectral coherency and maximum value of PSD in frequency band of 1–2 Hz of each signal, for all three groups. Our motivation for calculating maximum value of PSD is roughly

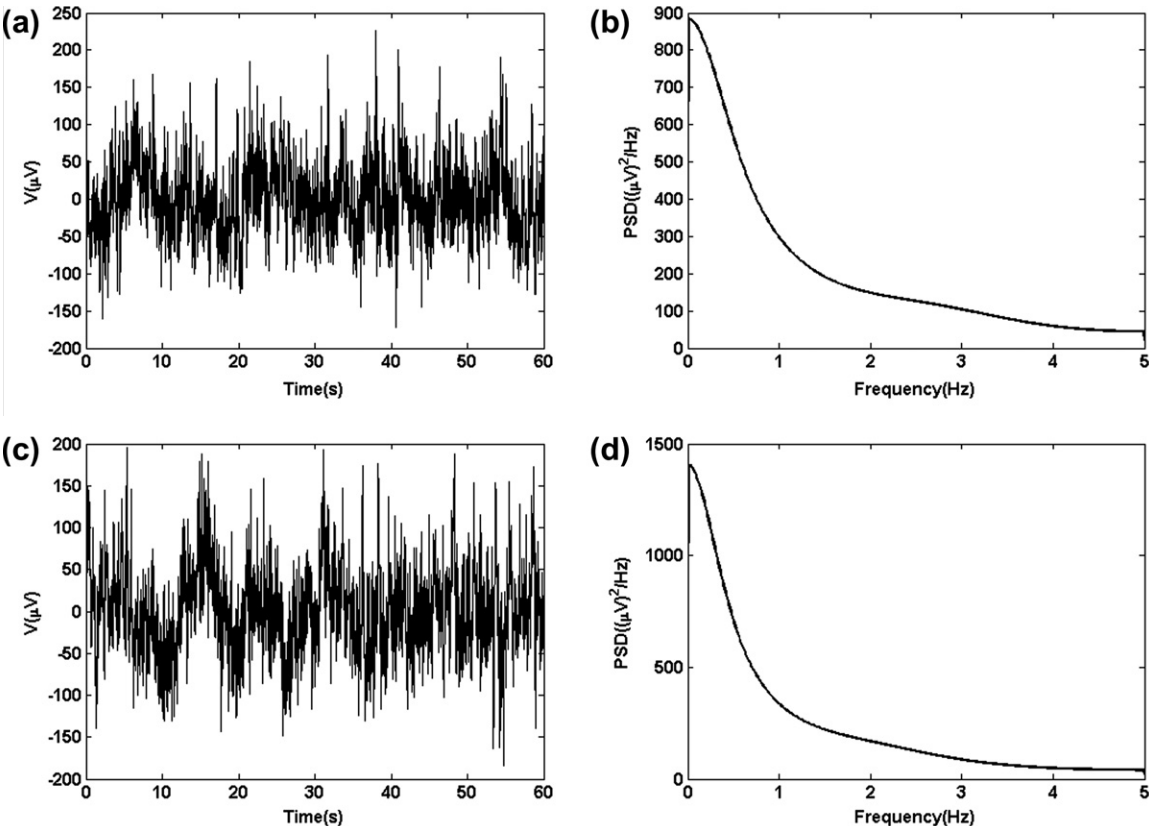

Fig. 2 – The EEG signals recorded on frontal lobe in healthy volunteer who performed various tasks. The first signal (a) and second signal (c), with corresponding power spectral densities (b), (d).

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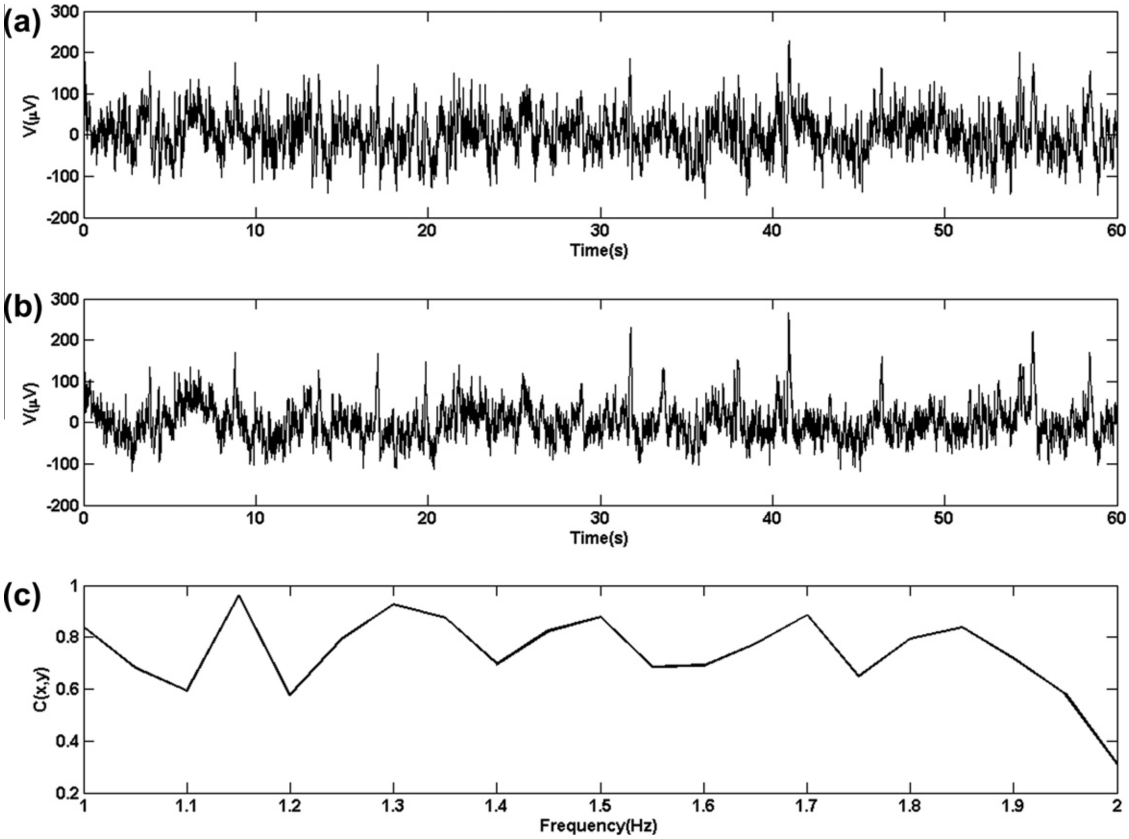

Fig. 3 – The values of parameter spectral coherency (c) in the frequency range 1–2 Hz, between two EEG signals (a), (b) recorded on frontal lobe.

speaking, to target frequency peak about 1.5 Hz. According to these results, we found a statistically significant differences between the maximum value of PSD between the group of subjects with global epileptic seizures (12,868 ± 12,452 $(\mu V)^2$/Hz) and the group of healthy volunteers (3100 ± 2542 $(\mu V)^2$/Hz, $p = 0$). In addition, significant statistical differences were established between the group of subject with focal epileptic seizures (3761 ± 2495 $(\mu V)^2$/Hz, $p = 0$) and healthy volunteers, as well as between global and focal epileptic seizures ($p = 0$). Also, interesting results were obtained in the case of parameter spectral coherence of two reference signals (frontal and parietal lobe). The mean value of this parameter in the range 1–2 Hz of global epileptic attacks (0.097 ± 0.08) is significantly lower, than the mean value in healthy volunteers (0.731 ± 0.150, $p = 0$). At the other hand, we haven't found statistical significant differences between global and focal groups (0.07 ± 0.05, $p = 0.34$). The statistical significant differences were found between groups of focal seizures and healthy volunteers ($p = 0$). Differences of spectral coherence between groups of epileptic subjects and healthy volunteers were dramatic, suggesting that spectral coherence in this band may be the key to understanding the origin and development of epileptic disorders.

4. Discussion

Properties of delta frequency range and infraslow oscillations are studied in different sleep stages of human subjects.[10] In this study, slow waves were detected in the cortical area and it was shown that there was very significant correlation ISOs with higher frequency bands. In this context, the prominent frequency bands are: 0.5–1 Hz, 1.5–4 Hz, 4–8 Hz and 7–18 Hz. It could be emphasized that the largest coupling of ISOs with higher bands was during the decline of their amplitude (the phase difference $\sim\pi$). These results point to a possible hypothesis that the oscillations represents excitability of cortical neural networks, which further increases modulated oscillations in frequency band,[11] 0.5–1 Hz. Furthermore, similar results were obtained in animals.[12,13] There were characteristic fluctuations observed around 0.1 Hz, which were coherent over longer distances. This means that the slow oscillations may have broader significance in the functioning of the brain and may represent a mechanism of coherency between different regions of the brain. This hypothesis is supported with our results in this paper. By visual inspection of Figs. 3 and 4, an array of maximum and minimum which recurring, could be seen every 0.05 Hz. In this picture, the values of parameter spectral coherence between different EEG signals in subject in the waking state, who performed a variety of mental and physical tasks, are shown. Since the signals were taken from different regions of the brain (frontal and parietal lobe), it can be concluded that the ISOs have an important role in the synchronization of neural networks of the brain. In addition, by visual inspection of the Fig. 2b and d, it can be seen that the values of power spectral density

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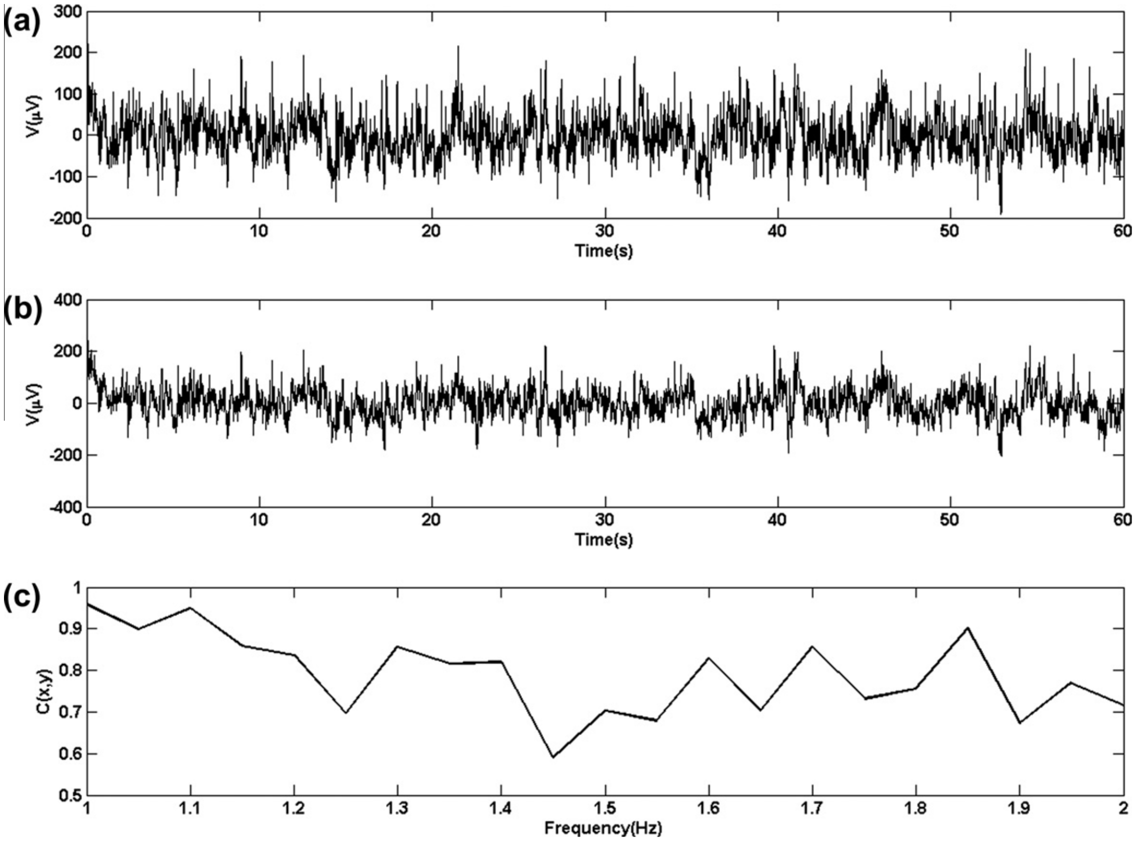

Fig. 4 – The shape of parameter spectral coherency (c) in the frequency range 1–2 Hz, between two EEG signals (a), (b) taken from parietal lobe.

were much higher in the area of infraslow oscillations. All these facts indicate that the ISOs have a significant impact on brain functioning in healthy individuals. It is important to point out that this array of 0.05 Hz was observed in all frequency bands, which means significant coupling exists between ISOs and higher frequency bands. The next important question is the role of slow oscillations in the pathophysiological states of the brain, such as for example, epilepsy. Number of studies, clearly indicate the possible role of ISOs in this neurobiological disorder. It has been shown that the negative peak or declining phase of ISOs triggers epileptic events.[10] But what was so far not discussed is whether these oscillations are characteristic for various types of epilepsy. In Fig. 1a waves with periods of 20 s in generalized epileptic discharge are clearly visible and modulate epileptic brain activity. However, in focal epileptic attack (Fig. 1c), this rhythmic activity was not visible, indicating occurrence of ISOs in synchronization of large neural networks. The activity of the ISOs was largest in generalized epileptic attack, when the most of the cortical neural network was affected by this disorder. These results were supported the hypothesis that the origin of ISOs could be rhythmic fluctuation of cortical neural networks. On the other hand, the observed peak around 1.5 Hz, confirms the hypothesis that ISOs may trigger increased activity in the delta frequency range. The possible explanation of this results could be found in an interesting study where the authors analyzed progression of the seizure activity in the animal model.[14] They showed that the coherency between the anterior thalamus and cortex plays an important role in the development of epileptic activity and that most of the coherence was expressed in the frequency range 1–3 Hz. Even after the removal signal contribution from the hippocampus, which is usually linked with the source of epileptic activity, coherence in the low frequency region still remains unchanged. The similar results were obtained during the research of spontaneus spike–wave discharges in animal model of absence epilepsy.[15] In this study, the distribution of EEG power in traditional frequency bands has been analyzed. It has been shown that the sudden increase of power in delta frequency range, could be used as an indicator of incoming epileptic seizure and peak frequencies of spontaneus spike–wave discharges in thalamus that appeared in the frequency range 0.5–1.5 Hz. Also, the important role of intracortical and cortical-thalamus associations in epileptice episodes was highlighted. Medically intractable seizures highly correlated with slow frequency ranges in humans.[16] With power training to decrease slow frequency ranges and increase the sensory motor rhythm (12–15 Hz), about 82% patients had significant reduction in seizure frequency.

The wavelet transform is particularly suitable tool[17,18] for detecting abrupt changes and various nonlinearities in the signal. In this sense, it has been demonstrated markedly

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increased activity in frequency band 0.8–1.6 Hz during the tonic phase[19] of epileptic seizure. Also, we used parameter relative wavelet energy (RWE) as a detector of epileptic events evoked by camphor essential and 1.8/cineole in rats brain activity and showed significant increase of relative wavelet energy in delta frequency range during epileptic seizures.[20]

5. Conclusion

Properties of slow rhythms and infraslow oscillations in the EEG, which are examined in this paper, indicate their importance in brain functioning. In that sense, their role is still enigmatic. So far, it is known that these types of oscillations are especially emphasized during sleep and epileptic discharges. In generalized epileptic seizures, ISOs of 0.05 Hz was dominant, with the occurrence of typical frequency peak of 1.5 Hz. However, we have shown that there was significant influence of the ISOs at 0.05 Hz, even in healthy individuals who carried out various mental and physical tasks. Also, the origin of these oscillations could be in fluctuations of cortical neural networks. Here the question naturally arises, are the cortical oscillations driver of brain activity. This question, now cannot be answered and further studies are needed to clarify coupling ISOs and delta band with higher frequency band. Solving this problem could be very important for understanding brain functioning.

Conflict of interest statement

None declared.

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