Parametrization of synchronization effects in bioelectrical signals of brain activity of subjects with varying degrees of the risk of psychiatric disorders manifestation based on Flicker-Noise Spectroscopy

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In this paper, we present the capabilities of Flicker-Noise Spectroscopy in searching for diagnostic criteria for psychiatric disorders of the schizophrenia spectrum. From the set of parameters calculated for the signals of bioelectrical brain activity of subjects with varying degrees of risk of psychiatric disorders manifestation, parameters characterizing the „depth" of frequency-phase synchronization and degree of high-frequency „noise" manifestation were selected. The qualitative assessment was determined by the structure of the calculated 3D cross-correlators. As a result of statistical analysis of the subjects' electroencephalograms, there were identified 4 groups with increasing risk of future development of schizophrenia. The maximum accuracy of the proposed single-parameter estimation was 78%.

Keywords: physics of complex systems, Flicker-Noise Spectroscopy, frequency-phase synchronization, psychiatric disorders, electroencephalograms, diagnostics.

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Objective early-stage diagnosing of psychiatric disorders, primarily schizophrenia, is difficult due to the lack of instrumental detection methods, although the association of disorders of this kind with inevitable changes in the activity of individual areas of cerebral cortex is obvious [1–3]. Therefore, it seems natural to combine the capabilities of diagnosing such pathologies with the analysis of electroencephalograms (EEG) or magnetoencephalograms (MEG) reflecting the functional activity of spatially separated areas of the patients' cerebral cortex. A more reason for this is that the studies conducted in this area have shown the promise of the developed approaches [3–5].

What is of undoubted informational significance for diagnosing psychiatric pathologies is revealing certain relationships between the characteristic excitation frequencies and phases in various cerebral cortex lobes (certain ensembles of neurons), since the minimal/optimal level of the frequency-phase synchronization revealed by analyzing simultaneously recorded EEG- or MEG-signals is a necessary condition for the brain functioning as an integral system [6].

In this work, objective information contained in the EEG signals of subjects with different levels of risk of schizophrenia-spectrum diseases manifestation in various leads was acquired by using a phenomenological approach, namely, Flicker-Noise Spectroscopy (FNS) [6,7]. Notice that previous studies have demonstrated the efficiency of this approach in parameterizing time signals, searching for predictors of abrupt structural changes in complex systems, and also in studying synchronization effects in the dynamics of simultaneously recorded experimental indicators.

As experimental data, clinical EEG-signals from 16 electrodes were used, which were obtained at the Scientific Center for Mental Health of the Russian Academy of Medical Sciences in order to clarify the signs of schizophrenia in children/adolescents $11-14$ years old [6,8,9]. The experimental group included 45 adolescent boys with established symptoms of schizophrenia-spectrum disorders. The reference group consisted of 39 adolescent boys free of those symptoms. The average age of the subjects was 12.25 years in both groups.

The diagnostic criteria were searched for on the basis of obtaining direct information on the degree of the frequency-phase synchronization of signals produced by cerebral cortex areas localized in different cerebral cortex lobes (F_3-F_4 refere to the frontal lobe, P_3-P_4 mean the parietal lobe, T_3-T_4 mean the temporal lobe). A number of studies [10] have shown that neurodegenerative processes develop mainly in the frontal brain lobes of people suffering from schizophrenia-spectrum disorders. Two other pairs, which are typically not considered as informationally relevant in schizophrenia research, were chosen for comparison.

To test the working hypothesis about the suppression of frequency-phase synchronization in the functional activity of the specified cerebral cortex areas in the schizophrenia-spectrum diseases, two FNS-parameters were selected: one of them determined the synchronization „depth" and the other was used as a measure of the impact of high-frequency „noise" destroying the synchronization.

In this work we do not present all the characteristics calculated within the framework of FNS [6,7,11,12]. Let us identify the simplest type of cross-correlators $q_{ij}(\tau, \theta_{ij})$,

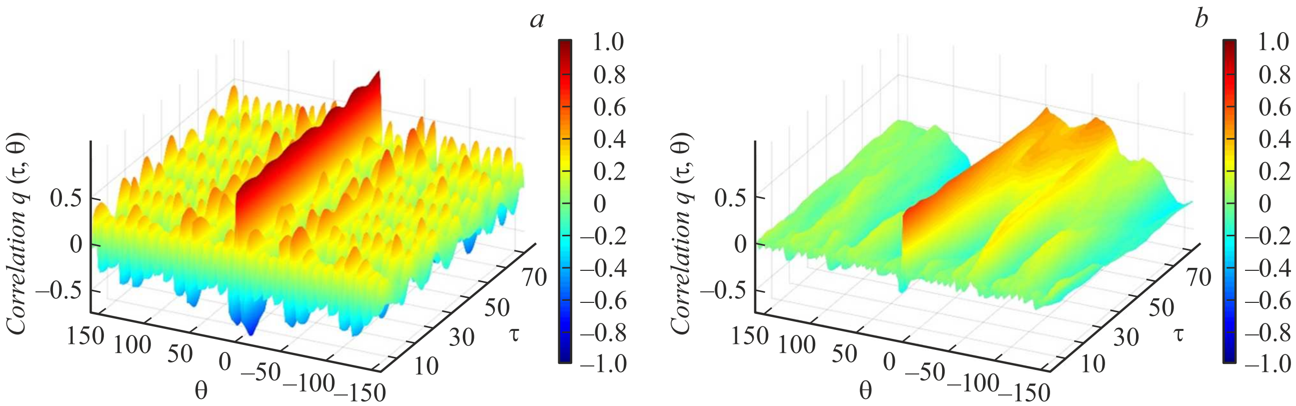

Figure 1. Representative 3D-structures of cross-correlators $q(\tau, \theta)$ calculated for electroencephalograms of a volunteer from the reference (healthy) group (a) and of a representative with clinically established symptoms of schizophrenic-type disorders (b).

which characterizes relationships between dynamic variables $V_i(t)$ and $V_j(t)$ measured at spatially separated points i and j of the system under study:

$$q_{ij}(\tau, \theta_{ij}) = \left\langle \left[\frac{V_i(t) - V_i(t+\tau)}{\sqrt{2}\sigma_i} \right] \times \left[\frac{V_j(t+\theta_{ij}) - V_j(t+\theta_{ij}+\tau)}{\sqrt{2}\sigma_j} \right] \right\rangle_{T-\tau-|\theta_{ij}|},$$

$$\sigma_i(\tau) = \left\{ \left\langle \left[V_i(t) - V_i(t+\tau) \right]^2 \right\rangle_{T-\tau-|\theta_{ij}|} \right\}^{1/2}. \quad (1)$$

Here τ is the „delay time" (we assume that $\tau > 0$), θ_{ij} is the „time shift" parameter. As a result, a „spatial" (3D) representation of the complex surface $q_{ij}(\tau, \theta_{ij})$ is considered depending on τ and θ_{ij} as time parameters. Of interest are the ranges of parameters τ and θ_{ij} where correlation $q_{ij}(\tau, \theta_{ij}) \to 1$ or anti-correlation $q_{ij}(\tau, \theta_{ij}) \to -1$ is expressed in variations in $V_i(t)$ and $V_j(t)$.

In the course of analyzing the effects of synchronization of bioelectrical activity signals for all the subjects, four groups of subjects were identified based on the calculated FNS-parameters. Fig. 1 presents the cross-correlators 3D structures for representatives of the first group (reference group, Fig. 1, a) and fourth group (subjects with the most pronounced symptoms, Fig. 1, b). Visual analysis allows, to a first approximation, assessing the degree of manifestation/violation of the effects of frequency-phase synchronization, including the „deformation" of the cross-correlators 3D structure. However, as the preliminary analysis shows, deformation of the cross-correlator 3D structure is also possible in the case of healthy subjects because of high individuality of their EEG-signals.

The first parameter proposed for quantitative assessment of the level of the frequency-phase synchronization will be determined based on analyzing the cross-correlator $q(\tau, \theta)$ projection at fixed $\tau = \tau_0$ in the θ range of $-150 f_d^{-1}$ to $150 f_d^{-1}$. As shown in Fig. 2, the dependence of the cross-correlator $q(\tau, \theta)$ projection is conditionally symmetrical with respect to $\theta = 0$ and decreases oscillatingly with θ increasing in the positive and negative directions. Based on this observation, parameter $m_{\min}$ was proposed, which is defined as the minimum number of intersections of the θ axis in its positive or negative directions within a certain interval fixed in modulus, the vicinity of $\theta = 0$ not belonging to this interval. Thereat, there exists an intermediate range containing subjects of both types, due to which the threshold value of $\hat{m}_{\min}$ may be introduced.

The second parameter is defined as „sharpness" factor $S_c(T_0^{-1})$ that is a measure of signal irregularities in the high-frequency part of the spectrum or, in other words, a measure of „sharpness". At very low values of $S_c(T_0^{-1})$, the control subjects dominate, while at large values predominant are the subjects suffering from schizophrenia-spectrum disorders. Thereat, there exists an intermediate range to which subjects of both types belong, due to which threshold value $\hat{S}_c(T_0^{-1})$ can be introduced.

The main characteristics of single-parameter classifications are listed in the Table for all three pairs of the electrodes considered. The Table also presents absolute errors, namely the number of wrong diagnoses made based on the calculated FNS-parameter in comparison with medical diagnoses for a sample of 84 children/adolescents. For instance, in the case of the electrode combination F_3–F_4 and $\hat{m}_{\min}$ criterion, 16 volunteers with identified symptoms of schizophrenia-spectrum disorders were classified as healthy subjects. Wrong diagnoses for the reference group representatives were made in 11 cases. In the case of classification by the $m_{\min}$ parameter, almost the same agreement with the diagnoses made by specialists was observed for all the three pairs of electrodes. Threshold values were determined by finding the maximum agreement between the obtained classification and diagnoses made by specialists from the RAMS Scientific Center for Mental Health.

To obtain a reliable estimate of the children/adolescents susceptibility to schizophrenia-spectrum disorders, more complex classification algorithms may be created on the

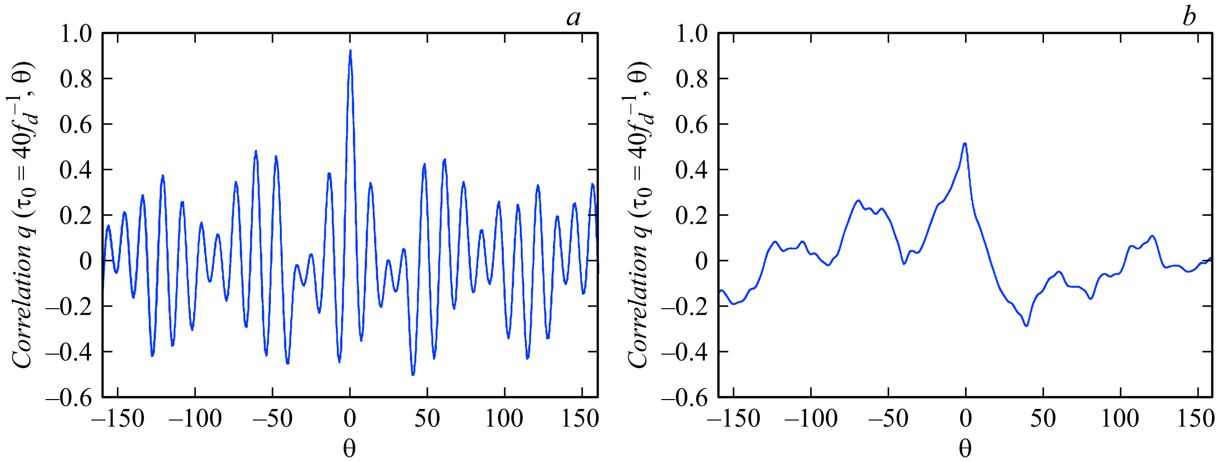

Figure 2. Projections of the $q(\tau_0, \theta)$ cross-correlator for the F_3-F_4 pair of a reference group volunteer (a) and experimental group representative (b) at $\tau_0 = 40 f_d^{-1}$. The projections are constructed for the cross-correlators presented in Fig. 1.

Table 1. Classification of EEG-signals depending on the FNS-parameters (threshold criterion values for different combinations of electrodes and number of wrong diagnoses in a sample of 84 volunteers are presented)

Electrodes	Classification criterion			
	$\hat{m}_{\min}$	Error	$\hat{S}_c(T_0^{-1}) \cdot 10^{-3}$	Error
F_3-F_4	8	27	2.36	21
P_3-P_4	10	27	0.26	18
T_3-T_4	6	29	1.76	23

basis of simultaneously analyzing two (or more) parameters. Such identification of certain types of regularities is aimed at improving the objectivity of diagnoses. If the optimization is performed by two parameters simultaneously with determining threshold values for each parameter based on the maximum compliance between the results of this classification and diagnosis made by specialists [8,9], then relative errors get reduced to 16–18%.

As a result of the general classification of the subjects' EEG-signals, four groups were identified based on manifestation of symptoms of schizophrenia-spectrum disorders. When comparing the result of that identification with the results of medical diagnostics at the RAMS Scientific Center for Mental Health, two groups with the lowest risk of the pathology development may be assigned to the „conditionally healthy" group, while two groups with the highest risk of the pathology development may be attributed to the „conditionally sick" group.

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Compliance with Ethical Standards

All the works included in the research involving human participants were carried out in accordance to the ethical standards of the national Scientific Ethics Committee and the 1964 Declaration of Helsinki with its subsequent supplements, or to similar ethical standards. The Informed Voluntary Consent was obtained from legal representatives of each participant of the study.

Conflict of interests

The authors declare that they have no conflict of interests.

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