Research of the Autonomic Regulation in the Formation of the Brain Microwave Radiation Restoration Processes during Rehabilitation of the Stroke Patients

Study by Means of the Multifractal Analysis of the Radiophysical Complex MRTHR Signals

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Abstract: The paper discusses the possibility of applying multifractal cross-correlation analysis method for the joint processing of transient biomedical signals received via the Radiophysical complex MRTHR (Medical Radio-Thermograph - Heart Rate) for rehabilitations estimations. The results of the multifractal cross-correlation analysis application are shown for research the role of the autonomic regulation in the formation of the brain microwave radiation (intrinsic electromagnetic radiation of the brain) in the treatment process. A pilot clinical study obtained by the multichannel Radiophysical complex MRTHR had shown the dynamics discrepancies of cross-correlation Hurst exponent coincides with the clinical data for patients after passing through the course of rehabilitation using techniques of the dynamic correction activity of the sympathetic nervous system.

1 INTRODUCTION

It is well known, that the main mechanism for ensuring the constancy of the internal environment of the body, is the autonomic nervous system (ANS). The ANS adapts all regulation systems to environmental changes (Guyton and Hall, 2011). The ANS can be considered as the complex of structures that are parts of the peripheral and central divisions of the nervous system that regulate the functions of organs and tissues. This regulation is aimed at maintaining the body relatively constant internal environment (homeostasis).

Among the main factors that contribute to changes in regulation of cerebral circulatory system are:

- the vascular tone change;
- the intravascular pressure;
- the shear stress on the vascular wall;
- the streaming blood characteristics;
- the chemical composition of the blood;
- the blood viscosity
- the activity of the autonomic regulation;
- the dependence of the perfusion pressure in the brain on the value of intracranial pressure (Moskalenko, 1992).

The actuator in the regulation mechanism of the cerebral circulation are the muscles of the vascular wall. The muscles perceive irritation of specialized receptor and chemical compounds released into the bloodstream and the environment. In addition, muscles perceive the mechanical stretching of the intravascular blood pressure and are sensitive to a variety of substances, which are the products of cellular metabolism (Pocock and Richards, 2013).

According to the anatomical criteria the ANS is divided into the segmental and suprasegmental divisions (Schmidt and Thews, 1989). The segmental division of the ANS provides the autonomic innervation of the individual segments of the body and internal organs, which belong to them. It is divided into the sympathetic and parasympathetic divisions (SNS and PSNS, respectively). The heart rate variability signal (HRV) is an example of the

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standard instruments of functional diagnostics.

This choice in our study is not accidental. The HRV signals are indicators of the ANS activity (Malik *et al.*, 1996). The role of the autonomic regulation of the formation of functional processes in the brain tissue is poorly understood. The suprasegmental divisions of the ANS are involved in organisation cerebral circulation. Although clinical trials of its activity depends on the effectiveness of rehabilitation of vascular lesions of the brain (Kublanov *et al.*, 2010). Particularly there is no data on the effect of the autonomic regulation on the formation of the brain microwave radiation.

Based on this, the aim of this paper is to apply the multifractal estimates for the autonomic regulation in the formation of brain microwave radiation restoration processes during rehabilitation of the patients.

2 MATERIALS AND METHODS

2.1 Radiophysical Complex MRTHR

In this study two signals forms the information channels of multichannel Radiophysical complex MRTHR: the HRV and brain microwave radiation (Kublanov, 2013). Figure 1: Structural diagram of the Radiophysical complex MRTHR for examining patients (Kublanov, 2013).

The HRV signals are obtained from the electrocardiography registered by means of the electrophysical signals channel. The microwave radiometer registers the brain microwave radiation in 650-850 MHz range.

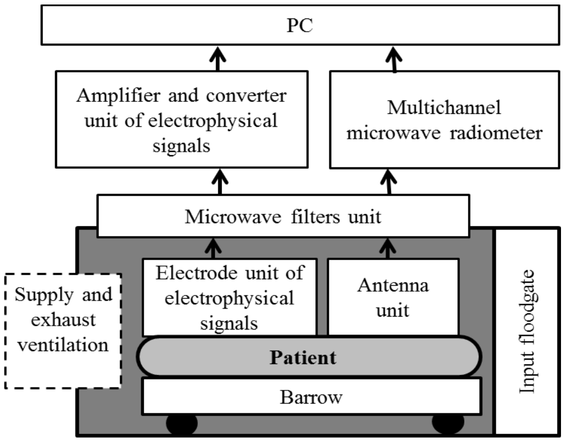

Figure 1: Structural diagram of the Radiophysical complex MRTHR for examining patients.

2.2 Patients

Signal analysis was made based on studies conducted in the Sverdlovsk regional clinical psycho-neurological Hospital for War Veterans (SRCPNH, Yekaterinburg). Investigations were carried out for the group of seven patients suffering from ischemic stroke (before and after rehabilitation treatment).

All patients gave their informed consent to voluntary participate in the study. The study was approved by the Ural State Medical University ethics committee (protocol №8 from 16.10.2015). The Table 1 shows the clinical data for group of patients.

The rehabilitation of patients after ischaemic stroke was performed in accordance with Guidelines for Management of Ischaemic Stroke and Transient Ischaemic Attack 2008 (Ringleb *et al.*, 2008).

Table 1: Clinical data of the studied patients group from the SRCPNH.

n	Patient/ sex	Age, years	Stroke localization. Clinical data.	ICD-10	Amount of the DCASNS séances
1	T.V.S./ male	53	Left middle cerebral artery basin, with elements of aphasia, early recovery period (up to the year)	I63.5	10
2	Z.I.G./ male	40	Ischemic stroke in Right Internal Carotid Artery basin 3 and 2 years ago. Arterial Hypertension III st.	I63.2, I10	10
3	G.V.L./ male	76	Ischemic stroke in Right middle cerebral artery 3 years ago, right hemiparesis. Diabetes mellitus. Arterial Hypertension III st.	I63.5, I10, E11.6	10
4	K.M.F./ female	73	Ischemic stroke in Left middle cerebral artery, residual effect. Ischemic heart disease. Heart failure.	I63.5, I25.8	10
5	D.L.I./ male	66	Chronic cerebral ischaemia III. Arterial Hypertension III st.	I69, I10	10
6	D.K.A./ female	71	Stroke in right internal carotid artery (1 month ago). Arterial Hypertension III st.	I63.2, I10	10
7	S.V.I./ male	49	Ischemic stroke in Right Internal Carotid Artery. Arterial Hypertension III st.	I63.2, I10	10

In addition, patients were treated with the neuro-electrostimulation device – “SYMPATHOCOR-01” course of the dynamic correction activity of the sympathetic nervous system (DCASNS) (Kublanov *et al.*, 2015). For these patients clinically proven improvement was observed after rehabilitation course.

2.3 Multifractal Cross-correlation Analysis

In our study, we propose to evaluate the information characteristics of the signals of the brain microwave radiation and HRV using method of multifractal formalism. Nowadays, application of the multifractal analysis is common in the brain research (Pavlov *et al.*, 2016; Whalley *et al.*, 2016; Závodszky *et al.*, 2015). Registration and analysis of these biomedical signals at the same time, gives a qualitatively new features that allow one to define a new integral indicator for the study of the functional changes in the brain in a state of preclinical and clinical practice in the early stages of development of these changes (Kublanov *et al.*, 2015).

Application of the multifractal cross-correlation analysis (MFCCA) method on two signals should be carried out at the same time windows (Podobnik and Stanley 2008). Based on this, in further signal analysis ten second time windows were considered. It can be assumed that the important properties of the signal, there are only in a certain range of scales, where properties are most distinct characteristic of multifractal structure (Di *et al.* 2015; Delignières *et al.* 2016).

Generally, in analysis of HRV signals applied:

- HF spectral component, which characterize activity of the parasympathetic department of the ANS and activity of the autonomic regulation loop;
- LF spectral component, which mainly characterize activity of the sympathetic vascular tone regulation centre. (Malik M. *et al.*, 1996).

The fluctuations of very low-frequency (VLF) spectral component of the HRV signal in range (25-300), sec are complex two- or three- formation (Fleishman 2005). Because of that the dynamics of changes in the aggregate analysis of signals obtained estimates of the HRV and brain microwave radiation signals is not advisable to carry out throughout the VLF range. It is appropriate to carry out analysis on a set of time windows.

To acquire summary estimation of the microwave radiation of biomedical signals, which indicate the ANS variability, one must transform the original biomedical signals to equidistant time series (TS) with the same sampling frequency 10 Hz (Example of signals is presented in Figure 2).

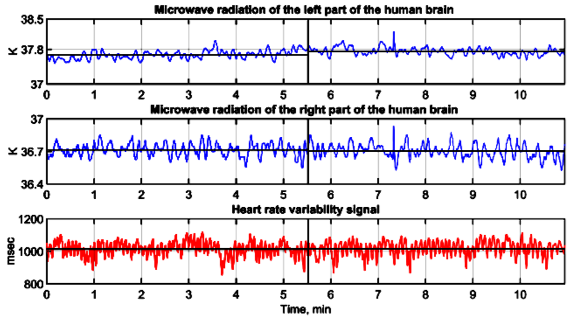

Figure 2: Simultaneously recorded signals of the Brain Microwave Radiation and HRV.

After interpolation, the investigated TS are accessed by the multifractal cross-correlation analysis. Stages of MFCCA are shown in Fig.3 (Kublanov *et al.*, 2016).

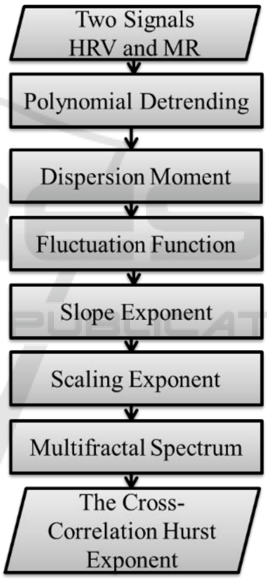

Figure 3: Stages of multifractal cross-correlation analysis.

The usage of multifractal analysis as an effective tool to study the possibilities and identify short-term series HRV was presented in (Kublanov *et al.*, 2015). There it was shown that one parameter – cross-correlation Hurst exponent H_2 is enough for obtaining information significant estimates of the autonomic regulation in the formation of brain microwave radiation.

In accordance with that article, simultaneous analysis of TS for signals the brain microwave radiation and HRV indicates the relationship between multifractal parameters for group for healthy subjects.

It was determined that:

- processes describing sympathetic activity of the ANS with fluctuation periods in the range from 6.5 to 25, sec and transport dynamics of the fluid in the intercellular and intracellular spaces brain tissue fluctuation periods ranging from 20 to 40, sec are similar.
- processes that characterize the activity of the central ergotrophic and humoral-metabolic mechanisms of heart rate regulation, defined by VLF fluctuations of the HRV in the range from 25 to 300, sec and the thermodynamic processes in the regulation of brain tissue fluctuations with range from 60 to 70, sec are similar.

As shown previously (Kublanov *et al*, 2016), the diagnostic capability of the computed multifractal characteristics in two functional states for the above mentioned time windows can be determined by a Bland-Altman's criteria (Bland and Altman, 1986) as follows:

- assessment of systematic differences calculated as the difference between each measurement pair;
- calculation of the mean and standard deviation for these differences, characterizing the degree of variation of results.

3 RESULTS AND DISCUSSIONS

Data analysis of multifractal estimates were provided for the HRV and brain microwave radiation signals obtained using the MFCCA method for the group of patients (shown in the Table 1). For signals of the HRV and brain microwave radiation multifractal estimates obtained by the MFCCA, difference of the Hurst exponents was calculated in two functional states: at rest and during antiorthostatic load. The analysis was conducted on time windows (20-30; 30-40;
60-70, sec) as specified in the article (Kublanov *et al*., 2015).

Obtained estimation are presented before and after the course of rehabilitation using techniques of the DCASNS. In all the tables below, negative values indicate a “shift” of the cross-correlation in direction of the antiorthostatic load, positive values – in direction of rest (Fig. 4).

Figure 4: State F ─ functional rest [0,300] sec; state A ─ antiorthostatic load (30^0) [300,600] sec.

3.1 Patient One

The clinical data of the patient T.V.S. showed reduction of the ataxia (instability) severity in Romberg’s sign, decreased effects of motor aphasia, rate of speech and articulation improvement. Blood pressure and heart rate indices - have not changed. During the period of treatment there were no hemodynamic deterioration.

The DCASNS method mode function stellate ganglion block (blocking the activity of the SNS) was used for this patient. Clinical outcome was accompanied by a decrease in LF / HF ratio from 2.64 (the predominance of sympathetic tone) to 1.56 (normal). This effect is associated with the SNS predominant tone with respective pathogenesis and clinical manifestations. Moreover, the duration of disease is relatively low: early post stroke recovery period - during the year.

Table 2: Systematic discrepancy assessments of the cross-correlation Hurst exponent for the HRV and brain microwave radiation signals for patient T.V.S.

Time window	20-30, sec	30-40, sec	60-70, sec
Before	-0,04460	-0,11771	-0,17561
After	0,02878	0,27910	0,00551

In accordance with the Table 2, the normalization of autonomic balance for the segmental divisions of the ANS was accompanied by an increase in conjunction with oscillatory processes that reflect the transport of tissue fluid in the matter of the brain at rest and during antiorthostatic load.

Based on that it can be assumed that the synchronization processes in the ANS (at the segmental level) have a relationship with the normalization of the function of suprasegmental (brain) autonomic structures. Synchronization of processes can be explained by activation (normalization) process and neuroplasticity of the nervous trophism, caused by the DCASNS method.

3.2 Patient Two

In accordance with the clinical data of the patient Z.I.G. headaches decreased (frequency, duration, intensity, reduced the number of analgesics taken to anesthesia). Achieved target blood pressure (less than 120 mm Hg). Decreased subjective phenomena of weakness. Decreased levels of anxiety (from 12 to 7 grades) (Boakye *et al.,* 2016).

For this patient mainly the DCASNS stimulation activity mode of the SNS was used. Initially, reduced tone of the SNS was accompanied by headaches, and anxiety disorders. As the result of the DCASNS tone of the SNS increased. LF / HF ratio increased from 0.25 to 1.05.

All patient's clinical parameters were determined by "shift" of autonomic regulation on the segmental level – reduction of HF and LF, and suprasegmental hypothalamic. The “shift” happened a long time (three years) after vascular accident and manifested itself in slowdown of the vascular tone regulation process. The leading treatment effect was a slight increase in power modulating effects of segmental structures of the ANS (the nerves of the heart). The disappearance of headaches was caused by the expansion of the adaptation corridor of vascular tone (in an increment of the total power spectrum of HRV - total power index).

Table 3: Systematic discrepancy assessments of the cross-correlation Hurst exponent for the HRV and brain microwave radiation signals for patient Z.I.G.

Time window	20-30, sec	30-40, sec	60-70, sec
Before	-0,18838	-0,24459	-0,12457
After	0,10135	0,03153	-0,05517

According to the data presented in the Table 3, the normalization of autonomic balance in the segmental divisions of the ANS in a state of rest was accompanied by an increase of cross-correlation level with oscillatory processes that reflect the transport of tissue fluid in the brain substance alone. At the same time, the relationship between the thermodynamic processes in the brain and VLF component of the spectrum of HRV increased. This finding indirectly confirms the currently existing ideas about the nature of VLF waves (as one that reflects the thermoregulatory processes) (Fleishman, 2005).

3.3 Patient Three

Pursuant to the clinical data of the patient G.V.L. systolic blood pressure decreased to target values (less than 120 mm Hg for patients with diabetes). Reflexes with limb asymmetry decreased. The appearance of hemiparetic gait reduced. The hemiparesis severity decreased from 3 to 2 grades.

The DCASNS stimulation biotropic field parameters were individually selected with predominant target – the activition of the SNS. It resulted in balance normalization of the sympathetic and parasympathetic regulation of the heart, coursed by diabetes and diabetic autonomic neuropathy. Improvement of the decreased tone of the SNS, allowed to achieve the normalization of segmental regulatory effects on vascular tone, and a significant regression of neurological symptoms.

Table 4: Systematic discrepancy assessments of the cross-correlation Hurst exponent for the HRV and brain microwave radiation signals for patient G.V.L.

Time window	20-30, sec	30-40, sec	60-70, sec
Before	-0,09742	0,04123	-0,09871
After	0,00758	0,06727	0,01680

According to the Table 4 for a patient with severe organic lesion of segmental and suprasegmental autonomic structures have achieved a certain normalization of autonomic balance in segmental divisions of the ANS in a state of rest. In other words, the DCASNS influence preserved insufficient regulation reserves by stimulating the processes of transport of tissue fluid (mechanisms of trophism and neuroplasticity) in the matter of the brain. This in turn provided normalization of autonomic reactivity in functional loads (within the stored reserves of the regulation) (Kessner *et al.*, 2016; Lundborg, 2005). At the same time, a positive impact of the DCASNS on segmental autonomic structures (the hypothalamus) was indicated by some normalization of reactivity of the thermodynamic processes in the brain at antiorthostatic load.

3.4 Patient Four

In conformity with the clinical data of the patient K.M.F. fatigue phenomenon decreased, disappeared noise in the head, dizziness. The blood pressure normalized - hypotension phenomena have disappeared. The symptoms of anxiety scale reduced (from 14 to 11 grades) (Hurley and Tizabi, 2013; Stetler *et al.*, 2014).

Application of the DCASNS method in the stimulation mode managed to maintain an increased tone of the SNS. Furthermore, it allowed maintaining a normal perfusion of blood through the arterial bed and the maintenance of normal values of blood pressure. These values ensure the normalization of blood flow through the brain and restoration of the cerebral blood flow performance after stroke. Little effect was associated with initially low levels of total power of HRV – *i.e* low modulating effects on the heart of segmental division.

Table 5: Systematic discrepancy assessments of the cross-correlation Hurst exponent for the HRV and brain microwave radiation signals for patient K.M.F.

Time window	20-30, sec	30-40, sec	60-70, sec
Before	-0,15419	0,03370	-0,06882
After	-0,04550	-0,02534	0,04625

In accordance with the Table 5 for this patient was observeddecreased HRV correlation of signals in LF- and of HF - bands with their brain microwave radiation in the respective time windows. This coincides with the target values of the blood pressure - the necessity to maintain high tone of the SNS. At the same time, there was a significant increase in correlation, both at rest and during antiorthostatic, for stress indicators of the brain microwave radiation (thermoregulation) with VLF-component of the HRV spectrum. This, in turn, may indicate a preferential activation of the suprasegmental autonomic structures (the hypothalamus) when this particular mode the DCASNS method is selected.

3.5 Patient Five

In appliance with the clinical data of the patient D.L.I. there was a normalization of elevated blood pressure. The target blood pressure was achieved - less than 130/80 mm Hg. It was possible to reduce the tone of the SNS by means of the DCASNS method in blocking mode. Which, in turn, resulted in lowering of blood pressure.

Table 6: Systematic discrepancy assessments of the cross-correlation Hurst exponent for the HRV and brain microwave radiation signals for patient D.L.I.

Time window	20-30, sec	30-40, sec	60-70, sec
Before	-0,05011	-0,03088	-0,07643
After	0,18664	-0,19695	0,30650

According to the data presented in the Table 6, the patient has a reduced correlation of HRV LF signals in the range, the effect associated with initially elevated tone SNS. At the same time, the relationship of the thermodynamic processes in the brain and VLF-component of the HRV spectrum increased (Togo *et al.*, 2006).

3.6 Patient Six

The clinical data of the patient D.K.A. provides insight of achieved gradual reduction for high blood pressure in the range of target values in the acute phase of stroke. There was an increase caused by a reduced stroke force of muscles on the left. At the same time, there was a decrease of pathologically elevated tone of the left limbs.

For the DCASNS method, biotropic parameters of physical fields were selected to block the SNS. By using that, it was possible to dramatically reduce increased tone of the SNS and to normalize the autonomic balance. This resulted in improvement of blood perfusion on the arterial bed by reducing the weakening of hypervasoconstriction degree. This, in turn, ensured the normalization of blood flow through the head brain and recovery rates of cerebral blood flow after stroke.

Table 7: Systematic discrepancy assessments of the cross-correlation Hurst exponent for the HRV and brain microwave radiation signals for patient D.K.A.

Time window	20-30, sec	30-40, sec	60-70, sec
Before	-0,04999	-0,06435	-0,10949
After	-0,14435	0,25473	0,01954

In accordance with the Table 7 for a patient with severe acute organic central nervous system disease (acute ischemic stroke) achieved normalization of autonomic maintenance - increase of the correlation between HF indicators of the HRV and the brain microwave radiation. Moreover, autonomic reactivity was moted - increased correlation of the module LF and the brain microwave radiation in a time window of 60-70 for state of antiortostic load.

This confirms the restoration of suprasegmental autonomic regulation processes in the brain. In other words, activation of a fluid transport processes (neuro-trophic, neuroplasticity), as thermoregulation processes.

3.7 Patient Seven

According to the clinical data of the patient S.V.I. high blood pressure failed to normalize after the first course the DCASNS method. This can be explained by the presence of comorbidity, in violation of the mechanisms of autonomic regulation of vascular tone. Also this complicates treatment and worsens the prognosis – anxiety and depressive disorders. Indicators of the Hospital Anxiety and Depression Scale patient had evidence of clinically significant depression (Varidaki *et al.*, 2016)

After re-hospitalization and new selection of the biotropic physical parameters for the DCASNS method it was possible to normalize blood pressure. The presence of depression, worsen cardiovascular disease due to a persistent increase of the tone of the SNS, were the factors that prolonged treatment and made difficult to achieve positive clinical (Jeong *et al.*, 2016).

The patient required repeated the DCASNS courses with individual selection of the biotropic field parameters. As a result, moderate decline in the tone of the SNS happened. The achievement of a significant antidepressant effect revealed in reduction of the severity of depressive symptoms at the hospital anxiety and depression scale. Moreover, it achieved normalization of blood pressure (Rial *et al.*, 2016). The effect can be associated with initially elevated tone of the SNS.

Table 8: Systematic discrepancy assessments of the cross-correlation Hurst exponent for the HRV and brain microwave radiation signals for patient S.V.I.

Time window	20-30, sec	30-40, sec	60-70, sec
Before	-0,14729	-0,25288	-0,05091
After	-0,03984	-0,02991	-0,08195

The data presented in the Table 8 show that this support of patient in the clinical observation of the results and gave an explanation concerning the difficulties to achieve a therapeutic effect. The patient showed the initial expression violations of the correlation between process of the segmental division modulation of heart rate at rest and during exercise in time windows. Which primarily reflects the phenomena of transport of fluid in the brain and is associated with the processes it neuro-trophic and neuroplasticity. As it is currently known and shown, these processes suffer significantly from patients with depressive disorders (Arnaud and Di, 2016).

Thus, the data of the cross-correlation analysis coincides with the clinical picture of the disease for the patient and fits into this particular clinical case. The data is the basis for predicting the difficulty in achieving a clinical effect of the DCASNS, which is associated with a profound impairment of nervous trophic and neuroplasticity.

3.8 Discussion

The analysis of data presented in Tables 2-8, showed that the dynamics of cross-correlation differences Hurst exponent coincides with the clinical data in the treatment of patients. The coincidence is representative for the variety of clinical cases, and can serve as a basis for forecasting and possible correction of the treatment course of patients.

Obtained in this study estimations are consistent with results received earlier. In (Kublanov *et al.*, 2016) it was found, that for the time windows 20–40 and 50–60 seconds in the functional rest and during the passive orthostatic load, the systematic discrepancy between the differences of the Hurst exponent of biomedical signals is minimal for the healthy patients. For patients suffering from ischemic stroke prior to the rehabilitation treatment, these values are greater.

4 CONLUSIONS

The article describes the pilot clinical study of the brain microwave radiation and HRV signals obtained by the multichannel Radiophysical complex MRTHR. Analysis of the HRV and brain microwave radiation signals, by means of the methods of the cross-correlation multifractal analysis allowed to obtain new knowledge about the studied biomedical signals.

Application of multifractal formalism allowed proving that at the minimum level of systematic differences of the HRV and the brain microwave radiation signals dynamic changes in these signals occur like. In this case, we can assume that the role of the autonomic regulation defined by characteristics of the HRV in the formation of the brain microwave radiation is high. The proposed approach can be used to manage the medical process.

Dynamics of the cross-correlation Hurst exponent differences coincides with the patients' clinical data. The treatment effectiveness depends on the duration of the disease, more amenable to correction processes arisen recently. Strokes to the three-year history and were treatable worse.

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