The search for statistical patterns of pathological activity in human EEG signals in focal epilepsy

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Abstract. Modern data science faces a lot of challenges, one of which is the search for diagnostic criteria for neurological diseases. New methods of statistical analysis are actively applied in the field of biophysics to solve this issue. In this paper we apply the Memory Functions Formalism to analyze electroencephalogram signal recordings in the sleeping state of 8 healthy subjects and 19 patients with nocturnal lobe epilepsy. We observe the considerable difference of statistical memory effects and fractal properties at the pathology in comparison with the control group. Furthermore, we reveal significant alterations in brain rhythms at power spectra of statistical memory functions for two groups of subjects. As a result, we show that the application of the statistical analysis methodology of bioelectrical brain cortex activity recordings, after appropriate verification, can be useful in the search for diagnostic criteria of nocturnal frontal lobe epilepsy.

1. Introduction
The determining of diagnostic criteria for neurological diseases is an important challenge in modern data science and biophysics. One of the most common neurological diseases is epilepsy, characterized by seizures associated with impaired brain function [1]. With the development of recording equipment and the accumulation of significant arrays of experimental data (for example, records of electroencephalograms, EEG), methods of statistical physics are increasingly used in diagnostics [2].

In [3] the authors applied the generalized Hurst exponent method to establish a statistically significant difference in multifractal patterns of the EEG signals of healthy (control group) and epileptic subjects. They discovered that the fractal degree was pronounced more in short variations for the control group and long variations for the subjects with epilepsy. For the validation of the obtained results, the authors performed three various statistical tests and concluded that their method can be used to distinguish signals of subjects in different groups.

This issue was also analyzed within the framework of Flicker-Noise Spectroscopy in paper [4] where similar data (interictal EEG signals recordings) were studied. Using this method they searched for differential characteristics of epilepsy in comparison with healthy subjects. As a result, they established specific collective dynamics in brain activity recordings of a subject with epilepsy.

Moreover, nowadays a combination of statistical analysis and machine learning methods is widely used. In the study [5] EEG signals of the healthy subjects and subjects with epilepsy during the seizure and their interical recordings are considered. The authors present an effective method based on convolutional neural networks for the pre-processing of raw epileptic-related EEG data. This method can also be used in a combination with other statistical analysis methodologies to increase diagnostic accuracy.
In this work, within the framework of Memory Functions Formalism (MFF) and the calculation of the Hurst parameter, we search for statistical patterns of pathological bioelectric activity in humans with nocturnal frontal lobe epilepsy (NFLE). Nocturnal frontal lobe epilepsy is genetic focal epilepsy characterized by cluster (alternating) short seizures emanating from the frontal lobe of the cerebral cortex during slow-wave sleep.

The aim of this work is to search for new diagnostic criteria for NFLE based on a statistical analysis of interictal EEG signals. Generally, nocturnal frontal epilepsy manifests itself in childhood (5–15 years), but its manifestations persist throughout life. Patients suffer from nocturnal hypermotor cluster seizures originating from the frontal lobe. Often, attacks are preceded by a feeling of lack of air, headache, auditory and visual hallucinations, somatic and autonomic disorders. Attacks are accompanied by sudden awakening. While the methods of searching for diagnostic criteria from EEG signals recorded during an epileptic seizure in NFLE are sufficiently developed, studies of interictal electroencephalograms are rare.

2. Memory Functions Formalism methodology
Memory Functions Formalism is a theoretical approach that studies the dynamics of stochastic processes in complex systems. During the analysis in the framework of MFF, a variety of parameters can be obtained. Based on Zwanzig-Mori projection operators [6, 7] the temporal dynamics of the studied parameter $X$ of a complex system is represented as a time series:

$$X = \{x(T), x(T+\tau), x(T+2\tau),..., x(T+(N-1)\tau)\}.$$ 

Then a chain of difference equations for autocorrelation function $a(t)$ and statistical memory functions $M_i (i=1,2,...,n)$ is obtained:

$$\frac{\Delta a(t)}{\Delta t} = \lambda_1 a(t) - \tau \Lambda \sum_{j=0}^{m-1} M_j(j\tau)a(t-j\tau),...,$$

$$\frac{\Delta M_{n-1}(t)}{\Delta t} = \lambda_n M_{n-1}(t) - \tau \Lambda \sum_{j=0}^{m-1} M_n(j\tau)M_{n-1}(t-j\tau).$$

Fourier images of the memory functions $M_i$ determine the spectral features of the studied parameter of the system:

$$\mu_0(\nu) = \left| \Delta t \sum_{j=0}^{N-1} a(t_j) \cos 2\pi \nu t_j \right|^2,$$

$$\mu_i(\nu) = \left| \Delta t \sum_{j=0}^{N-1} M_i(t_j) \cos 2\pi \nu t_j \right|^2.$$

For a quantitative description of statistical memory effects the authors proposed a frequency dependence of the non-Markov parameter:

$$\epsilon_i(\nu) = \left( \frac{\mu_{i+1}(\nu)}{\mu_i(\nu)} \right)^{1/2}.$$
In this paper, we consider the values of the non-Markov parameter at zero frequency $\varepsilon_i(0)$. In this case, the description of long-term periodic features of temporal signals is carried out. For example, if the values $\varepsilon_i(0) \gg 1$, then the investigated processes have a Markov character (short-term statistical memory appears). At values $\varepsilon_i(0) \sim 1$ the dynamics of temporal signals is characterized by long-term statistical memory, and the processes under study are of a non-Markov nature. The intermediate values of the non-Markov parameter determine the quasi-Markov processes (intermediate statistical memory).

3. Description of experimental data
Polysomnographic (recorded during sleep) multichannel EEG signals recordings of 8 healthy subjects with no history of neurological diseases and 19 subjects with nocturnal frontal lobe epilepsy were provided by the Sleep Disorders Center of the Ospedale Maggiore of Parma, Italy. The bioelectrical activity signals from the outer ear zone, parietal and frontal lobe (electrodes $A_1$, $P_4$ and $F_4$ respectively) were recorded, using central electrode $C_4$ as a reference electrode. Electrodes placement was performed by the International electrode placement system “10-20%” (figure 1); the experimental data were published in the Physionet database [8]. The average recording time duration is approximately 8 hours.

![Figure 1](image_url). The scheme of the “10-20%” International electrode placement system.
4. Results and Discussion
The statistical analysis of EEG signals was performed in three stages.
At the first stage, the areas of signal nonlinearity were determined by evaluating the nonlinearity coefficient:

\[ n = \frac{\sigma^2_t}{\sigma^2_0}, \tag{1} \]

where \( \sigma^2_t \) is the variance of the signal in the considered window, \( \sigma^2_0 \) is the variance of the signal over its entire duration. This data preprocessing is due to the significant duration of signals recordings, which results in an appearance of a large number of periodic overlapping artifacts that greatly complicate the analysis.

At the second stage, an autocorrelation analysis of the preprocessed polysomnographic EEG recordings for two groups of people was carried out. To quantify the correlation effects the mean values of non-Markov parameters for all electrodes were calculated. Then the ratios of these parameters were calculated to compare statistical memory effects manifestation for a group of patients with NFLE and a group of healthy subjects (see table 1). As a result, a “meaningful” electrode was identified, as an electrode for which the values of the studied parameters differed the most for both groups. Determination of this electrode allows narrowing the range of searching the diagnostic criteria by considering a localized area of cerebral cortex in which the pathological activity of neurons ensembles manifests the most significantly.

| Electrode | \( \bar{e}_1(0) \) | \( \bar{e}_2(0) \) | \( \bar{e}_3(0) \) | \( \bar{d}_1(0) \) |
|-----------|-----------------|-----------------|-----------------|-----------------|
| \( A_1 \)  | 1.07            | 1.02            | 1.03            | 1.45            |
| \( F_4 \)  | 1.24            | 1.02            | 1.05            | 3.40            |
| \( P_4 \)  | 1.13            | 0.98            | 1.02            | 2.16            |

Generally, the values of the non-marking parameter for the temporal signals of healthy subjects and patients with NFLE relate to the interval \( e_i(0) > 10 \). This allows evaluating the investigated processes as quasi-Markov with the manifestation of intermediate statistical memory.

The calculation of mean values of the Hurst parameter for all electrodes was also used as an additional criterion for the identification of a “meaningful” electrode. It showed significant differences in the fractal structure of signals from \( F_4 \) for patients with epilepsy and the control group (\( H = 0.34, \bar{H} = 0.5 \) respectively) in comparison with \( A_1 \) (\( H = 0.48, \bar{H} = 0.5 \) respectively) and \( P_4 \) (\( H = 0.53, \bar{H} = 0.5 \) respectively) electrodes. It should be noted that the obtained values of the Hurst parameter for healthy subjects, which correspond to a random walk, can be associated with the implementation of the first stage of this study. The reason for the difference in the values of the Hurst exponent for patients with NFLE will be disclosed below. Thus, the \( F_4 \) electrode is considered “meaningful” and signals from this electrode were analyzed at the next stage of the study. It should be noted that mean values of the non-Markov parameter \( \bar{e}_1(0) \) and \( \bar{d}_1(0) \), along with the Hurst parameter can be used as criteria for NFLE diagnosis.

For further study, from the control group and the group of patients, one subject was selected with the parameter values closest to the mean values for their group. In the control group, it is subject number 5, and in the patients group it is subject number 15.

At the final stage of the study, the spectral features of EEG signals for two groups of subjects were analyzed. On the graphs of the power spectra of statistical memory functions a manifestation of different types of brain rhythms is shown for the control group subject (figure 2) and patient with NFLE (figure 3).
Figure 2. Power spectra of the statistical memory functions of EEG signals for a healthy subject. Arrows denote frequencies with the most intense activity.

Figure 3. Power spectra of the statistical memory functions of EEG signals for a patient with NFLE. Arrows denote frequencies with the most intense activity.
For the healthy subject $\alpha$- and $\delta$-activity are manifested the most (12 Hz and 0.6 Hz respectively). These brain rhythms correspond to the natural restful sleep or resting state. On the contrary, for the patient with NFLE, in addition to the $\delta$-rhythm (0.5 Hz), which is natural for the sleeping state, the $\gamma$-rhythm (72 Hz) is also manifested. The $\gamma$-activity corresponds to active wakefulness when solving complex issues that require maximum concentration of attention.

Besides that, at the pathology the appearance of overlapping periodic processes in the form of high-amplitude bursts of brain activity was established. The manifestation of such bursts may indicate the presence of disease and serve as criteria for the diagnosis of NFLE. The presence of a significant number of overlapping periodic (resonant) processes leads to persistent and antipersistent correlations and a difference in the values of the Hurst exponent from the scenario of a random walk ($H=0.5$).

5. Conclusions
The human brain is a unique complex compound object, the study of which, as well as the study of changes in its activity, can be carried out by the methods of statistical analysis. This approach allows detecting diagnostic patterns in case of deviations from the normal functioning of the human brain. In the future, the discovered patterns can become the basis for automated intelligent systems for the analysis and diagnosis of various brain diseases.

In this paper autocorrelation analysis in the framework of Memory Functions Formalism was performed. The application of this methodology gives a variety of parameters that can be used as diagnostic criteria in the search for neurological [9–14] or psychiatric [15–17] diseases.

The obtained results allow determining the manifestations of pathological activity in neurological disease – nocturnal frontal lobe epilepsy, using the methods of statistical physics analysis. After additional verification, the methodology of Memory Functions Formalism, in combination with other methods of analysis, will make it possible to diagnose NFLE with greater accuracy. It should be noted that this is a rather difficult task when it comes to analyzing interictal signals (i.e. EEG signals recorded between epileptic seizures) [4, 18–20].

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