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INTERRELATIONS BETWEEN CHANGES IN PARAMETERS OF HRV, EEG AND HUMORAL IMMUNITY AT PATIENTS WITH CHRONIC PYELONEPHRITIS AND CHOLECYSTITIS

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Abstract
Background. The immunological homunculus conception considers somatotopic organization to CNS regulation of immune system. Previously, we have shown within the immunological homunculus conception that take place causal relationships parameters of EEG and HRV, on the one hand, and the parameters of cellular and humoral immunity as well as phagocytose, on the other hand. The purpose of this study is to find out the relationships between induced by balneotherapy **changes** in parameters of EEG and HRV, on the one hand, and the parameters of immunity, on the other hand. **Methods.** In basal conditions in 33 men and 10 women with chronic pyelonephritis and cholecystitis in remission, we recorded twice, before and after balneotherapy at the spa Truskavets', EEG ("NeuroCom Standard") and HRV ("Cardiolab+VSR"). In blood estimated routine parameters of Humoral Immunity on a set of I and II levels recommended by the WHO. **Results.** We detected that changes in relative level $CD22^+$ B-Lymphocytes upregulated by parasympathetic outflows and β-rhythm generating structures that are projected onto the loci O2, Fp1, F3 and F4, while downregulated by sympathetic outflows and θ-rhythm generating structures that are projected onto the locus T5. Serum level of IgA upregulated by parasympathetic outflows and α-rhythm generating structures that are projected onto the loci T3 and C3 as well as δ-rhythm generating structures onto F7 and T5, while downregulated by sympathetic outflows and θ-rhythm generating structures that are projected onto the loci T5, F7, Fp2, F3, F8 and F4. Serum level of CIC upregulated by parasympathetic outflows and α-rhythm generating structures that are projected onto the loci T4, Fp2, T3, F8 and C3 as well as θ-rhythm generating structures onto the loci T3 and T6, while downregulated by sympathetic outflows and β-rhythm generating structures that are projected onto the loci Fp1, F3 and P4 as well as δ-rhythm generating structures onto T4. Unlike the previous parameters serum level of IgM downregulated by parasympathetic outflows and α-rhythm generating structures that are projected onto the loci T3 and T6 as well as β-rhythm generating structures onto the locus T5, while upregulated by sympathetic outflows and θ-rhythm generating structures that are projected onto the loci

F3, Fp2, T5, F4, O1 and F8. Serum level of IgG downregulated by parasympathetic outflows, while upregulated by sympathetic outflows and δ-rhythm generating structures that are projected onto the loci O2 and F8 as well as α-rhythm generating structures onto C3. **Conclusion.** The results are supplemented and refined Tracey's immunological homunculus conception.

Keywords: HRV, EEG, B-Lymphocytes, Immunoglobulines M,G,A, Circulating immune complexes, correlations.

INRODUCTION

Previously, we have shown within the immunological homunculus conception [29] that blood level of Leukocytes and proportions of subset of Leukocytes (Leukocytogram) [16], Neutrophils phagocytic function [13,15] as well as proportions of subset of Lymphocytes and serum level Immunoglobulines M, G and A [14] subordinate modulation central and autonomic nervous systems. In this study we set a goal to analyze the causal relationships between **changes** in parameters of EEG and HRV, on the one hand, and the parameters of Immunity, on the other hand.

MATERIAL AND METHODS

The object of observation were 33 men and 10 women aged 24-70 years old, who came to the spa Truskavets' (Ukraine) for the treatment of chronic pyelonephritis combined with cholecystitis in remission. The survey was conducted twice, before and after balneotherapy.

We recorded electrocardiogram in II lead to assess the parameters of HRV [1,2,3-7] (software and hardware complex "CardioLab+HRV" production "KhAI-MEDICA", Kharkiv, Ukraine). For further analysis the following parameters heart rate variability (HRV) were selected. Temporal parameters (Time Domain Methods): the standart deviation of all NN intervals (SDNN), coefficient of variation (Cv), the square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD), the percent of interval differences of successive NN intervals greater then 50 ms (pNN_{50}); heart rate (HR), the moda (Mo), the amplitude of moda (AMo), variational sweep (MxDMn) as well as triangulary index (TI). Spectral parameters (Frequency Domain Methods): spectral power density (SPD) bands of HRV - high-frequency (HF, range 0,4÷0,15 Hz), low-frequency (LF, range 0,15÷0,04 Hz), very low-frequency (VLF, range 0,04÷0,015 Hz) and ultra low-frequency (ULF, range 0,015÷0,003 Hz). Expectant as classical indexes: LF/HF, LFnu=100%•LF/(LF+HF) and Baevskiy's Stress Index (BSI=AMo/2•Mo•MxDMn) as well as Baevskiy's Activity Regulatory Systems (BARS) [1].

Then EEG recorded a hardware-software complex "NeuroCom Standard" (KhAI Medica, Kharkiv, Ukraine) monopolar in 16 loci (Fp1, Fp2, F3, F4, F7, F8, C3, C4, T3, T4, P3, P4, T5, T6, O1, O2) by 10-20 international system, with the reference electrodes A and Ref tassels on the ears. Among the options considered the average EEG amplitude (µV), average frequency (Hz), frequency deviation (Hz), index (%), coefficient of asymmetry (%) as well as absolute ($\mu V^2/Hz$) and relative (%) SPD of basic rhythms: β (35÷13 Hz), α (13÷8 Hz), θ (8÷4 Hz) and δ (4÷0,5 Hz) in all loci, according to the instructions of the device. In addition, calculated Laterality Index (LI) for SPD each Rhythm using formula [20]:

$$LI, \% = \Sigma\,[200 \cdot (Right - Left)/(Right + Left)]/8$$

We calculated also for HRV and each locus EEG the Entropy (h) of normalized SPD using formula C Shannon [cit. by: 22]:

$$hHRV = -\,[SPD\ HF \cdot \log_2 SPD\ HF + SPD\ LF \cdot \log_2 SPD\ LF + SPD\ VLF \cdot \log_2 SPD\ VLF +$$

$+ SPD\ ULF \bullet \log_2 SPD\ ULF]/\log_2 4$

$hEEG = -[SPD\alpha \bullet \log_2 SPD\alpha + SPD\beta \bullet \log_2 SPD\beta + SPD\theta \bullet \log_2 SPD\theta + SPD\delta \bullet \log_2 SPD\delta]/\log_2 4$

Immune status evaluated on a set of I and II levels recommended by the WHO. For phenotyping subpopulations of lymphocytes used the methods of rosette formation with sheep erythrocytes on which adsorbed monoclonal antibodies against receptors CD3, CD4, CD8, CD22 and CD16 from company "Granum" (Kharkiv) with visualization under light microscope with immersion system. Subpopulation of T cells with receptors high affinity determined by test of “active” rosette formation [17]. The state of humoral immunity judged by the concentration in serum of Immunoglobulins classes G, A, M (ELISA, analyser “Immunochem”, USA) and circulating immune complexes (by polyethylene glycol precipitation method) [17].

Results processed by methods of correlation and canonical analyses, using the software package "Statistica 5.5".

RESULTS AND DISCUSSION

In this article, we will analyze the relationships between changes in parameters of EEG and HRV, on the one hand, and the parameters of **humoral** immunity only, on the other hand. Cellular immunity and phagocytosis will be the subject of following articles. A separate fragment is published in abstract format [12,24,25].

It is known that the connections between the nervous and immune systems are two-way. On the one hand, the nervous system, through its mediators (acetylcholine, norepinephrine, neuropeptides), affects proliferation, apoptosis and the function of lymphocytes, macrophages and microphages expressing the corresponding receptors. On the other hand, immunocytes release cytokines, hormones and even the same neurotransmitters that together affect neuron activity [8-11,18,21-23,26]. Therefore, the nature of cause-effect relationships can not be unambiguous. Proceeding from this, purely arbitrarily, we will consider the changes in the parameters of HRV and EEG as a factor (argument), instead of changing the parameters of immunity as a productive feature (function).

First of all, we, using a canonical analysis, found out what factors of nervous regulation and to what extent influence changes in the proportion of subset of B-lymphocytes in blood.

Unfortunately, because of the total lack of funding, in our cheap “NeuroCom Standard” device function “Thomography” is not involved, so we can not surely judge the localization of nerve structures that are projected onto those or other loci.

As can be seen from Table 1, the canonical root of nerve regulation receives predominantly **negative** factor loadings that reflect the **stimulating** effect on B-lymphocytes blood level by the side of HRV markers of vagal tone as well as β-rhythm generating structures that are projected onto the right occipitalis and medialis frontalis as well as left anterior and medialis frontalis loci as well as θ-rhythm generating structures that are projected onto the left anterior temporalis locus.

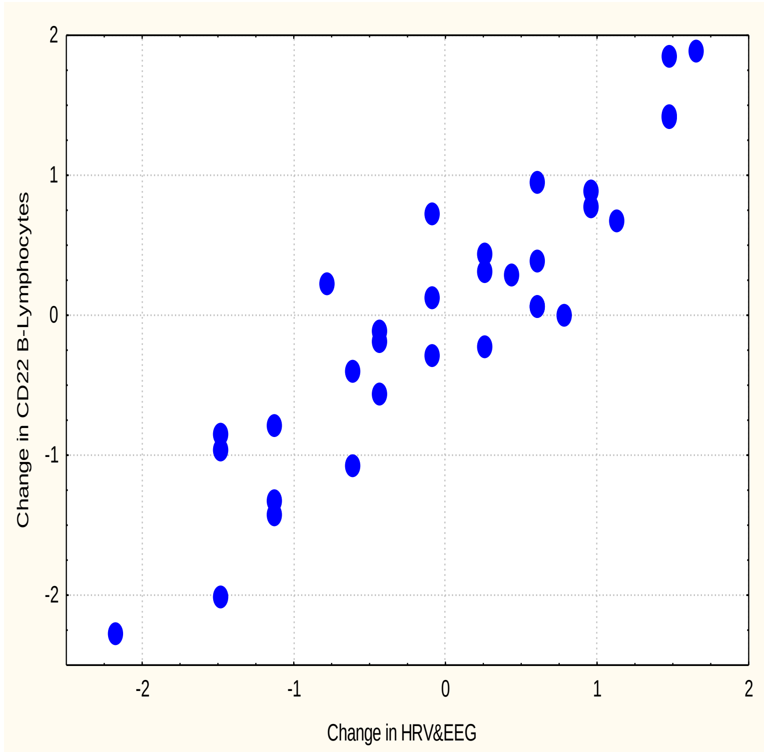
Table 1. Factor structure of canonical Roots representing Neural parameters and CD22$^+$ B-lymphocytes blood level

Right set	R
Cv HRV, %	**-,444**
SDNN HRV, ms	**-,430**
ULF HRV SPD, ms^2	**-,390**
VLF HRV SPD, ms^2	**-,389**
MxDMn HRV, ms	**-,359**
Bayevskiy Stress Index, ln	**,406**
AMo HRV, %	**,397**
O2-β SPD, %	**-,459**
Fp1-β SPD, %	**-,345**
T3-θ SPD, %	**-,338**
F4-β SPD, μV^2/Hz	**-,322**
F3-β SPD, %	**-,315**
α-Rhythm deviation, Hz	**-,393**
C3 Entropy	**-,391**
T5-θ SPD, %	**,275**
β-Rhythm Asymmetry, %	**,319**
β-Rhythm Index, %	**,294**
θ-Rhythm Frequency, Hz	**,258**
Left set	R
CD22$^+$ B-Lymphocytes, %	**-1**

It is speculated that ULF band (0,015÷0,003 Hz) associated with oscillation blood level of norepinephrine (0,002 Hz) as well as 17-OCS (0,0019 Hz) [cit by: 7], while VLF band HRV (0,04÷0,015 Hz) associated with oscillation blood levels of renin (0,04 Hz) and epinephrine (0,025 Hz), reflects thermoregulatory cycles [cit by: 2,7], cerebral ergotropic and metabolotropic outflows [cit by: 1], activation of cerebral sympathetic-adrenal system [cyt by: 4], sympathetic activity [cit by: 6]. But in this study we found that changes in the SPD ULF as well as VLF bands positively correlates with changes in vagal markers MxDMn (r=0,75 and 0,77), SDNN (r=0,66 and 0,88) and RMSSD (r=0,49 and 0,74 respectively), hence this parameter of HRV also reflects parasympathetic outflows.

Positive factor loadings reflect the **inhibting** effect on B-lymphocytes blood level by the side of HRV markers of sympathetic tone and θ-rhythm generating structures that are projected onto the left posterior temporalis locus. In addition, stimulating effect makes Deviation (variability) of α-rhythm and Entropy of relative SPD of the rhythms in the locus C3, which is probably projected the left hippocampus [27], while inhibiting effect makes Asymmetry and Index of β-rhythm as well as Frequency of θ-rhythm.

Judging by the coefficient of canonical correlation, changes in the nervous regulation determine changes in the level of B-lymphocytes by 84,4% (Fig. 1).



$R=0,919$; $R^2=0,844$; $\chi^2_{(18)}=39$; $p=0,003$; Λ Prime=0,156

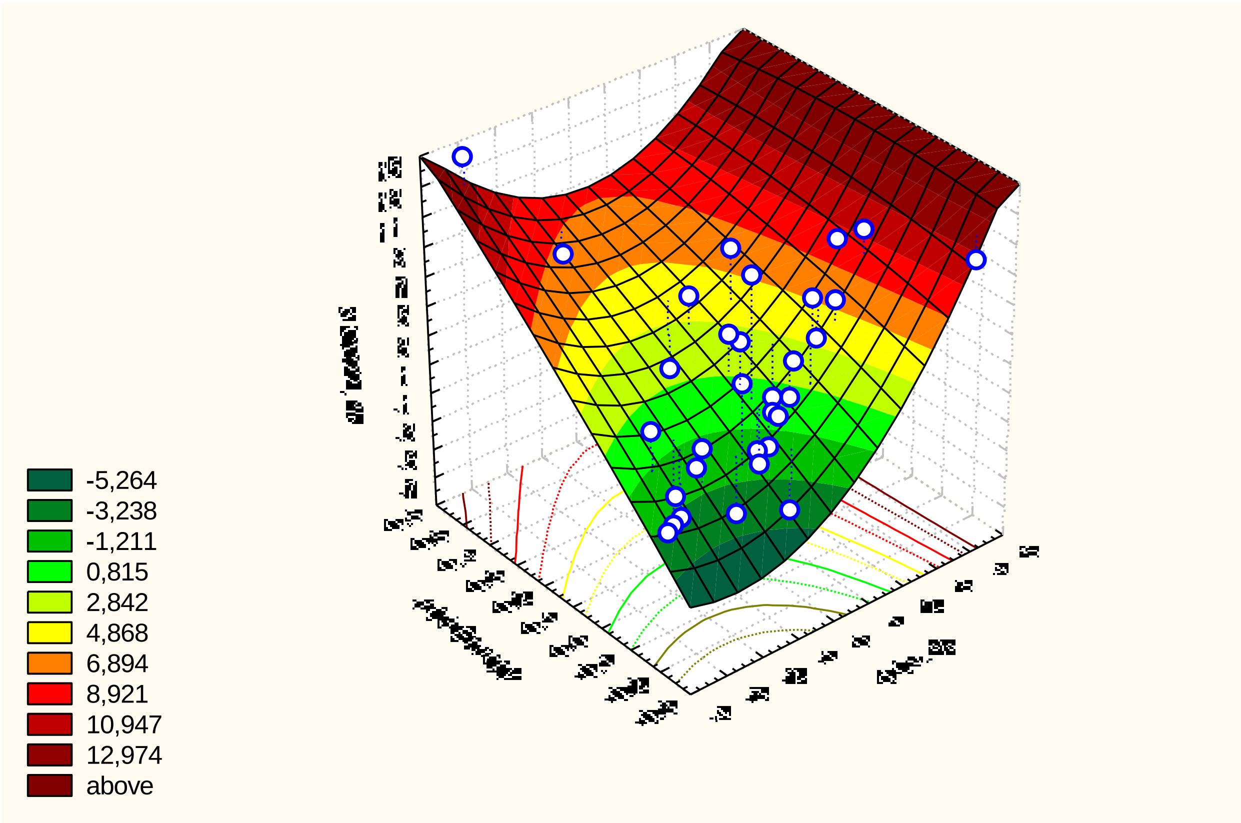
Figure 1. Canonical correlation between changes in parameters of HRV and EEG (line X) and blood $CD22^+$ B-lymphocytes level (line Y)

Among mentioned parameters HRV and EEG a regression model with stepwise exclusion included the following 9 only (Table 2).

Table 2. Regression Summary for Dependent Variable: change in CD22 B-Lymphocytes $R=0,893$; $R^2=0,798$; Adjusted $R^2=0,727$; $F_{(8,2)}=11,3$; $p<10^{-5}$; SE of estimate: 3,0%

		Beta	St. Err. of Beta	B	St. Err. of B	n=32 $t_{(23)}$	p-level
Change in Variables	r		Intercpt	1,855	,570	3,25	,004
Cv HRV, %	**0,41**	,279	,102	,891	,325	2,74	,012
C3 Entropy	**0,36**	,375	,109	12,47	3,63	3,43	,002
α-Rhythm Deviation, Hz	**0,36**	,296	,097	2,748	,903	3,04	,006
T3-θ SPD, %	**0,31**	,378	,108	,444	,127	3,50	,002
F4-β SPD, $\mu V^2/Hz$	**0,30**	,206	,097	,035	,016	2,13	,044
β-Rhythm Index, %	**-0,27**	-,317	,101	-,104	,033	-3,14	,005
T5-θ SPD, %	**-0,25**	-,459	,101	-,454	,100	-4,54	,0001
θ-Rhythm Frequency, Hz	**-0,24**	-,263	,101	-,932	,359	-2,60	,016

Fig. 2 visualizes the dependence of changes in the level of B-lymphocytes on changes in the tone of the Vagus and the Entropy of the rhythms in the locus C3.



dCD22 (%)=1,71+1,55•dCv(%)+14,8•dC3h

R=0,599; R^2=0,359; Adjusted R^2=0,314; $F_{(2,3)}$=8,1; p=0,002; SE of estimate: 4,8%

Figure 2. Interrelations between changes in coefficient of variation HRV (line X), rhythms entropy in locus C3 (line Y) and $CD22^+$ B-lymphocytes blood level (line Z)

Factor structure of canonical Roots representing Neural parameters and IgM serum level (Table 3) testifies that the latter **downregulated** by parasympathetic outflows as well as α- and θ-rhythm generating structures that are projected onto the left anterior temporalis locus as well as β-rhythm generating structures projected onto left posterior temporalis locus and α-rhythm generating structures projected onto right posterior temporalis locus, which all probably reflectes the amygdala [27], while **upregulated** by sympathetic outflows and θ-rhythm generating structures that are projected onto the 12 loci.

In addition, inhibiting effect makes Entropy of bands HRV, while stimulating effect makes Entropy of the rhythms in 7 loci.

In total, changes in the nervous regulation determine changes in the level of IgM by 97,2% (Fig. 3).

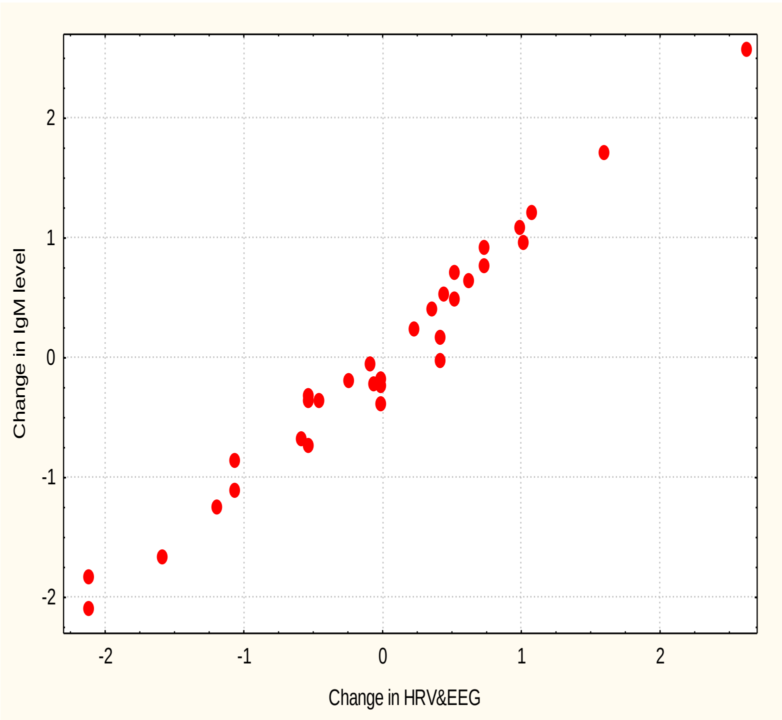
Table 3. Factor structure of canonical Roots representing Neural parameters and IgM level

Right set	R
ULF HRV SPD, ms^2	**,539**
ULF HRV SPD, %	**,463**
HRV SPD Entropy	**,355**
MxDMn HRV, ms	**,306**
LF HRV SPD, %	**-,293**
T3-α SPD, %	**,354**
T3-α SPD, $\mu V^2/Hz$	**,341**
T3-θ SPD, $\mu V^2/Hz$	**,311**
T5-β SPD, $\mu V^2/Hz$	**,340**
T6-α SPD, $\mu V^2/Hz$	**,327**
F3-θ SPD, %	**-,477**
Fp2-θ SPD, %	**-,469**
T5-θ SPD, %	**-,433**
F4-θ SPD, %	**-,422**
O1-θ SPD, %	**-,409**
F8-θ SPD, %	**-,390**
C4-θ SPD, %	**-,367**
C3-θ SPD, %	**-,363**
P4-θ SPD, %	**-,348**
F7-θ SPD, %	**-,340**
T6-θ SPD, %	**-,332**
T4-θ SPD, %	**-,313**
Fp1 Entropy	**-,345**
P4 Entropy	**-,331**
F4 Entropy	**-,329**
F3 Entropy	**-,431**
C3 Entropy	**-,397**
F7 Entropy	**-,381**
Fp2 Entropy	**-,373**
Left set	R
IgM	**-1**

Among mentioned parameters HRV and EEG a regression model with stepwise exclusion included 12 only (Table 4).

Table 4. Regression Summary for Dependent Variable: change in IgM serum level $R=0,848$; $R^2=0,719$; Adjusted $R^2=0,541$; $F_{(12)}=4,0$; $p=0,003$; SE of estimate: 0,26 g/l

		Beta	St. Err. of Beta	B	St. Err. of B	n=32 $t_{(19)}$	p-level
Change in Variables	r		Intercpt	,0438	,0596	0,73	,471
ULF HRV, ms^2	**-0,53**	-,304	,165	-,0006	,0003	-1,84	,081
T6-α SPD, $\mu V^2/Hz$	**-0,32**	-,594	,293	-,0017	,0008	-2,02	,057
T5-α SPD, $\mu V^2/Hz$	**-0,30**	-,407	,319	-,0010	,0008	-1,28	,217
Fp2-α SPD, $\mu V^2/Hz$	**-0,26**	,587	,358	,0024	,0014	1,64	,117
F3-θ SPD, %	**0,47**	,228	,236	,0089	,0092	0,97	,346
F3 Entropy	**0,43**	,250	,221	,6789	,5995	1,13	,272
O1-θ SPD, %	**0,40**	,376	,148	,0314	,0124	2,54	,020
F8-θ SPD, %	**0,39**	,418	,223	,0211	,0113	1,87	,077
C4-θ SPD, %	**0,36**	-,441	,245	-,0241	,0133	-1,80	,087
T6 Entropy	**0,31**	-,306	,208	-,5834	,3969	-1,47	,158
δ-Rhythm Laterality, %	**0,30**	,259	,142	,0016	,0009	1,83	,083
LF HRV SPD, %	**0,29**	,172	,147	,0047	,0040	1,17	,255



$R=0,986$; $R^2=0,972$; $\chi^2_{(29)}=56$; $p=0,002$; Λ Prime=0,028

Figure 3. Canonical correlation between changes in parameters of HRV and EEG (line X) and serum IgM level (line Y)

In Fig. 4-6, the closest partial neuro-immune interrelations are visualized.

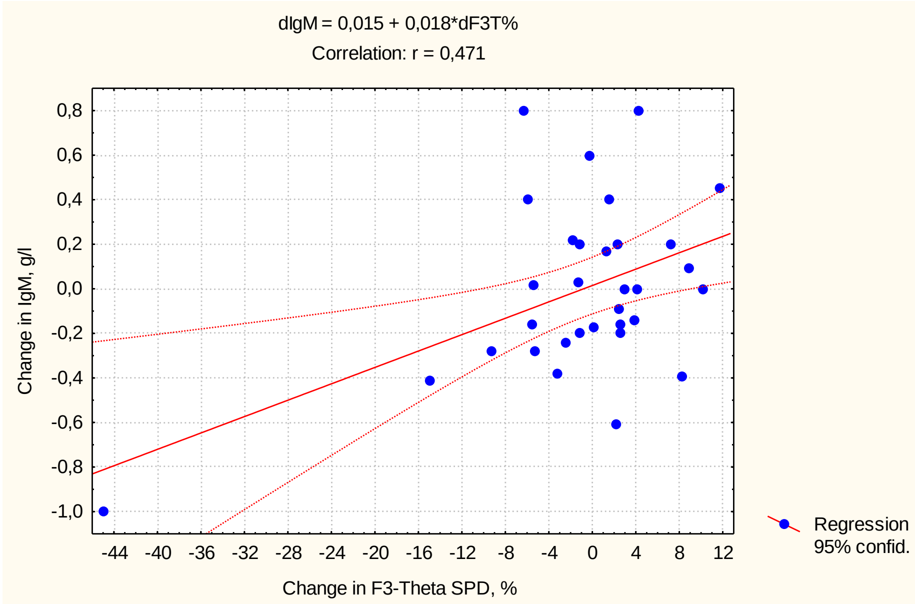
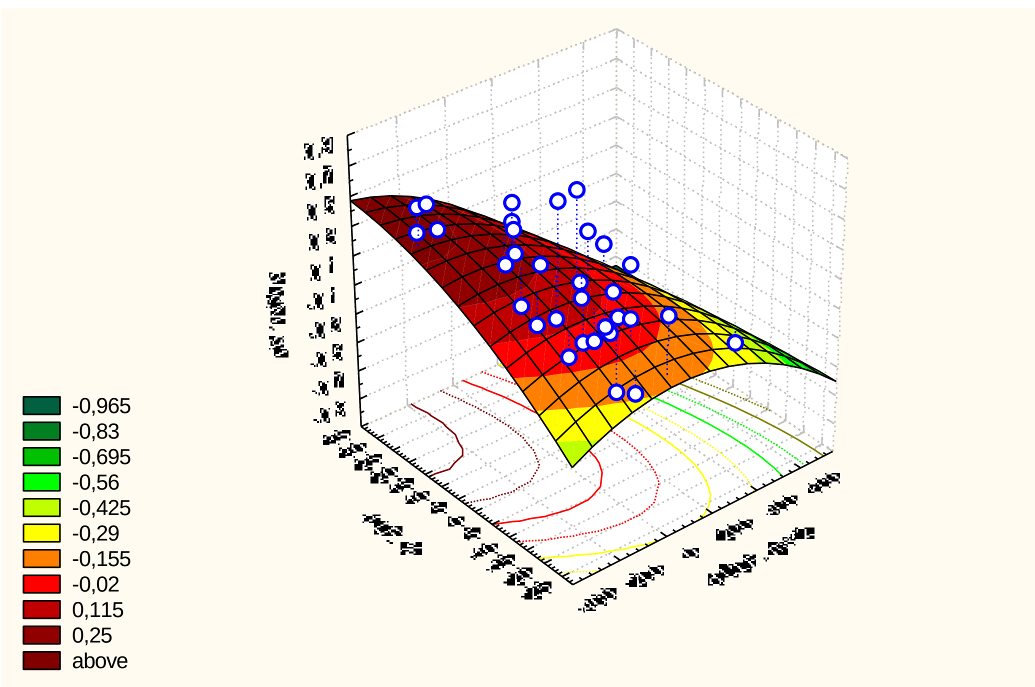
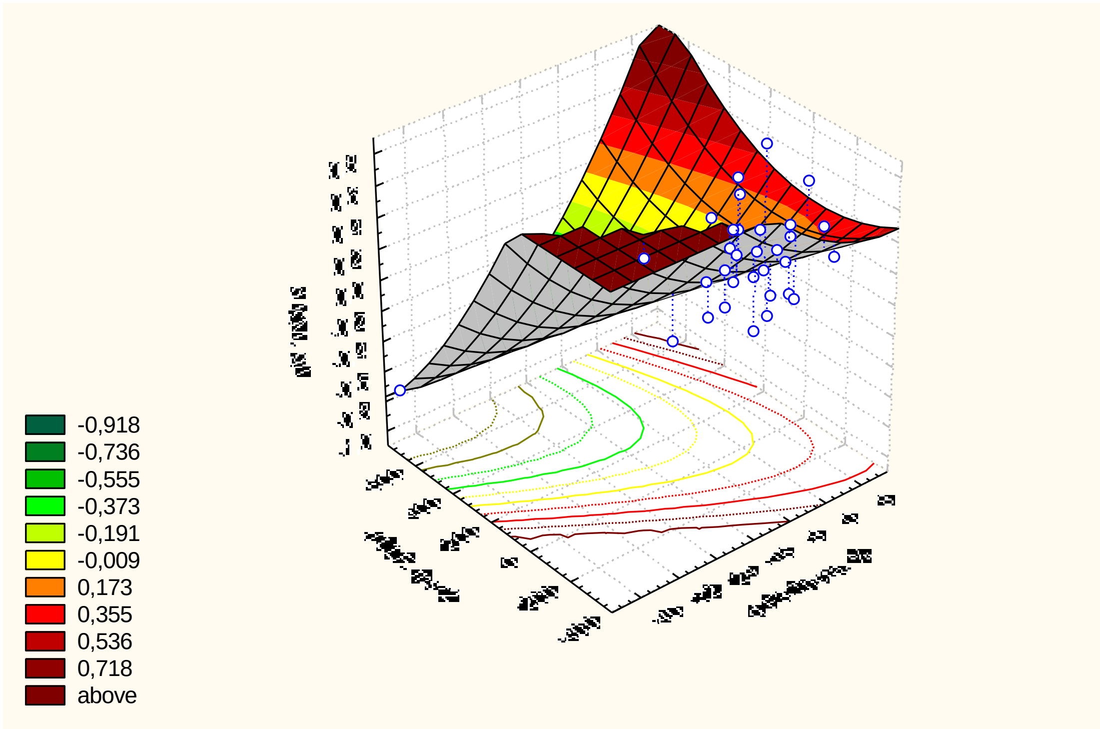


Figure 4. **Relationship between changes in relative SPD of θ-rhythm in locus F3 (line X) and serum IgM level (line Y)**



dIgM(g/l)=-0,006-0,001•dULF(ms^2)+0,005•dLF(%)
R=0,558; R^2=0,349; Adjusted R^2=0,280; $F_{(2,3)}$=6,5; p=0,005; SE of estimate: 0,33 g/l

Figure 5. Interrelations between changes in absolute SPD ULF band HRV (line X), relative SPD LF band HRV (line Y) and serum IgM level (line Z)



dIgM(g/l)=0,010+0,0097•dF3-θ(%)-0,0008•dULF(ms^2)

R=0,569; R^2=0,323; Adjusted R^2=0,277; $F_{(2,3)}$=6,9; p=0,003; SE of estimate: 0,33 g/l

Figure 6. Interrelations between changes in relative SPD θ-Rhythm in locus F3 (line X), absolute SPD ULF band HRV (line Y) and serum IgM level (line Z)

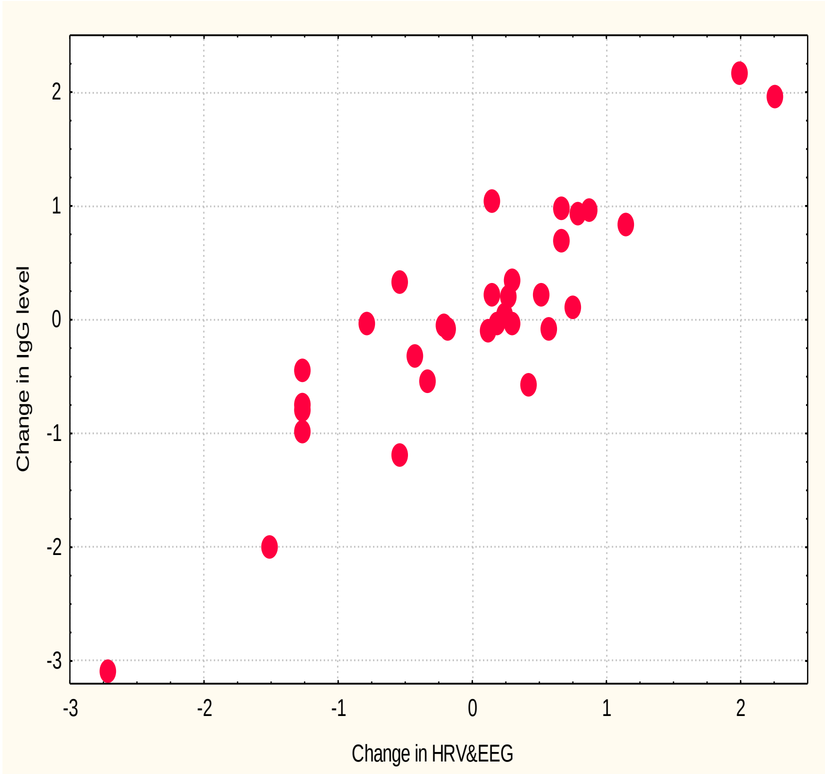
Serum level of IgG **downregulated** by parasympathetic outflows, while **upregulated** by sympathetic outflows.

Table 5. Factor structure of canonical Roots representing Neural parameters and IgG serum level

Right set	R
Moda HRV, ms	**,310**
HR, beats/min	**-,300**
HF HRV SPD, %	**,304**
AMo/Mo HRV, units	**-,291**
θ-Rhythm Index, %	**,680**
β-Rhythm Frequency, Hz	**,502**
δ-Rhythm Deviation, Hz	**,389**
α-Rhythm Frequency, Hz	**,338**
C4 Entropy	**,361**
O1 Entropy	**,342**
T5 Entropy	**,301**
T6 Entropy	**,290**
O2-δ SPD, $\mu V^2/Hz$	**-,462**
F8-δ SPD, $\mu V^2/Hz$	**-,341**
δ-Rhythm Asymmetry, %	**-,301**
C3 α SPD, %	**-,378**
Left set	R
IgG	**-1**

In addition, a decrease in IgG levels is associated with an increase in θ-rhythm Index, α- and β-rhythms Frequency and δ-rhythm Deviation as well as in Entropy of relative SPD of rhythms in loci C4, O1, T5 and T6. In return, a increase in IgG levels is associated with an decrease in δ-rhythm Asymmetry and SPD δ-rhythm generating structures that are projected onto the loci O2 and F8 as well as α-rhythm generating structures onto locus C3.

Changes in the nervous regulation determine changes in the level of IgG by 80,0% (Fig. 7).



$R=0,894$; $R^2=0,800$; $\chi^2_{(16)}=35$; $p=0,004$; Λ Prime=0,200

Figure 7. Canonical correlation between changes in parameters of HRV and EEG (line X) and serum IgG level (line Y)

Among mentioned parameters HRV and EEG a regression model with stepwise exclusion included 10 only (Table 6).

Table 6. Regression Summary for Dependent Variable: change in IgG serum level
$R=0,876$; $R^2=0,767$; Adjusted $R^2=0,656$; $F_{(10,2)}=6,9$; $p=10^{-4}$; SE of estimate: 1,98 g/l

		Beta	St. Err. of Beta	B	St. Err. of B	n=32 $t_{(21)}$	p-level
Change in Variables	r		Intercpt	,118	,435	0,27	,789
θ-Rhythm Index, %	**-0,61**	-,301	,134	-,023	,010	-2,25	,035
β-Rhythm Frequency, Hz	**-0,45**	-,360	,130	-,220	,079	-2,77	,012
δ-Rhythm Deviation, Hz	**-0,35**	-,178	,135	-1,510	1,143	-1,32	,201
HF HRV SPD, %	**-0,27**	-,319	,117	-,132	,048	-2,73	,013
T5 Entropy	**-0,27**	,248	,189	3,823	2,901	1,32	,202
T6 Entropy	**-0,26**	,266	,159	4,435	2,655	1,67	,110
O2-δ SPD, $\mu V^2/Hz$	**0,41**	1,155	,382	,0031	,0010	3,02	,006
C3 α SPD, %	**0,34**	,136	,118	,037	,032	1,16	,260
F8-δ SPD, $\mu V^2/Hz$	**0,31**	-,737	,306	-,0044	,0018	-2,41	,025
δ-Rhythm Asymmetry, %	**0,27**	,413	,126	,043	,013	3,28	,004

The most noticeable modulates the level of IgG Index of θ-rhythm (Fig. 8).

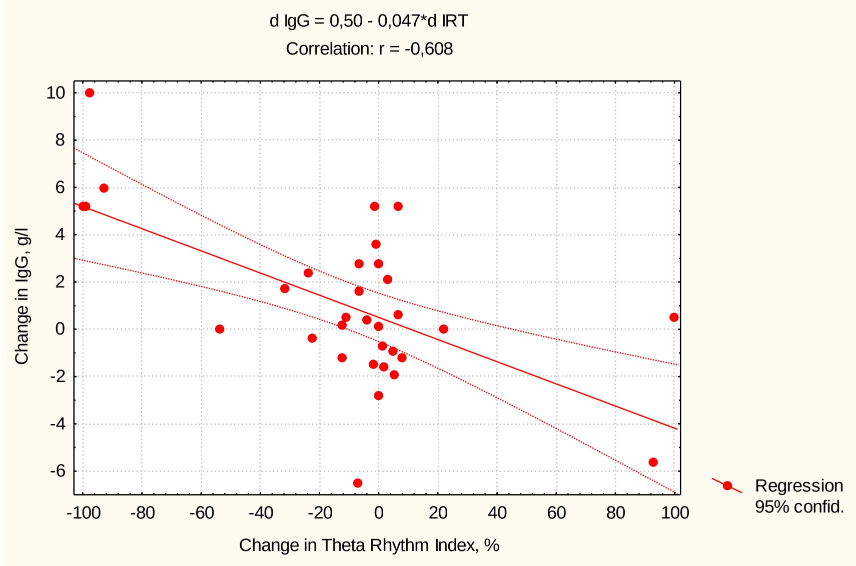


Figure 8. **Relationship between changes in θ-rhythm index (line X) and serum IgG level (line Y)**

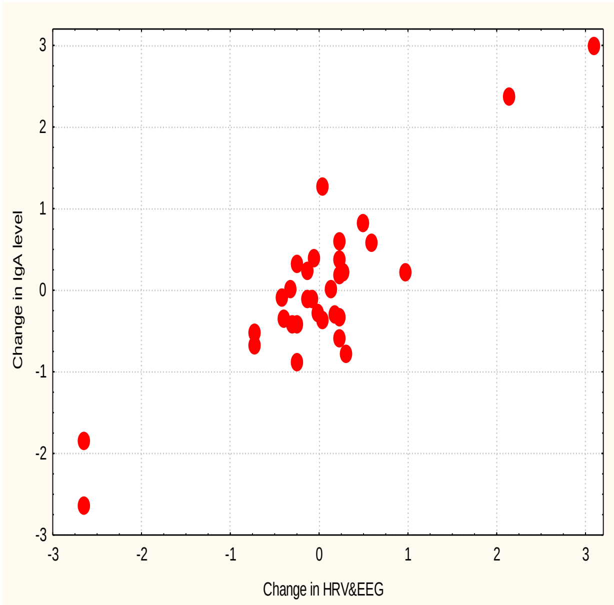
Factor structure of canonical Roots representing Neural parameters and IgA serum level (Table 7) testifies that the latter **upregulated** by parasympathetic outflows as well as δ-rhythm generating structures that are projected onto the left frontalis lateralis and temporalis posterior loci as well as α-rhythm generating structures are projected onto left temporalis anterior and centralis loci, and Index of β-rhythm.

Table 7. Factor structure of canonical Roots representing Neural parameters and IgA level

Right set	**R**
ULF HRV SPD, ms^2	**-,550**
F7-δ SPD, $\mu V^2/Hz$	**-,495**
T5-δ SPD, $\mu V^2/Hz$	**-,492**
T3-α SPD, %	**-,421**
C3-α SPD, %	**-,402**
β-Rhythm Index, %	**-,391**
θ-Rhythm Index, %	**,514**
T5-θ SPD, %	**,533**
F7-θ SPD, %	**,464**
Fp2-θ SPD, %	**,452**
F3-θ SPD, %	**,416**
F8-θ SPD, %	**,416**
F4-θ SPD, %	**,414**
T5 Entropy	**,625**
F7 Entropy	**,571**
T6 Entropy	**,529**
O1 Entropy	**,519**
Fp2 Entropy	**,472**
F8 Entropy	**,466**
Left set	**R**
IgA	**-1**

Instead, a **decrease** in IgA level is associated with an **increase** in the θ-rhythm Index and its SPD in 6 loci as well as in Entropy of relative SPS of rhythms in 6 loci.

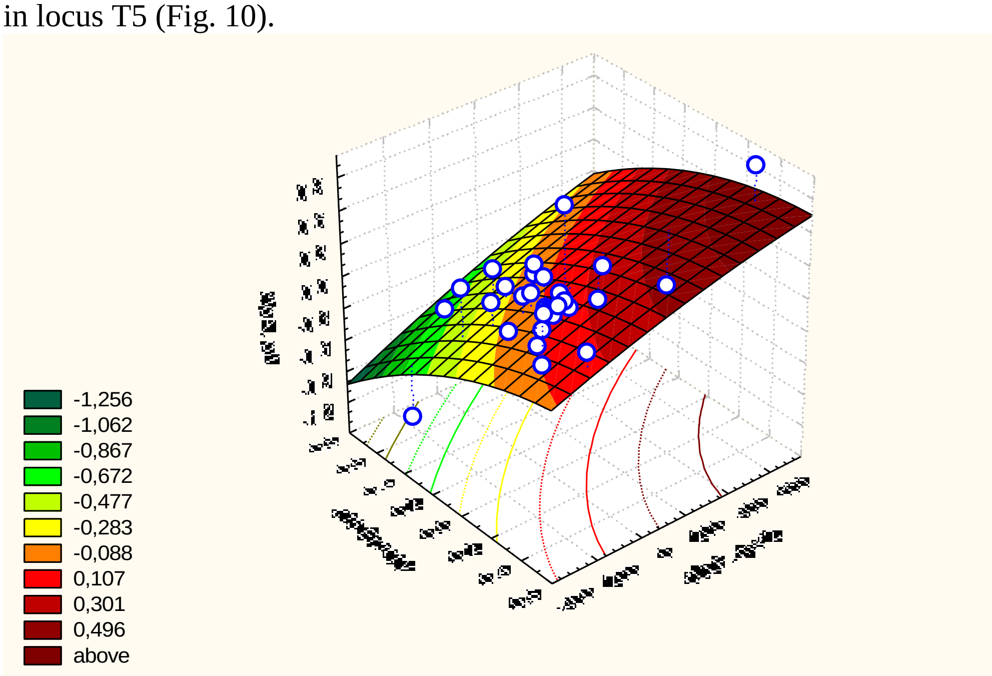
In total, changes in the nervous regulation determine changes in the level of IgA by 79,1% (Fig. 9).



$R=0{,}889$; $R^2=0{,}791$; $\chi^2_{(19)}=32$; $p=0{,}031$; Λ Prime=0,209

Figure 9. Canonical correlation between changes in parameters of HRV and EEG (line X) and serum IgA level (line Y)

The IgA level is most modulated by SPD ULF band HRV and Entropy PSD of rhythms EEG in locus T5 (Fig. 10).



dIgA(g/l)=-0,080+0,0008•dULF(ms^2)-0,873•dT5 entropy

$R=0{,}651$; $R^2=0{,}424$; Adjusted $R^2=0{,}384$; $F_{(2,3)}=10{,}7$; $p<10^{-3}$; SE of estimate: 0,33 g/l

Figure 10. Interrelations between changes in absolute SPD ULF band HRV (line X), rhythms entropy in locus T5 (line Y) and serum IgA level (line Z)

Among mentioned parameters HRV and EEG a regression model with stepwise exclusion included 9 only (Table 8).

Table 8. Regression Summary for Dependent Variable: change in IgA serum level $R=0,876$; $R^2=0,768$; Adjusted $R^2=0,673$; $F_{(9,2)}=8,1$; $p<10^{-4}$; SE of estimate: 0,24 g/l

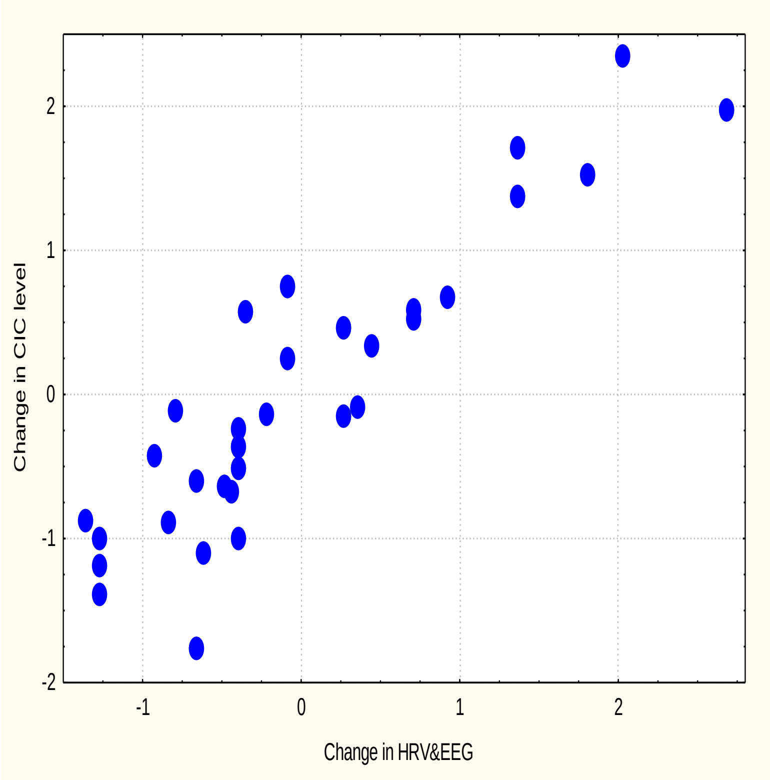
		Beta	St. Err. of Beta	B	St. Err. of B	n=32 $t_{(22)}$	p-level
Change in Variables	r		Intercpt	-,0826	,0486	-1,70	,103
F7 Entropy	**-0,51**	,473	,209	,9832	,4344	2,26	,034
O1 Entropy	**-0,46**	-,175	,137	-,3670	,2860	-1,28	,213
θ-Rhythm Index, %	**-0,46**	-,453	,121	-,0044	,0012	-3,74	,001
F7-θ SPD, %	**-0,41**	-,699	,186	-,0586	,0156	-3,76	,001
F8-θ SPD, %	**-0,37**	,193	,138	,0107	,0077	1,40	,176
ULF HRV SPD, ms^2	**0,49**	,391	,122	,0009	,0003	3,20	,004
T3-α SPD, %	**0,37**	,273	,117	,0065	,0028	2,33	,029
β-Rhythm Index, %	**0,35**	,416	,141	,0099	,0033	2,96	,007
VLF HRV SPD, %	**0,28**	,232	,122	,0057	,0030	1,90	,071

The last among the registered parameters of humoral immunity - circulating immune complexes – **downregulated** by sympathetic outflows as well as β-rhythm generating structures are projected onto right parietalis and left frontalis anterior and medialis loci as well as δ-rhythm generating structures are projected onto right temporalis anterior locus, while **upregulated** by parasympathetic outflows as well as θ- and α-rhythm generating structures are projected onto various loci (Table 9).

Table 9. Factor structure of canonical Roots representing Neural parameters and CIC serum level

Right set	**R**
$(MxDMn \cdot Mo)^{-1}$ HRV, units	**,377**
LF HRV SPD, %	**,361**
Heart Rate, beats/min	**,336**
Bayevskiy ARS Index, units	**,328**
Bayevskiy Stress Index, ln	**,321**
β-Rhythm Frequency, Hz	**,346**
P4-β SPD, %	**,318**
Fp1-β SPD, %	**,313**
F3-β SPD, %	**,297**
δ-Rhythm Laterality, %	**,343**
T4-δ SPD, %	**,338**
MxDMn HRV, ms	**-,332**
pNN_{50}, HRV, %	**-,302**
T3-θ SPD, %	**-,430**
T6-θ SPD, %	**-,307**
T4-α SPD, %	**-,403**
Fp2-α SPD, %	**-,386**
T3-α SPD, %	**-,338**
F8-α SPD, %	**-,323**
C3-α SPD, %	**-,315**
Left set	**R**
CIC	**-1**

In total, changes in the nervous regulation determine changes in the level of CIC by 82,1% (Fig. 11).



R=0,906; R^2=0,821; $\chi^2_{(20)}$=34; p=0,023; Λ Prime=0,179

Figure 11. Canonical correlation between changes in parameters of HRV and EEG (line X) and serum CIC level (line Y)

Among mentioned parameters HRV and EEG a regression model with stepwise exclusion included 7 only (Table 10).

Table 10. Regression Summary for Dependent Variable: change in CIC serum level R=0,811; R^2=0,658; Adjusted R^2=0,559; $F_{(7,2)}$=6,6; $p<10^{-3}$; SE of estimate: 15 units

		Beta	St. Err. of Beta	B	St. Err. of B	n=32 $t_{(24)}$	p-level
Change in Variables	r		Intercpt	-,970	2,87	-0,34	,738
T3-θ SPD, %	**0,39**	,444	,140	2,064	,651	3,17	,004
T4-α SPD, %	**0,36**	-,329	,187	-,599	,341	-1,76	,092
MxDMn HRV, ms	**0,30**	,267	,133	,094	,047	2,01	,056
C3-α SPD, %	**0,29**	,354	,143	,656	,265	2,48	,021
F8-α SPD, %	**0,29**	,564	,173	,817	,251	3,26	,003
δ-Rhythm Laterality, %	**-0,31**	-,211	,130	-,078	,048	-1,63	,116
P4-β, %	**-0,29**	-,671	,141	-1,418	,298	-4,76	,0001

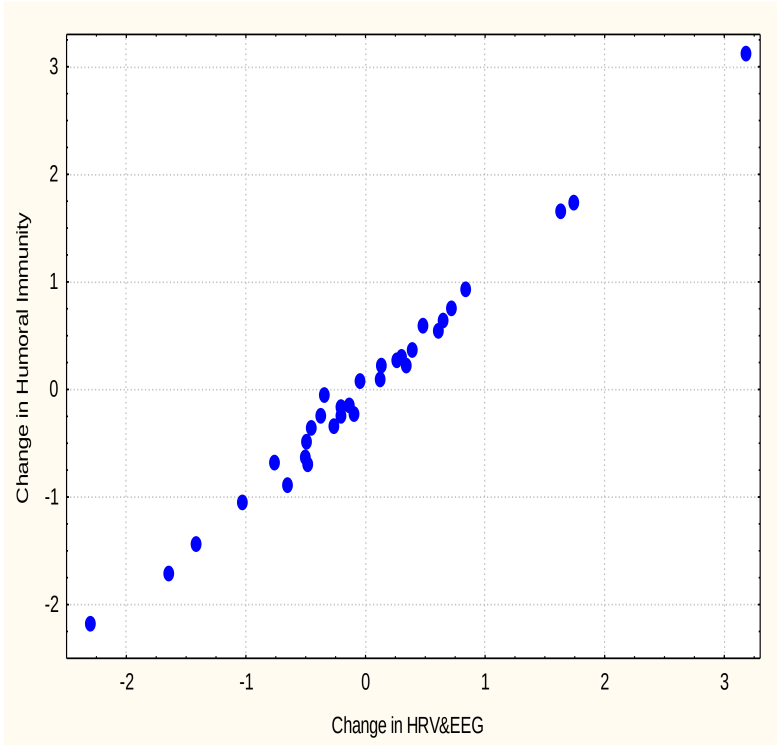
At the final stage, we analyzed the canonical correlation between changes in the parameters of the nerve regulation, on the one hand, and humoral immunity - on the other hand. The program identified two pairs of canonical roots (Table 11).

Table 11. Factor structure of canonical Roots representing Neural and Humoral Immune parameters

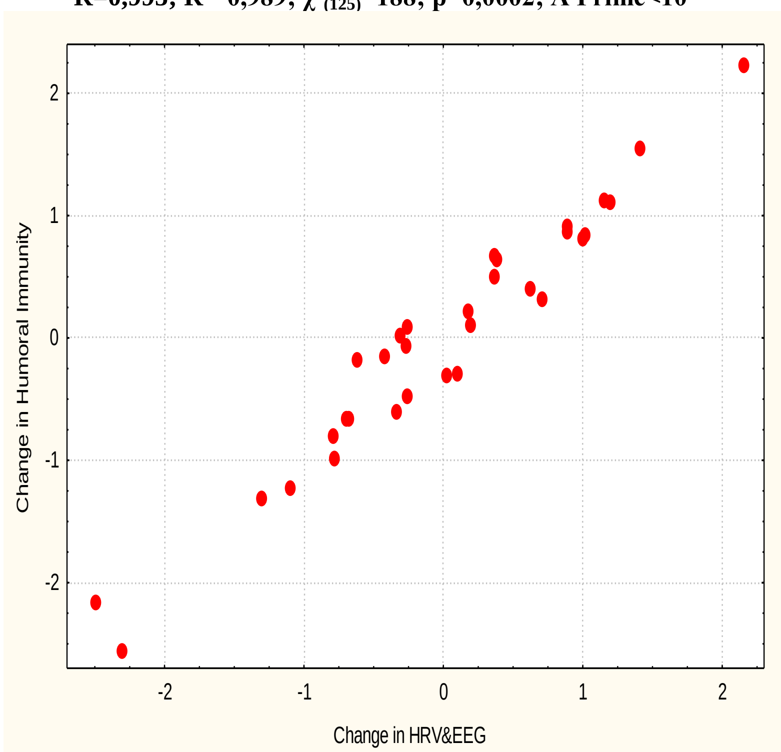
Right set	Root 1	Root 2
T5-θ SPD, %	**-,543**	-,292
F3-θ SPD, %	**-,525**	-,248
F7-θ SPD, %	**-,516**	-,168
F4-θ SPD, %	**-,465**	-,238
Fp2-θ SPD, %	**-,451**	-,341
F7 Entropy	**-,340**	-,341
AMo HRV, %	**-,206**	,167
ULF HRV SPD, ms^2	**,508**	,319
SDNN HRV, ms	**,234**	-,024
VLF HRV SPD, ms^2	**,140**	,093
O2-β SPD, %	**,451**	,072
O2-δ SPD, $\mu V^2/Hz$	-,062	**,318**
F7-δ SPD, $\mu V^2/Hz$	-,016	**,115**
β-Rhythm Frequency, Hz	,206	**-,541**
θ-Rhythm Index, %	,312	**-,443**
F8-θ SPD, %	-,226	**-,467**
O1-θ SPD, %	-,192	**-,315**
Fp2 Entropy	-,247	**-,481**
T6 Entropy	-,257	**-,440**
F3 Entropy	-,209	**-,432**
O1 Entropy	-,107	**-,381**
C3 Entropy	-,063	**-,371**
T5 Entropy	-,169	**-,323**
Left set	Root 1	Root 2
CD22	**,572**	,005
IgM	**-,559**	-,529
CIC	**-,314**	,284
IgG	-,468	**,685**
IgA	,170	**,475**

The neural root of the first pair receives **negative** factor loads from the relative SPD of θ-rhythm, which generates structures that are projected onto the left temporalis posterior, frontalis medialis and lateralis as well as right frontalis medialis and anterior loci as well as from sympathetic tone. Instead, **positive** factor loadings give a vagal tone and β-rhythm generating structures are projected onto right occipital locus. The immune root of the first pair receives positive factor loadings from the B-lymphocytes level, while negative loadings from IgM, CIC as well as IgG levels. Canonical correlation is very strong (Fig. 12, above).

The neural root of the second pair receives **positive** factor loadings from the δ-rhythm generating structures are projected onto right occipitalis and left frontalis lateralis loci while **negative** factor loads from the θ-rhythm generating structures that are projected onto the right frontalis lateralis and left occipitalis loci as well as from Index of θ-rhythm, Frequency of β-rhythm and Entropy of relative SPD of rhythms in various loci. The immune root of the second pair receives positive factor loadings from the IgG and IgA as well as CIC levels, while negative loadings from IgM level. Canonical correlation is very strong too (Fig. 12, below).



R=0,995; R^2=0,989; $\chi^2_{(125)}$=188; p=0,0002; Λ Prime<10^{-5}



R=0,974; R^2=0,949; $\chi^2_{(96)}$=118; p=0,066; Λ Prime=0,0005

Figure 12. Canonical correlation between changes in parameters of HRV and EEG (line X) and humoral Immunity (line Y). First (above) and second (below) pair of canonical roots

Discussion of the results we will carry out in the following article together with data on neural regulation of cellular immunity.

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ACCORDANCE TO ETHICS STANDARDS

Tests in patients are conducted in accordance with positions of Helsinki Declaration 1975, revised and complemented in 2002, and directive of National Committee on ethics of scientific researches. During realization of tests from all participants the informed consent is got and used all measures for providing of anonymity of participants.

For all authors any conflict of interests is absent.

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