Eur. Phys. J. Spec. Top. (2024) 233:519–530
https://doi.org/10.1140/epjs/s11734-023-01063-5

THE EUROPEAN PHYSICAL JOURNAL SPECIAL TOPICS

Regular Article

EEG markers of attention sustainability detected in neuropsychological testing in different age groups

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Received 30 August 2023 / Accepted 24 November 2023 / Published online 15 December 2023

Abstract This article presents the results of studies of physical processes in brain activity in patients of different age groups under strictly controlled experimental conditions. The patients selected for the study showed signs of normal age-related aging processes, being physically and socially active. We excluded from the study patients with anxiety disorder and depression, as capable of significantly altering brain activity and cognitive control. All 60 patients were divided into three age groups—middle-aged to elderly, according to WHO classification. The mathematical study was designed to look for changes in brain activity during neuropsychological testing with increasing age of the patients. Assuming that in functionally successful normal aging, such changes will keep some electrophysiological structure in brain activity unchanged, and independent of the patient's age, we evaluated the quantitative characteristics of oscillatory patterns in a set of standard bands for each of the patients and performed statistical analysis of the obtained patterns. As a result of the study, we identified a narrow zone of the left hemisphere characterized by stability and low variability of brain activity in all three age groups. In addition, brain activity in the right hemisphere changes significantly from age to age, characterized by maximum variability when reaching old age (over 60 years). The presented results provide a promising basis for further studies, in particular, repeated performance of these assessments in age-matched patients with similar independent control of their cognitive and emotional status. Thus, the method of estimating the number of oscillatory patterns in different frequency ranges of electroencephalographic recordings represents an opportunity for additional research in neurogeriatrics.

1 Introduction

At the beginning of the twenty-first century, the World Health Organization (WHO) officially introduced the concept of "healthy ageing", which implies a high level of quality of life for older people [1]. At the same time,

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their functional capacity is determined by the system of health–environment interaction. However, this concept was actively discussed earlier, starting from the 1960s and earlier, up to 1902 [2, 3]. Note that since 2015, the term "healthy ageing" has been understood in a comprehensive way, reflecting both a patient's subjective assessment of physical and cognitive parameters of the psyche, and an objective description based on measurements determined by researchers [4, 5].

Since the 2010s, research and publications have begun to show the importance of increasing functional capacity in aging by improving health and mental well-being already in middle age [6, 7]. Thus, the concept of preparation for functionally active aging has emerged in geriatrics, beginning already in the middle age of the patient [8]. In addition to clear and explicit recommendations for lifestyle modification and control, the interdisciplinary field of the actively developing neurogeriatrics verny2020neurogeriatrics is of particular interest. In this field, normal brain aging is understood as a legitimate involutional change that is tolerated in old age and is not the basis for any diagnosis such as benign age-related forgetfulness [9]. Perhaps, the most active pole of attraction in neurogeriatrics is the problem of early diagnosis of neurodegenerative diseases [10–12].

Today, population aging is accelerating worldwide, and this demographic transition will affect virtually every aspect of society [13]. Neurodegenerative diseases, including dementia, significantly increase the necessary costs of caring for patients suffering from them. The increased burden on social and medical organizations, relatives, and loved ones of patients leads to a significant reduction in the quality of life of the society. Early detection of preclinical manifestations and precursors of neurodegenerative diseases is one of the main goals of the currently active interdisciplinary studies of brain activity. However, it must be recognized that even if the earliest possible precursors to the development of neurodegenerative diseases such as Alzheimer's disease are detected, the possibilities of pharmacological treatment of these brain disorders are very limited [14]. This fact requires finding new ways to detect and influence living systems to reduce the harms of aging and neurodegeneration.

In neuroscience, delineated by the field of geriatrics, we can emphasize the search for characteristics of brain activity and structure that correlate with the processes of normal aging while preserving cognitive function [15]. With successful detection of such characteristics, it is possible to compare brains in conditionally normal ("healthy") and pathological aging [16, 17] or brain diseases [18]. One applied aspect of ongoing research into normal brain aging is the development of devices to assist elderly patients [19, 20] and to monitor and track brain aging [21, 22]. Such devices may be based on neurointerfaces that allow not only to monitor aging processes and emerging cognitive dysfunctions, but also non-invasively influence them [23]. Particular hopes are now pinned on technologies for non-invasive and non-pharmacological influences on the dynamics of the blood–brain barrier (BBB) permeability [24]. In particular, there are now works demonstrating certain effects of laser technology [25, 26] and auditory influences [27, 28] on BBB permeability. As it was shown in a number of works, an increase in BBB permeability accompanies the development of post-stroke dementia [29–31] and neurodegenerative diseases [32, 33]. At the same time, there is a hypothesis that when BBB permeability is increased, for example, at some stages of sleep, it is possible to trigger physiological processes that prevent pathological aging of the brain and the development of neurodegenerative diseases [34, 35]. In addition, the detection of stable patterns of brain activity during aging may provide scientists and clinicians with samples of "successful" brain dynamics, to which a brain with pathological dynamics can be brought on the basis of, for example, non-invasive technologies.

Interdisciplinary research in neuroscience standardly includes the use of methods of nonlinear physics and statistical analysis to process recordings of functional monitoring of brain activity. Of particular importance, especially in studies of age-related processes, are non-invasive methods of recording brain activity, the use of which in the future is possible not only in medical and scientific institutions, but also in the home, in contrast to, for example, magnetic resonance imaging. One of such methods is standard electroencephalography: the installation of sensors is not difficult, and the recording device is miniaturized and does not interfere with random activity, which makes it possible to comfortably carry out long-term observation, including night recordings. The analysis of the dynamic characteristics of electroencephalography is often based on the approach of estimating amplitudes andor energies in various frequency ranges characteristic of different states of the human brain and determined empirically. This approach is quite justified when analyzing short fragments of EEG signals, not exceeding 0.01 – 0.1 s, presumably corresponding, for the most part, to a specific neurophysiological process. In particular, during short-term image presentation, short phases of "relaxation" after stimulus perception and recognition can be identified, corresponding to increased alpha activity in the occipital region of the brain [36]. However, when analyzing long EEG time series and/or more complex experimental recordings combining not only stimulus perception but also, for example, motor activity, the use of such a technique becomes difficult.

We use a previously developed method for assessing the oscillatory patterns in electroencephalographic (EEG) [28, 37] recordings. Validation of this method for estimating the spatial and temporal structure of the EEG has been previously performed in the detection of cognitive disorders in patients [38], night sleep studies [39], and detection of cortical brain activity disorders in animals [37]. A special feature of the method is the possibility of complex selective filtering of multifrequency nonstationary EEG activity based on special sorting of the skeletal structure of the continuous wavelet transform (CWT). CWT - analysis of each EEG signal results in a transition from a one-dimensional nonstationary signal to a two-dimensional surface, "time (t) – frequency (f)".

Further computation allows us to reduce the amount of redundant information by moving to selected CWT oscillatory patterns, each described by a set of coordinates on the surface under study $(t; f)$". Of particular importance to this method is the fact that it has been used to detect abnormalities of BBB permeability [28] in animal models, making it potentially applicable for similar analyses in age-matched patients.

In the presented work, we aim to investigate changes in brain activity patterns during healthy aging. In this case, to search for these changes, we used electroencephalography recordings obtained during a long simple psychological test, which has been repeatedly used previously in the analyses of monotonous activity in humans. This test method has been tested previously when working with patients suffering from chronic headaches [40]. The analysis of the EEG recordings of patients obtained as part of this test made it possible to divide classes of patients according to the degree of pain chronicity, i.e., the severity of the disease. The present study included patients who could be described as demonstrating healthy aging. All participants had no subjective complaints about their health status, and clinical specialists did not diagnose them with cognitive impairment; existing age-related diseases and pathologies were compensated.

2 Materials and methods

2.1 Clinical materials

All clinical trials were conducted in accordance with the Declaration of Helsinki [41]. Local ethics committee approval was obtained prior to patient recruitment for the studies. All participants gave written informed consent to participate in the clinical study, digital data processing, and publication of results in the scientific press. The processing of the biomedical signals obtained was performed with the necessary respect for the confidentiality and anonymity of the study respondents.

Sixty patients aged between 20 and 70 years were included in this study. Medical procedures were performed by certified physicians. Psychiatric screening included assessment of neuropsychological status, including an elementary assessment of cognitive function based on the Montreal Cognitive Assessment (MoCA, > 26 points) [42] and anxiety and depression scale (HADS, < 7) [43]. A therapist with a certified somnologist monitored the absence of disorders of total sleep duration (< 30 min) to fall asleep, no more than one prolonged awakening (> 15 min) per night in the past 3–4 months. In addition, volunteers were interviewed to monitor psychological readiness for prolonged testing, adequate state of general cognitive background, and high level of subjective satisfaction with their physical condition and psychoemotional vibe.

Severely obese patients with a body mass index greater than 30 were excluded from the study. Patients with uncompensated conditions such as uncontrolled cardiac disease (hypertension, arrhythmia, etc.), neurological abnormalities (epilepsy, post-stroke paresis, etc.), and active infectious diseases were also excluded from participation in this clinical trial. In addition, patients with chronic pain syndromes were excluded.

The original number of volunteers was 81, of which 21 patients were excluded for the following reasons:

- one volunteer's HADS score exceeded 7;
- four volunteers had chronic migraine and one participant had cluster headache;
- ten volunteers described their significant sleep problems, including frequent awakenings, significant apnea, and difficulty falling asleep;
- five volunteers had uncontrolled arterial hypertension.

All patients were divided into three groups according to their age: Group **I** (20–44 years), Group **II** (45–59 years), and Group **III** (60–70 years). Table 1 summarizes the basic information of the above three groups of patients.

Table 1 Characteristics of the patients groups

	Group **I**	Group **II**	Group **III**
$age_{\min}$	23	46	60
$age_{\max}$	43	59	70
$\langle age \rangle$	32.1	52.9	63.35
$\delta(age)$	6.25	3.93	3.39

$Age_{\min}$—the minimal age of patients in the group, $age_{\max}$—the maximal age of patients in the group, $\langle age \rangle$—the mean age of patients in the group, $\delta(age)$—standard deviation of the age of patients in the group

All participants were invited for neuropsychological testing, which was performed in a standardly equipped electrophysiological testing room. The time of testing was selected from 9 to 14 h of the day, 2–3 h after awakening according to the participants' usual daily routine.

The patient was positioned semi-reclined on a couch chair with legs stretched out in front of himher. Pillows were placed under the test subject's lumbar and neck to eliminate muscle tension. A small table was placed at a distance from the patient's half-extended arms, on which a touch screen tablet was attached to perform the test. All patients performed a completely identical block of tasks during testing.

During testing, the stimulus images were displayed on the tablet screen, examples of which are shown in Fig 1a. The neuropsychological test took each patient approximately 40 min to complete ($t_{start} - t_{end}$ in Fig 1b). During testing, patients were presented with $M = 350$ short visual stimuli consisting of several geometric objects, ranging from 3 to 8 squares. Each stimulus was presented for a short period of time, $\Delta t_{ST}^{I,II,\cdots M}$. Before the next stimulus was presented, a blurred gray background was shown on the screen for $\Delta t_{P}^{I,II,\cdots M}$. The duration of stimulus presentation was significantly shorter than the duration of the pause between them, $\Delta t_{P}^{I,II,\cdots M} \gg \Delta t_{ST}^{I,II,\cdots M}$.

The patient was instructed to rate hisher sense of the number of objects at each stimulus presented. If the number was even, the patient pressed the right side of the tablet; if the number was odd, the patient pressed the left side of the tablet. The time from the onset of presentation of each stimulus until the patient pressed the tablet, i.e., made a choice, was denoted as $\Delta t_{R}^{I,II,\cdots M}$ reaction time. The order of stimulus presentation, the duration of presentation of all stimuli, and the duration of each pause between stimuli were the same for all subjects. The complete experimental protocol was previously published in the supplementary materials to the article Zhuravlev et al. [40].

During this neuropsychological testing, surface electroencephalography (EEG) was recorded in each patient using clinically certified equipment. Digital signals were recorded at a sampling rate of 500 Hz using a conventional monopolar recording technique in $n = 31$ leads, as shown in Fig. 1c. The two reference electrodes A1 and A2 were placed on the mastoid process, and the ground electrode (N) was placed above the forehead. EEG signals were filtered using a band-pass filter with cut-off frequencies of 0.5 Hz and 30 Hz, and a 50 Hz band-pass filter.

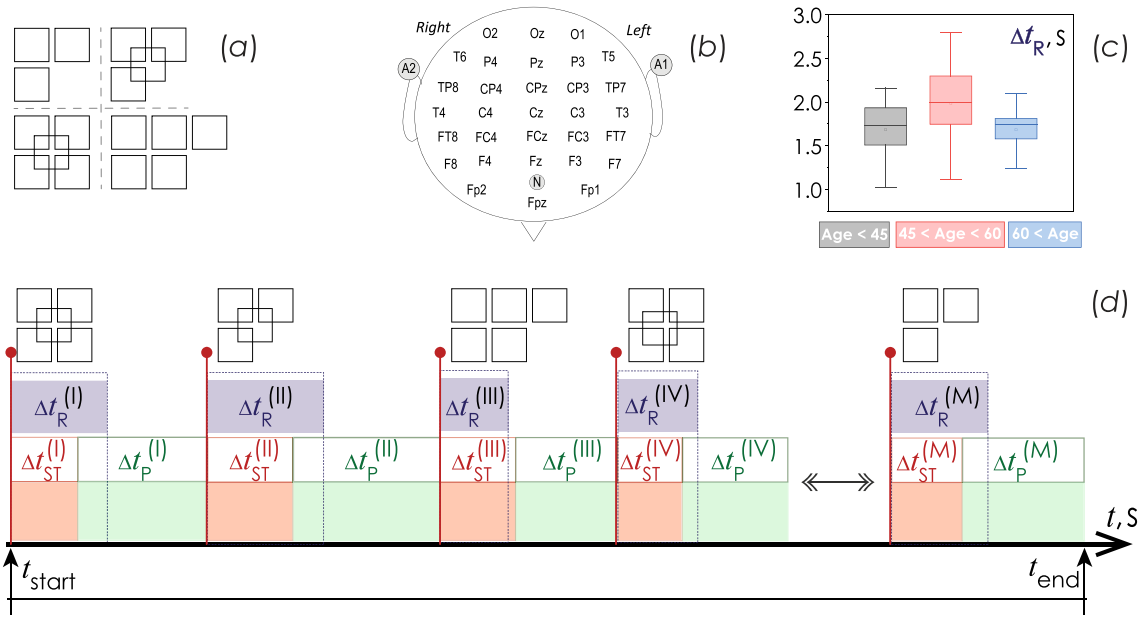

Fig. 1 **a** Examples of visual stimuli. **b** Scheme of experimental design and main time epoch selection: t_{start}, t_{end}]—test start and end times; M—number of presented stimuli; $\Delta t_{ST}^{(I)}$, $\Delta t_{ST}^{(II)}$, $\Delta t_{ST}^{(III)}$, $\Delta t_{ST}^{(IV)}$, $\Delta t_{ST}^{(M)}$—time intervals of stimulus presentation with ordinal number $I, \ldots, M$; $\Delta t_{p}^{(I)}$, $\Delta t_{p}^{(II)}$, $\Delta t_{p}^{(III)}$, $\Delta t_{p}^{(IV)}$, $\Delta t_{p}^{(M)}$—duration of pauses between presentation of stimuli with ordinal numbers $I, \ldots, M$; $\Delta t_{R}^{(I)}$, $\Delta t_{R}^{(II)}$, $\Delta t_{R}^{(III)}$, $\Delta t_{R}^{(IV)}$, $\Delta t_{R}^{(M)}$—reaction times for stimulus presentation with ordinal number $I, \ldots, M$; red vertical lines with dots at the top indicate the onset of each image presented at the top; epochs corresponding to stimulus presentation time intervals, $\Delta t_{ST}^{(i)}$, and pauses, $\Delta t_{p}^{(i)}$, respectively, are highlighted in light red and light green; light gray on top shows detected reaction time intervals; **c** EEG—electrode placement map; **d** distribution of reaction times for three age groups of patients, with results for groups **I**, **II** and **III** shown in gray, light red, and light blue, respectively

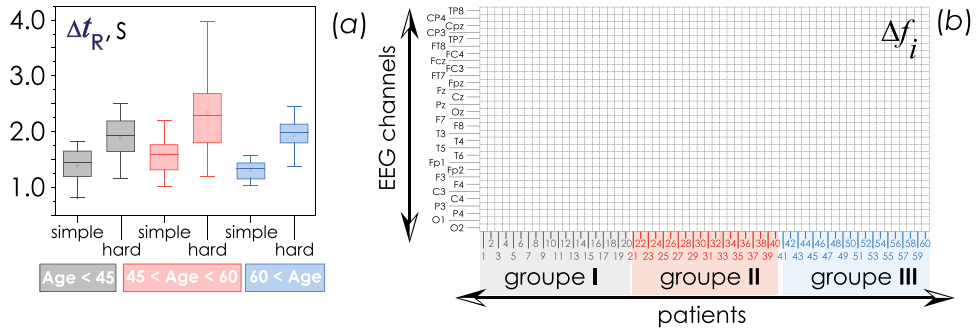

Fig. 2 **a** The distributions of reaction times for three age groups of patients, with results for groups I, II, and III shown in gray, light red, and light blue, correspondingly. **b** The scheme of demonstration of the results of estimation of the number and duration of oscillatory patterns for each of the frequency ranges. The X-axis corresponds to patient numbers, and the Y-axis demonstrates EEG channel numbers. Numbers of patients of groups **I**, **II** and **III** are shown in gray, red, and blue, respectively

2.2 Statistical data processing

Mean, median, and standard deviation were used in descriptive statistics of collected data. The Mann–Whitney U test for independent samples was performed for the comparison of quantitative data. Calculation and graph of distributions of Tr coefficients were made in OriginLab version 6.1. The results with a p value ≤ 0.001 were assumed statistically significant. Statistical analyses were conducted by SPSS version 22.0 software for Windows (IBM, Armonk, NY, USA).

2.3 Reaction time analysis

For each patient, an array of stimulus response durations was calculated, allowing the estimation of standard statistical characteristics of this parameter. Figure 1d shows the estimates of reaction time within the age groups of the study participants. It can be clearly seen that no significant differences were found in the patients' reaction times to the stimuli. This fact further emphasizes that there were no particular differences in the cognitive status of patients of different ages.

Further, all presented geometric stimuli were divided into two clusters, conventionally labeled as "simple" and "hard". We assigned to the "simple" cluster all stimuli comprising between three and five objects. In the "hard" stimuli cluster, we assigned all stimuli consisting of six-to-eight squares. In Fig. 2a, the results of the reaction times of the study participants to stimuli from the "simple" and "hard" clusters are shown. In general, reaction times Δt_R to stimuli from the "hard" cluster were superior to those of the "simple" cluster. A similar sample was observed in all three age groups. However, as the age of the participants increased, the duration of reaction time to the "simple" stimuli decreased slightly, while the duration of reaction time to the "hard" stimuli increased. Thus, the differences between reactions to "simple" and "hard" stimuli clusters for the group **III** were greater than for the group **II**, and those for the group **II** were greater than those for the group **I**. At the same time, there were still no statistically significant differences between groups **I**, **II** and **III**.

2.4 EEG processing

We denoted the array of EEG signals of each patient as $E_1(t_j); ...; E_e(t_j); ...; E_{19}(t_j)$, where $E_e(t_j)$ is the value of the signal registered in current EEG channel e-number at the moment of discrete time t_j. For each EEG signal $E_e(t_j)$, a CWT with the basic Morlet function of the following form was calculated:

$$W_e(f_i, t_j) = \sqrt{\frac{1}{f}} \sum_{j=1}^{N} \exp\left(\frac{-\left[f_i \cdot (t_j - \frac{1}{f_i})\right]^2}{2}\right) \times$$
$$\times E_e(t_j) \cdot \left[-\exp\left(\imath 2\pi f_i (t_j - \frac{1}{f_i})\right) - \exp(-\pi)\right] \cdot \Delta t. \quad (1)$$

In Eq. (1), the following notation was introduced: f_i is the signal frequency, similar to that for the usual Fourier transform, t_j is the discrete recording time, N is the number of time samples in the signal were analyzed, $\imath$ is the

imaginary unit, and $\Delta t = (t_{j+1} - t_j) = 0.002$ s is the time step of the signal sampling. We chose sampling along the frequency axis equal to 0.01, i.e., $\Delta f = (f_{i+1} - f_i) = 0.01$ Hz.

Next, on the surface line $W_e(f_i, t_0)$, all points of maxima, $extr[W_e(f_i, t_0)]_{t_0}$, were extracted. At the next time point, $t_1 = t_0 + \Delta t$, all maxima $extr[W_e(f_i, t_1)]_{t_1}$ for a given surface line $W_e(f_i, t_1)$ were detected again. For the two generated arrays of maximum points, the operation of controlling their location on the plane $(f;\ t)$ was performed, viz

$$\|(f_{i^0}, t_0) - (f_{i^1}, t_1)\| \leq \varsigma, \tag{2}$$

where $\varsigma = 0.001$.

Thus, of the two arrays of extreme maximum values $extr[W_e(f_i, t_0)]_{t_0}$ and $extr[W_e(f_i, t_1)]_{t_1}$, only those that formed continuous lines on the plane $(f;\ t)$, referred to as patterns, P, were retained. This procedure was repeated at each time step, $t_{i+1} = t_i + \Delta t$. This step-by-step processing resulted in a set of patterns that included only extreme CWT values

$$\begin{aligned} P = \Big\{ & extr\Big[W_e\big(f_{P1}^1, t_{P1}^1\big), W_e\big(f_{P1}^2, t_{P1}^2\big), \ldots, W_e\left(f_{P1}^{L_{P1}}, t_{P1}^{L_{P1}}\right)\Big]; \\ & extr\Big[W_e\big(f_{P2}^1, t_{P2}^1\big), W_e\big(f_{P2}^2, t_{P2}^2\big), \ldots, W_e; \left(f_{P2}^{L_{P2}}, t_{P2}^{L_{P2}}\right)\Big]; \ldots; \\ & extr\Big[W_e\big(f_{PN}^1, t_{P1}^1\big), W_e\big(f_{P1}^2, t_{P1}^2\big), \ldots, W_e; \left(f_{P1}^{L_{P1}}, t_{P1}^{L_{P1}}\right)\Big]\Big\}. \end{aligned} \tag{3}$$

After the processing of the entire duration of the EEG time series was completed, all detected patterns were checked for duration to exclude random noise interference. For each pattern, P, we calculated average frequency, $\langle f_P \rangle$

$$\langle f_P \rangle = \frac{\sum_{i=1}^{L_P} f^i}{L_P}, \tag{4}$$

and average duration, $\langle T_P \rangle$

$$\langle T_P \rangle = \sum_{i=1}^{L_P} t^i. \tag{5}$$

In this case, for each point (f_P, t_P) of the oscillatory pattern P, the particular energy value that was extreme in a particular $\delta - \delta$ – neighborhood (f_P, t_P) was ignored.

The entire EEG recording was divided into Δ_{30s} intervals of 30 s duration. Then, all patterns detected during this Δ_{30s} interval were sorted according to the frequency of oscillatory activity. Each pattern according to its mean frequency $\langle f_P \rangle$ (4) was assigned to one of the standard neurophysiological frequency ranges, namely, δ_1, [1.0; 2.5] Hz, δ_2, [2.5; 4.5] Hz, θ_1, [4.5; 6.5] Hz, θ_2, [5.0; 9.0] Hz, α_1, [9.0; 12.0] Hz, α_2, [12.0; 14.0] Hz, β_1, [14.0; 20.0] Hz, β_2, [20.0; 30.0] Hz. Accordingly, the number of $\tilde{N}$ patterns and their average duration $\tilde{T}$ were calculated for each of these ranges.

Further analyses made it possible to visually assess the dynamics of the number and duration of oscillatory patterns by constructing corresponding maps for all frequency ranges under consideration simultaneously for all study participants. Figure 2b shows a schematic of such an illustration. On the abscissa axis were plotted the numbers of all participants in the clinical trials, and on the ordinate axis each of the EEG channels were labeled. Accordingly, the entire plane was divided by the corresponding grid, as performed in this scheme (Fig. 2b). For each band, two similar planes were evaluated—for mean duration and number of oscillatory patterns. On these grids, each cell was colored according to the magnitude of the characteristic being demonstrated.

3 Results

In Figs. 3 and 4, the distributions for the number $\tilde{N}$ and duration $\tilde{T}$ of patterns in two typical frequency bands are demonstrated. These maps show the results of patient ratings of responses to “simple” stimuli. The characteristics of responses to “complex” stimuli cluster are similar to those presented, in general. To reduce the number of figures and ease of interpretation, we present distributions of characteristics of oscillatory patterns plotted in only two bands.

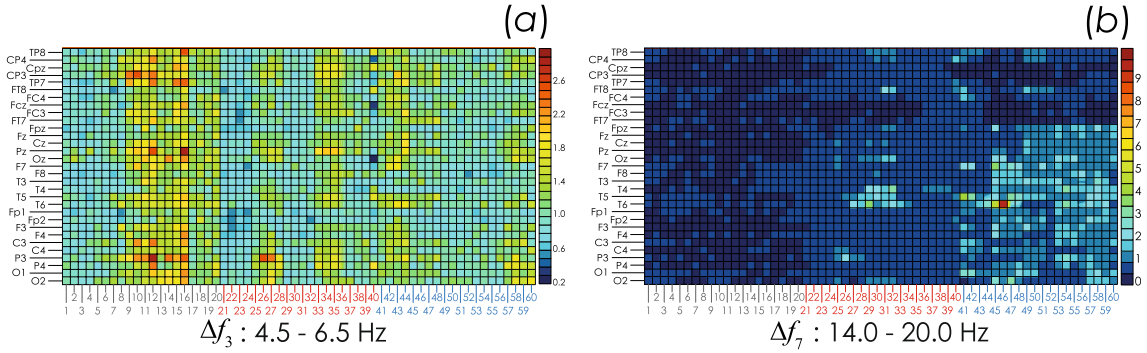

Fig. 3 **a** and **b**: Patterns' number $\tilde{N}$ distribution maps for frequency bands θ_1 and β_1, respectively. Numbers of patients of groups **I**, **II**, and **III**, shown in gray, light red, and light blue, respectively

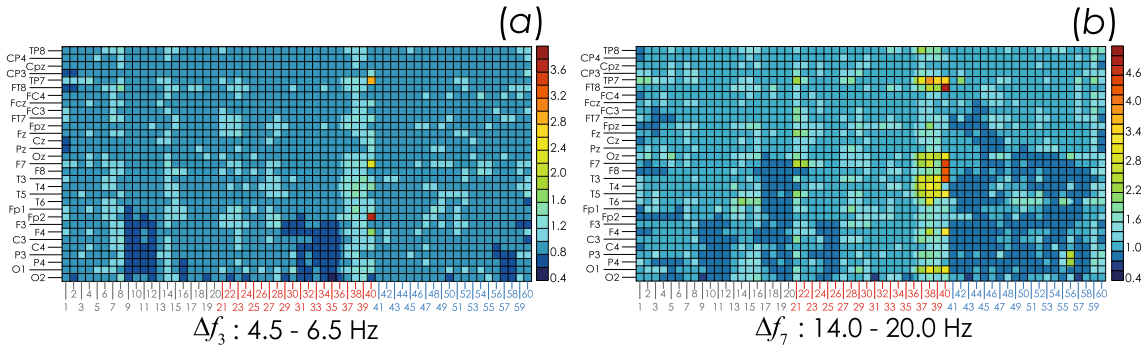

Fig. 4 **a** and **b**: Pattern duration $\tilde{T}$ distribution maps for frequency bands θ_1 and β_1, respectively. Numbers of patients of groups **I**, **II**, and **III** shown in gray, light red, and light blue, respectively

Examination of the changes occurring on the surface along the X-axis allows us to assess the age-related dynamics of brain activity in the groups of study participants. Most of the frequency bands of oscillatory dynamics for the analyzed group of patients do not show any age-related changes, similar to that shown in Fig. 3a and 4a. The most characteristic changes were observed in the Δf_7 (or β_1, [14.0; 20.0] Hz) band, as shown in Fig. 3b and 4b.

Further statistical analyses were performed for the allocated frequency band β_1. Returning to the division of all patients into three age groups, the number and duration of patterns in this frequency band were assessed for "simple" and "hard" stimuli clusters. The results of the statistical analysis are demonstrated in Figs. 5 and 6 for the number $\tilde{N}$ and duration $\tilde{T}$ of patterns, respectively. The series of these figures presents standard box plots showing the distributions of each of the quantitative characteristics of the patterns, $\tilde{N}$ and $\tilde{N}$, within the age groups. Results for groups **I**, **II**, and **III** are shown in gray, red, and blue, according to the previously selected color scheme.

Let us consider the dynamics of the number, $\tilde{N}$, of oscillatory patterns in different age groups. Note that in Fig. 5a and b, the names of EEG channels in which no statistically significant differences in characteristics are observed for at least one type of stimuli presented are typed in fine print. On the light green background are the results of numerical estimates that presented statistically significant differences in the perception of "simple" and "hard" stimuli clusters.

In general, the variability in the number of $\tilde{N}$ patterns increased with increasing age of the participants. In group **I**, which consists of the youngest participants, the variability of this quantitative characteristic is smallest compared to the data for groups **II** and **III**. The analyses revealed 24 statistically significant differences between groups **I** and **III** in EEG analyses for both "simple" and "hard" stimuli clusters. EEG analyses in groups by groups **I** and **II** revealed 14 and 13 instances of differences for the perception of "simple" and "hard" stimuli clusters, respectively. When EEG was analyzed in groups **II** and **III**, statistically significant differences were found 13 and 14 for the perception of "simple" and "hard" stimuli clusters, respectively. It is natural that statistically significant differences are most often found when comparing the groups **I** (20 – 44 years) and **III** (60 – 70 years), which are quite far apart in age. Brain activity during perception of "simple" and "hard" stimuli clusters appears to be similar and shows no significant differences. However, statistically significant differences in EEG brain activity during perception of "hard" stimuli cluster for all three age groups were found to be significantly less – 5 channels versus 8 in the case of "simple" stimuli cluster.

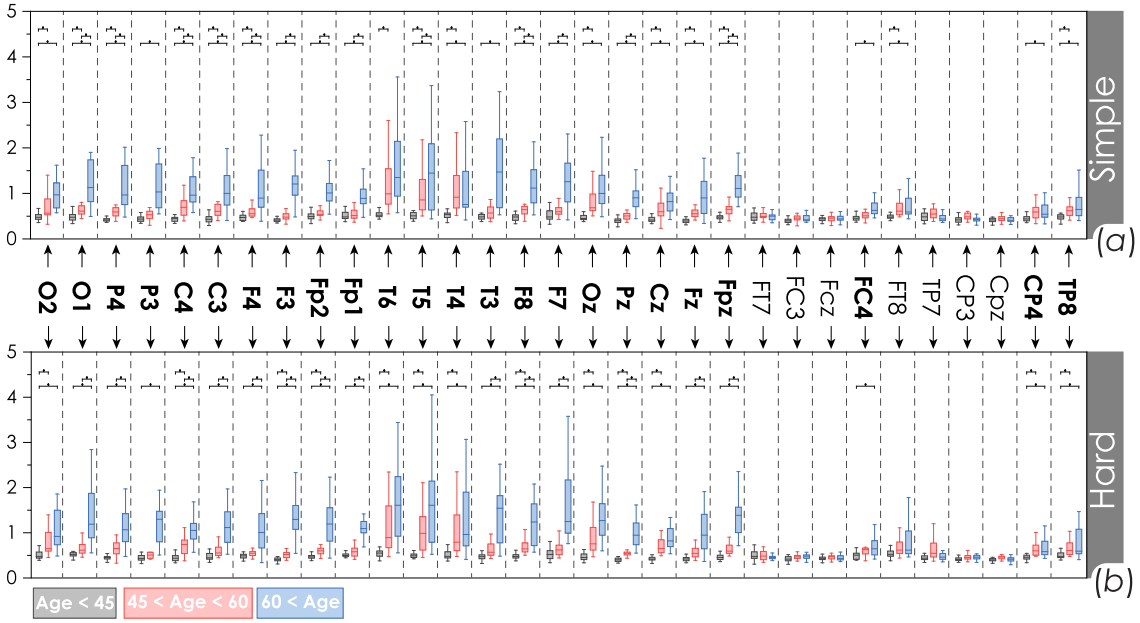

Fig. 5 **a**, **b** Values of number, $\tilde{N}$, of oscillatory patterns P estimated in every EEG channel in frequency band β_1, [14.0; 20.0] Hz, for visual perception of "simple" and "hard" stimuli clusters, respectively. The diagrams of the numerical characteristics calculated for three age groups: Group **I** (20 – 44 years), Group **II** (45 – 59 years), and Group **III** (60 – 70 years). The charts for Groups **I**, **II**, and **III** are shown in gray, red, and blue, correspondingly. 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. Above the diagrams, horizontal brackets show the results of the evaluation of differences between group characteristics calculated according to the Mann–Whitney U test, $p < 0.005$

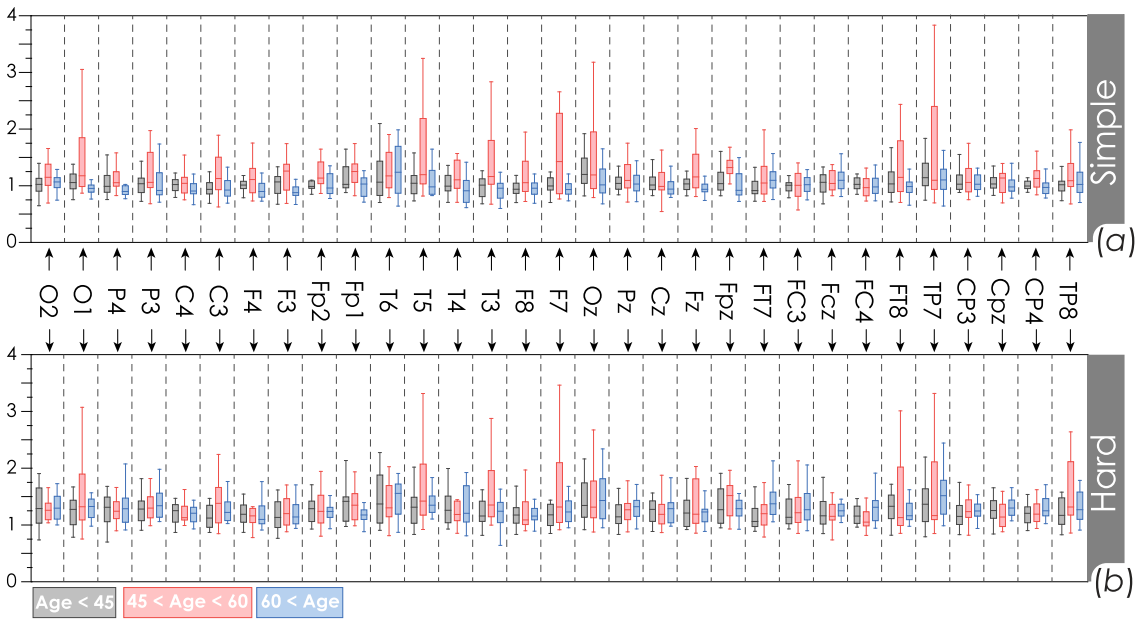

Fig. 6 **a**, **b** Values of time duration, $\langle T_P \rangle$, of oscillatory pattern P estimated in every EEG - channel in frequency band β_1, [14.0; 20.0] Hz, for visual perception of simple and complex stimuli objects, respectively. The diagrams of the numerical characteristics calculated for three age groups: Group **I** (20–44 years), Group **II** (45–59 years), and Group **III** (60–70 years). The charts for Groups **I**, **II**, and **III** are shown in gray, red, and blue, correspondingly. 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

EEG channels, C4 and F8, located in the right cerebral hemisphere, appear to be the most promising for differentiating different age groups **I**, **II** and **III**. For these EEG channels, estimations of the number $\tilde{N}$ of oscillatory patterns significantly differ during the perception of "simple" and "complex" stimuli.

Statistical analysis in values of time duration $\langle T_P \rangle$ of oscillatory patterns P did not reveal any significant differences, as demonstrated in Fig. 6. At the same time, in contrast to the regularities found by analyzing the number $\tilde{N}$ of patterns P, the variability of pattern's lifetime $\langle T_P \rangle$ is maximum for the Group **II** (45–59 years). In addition, we note that in occipital EEG channels Oz and O1, variability increases significantly in all three age groups. At the same time, for the previously identified right hemisphere EEG channels (C4 and F8), when considering the perception of conditionally "complex" stimuli, the duration of oscillatory patterns shows a completely similar distribution in all three age groups.

4 Discussion

The presented paper is the result of an interdisciplinary study involving digital analysis of oscillatory processes in brain activity recorded during medical clinical trials. From the point of view of nonlinear physics, the analyzed processes represent examples of recording the activity of a complex distributed system with pronounced nonlinear properties. In this case, the presented method allows us to observe the dynamics of strongly nonstationary processes recorded during some time intervals, evaluating both the change of the oscillation frequency and its amplitude. This approach is centered on the decomposition of the original signal into a set of oscillatory components. Traditional estimates of the energy attributable to different frequency bands represent an averaged and normalized measure of the energy of different oscillational complexes without separating them. Such a traditional approach allows the estimation of general regularities, such as the activation of the alpha – rhythm in pauses between the visual stimuli presentation andor the activation of beta activity in response to stimuli, as has been shown in [44] for perception of bistable images. Thus, such a standard approach allows us to assess the most pronounced trends in point-by-point EEG recordings of brain activity. At the same time, detection of more subtle abnormalities in the pattern of brain activity, which may be associated with neurodegenerative diseases [38] andor with aging processes, seems to be difficult to perform on the basis of such averages.

One of the manifestations of serious disorders accompanying human aging is a change in the functioning of complex complexes of brain structures that provide regulation of tone or wakefulness, receive, process, and store information from the outside world, and also regulate and control mental activity. With aging, there are serious disturbances in the clear regulation of mental processes, memories, and associations acquire a disorganized character and the directed performance of mental activity becomes inaccessible or difficult. To carry out organized activity, it is necessary to have such an optimal state of the cerebral cortex, when the nervous processes are characterized by concentration, balanced excitation and inhibition, and high mobility of the nervous system, allowing easy transition from one activity to another [45]. However, with healthy aging, traits of optimal neurodynamics can be found at very old ages. However, it remains an open question exactly how conditionally normal brain function is maintained in the case of healthy aging in "functionally healthy" participants. First, abstracting from specific neurophysiological bases of cognitive functions realization, we can assume that the basic principles of brain functioning and, accordingly, EEG recordings of its activity remain unchanged in the process of normal aging. Second, it is possible that compensatory mechanisms that reduce the effects of inevitably occurring regression processes during brain and organism aging are triggered. The results obtained seem to lie in the line of the second hypothesis, since, practically, the whole structure of brain activity retains its structure when analyzing EEG recordings of patients of different ages, with the exception of some areas of the right hemisphere, in particular, the temporal lead F8. Today, brain activity in the right temple is one of the important markers of the state of cognitive function. In particular, high education level was associated with greater parietal, occipital, and temporal resting-state EEG alpha power, as shown in Babiloni et al. [46].

5 Conclusion

The presented results demonstrate the prospect of further development of physical methods of nonstationary signal processing based on the refinement of the frequency–time pattern of oscillatory components present in complex recordings of biological nature. The presented approach allowed us to identify age-specific features in the structure of brain electrical activity in normal "healthy" aging patients. Comparison of brain activity of elderly patients without pronounced neurodegenerative diseases but with certain impairments of cognitive activity may be useful for the early detection of such disorders in patients in the preclinical stage.

Acknowledgements The study was conducted with the financial support of the Russian Science Foundation (Project No. 22-72-10061).

Data availability The datasets generated during and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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