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NEURO-IMMUNE RELATIONSHIPS AT PATIENTS WITH CHRONIC PYELONEPHRITE AND CHOLECYSTITE. Communication 3. CORRELATIONS BETWEEN PARAMETERS EEG, HRV AND IMMUNOGRAM

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Abstracts

Background. The immunological homunculus conception considers somatotopic organization to CNS regulation of immune system. We set a goal to analyze the causal relationships between parameters of EEG and HRV, on the one hand, and the parameters of immunity, on the other hand. **Methods.** In basal conditions in 23 men with chronic pyelonephrite and cholecystite in remission, we recorded EEG ("NeuroCom Standard") and HRV ("Cardiolab+VSR"). In blood estimated routine parameters of Immunity on a set of I and II levels recommended by the WHO. **Results.** Maximal coefficient canonical correlation (R) parameters of EEG and HRV detected with relative level $CD22^+$ B-Lymphocytes: 0,94 ($p<10^{-4}$), maximal relationships take place with Spectral Power Density (SPD) absolute (a) Fp1-α (r=-0,64) and relative (r) PSD Fp1-β (r=0,60). R with serum level IgM takes 0,90 ($p<10^{-4}$), maximal relationships with rSPD O1-θ (r=0,60) and rHF HRV (r=0,52), with serum level IgG takes 0,86 ($p<10^{-3}$), maximum with rSPD of β-rhythm in loci T6, O1 and O2 (r for all makes 0,40), with serum level IgA takes 0,84 ($p<10^{-4}$), maximum with Asymmetry of δ-rhythm (r=0,59) and aSPD T4-θ (r=-0,50) as well as with Circulating Immune Complexes: R=0,84 ($p<10^{-4}$), maximum with Bayevskiy's Stress Index HRV (r=0,45) and rSPD T3-α (r=0,39). R with relative level $CD8^+$ T-Lymphocytes makes 0,81 ($p<10^{-4}$), maximal relationships take place with aSPD of α-rhythm in loci P4 (r=-0,38) and P3 (r=-0,31) as well as with rVLF HRV (r=-0,29). R with relative level $CD4^+$ T-Lymphocytes makes 0,79 ($p<10^{-3}$), maximum with aSPD of β-rhythm in loci F4 (r=0,40) and T3 (r=0,39). R with level $CD16^+$ NK-Lymphocytes makes 0,71 (p=0,009), maximal relationships take place with Index of α-rhythm (r=-0,36) and Entropy SPD in locus C3. Minimal R detected with level "active" T-

Lymphocytes: 0,57 (p=0,029). **Conclusion.** Take place neuro-immune causal relationships in bounds of immunological homunculus conception.
Keywords: HRV, EEG, T-, NK-, B-Lymphocytes, Immunoglobulines M,G,A, Circulating immune complexes, correlations.

INRODUCTION

Previously, we [8-11,15,16] have shown within the immunological homunculus conception [17] that blood level of Leukocytes and parameters of Leukocytogram as well as Neutrophils phagocytic function subordinate modulation central and autonomic nervous systems. Revealed that canonical correlation between constellation EEG and HRV parameters form with blood level of Leukocytes 0,92 ($p<10^{-5}$), with relative content in Leukocytogram Stubnucleary Neutrophiles 0,93 ($p<10^{-5}$), Segmentonucleary Neutrophiles 0,89 ($p<10^{-3}$), Eosinophiles 0,87 (p=0,003), Lymphocytes 0,77 ($p<10^{-3}$) and with Monocytes 0,75 (p=0,003). Canonical correlation with Phagocytic Index form 0,94 and 0,93 for E. coli and Staph. aureus respectively. However neural regulation Killing Index as well as Microbial Count significantly distinguished for Gram-negative and Gram-positive Bacterias: R form 0,99 and 0,84 versus 0,66 and 0,69 respectively. Integrated parameter Bactericidity Capacity of blood Neutrophils correlated with EEG and HRV parameters equally: R makes 0,89 and 0,93 respectively. In this study we set a goal to analyze the causal relationships between 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 23 men aged 24-70 (mean 49,1±2,5) years old, who came to the spa Truskavets' (Ukraine) for the treatment of chronic pyelonephritis combined with cholecystitis in remission. The survey was conducted, as a rule, twice, before and after balneotherapy.

We recorded electrocardiogram in II lead to assess the parameters of HRV [1-3] (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), moda (Mo), the amplitude of moda (AMo), variational sweep (MxDMn). 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] both in supine and orthostatic positions.

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 (%) and absolute (μV^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 [13]:

LI, % = Σ [200•(Right – Left)/(Right + Left)]/8

We calculated also for each locus the Entropy (h) of normalized SPD using formula C Shannon [cit. by: 14]:

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

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 [12]. 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) [12].

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

RESULTS

Let's start with the analysis of parameters of humoral immunity. Screening of blood level B-Lymphocytes found their downregulation by Stress Index (SI) in supine position while upregulation by Vegetative Reactivity as (supine SI/orthostatic SI) ratio as well as by HRV markers of Vagal tone (Table 1). In general, the autonomic determination makes only 23%.

Table 1. Regression Summary for Dependent Variable: CD22 B-Lymphocytes, Independent Variables: parameters of HRV

R=0,617; R^2=0,381; Adjusted R^2=0,230; $F_{(8,3)}$=2,5; p=0,028; Std. Error of estimate: 4,4%

		Beta	St. Err. of Beta	B	St. Err. of B	n=37 $t_{(33)}$	p-level
Independent Variables	r		Intercpt	45,4	9,8	4,63	10^{-4}
BSI(s), units	-0,30	-,845	,314	-,0271	,0101	-2,69	,011
BSI(s)/BSI(o)	0,36	,377	,188	1,367	,6801	2,01	,053
Cv, %	0,34	1,001	,398	2,693	1,072	2,51	,017
SDNN, msec	0,29	-2,461	1,144	-,6717	,3123	-2,15	,039
TP HRV, $msec^2$	0,29	2,399	1,002	,0064	,0027	2,39	,022
MxDMn, msec	0,26	-1,046	,431	-,0803	,0331	-2,43	,021
pNN_{50}, %	0,25	,984	,398	,3562	,1442	2,47	,019
HF, $msec^2$	0,23	-1,356	,513	-,0101	,0038	-2,65	,012

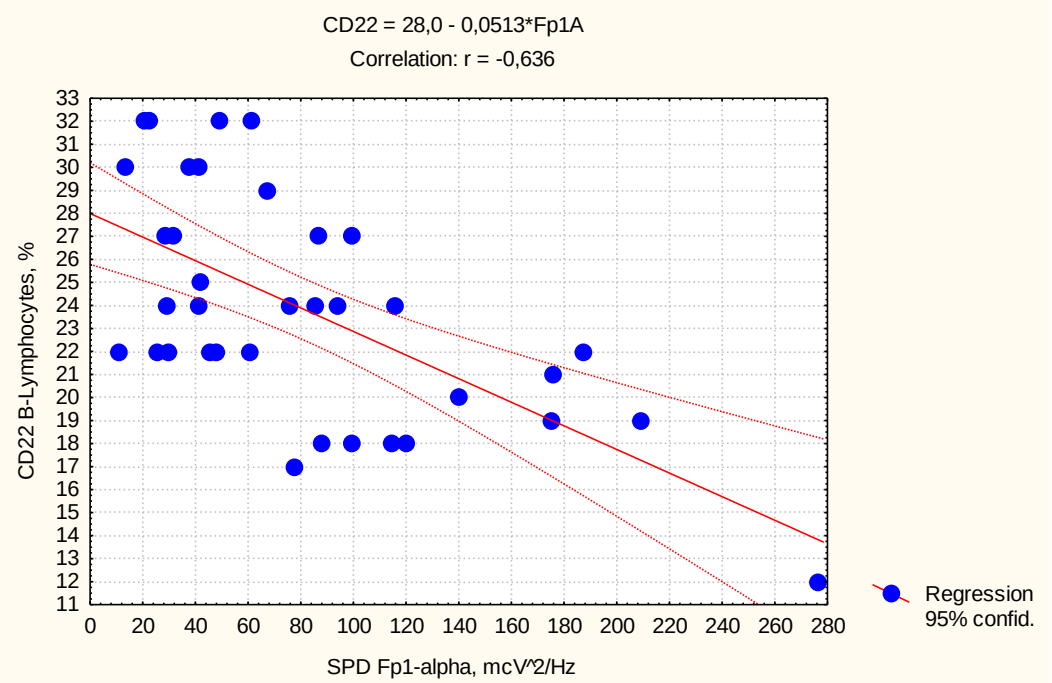

Fig. 1. Relationship between SPD Fp1-α (axis X) and blood level B-Lymphocytes (axis Y)

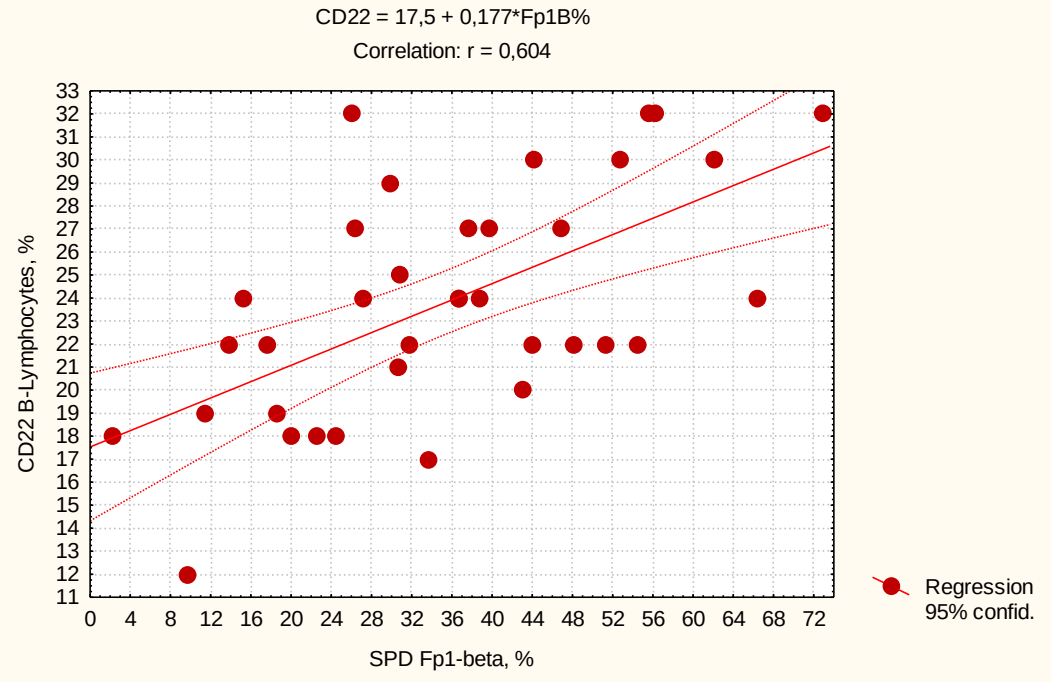

Fig. 2. Relationship between SPD Fp1-β (axis X) and blood level B-Lymphocytes (axis Y)

Much stronger influence on the blood level B-Lymphocytes causes neural structures that are projected on the locus Fp1. In particular, the structure generating α-Rhythm reduce it (Fig.1), whereas structure generating β-Rhythm increase it (Fig. 2).

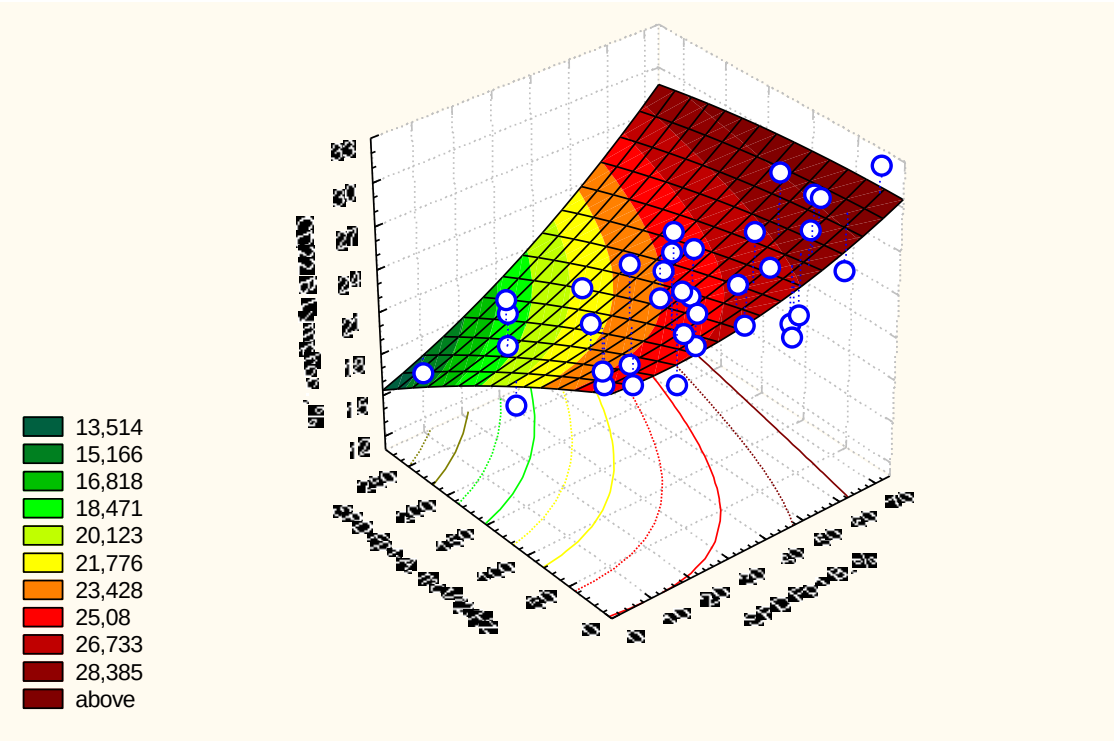

Fig. 3. Relationships between SPD Fp1-β (axis X), Fp1-α (axis Y) and blood level B-Lymphocytes (axis Z)

Taken together, these neural structures determine the blood level B-Lymphocytes to 43% (Fig. 3): R=0,679; R^2=0,462; Adjusted R^2=0,429; $F_{(2,3)}$=14,2; $p<10^{-4}$; Std. Error of estimate: 3,7%.

To a lesser extent correlated with blood level B-Lymphocytes SPD α- and β-Rhythm of neural structures projected on others loci. Taken together, these neural structures determine the blood level B-Lymphocytes on 77% (Table 2 and Fig. 4).

Table 2. Regression Summary for Dependent Variable: CD22 B-Lymphocytes, Independent Variables: parameters of EEG

R=0,936; R^2=0,877; Adjusted R^2=0,773; $F_{(16,2)}$=8,4; $\chi^2_{(16)}$=43,5; $p<10^{-4}$;
Std. Error of estimate: 2,4%

		Beta	St. Err. of Beta	B	St. Err. of B	n=36 $t_{(19)}$	p-level
Independent Variables	r		Intercpt	21,1	3,0	6,98	10^{-6}
Fp1-α, μV^2/Hz	-0,64	-3,565	,898	-,287	,072	-3,97	10^{-3}
F7-α, μV^2/Hz	-0,61	,517	,416	,075	,060	1,24	,229
Fp2-α, μV^2/Hz	-0,60	2,107	,743	,167	,059	2,84	,011
T6-α, μV^2/Hz	-0,57	-,728	,208	-,086	,025	-3,50	,002
C3-α, μV^2/Hz	-0,51	1,048	,376	,047	,017	2,79	,012
P3-α, μV^2/Hz	-0,50	1,047	,391	,022	,008	2,68	,015
F4-α, μV^2/Hz	-0,49	,439	,322	,029	,021	1,37	,188
T4-α, μV^2/Hz	-0,46	-1,273	,350	-,096	,026	-3,64	,002
T5-α, μV^2/Hz	-0,46	-,458	,252	-,041	,022	-1,82	,085
P4-α, μV^2/Hz	-0,42	,599	,274	,014	,006	2,19	,041
F8-α, μV^2/Hz	-0,39	,441	,227	,096	,050	1,94	,067
P3-δ, μV^2/Hz	-0,40	-,517	,159	-,035	,011	-3,26	,004
FP1-β, %	0,60	1,668	,307	,490	,090	5,43	10^{-4}
C3-β, %	0,48	,347	,235	,139	,094	1,47	,157
F3-β, %	0,43	-1,121	,275	-,396	,097	-4,08	10^{-3}
T6-β, %	0,42	-,560	,164	-,124	,036	-3,41	,003

On the other hand, found a negative correlation Moda HRV as Vagal tone marker with SPD T5-α (r=-0,44), P3-α (r=-0,37) and F8-α (r=-0,44). This casts suggested that downregulation blood level B-Lymphocytes by generating α-Rhythm neural structures is realized by downregulation activating influence of Parasympathetic nucleus of Brain Stem (probably Nucleus Ambiguous).

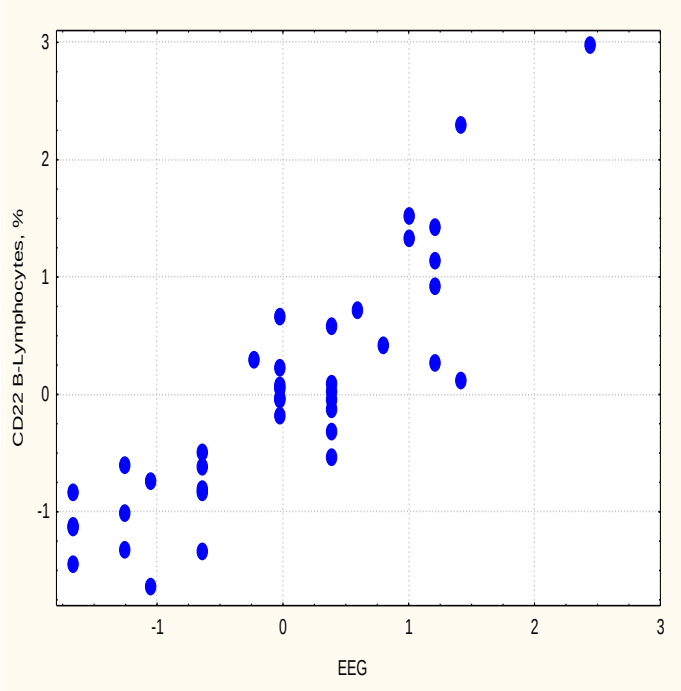

Fig. 4. Canonical correlation between parameters EEG (axis X) and blood level B-Lymphocytes (axis Y)

Serum level major fraction of Immunoglobulines IgG correlated negative with (VLF+LF)/HF ratio (r=-0,37) and LF/(LF+HF) ratio (r=-0,30) as HRV markers of sympathetic outflows [1-3,6]. A negative correlation was found also with θ-Rhythm Index as well as SPD of β-Rhythm in Right Temporalis Posterior and Occipitalis loci (Table 3).

Table 3. Regression Summary for Dependent Variable: IgG, Independent Variables: parameters of HRV and EEG

R=0,860; R^2=0,740; Adjusted R^2=0,575; $F_{(14,2)}$=4,5; $\chi^2_{(14)}$=38; $p<10^{-3}$; Std. Err of estimate: 2,4 g/l

		Beta	St. Err. of Beta	B	St. Err. of B	n=37 $t_{(22)}$	p-level
Independent Variables	r		Intercpt	20,3	4,8	4,26	10^{-3}
LFnu, %	-0,30	-,394	,131	-,077	,026	-3,01	,006
Index θ, %	-0,40	-,218	,128	-,021	,012	-1,70	,103
T6-β, %	-0,40	-,415	,224	-,068	,036	-1,85	,077
O2-β, %	-0,40	-,337	,199	-,073	,043	-1,69	,105
O2-β, μV^2/Hz	-0,27	-,391	,139	-,041	,015	-2,82	,010
Asymmetry β, %	-0,31	,221	,152	,055	,038	1,46	,159
T3-α, μV^2/Hz	0,38	,554	,201	,034	,012	2,75	,012
F3-α, μV^2/Hz	0,30	-1,491	,428	-,071	,020	-3,49	,002
F3-α, %	0,28	,810	,313	,188	,073	2,59	,017
C3-α, %	0,29	-,806	,380	-,199	,094	-2,12	,045
C3-α, μV^2/Hz	0,28	,565	,383	,019	,013	1,48	,154
Asymmetry δ, %	0,26	,512	,156	,094	,029	3,28	,003
P4-θ, μV^2/Hz	0,25	,378	,194	,033	,017	1,95	,064
Frequency δ, Hz	0,25	,238	,122	5,60	2,87	1,95	,064

Instead, the opposite of dependence detected by SPD of α-Rhythm in Left Frontalis Medialis and Centralis loci. Taken together, these neural structures determine the serum level IgG to 77% (Table 3 and Fig. 5).

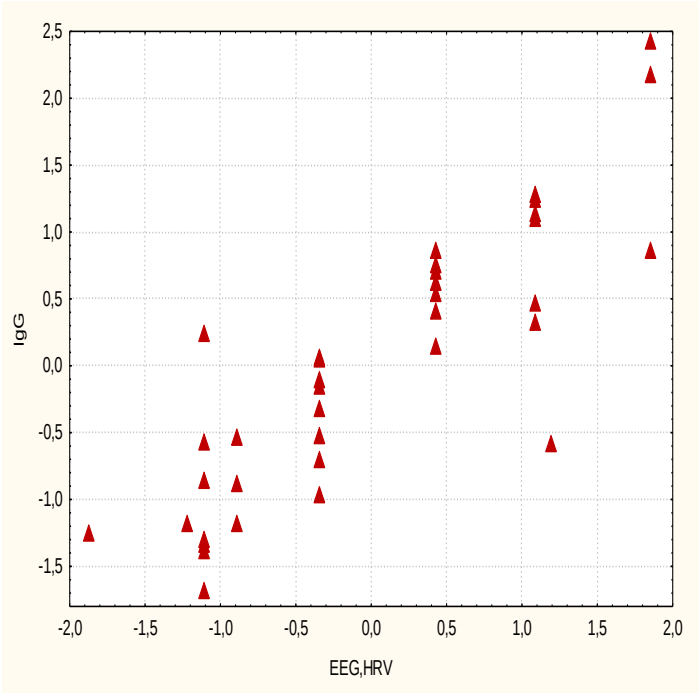

Fig. 5. Canonical correlation between parameters EEG and HRV (axis X) and serum level Immunoglobulines G (axis Y)

Found a positive correlation θ-Rhythm Index with SPD LF (r=0,39) and VLF (r=0,29) bands as well as SPD O2-β with ULF (r=0,25) band while negative correlation SPD C3-α (r=-0,32) and F3-α (r=-0,31) with LFnu. Last is admitted HRV markers of Sympathetic tone [1,3]. It is speculated that absolute SPD LF band reflects mainly Sympathetic outflow or both Sympathetic and Vagal origin [2]; VLF band (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 sympatho-adrenal system [cyt by: 4], sympathetic activity [cit by: 6]; 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].

This suggested hypothesis that downregulation serum level IgG by generating θ- and β-Rhythms neural structures is realized by upregulation of inhibiting influence of Sympathetic nucleus of Brain Stem (probably caudal and rostral ventro-lateral medulla). On the other hand, generating α-Rhythm neural structures realizes upregulation IgG by inhibition inhibiting (disinhibition) Sympathetic nucleus.

Serum level of Immunoglobuline A, in contrast to the IgG, does not correlate with any parameter of HRV. Among parameters of EEG found a positive correlation with Asymmetry of δ-Rhythm (Fig. 6) and θ-Rhythm while negative correlation with SPD of θ-Rhythm in Right (Fig. 7) and Left loci, its Amplitude as well as with SPD of β-Rhythm in Left loci. SPD C3-α correlate with IgA positively (Table 4).

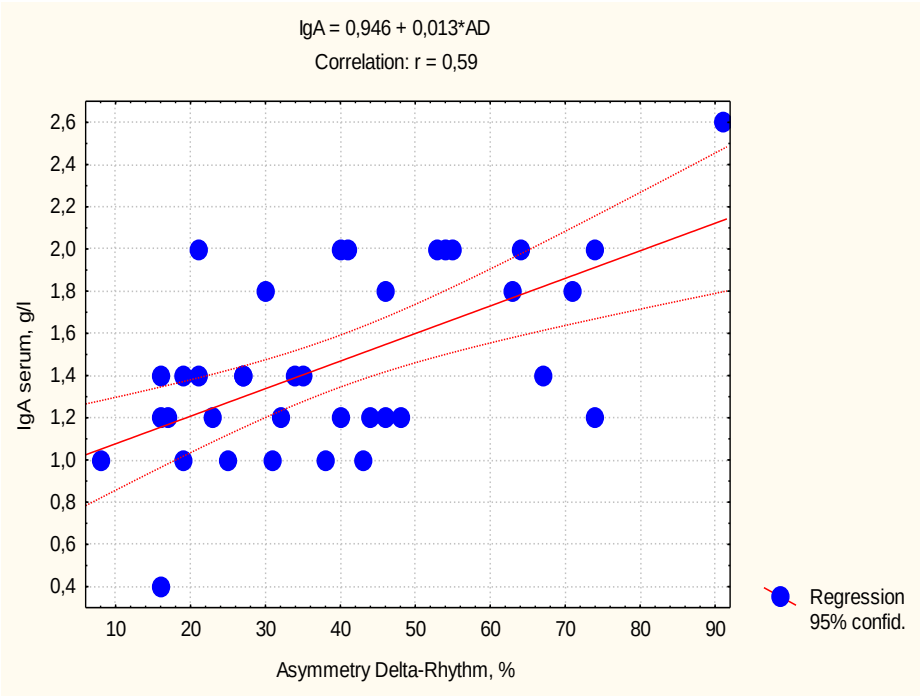

Fig. 6. Relationship between Asymmetry δ-Rhythm (axis X) and serum level Immunoglobuline A (axis Y)

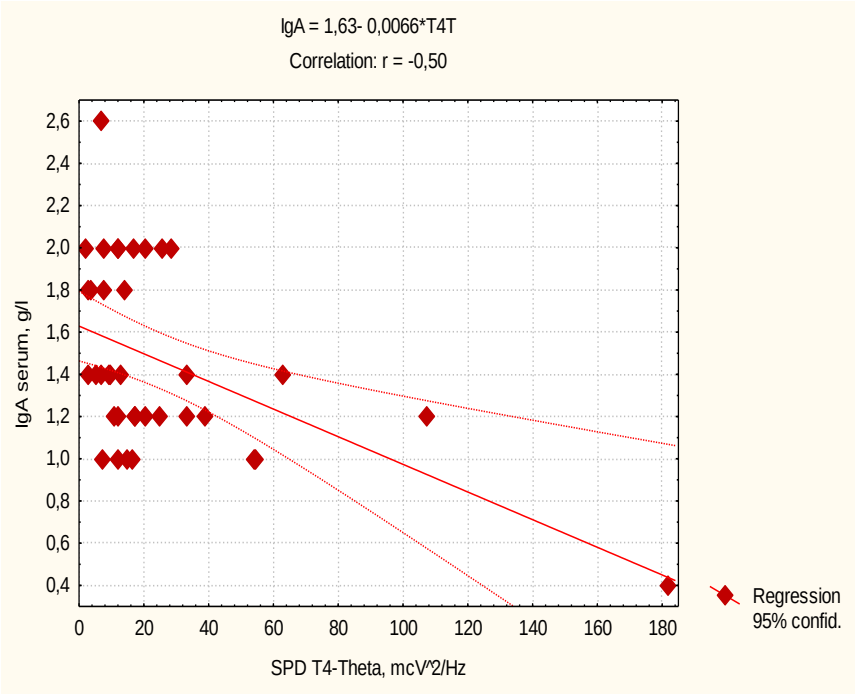

Fig. 7. Relationship between SPD T4-θ (axis X) and serum level IgA (axis Y)

Taken together, these neural structures determine the serum level IgA to 61,5% (Table 4 and Fig. 8).

Table 4. Regression Summary for Dependent Variable: IgA, Independent Variables: parameters of EEG

R=0,843; R^2=0,711; Adjusted R^2=0,615; $F_{(9,3)}$=7,4; $\chi^2_{(9)}$=38; $p<10^{-4}$; Std. Err of estimate: 0,28 g/l

		Beta	St. Err. of Beta	B	St. Err. of B	n=37 $t_{(27)}$	p-level
Independent Vars	r		Intercpt	,6329	,3279	1,93	,064
T4-θ, μV^2/Hz	-0,50	-1,717	,411	-,0227	,0054	-4,18	10^{-3}
P4-θ, %	-0,45	,738	,281	,0688	,0262	2,62	,014
Fp1-θ, μV^2/Hz	-0,37	,676	,309	,0084	,0038	2,19	,037
T5-θ, %	-0,30	-,472	,131	-,0384	,0106	-3,61	,001
Amplitude θ, μV	-0,35	,567	,262	,0676	,0313	2,16	,040
Asymmetry θ, %	0,44	,612	,145	,0144	,0034	4,23	10^{-3}
F7-β, μV^2/Hz	-0,35	,363	,173	,0031	,0015	2,10	,045
T5-β, μV^2/Hz	-0,35	-,755	,189	-,0050	,0013	-4,00	10^{-3}
C3-α, %	0,36	,240	,133	,0071	,0040	1,80	,084

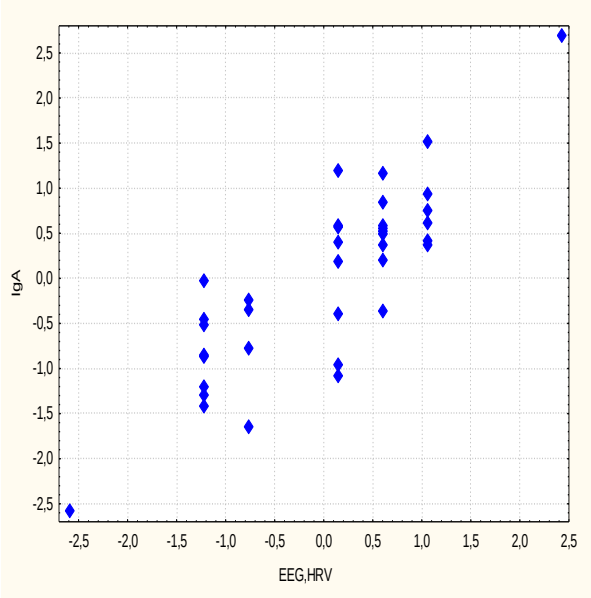

Fig. 8. Canonical correlation between parameters EEG and HRV (axis X) and serum level Immunoglobulines A (axis Y)

Table 5. Regression Summary for Dependent Variable: IgM, Independent Variables: parameters of HRV

R=0,749; R^2=0,562; Adjusted R^2=0,487; $F_{(6,4)}$=7,5; $p<10^{-4}$; Std. Error of estimate: 0,26 g/l

		Beta	St. Err. of Beta	B	St. Err. of B	n=37 $t_{(35)}$	p-level
Independ Vars	r		Intercpt	-1,747	,8328	-2,10	,043
HF, %	0,52	1,528	,418	,0448	,0122	3,66	10^{-3}
RMSSD, msec	0,47	2,401	,639	,0466	,0124	3,76	10^{-3}
pNN_{50}, %	0,43	-1,563	,482	-,0412	,0127	-3,24	,003
SDNN, msec	0,28	-,706	,297	-,0140	,0059	-2,37	,023
VLF, %	-0,32	,521	,218	,0107	,0045	2,39	,022
LFnu, %	-0,28	1,222	,328	,0236	,0063	3,72	10^{-3}

The level of IgM positively correlated with HRV markers of Vagal tone, while negative with markers of Sympathetic tone, which together determine its to 49% (Table 5, Fig. 9).

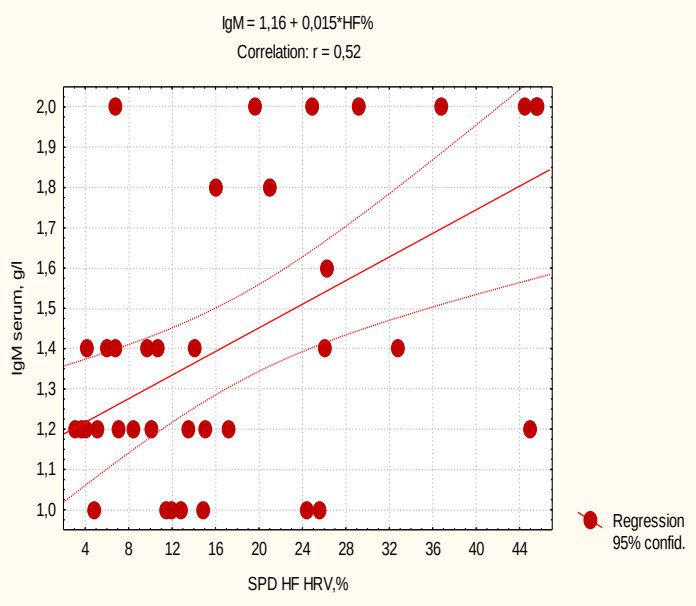

Fig. 9. Relationship between SPD HF band HRV (axis X) and serum level IgM (axis Y)

Among the parameters EEG closest correlation was found for the SPD of θ-Rhythm in Left Occipitale locus (Fig. 10). The outflows of these neural structures determines the level of IgM to 44,5% (Fig. 11).

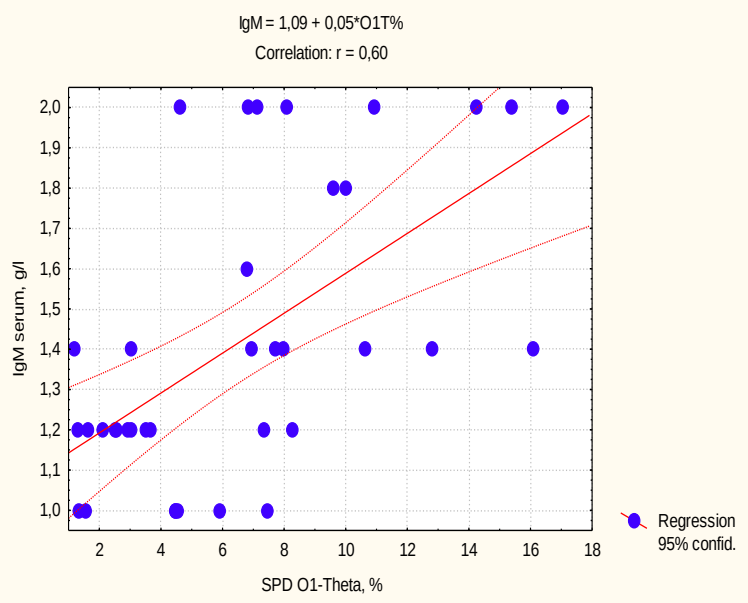

Fig. 10. Relationship between SPD O1-θ (axis X) and serum level Immunoglobuline M (axis Y)

Table 6 shows the parameters of HRV and EEG included in the regression model by step exclusion, which taken together determine the level of IgM to 71% (Fig. 12).

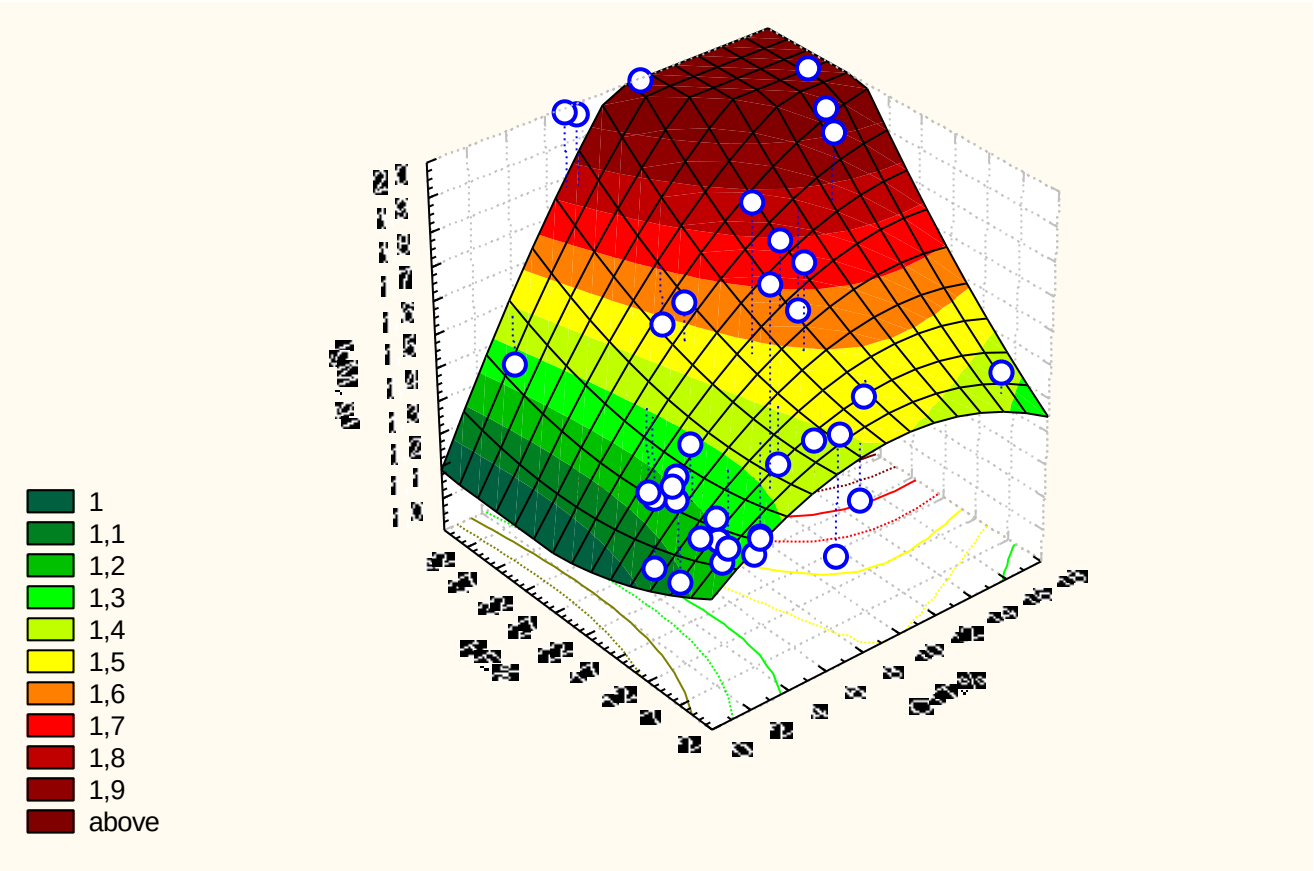

Fig. 11. Relationships between SPD O1-θ (axis X), HF band HRV (axis Y) and serum level Immunoglobuline M (axis Y)

Table 6. Regression Summary for Dependent Variable: IgM, Independent Variables: parameters of HRV and EEG
R=0,899; R^2=0,808; Adjusted R^2=0,712; $F_{(12,2)}$=8,4; $\chi^2_{(12)}$=37,5; $p<10^{-4}$; Std. Err of estim: 0,20 g/l

		Beta	St. Err. of Beta	B	St. Err. of B	n=37 $t_{(24)}$	p-level
Independ Vars	r		Intercpt	-,7821	,8023	-,97	,339
HF, %	0,52	1,185	,384	,0333	,0108	3,08	,005
pNN_{50}, %	0,43	-,537	,173	-,0142	,0046	-3,11	,005
(VLF+LF)/HF	-0,34	-,558	,205	-,0262	,0096	-2,73	,012
VLF, %	-0,32	,576	,219	,0123	,0047	2,62	,015
LFnu, %	-0,28	,879	,341	,0169	,0066	2,58	,016
O1-θ, %	0,60	,641	,149	,0529	,0123	4,29	,000
F8-θ, %	0,46	,312	,165	,0179	,0094	1,90	,070
Fp1-θ, %	0,40	1,267	,477	,0558	,0210	2,65	,014
Fp2-θ, %	0,39	-1,128	,479	-,0510	,0216	-2,35	,027
F7-θ, %	0,30	-,468	,152	-,0345	,0112	-3,08	,005
T3-β, %	0,27	,305	,106	,0060	,0021	2,88	,008
O1-α, μV^2/Hz	-0,33	-,357	,134	-,0008	,0003	-2,67	,013

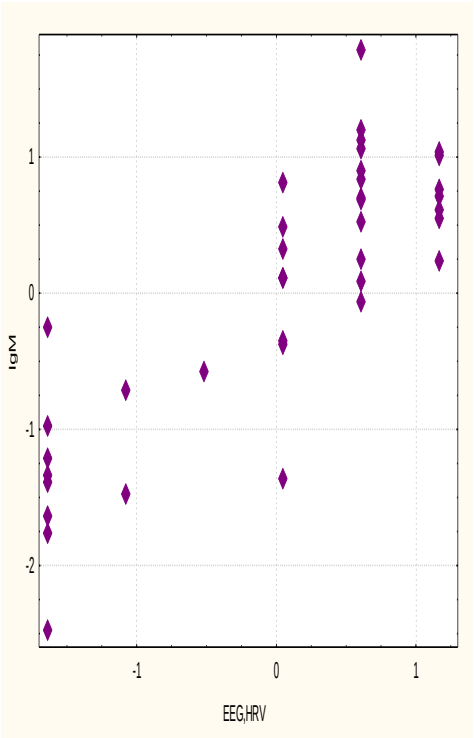

Fig. 12. Canonical correlation between parameters EEG and HRV (axis X) and serum level Immunoglobulines M (axis Y)

As you can see, a stimulating effect on the level of IgM causes generating θ-Rhythm structures CNS, which are projected to Occipital Left as well as Frontal Anterior and Lateral loci, while generating α-Rhythm structures that are designed to Occipital Left locus, reduce the level of IgM. On the other hand, found positive relationships SPD Fp1-θ and Fp2-θ with vagal markers rHF and pNN_{50} (r=0,44 and 0,45 as well as 0,41 and 0,37 respectively) while negative relationships with sympathetic markers LFnu (r=-0,30 and -0,34 respectively). SPD O1-θ correlated oppositely with pNN_{50} and rVLF (r=0,31 and -0,39 respectively). SPD O1-α correlated negatively with vagal markers Moda (r=-0,52) and aLF (r=-0,28).

This suggested hypothesis that upregulation serum level IgM by generating θ-Rhythm neural structures is realized by upregulation activating influence of Parasympathetic nucleus of Brain Stem (probably nucleus ambiguous) as well as downregulation of inhibiting influence of Sympathetic nucleus of Brain Stem (probably caudal and rostral ventro-lateral medulla). On the other hand, generating α-Rhythm neural structures realizes downregulation IgM by inhibition activating Parasympathetic nucleus.

The level of Circulating Immune Complexes moderate positively correlated with Baevskiy's Stresss Index (both in supine and orthostatic positions) as marker of Sympatho-Vagal balance as well as with Amplitude of Moda as HRV marker of Sympathetic tone, while negative correlated with aSPD of LF band, Cv and SDNN as markers of Vagal tone, which together determine its to 22% (Table 7).

Among the parameters of EEG level of CIC correlated with Frequency of δ-Rhythm (r=0,38), its Laterality (r=-0,32) and absolute SPD in loci Fp1 (r=0,36), F7 (r=0,34), T5 (r=0,30) and T3 (r=-0,30). Also found links with relative SPD T3-α (r=0,39), P3-β (r=-0,34) and C3-β (r=-0,31).

Table 7. Regression Summary for Dependent Variable: CIC, Independent Variables: parameters of HRV
R=0,575; R^2=0,331; Adjusted R^2=0,216; $F_{(6,4)}$=2,9; p=0,022; Std. Error of estimate:16 units

		Beta	St. Err. of Beta	B	St. Err. of B	n=37 $t_{(35)}$	p-level
Independent Variables	r		Intercpt	35,5	28,0	1,27	,214
BSI(s), units	0,39	,786	,310	,092	,036	2,53	,016
BSI(o), units	0,34	,288	,192	,018	,012	1,50	,143
AMo, %	0,28	-,494	,354	-,626	,449	-1,40	,172
LF, $msec^2$	-0,30	-,543	,299	-,015	,008	-1,82	,078
Cv, %	-0,29	-,588	,331	-5,780	3,251	-1,78	,084
SDNN, msec	-0,26	1,025	,488	1,023	,487	2,10	,043

Table 8. Regression Summary for Dependent Variable: CIC, Independent Variables: parameters of HRV and EEG
R=0,837; R^2=0,701; Adjusted R^2=0,616; $F_{(8,3)}$=8,2; $\chi^2_{(8)}$=37; $p=10^{-5}$; Std. Err of estimate:12 units

		Beta	St. Err. of Beta	B	St. Err. of B	n=37 $t_{(28)}$	p-level
Independent Variables	r		Intercpt	60,70	20,15	3,01	,0054
BSI(s), units	0,39	,488	,255	,058	,031	1,91	,0658
AMo, %	0,28	-,819	,265	-1,054	,341	-3,09	,0045
Frequency δ, Hz	0,38	,392	,118	47,5	14,4	3,31	,0026
T5-δ, μV^2/Hz	0,30	,308	,157	,006	,003	1,96	,0596
Cv, %	-0,29	-,465	,162	-4,527	1,581	-2,86	,0079
Laterality δ, %	-0,32	-,430	,111	-,168	,043	-3,88	,0006
T3-δ, μV^2/Hz	-0,30	-,479	,111	-,061	,014	-4,31	,0002
C3-β, %	-0,31	-,235	,116	-,352	,174	-2,02	,0536

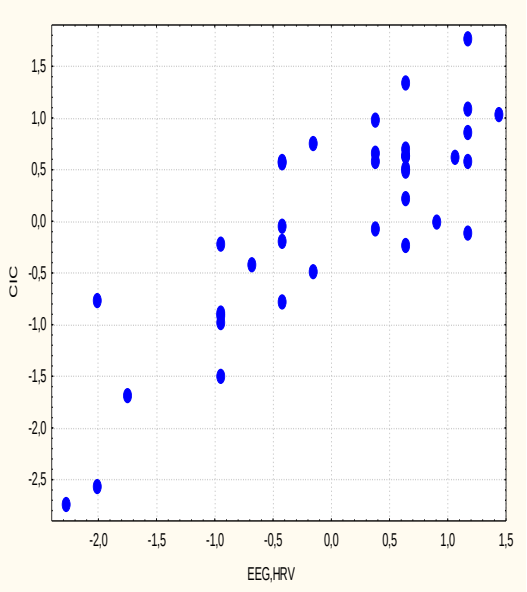

Fig. 13. Canonical correlation between parameters EEG and HRV (axis X) and serum level Circulating Immune Complexes (axis Y)

But the program has included in the regression model by step exclusion only five parameters of EEG, which together with three parameters of HRV determine the level of CIC to 62% (Table 8, Fig. 13).

It seems that the upregulation level CIC by generating δ-Rhythm structures projected on locus T5 (left amygdala?) is realized by upregulation Sympathetic nuclei, because take place correlation absolute SPD T5-δ with SIB (r=0,66) and AMo (r=0,48).

Relative blood level subpopulation of T-helpers correlates very poorly negatively with HRV markers Vagal tone pNN_{50} (r=-0,25) and HF (r=-0,24) while positively with SPD α- and β-Rhythms in some loci. The combined effect of neural structures determines the blood level T-helpers to 50% (Table 9).

Table 9. Regression Summary for Dependent Variable: $CD4^+$ T-Lymphocytes, Independent Variables: parameters of HRV and EEG

R=0,791; R^2=0,626; Adjusted R^2=0,502; $F_{(9,3)}$=5,0; $\chi^2_{(9)}$=23; $p<10^{-3}$; Std. Error of estimate: 3,8%

		Beta	St. Err. of Beta	B	St. Err. of B	n=37 $t_{(27)}$	p-level
Independent Variables	r		Intercpt	29,0	2,1	13,6	10^{-6}
pNN_{50}, %	-0,25	-,413	,142	-,160	,055	-2,90	,007
T5-α, μV^2/Hz	0,27	-,629	,285	-,060	,027	-2,21	,036
C4-β, μV^2/Hz	0,31	-,685	,354	-,072	,037	-1,94	,063
F4-β, μV^2/Hz	0,40	1,182	,439	,115	,043	2,69	,012
T3-β, μV^2/Hz	0,39	,615	,164	,047	,013	3,75	,001
Fp1-β, μV^2/Hz	0,29	-,587	,334	-,086	,049	-1,76	,089
T3-α, μV^2/Hz	0,31	,429	,215	,038	,019	1,99	,056
T5-θ, μV^2/Hz	0,25	,510	,220	,118	,051	2,32	,028
O2-β, μV^2/Hz	-0,27	-,416	,145	-,063	,022	-2,88	,008

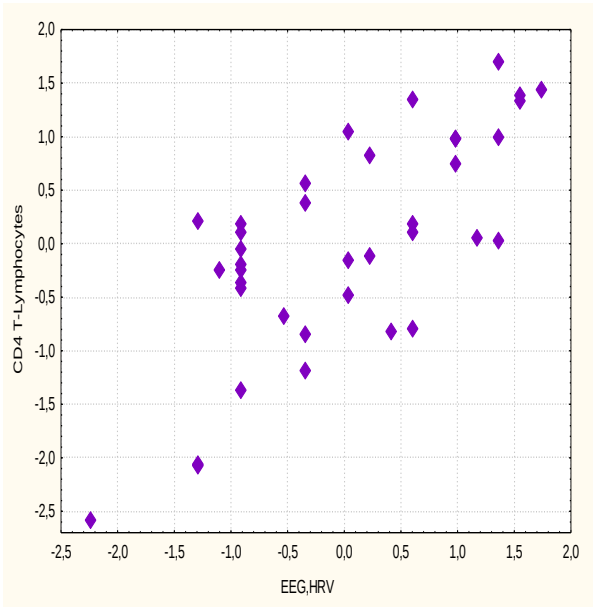

Fig. 14. Canonical correlation between parameters EEG and HRV (axis X) and blood level T-helper Lymphocytes (axis Y)

On the other hand, revealed relationships between SPD T5-α and other Vagal marker Moda (r=-0,44) as well as SPD C4-β and aLF (r=-0,30). These facts give reason to believe that upregulation level of T-helpers by generating α-Rhythm left Amygdala (?) and generating β-Rhythm right Hippocamp (?) is realized by downregulation inhibiting Parasympathetic nuclei.

Relative blood level Cytolyc subpopulation of T-Lymphocytes correlates very poorly negatively with SPD VLF band HRV as marker activation of cerebral sympatho-adrenal system while positively with SPD HF band HRV as marker of Vagal outflows. Among parameters of EEG level T-killers correlates very poorly with SPD α- and δ-Rhythms in some loci. The combined effect of neural structures determines the blood level T-killers to 55% (Table 10, Fig. 15).

Table 10. Regression Summary for Dependent Variable: $CD8^+$ T-Lymphocytes, Independent Variables: parameters of HRV and EEG
R=0,808; R^2=0,653; Adjusted R^2=0,554; $F_{(8,3)}$=6,6; $\chi^2_{(8)}$=30; $p<10^{-4}$; Std. Error of estimate: 3,5%

		Beta	St. Err. of Beta	B	St. Err. of B	n=37 $t_{(28)}$	p-level
Independent Variables	r		Intercpt	22,2	3,8	5,80	10^{-5}
VLF, $msec^2$	-0,28	-,487	,121	-,004	,001	-4,04	10^{-3}
HF, %	0,28	,362	,115	,145	,046	3,15	,004
P4-α, %	-0,36	-,531	,289	-,169	,092	-1,84	,076
Fp2-α, %	-0,27	-,606	,167	-,205	,057	-3,62	,001
P3-α, %	-0,25	,949	,288	,295	,090	3,29	,003
Fp2-δ, $\mu V^2/Hz$	-0,27	-1,790	,562	-,035	,011	-3,18	,003
F7-δ, $\mu V^2/Hz$	-0,26	1,085	,514	,007	,003	2,11	,044
P3-δ, %	0,27	,395	,163	,170	,070	2,43	,022

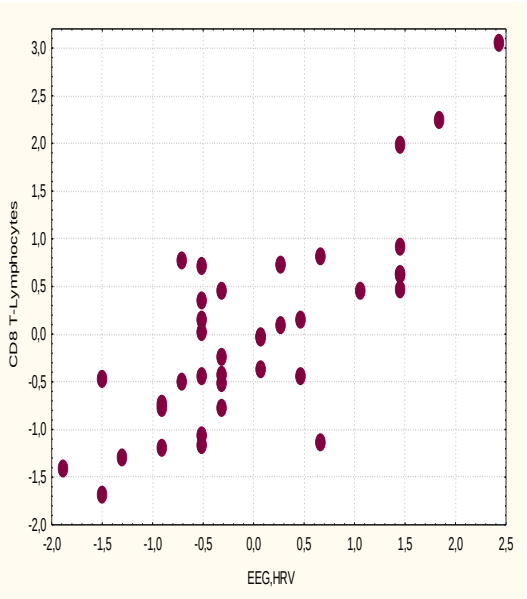

Fig. 15. Canonical correlation between parameters EEG and HRV (axis X) and blood level T-cytolytic Lymphocytes (axis Y)

On the other hand, revealed relationships between SPD F7-δ and other Sympathetic marker AMo (r=0,47). These facts give reason to believe that downregulation level of T-killers by

generating δ-Rhythm prefrontal neural structures is realized by upregulation inhibiting Sympathetic nuclei.

Relative blood level of Natural Killers correlates very poorly positively with relative SPD LF band HRV (r=0,28) as marker of Sympathetic tone and with Stress Index as marker of Sympatho-Vagal balance while negatively with Entropy SPD in locus C3, Index of α-Rhythm, SPD P4-α (r=-0,27) as well as SPD of θ-, δ- and β-Rhythms in some loci. The combined effect of neural structures determines the blood level NK-Lymphocytes to 35% (Table 11, Fig. 16).

Table 11. Regression Summary for Dependent Variable: $CD16^+$ NK-Lymphocytes, Independent Variables: parameters of HRV and EEG
R=0,712; R^2=0,507; Adjusted R^2=0,349; $F_{(9,3)}$=3,2; $\chi^2_{(9)}$=15,8; p=0,009; Std. Err of estimate:1,9%

		Beta	St. Err. of Beta	B	St. Err. of B	n=38 $t_{(28)}$	p-level
Independent Variables	r		Intercpt	21,2	4,3	4,96	10^{-4}
BSI (o)	0,28	,244	,151	,0024	,0015	1,62	,117
Index α, %	-0,36	-,482	,193	-,0429	,0172	-2,50	,018
Entropy SPD C3	-0,35	-,458	,183	-10,65	4,26	-2,50	,018
P3-θ, μV^2/Hz	-0,32	-,494	,366	-,0331	,0245	-1,35	,188
P4-θ, μV^2/Hz	-0,28	,466	,368	,0273	,0215	1,27	,215
O2-θ, μV^2/Hz	-0,26	,408	,208	,0484	,0246	1,97	,059
Fp2-δ, μV^2/Hz	-0,26	-,234	,174	-,0022	,0016	-1,35	,188
O2-β, μV^2/Hz	-0,26	-,251	,161	-,0156	,0100	-1,56	,129
Deviation α, Hz	0,28	,216	,156	,8865	,6408	1,38	,177

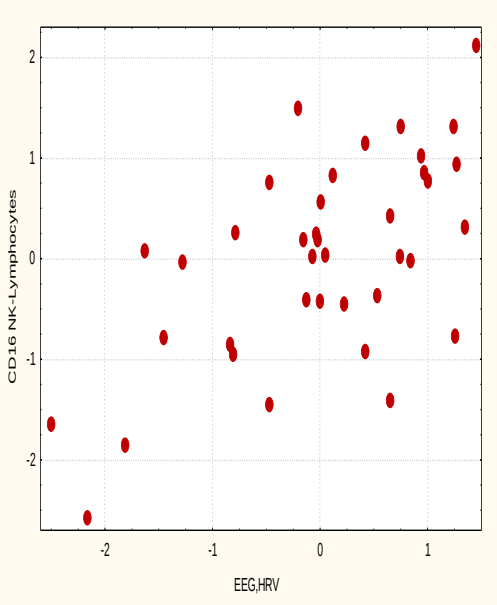

Fig. 16. Canonical correlation between parameters EEG and HRV (axis X) and blood level Natural Killers (axis Y)

The observed correlation between Index of α-Rhythm and other marker of Sympatho-Vagal balance LF/HF ratio (r=-0,32). These facts give reason to believe that downregulation level of Natural Killers by generating α-Rhythm neural structures is realized by upregulation inhibiting Sympathetic nuclei.

Finally, the "active" subpopulation of T-Lymphocytes, judging by the correlation coefficient, is very weak subordinate regulatory influence neural structures. However, the force of canonical correlation revealed statistically significant (Table 12, Fig. 17).

Table 12. Regression Summary for Dependent Variable: "Active" T-Lymphocytes, Independent Variables: parameters of HRV and EEG
R=0,566; R^2=0,320; Adjusted R^2=0,210; $F_{(5,3)}$=2,9; $\chi^2_{(5)}$=12,7; p=0,029;
Std. Error of estimate: 4,2%

		Beta	St. Err. of Beta	B	St. Err. of B	n=37 $t_{(31)}$	p-level
Independent Variables	r		Intercpt	13,3	10,1	1,32	,197
F8-α, μV^2/Hz	0,21	,403	,160	,085	,034	2,51	,017
Frequency α, Hz	0,22	,191	,157	1,034	,850	1,22	,233
Frequency θ, Hz	0,20	-,213	,157	-,801	,591	-1,36	,185
Asymmetry θ, %	0,23	,316	,158	,080	,040	2,00	,055
Asymmetry β, %	0,25	,309	,156	,099	,050	1,98	,057

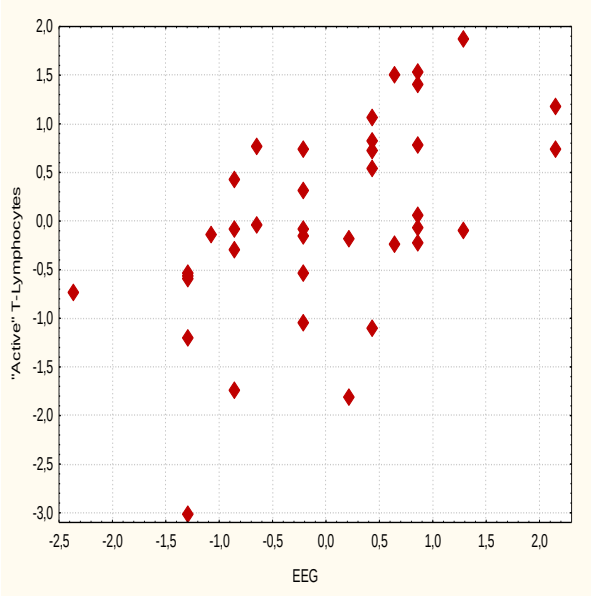

Fig. 17. Canonical correlation between parameters EEG (axis X) and blood level "Active" T-Lymphocytes (axis Y)

Found negative correlations markers of vagal tone Moda with SPD F8-α (r=-0,37) and Frequency of θ-Rhythm (r=-0,35), pNN_{50} and aHF with Asymmetry of β-Rhythm (r=-0,33 and -0,31 respectively) while positive correlation Asymmetry of θ-Rhythm with Sympathetic markers rLF (r=0,29) and ULF (r=0,28) as well as Frequency of α-Rhythm with ULF (r=0,27). These facts give reason to believe that upregulation level of "active" T-Lymphocytes by generating α- and θ-Rhythms neural structures is realized by downregulation inhibiting Parasympathetic nuclei and upregulation activating Sympathetic nuclei.

Limited extent article does not allow us to discuss the results, so we will move it to the next article.

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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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