RELATIONSHIPS BETWEEN THE ENTROPIES OF EEG, HRV, IMMUNOCYTOGRAM AND LEUKOCYTOGRAM

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Background. In mathematics the entropy is a measure of uncertainty of a random function; in the theory of information entropy is a measure of uncertainty in a situation, any experience (test) that can have different consequences. The entropy is also a measure of disorder, the degree of chaos present in the system. CE Shannon linked the mathematical dependence of the concept of information and entropy, which characterizes the degree of ordering of the system. This estimate of the amount of information coincides with the estimation of the quantitative measure of elimination of uncertainty of entropy, the degree of organization of the system. It is well known about functional interactions between central and autonomic nervous and immune systems. In the context of this concept, we have prioritized research on the interconnections between the entropies of these systems. **Material and methods.** In basal conditions in 37 men and 14 women with chronic pyelonephritis and cholecystitis in remission as well as without clinical diagnose but with dysfunction of neuro-endocrine-immune complex and metabolism, we recorded twice, before and after balneotherapy at the spa Truskavets', EEG ("NeuroCom Standard") and HRV ("Cardiolab+VSR"). In blood we determined relative content of components (RCC) of Immunocytogram (ICG) (T helper, T cytolytic, B and NK lymphocytes) and Leukocytogram (LCG) (Eosinophils, Stub and Segmentonucleary Neutrophils, Lymphocytes and Monocytes). Than we calculated for each locus of EEG and HRV as well as for ICG and LCG the Entropy (h) of normalized spectral power density (SPD) or RCC using Shannon's formula: **Results.** There was a complete absence of correlation between hHRV and hLCG (r=-0,03) as well as hICG (r=-0,03), whereas the relationship between hLCG and hICG is significant (r=-0,40; p<0,001). Accepting the entropy of EEG HRV as a factor, using the correlation analysis with step-by-step exclusion, we obtain the equations for dependent variables. Canonical correlation between hHRV&EEG, on the one hand, and hLCG&Immunity, on the other hand, is strong: R=0,814; R^2=0,663; $\chi^2_{(240)}$=296; p=0,008. **Conclusion**. The enropy of HRV and EEG significantly correlate with the entropy and parameters of immunity, which testifies to their modulating regulatory effects.

Keywords: EEG, HRV, Leukocytogram, Immunocytogram, Entropy, Correlations, Women and Man.

INTRODUCTION

In physics, entropy is a quantity which, in observed phenomena and processes, characterizes the devaluation (scattering) of energy due to the transformation of all its types into heat with a uniform distribution of heat between bodies; in chemistry and thermodynamics it is a measure of the amount of energy in the physical system, which can not be used to perform work; in mathematics it is a measure of uncertainty of a random function; in the theory of information entropy is a measure of uncertainty in a situation, any experience (test) that can have different consequences. The entropy is also a measure of disorder, the degree of chaos present in the system. CE Shannon [27] linked the mathematical dependence of the concept of information and entropy, which characterizes the degree of ordering of the system. This estimate of the amount of information coincides with the estimation of the

quantitative measure of elimination of uncertainty of entropy, the degree of organization of the system.

According to PV Biloshytskyi [5,6], the mathematical formula directly indicates the possibility of quantitative change in information to change the ordering of the system, which, in relation to biosystems, can mean a change in quality (stability, workability, health, etc.), and thus indicate the path of purposeful use of bioinformatics in medical practice. Accordingly, the author suggests that instead of the term entropy, we use the term of the **reliability of the functioning of the organism**, which is very impressive to us, as well as his assumption that the dependence of the reliability of the biosystem on information is precisely the elusive **vis vitalis** (life force).

The calculation of entropy is acceptable, in particular, with respect to closed systems of various shaped elements, such as leukocytogram, immune-, spleno- and thymocytogram. Information analysis of cytograms allows us to assess the state of morpho-functional adaptive-protective systems, information about which contained in their cytograms [1,22,29].

Other objects for calculating entropy are the normalized spectral power density of the HRV and EEG [15-17].

It is well known about functional interactions between central and autonomic nervous and immune systems [14-17,23,24,28]. In the context of this concept, we have prioritized research on the interconnections between the entropies of these systems.

MATERIAL AND METHODS

The object of observation were 37 men and 14 women aged 23-76 years old, who came to the spa Truskavets' (Ukraine) for the treatment of chronic pyelonephritis and cholecystitis in remission as well as without clinical diagnose but with dysfunction of neuro-endocrine-immune complex and metabolism. The survey was conducted twice, before and after weekly balneotherapy.

We recorded electrocardiogram in II lead (hardware-software complex "CardioLab+HRV" produced by "KhAI-MEDICA", Kharkiv, Ukraine) to assess the parameters of heart rate variability (HRV). For further analysis (Frequency Domain Methods) were selected spectral power (SP) 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) [2,4,12].

Simultaneosly we recorded EEG (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 on the tassels of ears. Among the options considered the average EEG amplitude (μV), average frequency (Hz), frequency deviation (Hz), index (%), coefficient of asymmetry (%) as well as absolute (μV^2/Hz) and relative (%) spectral power density (SPD) in the standard frequency bands: 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 [19]:

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

We calculated also for HRV and each locus EEG the Entropy (h) of normalized SPD using formula CE Shannon [27]:

$$hHRV = - [SPDHF \bullet \log_2 SPDHF + SPDLF \bullet \log_2 SPDLF + SPDVLF \bullet \log_2 SPDVLF + SPDULF \bullet \log_2 SPDULF]/\log_2 4;$$
$$hEEG = - [SP D\alpha \bullet \log_2 SP D\alpha + SP D\beta \bullet \log_2 SP D\beta + SP D\theta \bullet \log_2 SP D\theta + SP D\delta \bullet \log_2 SP D\delta]/\log_2 4$$

In portion of capillary blood we counted up Leukocytogram (LCG) (Eosinophils, Stub and Segmentonucleary Neutrophils, Lymphocytes and Monocytes) and calculated its Adaptation Index as well as Strain Index by IL Popovych [7,13,21].

The informativeness of these indices was demonstrated by other authors [3,20], as well as its advantage over the Lymphocytes/Segmentonucleary Neutrophils ratio [10,25].

We remind that the algorithm of quantization of the Popovych's indexes is based on the proposed LKh Garkavi et al [9,10] ranges of relative content in the leukocytogram of lymphocytes, which determines the type of General Adaptation Reaction of Organism as well as other components of leukocytogram and total leukocyte levels indicating harmonic or disharmonious character of GARO.

Leukocyto-gram Lymphocy-tes level, %	**G**eneral **A**daptation **R**eaction of **O**rganism	Eosinophiles and Stub Neutrophiles: 1÷6 %; Monocytes: 4÷7 %; Leukocytes: 4÷8 G/l	Eosinophiles and Stub Neutrophiles: <1; >6; Monocytes: <4; >7; Leukocytes: <4; >8 G/l
<21	Stress	**1,22**	**0,02**
21÷27	Training	**1,46**	**0,74**
28÷33	Quiet Activation	**1,95**	**0,98**
34÷43,5	Heightened Activation	**1,70**	**0,50**
≥44	Superactivation	**0,26**	

Strain Index-1 = $[(Eo/3,5\text{-}1)^2 + (SN/3,5\text{-}1)^2 + (Mon/5,5\text{-}1)^2 + (Leu/6\text{-}1)^2]/4$

Later, LKh Garkavi et al [11] proposed some other boundaries of ranges, on the basis of which we calculated the second version of the indices, testing of which will debuted in this article.

Leukocyto-gram Lymphocy-tes level, %	**G**eneral **A**daptation **R**eaction of **O**rganism	Eosinophiles: 1÷4,5 %; Stub Neutrophiles: 3÷5,5 %; Monocytes: 5÷7 %; Leukocytes: 4÷6 G/l	Eosinophiles: <1;>4,5% Stub Neutrophiles: <3; >5,5; Monocytes: <5; >7; Leukocytes: <4; >6 G/l
<21	Stress	**1,22**	**0,02**
21÷27	Training	**1,46**	**0,74**
28÷33	Quiet Activation	**1,95**	**0,98**
34÷43,5	Heightened Activation	**1,70**	**0,50**
≥44	Superactivation	**0,26**	

Strain Index-2 = $[(Eo/2,75\text{-}1)^2 + (SN/4,25\text{-}1)^2 + (Mon/6\text{-}1)^2 + (Leu/5\text{-}1)^2]/4$

Immune status evaluated on a set of I and II levels recommended by the WHO as described in the manual [18]. 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. 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).

We calculated also the Entropy (h) of Immunocytogram (ICG) and Leukocytogram (LCG) using classical CE Shannon's formula [27]:

$hICG = - [CD4 \bullet \log_2 CD4 + CD8 \bullet \log_2 CD8 + CD22 \bullet \log_2 CD22 + CD16 \bullet \log_2 CD16]/\log_2 4$

$hLCG = - [Lymph \bullet \log_2 Lymph + Mon \bullet \log_2 Mon + Eos \bullet \log_2 Eos + SNN \bullet \log_2 SNN + StubN \bullet \log_2 StubN]/\log_2 5$

Parameters of phagocytic function of neutrophils estimated as described by SD Douglas and PG Quie [8] with moderately modification by MM Kovbasnyuk [16]. To do this, 5 drops of blood immediately after collection, made in glass centrifuge tubes with 2 ml of 4% solution of sodium citrate. Blood samples were stored in a refrigerator at a temperature of 4^0C. Further

samples were centrifuged (5000 rev/min for 5 min). The supernatant was removed with the help of the Pasteur's pipette. We used a fraction of leukocytes with traces of erythrocytes. The objects of phagocytosis served daily cultures of Staphylococcus aureus (ATCC N 25423 F49) as typical specimen for Gram-positive Bacteria and Escherichia coli (O55 K59) as typical representative of Gram-negative Bacteria. Both cultures obtained from Laboratory of Hydro-Geological Regime-Operational Station JSC "Truskavets'kurort". To prepare the suspension microbes did wipes with relevant shoals sterile saline, immersed tubes in boiling water for 3 seconds, cooled to room temperature. Integrity microbes controlled with the aid of a microscope. To do this, drop the suspension of microbes applied to skimmed substantive piece of glass, fixed in alcohol lamp flame. Ready preparations stained by Papenheim, microscoped during immersion, lense h90, eyepiece x10. The test samples were prepared as follows. In Vidal's plastic tubes made in the following order of 0,05 mL of heparin, 0,05 mL of sterile saline, 0,1 mL suspension of leukocytes, 0,05 mL suspension of microbial bodies. Samples shaked and placed in thermostat at 37^0C for 30 min, shaking them with every 10 mins. Then, to stop phagocytosis, the sample was cooled under running water for 10 min. In further samples are centrifuged (5000 rev/min, for 5 min), the supernatant removed with the help of the Pasteur's pipette. From the suspension of leukocytes (with traces of red blood cells) prepared strokes, dried in air at room temperature and stained by Papenheim. Microscoped during immersion lens h90, x10 eyepiece. Take into account the following parameters of phagocytosis: activity as percentage of neutrophils, in which found microbes - Hamburger's Phagocytic Index; intensity as number of microbes absorbed one phagocytes - Microbial Count (MC) or Right's Index; completeness as percentage of dead microbes - Killing Index (KI). Microbial number and index their digestion is determined for each phagocyte and fixed in phagocytic frame.

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

RESULTS AND DISCUSSION

In the first stage, screening of correlation relationships between the levels of entropy of HRV and loci of EEG, on the one hand, and the entropy of LCG and ICG, as well as immune parameters, was performed on the other.

According to calculations by the formula [23]:

$|r|=\{\exp[2t/(n-1,5)^{0,5}]-1\}/\{\exp[2t/(n-1,5)^{0,5}]+1\}$

for a sample of n=102 critical value |r| at $p<0,05$ ($t>2,00$) is 0,20, at $p<0,02$ ($t>2,39$) is 0,23, at $p<0,01$ ($t>2,66$) is 0,26, at $p<0,001$ ($t>3,46$) is 0,33.

Based on the results of the screening, a matrix (Table 1) is created, which includes only those parameters that have at least one significant correlation with the parameters of another set. As we see, the locus of F8 and P4, on the one hand, and Phagocytic Index, Stub Neutrophils, Monocytes, $CD22^+$ B Lymphocytes, IgG, on the other hand, were located outside the matrix.

There was a complete absence of correlation between enropies of HRV and LCG as well as ICG, whereas the relationship between enropies of LCG and ICG is maximal for matrix ($r=-0,40$; $p<0,001$).

Table 1. Matrix of Correlations, left set with right set
$_{0,05}|r|\geq 0,20$; $_{0,02}|r|\geq 0,23$; $_{0,01}|r|\geq 0,26$; $_{0,001}|r|\geq 0,33$

	HRV H	Fp1 H	Fp2 H	F3 H	F4 H	F7 H	T3 H	T4 H	C3 H	C4 H	T5 H	T6 H	P3 H	O1 H	O2 H
LCGH	-,03	-,07	-,12	,19	,09	-,09	-,03	-,03	,12	,03	**-,23**	-,17	**-,22**	**-,31**	**-,20**
ICGH	-,03	,09	,15	-,16	-,10	,16	-,07	-,04	-,13	-,03	**,20**	**,22**	**,22**	,13	,18

MC Sa	-,12	**,21**	**,24**	**,23**	**,23**	,18	,14	,08	,13	**,27**	,10	,16	,02	,13	,09
KI Sa	**,28**	-,14	**-,29**	-,09	-,06	**-,20**	**-,23**	**-,21**	-,08	-,09	-,16	**-,22**	-,19	**-,20**	**-,23**
MC Ec	**-,27**	**,25**	**,23**	**,28**	**,27**	,18	,13	,10	,18	**,20**	,10	,17	,11	,16	,00
KI Ec	**,27**	-,07	-,04	,03	-,09	-,11	-,12	-,05	-,07	-,05	-,08	-,01	**-,23**	-,12	-,14
Leukoc	-,18	,09	-,00	,18	,19	,02	,03	,01	,09	,07	-,10	-,07	-,11	**-,21**	-,11
SNN	**-,25**	-,03	,06	**-,25**	**-,24**	,09	-,02	-,01	**-,24**	-,17	,12	,14	**,24**	,15	,19
Eosin	**-,21**	-,10	-,07	,01	-,00	,03	-,04	-,01	,00	,01	-,11	-,02	**-,20**	-,18	-,15
Lymph	**,36**	,06	-,05	**,21**	**,24**	-,09	,03	,01	**,23**	,18	-,03	-,08	**-,20**	-,01	-,15
CD4	-,03	-,02	,01	**-,23**	-,18	,11	-,10	-,09	-,11	-,07	,10	,13	,17	,01	,08
CD8	,17	,16	,14	,02	,16	,06	,07	,11	,08	**,20**	**,20**	,18	,09	,03	,11
Ta	-,13	,07	,17	-,02	-,16	**,21**	-,08	,01	-,19	-,10	,01	,07	,08	,12	,18
CIC	,04	-,11	-,07	-,17	**-,28**	-,16	-,06	,00	-,06	-,16	-,06	-,06	-,05	-,14	-,09
IgA	-,10	-,07	,00	-,08	-,20	,12	,02	-,03	**-,23**	-,16	-,06	,09	-,00	,04	,05
IgM	,09	,14	,14	,13	,04	,11	,08	,09	**,25**	,17	,12	,11	,10	,17	,11
CD16	-,04	,02	,12	**-,26**	**-,22**	,17	-,04	-,04	-,18	-,07	,16	**,25**	**,21**	,08	**,20**
PSI-1	-,18	,00	,07	,05	,10	,04	,07	,10	,12	,09	-,07	-,09	,01	**-,23**	-,10
PSI-2	**-,23**	-,03	,04	,03	,07	,04	,07	,09	,10	,08	-,06	-,07	-,07	**-,26**	-,17
PAI-1	-,04	**-,28**	**-,28**	-,12	**-,29**	-,05	-,01	-,17	-,16	-,17	-,03	-,14	-,01	-,08	-,05
PAI-2	**-,21**	-,07	-,14	,06	-,11	-,06	,10	-,09	,01	-,07	,04	-,11	**,20**	-,04	,03

At the second stage, coefficients of the multiplicity correlation of the entropy indices with each other (Tables 2-4) and immunity parameters (Tables 5-19) were calculated on the basis of a regression model with step-by-step exclusion to reach the maximum Adjusted R^2.

Table 2. Regression Summary for HRVH
R=0,268; R^2=0,072; Adjusted R^2=0,049; $F_{(2,8)}$=3,2; p=0,046

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(83)}$	p-level
Variable	r		Intercpt	,940	,088	10,7	10^{-6}
Fp2H	-0,21	-,169	,109	-,141	,091	-1,55	,126
F3H	-0,21	-,170	,109	-,130	,084	-1,55	,124

Table 3. Regression Summary for ICGH
R=0,346; R^2=0,120; Adjusted R^2=0,087; $F_{(3,8)}$=3,7; p=0,015

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(82)}$	p-level
Variable	r		Intercpt	,894	,045	20,1	10^{-6}
T6H	0,22	,183	,112	,058	,036	1,64	,106
P3H	0,22	,198	,113	,086	,049	1,75	,084
F3H	-0,16	-,228	,106	-,080	,037	-2,14	,035

Table 4. Regression Summary for LCGH
R=0,403; R^2=0,162; Adjusted R^2=0,142; $F_{(2,8)}$=8,0; p=0,0006

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(83)}$	p-level
Variable	r		Intercpt	,669	,030	22,0	10^{-6}
O1H	-0,31	-,360	,102	-,100	,028	-3,53	,001
F3H	0,19	,257	,102	,077	,031	2,51	,014

Table 5. Regression Summary for Fp1H
R=0,362; R^2=0,131; Adjusted R^2=0,110; $F_{(2,8)}$=6,3; p=0,003

	Beta	St. Err.		St. Err.		p-

			of Beta	B	of B	$t_{(83)}$	level
Variable	r		Intercpt	,5987	,1416	4,23	10^{-4}
Microbian Count vs E. coli	0,25	,226	,103	,0045	,0021	2,20	,031
Popovych's Adaptation Index-1	-0,28	-,263	,103	-,0692	,0271	-2,56	,012

Table 6. Regression Summary for Fp2H
R=0,470; R^2=0,220; Adjusted R^2=0,182; $F_{(4,8)}$=5,7; $p<10^{-3}$

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(81)}$	p-level
Variable	r		Intercpt	,8547	,1842	4,64	10^{-5}
Killing Index vs Staphyl. aureus	-0,29	-,287	,100	-,0052	,0018	-2,87	,005
Popovych's Adaptation Index-1	-0,28	-,289	,099	-,0734	,0252	-2,91	,005
Microbian Count vs Staph. aur.	0,24	,160	,100	,0030	,0019	1,60	,114
Immunoglobuline M	0,14	,134	,098	,0705	,0518	1,36	,177

Table 7. Regression Summary for F3H
R=0,444; R^2=0,197; Adjusted R^2=0,157; $F_{(4,8)}$=5,0; p=0,001

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(81)}$	p-level
Variable	r		Intercpt	,1954	,2813	,69	,489
Microbian Count vs E. coli	0,28	,314	,101	,0066	,0021	3,11	,003
Entropy of Leukocytogramm	0,19	,180	,102	,5989	,3401	1,76	,082
$CD4^+$ T-helper Lymphocytes	-0,23	-,221	,104	-,0046	,0021	-2,13	,036
Circulating Immune Complexes	-0,17	-,131	,102	-,0013	,0010	-1,29	,200

Table 8. Regression Summary for F4H
R=0,529; R^2=0,280; Adjusted R^2=0,215; $F_{(7,8)}$=4,3; $p<10^{-3}$

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(78)}$	p-level
Variable	r		Intercpt	,5714	,1915	2,98	,004
Popovych's Adaptation Index-1	-0,29	-,170	,103	-,0491	,0298	-1,65	,103
Circulating Immune Complexes	-0,28	-,197	,098	-,0021	,0011	-2,02	,047
$CD16^+$ NK Lymphocytes	-0,22	-,164	,124	-,0048	,0037	-1,32	,189
T Active Lymphocytes	-0,16	-,157	,109	-,0052	,0036	-1,44	,153
Microbian Count vs E. coli	0,27	,235	,101	,0052	,0022	2,33	,022
Leukocytes	0,19	,128	,101	,0212	,0167	1,27	,207
$CD8^+$ T-cytolytic Lymphocytes	0,16	,175	,109	,0055	,0035	1,60	,114

Table 9. Regression Summary for F7H
R=0,333; R^2=0,111; Adjusted R^2=0,067; $F_{(4,8)}$=2,5; p=0,047

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(81)}$	p-level
Variable	r		Intercpt	,3465	,2121	1,63	,106
T Active Lymphocytes	0,21	,153	,116	,0062	,0048	1,31	,194
Microbian Count vs Staph. aur.	0,18	,157	,106	,0041	,0028	1,48	,142
$CD16^+$ NK Lymphocytes	0,17	,128	,117	,0047	,0043	1,10	,275
Circulating Immune Complexes	-0,16	-,180	,106	-,0024	,0014	-1,70	,093

Table 10. Regression Summary for F8H
R=0,270; R^2=0,073; Adjusted R^2=0,051; $F_{(2,8)}$=3,3; p=0,043

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(83)}$	p-level
Variable	r		Intercpt	,5860	,2113	2,77	,007

Microbian Count vs E. coli	-0,16	,135	,106	,0039	,0031	1,27	,206
Popovych's Adaptation Index-1	-0,23	-,222	,106	-,0844	,0404	-2,09	,040

Table 11. Regression Summary for T3H
R=0,233; R^2=0,054; Adjusted R^2=0,043; $F_{(1,8)}$=4,8; p=0,031

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(84)}$	p-level
Variable	r		Intercpt	1,0430	,1048	9,95	10^{-6}
Killing Index vs Staphyl. aureus	-0,23	-,233	,106	-,0046	,0021	-2,19	,031

Table 12. Regression Summary for T4H
R=0,282; R^2=0,080; Adjusted R^2=0,057; $F_{(2,8)}$=3,6; p=0,032

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(83)}$	p-level
Variable	r		Intercpt	1,0583	,1011	10,5	10^{-6}
Killing Index vs Staphyl. aureus	-0,21	-,224	,106	-,0040	,0019	-2,12	,037
Popovych's Adaptation Index-1	-0,17	-,193	,106	-,0473	,0260	-1,82	,072

Table 13. Regression Summary for C3H
R=0,390; R^2=0,152; Adjusted R^2=0,110; $F_{(4,8)}$=3,6; p=0,009

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(81)}$	p-level
Variable	r		Intercpt	,7265	,1317	5,52	10^{-6}
Immunoglobuline M	0,25	,210	,106	,0926	,0464	1,99	,049
Microbian Count vs E. coli	0,18	,161	,106	,0026	,0017	1,52	,133
Immunoglobuline A	-0,23	-,175	,109	-,0455	,0283	-1,61	,112
T Active Lymphocytes	-0,19	-,158	,109	-,0039	,0027	-1,45	,152

Table 14. Regression Summary for C4H
R=0,358; R^2=0,129; Adjusted R^2=0,085; $F_{(4,8)}$=3,0; p=0,024

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(81)}$	p-level
Variable	r		Intercpt	,5516	,1460	3,78	,0003
Microbian Count vs Staph. aur.	0,27	,244	,104	,0042	,0018	2,34	,022
Immunoglobuline M	0,17	,143	,105	,0686	,0502	1,37	,175
Popovych's Adaptation Index-1	-0,17	-,133	,105	-,0306	,0242	-1,27	,209
Circulating Immune Complexes	-0,16	-,110	,105	-,0009	,0009	-1,05	,298

Table 15. Regression Summary for T5H
R=0,302; R^2=0,091; Adjusted R^2=0,058; $F_{(3,8)}$=2,7; p=0,049

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(82)}$	p-level
Variable	r		Intercpt	1,192	,2985	3,99	,0001
Entropy of LCG	-0,23	-,165	,111	-,6284	,4257	-1,48	,144
Killing Index vs Staphyl. aureus	-0,16	-,121	,110	-,0027	,0025	-1,10	,274
$CD8^+$ T-cytolytic Lymphocytes	0,20	,173	,107	,0060	,0037	1,61	,111

Table 16. Regression Summary for T6H
R=0,329; R^2=0,108; Adjusted R^2=0,075; $F_{(3,8)}$=3,3; p=0,024

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(82)}$	p-level
Variable	r		Intercpt	,6442	,2218	2,90	,005

$CD16^+$ NK Lymphocytes	0,25	,218	,108	,0067	,0033	2,02	,047
Microbian Count vs Staph. aur.	0,16	,142	,106	,0032	,0024	1,34	,185
Killing Index vs Staphyl. aureus	-0,22	-,140	,109	-,0030	,0024	-1,28	,204

Table 17. Regression Summary for P3H
R=0,389; R^2=0,152; Adjusted R^2=0,099; $F_{(5,8)}$=2,9; p=0,020

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(80)}$	p-level
Variable	r		Intercpt	2,589	1,501	1,72	,089
SN Neutrophils	0,24	-,684	,699	-,0111	,0114	-,98	,331
Killing Index vs E. coli	-0,23	-,246	,123	-,0024	,0012	-2,00	,048
Entropy of LCG	-0,22	-,355	,337	-,9487	,8993	-1,06	,295
Eosinophils	-0,20	-,244	,119	-,0164	,0080	-2,04	,044
Lymphocytes	-0,20	-,661	,545	-,0117	,0096	-1,21	,229

Table 18. Regression Summary for O1H
R=0,464; R^2=0,215; Adjusted R^2=0,156; $F_{(6,8)}$=3,6; p=0,003

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(79)}$	p-level
Variable	r		Intercpt	1,645	,3186	5,17	10^{-5}
Entropy of LCG	-0,31	-,427	,157	-1,541	,5677	-2,71	,008
Popovych's Strain Index-2	-0,26	-1,289	,576	-,5618	,2510	-2,24	,028
Popovych's Strain Index-1	-0,23	1,040	,526	,5748	,2908	1,98	,052
Killing Index vs Staphyl. aureus	-0,20	-,151	,107	-,0032	,0023	-1,41	,163
Eosinophils	-0,18	,444	,276	,0404	,0251	1,61	,111
Immunoglobuline M	0,17	,199	,101	,1235	,0630	1,96	,053

Table 19. Regression Summary for O2H
R=0,321; R^2=0,103; Adjusted R^2=0,071; $F_{(3,8)}$=3,2; p=0,027

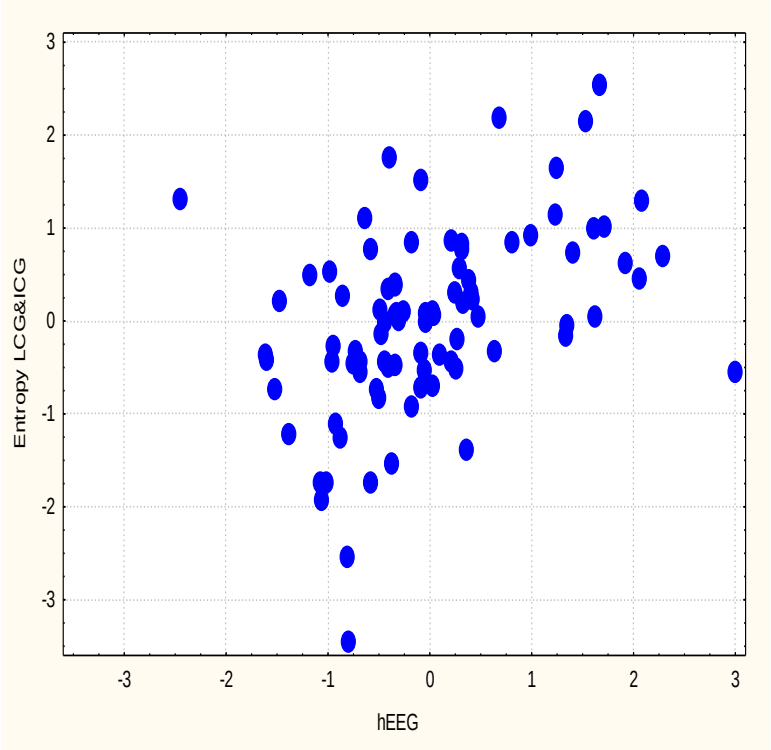
		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(84)}$	p-level
Variable	r		Intercpt	,5817	,3440	1,69	,095
Killing Index vs Staphyl. aureus	-0,23	-,233	,104	-,0048	,0022	-2,23	,028
Popovych's Strain Index-2	-0,17	-,130	,105	-,0558	,0448	-1,24	,217
Entropy of ICG	0,18	,141	,105	,4419	,3292	1,34	,183

As we see, the coefficients of the multiplicity correlation, despite the statistical significance, are very moderate, being in the range of 0,233÷0,529.

A similar situation with respect to the influence of entropy of the constellation of EEG loci on the entropy of LCG and ICG is revealed also in the result of canonical correlation analysis (Table 20 and Fig. 1).

Table 20. Factor Structure Matrix for Entropy of EEG vs Entropy of LCG and ICG

Right set	R
O1H	**-,681**
T5H	**-,564**
P3H	**-,563**
O2H	**-,507**
T6H	**-,481**
F3H	**,491**
Left set	R
LCGH	**,952**
ICGH	**-,661**



R=0,433; R^2=0,188; $\chi^2_{(12)}$=23; p=0,024; Λ Prime=0,750

Figure 1. Scatterplot of canonical correlation between Entropy of EEG (X-line) and LCG and ICG (Y-line)

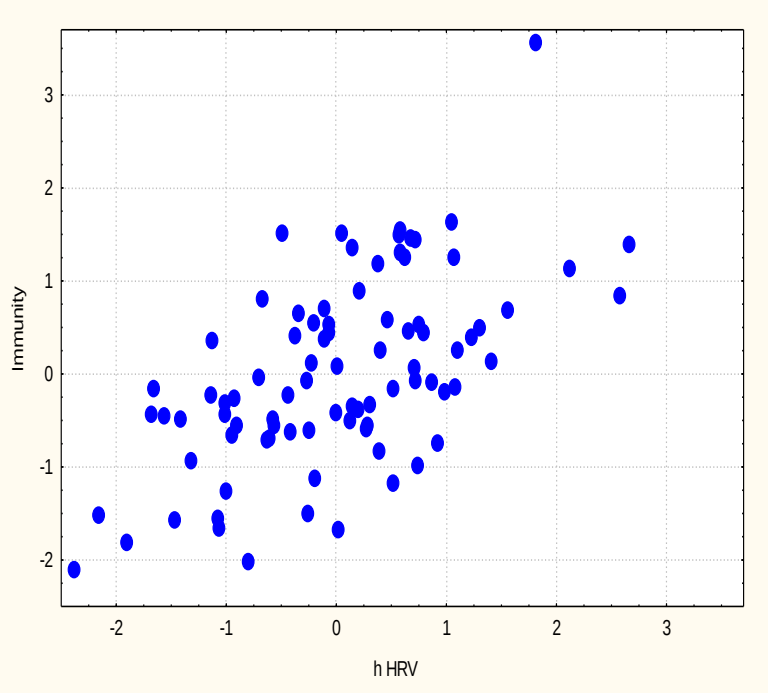
Instead, the maximum determinant influence on the parameters of immunity is the entropy of HRV (Table 20).

This is consistent with the concept [14-17,23,24,28] that the sympathetic and vagal nerves directly affect the immunocytes, more precisely the norepinephrine and acetylcholine released by their terminals, whereas cortical and subcortical neural structures directly regulate the nucleus of the autonomic nervous system (nucleus coeruleus, ambiguus, dorsalis motoris etc).

Table 21. Regression Summary for HRVH

R=0,597; R^2=0,355; Adjusted R^2=0,278; $F_{(9,8)}$=4,6; $p<10^{-4}$

		Beta	St. Err. of Beta	B	St. Err. of B	$t_{(76)}$	p-level
Variable	r		Intercpt	1,2477	,2009	6,21	10^{-6}
Killing Index vs Staphyl. aureus	0,28	,150	,104	,0023	,0016	1,44	,154
$CD8^+$ T-cytolytic Lymphocytes	0,17	,221	,102	,0051	,0024	2,16	,034
Microbian Count vs E. coli	-0,27	-,310	,101	-,0050	,0016	-3,07	,003
Segmentonucleary Neutrophiles	-0,25	-,235	,117	-,0037	,0018	-2,02	,047
Popovych's Strain Index-2	-0,23	,635	,437	,1957	,1346	1,45	,150
Popovych's Adaptation Index-2	-0,21	-,190	,104	-,0513	,0282	-1,82	,072
Eosinophiles	-0,21	-,312	,195	-,0201	,0126	-1,60	,114
Leukocytes	-0,18	-,168	,103	-,0204	,0125	-1,63	,106
Popovych's Strain Index-1	-0,18	-,767	,397	-,2999	,1555	-1,93	,057



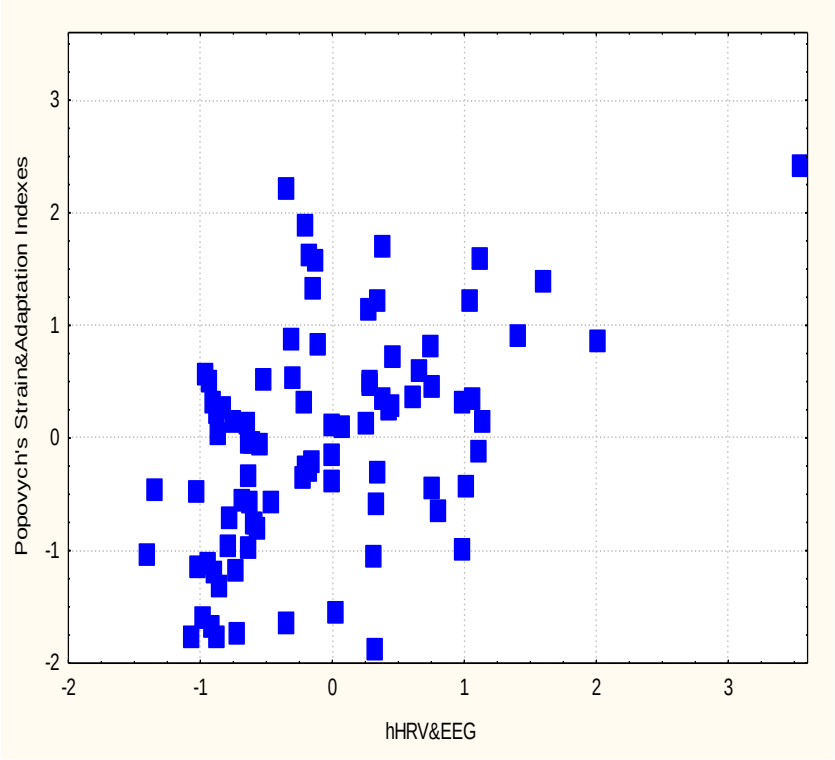
R=0,597; R^2=0,355; $\chi^2_{(9)}$=35; $p<10^{-4}$; Λ Prime=0,645

Figure 2. Scatterplot of canonical correlation between Entropy of HRV (X-line) and Immunity (Y-line)

A special canonical analysis has shown that the newly proposed modifications of Popovych's Strain and Adaptation Indices are more closely correlated with the entropies of the neural regulatory structures compared to the previous version(Table 22 and Fig. 3).

Table 22. Factor Structure Matrix for Entropy of HRV and EEG vs Popovych's Strain and Adaptation Indices

Right set	**R**
HRVH	**-,657**
O1H	**-,444**
FP1H	**-,112**
FP2H	**-,051**
P3H	**,204**
F4H	**,018**
Left set	**R**
PSI-2	**,739**
PSI-1	**,709**
PAI-2	**,510**
PAI-1	,100



R=0,540; R^2=0,291; $\chi^2_{(24)}$=54; p=0,0005; Λ Prime=0,514

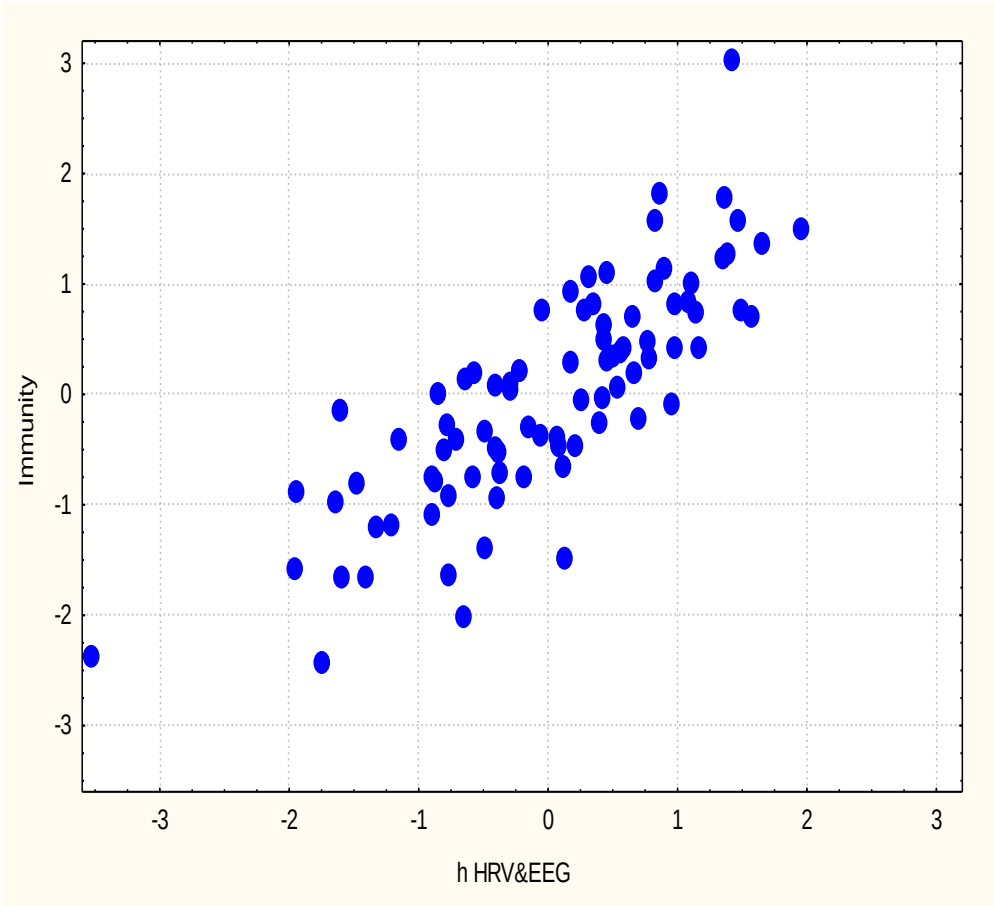
Figure 3. Scatterplot of canonical correlation between Entropy of HRV and EEG (X-line) and Popovych's Strain and Adaptation Indices (Y-line)

At the final stage, we investigated the canonical correlation between the entropy of HRV and EEG, on the one hand, and the actual and **informational** parameters of immunity, on the other hand (Table 23 and Fig. 4).

Table 23. Factor Structure Matrix for Entropy of HRV and EEG vs Immunity in total

Right set	**R**
HRVH	**,635**
C3H	**,214**
F3H	**,102**
C4H	**,100**
F4H	**,073**
T5H	**,046**
T6H	**,037**
P3H	**-,290**
O2H	**-,260**
F7H	**-,212**
FP2H	**-,098**
O1H	**-,037**
Left set	**R**
Lymphocytes in total	**,715**
Killing Index vs E. coli	**,412**
Killing Index vs Staph. aureus	**,305**
Immunoglobuline M	**,286**
$CD8^+$ T-cytolytic Lymphocytes	**,141**
Circulating Immune Complex	**,088**
Entropy of LCG	**,064**
Segmentonucleary Neutrophils	**-,535**
T-active Lymphocytes	**-,420**

$CD16^+$ NK Lymphocytes	**-,345**
Popovych's Adaptation Index-2	**-,304**
Immunoglobuline A	**-,283**
Popovych's Strain Index-1	**-,280**
$CD4^+$ T-helper Lymphocytes	**-,242**
Popovych's Strain Index-2	**-,226**
Leukocytes	**-,167**
Popovych's Adaptation Index-1	**-,124**
Microbial Count vs E. coli	**-,109**
Eosinophils	**-,102**
Microbial Count vs Staph. aureus	**-,029**



R=0,814; R^2=0,663; $\chi^2_{(240)}$=296; p=0,008; Λ Prime=0,013

Figure 4. Scatterplot of canonical correlation between Entropy of HRV and EEG (X-line) and Immunity (Y-line)

Our data on the significant factor loads on the F3, F4, P3, T5, T6 and Fp2 loci are consistent with the KJ Tracey's [28] scheme of immunological homunculus (Fig. 5) by which the neural structures that are projected onto these loci responsible for the immune compartment cytokines release (F3 and F4), clonal expansion (P3), regulation of T cells (T5 and T6) and activation of memory B cells (Fp2) respectively.

However, we did not find in the factor structure matrix of the anterior temporal locus, on which projected nerve structures responsible for maturation of dendritic cells. Instead, we have reason to supplement the KJ Tracey's scheme with the assumption that the structures (hippocampus? [26]) that projected on the left central locus are responsible for increasing the content in blood of IgM and total lymphocytes and reducing the content of IgA and segmentonuclear neutrophils. Instead, the structures responsible for increasing the intensity

phagocytosis by neutrophils of gram-positive and gram-negative microbes are plotted on the right central locus.

Another addition may be the assumption of localization in the occipital loci of the structures responsible for the entropy of the leukocytogram, its strain, as well as the inhibition of completeness of phagocytosis of Staph. aureus, but not E. coli. Differences in the neural regulation of these two types of bacteria have been detected by us before [16].

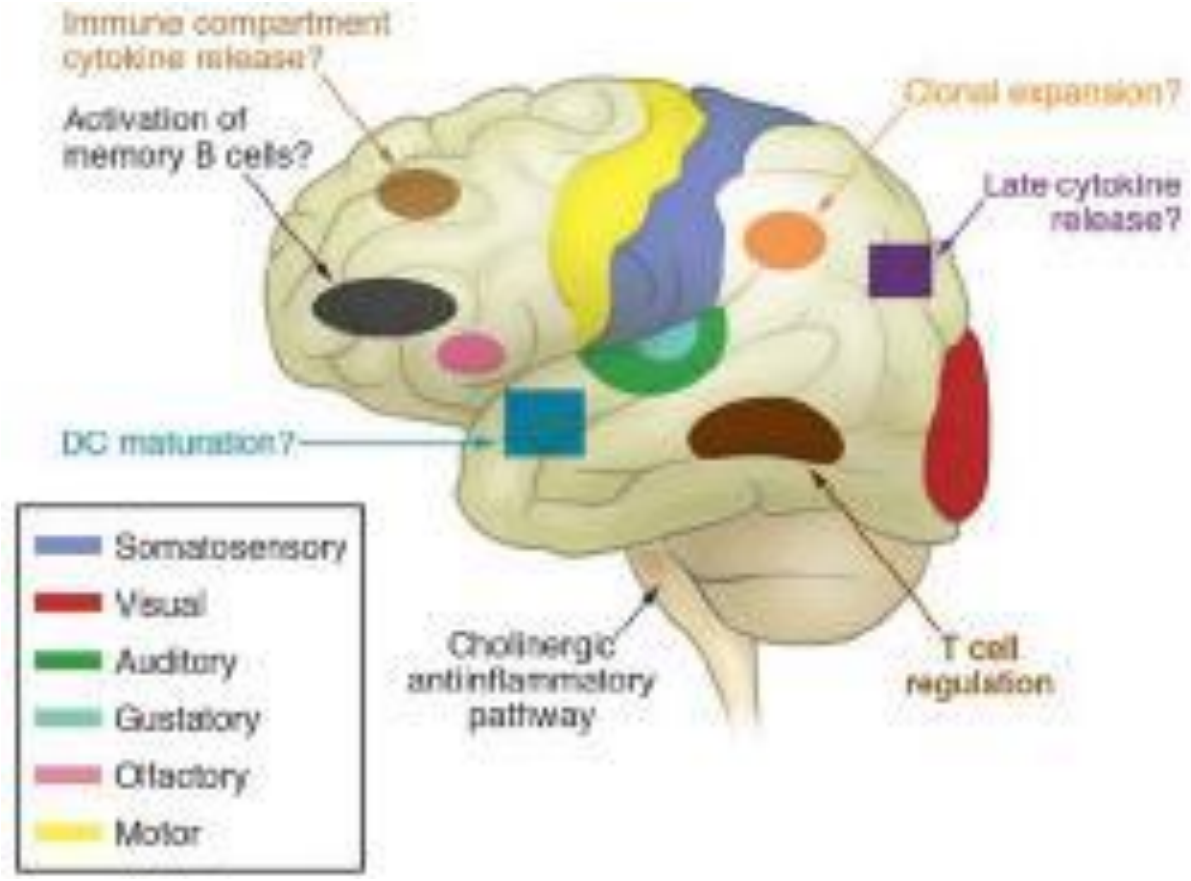


Figure 5. KJ Tracey's scheme of immunological homunculus [28]

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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