DOI: 10.18721/JPM.13309
УДК 53.023, 57.023, 57.087.1

A NOVEL PHYSICO-MATHEMATICAL TECHNIQUE OF ANALYZING THE QUANTITATIVE ELECTROENCEPHALOGRAMS: DEVELOPMENT AND APPLICATION

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The article presents a physical and mathematical model developed by the authors. The model allows analyzing the amplitude-frequency characteristic (AFC) of electroencephalograms (EEG) of a human brain. The proposed method of EEG processing, in contrast to the previously used one, is based on approximating the AFC by an equation that contains a set of coefficients. This method is convenient for comparing data obtained from different subjects and, as found, has diagnostic significance. Previously, only the frequency / amplitude ratio or its inverse was used for evaluations. The results achieved indicate the possibility of differentiating patients of various neuropsychic profiles according to the values of the parametric indicators obtained by approximating the EEG amplitude-frequency response.

Keywords: quantitative EEG, amplitude-frequency characteristic, EEG mathematical analysis, schizophrenia, dementia

Citation: Sobolev M.E., Gorelik A.L., Vlasova O.L. A novel physico-mathematical technique of analyzing the quantitative electroencephalograms: development and application, St. Petersburg Polytechnical State University Journal. Physics and Mathematics. 13 (3) (2020) 102–110. DOI: 10.18721/JPM.13309

РАЗРАБОТКА И ПРИМЕНЕНИЕ НОВОГО ФИЗИКО-МАТЕМАТИЧЕСКОГО МЕТОДА АНАЛИЗА КОЛИЧЕСТВЕННЫХ ЭЛЕКТРОЭНЦЕФАЛОГРАММ

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В статье представлена разработанная авторами физико-математическая модель, позволяющая анализировать амплитудно-частотную характеристику (АЧХ) электроэнцефалограмм (ЭЭГ) головного мозга человека. Предлагаемый метод обработки ЭЭГ, в отличие от применявшегося ранее, основан на аппроксимации АЧХ уравнением, которое содержит набор коэффициентов, удобных для сравнения данных, полученных от разных испытуемых и, как установлено, обладающих диагностической значимостью. Ранее для оценок использовалось лишь отношение частота/амплитуда либо обратное ему. Полученные результаты указывают на возможность дифференциации пациентов различных нервно-психических профилей по значениям параметрических показателей, получаемых при аппроксимации АЧХ ЭЭГ.

Ключевые слова: количественная ЭЭГ, амплитудно-частотная характеристика, математический анализ ЭЭГ, шизофрения, деменция

Ссылка при цитировании: Соболев М.Е., Горелик А.Л., Власова О.Л. Разработка и применение нового физико-математического метода анализа количественных электроэнцефалограмм // Научно-технические ведомости СПбГПУ. Физико-математические науки. 2020. Т. 13. № 3. С. 119–129. DOI: 10.18721/JPM.13309

Introduction

The share of interdisciplinary research in biomedical applications is growing steadily. One potential direction for this approach are modern computer technologies and methods of mathematical data processing in neurophysiological research. These studies consider neurodynamic processes occurring in the brains of animals belonging to different types and classes, as well as in the human brain. Researchers aim to gain an understanding of the mechanisms governing the nervous system and the mind, working with individual neurons, cell populations, brain slices, and the brain as a whole, as well as with their computer models.

Electroencephalography (EEG) is a non-invasive method for recording brain activity, widely used in research and in clinical practice, along with magnetic resonance imaging (MRI), positron emission tomography (PET), computed tomography (CT). EEG records bioelectric signals of the brain taken from the electrodes placed on the surface of the scalp by measuring the voltage differences between the electrodes applied and the references [1]. The images obtained by EEG, characterizing the recorded voltage differences, are called electroencephalograms.

EEG readings reflect the synchronous synaptic activity of neuron populations. Electrical excitation of neurons generates an extracellular voltage that allows the opposing ends of the neuron (dendrites and axons) to have different charges. The general purpose of EEG is to interpret the changes in measured signals reflecting the changes in the activity of certain regions of the brain. Identifying these regions is a crucial problem, since the measurements in the surface of the scalp reflect the sum of the signals taken from different spatially distributed regions of the brain. Because neural activity is cyclic, the measured voltage fluctuates between positive and negative, and the rate of this cycle reflects the frequency of the signal.

EEG is a highly sensitive method with a resolution of up to tens of milliseconds, allowing to observe the evolution of various bioelectric processes over time, which cannot be achieved by other methods. In addition, EEG makes it possible to explore the response of such a highly complex biological system as the brain to various stimuli. However, a high-quality amplifier is necessary to adequately record and then interpret electroencephalograms, since the amplitude of the measured signal is small: it ranges from units to several tens of microvolts.

Several frequency ranges are observed in the bioelectric signal of the brain [2]: delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz), and gamma (over 30Hz). It can be seen from Fig. 1 that the measured signal contains all of these rhythms in a certain proportion which changes depending on the brain's activity.

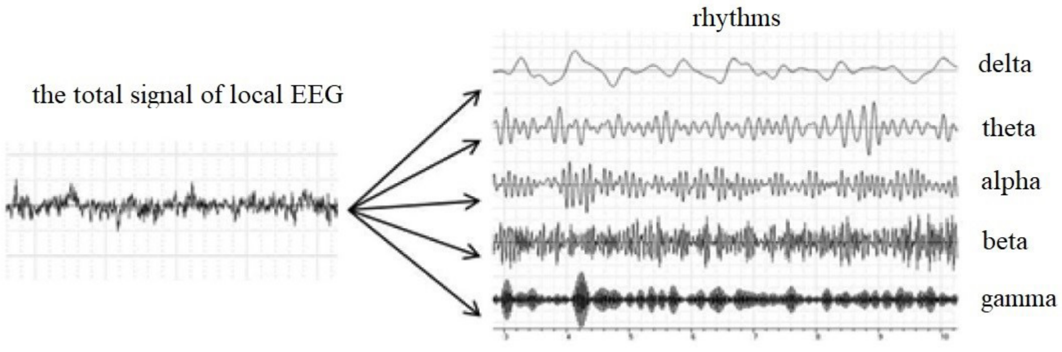

Fig. 1. Total signal of local EEG and brain rhythms: delta, theta, alpha, beta, gamma [3]

In general, quantitative studies of electroencephalograms rely on various methods of analysis, including cross-correlation coefficients, coherence coefficients, the method of evoked potentials, etc. Different methods are also used to study the frequency response of the bioelectric signal of the brain. One of these methods is considered in our study.

The method of evoked potentials (EP) consists of recording the electrical activity of the brain in response to an external stimulus. This method is used to study such properties of the brain as excitability and susceptibility to stimuli [4]. The amplitude and the delay in the response of evoked potentials of EEG signals provide valuable data on the functional capabilities of the brain in different conditions and in different target groups. For example, an increase in time delay may be associated with attention deficit hyperactivity disorder (ADHD) in children [5], aging [6], mild cognitive impairment [7], and various psychotic conditions [8].

Applying energy-dispersive spectroscopy [9] for analysis of evoked potentials - is one of the most successful methods for identifying biomarkers. In addition, it can yield important data on the frequency composition of EEG oscillations. Typically, spectral estimates are calculated for discrete frequencies (for example, 8.5–10.0 Hz, that is, for the lower alpha band). The RMS amplitude or power (squared amplitude) of the given EEG signal frequency is used to quantify its contribution to the measured signal.

Unfortunately, spectral analysis does not provide data for the temporal evolution, that is, for the moments when frequency shifts occur over time. This problem can be solved by different methods of time-frequency analysis, including short-term Fourier transform, and wavelet analysis, which has gained popularity in recent years, making it possible to accurately convert EEG signal shapes into specific time and frequency components. EEG signals are regarded within this approach as shifted and scaled versions of a particular mathematical function (wavelet) rather than the composition of sinusoidal waves with different frequencies, as is the case with Fourier transforms. It has been found that the spectral power of alpha waves at rest and the peak frequency of the alpha rhythm can be reduced in patients with psychotic disorders [10]. A possible reason for this is that decreased alpha power is correlated with negative symptoms in schizophrenia.

Schizophrenia is a severe mental illness that affects approximately 1% of the population. Because this disabling disorder may be caused by diverse genetic and neurobiological factors, many trials have been carried out to identify its biomarkers with a view to its early diagnosis. The biomarkers most commonly used for schizophrenia are associated with the neuroimmune and neuroendocrine systems, metabolism, various neurotransmitter systems, and neurotrophic factors. Quantitative electroencephalography has also been applied to identify possible biomarkers but such studies are very scarce. A notable paper [11] considers the theta-phase gamma-amplitude relationship as an evidence-based tool for the detection of schizophrenia.

Russian researchers compared various indicators of the alpha rhythm in the electroencephalograms of healthy subjects with the corresponding indicators in patients with arterial hypertension [12]. The values of the amplitude and frequency observed for patients with hypertension were lower than those in healthy subjects. An increase in the frequency-amplitude ratio in the frontal, parietal and occipital electrodes was found for diseased subjects, without any changes in the temporal electrodes.

Several cerebrovascular and cardiovascular diseases are associated with the onset of dementia. The neuropsychological profile of patients with such disorders [13] depends on the location and depth of vascular damage to the brain, as well as on the types of cerebrovascular pathologies. Quite often, such pathologies affect the frontal lobes; consequently, the patient’s motivation begins to decrease and control over the actions deteriorates. In addition, such symptoms as forgetfulness and confusion are observed. Ref. [14] reported an increase in the spectral power in the delta range, proportional to the damage to the cardiovascular system, and a decrease in the power of the alpha rhythm in diseased subjects. Furthermore, it was found that the ratio of theta to the alpha power can serve as a reliable marker for assessing the individual degree of brain damage in cardiovascular diseases.

Our study describes a new mathematical model that adequately describes the amplitude-frequency response of the EEG.

We found the statistical distribution of the coefficient values determined by fitting the EEG frequency response obtained during examination of healthy subjects, comparing the obtained parameters between the groups of healthy subjects and those suffering from schizophrenia and age-related vascular dementia.

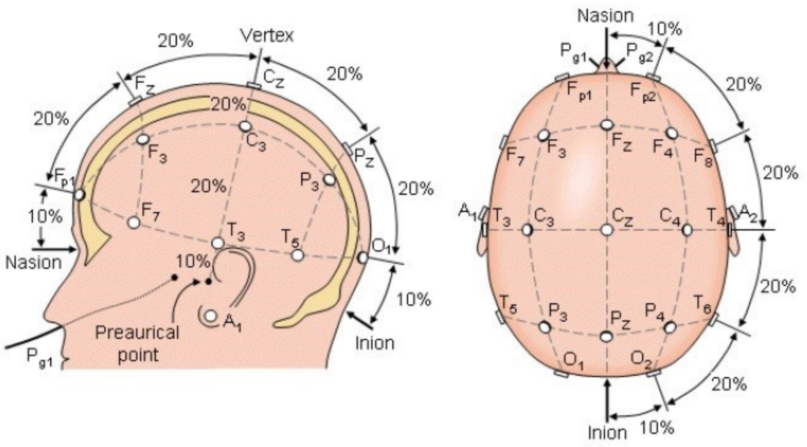

Fig. 2. International 10–20 system [15]; the human skull is shown in two projections (*a* and *b*) with characteristic points on it: bridge of the nose (Nasion), the crown (Vertex) and occipital protuberance (Inion); see also the explanations in the text

Materials and methods

Electroencephalograms of the subjects were obtained at the Department of Functional Diagnostics of the V.M. Bekhterev National Medical Research Center for Psychiatry and Neurology (St. Petersburg) from 2010 to 2018. A Telepath-104 electroencephalograph was used for the recordings. The electrodes were positioned in accordance with the international 10–20 system (Fig. 2) [15].

The following notations and abbreviations were introduced in the figure for the electrodes and the anatomical structures: Nasion for bridge of the nose, Inion for occipital protuberance, Vertex for crown, Preaurical point for external auditory meatus, F for lobus frontalis (frontal lobe), C for sulcus centralis cerebri (central sulcus), T for lobus temporalis (temporal lobe), P for lobus parietalis (parietal lobe), O for lobus occipitalis (occipital lobe), A for auricula (earlobe); the electrodes in the left hemisphere are denoted by odd indices, and the electrodes in the right hemisphere by even indices.

The sampling rate of the electroencephalograph was 250 Hz. A cap consisting of silicone tubes and silver chloride non-polarizing bridge electrodes were used.

Three groups of subjects were considered: relatively healthy (normal) subjects, patients with schizophrenia and patients with age-related vascular dementia. The ‘normal’ group consisted of relatively healthy subjects and included 17 people aged 20 to 64 (3 men and 14 women). The ‘schizophrenia’ group included 9 patients with schizophrenia aged 22 to 49 (4 men and 5 women). The ‘age-related vascular dementia’ group included 17 people aged from 54 to 80 (6 men and 11 women) suffering from age-related cerebrovascular disorders with pronounced cognitive decline.

EEG recordings were examined in the WinEEG 2.90.53 program using average-reference montage, with 16 electrodes, or (Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, T6) channels. The high-pass filter was set to 0.5 Hz, the low-pass filter - to 50 Hz, with a notch filter at 50 Hz. Epoch length was 5 s. Artifact-free epochs recorded while the subjects were at rest with their eyes closed (the so-called quiet wakefulness) were chosen for analysis. About 45 different values of amplitudes and frequencies were obtained for each subject. Analysis of the coefficients was carried out using the MagicPlot 2.7.2 software. We used Student’s *t*-test for statistical analysis.

A physico-mathematical model was developed for quantitative analysis of electroencephalograms, reflecting the relationship between the amplitude and frequency of the bioelectric signal of the brain, which is described by the following formula:

$$\begin{aligned} A(f) &= af + b + \\ &+ a_1 \exp[-(f - f_0)^2 \ln 2/\sigma^2], \end{aligned} \tag{1}$$

where A, V, is the amplitude of the wave; f, Hz, is the wave frequency; a, b, a_1, f_0, σ are the numerical coefficients in different units: a in V/Hz; b, a_1 in V; f_0, σ in Hz.

Eq. (1) was derived empirically by approximating the frequency response. It provides the best description, giving the

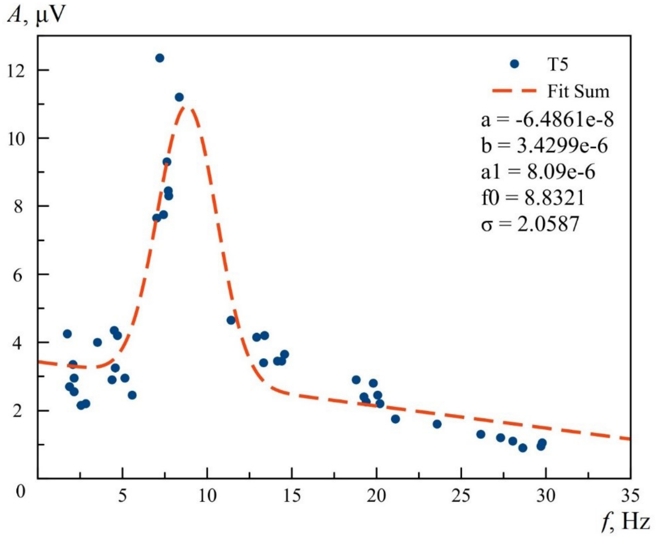

Fig. 3. Example of approximated (dashed line) experimental frequency response (points) for T5 electrode for one of the subjects in the ‘normal’ group; the values of the obtained parameters are given

minimum error of deviation from the given response curve. The frequency response was calculated in earlier studies using simply the ratio of amplitude to frequency or the inverse ratio, which is certainly convenient for obtaining a simple estimate but has no physical basis. Eq. (1) complicates calculations but reflects the behavior of the measured signal curve, therefore, it best describes the curve corresponding to the amplitude versus frequency function. Based on these considerations, the amplitudes and frequencies for each electrode, obtained from the electroencephalograms for each subject, were approximated by Eq. (1). The biophysical nature of the proposed relationship is undoubtedly intriguing and may be the subject of a separate study. However, this task is beyond the scope of our analysis.

Results and discussion

Let us first consider the results for the ‘normal’ group. An example of the approximated frequency response obtained for one of the subjects using the T5 electrode is shown in Fig. 3. The frequency response for other channels had a similar appearance for each subject from the ‘normal’ group.

Because we observed no significant differences in the coefficient values between the channels in each of the three study groups, data for each parameter were analyzed simultaneously for all electrodes (without separating the data for different electrodes). As a result, statistical distributions of the coefficient values were obtained for the ‘normal’ group (Fig. 4). Evidently, the peak frequency f_0 lies in the alpha range, and so the obtained data are consistent with the general notion that the maximum amplitude of alpha waves occurs in a state of passive wakefulness with eyes closed (at rest).

Comparing the obtained values of the parameters between the three groups, we found the following differences (the paragraphs are lettered in accordance with the letters in Fig. 5):

a) in the coefficient a_1 between the ‘normal’ and ‘age-related vascular dementia’ groups ($p < 0.05$); between the ‘schizophrenia’ and ‘age-related vascular dementia’ groups ($p < 0.05$);

b) in the coefficient f_0 between the the ‘normal’ and ‘age-related vascular dementia’ groups ($p < 0.05$); between the ‘schizophrenia’ and ‘age-related vascular dementia’ groups ($p < 0.05$); between the ‘normal’ and ‘schizophrenia’ groups ($p < 0.20$);

c) in the coefficient σ between the ‘normal’ and ‘schizophrenia’ groups ($p < 0.05$); between the ‘schizophrenia’ and ‘age-related vascular dementia’ groups ($p < 0.05$).

These differences are shown graphically in Fig. 5. No other differences were found between the coefficients.

Thus, it was found that there are distinct characteristics in the behavior of the frequency response for each of the three groups, different from the other groups. For example, the

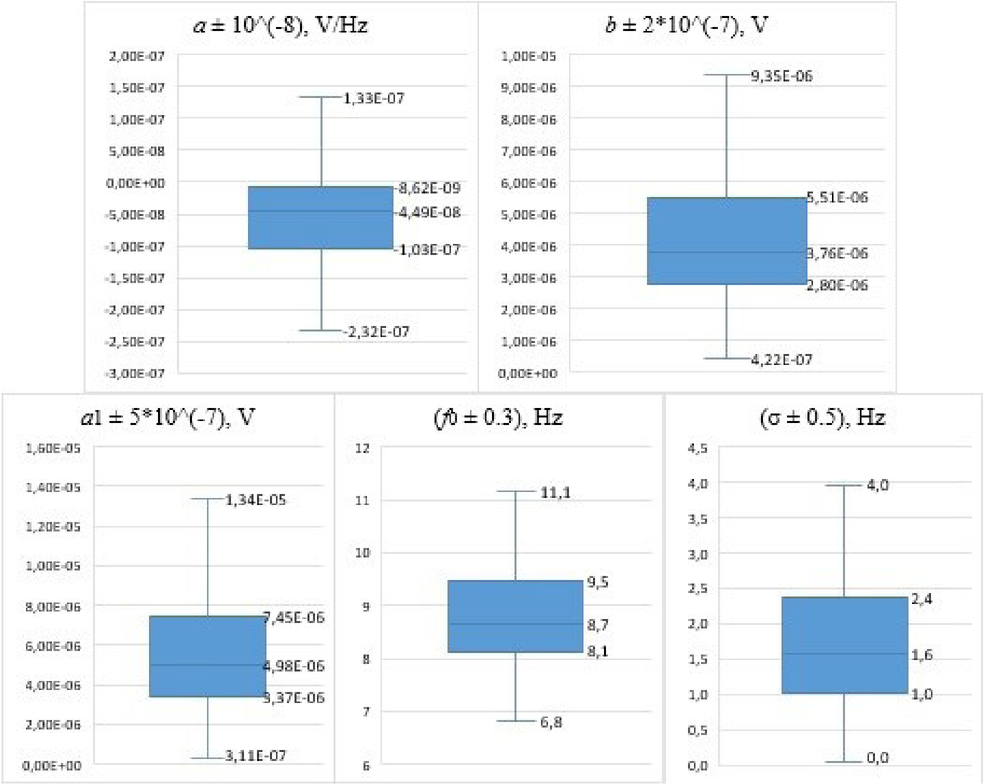

Fig. 4. Statistical distributions of frequency response coefficients (1) for subjects of the 'normal' group

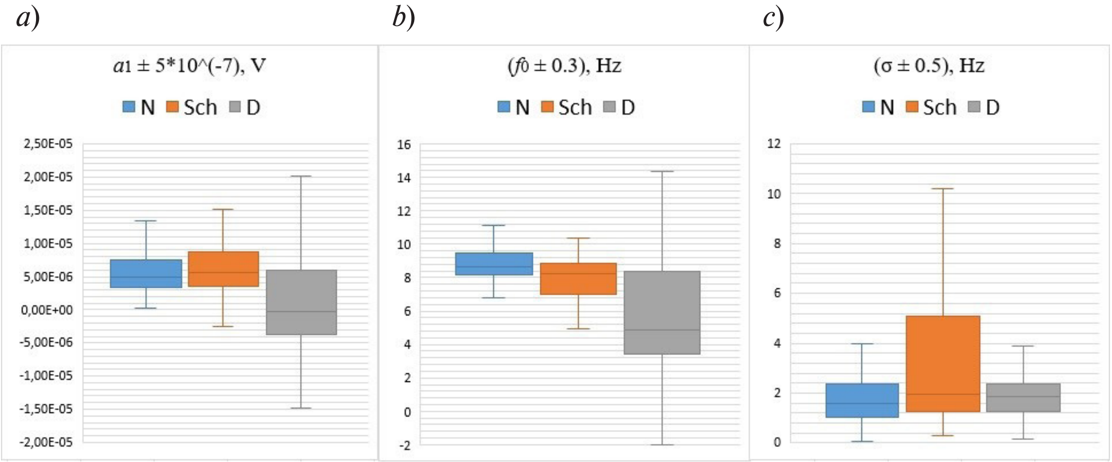

Fig. 5. Statistical distributions of coefficients a_1 (*a*), f_0 (*b*) and σ (*c*) for all electrodes for three groups of subjects: 'normal' (N), 'schizophrenia' (Sch), 'dementia' (D); the differences observed between the data are given in the text

characteristics for the 'schizophrenia' group are a slightly reduced peak frequency f_0, compared to the 'normal' group (but still falling into the upper theta and lower alpha frequency ranges) and increased half-width at half-maximum σ, compared to similar coefficients from the other two groups. In the meantime, the 'age-related vascular dementia' group is characterized by a negative value of the coefficient a_1 (i.e., the Gaussian peak is deflected downwards rather than upwards) and a reduced value of the peak frequency f_0.

Notably, the differences in data between the groups should be assessed by the entire set of values of the obtained parameters, and not by one single parameter value.

Analysis of the results has lead us to conclude that the proposed mathematical model (1) can be used to divide the subjects into groups in accordance with their specific diseases.

Conclusion

Electroencephalography is a popular method used to diagnose various neuropsychiatric disorders. Because of its high temporal resolution, EEG allows to almost instantly track the changes in brain activity. In contrast to several other methods, the procedure is non-invasive and absolutely harmless for the subjects.

EEG signals are electrophysiological responses reflecting basic neural activities that depend on the physiological states of the subject (for example, emotions, attention, and many others). The key parameters obtained by EEG are the amplitude and frequency of the measured signal. Determining these parameters visually can produce serious errors; for this reason, they are calculated by various software packages and methods. Furthermore, understanding different manifestations and biomarkers of certain functional states of the brain, identified, in particular, by mathematical methods of EEG analysis, is important for clinical practice.

This study presents a physico-mathematical model that we have developed, approximating the amplitude-frequency characteristic of human electroencephalograms. We have found pronounced differences in the values of the coefficients obtained for different clinical groups of subjects. It has been established that the selected empirical parameters have actual diagnostic significance rather than serve for fitting purposes only.

Thus, we have confirmed the practical significance of the proposed method for differentiating neuropsychic disorders in patients.

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Received 04.04.2020, accepted 28.05.2020.

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Статья поступила в редакцию 04.04.2020, принята к публикации 28.05.2020.

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