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Studying electrical activity of the brain within the concept of coordination of rhythmic processes

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Abstract. *Purpose* of this work is to study the effects of one-day sleep deprivation using the concept of coordination between brain rhythms as a complex network. The research *method* is the cross-correlation analysis of non-stationary processes, which is an extension of fluctuation analysis to the case of two signals. Recordings of electrocorticograms of mice in two states are considered: before and after sleep deprivation. As a *result* of the studies carried out, differences have been established between functional states, the diagnosis and quantitative description of which can be carried out using local scaling exponent. *Conclusion.* Additional possibilities for analyzing the complex dynamics of electrical activity of the brain within the framework of the concept of rhythm coordination are illustrated.

Keywords: rhythmic dynamics, cross-correlation analysis, nonstationarity, scaling exponent, electrocorticogram.

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Introduction

Networks of interacting elements are found in various fields of science and technology. The human body can be viewed in the context of a complex network in which multicomponent physiological systems, each with its own regulatory mechanism, constantly interact to coordinate their functions [1–4]. However, despite significant progress and achievements in physiology over the past decades, the principles and mechanisms by which various systems and subsystems in the human body dynamically interact as a single network and integrate their functions to form physiological states in health and disease remain unknown. The search for answers to these fundamental questions is undertaken within the framework of the interdisciplinary concept of "Network Physiology" [5, 6]. In addition to defining health and disease through

structural, dynamic, and regulatory changes in individual physiological systems, it focuses on the coordination and network interactions between different systems and subsystems. Identifying and quantifying interactions is an actual problem due to the complex dynamics of body systems [7,8], and improving the relevant tools is an important task [9,10].

The development of network physiology has allowed us to look at many problems from a different perspective, in particular, at the study of the dynamics of brain rhythms. Rhythms have been known in the nervous system for a long time, but it remains a mystery what biophysical mechanisms produce them and what functions they serve. In the last decade, many studies have appeared linking rhythms at different frequencies with attention [11], perception [12], learning and memory [13,14], as well as with motor behavior [15]. Research in neuroscience has traditionally focused on studying the frequency of action potential generation by neurons at the micro level, while at the macro level, the areas of the brain involved in solving various problems are studied. Much less clear, however, are the principles by which lower-level signals are organized to produce the effects observed in macrodynamics. A number of studies at the micro level focus on local field potentials and the corresponding interactions between neural oscillations [16]. At the macroscopic level, studies have traditionally examined the coherence of the same rhythm in different brain regions [17] with limited studies of the synchronous occurrence of specific pairs of cortical rhythms [18–20].

Recently, a paradigm of network interactions of physiologically significant rhythms was proposed and various classes of coupling forms were found that coexist during a certain physiological state and are reorganized during transitions between physiological states [21,22]. These studies demonstrated the presence of dynamic networks of interactions between brain rhythms and showed that physiological states cannot be fully described by focusing only on individual rhythms and on certain paired interactions. According to the conclusions of these studies, the continuous coordination between all brain rhythms as a complex network underlies physiological function. At the same time, the microarchitecture of the modulation of wave processes over short time intervals carries important information about the nature of rhythm interactions. The authors of the works [21, 22] substantiated that the interaction between each pair of brain rhythms is characterized by a certain profile and in general these interactions are represented by an ensemble of profiles that is typical for a particular physiological state.

Based on the ideas presented in the works by [21, 22], this paper investigates the effects of brain rhythm coordination in experiments on mice subjected to one-day sleep deprivation. Although short-term effects of sleep deprivation have been studied less than long-term sleep deprivation, they also lead to changes in brain electrical activity [23]. The paper studies the possibility of detecting changes in rhythm coordination based on cross-correlation analysis adapted to the case of non-stationary dynamics [24, 25].

1. Metods

1.1. DCCA. Given the limitations of classical probabilistic methods of signal analysis when considering the dynamics of systems with time-varying characteristics, approaches using various variants of fluctuation analysis [26–28] are quite popular. Their main feature is the removal of slow non-stationarity (trend) from the signal profile, which can formally be interpreted as a procedure for reducing to stationarity. However, such a procedure is far from always effective, and it is advisable to use it after preliminary data processing, which follows, in particular, from the work of [27]. Another feature of fluctuation analysis methods is the construction of an increasing function depending on the scale parameter, in contrast to a decreasing autocorrelation

function, and this circumstance simplifies the analysis of long-range correlations, reducing the error of the estimates of the scaling exponent [26]. In studying the dynamics of physiological systems, fluctuation analysis methods are used quite often, especially detrended fluctuation analysis (DFA) [26], allowing to obtain diagnostically significant results.

In the works [24, 25], a generalization of fluctuation analysis was proposed for the case of two simultaneously recorded signals of a dynamic system and a method for the quantitative description of long-range cross-correlations in non-stationary dynamics — the DCCA (detrended cross-correlation analysis) method was proposed. This method involves constructing profiles [26] of the analyzed signals x_i and $\tilde{x}_i$, $i = 1, \ldots, N$:

$$y_k = \sum_{i=1}^{k} x_i, \quad \tilde{y}_k = \sum_{i=1}^{k} \tilde{x}_i. \tag{1}$$

Sometimes the signals x_i and $\tilde{x}_i$ are first reduced to a zero mean [26], but this is not a mandatory procedure and does not affect the calculation results due to subsequent approximation and local trend removal. The profiles y_k and $\tilde{y}_k$ are divided into segments of length n that may not overlap, in which case their number $M = [N/n]$, or overlap, increasing the number of segments to $M = [(N-n)/\Delta] + 1$, and then M is determined by the degree of overlap Δ of the corresponding sections. Within each segment, the local trend z_k and $\tilde{z}_k$ is approximated, for which a linear approximation is usually performed, and the resulting dependencies z_k and $\tilde{z}_k$ are piecewise linear functions.

By analogy with DFA, approximation options using nonlinear functions can also be considered.

Cross-correlations of profiles y_k and $\tilde{y}_k$ after trend removal are first calculated for individual segments j

$$f^2_{\mathrm{DCCA}}(n, j) = \frac{1}{n} \sum_{k=1+(j-1)\Delta}^{(j-1)\Delta+n} (y_k - z_k)(\tilde{y}_k - \tilde{z}_k), \tag{2}$$

and then the averaging procedure is performed

$$F^2_{\mathrm{DCCA}}(n) = \frac{1}{M} \sum_{j=1}^{M} f^2_{\mathrm{DCCA}}(n, j). \tag{3}$$

It is assumed that in the presence of long-range cross-correlations of the original signals x_i and $\tilde{x}_i$, which are of a power-law nature, the dependence $F_{\mathrm{DCCA}}(n)$ has the form

$$F_{\mathrm{DCCA}}(n) \sim n^{\lambda} \tag{4}$$

and is characterized by the scaling exponent λ. It is calculated by linear approximation of $\lg F_{\mathrm{DCCA}}$ $(\lg n)$. The value λ allows us to capture positive power-law correlations $(0.5 < \lambda < 1)$, anticorrelations $(0 < \lambda < 0.5)$, uncorrelated behavior $(\lambda = 0.5)$, etc. If we select the same signal as x_i and $\tilde{x}_i$, the DCCA method is transformed into a simpler approach — DFA. Note that the scaling exponent λ calculated in this case is related to the exponents describing the frequency dependence of the spectral density function or the decay of the autocorrelation function. The paper [24] provides examples of DCCA application to the analysis of signals of electrical activity of the brain — electroencephalograms, for which the presence of power laws of the form (4) was established.

1.2. Experimental data. The database of experiments performed on mice used in the work contained two-channel recordings of electrocorticograms (ECoG) recorded from the left and right hemispheres using silver microelectrodes with a tip diameter of 2-3 mkm implanted to a depth of 150 mkm. The experiments were performed 10 days after electrode implantation and included ECoG recordings in a normal waking state and immediately after a 24-hour sleep deprivation, which was performed from 8:00 PM to 8:00 AM using the [29, 30] method. The signals were recorded for 2 hours at a sampling frequency of 2 kHz. At the pre-processing stage, artifacts were removed using filtering or bad segments were excluded to obtain relatively "clean" ECoG recordings.

Next, electrical activity corresponding to the main frequency ranges was extracted: wave processes in the ranges of delta waves (0.25...4 Hz), theta (4...8 Hz), alpha (8...13 Hz), beta (13...20 Hz) and low gamma activity (20...30 Hz) [31]. For this purpose, bandpass filtering was carried out in the specified ranges, and the resulting signals were used in studying the coordination of brain rhythms.

1.3. Results. According to the theoretical foundations of the DCCA [24,25] or DFA [26] method, the scaling exponent is estimated in the presence of power-law dependencies of the form (4). Such power-law features are quite common in practice, including the analysis of the dynamics of physiological systems. However, a simple form of dependence $\lg F_{\mathrm{DCCA}}\,(\lg n)$, which is characterized by its identical slope regardless of the range of n, is not always observed, and this may be due not only to the dynamics of the system, but also to other factors. For example, a signal recorded from an electroencephalograph usually undergoes a filtering procedure using a high-pass filter with a cutoff frequency of up to 1 Hz. In this case, the range of scales for calculating dependencies (4) will be limited. For illustration purposes, let us consider the case of analyzing a single signal (the DFA method instead of DCCA) and compare the results for the original ECoG signal and the dynamics of individual rhythms (Fig. 1). In the first case, the dependence $\lg F_{\mathrm{DFA}}\,(\lg n)$ is close to linear in the considered range of scales, and for the dynamics of individual rhythms, the upper limit of the linear section decreases with increasing rhythm frequency. It is worth paying attention to an important circumstance. On the one hand, the DFA scaling exponent is related to the scaling exponent of the autocorrelation function, which, in turn, is related to the Hurst exponent and the fractal dimension [32]. But if the dependence $\lg F_{\mathrm{DFA}}\,(\lg n)$ is not strictly linear, then the question of the presence of such a connection becomes unclear, revealing the limitations of the applied analysis method. On the other hand, if the specified dependence deviates from linear, but can be approximately described (fitted) by a linear function in the considered range of scales, then the calculated local scaling exponent often

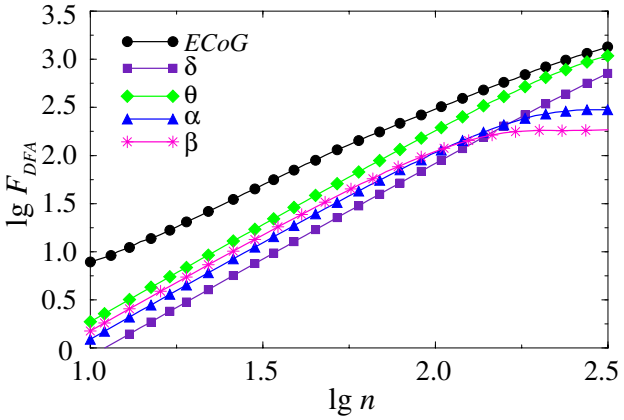

Fig 1. Dependencies $\lg F_{\mathrm{DFA}}(\lg n)$ for original ECoG signal and individual rhythms (color online)

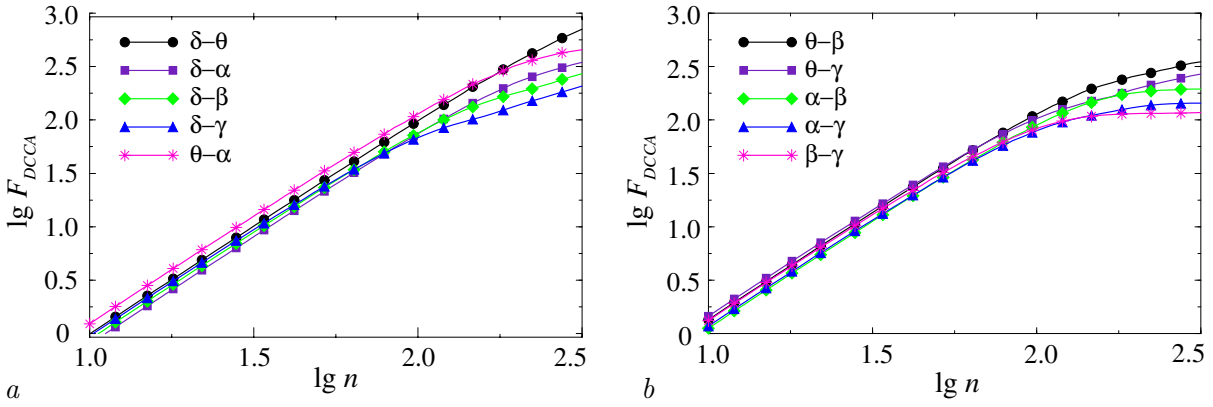

Fig 2. Dependencies $\lg F_{\mathrm{DCCA}}(\lg n)$ for different pairs of rhythms of a typical ECoG recording: *a* — pairs δ – θ, δ – α, δ – β, δ – γ, θ – α; *b* — pairs θ – β, θ – γ, α – β, α – γ, β – γ (color online)

turns out to be a useful quantitative measure that allows solving various diagnostic problems, e.g. in neurodynamics [33, 34].

A picture similar to Fig. 1 is also observed when applying the DCCA method to different pairs of rhythms of a single ECoG (Fig. 2). In the case of slow rhythms (for example, coordination of delta waves with other rhythmic processes, Fig. 2, *a*), deviations from the nearly linear dependence $\lg F_{\mathrm{DCCA}}\ (\lg n)$ are observed at higher values of $\lg n$, and for faster rhythms the range of $\lg n$ that can be considered is reduced. This circumstance should be taken into account when performing calculations.

Having carried out a preliminary assessment of the parts of the $F_{\mathrm{DCCA}}(n)$ dependences that are appropriate to consider for each pair of rhythms, we then compared the ECoG signals in the states before and after sleep deprivation. The range for calculating the scaling exponents was selected until significant deviations from the linear dependence appeared. Let us first carry out a comparison for one mouse (the most "clean" recording was selected, least susceptible to distortion due to artifacts, bad segments, etc.). Fig. 3 shows examples of λ estimates for three pairs of rhythms, where the differences between the states of normal wakefulness and sleep deprivation were most pronounced (which was confirmed using the Mann–Whitney test with a significance level $p < 0.01$). The calculations were performed on 10-minute ECoG fragments, after which averaging was performed, and Fig. 3 shows the mean values together with the standard error

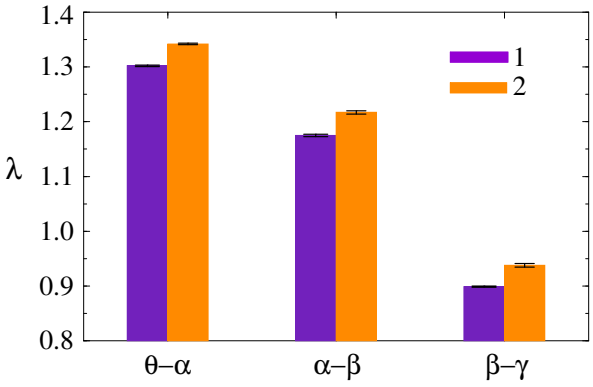

Fig 3. Values of DCCA scaling exponent for typical ECoG recording before (1) and after (2) sleep deprivation (color online)

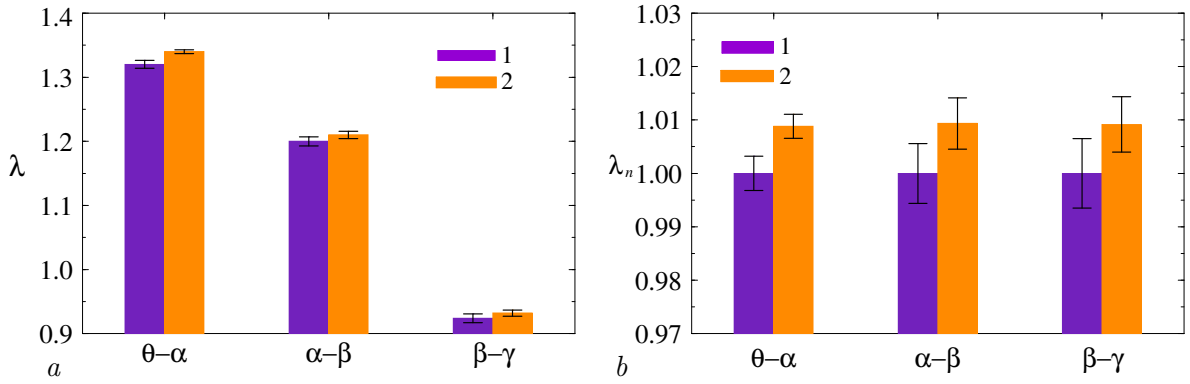

Fig 4. Group averaged values of DCCA scaling exponent before (1) and after (2) sleep deprivation: a — original, b — normalized (color online)

of the mean. Note that for all the given pairs of rhythms, significant changes in λ are revealed, which allows using the scaling exponent as a diagnostically significant measure.

Statistical analysis for the group of mice confirms the conclusion about the differences between the functional states, the diagnostics and quantitative description of which for individual rhythm pairs can be carried out using the DCCA method, but for the group the differences are less pronounced (Fig. 4, a). For clarity, Fig. 4, b shows the normalized scaling exponents λ_n (normalization was carried out to the value of λ in the state before sleep deprivation). Changes in λ_n caused by sleep deprivation are clearly distinguishable, especially for the rhythm pair θ – α. Note the following circumstances. When choosing the significance level $p < 0.05$, the separation of states was carried out only for the rhythm pair θ – α. For the pair α – β, the separation is performed at the level $p < 0.1$. Nevertheless, the obtained results indicate the diagnostic potential of the DCCA method when considering the problems of changing the functional state of the organism. In this work, the goal was not to find the most effective markers of state change, which requires a comparative analysis of different methods for studying the structure of signals. The task was to show that the proposed rhythm coordination paradigm [21,22] provides additional opportunities for analyzing the complex dynamics of electrical activity of the brain, including from the point of view of the concept of network physiology, and the obtained results illustrate this.

Conclusion

The paper studies the effects of short-term sleep deprivation on the dynamics of electrical activity of the brain using the concepts of network interactions of cortical rhythms. The experimental data were processed using the method of cross-correlation analysis of non-stationary dynamics (DCCA), considered within the framework of the concept [21,22], the authors of which, in addition to the traditional approach to determining states and functions through individual brain rhythms, suggested that coordinated interactions between different rhythms are necessary for the formation of physiological states. In other words, based on the actively developing theory of complex networks, they attempted to expand the understanding of the cooperative dynamics of neural ensembles of the brain in order to extract additional information about the features of its functioning, which may be of interest for both fundamental scientific and diagnostic purposes. Given that daily sleep deprivation has previously been shown to result in differences in EEG and ECoG signal characteristics compared to normal wakefulness [23], it was expected that differences could also be found in the coordination of brain rhythm pairs. This assumption was confirmed

using the local scaling exponent λ, which allowed us to establish differences in the dynamics of several rhythm pairs for individual animals. Statistical analysis of the exponents for a group of laboratory mice revealed statistically significant differences, but not for all rhythm pairs. Note that specific values of the scaling exponent depend on the range of scales, the choice of which affects the result, so a more thorough analysis with automatic selection of this range seems preferable for maximizing the differences in the characteristics of the two diagnosed states.

The concept of rhythm coordination, which implies the presence of dynamic networks of interactions between the corresponding processes [21, 22], is of considerable interest, and recent works investigating the functional networks of the brain [35–38] confirm the above. Although some ideas have been discussed before [39], the works [21, 22] represent a significant result that can become the basis for extensive studies by many scientific teams. This paper is one of the first attempts to use the ideology of the noted publications. It is the first to consider the application of the DCCA method in this context. Like any other approach, the DCCA method and its simplified version DFA have their drawbacks, and one can note some studies where the limitations of fluctuation analysis have been widely discussed [27, 40]. Nevertheless, a more effective tool for studying long-range correlations in the non-stationary dynamics of complex systems compared to fluctuation analysis has not yet been proposed. From the point of view of the tasks of studying the physiological state of the organism, the characteristics of fluctuation analysis often turn out to be diagnostically significant measures, therefore the range of issues considered in this article has practical significance, and not only in application to neurophysiological problems. Further research may include both improving the methodology for analyzing the effects of brain rhythm coordination taking into account the specifics of experimental data, and accumulating information on the features of their coordination for different physiological states.

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