



Recurrence quantification analysis and theta-band functional networks detect age-related changes in brain sensorimotor system: VR-based approach

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Received 10 December 2024 / Accepted 6 February 2025 / Published online 13 February 2025
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Abstract In this paper, we present the results of spectral, complexity and functional connectivity analysis of EEG signals recorded during VR-based experimental session in two groups of subjects. We focus on the analysis of aging biomarkers associated with theta-rhythm alterations associated with sensorimotor task performance. Recurrence quantification analysis-based measures of EEG complexity show the potential to reveal the aging indicators that are otherwise omitted by the conventional spectral power analysis, demonstrating that the group of elderly subjects induce the neural activity associated with working memory load more actively during the sequential sensorimotor integration task performance. The RQA is supplemented by the functional connectivity analysis, revealing the hyper-compensation in the elderly group of subjects.

1 Introduction

Research based on the analysis of neurophysiological signals involves the development of effective mathematical methods for detecting, classifying, and processing biomarkers of various types of human activity. Variability of the effects on EEG signals can be observed on the level of group as well as on the level of subject from one experiment to another, which significantly complicates the identification of reliable neurophysiological patterns [1]. In particular, developing methods capable of accurately identifying neurophysiological effects of interest from individual fragments of EEG signals is of high scientific significance, which is especially important for the development of brain-computer interfaces operating in real time. In addition, an important requirement for mathematical methods of processing EEG signals is the interpretability of the results, which is especially important in the field of application of machine learning and artificial intelligence methods in clinical neurorehabilitation [2, 3].

In the present paper, we propose an approach for analyzing signals of electrical activity of the sensorimotor system of the brain to identify biomarkers of healthy aging. With age, the human body undergoes structural changes affecting many physiological processes, including a decrease in the thickness of the cortex, a decrease in the volume of gray and white matter, and a decrease in the elasticity of blood vessels. According to the World Health Organization, age-related diseases of the nervous system are one of the leading causes of death in 2019 [4]. At the same time, neurodegenerative processes caused by aging have a significant impact on the quality of life of the older population, and their diagnosis is quite a complex task. In this context, dysfunctions of the human sensorimotor system revealed by EEG analysis can act as relevant markers of age-related changes. Sensorimotor integration is a multifactorial interaction of various brain regions in the process of forming a motor response to external multimodal stimuli, and includes the simultaneous involvement of cognitive, motor and perceptual activity [5, 6].

We propose a complex approach to analyze EEG data recorded during VR-based experiment involving sensorimotor area activation in different age groups of subjects. We demonstrated that theta rhythm plays a crucial role in the detection of age-related changes in the neural processing of motor tasks. Besides, we show that recurrence quantification analysis of EEG time series allows us to reveal how neural reaction on motor preparation alters with

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advanced age, possibly uncovering the underlying cognitive mechanisms of sensorimotor integration, otherwise undetected by traditional spectral features of EEG.

2 Methods

2.1 Dataset

The VR-based sensorimotor integration experiment was conducted by the Institute of Neurosciences of Samara State Medical University. The experiment was aimed at recording a complex sensorimotor response to target visual and auditory stimuli in several age groups of subjects. The following equipment was used: a Faraday cage, a BrainAmp128 EEG amplifier system (64 channels, sampling frequency – 500 Hz), Oculus Rift VR glasses, virtual environment software with audio-visual stimuli, a gamepad, an infrared camera and an audio system for communication with subjects. The subjects were seated in a comfortable chair for neurophysiological experiments. They were instructed to identify target auditory and visual stimuli by pressing the gamepad button when presented with target stimuli and ignoring non-target ones. All subjects were right-handed and, therefore, were holding the gamepad with their right hand. The experimental environment was implemented as a VR mini-game “fishing”, with the target stimuli being the croaking of a frog (audio) and the complete immersion of a float underwater (visual). The experiment involved 54 subjects divided into 5 age groups:

1. group I – 19–25 y.o., 18 subjects (9F);
2. group II – 26–35 y.o., 9 subjects (3F);
3. group III – 36–55 y.o., 9 subjects (7F);
4. group IV – 57–65 y.o., 9 subjects (6F);
5. group V – 65–76 y.o., 9 subjects (6F);

For each subject, the auditory and visual stimuli were presented in the course of single experimental session that lasted for approx. 10 min. For the present study, we used the auditory part of the experiment and conducted the research on group I (young adults, YA) and merged IV and V groups (elderly adult, EA). We sliced EEG signals into epochs time-locked at $[-2, 5]$ seconds in accordance with stimuli presentation. For each subject, we've selected 25 manually inspected epochs to proceed with the research.

2.2 Time-frequency analysis

We used continuous wavelet transform (CWT) [7] in the theta range (5–8 Hz) with Morlet mother wavelet to reveal age-specific spectral biomarkers of sensorimotor integration in different age groups. A similar approach was previously applied to the motor-related alpha- and beta-rhythms to analyze the motor-related activity [8]. In the present research, however, we focus on the theta-rhythm, as it was previously shown the great potential in revealing age-related alterations of the brain sensorimotor system [9].

The epochs for each age group of subjects were tested using the cluster permutation t -test in the spatio-temporal domain. The CWT and permutation tests were calculated using MNE package for Python [10].

2.3 Functional connectivity

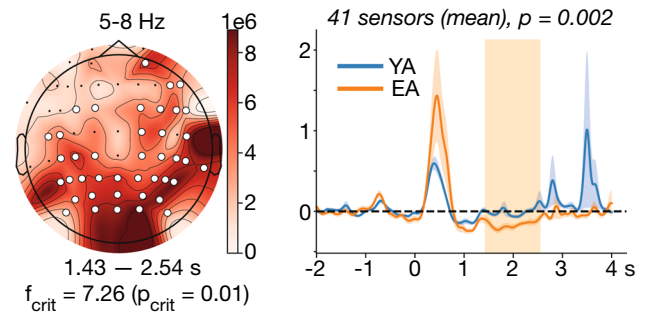
As a result of time-frequency analysis, we defined the time intervals of interest to show the topology of functional connectivity network on the different stages of the VR-based sensorimotor task performance. We chose phase lag index (PLI) as a coupling metric [11, 12]. PLI measures phase synchronization and, at the same time, avoids the underlying problems inherent for sensor-level EEG analysis. In particular, PLI levels out the common sources problem by introducing an asymmetry index for the distribution of the phase differences between two-time series centered around $0 \bmod \pi$:

$$PLI = |\langle \text{sign}[\Delta\phi(t_k)] \rangle|, \quad (1)$$

where $k = 1 \dots N$, $\langle \dots \rangle$ operator means time averaging and N is a number of samples. PLI takes value between 0 and 1, 0 meaning no synchronization (or coupling with $\Delta\phi(t_k)$ around $0 \bmod \pi$), and 1 corresponding to perfect phase locking.

For the chosen FOIs, we calculated 62×62 adjacency matrices. We applied network-based statistic [13] to analyze between-group differences in functional connectivity topologies. PLI was calculated using SciPy library for Python [14], and network-based statistic was implemented using Brain Connectivity Toolbox for Python.

Fig. 1 Results of between-groups spatio-temporal cluster test for theta frequency range



2.4 Recurrence quantification analysis

Recurrence quantification analysis (RQA) is a toolbox for numerical interpretation of recurrence plots (RPs). Introduced by Eckmann [15] in 1987, RPs efficiently visualize recurrences of dynamical systems through analysis of corresponding time series and allow to interpret the dynamical properties of the systems based on RP's appearance. RQA measures allowed us to quantify the “black” and “white” structures formed by recurrent and non-recurrent dots on RP, respectively.

RPs are constructed from time series. The classic approach is to determine the embedding of the system using Taken's theorem [16] and chosen values of embedding dimension m and delay τ . For each EEG epoch, we calculated m using the false nearest neighbors method, and τ using the mutual information method. Since those values deviated slightly for each epoch, we chose the median values of dataset $m = 4$ and $\tau = 13$.

The incorrect choice of embedding parameters can greatly affect the result of RP calculation and cause misrepresentation of important features of the time series. To compensate for the possible distortion of the results caused by the deviation of the chosen median embedding values, we used a method to calculate the recurrence threshold ϵ proposed by Kraemer et al. [17], according to which ϵ is set as the 4th percentile of the distribution of pairwise distances.

We performed windowed RQA on the global RP with a window size of 500 d.p. (1 s of recording) and step of 10 d.p. (20 ms of recording) and obtained time dependencies of determinism (DET), laminarity (LAM), recurrence rate (RR) and recurrence time entropy (RTE) RQA measures. In further analysis, we considered the variations of these measures from the pre-stimulus level ΔDET , ΔLAM , ΔRR and ΔRTE by extracting the corresponding mean baseline values.

RQA was implemented using DynamicalSystems library for Julia [18].

3 Results

3.1 Time-frequency analysis

We show (see Fig. 1a) that elderly subjects demonstrate ERD in theta rhythm (5–8 Hz) after the motor execution ($f_{\text{crit}} = 7.26$, $p_{\text{crit}} = 0.01$). This effect is widespread, encompassing 41 sensors in bilateral parieto-occipital lobe and left and right central and fronto-central areas.

3.2 RQA

Figure 2 shows the spatio-temporal clusters identified via between-groups permutation test for RQA measures calculated for theta-rhythm. EA group demonstrates a rapid decrease of both ΔRR and ΔRTE in the pre-movement stage localized at bilateral occipito-parietal sensors (ΔRR : –360–550 ms, ΔRTE : –360–740 ms, $f_{\text{crit}} = 4.07$, $p_{\text{crit}} = 0.05$). While the complexity of EEG signals of YA group is preserved on the baseline level, EA group is characterized by the decrease of EEG complexity associated with both stimuli presentation and motor preparation stage. In our earlier work, the decrease of EEG complexity was linked to event-related desynchronization (ERD) of mu-rhythm during motor execution [19]. We believe that the demonstrated effect in the EA group is of similar origin, reflecting the peak of theta-power associated with stimuli presentation and motor planning. Note that, although this effect can be visually inspected on the averaged spectral power time series, RQA measure were sensitive enough to detect it via statistical analysis.

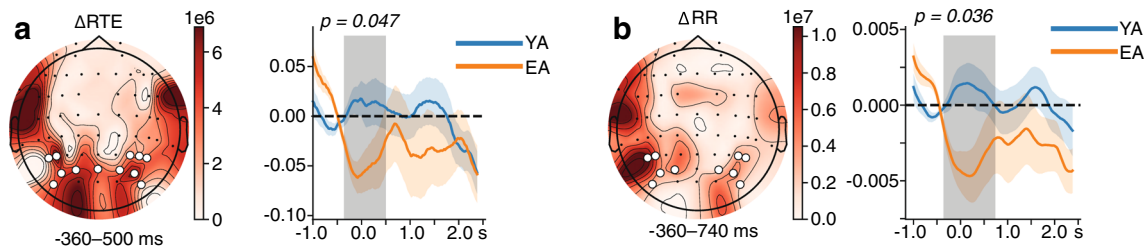
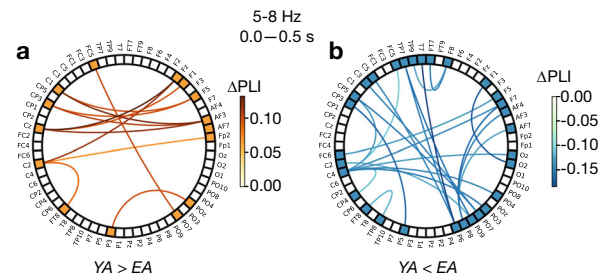


Fig. 2 Results of between-groups spatio-temporal cluster test of RQA measures time series: **a** ΔRTE and **b** ΔRR . Gray areas on the plots highlight the time interval where the significant differences between groups were found. The lineplots are presented as mean $\pm$ SE

Fig. 3 Functional connectivity networks revealed by NBS in theta frequency range during motor preparation stage. **a** Topology of stronger couplings in YA group and **b** in EA group



3.3 Brain functional connectivity

Connectivity matrices were calculated for each subject in the identified theta (5–8 Hz) rhythm. Between-subject analysis identified two groups of statistically relevant connectivity topologies corresponding to subnetworks with significantly stronger coupling in the YA group and EA group. Figure 3 shows the obtained topologies for the motor planning stage (0.0–0.5 s).

The EA group demonstrates more connections in the right parietal area (sensors P4, P6, P8) and the left occipital-parietal area (PO9, PO7, PO3). Sensor C4 was also identified as a hub associated with the left motor area (FC5 and CP5) and the left frontal cortex. At the same time, we show an age-related decrease in the strength of connections between the motor area (sensors CP3, C1, FC5, Cz) and the frontal cortex (Fz, F1, F5) with a shift to the left.

4 Discussion and conclusion

We report the results of the EEG study of age-related changes in the sensorimotor system. The EEG dataset under investigation was recorded in VR-based experimental environment during target stimuli detection tasks by different age groups of subjects. To reveal the effect of aging on the neural processing of repetitive sensorimotor task performance, we applied conventional time-frequency analysis, recurrence quantification analysis and functional connectivity analysis to study the effects from different perspectives and to form a more comprehensive picture of how healthy aging alters the neural mechanisms underlying the processing of these experimental conditions.

At the first stage, we demonstrated a significant spatio-temporal cluster of between-groups differences in theta spectral power involving 41 EEG sensors and emerging during motor execution. Elderly group of subjects, unlike the young adult group, demonstrate theta ERD associated with a reaction on stimuli (pressing the button). Although motor processing is conventionally associated with mu- (8–13 Hz) and beta-ERD (15–25 Hz), there is evidence that with advanced age, the brain activity usually associated with alpha-oscillations can tent to slow down towards the theta-band [20–22]. It is possible that the observed cluster is associated with motor action processing, with theta-ERD “inherited” from mu-ERD.

Note that a peak of theta rhythm is noticeable in both groups of subjects after the presentation of the stimulus, more pronounced in the group of elderly subjects (Fig. 1). Despite the fact that this effect was not significant, we note that a surge in theta activity in the elderly group as a response to the stimulus was observed earlier [9], where a similar process was associated with Bland’s model of sensorimotor integration. In their early work on rodents [23], Bland et al. considered theta activity of the hippocampal formation as a channel of communication between sensory processing and motor initiation. Synchronization of theta rhythm during the motor planning phase in

elderly subjects has been repeatedly observed in other studies [24]. This effect was previously tied to the retrieval of information from working memory associated with the performance of sequential motor tasks [25]. In the study [26], the theta power was positively associated with motor learning.

We proceeded with windowed RQA to explore how aging changes the complexity of EEG in theta-band. We showed a significant decrease in theta-band EEG complexity in EA, but not in YA group, during the motor preparation stage, most likely associated with the peak of theta-power shown before. As we stated previously, theta-power increase can be associated with the working memory load. Theta rhythm, particularly in parietal, temporal and occipital cortex, is known to be involved in the establishment of associations between different sources of information [27]. In the study [28], a conceptually similar experimental paradigm based on switching auditory-visual stimulation shown to cause bursts in occipital theta oscillations.

The age-related changes in EEG complexity are a rather rarely covered area of research. There's a well-established "decrease of complexity" theory that states that aging causes the loss of complexity in all physiological aspects [29], including the brain activity [30, 31]. EEG complexity is a good indicator of pathological processes and can be used as a biomarker of Autism Spectrum Disorder [32, 33] and various mental disorders [34, 35]. RQA-based complexity measure correlate with conventional biomarkers of aging, such as spectral properties of task-related EEG [36]. In general, we believe that the demonstrated effect is associated with the burst of theta-rhythm preceding motor reaction on the target stimuli, which links this biomarker to the increased working memory load. The observation of this pattern in EA group, but not in YA, can be linked to the more challenging access to the working memory in the elderly population, as it was demonstrated previously in [9].

The results were reinforced by the analysis of functional connectivity network topology on the motor preparation time interval. Network-based statistic revealed the fronto-parietal and occipital connections in the theta rhythm that most likely indicate the formation of an attention network in the EA group, the activation of which is associated with attention control [37]. In addition, a relationship was indicated between theta rhythm power, the fronto-parietal network, and access to working memory and cognitive abilities [38]. Note that the CPz sensor is a strong node in the EA group, having connections with temporal, parietal and occipital regions. Previous studies of age-related changes in neural responses to movement execution reported a similar result in the theta rhythm, which was interpreted as a sign of age-related decline in working memory [39]. These results may indicate a compensatory increase in the number and strength of connections in the group of elderly subjects. The compensatory mechanism is a reorganization mechanism that prevents cognitive decline by recruiting additional areas to process tasks that require fewer resources in the control group. The structure of the functional network shown in Fig. 3 can be explained by the age-related requirement for additional neural resources, which forms a much more extensive structure of the functional brain network for processing motor tasks in the group of elderly subjects.

In conclusion, we show age-related differences in neural activity during the sensorimotor integration tasks performance using time-frequency, functional connectivity and recurrence quantification analysis of EEG signals. We demonstrate the emergence of age-related compensation mechanisms of neural resources for the performance of simple sensorimotor tasks. The involvement of neural connections by elderly people indicating high involvement of the attention control network and difficult access to working memory were demonstrated. It was shown that RQA measures are capable of detecting biomarkers of healthy aging, such as a burst of theta-rhythm complexity during the motor planning stage.

Acknowledgements This research was supported by Russian Science Foundation (Grant no. 23-71-01064). The author expresses gratitude to Dr. Alexander Zakharov, the head of the Institute of Neurosciences of Samara State Medical University, for providing experimental data.

Data availability The data presented in this study are available on request from the corresponding author.

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