# CHARACTERISTICS OF SPATIAL SYNCHRONIZATION OF ENCEPHALOGRAMS IN LEFT- AND RIGHT-HANDED SUBJECTS IN RESTING STATE AND DURING COGNITIVE TESTING: A GRAPH-THEORY ANALYSIS

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Hand preference is one of the most striking manifestations of functional brain asymmetry. However, the nature of the phenomenon, as well as its interaction with other brain functions has not been fully understood. Therefore, the study of brain peculiarities of left- and right-handed subjects by neuronal network analysis is of particular interest.

**The aim of the investigation** was to analyze brain network structures according to electroencephalography findings in left- and right-handed subjects in resting state and during cognitive testing (memorizing) using a graph theory.

**Materials and Methods.** 44 volunteers (20 left-handed, 24 right-handed) took part in the experiment. We used three techniques to calculate the degree of spatial synchronization of EEG-signals: coherence, an imaginary part of coherence, and synchronization likelihood. On basis of the obtained graphs we built minimum spanning trees (MST) and calculated some of their characteristics.

**Results.** Left-handers compared to right-handers were found to have more linear MST in theta band (coherence-based MST). Memorizing was characterized by the increase of MST regularity structure in alpha band for all three signal measures (coherence, an imaginary part of coherence, and synchronization likelihood). And only right-handers showed the increase in regularity for MST built on the basis of synchronization likelihood and imaginary part of coherence. Regularity increase in alpha band for coherence-based MST was not associated with handedness. Thus, MST based on synchronization likelihood and an imaginary part of coherence are more sensitive to differences between left- and right-handers during memorizing.

**Key words:** brain functional relationship; neuronal network; graph theory; minimum spanning tree; hand preference; electroencephalography.

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Hand preference is one of the brightest manifestations of functional asymmetry of the brain. However, there is no clear understanding of the nature of handedness and its interaction with other brain functions [1]. Previous studies of EEG functional connectivity related to handedness were not numerous and not well comparable. Thus, the opposite changes between rest and spatial imaginary task conditions were found in inter-hemisphere EEG coherence in the alpha band, using only two pairs of electrodes (Fz-P3 and Fz-P4) [2]. For right handers there were found higher coherence in the alpha band, and lower coherence in the 29 and 33 Hz band [3]. On the other hand, no differences between the groups with different manual preferences were also found [4]. Coherence values were larger for left-handed subjects over the occipital region during wakefulness, stage 2, and the stage of rapid eye movement sleep, but not during stage 3/4 sleep [5]. Average levels of coherence were greater for right handers in the left hemisphere in a resting state. On the contrary, for the left-handers higher coherence values were located in the right hemisphere [6]. The results are ambiguous and the analysis of physiological data parameters of the brain, in particular EEG, may shade some light on this problem.

In recent years, it becomes more evident that neuron networks play an important role in the structure of brain activity. Networks themselves and their interaction are the basis and driving force for all processes in the brain such as speech, learning, memory and others. Inter-individual differences at any level (genetic, environmental etc.) display themselves in the organization of neuron networks, and a systemic approach is necessary for their analysis and understanding.

Graph theory, as the example of such a systemic approach appears to be a useful tool for network analysis of different neuroimaging data (EEG, MEG, fMRT) [7–9].

**The aim of this investigation** is to analyze the network qualities of EEG of left- and right-handed people in a resting state and during cognitive performance using graph theory.

**Materials and Methods.** 44 volunteers, ranging in age from 18 to 25, took part in the experiments. They were divided into groups of left-handers (8 men, 12 women) and right-handers (9 men, 15 women) using the Edinburgh questionnaire [10]. The study complied with the Declaration of Helsinki (The Declaration was passed in Helsenki, Finland, June, 1964 and revised in October, 2000 (Edinburgh, Scotland), and was performed following approval by the ethic committee of Nizhny Novgorod State Medical Academy. Written informed consent was obtained from every participant.

*EEG recording.* EEG was recorded monopolar with ipsilateral ear reference using Neuron-Spectrum-4/EPM system (Russia). The electrodes were mounted using the "10–20" scheme (Fig. 1, *a*) in the following locations: FP1, FP2, F3, F4, Fz, C3, C4, Cz, P3, P4, Pz, O1, O2, F7, F8, T3, T4, T5, T6. The ground electrode was placed on the forehead. EEG signal was digitally filtered at 0.5–30 Hz. Sampling rate was 500 Hz. Artifacts of EEG recording were removed using Independent Component Analysis (ICA).

*The experiment procedure*. The experiment consisted of memory (cognitive) tests and two background records in the resting state before and after the test. During the background testing, the subjects were asked to look at the monitor, without any additional tasks. A white screen was demonstrated to them during 30 s ("Background 1"), and then the lines with different angle of inclination were displayed during 60 s ("Background 2"). Each line was demonstrated during 2 s. The sequence of lines with different angles was pseudorandom and identical for every participant. The memory test consisted of a single line presented during 5 s ("Memorizing"). The angle of the line for "Memorizing" was 0, 45, 60, 90, 120, 135 degrees. 3 sessions for each angle were recorded. 18 sessions of memory test (5 s each) were recorded for each participant. The duration of "Memorizing" set was 90 s in total.

*Graph analysis.* Graph is a mathematical model of network consisted of nodes and edges. From the position of graph theory brain connectivity has small-world organization characterizes by an optimal parameters for information processing [11, 12]. There are two main measures of such a graph: path length and cluster coefficient. Path length is the mean of the shortest path (expressed in the number of edges) connecting any two nodes on the graph, and cluster coefficient is the likelihood that a certain number of adjacent nodes, connected to one node, are also connected to each other, averaged for all graph nodes [12]. But, these graph measures can be influenced by a number of nodes and the average degree of the network. This makes the network comparison difficult [13]. A possible solution of the problem is constructing the so-called minimum spanning tree (MST). MST method built on the basis of EEG data was introduced by Boersma et al. [14] to examine developmental changes in functional brain network topology of children in the process of their development. MST is a graph which is built from connected and undirected graph with given edge-weights in such a way that the graph is a tree, i.e. connected graph without cycles, which connects all the given nodes, and it has minimal weight (set of edges included in MST). Thus, EEG based MST is the most connected part of network.

Functional networks in our study consisted of 19 nodes (Fig. 1, *b*), which represented the electrodes used for EEG recording. Edge weight between any two nodes was characterized by the degree of connectivity of signals registered on two electrodes corresponding to these nodes. We used three connectivity measures: coherence (COH), imaginary part of coherence (COH-IM) [15] and synchronization likelihood (SL) [16]. First,

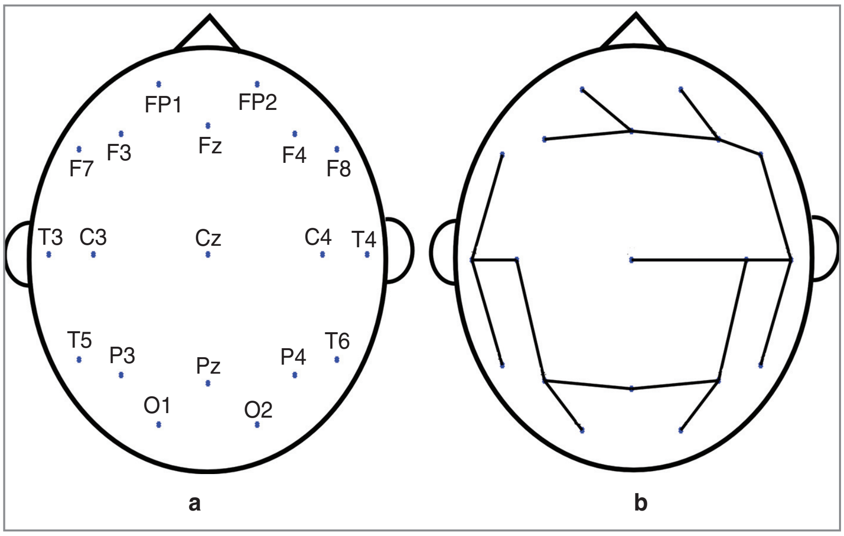


**Fig. 1.** Electrodes placement according to “10–20” system (*a*) and example of minimum spanning tree (*b*). Minimum spanning tree is a mathematical model of network, consisting of nodes and (connections between them) edges. For the given tree average unweighted distance is 4.4654 edges, radius — 6 edges, diameter — 11 edges, maximum degree — 3 edges, leaf number — 9 and maximal betweenness centrality is 58.17%

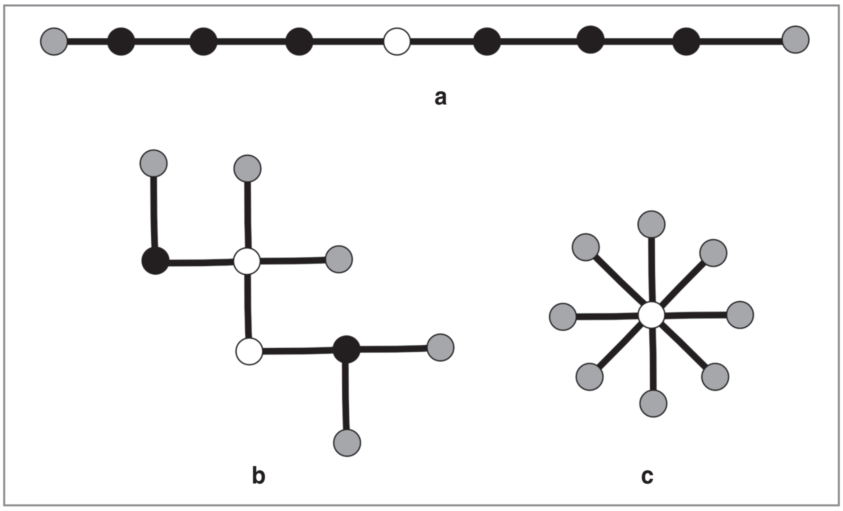


**Fig. 2.** Examples of different types of minimum spanning tree topology. Nodes colored in grey are leaves. Nodes with maximal betweenness centrality are colored in white. Nodes without special characteristics are colored in black. Minimum spanning tree with linear topology (*a*) has the following characteristics: leaf number is 2, radius — 4, diameter — 8, maximal degree — 2 and maximal betweenness centrality is 0.57. Tree with a star-like structure (*b*) has leaf number 8, radius — 1, diameter — 2, maximal degree — 8 and maximal betweenness centrality is 1. The tree with intermediate topology (*c*) has: radius equal to 3, diameter — 5, leaf number — 5, maximal degree — 4 and maximal betweenness centrality to 0.7

EEG records were segmented into 1500 samples (3 s) epochs. For each epoch COH, COH-IM and SL were calculated between all pairs of 19 leads (171 pairs). The values obtained for the COH and COH-IM of different frequencies were averaged for the following frequency bands: theta-1 (4–5 Hz), theta-2 (6–7 Hz), alpha-1 (8–10 Hz), alpha-2 (11–13 Hz), beta-1 (14–20 Hz), beta-2 (20–30 Hz). For SL calculation the signal was digitally filtered for the same band before epoching. Value of COH-IM was squared. Obtained connectivity matrices were averaged for each participant and for each condition separately. Before building MST matrices were inverted. Thus, a full graph consisting of 171 edges was obtained with each edge having its own weight. The edge weight was 0 if signals from two edges were absolutely identical, and was 1 if signals were absolutely different.

The next step was constructing of MST. Kruskal’s algorithm [17] realized in MATLAB® was used for construction of MST. Firstly, this algorithm ranges all the edges in our complete graph by weights — from minimal to maximal. After that, it consequentially adds the edges to the empty graph in the order of their weight increase. However, if an added edge forms a cycle with the previously added edges, algorithm will remove it from the network and proceed to checking the next edge.

The following parameters for each MST: radius, diameter, unweighted distance, weighted distance, maximal degree, leaf number, maximal betweenness centrality (Fig. 2) were calculated.

Radius is a minimal eccentricity amongst all nodes in the tree. Eccentricity of a node is a characteristic of a node, presenting the length of the longest path amongst all the shortest paths from this node to the other nodes. The shortest path between 2 nodes is a path that has minimal weight. It may be weighted (edge weights may be various) and unweighted (edge weight is always equal 1). Diameter is a characteristic of a tree, maximal eccentricity amongst all nodes in the tree. We used unweighted radius and diameter. Mean distance is a mean value of all the shortest paths in the tree. It may be weighted and unweighted (we used both).

Degree is a number of edges, adjacent to the node. A maximal degree among all nodes was used in this work. Leaf number is a number of nodes with a degree equal to 1. Betweenness centrality is a characteristic of a node, being a ratio between the number of the shortest paths passing through the node and the total number of the shortest paths. Maximal betweenness centrality is a characteristic of a node, it is maximal betweenness centrality amongst all nodes.

*Statistical analysis.* A variance analysis ANOVA with repeated measures was carried out for data analysis utilizing package "ez" for R programming language [18]. As for the intergroup factors, there were used manual preferences (left or right handedness) and sex (male or female); an experiment stage ("Background 1", "Background 2" and "Memorizing") were used as intra-group factors. The difference between groups was considered statistically significant when p<0.05.

**Results.** The main task of our investigation was to compare characteristics of MST for left- and right-handers. We analyzed only systematic differences in specific frequency bands i.e. when simultaneously in the given frequency band not less than three MST characteristics differed significantly for one factor or intercept of the factors.

Significant differences between left- and right-handers were observed regularly only for COH-based MST in theta-1 (diameter, radius and unweighted distance) and theta-2 band (diameter, radius, unweighted distance and maximal degree) (Fig. 3). Diameter, radius and unweighted distance were higher for left-handers, while maximal node degree was lower in both cases.

Effect of sex was found regularly only for COH-IM-based MST in theta-2 band for diameter, radius and unweighted distance. All three characteristics were higher for males.

Stages as the main factor, were significant for COH-based MST in theta-2 (diameter, radius, unweighted distance), alpha-2 (maximal betweenness centrality, radius, unweighted and weighted distance) (Fig. 4), and beta-2 band (diameter, radius, leaf number, unweighted distance). In theta-2 band, all three characteristics decried during "Memorizing" stage in comparison with the backgrounds as revealed by post-hoc comparisons using the Tuky test. Changes in alpha-2 and beta-2 band were opposite and manifested themselves in the increase of diameter, radius, unweighted and weighted distance simultaneously with the decrease in maximal betweenness centrality and leaf number.

For SL based MST stage as main factor, was significant for alpha-1 band (diameter, radius, unweighted and weighted distance). For all four characteristics, values were significantly less during "Memorizing" than during "Background 2".

Maximum degree was significantly higher during "Memorizing" in comparison with "Background 1" for left-handers in SL-based MST. At the same time in right-

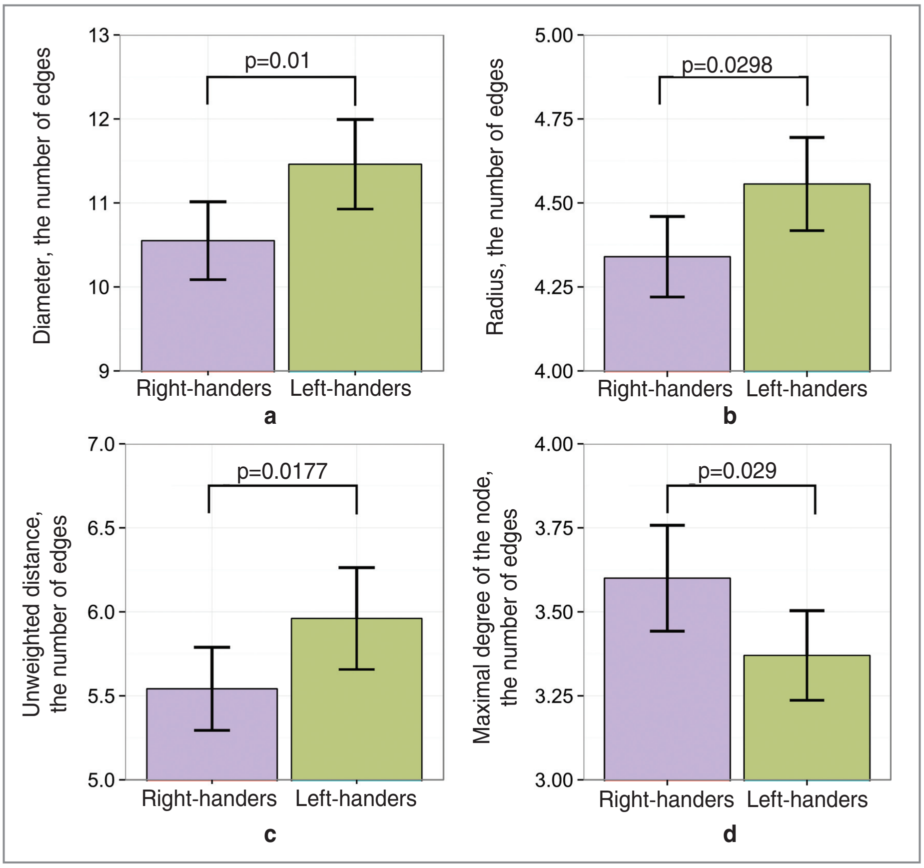


**Fig. 3.** Comparison of characteristics of COH-based minimum spanning tree in the theta-2 band during different stages. Error bars represent 95% confidence intervals. Note higher level of diameter (*a*), radius (*b*), unweighted distances (*c*) in left-handers, while maximal degree of the node (*d*) is higher in right-handers. Minimum spanning tree topology was more linear in left-handers in comparison with right-handers

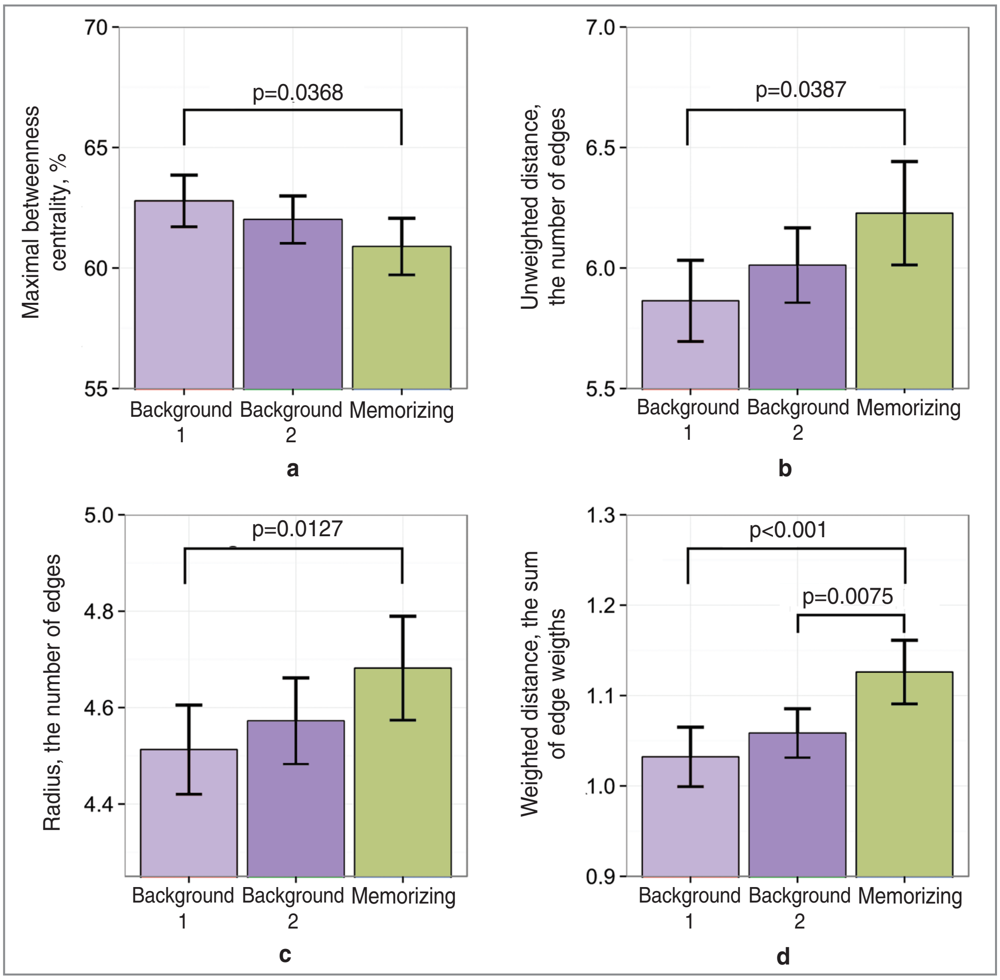


**Fig. 4.** Changes in characteristics of COH-based minimum spanning tree in the alpha-2 band during different stages. Error bars represent 95% confidence intervals. Note a decrease of maximal betweenness centrality (*a*) and, on the contrary, an increase of unweighted distance (*b*), radius (*c*) and weighted distance (*d*) during “Memorizing”. Minimum spanning tree becomes more linear during “Memorizing”, while importance of particular node becomes lower

hander levels of weighted and unweighted distances were higher during “Memorizing” in comparison with “Background 1” and “Background 2” (Fig. 5). The same picture occurred in COH-IM based MST in alpha-1 band. Maximal degree decreased in right-handers in “Memorizing” in comparison with “Background 1” (p=0.03694). Leaf number increased in “Memorizing” in comparison with “Background 1” and “Background 2” in left-handers, and weighted distance in right-handers.

Our results revealed that the brain networks of left-handers have an altered functional connectivity pattern compared to right-handers.

As it was mentioned above, we analyzed only regular differences in characteristics of MST. The most common pattern of the regular differences was simultaneous changing in diameter and/or radius and unweighted distance. Higher values of diameter and distance refer to a more regular (ordered) pattern of the MST. Such pattern of changes was often accompanied by the opposite changes in maximal degree.

Usually, obtained MSTs have multiple nodes with a maximal degree. The lower was the maximal degree, the higher was the number of nodes with the maximal degree, i.e. the value of the maximal degree was inversely related to the number of nodes where this maximal degree was observed (Fig. 6). For COH-based MST in theta-2 band nodes with the highest percentage of subjects in which a particular node had maximal degree were F3, F4, C3, P3, P4. For SL-based MST in alpha-2 band during “Memorizing” most “popular” nodes were Fz, P3 and P4. For COH-IM-based MST distribution was different and most commonly nodes with maximal degree were located in post-central regions. Thus, the distribution of nodes with maximal degree was similar for COH- and SL-based MST as well as MST for left- and right-handers. But it is worth mentioning that in left-handers in the theta-2 band in COH-based MST each separate node possessed the maximal degree in the majority of the participants. Along with the lower maximal degree (See Fig. 3, *d*) it means that the number of nodes, the most significant for

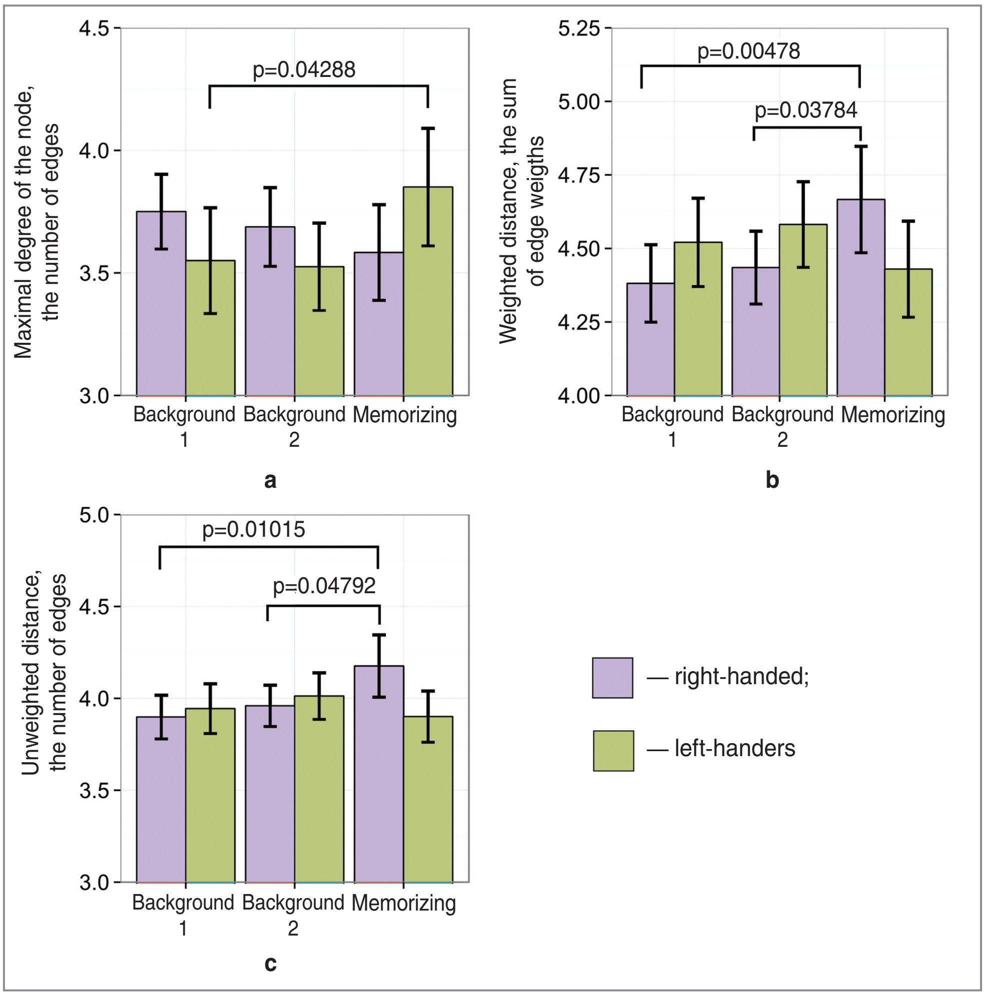


**Fig. 5.** Changes in characteristic of SL-based minimum spanning tree in the alpha-2 band during different stages. Error bars represent 95% confidence intervals. Note higher values of maximal degree (*a*) for left-handers, and weighted (*b*) and unweighted (*c*) distances for right-handed subjects during "Memorizing" in comparison with the backgrounds. For right-handed subjects minimum spanning tree become more linear during "Memorizing"

information transfer between the brain parts, was higher for left-handed subjects, with less significance of each particular node.

The reasons of changes in EEG-based graph structure are not yet clear enough. As one of the possible mechanism of the increase in diameter and unweighted distance level and the decrease in the level of the maximal degree, we can assume a non-specific activation of subcortical centers. In such a way, activation of subcortical structures can cause smoothing of the level of connection strength between electrodes, and shifting MST structure to a more linear type.

Higher values of the diameter, radius and unweighted distance for COH-based MST in the theta-bands for left-handers in all stages of the experiment (See Fig. 3), supports the theory that right-handers have more local and specialized networks, whereas left-handers have more distributed networks [19]. It also may be the result of a higher influence of subcortical sources of theta-band activity, such as hypothalamus in left-handed.

Statistically significant differences between stages in alpha-2 and beta-2 bands for COH-based MST were found in the increase of radius, unweighted and weighted distance, and the decrease in the level of maximal betweenness centrality in alpha-2 (See Fig. 4) and level of leaf number in beta-2. So during "Memorizing" brain network tends to become more ordered and linear in both group of participants. Similar pattern in the alpha-2 band was observed for SL-based MST. Unweighted and weighted distances increased only in the right-handed group (See Fig. 5, *b, c*). An increase the in the level of maximal degree of the node was found in left-handers (Fig. 5, *a*). The features of changing COH-IM-based MST characteristics in the alpha-1 band were similar. Thus, MST topology did not differ between handedness groups during backgrounds record, but had opposite changes during "Memorizing". The topology of the supposed neuronal networks becomes more linear in left-handers in comparison with right-handers as have been found in the results of SL- and COH-IM-based MST analysis.

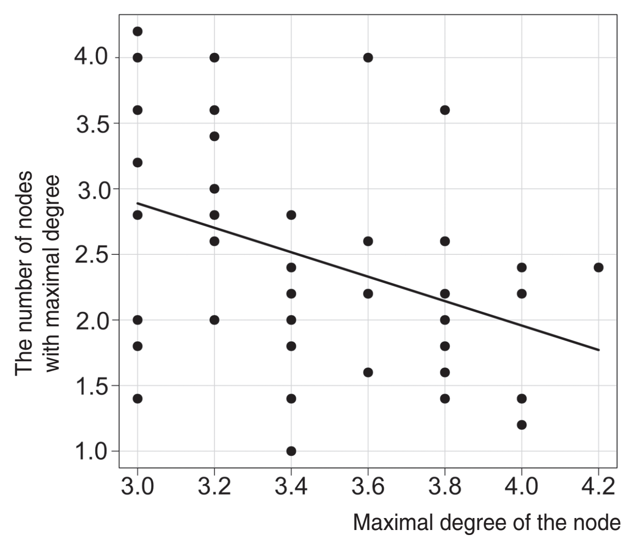


**Fig. 6.** Relation of the number of nodes with maximal degree to the value of maximal degree in COH-based in the theta-2 band. Dots represents single values, line is a line model of data; r=–0.3725371; p=0.01276. It may be concluded, that the higher the value of minimum spanning tree maximal degree, the lower the number of nodes with this maximal degree. Thus, the value of minimum spanning tree maximal degree may serve as an indicator of topology linearity of supposed neuronal networks modeled by minimum spanning trees

We can conclude that, SL-based as well as COH-based MST reflected the changes in brain network during memorization, but have greater sensitivity for separating the groups with different manual preference.

In the alpha-1 band dynamics in parameters of SL-based MST was slightly different from that in the alpha-2 in the course of the experiment. The greatest difference was found between "Background 2" and other stages of the experiment. It may be related to the rate of stimuli presenting, because in "Background 2", stimuli changed every 2 s, while during "Background 1" and "Memorizing" no changes of the stimuli occurred. It also may be associated with functional changes of different bands. Thus, in the theta-2 band in COH-based MST, the direction of changes, related to the course of the experiment, was opposite to that in the alpha-2. With great caution we can conclude, that during cognitive loads changes in low frequency neuronal networks occur in other ways compared to high frequency networks.

Notably, stage-related changes in characteristic of MST occurred primarily in the alpha bands during the experiment. Alpha-wave synchronization is important for efficient performance in cognitive or motor tasks [20]. So the analysis based on MST can detect related network changes in the alpha band regardless of connectivity measure of the registered signals.

**Conclusions.** The obtained results demonstrate handedness-related differences in brain connectivity by analyzing minimum spanning trees of EEG based graphs during resting state and memorizing conditions. Left-handers have more linear MST than right-handers in the theta band for coherence-based MST. Memorizing was associated with increasing in regularity of MST for alpha band for all three measures. For synchronization likelihood and imaginary part of coherency this increase of regularity was handedness specified and occurred in right-handers. No differences between handedness groups in coherence-based MST in alpha band were found. Consequently, synchronization likelihood and imaginary part of coherency based MST were more sensitive to differences between groups during memorizing.

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