FNS-parameterization of human magnetoencephalograms for the diagnosis of photosensitive epilepsy

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Abstract. This work presents the results of parameterization of magnetoencephalogram signals from healthy subjects and a patient with photosensitive epilepsy. Diagnostic criteria were established during the extraction of resonant and high-frequency (chaotic) components of the initial time signals. It is shown that an increase in the intensity of the chaotic components of the studied signals in the high-frequency region leads to a violation of cross-correlation relationships and a decrease in the level of manifestation of frequency-phase synchronization. The discovered signs of photosensitive epilepsy will contribute to the development of new methods for the diagnosis and medical control of this disease based on Flicker-Noise Spectroscopy.

1. Introduction
A high level of the individuality of the external and behavioral traits of each person is manifested in the spatio-temporal structure of biomedical signals – electrocardiograms, electroencephalograms, magnetoencephalograms (ECG, EEG, MEG), measured during medical examination procedures. Each of the signals \( V(t) \), where \( t \) – is the time, recorded at a certain time interval \( T \) with a sampling rate \( f_s \), is a manifestation of a complex set of physiological processes, which leads to the accumulation of information about the state of both an individual organ and the organism as a whole [1]. Currently, active development of methods for analyzing physiological signals is being carried out – digitized time series, which allow identifying the required individuality characteristic of each organism in normal conditions and a case of disturbances in its functioning.

To solve these problems, we propose to use the capabilities of Flicker-Noise Spectroscopy (FNS) [2, 3]. Within the framework of the FNS, information parameters are introduced to describe the studied signals in different frequency ranges. The individual characteristics of the evolution of the complex systems are manifested in the low-frequency and high-frequency (chaotic) components of the produced signals. At the same time, in the sequences of these chaotic components, highly individual for each system, informational significant correlation relationships are almost always revealed. Magnetoencephalogram signals are considered as such signals. Neuromagnetic signals-responses of the cerebral cortex to the effects of a flickering red-blue stimulus were recorded in a group of healthy subjects and a patient with photosensitive epilepsy (PSE). PSE is a disease in which there is excessive neural activity that occurs during flickering light exposure, especially in children, and is accompanied by various clinical and paraclinical signs. Signals-responses with a sampling rate of 500 Hz to the effects of color stimuli were recorded by 61 SQUID (superconducting quantum interference sensor) [4].

Earlier, in the works of the authors [5, 6], it was shown that individual areas of the human cerebral cortex, for example, in the vicinity of 10 and 59 sensors, are localization zones that activate the pathological mechanisms of PSE. Primarily, it manifested in the appearance of characteristic
resonance processes at certain frequencies (50 Hz and/or 100 Hz). However, such high-frequency components were not detected in the response signals of many other sensors of the patient, which allowed assuming that the corresponding parts of the cerebral cortex are not subject to pathological changes.

The purpose of this work is to search for new diagnostic criteria for photosensitive epilepsy, revealed by studying the statistical regularities of MEG signals from additional sensors in the framework of Flicker-Noise Spectroscopy. This will allow increasing the efficiency of FNS in the diagnosis of photosensitive epilepsy and obtaining a more complete picture of the features of neuromagnetic activity in different parts of the cerebral cortex of patients when exposed to flickering light stimuli. We also evaluate the possibility of using these diagnostic criteria to detect foci of excitation of abnormal activity in PSE.

To analyze the resonant and chaotic components, algorithms for the separation of the signals under study were proposed. Experimental dependencies of power spectra, structural transient functions – difference moments of the second order are presented, and parameters for constructing their interpolation representations are calculated.

2. Flicker-Noise Spectroscopy parameters
The parameters of Flicker-Noise Spectroscopy are introduced based on basic functions for statistical physics: autocorrelation function $\psi(\tau)$, its cosine transform or power spectrum $S(f)$, second-order difference moments or transient “structural” Kolmogorov functions $\Phi^{(2)}(\tau)$ [2, 3, 5, 6].

As is known, the $S(f)$ dependencies exhibit specific frequencies to the studied signal, which can be associated with resonances inherent in signal sources. Chaotic, higher-frequency components of the signal give monotonically varying contributions to the $S(f)$ dependencies. While extracting such contributions of chaotic components $S_c(f)$ in $S(f)$, the “intermittency” of the considerable dynamics is taken into account, when sections of relatively small changes of the dynamic variable $V(t)$ are interspersed with short-term sharp and significant changes of the variable [7]. In this case, two frequency regions are distinguished – less high-frequency irregularities-jumps and higher-frequency ones – irregularities-bursts, accompanied by a change in the characteristic values of the signal $V(t)$. The chaotic components $\Phi^{(2)}(\tau)$ of the $\Phi^{(2)}(\tau)$ dependence calculated for such a process are determined by the algebraic sum of the differences of displacements occurring on the interval $\tau$ – “irregularities-jumps”. A consistent rationale for this conclusion is presented in the works [2, 3].

3. Results and Discussion
Neuromagnetic responses of the cerebral cortex to the effects of a red-blue flickering light stimulus were recorded in a group of healthy subjects (9 people) and a patient with photosensitive epilepsy. 61 SQUID sensors were located on the entire surface of the head and were recording weak gradients of magnetic induction generated by areas of the human cerebral cortex [4, 8]. The allocation of the sensors corresponds to the following areas of the subjects cerebral cortex: frontal (9–21), vertex (7, 8, 25–27, 31–33, 37, 45, 50, 59–61), parietal (3, 6–8, 24–26, 30–32, 36, 37, 40, 44, 45, 49, 50, 55, 58–61), temporal (1–7, 22–25, 28–31, 34–37, 22, 56–60), occipital (38–43, 46–48, 51–55). The duration of each analyzed signal was $T \approx 1.7$ s (845 counts).

The FNS analysis carried out in [5, 6] revealed some differences in the nature of the correlation relationships manifested in the MEG signals of the patient in comparison with the corresponding signals of the subjects. It was shown that the areas of the human cerebral cortex in the vicinity of the 10th and 59th sensors, with some others, are the zones of localization of the pathological mechanisms of PSE. In this regard, in this work the results of the FNS analysis of the signal recorded by the 59th sensor, as well as the signal recorded by the less specific sensor 30th are presented for an example. Further, we will limit the results of FNS analysis of the neuromagnetic responses to only 1st and 6th healthy subjects and the patient with PSE.

Figures 1–3 demonstrate the examples, respectively, of the time dependencies of the signals recorded on the 30th sensor (Figures 1a, 2a, 3a), as well as of the power spectra $S(f)$ obtained based on
these signals (Figures 1b, 2b, 3b), of the second-order difference moments $\Phi^{(2)}(\tau)$ (Figures 1c, 2c, 3c), of the chaotic contributions of structure functions $\Phi_c^{(2)}(\tau)$ (Figure 1d, 2d, 3d), and the examples of the similar data for the 59th sensor on figures 4–6.

The differences between the recorded responses of healthy subjects and the patient are manifested, primarily, in the spectra $S(f)$. In all healthy subjects, only “normal” physiological rhythms with frequencies less than 30 Hz appeared in the power spectra under the influence of a color stimulus. At the same time, in the patient suffering from PSE, abnormally high frequencies appeared in the corresponding power spectra in the region of 50 Hz and 100 Hz (for the 59th sensor) (Figure 6b). However, such high-frequency components were not detected in the signals of many other sensors of the patient, for example, sensor 30th (Figure 3b), which suggests that the regions of the cerebral cortex corresponding to such sensors are not subject to pathological changes.

The individuality of the signals of healthy subjects and the patient was significantly manifested in the behavior of the dependences of the second-order difference moment $\Phi^{(2)}(\tau)$. There is a good agreement between the dependences constructed based on the experimental data and the calculated dependences: the difference in the values of the areas does not exceed 1.5% for the representatives of the control group and 4.5% for the patient with PSE.

Figure 1. a – magnetoencephalogram signal for healthy subject № 1, recorded by 30th sensor; b – power spectrum $S(f)$ of the signal; c – structure functions $\Phi^{(2)}(\tau)$, where the solid line is the experimental dependence, square markers correspond to the calculated dependence (resonance frequencies and the contribution of irregularities-jumps), dashed markers are the contribution of resonance frequencies; d – is the chaotic contribution of the structure function $\Phi_c^{(2)}(\tau)$, where the solid line is the difference between the experimental dependence $\Phi^{(2)}(\tau)$ and the resonance component $\Phi_r^{(2)}(\tau)$, square markers correspond to the interpolation dependence for $\Phi_c^{(2)}(\tau)$. 
Figure 2. a – magnetoencephalogram signal for healthy subject № 6, recorded by 30th sensor. Letters (b)–(d) are interpreted in the same way as in Figure 1.

Figure 3. a – magnetoencephalogram signal for a patient with photosensitive epilepsy, recorded by 30th sensor. Letters (b)–(d) are interpreted in the same way as in Figure 1.
Figure 4. a – magnetoencephalogram signal for healthy subject № 1, recorded by 59th sensor. Letters (b)–(d) are interpreted in the same way as in Figure 1.

Figure 5. a – magnetoencephalogram signal for healthy subject № 6, recorded by 59th sensor. Letters (b)–(d) are interpreted in the same way as in Figure 1.
Figure 6. a – magnetoencephalogram signal for a patient with photosensitive epilepsy, recorded by 59th sensor. Letters (b)–(d) are interpreted in the same way as in Figure 1.

As a measure of the chaotic component of the signal, formed by irregularities-bursts and irregularities-jumps in the high-frequency region, the FNS uses the “sharpness” factor $S_c(T_0^{-1})$ [2, 3, 5, 6]. Moreover, in [6] it was shown that an increase in this parameter leads to a violation of cross-correlation relationships and a decrease in the degree of synchronization effects manifestation. Comparative analysis of the values of this parameter (see Table 1) for the signals of healthy subjects and a patient with PSE shows that large values of $S_c(T_0^{-1})$ can be considered as a sufficient condition for pathological changes indicating violations of frequency-phase synchronization. Therefore, the choice and adjustment of therapy for photosensitive epilepsy, and possibly other neurological diseases, should be oriented towards restoring a certain level of signal synchronization.

Table 1. The values of the sharpness factor $S_c(T_0^{-1})$, $\text{fT}^2/(\text{cm}^2\text{f}_0)$, for the magnetoencephalogram signals of the patient and healthy subjects when exposed to a red-blue flickering stimulus.

| No. of sensor | 25   | 30 | 37  |
|---------------|------|----|-----|
| 1st healthy   | 8.6  | 36.2| 79  |
| 6th healthy   | 5    | 29 | 167.9|
| Patient       | 956  | 1474| 579 |

4. Conclusions
The physics of the complex systems, as one of the dynamically developing scientific directions, allows revealing to a large extent the hidden regularities in the evolution and structure of natural composite objects. The interactions between the elements of the complex systems lead to unique properties: nonlinearity, nonequilibrium, dynamic intermittency, self-organization [9–12].

The most difficult object for studying complex systems is the human brain. The analysis of signals of the cerebral cortex bioelectrical activity contributes to the search for indicators of human neurological diseases [13–15], psychiatric disorders [16–19], changes in psychoemotional states [20, 21].
The performed studies allowed establishing additional diagnostic criteria corresponding to the spread of abnormal collective excitation of neurons in the cortex and subcortical structures, leading to an epileptic seizure when exposed to flickering color stimuli. Particularly, differences were discovered in the behavior of the power spectra, as well as in the difference moments of the second order for magnetoencephalograms of healthy subjects and a patient with photosensitive epilepsy. The calculation of the chaotic component measure of the MEG signals of healthy subjects and a patient with PSE was performed. An increase in the values of this measure, which characterizes dynamic intermittency, leads to a weakening of the frequency-phase synchronization effects between informational significant sensors. Due to a wider range of informational significant sensors, it turned out to be possible not only to diagnose PSE but also to quantify the effectiveness of therapeutic effects.

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