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Recurrence quantification analysis provides the link between age-related decline in motor brain response and complexity of the baseline EEG

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Abstract. The *goal* of the present study is to investigate the effect of healthy aging on the neuronal mechanisms supporting human brain activity during motor task performance. Such biomarkers of the age-related changes can be detected using mathematical methods of time-series analysis and complexity analysis. *Methods*. In the present paper, recurrence quantification analysis (RQA) measures are employed to explore the complexity of the pre-movement EEG in young and elderly adult groups. To evaluate the neural brain response during motor execution, we applied the traditional methods of time-frequency analysis. *Results*. The proposed approach demonstrated that (i) the RQA measures show a significant increase of complexity in elderly adults; (ii) increased pre-movement EEG complexity comes with the reduced motor-related brain response in the α/μ-band ($p < 0.01$), estimated via the traditional methods of time-frequency analysis. It allows to conclude that the increased pre-movement EEG complexity indicates the weak neuronal plasticity degenerated under the factor of age. *Conclusion*. The complexity of the pre-movement α/μ-band neuronal oscillations could be considered as a relevant measure for the detection of age-related cognitive or motor impairments. Besides, applied RQA method demonstrated a good ability to assess the complexity features of pre-stimulus EEG and provided a clear interpretation of age-related changes in electrical activity of the brain cortex.

Keywords: complexity, recurrence quantification analysis, EEG, age-related changes, event-related desynchronization.

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Рекуррентный анализ сложности предстимульных сигналов ЭЭГ и их связь с возрастными изменениями в двигательной активности мозга

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Аннотация. *Целью* данного исследования является изучение влияния процессов естественного старения на нейронные механизмы мозга, ответственные за обработку двигательной активности человека. Подобные биомаркеры возрастных изменений могут быть обнаружены с помощью математических методов анализа временных рядов и анализа сложности сигналов. *Методы*. В данном исследовании для анализа сложности предстимульных сигналов ЭЭГ в двух возрастных группах испытуемых были использованы меры рекуррентного анализа. Для оценки нейронной реакции во время выполнения движений, были применены традиционные методы частотно-временного анализа сигналов ЭЭГ. *Результаты*. Предложенный подход продемонстрировал следующее: 1) меры рекуррентного анализа показывают значительный рост сложности предстимульных сигналов ЭЭГ в группе возрастных испытуемых; 2) повышенная сложность ЭЭГ связана со сниженным нейронным ответом в α/μ-ритме ($p < 0.01$), измеренным с помощью частотно-временного анализа. Данные результаты позволяют сделать вывод о том, что повышенная сложности предстимульных сигналов ЭЭГ указывает на возрастное снижение нейронной пластичности. *Заключение*. Сложность предстимульных колебаний в α/μ-ритме может быть рассмотрена как релевантная мера для детектирования возрастных когнитивных и двигательных изменений. Кроме того, рекуррентный анализ продемонстрировал возможность оценить сложность предстимульных сигналов ЭЭГ и дать чёткую интерпретацию возрастным изменениям электрической активности коры головного мозга.

Ключевые слова: сложность, рекуррентный анализ, ЭЭГ, возрастные изменения, вызванная десинхронизация.

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Introduction

Studying the age-related changes in brain activity is a complex task of high social significance. Besides the commonly used clinical approaches to the diagnosis of neurological disorders, recent studies actively focus on the features of brain electrical activity extracted via the mathematical methods of time-series analysis [1]. Traditionally, hallmarks of the age-related pathological states are observed in the spectral power of electroencephalogram (EEG) rhythms. In particular, a well-known pattern of Alzheimer's disease is a generalized slowing of the EEG, i.e., a shift in the EEG spectral power towards the low-frequency θ- (4–8 Hz) and δ-bands (1–4 Hz) [2, 3].

Another group of studies focus on the dynamical properties of EEG reflecting the changes in brain behavior under healthy aging. In this context, the complexity features of EEG, which are known to reflect the current dynamical state of the EEG time series as well as to detect the transitions from periodic and chaotic behavior and *vice versa* [4, 5], are of special interest. In particular, the entropy-based estimations of complexity provide an insight into various pathological processes, such as abnormalities in sleep-related EEG [6] and cardiac rhythm [7], epileptic brain activity [8], etc. Regarding the age-related changes, a decreased resting-state EEG complexity is a well-established marker of healthy aging [9, 10].

In Ref. [11] the authors demonstrate that the response of EEG to the changes in environmental conditions weakens with age based on the analysis of dimensional complexity in the eyes-open and eyes-closed state. In Ref. [12] the authors show that the age-related slowing down in the motor initiation before the dominant hand movements is accompanied by the growth of the θ-activity within sensorimotor area and reconfiguration of the θ-band functional connectivity in elderly adults.

However, entropy-based methods have certain limitations. For instance, the fractal dimension methods, despite their simplicity and universality, are often criticized for sensitivity to the noisiness of the signal and narrow interval of the values, which can lead to identical results for different signals [13]. On the other hand, the entropy-based methods are known to be sensitive to the length of time series [14], which resulted in the development of several modifications depending on the research goal [15, 16]. All these methods in their present form satisfy the most requirements of modern EEG studies. In our previous work [17], we used long-range correlations technique [18, 19] to analyze age-related distinctions in EEG signals during execution of motor tasks. However, the application of new methods is also important to enhance the physiological interpretation of the brain signals complexity.

In the present study, the recurrence quantification analysis (RQA) is proposed to quantify the complexity of the baseline EEG preceding motor task [20]. RQA is a powerful tool that has been developed to explore the recurrent states of complex dynamical systems through the analysis of time series. The measures of RQA estimate the system's complexity using the natural property of dynamical systems to recur to their previous substantially similar states. RQA was widely used for analysis of climate data [21, 22], in natural sciences and engineering [23–25], for natural language processing [26] and etc. One can witness a rapidly developing trend to apply RQA to the processing of biological signals. In particular, RQA measures demonstrated an advantage over the frequency domain analysis during the detection of pathological states on EEG, such as early stages of Autism Spectrum Disorder [27], multiple sclerosis [28] and stress-related conditions [29, 30]. In addition, in our previous study, the RQA measures demonstrated an ability to quantify properly the features of motor-related brain activity [31]. It should be noted that RQA provides a clear interpretation of the system's complexity in terms of concepts of statistical physics and nonlinear dynamics.

Summarizing the above, the goal of the present paper is to demonstrate the relevance of the RQA measures in the analysis of age-related changes in brain behavior through the quantification of EEG complexity. We consider motor-related activity since recent studies indicate that the brain motor system is susceptible to the age-related degenerative changes [32, 33]. The disintegration of the brain network connectivity leads to over-activation of the sensorimotor cortex, often addressed as a compensatory mechanism, which causes the different patterns of cognitive and motor-related activity processing in the elderly population [32, 34, 35]. Despite a large number of studies, the particular effects of aging on the motor-related response remain unclear. The main hypothesis of this study is that the complexity of pre-movement neural activity captured by EEG is connected with the ability of individuals to induce a proper motor-related cortical response, and healthy aging has a direct effect on this connection. To address this hypothesis, the relationships are investigated between the complexity of the pre-movement α/μ (8–14 Hz) brain rhythm and motor-related cortical activation in young and elderly adult groups. The results demonstrate that the RQA-based complexity of the pre-movement EEG significantly increases with age. Finally, the correlation is uncovered between the pre-movement EEG complexity and the motor-related cortical activation. The significant differences dominate in the sensorimotor area.

1. Methods

1.1. Experimental design. The experiments were performed in two age groups consisting of 10 healthy elderly adults (65.0 ± 5.7 years, 6 females, 4 males) and a control group of 10 healthy young individuals (26.1 ± 5.2 years, 3 females, 7 males). Selected subjects had no medical history of head trauma, stroke, depression, and other neurological conditions that can affect the EEG features.

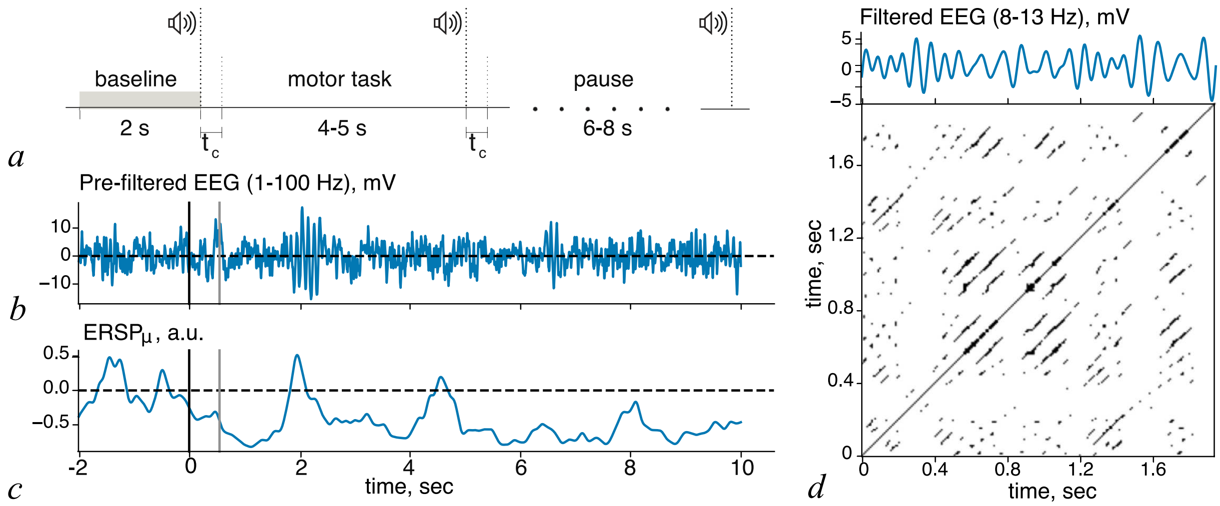

Fig. 1. *a* – the timeline of a single trial. Here, t_c is the duration of the audio command: 0.55 s for the right hand and 0.75 s for the left. *b* – a raw EEG sample corresponding to the single trial of the right hand motor execution and *c* – wavelet energy for this trial averaged over μ-rhythm (8–13 Hz). Solid black and gray vertical lines correspond to the time interval of the audio command. *d* – sample of EEG baseline time series (upper plot) and corresponding RP (lower plot)

The experimental study was approved by the local ethics committee and performed in accordance with the Declaration of Helsinki. Each experimental session started with 5 minutes of eyes-open EEG recording. After that, the participants were instructed to perform fine motor tasks according to the audio instruction. Following either long or short audio signal ($t_c = 0.75$ sec or $t_c = 0.55$ sec for the left and right hand, respectively), the participants were asked to squeeze the corresponding hand into a fist and relax it after the second audio command (see Fig. 1, *a*). After the movement was completed, the 6–8 seconds long pause was given before the next motor task.

Each participant performed $N = 60$ trials (30 with each hand).

1.2. EEG recordings and preprocessing. For EEG acquisition, the EEG amplifier Encephalan-EEGR-19/26 (Medicom MTD, Russia) with a sampling rate 250 Hz was used. EEG dataset was recorded with 31 Ag/AgCl electrodes according to the “10-10” international system [36]. Acquired EEG signals were filtered using the 50 Hz Notch filter to avoid the power-line interference.

Next, the low-frequency artifacts were removed by applying the 5^{th}-order Butterworth filter in the range 1–100 Hz to the EEG dataset (see Fig. 1, *b*). The ocular and cardiac artifacts were also removed using the independent component analysis (ICA) [37]. Then, EEG recordings were sliced into epochs. Each epoch included 2s of the baseline EEG and 10s of the motor-related activity. Finally, a visual inspection of the EEG epochs was performed to exclude those containing the artifacts that could not be removed via described preprocessing steps, leaving 15 epochs for each hand.

The preprocessing steps, including filtering, ICA, and epoching, were performed using the MNE package for Python 3.7 (ver. 0.20.0) [38]. The experimental data underlying the results presented in the study are available online at [39].

1.3. Recurrence quantification analysis. The RQA was applied to the EEG signals filtered in the α/μ-rhythm (8–14 Hz, see Fig. 1, *d*) to access the complexity of the brain activity preceding motor task. For proper estimation of the EEG complexity via RQA, one should consider the reconstructed phase space trajectory of the EEG time series using Taken’s theorem [40]. The embedding parameters were chosen as follows: the time delay of EEG filtered in α/μ-rhythm is $\tau = 5$ defined with the mutual information method [41], and the embedding dimension is $m = 3$ according to the Kennel’s false nearest neighbors method [42].

In the reconstructed phase space trajectory $\vec{x}_k$, the two states are considered as similar if they are in each other neighborhood defined by the threshold ε [43]. Recurrence matrix can be constructed by evaluation of all neighboring states of the trajectory as follows:

$$R_{i,j}(\varepsilon) = \Theta(\varepsilon - ||\vec{x_k}(t_i) - \vec{x_k}(t_j)||), \tag{1}$$

where $i, j = 1, ..., T - 2\tau$, Θ is the Heaviside function, and $||\cdot||$ is the norm (Euclidean norm in the present study). The recurrence plot (RP) is a visualization of the recurrence matrix that shows recurrent/non-recurrent states as black and white dots, respectively. Note that the value of the recurrence threshold ε is crucial for the assessment of the correct structure of the RP. In the present study, the ε was chosen as the 3^{rd} percentile of the pairwise distance distribution according to Kraemer et al. [44]. RP consists of various structures formed by the recurrent "black" dots and non-recurrent "white" dots, that represent different aspects of the system's dynamics in the state space. For example, the "black" diagonal lines quantified by the measure of determinism (DET) mean that the part of the system's trajectory moves almost parallel to another part for a time equal to the line length [43]:

$$DET = \frac{\sum_{l=l_{\min}}^{N} lP(l)}{\sum_{l=1}^{N} lP(l)}. \tag{2}$$

Therefore, DET represents the ratio of the recurrent dots that are included in the diagonal lines to the all recurrent dots of RP. In Eq. 2, $l_{\min}$ is the minimal length of diagonal line ($l_{\min} = 20$ in this study) and the $P(l)$ is the histogram of diagonal lines of length l.

Another measure of complexity is a recurrence time entropy (RTE) based on the "white" vertical lines analysis, which uses Shannon's definition of entropy and reflects the transitions of the considered system from regular to chaotic state and *vice versa* [44]. RTE is defined as follows:

$$RTE = -\frac{1}{\ln T_{\max}} \sum_{t_w=1}^{T_{\max}} p(t_w) \ln p(t_w), \tag{3}$$

where $p(t_w)$ is the probability of recurrence time t_w, and $T_{\max}$ is the largest recurrence time.

The RQA measures were applied to the 2 s time window of EEG before the first audio signal which corresponded to the pre-movement activity. DET and RTE were computed for each of 31 EEG channels and averaged over 30 epochs for each of 20 subjects (15 LH epochs and 15 RH epochs). Between-subject comparison of $\overline{DET}$ and $\overline{RTE}$ in spatial domain aimed at uncovering age-related changes in the brain signals complexity was performed using the non-parametric clustering permutation test following Ref. [45]. Effect was evaluated at each sensor-pair using two-tailed F-test for independent samples **(**$DF1 = 1$**,** $DF2 = 18$**,** $p = 0.05$**,** $F_{\text{critical}} = 4.41$**)**.

The RQA was performed using pyunicorn package for Python 3.7 (ver.0.6.0) [46].

1.4. Time-frequency analysis. To support the findings regarding EEG signals complexity, its link with the motor-related changes of EEG spectral power was explored in both age groups. A priory knowledge about the cortical activation during movements execution implies a pronounced event-related desynchronization of α/μ-oscillations (ERD_μ) in the contralateral area of the primary motor cortex [47–51].

First, time-series of the α/μ-band event-related spectral power ($ERSP_\mu$) were evaluated in symmetrical C4 (in right hemisphere for LH) and C3 (in left hemisphere for RH) sensors using Morlet-based wavelet transform [52, 53] implemented in the MNE package (see an example of $ERSP_\mu$ time series in Fig. 1, *c*). Baseline correction was applied by subtracting the mean of the 2 s baseline preceding audio command and then dividing by the mean of the baseline ("percent" mode). To investigate the effect of age, a between-subject comparison of the motor-related $ERSP_\mu$ averaged over the time interval

1–4 s was performed in each condition (LH and RH) via the unpaired t-test ($DF = 9$). The normality of the α/μ-band spectral power samples was validated via the Shapiro–Wilk test. Then, the correlation between the complexity of the pre-movement EEG and corresponding values of the averaged α/μ-band spectral power was analyzed using Pearson's coefficient and linear regression.

2. Results and Discussion

2.1. Pre-movement EEG complexity versus age. Fig. 2, *a* shows the results of the sensor-level between-subject comparison of the pre-movement EEG complexity. Both RQA measures demonstrated the presence of significant clusters, with 26 channels in $\overline{DET}$ (except F8, F7, and those placed over occipital cortex) and 13 channels for $\overline{RTE}$ (Tp8, Tp7, Pz, Oz, Fc-, C-, Cp-channels). These differences revealed via non-parametric permutation test can be interpreted as almost whole-head increased complexity of the pre-movement α/μ-band oscillations in elderly adults (reduced DET and increased RTE). Specifically, the pronounced differences are observed in the bilateral motor cortex with a skew towards the left hemisphere.

Next, we selected RQA data from the channels included in significant clusters only, and obtained the mean values of RQA complexity measures $\overline{DET}$ and $\overline{RTE}$ for each subject:

$$\overline{DET} = \frac{1}{N_{S_{DET}}} \sum_{s \in S_{DET}} DET_s, \tag{4}$$

$$\overline{RTE} = \frac{1}{N_{S_{RTE}}} \sum_{s \in S_{RTE}} RTE_s, \tag{5}$$

where S_{DET} and S_{RTE} are the sensor clusters of significant DET and RTE changes respectively,

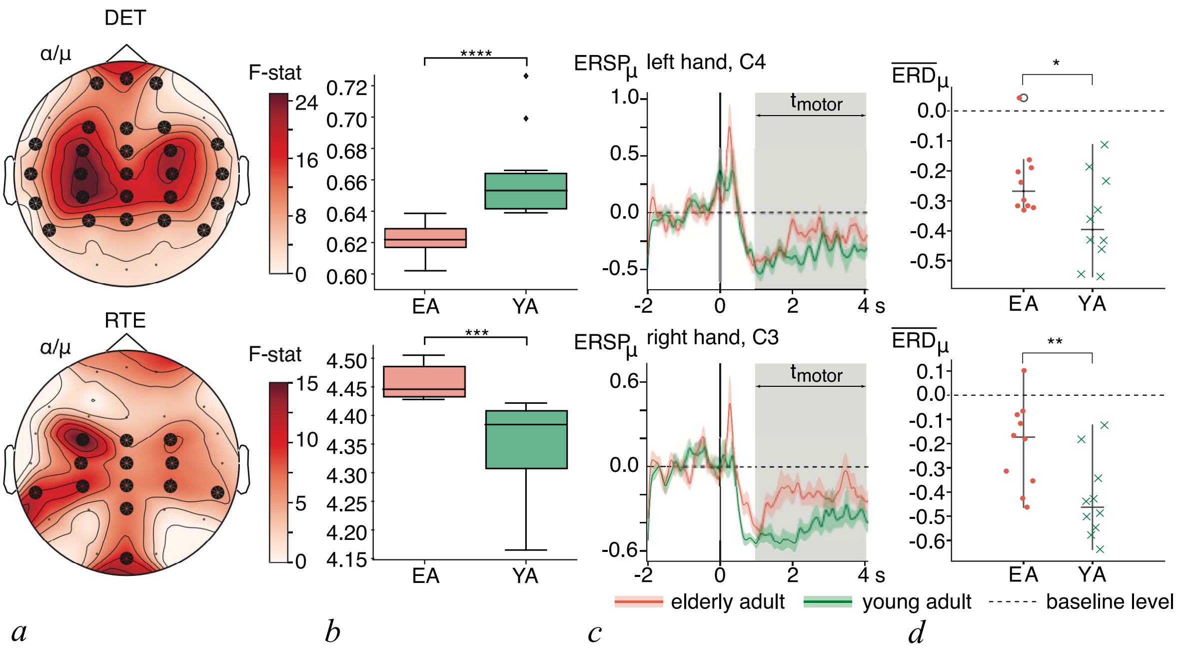

Fig. 2. *a* – Between-subject differences in DET (upper row) and RTE (lower row) calculated via a non-parametric cluster-based permutation test. The black dots correspond to the sensors composing significant clusters. *b* – Dependencies between the age and the RQA measures of complexity. Here, '***' indicates $p = 0.001$ and '****' indicates $p = 0.0001$ according to Mann–Whitney U-test. *c* – $ERSP_{\alpha/\mu}$ averaged across the subjects (mean ± SE) for the left-hand (top panel) and right-hand (bottom panel) movements. The shaded area corresponds to the time interval t_{motor}, where the motor execution takes place. *d* – The distributions of $\overline{ERD}_{\mu}$ for both age groups in the case of left-hand (top panel) and right-hand (bottom panel) movement

$N_{S_{DET}}$ and $N_{S_{RTE}}$ are the sizes of these clusters, DET_s and RTE_s are measures of EEG signal complexity at the s^{th} sensor.

Fig. 2, *b* shows the obtained dependencies. In particular, elderly group demonstrated decreased $\overline{DET}$ compared with young individuals with $p = 0.0001$ according to Mann–Whitney test. At the same time, $\overline{RTE}$ significantly increases with age ($p = 0.001$).

According to the demonstrated dependencies, the age-related changes in the α/μ-band EEG are associated with the increased complexity of these signals. In previous research, the entropy characteristics were considered that demonstrated the age-related decrease of the complexity of the resting state brain activity of different modality [54–56]. The age-related changes in brain activity were usually associated with reduced complexity due to the destructive changes in the cortical network structure [57]. However, in the present paper, the periods of rest between sequential motor executions are considered, which significantly deviates from the resting-state EEG due to the presence of the traces of task specific activity. Note that in our previous work considering the motor-related activity in the young population, the reduced EEG complexity was associated with ERD pattern during motor execution [31]. Besides, the motor-related ERD/S was previously connected with lower/higher EEG complexity estimated via Kolmogorov entropy [48]. We can conclude that in the young adult group the increase of the EEG oscillation regularity in the task-specific area corresponds to the better responsivity and stabilization of the brain state associates with the motor execution. At the same time, in the elderly population the motor-related baseline EEG demonstrated increased complexity in α/μ-rhythm also can be an illustration of poor neural response on stimuli or actions under healthy aging.

2.2. Motor-related spectral power and age. Fig. 2, *c* shows the $ERSP_{\mu}$ averaged across the subjects in each group and illustrates the motor-related desynchronization of the μ-rhythm soon after the audio command. The gray area in Fig. 2, *c* highlights to the time interval t_{motor} = [1,4]s corresponding to the motor task execution. To compare the level of the motor-related desynchronization between the age groups and experimental conditions, $ERSP_{\mu}$ was averaged within t_{motor} time interval so that $\overline{ERD}_{\mu}$ was obtained.

Fig. 2, *d* shows the distributions of the $\overline{ERPS}_{\mu}$ for both age groups in the case of the left-hand (C4 sensor top panel) and the right-hand (C3 sensor bottom panel) movements. As expected, young adults demonstrated more pronounced desynchronization compared with elderly adults. The mixed-design ANOVA (see Table) yielded the age as the only significant factor that affects the motor-related neural response ($F = 9.049$, $p = 0.008$). The within-subject factor of motor task (right or left hand) did not have significant influence on the $\overline{ERD}_{\mu}$ value ($F = 0.255$, $p = 0.641$), as well as the interaction between the factors ($F = 1.471$, $p = 0.241$). This observation confirms the known neurophysiological effects of healthy aging. Several studies on age-related changes evidenced that unilateral motor activation is less pronounced in elderly individuals. Instead, they employed a compensatory mechanism involving larger cortical areas including the regions of ipsilateral motor and prefrontal cortices [58–60]. The white matter tract disruption and volume decrease underlie such functional reorganization of brain regions [61, 62].

Table. Time-averaged $\overline{ERD}_{\mu}$, two-way mixed ANOVA

Cases	df1	df2	Mean Square	F	p
Age (between-subject factor)	**1**	**18**	**0.308**	**9.049**	**0.008**
Motor task (within-subject factor)	1	18	0.003	0.225	0.641
Motor task × Age	1	18	0.020	1.471	0.241

2.3. Relationship between the pre-movement complexity and the motor-related spectral power. Fig. 3 demonstrates the results of the correlation between the RQA complexity measures and $\overline{ERD}_{\mu}$. The correlation was evaluated at the same EEG sensors in the motor area (C4 for left-hand movements and C3 for right-hand movements).

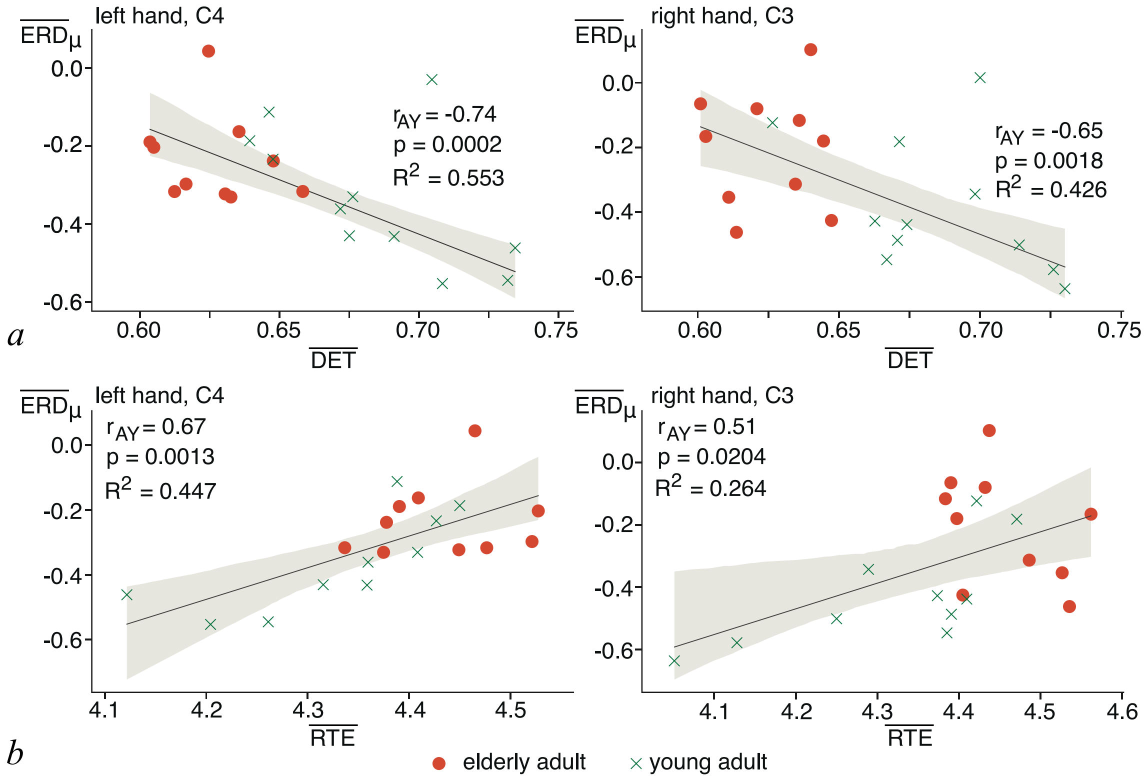

Fig. 3. Correlations between the averaged μ-band spectral power $\overline{ERD}_\mu$ and pre-movement EEG complexity measured by $\overline{DET}$ (*a*) and $\overline{RTE}$ (*b*). Left and right columns illustrate correlations in the case of the left-hand and right-hand movements, respectively. The black line represents the linear law fitted by the linear regression with a coefficient of determination R^2. The shaded area highlights the 95% confidence interval. Pearson's correlation coefficient r_{AY} and its p-value are shown on the corresponding scatter plots

The results demonstrate that the considered variables have significant linear relationships. The Pearson's correlation show that $\overline{DET}$ is negatively correlated with $\overline{ERD}_\mu$ (for the left hand movement, C4: $r_{AY} = -0.74$, $p = 0.0002$, for the right hand movement, C3: $r_{AY} = -0.65$, $p = 0.0018$), whereas $\overline{RTE}$ demonstrated positive trend (for the left hand movement, C4: $r_{AY} = 0.67$, $p = 0.0013$, for the right hand movement, C3: $r_{AY} = 0.51$, $p = 0.0204$). Despite the demonstrated regression was rather moderate, the Pearson's p-value indicated the significance of linear relationship between the considered variables. We assume that the computed R^2 values are affected by the relatively small and individual deviations caused by non-age factors.

In summary, the results demonstrated the correlation between the pre-movement brain μ-rhythm's complexity estimated via the RQA and the value of motor-related μ-band desynchronization $\overline{ERPS}_\mu$. In particular, the higher regularity of the pre-movement EEG precedes the more pronounced suppression of the $\overline{ERD}_\mu$. Both measures were considered as the biomarkers of the well-established neural response in the brain motor cortex, which were mostly manifest in young adults. These results provide the link between the known effects of aging and verify the RQA-based complexity analysis as a proper approach to reveal the markers of the age-related changes in the human EEG recordings.

Conclusions

The Recurrence Quantification Analysis was applied to evaluate the pre-movement EEG complexity of the aging brain and to explore its relationship with a motor-related neural response. The RQA-based measures demonstrated a strong age-related increase in the baseline level of EEG complexity.

In particular, pre-movement EEG of the elderly adults demonstrated the low value DET and high value of RTE, suggesting that sequential execution of the fine motor tasks affect the structure of the baseline EEG in a different way in different age groups. Elderly adults also showed a weaker motor-related μ-band desynchronization compared with young individuals. The results of the two-way mixed ANOVA verified that age was the only significant factor affecting neural activation on the brain motor cortex. Finally, the motor-related neural response was found to be correlated with the complexity of the pre-movement EEG. This observation confirmed the prior hypothesis that the age-related abnormalities in the complexity of pre-movement EEG anticipate the quality of motor-related neural response. Besides, the results of the RQA provided a robust and clearly interpreted measurement of the EEG signal complexity.

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