

The Relationship Between Elemental Status and the Expression of fNIRS Indicators in Residents of the European Part of Russia

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ARTICLE INFO

Received: 📅 October 13, 2025

Published: 📅 October 23, 2025

Citation: Yulia Shatyr, Michail Kunavin, Irina Ulesikova and Alexander Mulik. The Relationship Between Elemental Status and the Expression of fNIRS Indicators in Residents of the European Part of Russia. Biomed J Sci & Tech Res 63(4)-2025. BJSTR.MS.ID.009923.

ABSTRACT

The study aims to identify the presence of links between the levels of biologically significant micro- and macroelements in the human body and the expression of standard fNIRS indicators. The study involved native residents of three regions of the European part of Russia, aged 18-25 years (49 men and 51 women). The subjects' elemental status was assessed based on the levels of biologically significant micro- and macroelements (Al, As, B, Be, Ca, Cd, Co, Cr, Cu, Fe, Hg, I, K, Li, Mg, Mn, Na, Ni, P, Pb, Se, Si, Sn, V, and Zn) in hair samples. To assess the hemodynamic response of the cerebral cortex in the near infrared range, a Cortivision Poton Cap C20 device (Cortivision, Poland) equipped with 20 optodes with a sampling frequency of 7.8125 Hz was used. The obtained results showed that the concentration of hemoglobin in the cerebral circulation, reflecting the overall level of activation of metabolic processes, is directly related to the content of the main cationic macroelements (Na, K, Ca, Mg), and inversely related to the content of heavy metals and toxicants (Pb, Hg, Sn, As, Ni). The presented data necessitate further development of issues of individualization of cerebral metabolism taking into account the elemental status of the body, especially with regard to individuals with cardiometabolic and neurocognitive disorders. In addition, the prospects for the widespread implementation of functional near-infrared spectroscopy in research activities and clinical practice as a simple and effective method for neuroimaging brain functions are determined.

Keywords: Cerebral Homeostasis; Macroelements; Microelements; Elemental Status; fNIRS

Introduction

The human body contains numerous chemical elements, the levels and ratios of which collectively determine metabolism, growth and development processes, functional state, and the body's defenses, including its adaptive potential. The balance of micro- and macroelements is one of the main factors in the individualization of cerebral metabolism. Chemical elements are involved in the regulation of energy and plastic processes in nervous tissue, their content and ratio influences the functioning of the brain. The main research in this area focuses on a limited number of biologically significant macro- and microelements. Thus, Mg, Na, K, and Ca influence the activity of blood vessels in the brain. Mg also prevents damage to the white matter of the brain, participates in the regulation of metabolism and the maintenance of homeostasis in the brain, thereby preserving the functional potential of the brain and regulating the transmission of nerve

signals [1,2]. Fe, I, Cu, and Zn deficiencies cause neuroanatomical (neuronal degeneration), neurochemical (changes in the synthesis of neurotransmitters and receptors), and neurophysiological (changes in metabolism and signal transmission along pathways) disturbances [3-5]. At the same time, excess Zn, Fe and Cu provoke mitochondrial dysfunction, disruption of Ca homeostasis in neuroaccumulation of damaged molecules, disruption of DNA repair, decreased neurogenesis and disruption of energy metabolism [6].

Tissue samples from various brain regions in suicide victims were found to have elevated levels of Fe, Cu, P, and Ag [7]. Hg, Ni, and Mn have a negative impact on developing neurons [8,9]. The presented results, reflecting the final effects of chemical elements on cerebral homeostasis, nevertheless do not adequately reveal the specifics of the organization of metabolic activity in the nervous tissues of various regions of the brain depending on the elemental status of a particular

organism. This kind of knowledge opens up the possibility of regulating cerebral metabolism by correcting the content of chemical elements in the human body, which allows not only to prevent possible health problems, but also to modulate the desired neurophysiological states of the central nervous system. For studying the influence of biologically significant chemical elements on cerebral metabolism, there are two most effective noninvasive functional neuroimaging methods: electroencephalography (EEG) and functional near-infrared spectroscopy (fNIRS). EEG has better temporal but low spatial resolution, while fNIRS, in contrast, provides better spatial resolution but has low temporal resolution [10]. Since the issue under study requires an objective assessment of the severity and localization of metabolic activity of brain tissue at rest, fNIRS is the most optimal tool for solving this problem.

Material & Methods

For our study there were selected students of state universities, native residents of three regions of the European part of Russia: Arkhangelsk region (16 men 20.1 (SD 1.82) years old and 17 women 18.8 (SD 1.48) years old), Volgograd region (16 men 20.4 (SD 2.44) years old and 17 women 19.8 (SD 1.56) years old) and the Republic of Crimea (17 men 19.3 (SD 1.26) years old and 17 women 19.9 (SD 2.59) years old), a total of 49 men and 51 women. The conditions for inclusion of students in the sample were: age 18-25 years, sufficient for stable formation of the functional and structural status of the body, but not beyond the ascending period of human development; absence of chronic somatic and neurological diseases; presence of a complete, socially prosperous parental family; absence of financial and domestic problems. All studies were conducted in accordance with the principles of the Universal Declaration on Bioethics and Human Rights, including Articles 4, 5, 6, 9. The study was approved by the Ethics Committee of the S.M. Kirov Military Medical Academy (St. Petersburg, Russia), protocol No. 295 dated October 22, 2024. The elemental status of the subjects was assessed based on the content of biologically significant micro- and macroelements (Al, As, B, Be, Ca, Cd, Co, Cr, Cu, Fe, Hg, I, K, Li, Mg, Mn, Na, Ni, P, Pb, Se, Si, Sn, V, Zn) in hair samples. Chemical analysis of the biological material was performed using standard methods of inductively coupled plasma atomic emission spectroscopy at the Center for Biotic Medicine (Moscow).

To assess brain activity, the Cortivision Poton Cap C20 device (Cortivision, Poland) was used. The device is certified and complies with the requirements of the technical regulations of the Eurasian Economic Union (EAEU N RU D-PL.RA03.B.20841/21 dated 03.12.2021, valid until 02.12.2026). The Cortivision Poton Cap C20 is equipped with 20 optodes (10 sources and 10 detectors) with a sampling frequency of 7.8125 Hz. The optodes are non-invasively fixed to the subject's head using an elastic cap "EasyCap". The optode distribution scheme was developed in our own previously conducted study [11]. In this case, 8 pairs of optodes were placed according to the international 10-20 system in the frontal, parietal, temporal and

occipital regions in the left and right hemispheres (F3 and F4; P3 and P4; T7 and T8; O1 and O2, respectively); another 2 pairs of optodes were placed to study the prefrontal cortex (AF3 and AF4) (Table 1). The fNIRS study was performed for 30 seconds, with subjects sitting in a comfortable position with their eyes open. For subsequent data analysis, the arithmetic mean values of the concentrations of oxygenated (HbO) and deoxygenated (HbR) hemoglobin (mmol/l) were taken into account. During the statistical data analysis stage, Pearson's r-correlation coefficients were calculated between fNIRS parameters and the concentrations of biologically significant chemical elements in hair samples. The resulting correlation matrix served as the basis for hierarchical cluster analysis, which resulted in a dendrogram grouping various macro- and microelements based on the similarity of their correlation patterns.

Table 1: Schematic diagram of optodes for functional near-infrared spectroscopy.

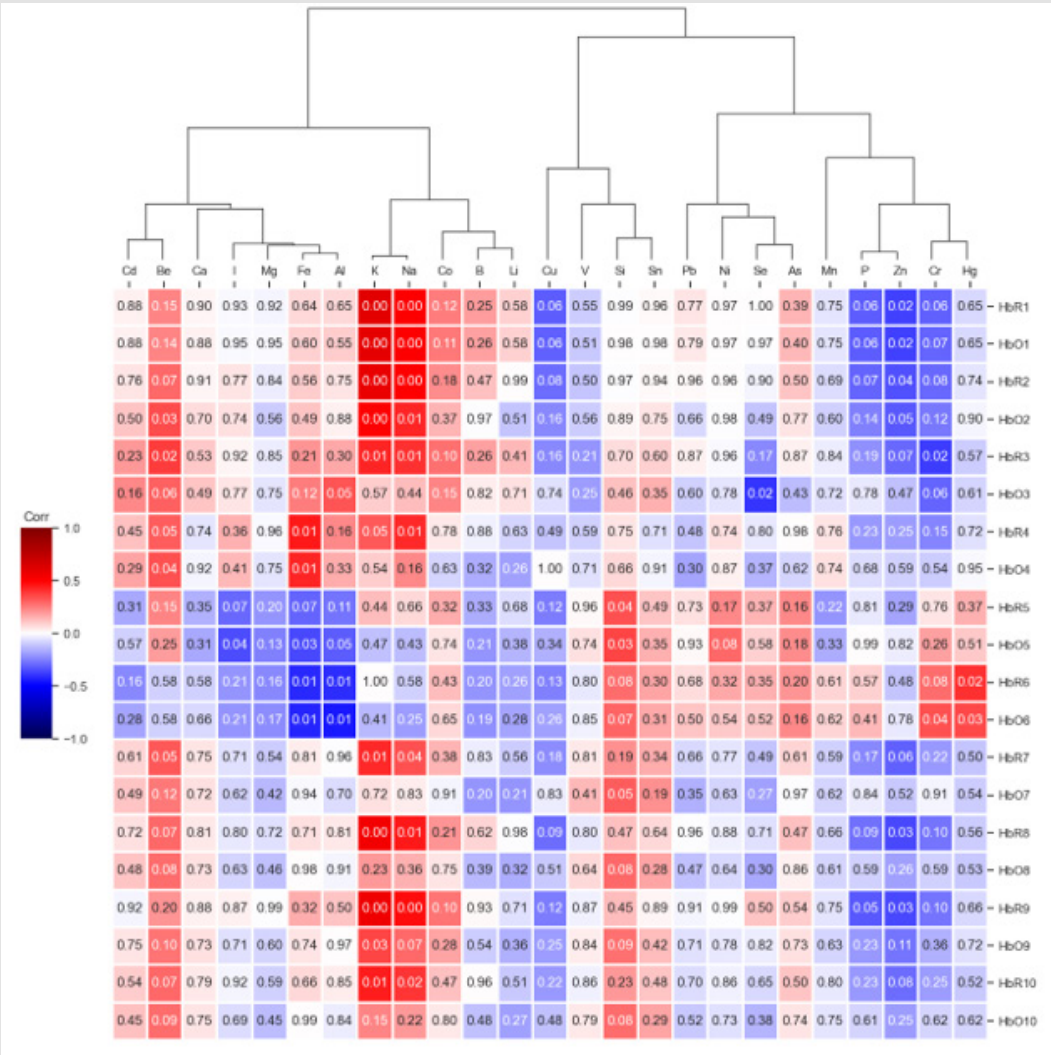
Channel number	Sensor type	Correspondence of the sensor to the EEG leads	Pickup location
1	Source	F4	Right frontal cortex
	Detector	F6	
2	Source	F3	Left frontal cortex
	Detector	F5	
3	Source	AF4	Right frontal cortex
	Detector	AFp2	
4	Source	AF3	Left frontal cortex
	Detector	AFp1	
5	Source	FTT8h	Right temporal cortex
	Detector	T8	
6	Source	FTT7h	Left temporal cortex
	Detector	T7	
7	Source	P3	Left parietal cortex
	Detector	CPP5h	
8	Source	P4	Right parietal cortex
	Detector	CPP6h	
9	Source	O1	Left occipital cortex
	Detector	OL1h	
10	Source	O2	Right occipital cortex
	Detector	OL2h	

Clustering of elements and dendrogram construction were performed in the Spyder development environment using the Pandas and Seaborn packages. Clusters were identified using the nearest neighbor method. Correlations were considered statistically significant at $p < 0.05$, and p values in the range of 0.05 to 0.1 were considered a trend toward statistical significance.

Results/Observations

The study revealed the presence of moderate-strength relationships between the concentration of some biologically significant chemical elements in hair samples and the levels of HbO and HbR in various parts of the subjects’ brains (Figure 1). All analyzed chemical elements were divided into two large clusters, depending on the prevalence of positive or negative correlations with fNIRS parameters. The first cluster, which is characterized by direct links with hemoglobin levels in the frontal and parietal-occipital regions of the brain, included 12 chemical elements, including Na, K, Ca, and Mg, which belong to the category of macroelements; Fe, Co, and I, which are included in the group of essential microelements; as well as Cd, Be, and Al, which

can be considered toxic or conditionally toxic elements. The identified positive correlations may be based on various aspects of the neuro-humoral balance, which are reflected in changes in the fNIRS signal. Most likely, they may be associated with the total concentration of hemoglobin in the blood, the ratio of oxy- and carbohemoglobin. Indirectly identified correlations may reflect the metabolic activity of brain tissue, and at the systemic level, depend on the nature of the regulation of vascular tone, cardiac function, and the overall activity of metabolic processes in the human organism. In each of these cases, a positive correlation with the concentration of a chemical element indicates its role in activating the corresponding metabolic pathways and reactions.



Note: The heat map demonstrates the strength and direction of correlations, with cells indicating the significance levels of correlations. The dendrogram groups chemical elements based on the similarity of their correlation patterns.

Figure 1: Results of hierarchical cluster analysis based on correlations between the concentration of biologically significant chemical elements in hair samples and fNIRS parameters.

Thus, direct correlations with the Fe content in the body can be interpreted, on the one hand, through its participation in the synthesis of heme and the key role in the transport of respiratory gases; on the other hand, at the systemic level, Fe is an important activator of cellular metabolism, being involved in the reactions of fatty acid breakdown and ATP synthesis in mitochondria. The largest number of statistically significant positive correlations, as well as their greatest strength ($r = 0.33-0.6$), were obtained for Na and K concentrations. Na and K are among the body's essential macronutrients. They are involved in maintaining the electrolyte balance of the intracellular and intercellular environments and are crucial osmotically active elements that contribute, among other things, to maintaining blood pressure. The excitability of nervous tissue and the formation of resting potentials and action potentials of neurons are realized through the redistribution of Na and K ions, and the functioning of transmembrane Na-K pumps. The strongest positive correlations between Na and K levels and fNIRS parameters were found in the right and left frontal, occipital, and parietal cortex. Moreover, for the third, fourth, seventh, eighth, ninth, and tenth channels, these connections are only valid for deoxygenated hemoglobin. This may indicate that elevated Na and K levels promote functional activation of the prefrontal, parietal, and occipital lobes of the brain due to enhanced oxygen metabolism, which leads to the conversion of oxy-Hb to deoxy-Hb.

Ca and Mg, macronutrients known for their role as universal activators of metabolic processes, were also included in the general cluster with Na and K. Particularly important in this context is the role of Ca, which is involved in the regulation of both the cardiovascular and nervous systems. It is well known that the transmembrane potential of Ca maintains cardiac muscle contractility and regulates heart rate. The release of neurotransmitters during synaptic transmission within and outside the central nervous system also involves Ca ions. Thus, the discovered correlations between the main cationic macronutrients and fNIRS parameters may simultaneously reflect both the overall activity of the brain's neural substrate and the activity of the cardiovascular tone regulation system. Direct correlations between fNIRS parameters and the concentration of several toxic elements (especially Ca and Be), which were also included in the same cluster as cationic macronutrients, can also be explained by activation processes, which in this case may have a compensatory nature. These trace elements are classic industrial pollutants and can enter the body through the inhalation of atmospheric dust, exhaust fumes, and tobacco smoke. Living in environments with elevated Cd loads is characterized by higher cardiovascular stress index values, manifested by higher heart rates and lower heart rate variability compared to similar indicators in individuals living in ecologically safe regions with lower Ca pollution levels.

Conversely, Be accumulation typically impacts respiratory function, reducing the diffusion of oxygen and carbon dioxide in the alveolar system of the lungs. Another cluster (13 chemical elements),

formed based on correlation matrix analysis, is characterized by a significant number of negative correlations between fNIRS parameters and the levels of various chemical elements in hair samples. It included significantly higher amounts of heavy metals (Pb, Hg, Sn), as well as other elements with pronounced toxic effects, often associated with industrial pollution (Ni, As, V). This cluster is practically not represented by macroelements (with the exception of P), but contains a number of microelements that play an important role in the antioxidant defense system (Se, Zn, Cr). It should be assumed that the combination of toxicants and essential microelements of the antioxidant defense system in a single cluster may be associated with their antagonism. Thus, Se is a factor in reducing the toxic effects of As. This effect of Se can be realized in several ways: through the formation of biologically inert complexes with As and/or through the action of antioxidant enzymes, whose synthesis depends on the concentration of Se. Similar protective mechanisms may be implemented in relation to Zn. Furthermore, Zn is known for its regulatory role in vasoconstriction and vasodilation, but the direction of these effects is heterogeneous. There is evidence indicating both direct and inverse relationships between Zn status and cardiovascular health.

Furthermore, the inclusion of certain essential trace elements in the negative cluster may be due to antagonism between their metabolism and elements in the positive cluster. For example, data have been obtained for Cu showing an inverse relationship between its content and Fe content. A separate point requiring consideration is the manifestation of multidirectional correlations between the content of the same chemical elements and the concentration of HbO and HbR in different lobes of the brain. Thus, Al, Fe, and I, assigned to the first cluster, exhibit negative correlations with the concentration of HbO and HbR in the temporal lobes, against a background of positive correlations with fNIRS indices in the prefrontal lobes. In contrast, Cr and Hg, classified in the second cluster, are characterized by direct associations with HbO and HbR concentrations in the temporal lobes, along with inverse associations with fNIRS values in the frontal, parietal, and occipital lobes. Only in the temporal lobes is the relationship between the levels of certain chemical elements and fNIRS readings observed to be diametrically opposed to the relationship between these same chemical elements and fNIRS readings in the frontal, parietal, and occipital leads. This phenomenon requires further study of the neuroanatomical, neurochemical, and neurofunctional relationships between the various lobes of the cerebral cortex.

Conclusion

A correlation analysis of hair elemental composition and fNIRS readings revealed a complex system of relationships, clustering which allowed us to identify general patterns indicating the role of various biologically active macro- and microelements in regulating the blood supply to the cortical regions of the central nervous system. The results showed that hemoglobin concentration in the cerebral circu-

lation, reflecting the overall level of metabolic activation, is directly related to the content of essential cationic macroelements (Na, K, Ca, Mg) and inversely related to the content of heavy metals and toxicants (Pb, Hg, Sn, As, Ni). Problematic issues related to the different directions of the relationship between the levels of certain chemical elements and fNIRS readings in the temporal lobes, compared to the relationship of these same elements with fNIRS readings in the frontal, parietal, and occipital leads, were identified. The presented data necessitate further development of individualized cerebral metabolism based on the body's elemental status, particularly for individuals with cardiometabolic and neurocognitive disorders. In addition, the prospects for the widespread implementation of fNIRS in research activities and clinical practice as a simple and effective method for neuroimaging brain functions are determined.

Conflict of Interest Statement

The authors declare no conflict of interest.

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2025.63.009923

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