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Oscillatory characteristics in the brain activity of the newborns and their correlation with different gestational ages

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Abstract. *The purpose* of this study is to detect the characteristic features of the oscillatory electrical activity of the brain in early postnatal development, depending on the gestational age of newborns. *Methods.* The study is based on automatic processing of clinical data from electroencephalography of newborns on the third day after birth. Behavioral characteristics assessed periods of sleep and wakefulness, without a precise division into stages of sleep and various states of wakefulness. The processing of multichannel electroencephalography signals was carried out on the basis of the method of modifying the continuous wavelet transform (CWT), which makes it possible to estimate the average characteristics of the number, duration and energy of oscillatory components (patterns) developing in different frequency ranges. *Results.* A paradoxical picture has been demonstrated describing the state of sleep and wakefulness in weakly preterm infants. For this group of children, the number and average energy of patterns detected in the frequency ranges from 1 to 20 Hz behave in a reflected way during sleep compared to children born at the usual time. At the same time, the average duration of oscillatory patterns remains unchanged. *Conclusion.* In the first days of a child's life, it is possible to detect significant differences in the activity of the brain of newborns with slightly different gestational age during sleep/wake behavioral states. Quantitative estimates of the parameters of oscillatory CWT patterns are promising for use as the basis for systems for automatic processing of neonatal brain activity, additional to amplitude electroencephalography estimates. Such systems may be relevant for the search for early signs of anomalies in the development of the central nervous system.

Keywords: continuous wavelet analysis, automatic recognition, oscillatory patterns, brain activity, sleep, newborns.

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Introduction

Today, the problem of human sleep research is among the most important topics that unite neuroscientists, physiologists, physicists and specialists in the field of information technology [1–3]. A special role is played by understanding the patterns of changes in the functioning of the brain during the transition from sleep to wakefulness at the very beginning of ontogenesis, the first days of human life. Electroencephalography (EEG) recording is most often used to analyze brain activity, which is due to the simplicity of its registration. The fundamental interest in the problem of human brain development is complemented by the need to solve humanistic problems of early detection of risks of central nervous system (CNS) injuries and appropriate therapeutic measures for the correction of neurological dysfunctions.

Today, in the clinical practice of working with newborns, EEG analysis is often based on the method of amplitude-integrated EEG (aEEG), based on a compressed one-dimensional representation of a long-term recording of two or more EEG channels together and allowing, based on the identification of typical trends, to quickly and relatively objectively draw a conclusion about the current state of cerebral function and assess its dynamics. In addition, the EEG is used to develop fully automated methods of monitoring a child, for example, when assessing brain maturation [4, 5] and classifying sleep states [6, 7]. At the same time, the use of aEEG is obviously a significant simplification of the processes of brain activity, reducing the entire complex multi-frequency distributed oscillatory dynamics of electrical potentials to an average characteristic obtained from spatially distributed electrode points. Thus, although characteristic aEEG trends have been quite successfully identified for critical and convulsive conditions of premature newborns, markers of normal or mildly pathological processes of the development of electrical activity of the brain in the immediate period after birth in full-term and mildly premature infants remain unknown.

Earlier, in the work [8], the team evaluated the appearance and dynamics during the first weeks of life of deep sleep markers in newborns of different gestation periods from the point of view of classical time-frequency analysis based on continuous wavelet transform (CWT). The use of the classical approach to assessing the vibrational dynamics of the EEG provides a significant amount of information for an objective assessment of the development of deep sleep in newborns, but requires careful preliminary detection of the stages of calm and active sleep [9–11], which is very laborious and not always feasible. In this paper, we propose the use of the method of oscillatory CWT patterns to study the EEG activity of newborns based on a simple behavioral assessment of the child's condition — sleep or wakefulness. The study of the number, duration and energy of oscillatory components allows us to observe significantly different characteristics of the brain activity of newborns with different gestation periods. The use of such methods may be promising for the creation of automatic systems to support medical decisions for the purpose of early detection of damage to the development of the central nervous system of newborns.

1. Materials and methods

1.1. Clinical materials. The collection of clinical materials was carried out in compliance with all ethical standards [12], the clinical study was approved by the local Ethics Committee of the SSMU named after V.,I. Razumovsky Ministry of Health of Russia. Prior to the start of the study, written parental consent was obtained for monitoring, subsequent mathematical processing of data and publication of the results. The material was collected in 28 full-term and late premature newborns with a gestation period of more than 34 weeks. For all newborns, the birth weight exceeded 1.5 kg, the birth took place naturally, excluding cases of cesarean sections.

Children with severe genetic pathology, diagnosed traumatic CNS lesion, intraventricular bleeding of the 3rd degree with a breakthrough into the brain substance were also excluded. All newborns were divided into groups #1 (N_1 =15) and #2 (N_2 =13) with gestation periods of 38–41 and 34–36 weeks, respectively.

Each child underwent a superficial and painless functional monitoring procedure 48-52 hours after birth. Two occipital EEG signals O1, O2 were recorded using an electroencephalograph «Encephalan-EEGR-19/26» («Medikom MTD», RF) with a sampling frequency of 250 Hz according to the scheme «10–20». The EEG signals were filtered by a bandpass filter with cut-off points of 1–20 Hz. The duration of monitoring was 160–180 minutes, and the entire duration was divided into two stages — wakefulness and sleep — in accordance with the activity of the child according to the assessment of the neonatologist.

1.2. Nonlinear methods of processing biomedical signals. To study the frequency-time characteristics of electroencephalography, the method of oscillatory patterns based on classical CWT was used, developed and tested earlier in the works of [13,14]. The CWT $W(f,t)$ was calculated for each EEG channel $x(t)$ based on the morlaix-basis with the parameter $\Omega_0 = 2\pi$:

$$W(f,t) = \sqrt{f} \cdot \int\limits_{t-4/f}^{t+4/f} x(t) \cdot \left(\sqrt{f} \cdot \pi^{1/4} \cdot e^{j\omega_0 f(t-t_0)} \cdot e^{\frac{f(t-t_0)^2}{2}} \right) \cdot dt. \quad (1)$$

(1) For each EEG channel, the energy power $E(f,t)$ was calculated for the frequency range $[1;20]$ Hz, according to

$$E(f,t) = W(f,t)^2. \quad (2)$$

(2) The procedure of the classical skeletal method [15,16] was performed, according to which for each moment of time t_s it is possible to allocate a set of m_s points $f_1, \dots f_{m_s}$, in which the function $E(f_s,t_s)$(2) demonstrates local maxima. As a result of processing the entire surface $E(f,t)$ in a certain frequency range throughout the entire time interval $[t_0;t_{\text{end}}]$ of signal registration $x(t)$, a multidimensional array of skeletons is formed

$$\begin{aligned} \text{extr}(E(f,t)) = \{ (t_0; f_1; E(f_1,t_0)), (t_0; f_2; E(f_2,t_0)), \dots (t_0; f_{m_0}; E(f_{m_0},t_0)), \dots \\ \dots, (t_s; f_{m_s}; E(f_{m_s},t_s)), \dots, (t_{\text{end}}; f_{m_{\text{end}}}; E(f_{m_{\text{end}}},t_{\text{end}})) \}. \end{aligned} \quad (3)$$

For each moment of time t_s, the ordinal number $\{1, \dots m_s\}$ of skeletons characterizes only the ordinal number of extremes, which is not related to the magnitude of the amplitude $E(f,t)$. However, information about the value of the vibrational energy E is stored in the array $\text{extr}(E(f,t))$(3) for each point of the surface (t,f). The method of estimating oscillatory patterns is based on a special sorting of skeletons data arrays $\text{extr}(E(f,t))$ (3).

(3) At each time step $[t_n;t_{n+1}]$, the condition was checked for each frequency f_j

$$\left| f_j^n - f_s^{n+1} \right| < \sigma, \quad (4)$$

where f_j^n – is the set of frequencies in which there are local maxima $E(f_j,t_n)$ at the time step t_n; f_j^{n+1} — frequencies in which the maxima of t_{n+1} are realized at the next time step $E(f_j,t_{n+1})$; σ— constant. The threshold value of the constant σ was selected in order to minimize the loss of information about frequency patterns existing in the analyzed signal. The determination of a specific value σ was based on the sampling frequency of the original EEG signal $x(t)$, exceeding this by 1-2 orders of magnitude, and on the sampling step of the frequency Δf used in the calculations of the NVP, according to [13] $\Delta f < \sigma$. Within the framework of this work , the values of these constants were as follows: $\Delta f = 0.1$, $\sigma = 0.4$.

Denoting the frequencies $f_{(a1)^n}$ and $f_{(a2)^{n+1}}$ as $(a1)$ and $(a2)$, respectively, note that if for some frequencies $(a1)$ and $(a2)$ the condition (4) was met, then activity at these frequencies in the time interval $[t_n; t_{n+1}]$ was considered as the development of a single oscillatory pattern in time. Further, for the frequency $(a2)$, this condition was analyzed again at the next time step t_{n+2}. If the condition is met, then the development of the identified pattern continued further with a certain frequency $(a3)$ in the time step t_{n+3}.

The actions described above were cyclically repeated until the condition (4) became incorrect, as a result of which the identified oscillatory pattern was considered to have ceased to exist in the analyzed signal. Each identified oscillatory pattern is P, $P(f,t) = \{((a1), t_n), ((a2), t_{n+1}), \ldots, ((am), t_{n+m})\}$, where m is the duration of the pattern's existence, was described by the average frequency of f_{md}

$$f_{md} = \sum_{i=1}^{m} (ai)/m, \tag{5}$$

and the lifetime of T

$$T = t_{n+m} - t_n = m\Delta t, \tag{6}$$

where Δt is the sampling step of the analyzed signal. If the lifetime T of the identified oscillatory pattern P did not exceed the oscillation period, which corresponds to the average frequency f_{md}, that is, the condition $T < (f_{md})^{-1}$ was fulfilled, then such an oscillatory pattern was considered as a random noise interference and/or an artifact of numerical calculations and was not taken into account in the further analysis of the signal $x(t)$.

(4) In the work [17] it is shown that for the identified oscillatory pattern P, an additional parameter of the average energy characteristic can be introduced. To do this, it is necessary to estimate the conserved energy value $E_{i,j}$ n of each point (f_i, t_j) representing a part of the detected patterns P. At each moment of time t_j, an array of all energy values $\{E_{1,j}, \ldots, E_{k,j}, \ldots\}$ was formed, where k varied from 1 to r, that is, the number of all frequencies, observed for the moment of time t_j on the calculated surface of the patterns P. In the array $\{E_{1,j}, \ldots, E_{k,j}, \ldots, E_{r,j}\}$, the maximum energy value of $E_{max,j}$ was found and normalization was carried out:

$$\begin{aligned} &\{\langle E_{1,j}\rangle, \ldots, \langle E_{k,j}\rangle, \ldots, \langle E_{r,j}\rangle\} = \\ &\qquad = \{E_{1,j}/E_{\max,j}, \ldots, E_{k,j}/E_{\max,j}, \ldots, E_{r,j}/E_{\max,j}\}. \end{aligned} \tag{7}$$

Normalization (7) was performed separately for each moment of time, which made it possible to use parallel computing methods for numerical calculations. Further, for all points $(f,t)_p$ that make up one P pattern with a duration of m, the average energy characteristic of the E pattern was calculated

$$E = \sum_{p=1}^{m} \langle E(f,t)_p \rangle / m. \tag{8}$$

Thus, each oscillatory pattern is characterized by three parameters: average frequency — f_{md} (ratio (5)), lifetime or duration —T (ratio (6)), and average energy E (the ratio (8)). In Fig. 1 an example of the dependencies on the time t of the quantity N, the average duration T

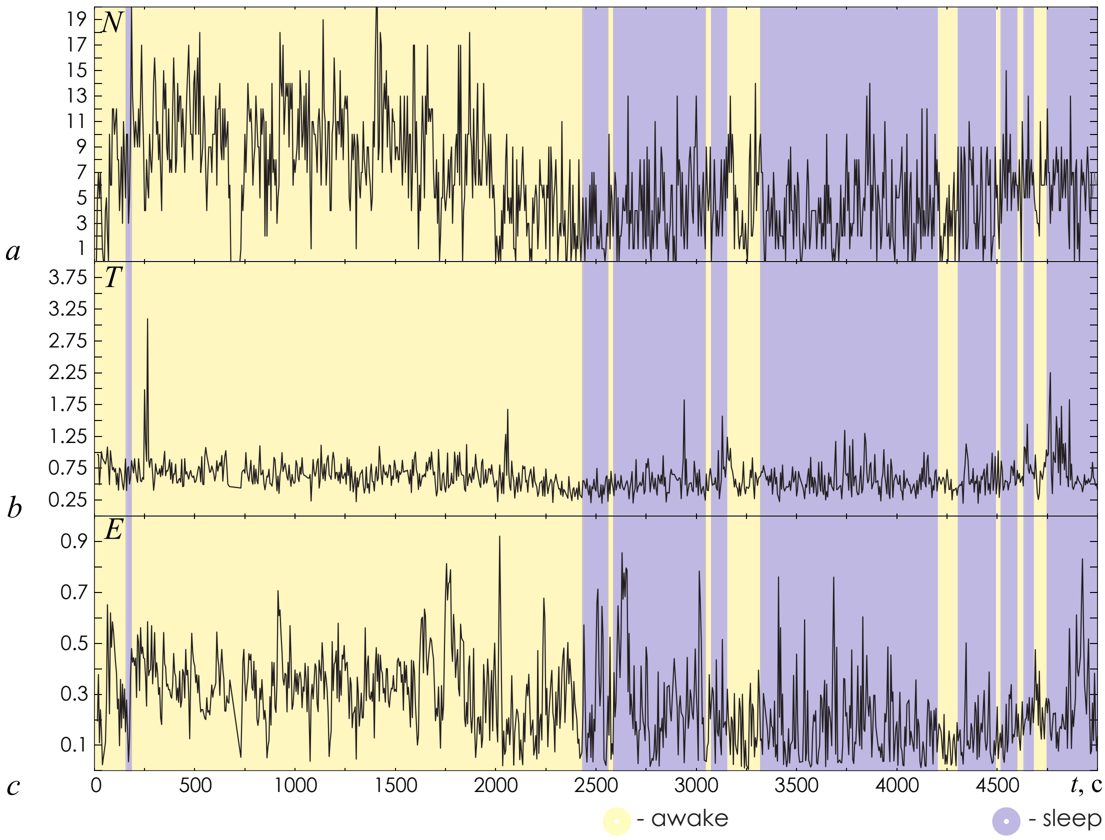

Fig 1. Dependences on time t of the number N (a), average duration T (b) and energy E (c) for patterns calculated from the EEG signal registered in the channel O1 when monitoring a baby # 12 from group # 1. The yellow and purple backgrounds colors correspond the awake and sleep stages, respectively (color online)

and energy E for patterns calculated from the EEG signal of one of the newborns in the entire frequency range is demonstrated $[1; 20]$.

The entire frequency range was divided into 10 intervals of 2 Hz: $\Delta f_1[1;2]$, $\Delta f_2[2;4]$, $\Delta f_3[4;6]$, $\Delta f_4[6;8]$, $\Delta f_5[8;10]$, $\Delta f_6[10;12]$, $\Delta f_7[12;14]$, $\Delta f_8[14;16]$, $\Delta f_9[16;18]$, $\Delta f_{10}[19;20]$. For each frequency interval, a statistical evaluation of the characteristics of the number N, average duration T and energy E of oscillatory patterns identified in the sleep and wakefulness states of two groups of newborns was carried out.

2. Results

In Fig. 2 statistical estimates of the quantitative characteristics of N, E and T of oscillatory CWT patterns for frequency intervals are presented $\Delta f_1 - \Delta f_{10}$.

The oscillatory characteristics of the EEG in the sleep and waking states of the # 1 and # 2 groups of newborns differ significantly. In general, the dynamics in the left (O1) and right (O2) hemispheres are very similar, but the evaluation of the oscillatory structure in the left hemisphere, that is, the O1 channel (left column in Fig. 2). At the same time, a comparison of the structure of activity during sleep and wakefulness for # 1 and # 2 groups demonstrates significant differences. For the number of N patterns, the frequency ranges Δf_1 and Δf_2 are especially indicative (Fig. 2, a, b). Full-term newborns demonstrate a decrease in the number of N patterns during wakefulness and an increase in this characteristic during sleep, and in

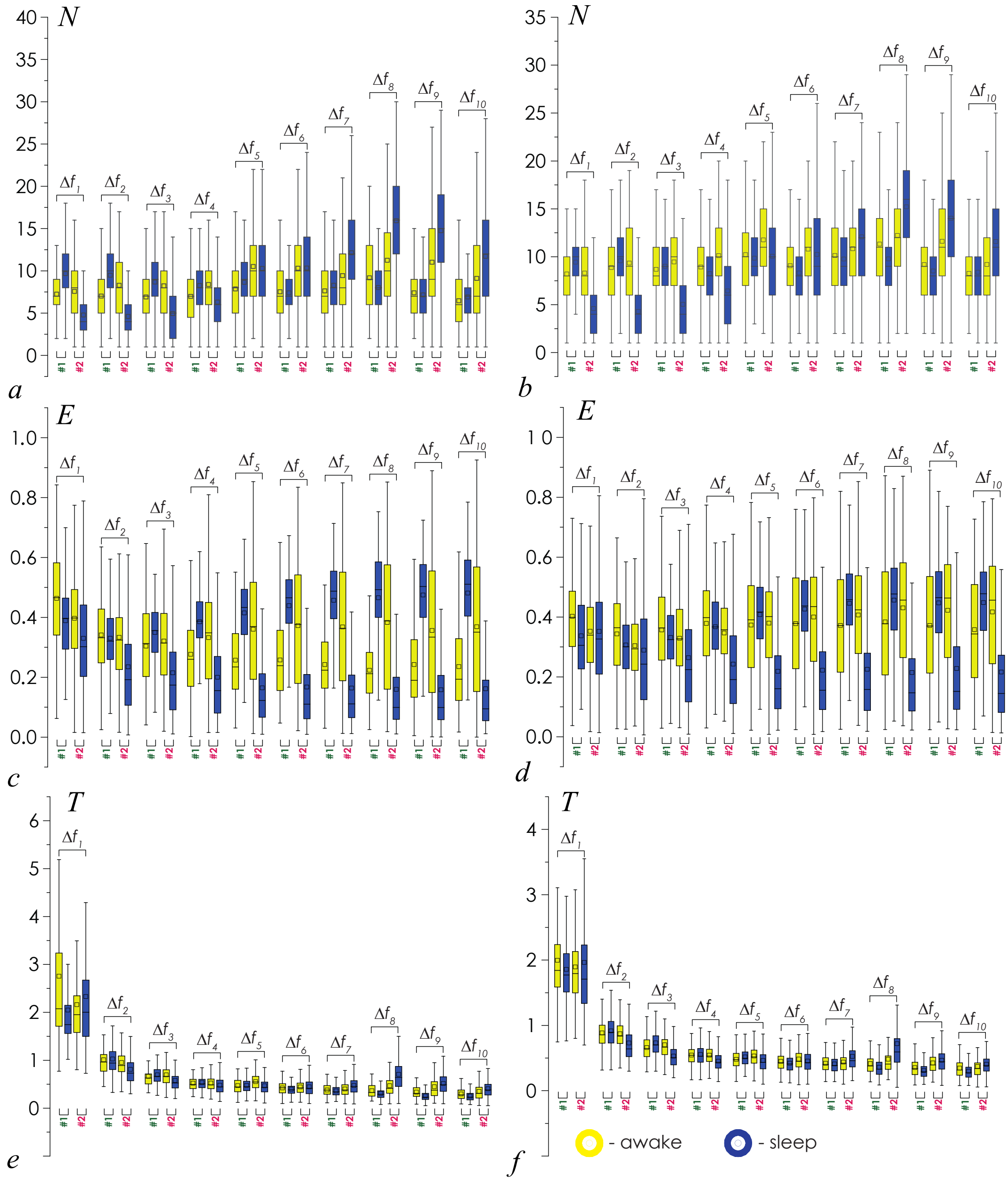

Fig 2. The diagrams of pattern's numbers N, duration T and energy E in ranges $\Delta f_1 \dots \Delta f_{10}$, calculated on EEG channels O1 and O2 for two groupes of newborn: a and b — N estimations for O2 and O1 channels recorded in #1 and #2 groups of newborns, respectively; c, d, e, f — similar diagrams for the evaluation of T and E. The diagrams depict the following statistical characteristics of numerical indicators: the first and the third quartiles (25–75 %, inside the box); the median and the mean (transverse line and point inside the box, respectively); 1.5 interquartile range (shown by whiskers); and outliers represented by asterisks. The yellow color shows the characteristics for the waking state, and the blue color for the sleep state. The neonatal groups #1 and #2 are shown in each diagram and highlighted in green (group #1) and red (group #2) (color online)

the second group the opposite process occurs — an increase in the number of low-frequency patterns during wakefulness. The energy in the Δf_1 and Δf_2 ranges during the child's waking hours paradoxically exceeds that during sleep (Fig. 2, *c*, *d*).

The following frequency ranges Δf_3 and Δf_4 are characterized by the stability of the characteristics of the number and energy of patterns during all states of the group # 1 and the wakefulness of the group # 2. At the same time, the sleep state for slightly premature newborns significantly «subsides» according to the characteristics of the selected oscillatory patterns. With a further increase in frequency in the left hemisphere (channel O1), a similar structure of vibrational activity in the energy region E remains (Fig. 2, *c*). Brain activity during sleep and wakefulness of newborns # groups 1 demonstrate clusters within a cloud of values of brain activity during wakefulness # groups 2 of weakly premature newborns, and EEG recorded during sleep for group # 2, demonstrate a significant decrease in the energy of oscillatory patterns in the range of $[4; 20]$ Hz.

For the highest frequency of the considered intervals $\Delta f_8 \ldots \Delta f_{10}$, a paradoxical picture is again observed. In slightly premature infants, the number of N oscillatory patterns of high frequencies exceeds that for wakefulness and, at the same time, is significantly greater than in newborns of group 1. At the same time, the evaluation of the energy of E patterns demonstrates the opposite processes during the sleep of newborns of different groups. In the first group, the energy increases, and in the second — decreases.

Note that the estimation of the duration of T patterns in all frequency ranges does not allow us to distinguish the features of the development of sleep and wakefulness states of newborns of different gestation periods (Fig. 2, *e*, *f*). To some extent, the only promising exception is the oscillatory range Δf_8, in which the average duration of detected patterns of newborns # 2 groups during sleep significantly increases.

The analysis performed is a detailed representation of nonlinear dynamics processes of oscillatory components with fundamental frequencies belonging to different frequency intervals $\Delta f_1 \ldots \Delta f_{10}$. The commonly used estimate of the integral energy of the CWT, which falls on a certain frequency range, demonstrates average characteristics that do not reflect all the internal processes of the development of specific patterns.

Conclusion

The study of the oscillatory structure of the occipital EEG of newborns with gestation periods of 38-41 and 34-36 weeks demonstrated significant differences in the formation of patterns detected on the basis of CWT. The use of the developed modification made it possible to identify promising quantitative characteristics of patterns for the left channel O1, namely the average energy E and the number of N patterns during the behavioral states of sleep and wakefulness of newborns in the frequency ranges $\Delta f_1 \ldots \Delta f_{10}$. Further development of this approach will be aimed at developing a system for automatic diagnosis of changes in the characteristics of brain activity in full-term newborns as a result of various pathological processes of childbirth and/or postnatal disorders, as well as studying their impact on the neurological development of the child.

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