Age-related changes in the brain functional connectivity during motor initiation

Frolov, Nikita, Pitsik, Elena

Nikita Frolov, Elena Pitsik, "Age-related changes in the brain functional connectivity during motor initiation," Proc. SPIE 11847, Saratov Fall Meeting 2020: Computations and Data Analysis: from Molecular Processes to Brain Functions, 118470V (4 May 2021); doi: 10.1117/12.2591775

Event: Saratov Fall Meeting 2020, 2020, Saratov, Russian Federation

Age-related changes in the brain functional connectivity during motor initiation

Nikita Frolov, Elena Pitsik

Neuroscience and Cognitive Technology Laboratory, Center for Technologies in Robotics and Mechatronics Components, Innopolis University, 420500, Innopolis, The Republic of Tatarstan, Russia

ABSTRACT

Healthy aging affects structural and neurochemical properties of the human brain neural network. It also changes the brain functioning via the transformation of neural interactions both within and between functionally distinct brain areas. The age-related degradation of the brain functioning is evident on the behavioral level in terms of the decline in reaction time, low ability to execute and control complex motor actions, weak flexibility in learning new skills. In this paper we apply functional connectivity analysis to reveal the age-related changes in the integrative brain dynamic during the motor initiation before the dominant hand movements accompanied. Analyzing the whole-scalp electroencephalography (EEG) signals on the sensor level, we find higher theta-band coupling in the ipsilateral hemisphere.

Keywords: Aging, motor initiation, EEG, functional connectivity

1. INTRODUCTION

Healthy aging affects normal brain functioning due to the disruption of structural links and changes in neurochemical composition of the brain.[1] It conditions the degradation of motor and cognitive performance of elderly people negatively affecting their daily activity and overall life quality. The hallmarks of such impairments are mostly evident in their behavior: lower ability to control and coordinate complex movements, longer reaction time (RT), etc.[2]

As, upper limbs demonstrate highest activity over the human lifespan and are mostly used for complex motor tasks accomplishment, the age-related degradation of their performance is the most notable.[3] While the differences in motor-related cortical activation under aging directly related are extensively studied and well-documented, less is known about age-related changes in the motor planning phase and how it affects motor performance, especially RT. Studying of these mechanisms is of strong interest in terms of deeper understanding of human's motor control. To our knowledge, the motor planning processes are also subjected to the age-related changes as: (i) this process requires activation of higher cognitive functions, i.e., motor memory, motor embodiment, sensory processing, and sensorimotor integration,[4,5] which are known to degrade strongly under healthy ageing and disease; (ii) the low-frequency (theta, 4-8 Hz) activity subserving the majority of these functions manifests a considerable age-related transformation - increased theta spectral power in elderly adults is linked with subjective cognitive decline and suspected dementia.[6]

In our recent study,[7] we uncovered that age-related slow-down of the motor initiation phase largely activates theta oscillations captured by the central-parental EEG sensors. Besides the activation, interaction between the brain areas measured by the functional connectivity provides relevant information about the brain's functioning.[8] At the same time, the integrative brain dynamics behind this phenomenon is still of interest. Here, we report the age-related changes in the brain functional connectivity preceding the fine motor task executed with the dominant hand.

Further author information: (Send correspondence to N. Frolov)
N.F.: E-mail: n.frolov@innopolis.ru
E.P.: E-mail: e.pitsik@innopolis.ru

Saratov Fall Meeting 2020: Computations and Data Analysis: from Molecular Processes to Brain Functions, edited by Dmitry E. Postnov, Proc. of SPIE Vol. 11847, 118470V
 · doi: 10.1117/12.2591775

2. MATERIALS AND METHODS

Participants and Experimental Paradigm

Twenty healthy right-handed volunteers having no history of nervous diseases or brain trauma participated in the experiments. They were equally divided in two age groups: Young adults (YA, aged 26.1±5.15 (MEAN±SD), 3 females) and Elderly adults (EA, aged 65±5.69 (MEAN±SD)).

The experiment aimed at revealing the age-related differences in sensorimotor integration process, i.e., a perception and classification of the audio command followed by motor execution based on the type of command. The duration of short audio signal (beep) determined whether a participant should execute clenching his/her right (750 ms) or left (300ms) hand. Audio stimuli were presented sequentially with time interval 10-13 s. A total number of presented stimuli was 60, including 30 short and 30 long signals uniformly distributed over the timeline of experimental session.

EEG Acquisition and Preprocessing

We acquired EEG signals using the monopolar registration method (a 10—10 system proposed by the American Electroencephalographic Society[9]). We recorded EEG signals with 31 sensors and two reference electrodes A1 and A2 on the earlobes and a ground electrode N just above the forehead. We used the cup adhesive Ag/AgCl electrodes placed on the "Tien–20" paste (Weaver and Company, Colorado, USA). The variation of impedance was controlled during the experiment within a range of 2–5 kOhm. The electroencephalograph "Encephalan-EEG-19/26" (Medicom MTD company, Taganrog, Russian Federation) with multiple EEG and two EMG channels performed amplification and analog-to-digital conversion of the recorded signals. The EMG signals were acquired to verify the correctness of the epochs segmentation. Each experimental session started and ended with 5 min Eyes Open Resting State recordings.

The raw EEG and EMG signals were sampled at 250 Hz and filtered by a 50–Hz notch filter by embedded hardware-software data acquisition complex. Additionally, raw EEG signals were filtered by the 5th-order Butterworth filter with cut-off points at 1 Hz and 100 Hz. Eyes blinking and heartbeat artifact removal was performed by the Independent Component Analysis (ICA).[10] The recorded EEG and EMG signals presented in proper physical units (millivolts) were segmented into two sets of epochs associated with the dominant hand movements in different age groups. Each epoch was 3 s long, including 2s pre-stimulus (baseline) activity and 1s post-stimulus activity. Data was then inspected manually and corrected for remaining artifacts. Epochs which we failed to correct manually mostly due to the strong muscle artifacts were rejected. Finally, each set contained 15 corrected epochs, which was equal to the minimal number of the artifact-free epochs over all participants.

All preprocessing steps including filtering, artifact removal and epoching were performed using MNE package (ver. 0.20.0) for Python 3.7.[11]

Connectivity Analysis

We considered functional connectivity in terms of established relationships between the band-pass filtered EEG signals.[12] With the aim of evaluating functional connectivity on the sensor level, we used phase lag index (PLI),[13] which was defined in frequency domain as

$$PLI_{i,j}(f,t) = |\langle \text{sign}(\Im[S_{i,j}(f,t)]) \rangle|, \tag{1}$$

where i, j were the indices of EEG sensors between which functional connectivity was assessed, $S_{i,j}(f,t)$ was the cross-spectral density and $\Im[\bullet]$ defined imaginary part of the complex-valued variable. Theta-band coupling which was of special interest in terms of the study was estimated by averaging $PLI(f,t)$ within a frequency band $[4, 8]$ Hz:

$$PLI^{\theta}_{i,j}(t) = \frac{1}{f_{max} - f_{min}} \int_{f_{min}=4Hz}^{f_{max}=8Hz} |\langle \text{sign}(\Im[S_{i,j}(f,t)]) \rangle|. \tag{2}$$

Using 2 we filled the weight tensor $W'_{i,j,k} = PLI^{\theta}_{i,j}(t_k)$ representing a time evolution the weighted connectivity for each epoch. Thus, each subject was characterized by the tensor $W_{i,j,k}$ averaged over all 15 epochs. Employing

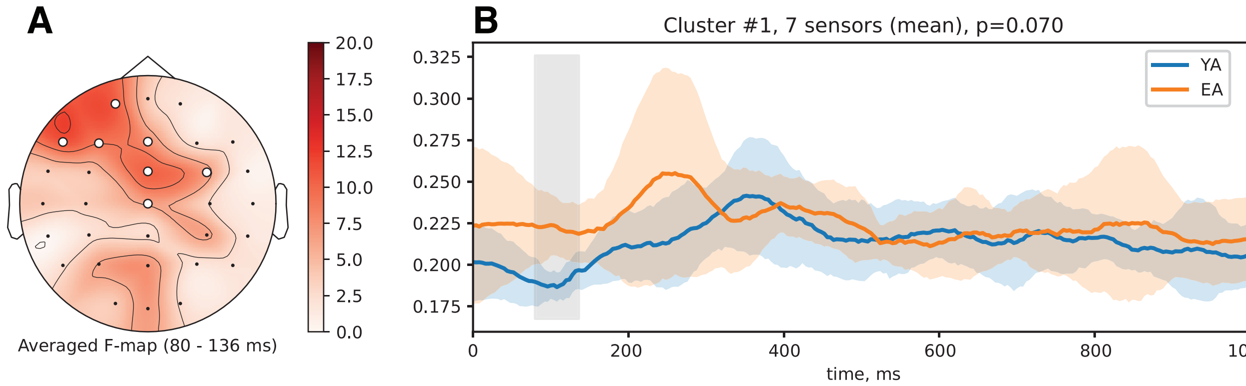

Figure 1. **Statistical inference of significant between-group differences in node strength via non-parametric cluster test** Toporgaphic plot of cluster-averaged F-statistic (**A**) and cluster-averaged evolution of the node strength (mean±SD, **B**). White dots in the topographic plot indicate EEG sensors demonstrating significant effect. Shading indicate the time interval characterized by significant between-group difference.

graph-theoretical approach we quantified each EEG sensor, i.e., a node of the weighted tensor $W_{i,j,k}$, with the measure of node strength defined as a sum of the coupling weights between current node and all the graph nodes:

$$D_i(t_k) = \sum_{j=1}^{N=31} W_{i,j,k}. \tag{3}$$

The node strength D_i is an extension of the node degree measure for the case of a weighted graph which also aims at identification of the most influential graph nodes.[14] To infer statistically significant changes in the functional connectivity between age groups YA and EA during the process of sensorimotor integration we tested the difference in $D_i(t)$ in spatiotemporal domain via non-parametric cluster test with $r = 1024$ permutations and pairwise comparison threshold $F_{tr}(1, 18) = 8.285$ corresponding to the significance level $p = 0.01$.[15]

3. RESULTS AND DISCUSSION

First, we evaluated the effect of between-group node strength difference in spatiotemporal domain. Non-parametric cluster test did not show any significant cluster with $p < 0.05$. However, it revealed a spatiotemporal cluster covering left frontal and midline EEG sensors (Fig. 1A) which occurred immediately after audio signal onset (80-136 ms, Fig. 1B) and achieved the level of significance $p = 0.07$. Despite, estimated cluster-level p-value was slightly greater than 0.05, it showed a tendency to demonstrate statistically significant between-group differences that should be taken into account. One of the possible explanations of such observation was small sample size collected during experimental study. Post-hoc comparison via t-test for independent samples showed that EA subjects demonstrated significantly greater ($t = 4.967$, $p < 0.001$) cluster-averaged node strength (0.222±0.018, mean±SD) compared with YA subjects (0.189±0.009, mean±SD). We could interpret these observations as a meaning that sensorimotor integration in EA subjects required stronger interactions within functional cortical network with dominating role of frontal and midline EEG sensors as opposed to YA participants.

Second, we took a closer look at the functional connectivity links related with the nodes in Fig. 1A. With this aim, we averaged tensors $W_{i,j,k}$ over the time interval 80-136 ms and considered only the links between these nodes and all other nodes of the network (Fig. 2A,B for YA and EA respectively). Afterwards, we considered only 15% of the strongest links within those subgraphs, constructed their adjacency matrices (Fig. 2C,D) and visualized them on a scalp (Fig. 2E,F). It is seen, that sensorimotor integration activates similar links in both age groups: bilateral frontal-temporal-parietal connections (F3-T7,F3-P7,FC4-TP8),and midline links between Fz, FCz and Cz sensors. These links could be interpreted as activation of audio information processing circuits and accessing working memory as parts of audio signal classification. However, EA subjects demonstrated large involvement of the coupling between right central, right temporal and midline sensors (Fz-FC4, Fz-TP8,Fz-Cp4,FCz-Cp4FC4-TP8). Stronger activation of the interaction between these sensors could be interpreted as

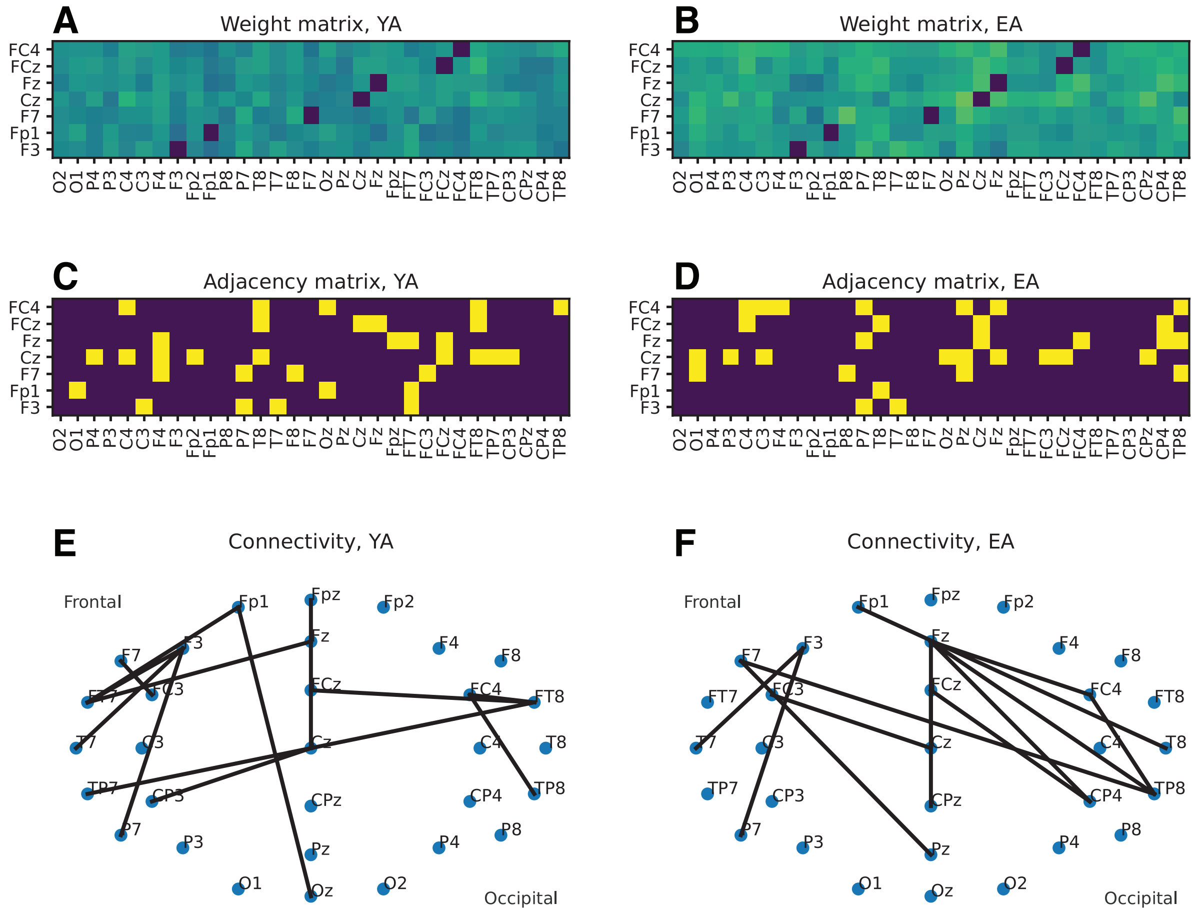

Figure 2. **Age-related difference in functional connectivity.** Cluster-averaged weight matrices $W_{i,j}$ for YA (**A**) and EA (**B**). Corresponding adjacency matrices $A_{i,j}$ obtained by removing 85% links from $W_{i,j}$ for YA (**C**) and EA (**D**). Structure of functional connectivity visualized on the scalp from $A_{i,j}$ for YA (**E**) and EA (**F**)

recruitment of additional brain areas for audio signal processing. It could be also treated as an increased access to the working memory in EA in an attempt to a correct classification of the presented stimulus.

4. CONCLUSION

Elderly adults exhibited greater activation of the theta-band cortical interactions immediately after the presentation of audio stimulus. We demonstrated that left frontal and midline EEG sensors played a leading role in these overactivated functional links. It was also shown that besides bilateral frontal-temporal-parietal links common for both age groups, elderly adult subjects demonstrated increased coupling between right central, temporal and midline sensors. Taken together, our results on functional interactions within cortical network suggest the utilization of more demanding sensorimotor integration processes in elderly adults.

ACKNOWLEDGMENTS

This work was supported by the Russian Foundation for Basic Research and the National Natural Science Foundation of China (research project no. 19–52–55001) and the Council on grants of the President of the Russian Federation (Grant Nos. NSh-2594.2020.2 and MK-2080.2020.2).

REFERENCES

[1] Seidler, R. D., Bernard, J. A., Burutolu, T. B., Fling, B. W., Gordon, M. T., Gwin, J. T., Kwak, Y., and Lipps, D. B., "Motor control and aging: links to age-related brain structural, functional, and biochemical effects," *Neuroscience & Biobehavioral Reviews* **34**(5), 721–733 (2010).

[2] Voelcker-Rehage, C., "Motor-skill learning in older adults—a review of studies on age-related differences," *European Review of Aging and Physical Activity* **5**(1), 5–16 (2008).

[3] Kalisch, T., Wilimzig, C., Kleibel, N., Tegenthoff, M., and Dinse, H. R., "Age-related attenuation of dominant hand superiority," *PLoS One* **1**(1), e90 (2006).

[4] Leisman, G., Moustafa, A. A., and Shafir, T., "Thinking, walking, talking: integratory motor and cognitive brain function," *Frontiers in public health* **4**, 94 (2016).

[5] Sepp, S., Howard, S. J., Tindall-Ford, S., Agostinho, S., and Paas, F., "Cognitive load theory and human movement: Towards an integrated model of working memory," *Educational Psychology Review* , 1–25 (2019).

[6] Stomrud, E., Hansson, O., Minthon, L., Blennow, K., Rosén, I., and Londos, E., "Slowing of eeg correlates with csf biomarkers and reduced cognitive speed in elderly with normal cognition over 4 years," *Neurobiology of aging* **31**(2), 215–223 (2010).

[7] Frolov, N. S., Pitsik, E. N., Maksimenko, V. A., Grubov, V. V., Kiselev, A. R., Wang, Z., and Hramov, A. E., "Age-related slowing down in the motor initiation in elderly adults," *Plos one* **15**(9), e0233942 (2020).

[8] Bassett, D. S. and Bullmore, E. T., "Human brain networks in health and disease," *Current opinion in neurology* **22**(4), 340 (2009).

[9] Nuwer, M. R., Comi, G., Emerson, R., Fuglsang-Frederiksen, A., Guérit, J.-M., Hinrichs, H., Ikeda, A., Luccas, F. J. C., and Rappelsburger, P., "Ifcn standards for digital recording of clinical eeg," *Electroencephalography and clinical Neurophysiology* **106**(3), 259–261 (1998).

[10] Hyvärinen, A. and Oja, E., "Independent component analysis: algorithms and applications," *Neural networks* **13**(4-5), 411–430 (2000).

[11] Gramfort, A., Luessi, M., Larson, E., Engemann, D. A., Strohmeier, D., Brodbeck, C., Goj, R., Jas, M., Brooks, T., Parkkonen, L., et al., "Meg and eeg data analysis with mne-python," *Frontiers in neuroscience* **7**, 267 (2013).

[12] Hramov, A. E., Frolov, N. S., Maksimenko, V. A., Kurkin, S. A., Kazantsev, V. B., and Pisarchik, A. N., "Functional networks of the brain: from connectivity restoration to dynamic integration," *Physics-Uspekhi* **64**(12) (2020).

[13] Stam, C. J., Nolte, G., and Daffertshofer, A., "Phase lag index: assessment of functional connectivity from multi channel eeg and meg with diminished bias from common sources," *Human brain mapping* **28**(11), 1178–1193 (2007).

[14] Boccaletti, S., Latora, V., Moreno, Y., Chavez, M., and Hwang, D.-U., "Complex networks: Structure and dynamics," *Physics reports* **424**(4-5), 175–308 (2006).

[15] Maris, E. and Oostenveld, R., "Nonparametric statistical testing of eeg-and meg-data," *Journal of neuroscience methods* **164**(1), 177–190 (2007).