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Evaluation of quantitative-qualitative levels of blood pressure by Tensioregulome

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Abstract

Background. Earlier we showed that the qualitative-quantitative clusters of blood pressure (BP) are very clearly different from each other by age, sex and the constellation of neuro-endocrine, immune and metabolic variables, which we called the **Tensioregulome** by analogy with the metabolome and the microbiome. The purpose of this study is detailing this concept. **Materials and methods.** Under an observations were 44 patients with chronic pyelonephritis and cholecystitis in the phase of remission. Testing was performed twice - on admission and after 7-10 days of standard balneotherapy. The main object of the study was BP. We determined parameters of EEG and HRV, plasma levels of adaptation hormones, electrolytes, lipids, and nitrogenous metabolites, components of humoral, cellular, and phagocytic links of immunity and microbiota as well as markers of pyelonephritis. **Results**. The forward stepwise program identified 42 Tensioregulome parameters as characteristic of quantitative-qualitative blood pressure clusters: 25 EEGs, sympathetic tone, cortisol, calcitonin, *Bifidobacteria* faeces, 5 metabolic and 5 immune parameters as well as sex and age. The accuracy of patient classification is 97,7%. Another 15 parameters were found to be characteristic, but were outside the discriminant model. Non-linear correlations between the BP and Tensioregulome parameters were revealed. **Conclusion**. The Tensioregulome allows us to reliably evaluate quantitative-qualitative levels of blood pressure without measuring it with a tonometer.
Keywords: blood pressure, EEG, HRV, hormones, immunity, metabolome, pyelonephritis.

INTRODUCTION

Earlier we showed that the qualitative-quantitative clusters of blood pressure are very clearly different from each other by age, sex and the constellation of neuro-endocrine, immune and metabolic variables [13-17], which we called the **Tensioregulome** [30] by analogy with the metabolome and the microbiome. The purpose of this study is detailing this concept.

MATERIALS AND METHODS

Under an observations were 34 males and 10 females by age 24-76 years with chronic pyelonephritis and cholecystitis in the phase of remission. Testing was performed twice - on admission and after 7-10 days of standard balneotherapy (drinking of bioactive water Naftussya, applications of ozokerite, mineral pools) [4,29].

The main object of the study was blood pressure (BP). Systolic and diastolic BP was measured (by tonometer "Omron M4-I", Netherlands) in a sitting position three times in a row.

Retrospectively, 5 quantitative-qualitative blood pressure clusters were created (Fig. 1) according to the existing gradation [25,28].

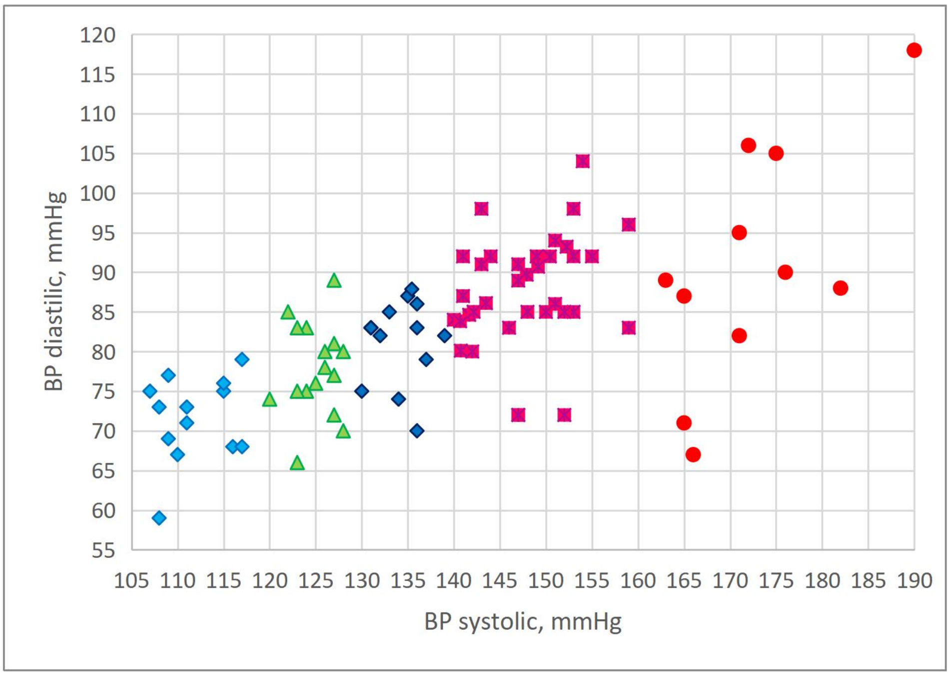

Fig. 1. Diagram of scattering of systolic and diastolic blood pressure of patients of Truskavets' spa

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 on the earlobes. Two minutes after the eyes had been closed, 25 sec of artifact free EEG data were collected by computer. Among the options considered the average EEG amplitude (μV), average frequency (Hz), frequency deviation (Hz), index (%), absolute (μV^2/Hz) and relative (%) PSD 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 coefficient of Asymmetry (As) and Laterality Index (LI) for PSD each Rhythm using equations [29]:

As, % = 100•(Max – Min)/Min; LI, % = Σ [200•(Right – Left)/(Right + Left)]/8.

We calculated for each locus EEG the Entropy (h) of normalized PSD using IL Popovych's [9,29] equation:

$$hEEG = - [PSD\alpha \cdot \log_2 PSD\alpha + PSD\beta \cdot \log_2 PSD\beta + PSD\theta \cdot \log_2 PSD\theta + PSD\delta \cdot \log_2 PSD\delta]/\log_2 4.$$

Simultaneosly recorded electrocardiogram in II lead to assess the parameters of HRV (software and hardware complex "CardioLab+HRV" produced by "KhAI-MEDICA", Kharkiv, Ukraine). For further analysis the following parameters heart rate variability (HRV) were selected. Temporal parameters (Time Domain Methods): heart rate (HR), mode (Mo), the standart deviation of all NN intervals (SDNN), 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 than 50 msec (pNN_{50}); triangular index (TNN). Spectral parameters (Frequency Domain Methods): power spectral density (PSD) 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 ultralow-frequency (ULF, range 0,015÷0,003 Hz). We calculated the Entropy of HRV band [9] and classical indexes LF/HF and LFnu=100%•LF/(LF+HF) as well as (VLF+LF)/HF as Centralization Index. RM Baevskiy's parameters: the amplitude of mode (AMo) and variational scope (MxDMn) as well as author's indexes: Baevskiy's Stress Index (BSI=AMo/2•Mo•MxDMn) and Baevskiy's Activity Regulatory Systems Index (BARSI) [3].

Among hormones determined main adaptation hormones such as Cortisol, Aldosterone, Testosterone, Triiodothyronine as well as Calcitonin (by the ELISA with the use of analyzers "Tecan" and "RT-2100C" and corresponding sets of reagents from "Алкор Био", XEMA Co, Ltd and DRG International Inc).

The author of the concept of stress-age syndrome VV Frolkis [5] proposed a stress coefficient, the numerator of which is represented by the blood concentration of catecholamines, ACTH, cortisol, vasopressin, and the denominator is the blood concentration of sex steroid hormones, thyroxine, TSH, as well as anti-stress neuropeptides. The authors of the concept of general adaptation reactions LKh Garkavi et al [6] added aldosterone to the list of anti-stress hormones. Based on the available data and the algorithm of the Truskavetsian Scientific School of Balneology [9,29], we offer our own modification of the neuro-hormonal stress index (NHSI) by combining Z-scores of BSI and hormones:

Frolkis's NHSI = (**BSI + cortisol** - **testosterone – triiodothyronine**)/4;

Garkavi's NHSI = (**BSI + cortisol** - **testosterone – triiodothyronine - aldosterone**)/5.

Immune status evaluated as described in the manual [24]. For phenotyping subpopulations of lymphocytes used the methods of rosette formation with sheep erythrocytes on which adsorbed monoclonal antibodies against receptors CD3, CD4, CD8, CD25, CD22 and CD56 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 of classes G, A, M (ELISA, analyser "Immunochem", USA) and circulating immune complexes (by polyethylene glycol precipitation method) as well as C-reactive protein (by the ELISA with the use of analyzer "RT-2100C"), Tumor Necrosis Factor-α, Interleukins 1β and 6 (ELISA, analyzer "Stat Fax 303", USA, reagents from "Vector-Best", RF).

In portion of the capillary blood we counted up Leukocytogram and calculated the Entropy (h) of Leukocytogram (LCG) as well as its Strain Index using IL Popovych's [9] equations:

$$hLCG = - [L \cdot \log_2 L + M \cdot \log_2 M + E \cdot \log_2 E + SNN \cdot \log_2 SNN + StubN \cdot \log_2 StubN]/\log_2 5;$$

$$\text{Strain Index-1} = [(Eos/3,5-1)^2 + (StubN/3,5-1)^2 + (Mon/5,5-1)^2 + (Leuk/6-1)^2]/4.$$

Parameters of phagocytic function of neutrophils estimated as described by MM Kovbasnyuk [19,31]. 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. Take into account the following parameters of Phagocytosis: activity (percentage of neutrophils, in which found microbes - Hamburger's Phagocytic Index PhI), intensity (number of microbes absorbed one phagocytes - Microbial Count MC or Right's Index) and completeness (percentage of dead microbes - Killing Index KI).

The condition of microbiota is evaluated on the results of sowing of feces. The levels of bacteriuria, leukocyturia, and erythrocyturia were also assessed by routine methods.

Daily urine was collected, in which was determined the concentration of electrolytes: calcium (by reaction with arsenase III), magnesium (by reaction with colgamite), phosphates (phosphate-molybdate method), chloride (mercury-rhodanidine method), sodium and potassium (flamming photometry); nitric metabolites: creatinine (by Jaffe's color reaction by Popper's method), urea (urease method by reaction with phenolhypochlorite), uric acid (uricase method). The same metabolic parameters were determined in plasma as well as glucose (glucose-oxidase method), triglycerides (by a certain meta-periodate method), total cholesterol (by a direct method after the classic reaction by Zlatkis-Zack) and content of him in composition of α-lipoproteins (HDLP) (by the enzyme method after precipitation of notα-lipoproteins); pre-β-lipoproteins (VLDLP) (expected by the level of triglycerides); β-lipoproteins (LDLP) (expected by a difference between a total cholesterol and cholesterol in composition α-and pre-β-lipoproteins). The analysis carried out according to instructions [7] with the use of analyzers "Reflotron" (BRD) and "Pointe-180" (USA) and corresponding sets of reagents.

Given its integral physiological nature [8,20-23], we determined also the electrokinetics index (EKI) as rate of electronegative nuclei of buccal epithelium by intracellular microelectrophoresis on the device "Biotest" (Kharkiv State University).

Normal (reference) values of variables are taken from the instructions and/or database of the Truskavetsian Scientific School of Balneology [29].

For statistical analysis used the software package "Statistica 6.4".

RESULTS AND DISCUSSION

In order to identify among the registered parameters, those for which the blood pressure clusters differ from each other, a discriminant analysis was performed [11]. The program forward stepwise included in the discriminant model 42 parameters. The following variables were identified as characteristic. Integral parameters of the organism: **age** and **sex index** (as a ratio between the number of the male and female in the cluster); 25 EEG parameters that reflect main rhythms – **delta** (5), **theta** (5), **alpha** (6) and **beta** (4) as well as **entropy** (5); HRV-marker of **sympathetic tone**, two hormones such as **cortisol** (actual) and **calcitonin** (standardized by sex [12]), 5 parameters of **immunity** and 5 parameters of **metabolome** as well as **Bifidobacteria** as representative of microbiome (Tables 1 and 2).

Table 1. Discriminant Function Analysis Summary for Variables, their actual levels for Clusters of Blood Pressure as well as Reference levels and Coefficients of Variability
Step 42, N of vars in model: 42; Grouping: 5 grs; Wilks' Λ: 0,0018; approx. $F_{(168)}$=3,9; $p<10^{-6}$

Variables currently in the model	Clusters of Blood Pressure (n)					Parameters of Wilk's Statistics						
	No-rm (16)	High N (13)	AH I (35)	Low N (13)	AH II (11)	Wil ks' Λ	Par-tial Λ	F-re-move (4,42)	p-level	Tole-rancy	Refe-rence (88)	Cv
Sex Index (M=1; F=2)	1,25 0,11	1,00 0,00	1,11 0,05	1,62 0,14	1,36 0,15	0,003	0,664	5,31	0,001	0,285	1,23 0,04	,343
Age, years	47,3 2,6	50,9 2,5	49,2 2,6	43,1 2,1	61,3 2,5	0,002	0,862	1,68	0,172	0,332	49,7 1,4	,257
Deviation-δ, Hz	0,66 0,08	0,55 0,04	0,70 0,04	0,85 0,10	0,64 0,07	0,003	0,709	4,30	0,005	0,365	0,67 0,03	,395
F4-δ PSD, %	40,5 6,5	35,5 8,4	30,2 3,0	44,1 8,0	40,1 9,3	0,003	0,550	8,61	10^{-4}	0,025	31,25 2,1	,624
T3-δ PSD, %	44,3 6,4	27,3 5,8	29,6 2,1	40,9 7,7	28,8 6,6	0,002	0,823	2,25	0,079	0,088	28,6 1,8	,596
C3-δ PSD, %	28,8 3,3	37,5 7,5	27,9 2,7	43,5 7,4	30,4 6,8	0,003	0,578	7,68	10^{-4}	0,032	28,0 1,8	,602
P3-δ PSD, %	24,8 3,5	26,0 5,6	27,7 2,8	36,7 7,1	25,2 6,0	0,003	0,683	4,88	0,003	0,088	25,6 1,9	,694
Amplitude-θ, μV	9,4 0,9	7,7 0,6	9,7 0,9	8,6 1,0	7,7 1,0	0,003	0,718	4,13	0,007	0,184	7,75 0,3	,376
F8-θ PSD, %	8,1 1,3	7,3 0,6	11,3 1,2	10,5 2,0	7,2 1,2	0,003	0,615	6,56	10^{-3}	0,131	9,8 0,5	,492
C4-θ PSD, %	9,8 1,1	9,5 1,4	13,9 1,1	11,9 1,3	9,4 1,1	0,003	0,636	6,01	0,001	0,110	11,1 0,5	,442
P4-θ PSD, %	7,3 0,7	7,2 0,8	10,2 0,9	9,3 1,3	9,4 1,6	0,004	0,432	13,8	10^{-6}	0,073	8,75 0,5	,545
O1-θ PSD, %	7,0 0,9	8,2 1,4	8,2 0,8	10,3 1,7	8,5 1,6	0,003	0,699	4,52	0,004	0,167	8,2 0,5	,584
Index-α, %	62,6 6,0	47,3 8,7	48,4 5,7	53,4 6,6	49,5 8,5	0,003	0,714	4,20	0,006	0,099	50,7 3,0	,560
Deviation-α, Hz	0,81 0,10	0,91 0,10	1,11 0,12	1,23 0,15	0,86 0,10	0,003	0,604	6,89	10^{-3}	0,313	1,02 0,06	,527
Fp2-α PSD, %	34,3 4,7	27,2 4,1	31,3 2,4	31,9 5,1	27,9 4,2	0,003	0,720	4,09	0,007	0,078	32,9 1,6	,448
F4-α PSD, %	31,1 4,0	27,5 6,5	28,7 2,0	28,1 5,6	27,2 5,7	0,002	0,783	2,91	0,033	0,025	31,1 1,6	,485
F7-α PSD, %	18,4 3,4	21,1 3,9	27,1 2,5	26,6 3,7	28,9 6,1	0,003	0,591	7,26	10^{-4}	0,138	27,6 1,5	,522
T4-α PSD, %	26,7 3,1	22,0 4,4	29,3 2,5	24,5 4,7	31,6 5,9	0,003	0,600	7,01	10^{-3}	0,072	29,0 1,6	,500
Laterality-β, %	-13 5,5	-13,0 10,8	-3,1 4,7	-6,2 7,2	-34 6,4	0,003	0,539	9,00	10^{-4}	0,268	-0,9 3,6	**SD** **34**
T3-β PSD, %	19,5 3,3	38,5 6,1	28,5 2,1	28,55 5,1	28,6 3,7	0,003	0,576	7,74	10^{-4}	0,072	30,7 1,5	,462
C3-β PSD, %	21,6 2,8	26,7 3,8	26,3 2,0	16,6 2,4	27,1 3,6	0,004	0,515	9,89	10^{-5}	0,029	25,45 1,1	,420
O1-β PSD, %	16,4 3,1	26,1 4,4	28,0 3,2	18,4 2,7	31,6 4,8	0,003	0,677	5,02	0,002	0,167	26,3 1,5	,542
Entropy PSD F3	0,78 0,05	0,81 0,04	0,89 0,02	0,76 0,05	0,81 0,04	0,003	0,559	8,29	10^{-4}	0,126	0,862 0,012	,130

Entropy PSD T3	0,78 0,04	0,75 0,04	0,90 0,01	0,76 0,05	0,83 0,04	0,004	0,512	10,0	10^{-5}	0,111	0,857 0,012	,131
Entropy PSD T5	0,81 0,05	0,77 0,04	0,83 0,02	0,73 0,04	0,74 0,08	0,002	0,851	1,83	0,140	0,256	0,825 0,014	,156
Entropy PSD T6	0,76 0,05	0,80 0,03	0,83 0,03	0,85 0,02	0,74 0,07	0,002	0,777	3,01	0,028	0,160	0,825 0,013	,149
Entropy PSD P3	0,82 0,02	0,81 0,03	0,82 0,02	0,77 0,05	0,80 0,05	0,002	0,758	3,35	0,018	0,132	0,802 0,014	,167
LF PSD nu, %	79,4 3,6	68,6 5,1	71,1 2,5	58,7 5,7	74,9 3,9	0,003	0,533	9,19	10^{-4}	0,324	64,2 1,4	,201
Cortisol, nM/L	386 47	446 56	374 26	391 44	469 49	0,002	0,897	1,21	0,321	0,474	370 12	,303
Calcitonin, Z	-0,47 0,33	-0,94 0,19	-0,78 0,09	-0,13 0,35	-0,69 0,30	0,002	0,862	1,68	0,172	0,481	0	
Interleukin-6, ng/L	3,64 0,81	4,76 0,91	4,62 0,55	4,61 0,88	7,22 0,76	0,002	0,810	2,46	0,060	0,346	4,25 0,15	,324
CIC, units	34 4	30 3	34 2	43 5	42 6	0,002	0,776	3,03	0,028	0,461	45 2	,389
$CD4^+$ T-helper Lym, %	30,5 2,2	33,1 1,9	27,4 1,0	35,9 2,6	33,7 1,9	0,002	0,835	2,07	0,102	0,189	39,5 0,7	,164
Phag Ind vs St. aur., %	99,2 0,19	99,3 0,21	98,6 0,24	98,9 0,32	98,5 0,34	0,002	0,764	3,25	0,021	0,224	98,3 0,19	,018
Micr. Count St. aur., B/Ph	64,1 1,9	63,2 1,9	61,3 1,6	63,9 1,9	59,7 1,9	0,002	0,837	2,05	0,105	0,327	61,6 1,1	,160
Sodium Plasma, mM/L	145 2,0	140,4 2,1	140 1,5	148,2 1,2	149 2,8	0,004	0,452	12,7	10^{-6}	0,288	145 0,5	,034
Magnesium P, mM/L	0,84 0,01	0,84 0,01	0,83 0,01	0,82 0,01	0,85 0,02	0,003	0,700	4,50	0,004	0,279	0,90 0,01	,056
Phosphate P, mM/L	1,00 0,04	1,09 0,07	1,02 0,03	0,90 0,05	1,08 0,07	0,004	0,453	12,7	10^{-6}	0,127	1,20 0,02	,167
Potassium P, mM/L	4,22 0,14	4,35 0,15	4,22 0,09	4,72 0,16	4,49 0,14	0,004	0,452	12,7	10^{-6}	0,288	4,55 0,05	,104
Potassium Excr, mM/d	66 5	71 13	79 7	63 9	72 8	0,002	0,868	1,60	0,192	0,374	65 2	,269
Calcium Excretion, mM/d	3,92 0,44	4,88 0,86	6,17 0,60	4,82 0,79	3,74 0,72	0,002	0,845	1,93	0,123	0,454	4,38 0,10	,214
Bifidobacteria,lgCFU/g	5,52 0,36	5,78 0,24	5,69 0,19	5,38 0,35	5,35 0,30	0,002	0,846	1,92	0,125	0,282	6,94 0,01	,011

Table 2. Summary of Stepwise Analysis for Variables, ranked by criterion Lambda

Variables currently in the model	F to enter	p-level	Λ	F-value	p-value
Sex Index (M=1; F=2)	5,61	10^{-3}	0,787	5,61	10^{-3}
Sodium Plasma, mM/L	4,45	0,003	0,647	4,99	10^{-4}
Entropy PSD T3	4,29	0,003	0,534	4,79	10^{-6}
Age, years	3,69	0,008	0,451	4,56	10^{-6}
Deviation-δ, Hz	3,63	0,009	0,381	4,44	10^{-6}
Phagocytic Ind vs St. aur., %	3,52	0,011	0,323	4,36	10^{-6}
$CD4^+$ T-helper Lymphoc, %	3,23	0,017	0,276	4,27	10^{-6}
LF PSD nu, %	3,79	0,007	0,230	4,31	10^{-6}
T3-β PSD, %	2,79	0,032	0,201	4,21	10^{-6}
P3-δ PSD, %	2,53	0,048	0,176	4,10	10^{-6}
F7-α PSD, %	2,11	0,089	0,158	3,96	10^{-6}
O1-β PSD, %	2,24	0,073	0,141	3,86	10^{-6}

Laterality-β, %	2,51	0,050	0,123	3,82	10^{-6}
Phosphate Plasma, mM/L	2,67	0,039	0,107	3,81	10^{-6}
Magnesium Plasma, mM/L	3,02	0,024	0,091	3,84	10^{-6}
Interleukin-6, ng/L	2,51	0,050	0,079	3,82	10^{-6}
F8-θ PSD, %	2,42	0,057	0,069	3,80	10^{-6}
Fp2-α PSD, %	2,27	0,071	0,061	3,77	10^{-6}
CIC, units	1,89	0,123	0,055	3,71	10^{-6}
O1-θ PSD, %	2,12	0,089	0,048	3,69	10^{-6}
T3-δ PSD, %	1,87	0,127	0,043	3,64	10^{-6}
Deviation-α, Hz	2,08	0,095	0,038	3,62	10^{-6}
Calcium Excretion, mM/d	2,07	0,095	0,033	3,60	10^{-6}
F4-α PSD, %	1,97	0,110	0,030	3,58	10^{-6}
C4-θ PSD, %	2,03	0,102	0,026	3,57	10^{-6}
Amplitude-θ, μV	2,44	0,057	0,022	3,60	10^{-6}
Index-α, %	2,23	0,077	0,019	3,61	10^{-6}
P4-θ PSD, %	2,90	0,030	0,016	3,69	10^{-6}
Entropy PSD P3	3,29	0,017	0,013	3,80	10^{-6}
Entropy PSD T6	2,83	0,033	0,011	3,87	10^{-6}
Entropy PSD F3	2,40	0,061	0,009	3,91	10^{-6}
$CD4^+CD25^+$ T-regulatory, %	2,09	0,095	0,008	3,92	10^{-6}
Microb Count St. aur., B/Ph	1,74	0,156	0,007	3,90	10^{-6}
Cortisol, nM/L	1,77	0,150	0,006	3,88	10^{-6}
F4-δ PSD, %	1,73	0,159	0,005	3,87	10^{-6}
T4-α PSD, %	1,78	0,148	0,005	3,86	10^{-6}
C3-β PSD, %	1,47	0,225	0,004	3,83	10^{-6}
C3-δ PSD, %	4,29	0,005	0,003	4,06	10^{-6}
Calcitonin, Z	1,36	0,263	0,003	4,01	10^{-6}
Entropy PSD T5	1,53	0,211	0,002	3,99	10^{-6}
Bifidobacteria feces, lgCFU/g	1,21	0,322	0,002	3,94	10^{-6}
Potassium Excretion, mM/d	1,60	0,192	0,002	3,93	10^{-6}

Another 14 variables also were found to be characteristic, but were outside the discriminant model due to duplication/redundancy of information (Table 3).

Table 3. Discriminant Function Analysis Summary for Variables currently not in the model

Variables	**No-rm (16)**	**High N (13)**	**AH I (35)**	**Low N (13)**	**AH II (11)**	Wilks' Λ	Partial Λ	F to enter	p-level	Tolerancy	Reference (88)	Cv
Electrokinetic Index, %	46,6 2,7	42,7 2,6	44,7 2,3	50,1 2,5	31,7 2,1	0,002	0,836	2,06	0,103	0,291	40,9 1,1	,250
T5-β PSD, %	19,9 2,5	35,4 5,9	31,2 3,2	24,9 5,3	26,4 4,9	0,143	0,939	0,64	0,634	0,394	29,0 1,7	,536
Baevskiy's' Stress In, Z	1,26 0,94	-0,25 0,20	0,75 0,44	-0,62 0,26	1,51 1,14	0,002	0,865	1,64	0,181	0,445	0	
Triangular Index, units	10,2 1,1	10,8 0,7	11,1 0,7	13,7 1,0	8,5 0,9	0,002	0,682	4,89	0,002	0,102	11,2 0,26	,217
Testosterone, Z	-0,35 0,34	0,74 0,74	0,37 0,46	-0,11 0,41	0,84 0,71	0,140	0,920	0,86	0,494	0,395	0	
Aldosterone, pM/L	227 6	232 11	229 4	221 5	226 5	0,149	0,976	0,24	0,913	0,286	238 5	,187
Triiodothyronine, nM/l	2,17 0,31	1,72 0,24	1,95 0,11	2,24 0,20	1,90 0,16	0,147	0,964	0,38	0,825	0,292	2,20 0,05	,227
Frolkis's	0,46	0,23	0,23	-0,10	0,54	0,002	0,827	2,19	0,086	0,093	0	

NHSI	0,35	0,25	0,19	0,22	0,29							
Garkavi's NHSI	0,41 0,28	0,21 0,20	0,22 0,15	-0,01 0,18	0,49 0,25	0,002	0,903	1,13	0,357	0,160	0	
Popovych's Strain Ind-1	0,16 0,03	0,14 0,02	0,18 0,02	0,11 0,02	0,11 0,02	0,143	0,939	0,64	0,634	0,394	0,10 0,01	,559
Monocytes, %	5,38 0,49	6,39 0,55	6,55 0,36	5,15 0,61	5,05 0,48	0,144	0,948	0,54	0,704	0,449	6,00 0,05	,166
IgA Serum, g/L	1,78 0,11	1,91 0,14	1,58 0,09	1,92 0,12	2,03 0,05	0,147	0,966	0,36	0,837	0,312	1,875 0,03	,167
Cholesterol, mM/L	4,88 0,27	5,55 0,35	5,43 0,15	5,36 0,20	5,93 0,24	0,002	0,697	4,57	0,004	0,284	5,37 0,11	,192
VLD Lipo-prot Chol, Z	0,16 0,26	-0,51 0,19	0,39 0,16	-0,41 0,18	0,19 0,21	0,002	0,682	4,89	0,002	0,102	0	

The 42-dimensional space of discriminant variables transforms into 4-dimensional space of a canonical roots. For Root 1 r*=0,956 (Wilks' Λ=0,0018; $\chi^2_{(168)}=401$; $p<10^{-6}$), for Root 2 r*=0,908 (Wilks' Λ=0,0207; $\chi^2_{(123)}=246$; $p<10^{-6}$), for Root 3 r*=0,825 (Wilks' Λ=0,118; $\chi^2_{(80)}=136$; $p=10^{-4}$), and for Root 4 r*=0,794 (Wilks' Λ=0,370; $\chi^2_{(39)}=63$; p=0,008). The first root contains 55,2% of discriminative opportunities, the II 24,6%, the III 12,2%, the last 9,0%.

Table 4 presents standardized and raw coefficients for discriminant variables, which are used for the calculation of the discriminant root values for each person, that enables the visualization of each patient in the information space of the roots.

Table 4. Standardized and Raw Coefficients and Constants for Blood Pressure and Neuro-Endocrine Variables

Coefficients	Standardized				Raw			
Variables currently in the model	Root 1	Root 2	Root 3	Root 4	Root 1	Root 2	Root 3	Root 4
Sex Index (M=1; F=2)	-0,539	0,175	-1,140	0,031	-1,407	0,457	-2,978	0,080
Sodium Plasma, mM/L	-1,397	0,196	-0,341	-0,118	-0,176	0,025	-0,043	-0,015
Entropy PSD T3	-0,301	-2,072	-0,671	0,855	-2,391	-16,44	-5,320	6,779
Age, years	0,573	0,229	0,158	-0,297	0,048	0,0193	0,0133	-0,0249
Deviation-δ, Hz	-0,752	-0,123	-0,592	0,206	-2,998	-0,492	-2,360	0,820
Phagoc. Ind vs St. aur., %	0,710	-0,439	0,700	0,406	0,613	-0,379	0,605	0,351
$CD4^+$ T-helper Lymph, %	-0,861	-0,057	0,333	-0,432	-0,120	-0,008	0,046	-0,060
LF PSD nu, %	0,657	-0,933	-0,681	0,152	0,041	-0,059	-0,043	0,010
T3-β PSD, %	1,606	2,057	-0,284	0,199	0,113	0,145	-0,020	0,014
P3-δ PSD, %	0,621	1,914	0,612	-0,037	0,036	0,110	0,035	-0,002
F7-α PSD, %	-1,573	-0,165	0,800	0,631	-0,113	-0,012	0,058	0,045
O1-β PSD, %	-1,128	-0,936	-0,250	-0,092	-0,080	-0,066	-0,018	-0,006
Laterality-β, %	-0,022	1,337	0,562	0,224	-0,001	0,053	0,022	0,009
Phosphate Plasma, mM/L	1,347	1,499	0,431	-1,026	6,800	7,569	2,175	-5,181
Magnesium Plasma, mM/L	0,657	0,479	0,429	-0,761	16,93	12,35	11,08	-19,61
Interleukin-6, ng/L	-0,741	-0,119	0,228	0,005	-0,296	-0,048	0,091	0,002
F8-θ PSD, %	0,933	-1,528	-0,414	0,385	0,174	-0,285	-0,077	0,072
Fp2-α PSD, %	1,770	-0,192	-1,018	0,150	0,120	-0,013	-0,069	0,010
CIC, units	-0,197	0,628	-0,421	0,083	-0,013	0,040	-0,027	0,005
O1-θ PSD, %	-0,756	1,182	0,076	-0,449	-0,170	0,265	0,017	-0,101
T3-δ PSD, %	0,831	0,142	-1,147	0,858	0,042	0,007	-0,058	0,044
Deviation-α, Hz	0,862	0,631	0,465	0,419	1,789	1,308	0,965	0,869
Calcium Excretion, mM/d	0,444	0,117	0,379	0,291	0,148	0,039	0,126	0,097
F4-α PSD, %	-2,541	0,761	1,660	-0,811	-0,159	0,048	0,104	-0,051
C4-θ PSD, %	0,884	1,545	0,965	-0,014	0,187	0,327	0,204	-0,003

Amplitude-θ, µV	0,678	-1,087	-0,415	0,207	0,183	-0,294	-0,112	0,056
Index-α, %	0,300	1,644	0,754	0,562	0,011	0,062	0,028	0,021
P4-θ PSD, %	-2,806	-0,450	0,162	0,820	-0,684	-0,110	0,040	0,200
Entropy PSD P3	1,005	0,812	-0,147	-0,738	8,335	6,735	-1,219	-6,124
Entropy PSD T6	0,626	0,999	0,525	-0,191	4,183	6,672	3,504	-1,275
Entropy PSD F3	-1,753	-0,836	0,403	0,001	-12,75	-6,080	2,932	0,007
$CD4^+CD25^+$ T-regulator, %	-0,026	-0,639	0,451	-0,034	-0,006	-0,157	0,111	-0,008
Micr Count St. aur., B/Ph	-0,141	0,016	-0,795	-0,284	-0,017	0,002	-0,097	-0,035
Cortisol, nM/L	-0,345	0,018	-0,036	-0,414	-0,002	0,0001	-0,0002	-0,0024
F4-δ PSD, %	-3,947	-1,438	1,639	-0,335	-0,167	-0,061	0,069	-0,014
T4-α PSD, %	-2,291	-0,633	0,801	0,121	-0,161	-0,044	0,056	0,009
C3-β PSD, %	-3,618	-0,781	2,312	0,802	-0,342	-0,074	0,218	0,076
C3-δ PSD, %	-3,216	-0,440	2,224	0,808	-0,172	-0,023	0,119	0,043
Calcitonin, Z	0,461	0,208	-0,281	-0,078	0,540	0,244	-0,330	-0,091
Entropy PSD T5	0,750	0,200	0,058	-0,230	4,760	1,272	0,368	-1,457
Bifidobacteria fec, lgCFU/g	0,608	-0,034	-0,456	-0,327	0,521	-0,029	-0,390	-0,281
Potassium Excretio, mM/d	-0,365	0,095	0,404	0,424	-0,010	0,003	0,011	0,012
	Constants				-30,81	23,14	-70,51	-12,82
	Eigenvalues				10,49	4,688	2,135	1,706
	Cumulative proportions				0,552	0,798	0,910	1

The localization along the major root axis of the patients with **AH II** (Fig. 2) in the extreme left (negative) zone reflects combination of maximum for sampling BP levels with **maximally increased** plasma IL-6 and testosterone levels, as well as normal, but maximum for the sample levels of cholesterol and PSD of beta-rhythm in O1 locus and alpha-rhythm in F7 locus. On the other hand, **AH II** is accompanied by normal, but minimum for the sample levels of the index and PSD of alpha-rhythm in F4 locus, amplitude of theta-rhythm, PSD of delta-rhythm in T3 locus as well as intensity of phagocytosis of Staph. aureus (Table 5).

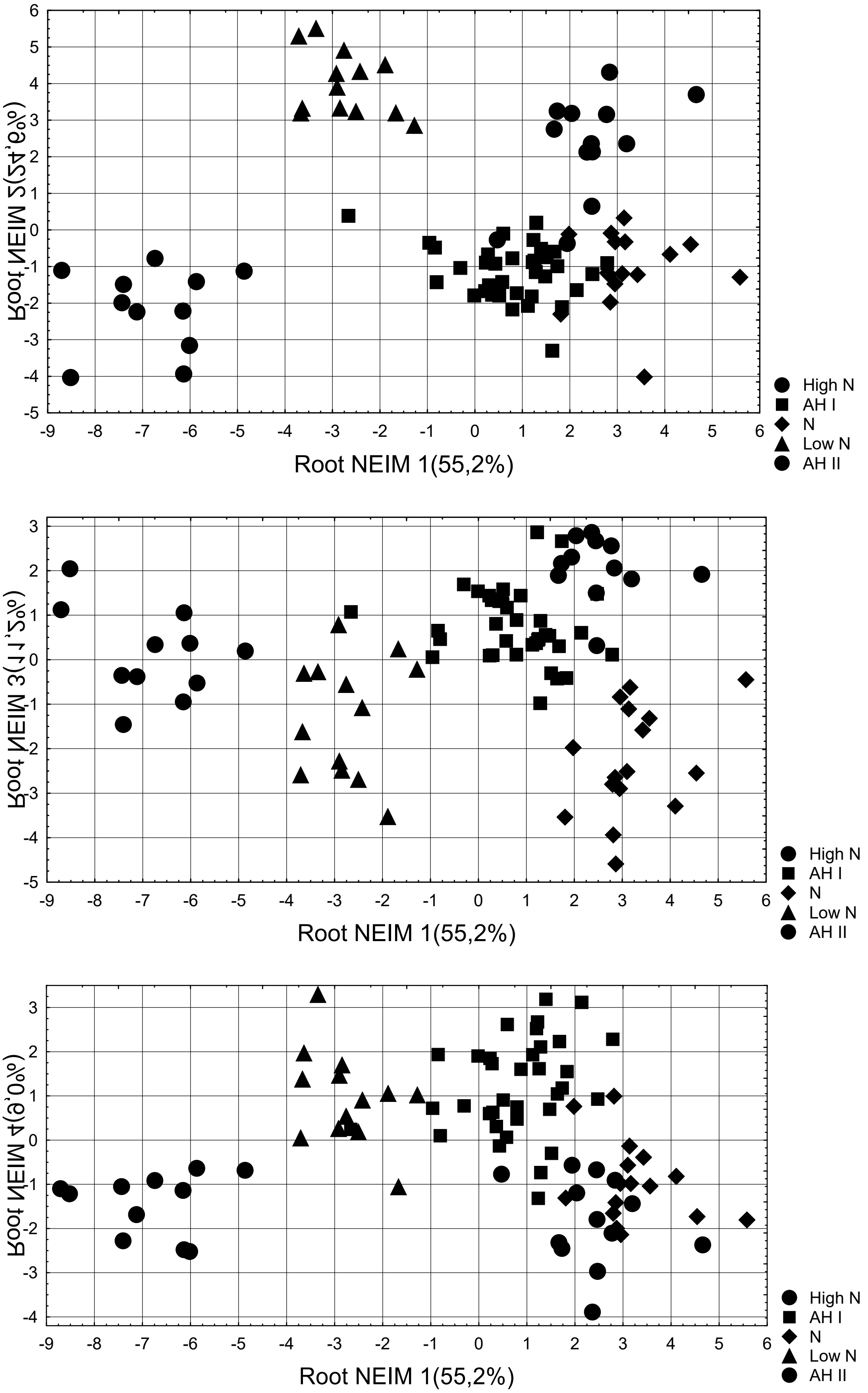

Fig. 2. Scattering of individual values of the discriminant roots of patients of different blood pressure clusters

At the opposite pole of the axis of the first root, there are patients with **Norm** BP, which are characterized, as a rule, by the **minimum**/**maximum** levels of the listed variables comparable to those in patients with **AH II**. It is interesting that in the latter patients (as well as with **AH I**), the sex- and age-normalized testosterone levels are increased almost equally in men and women, while among patients with **Norm** BP, the testosterone level in men is in the lower normal range, and in women - in the upper range.

The projections of patients with **High Norm** BP on the axis of the first root are only slightly shifted to the left and are densely intertwined, which is understandable, instead, the cluster of patients with **Low Norm** BP is localized close to patients with **AH II** (a situation where the extremes paradoxically converge). The separation of this cluster from others occurs along the axis of the second root. The top position of patients with minimum BP reflects, first of all, their youngest age as well as **maximally decreased** levels of plasma phosphate and magnesium, PSD of beta-rhythm in C3 locus, entropy of PSD in F3 and T5 loci, **minimum** for the sample lower border levels of entropy of PSD in P3 locus, sympathetic tone markers, and aldosterone as well as normal, but minimum for the sample levels of T-regulatory lymphocytes, potassium excretion and Frolkis's and Garkavi's NHSI. On the other hand, minimum BP is accompanied by maximum electrokinetic index (which reflects, first of all, biological age [8,20-23]), upper limit levels of vagal tone, PSD of delta-rhythm in F4, C3 and P3 loci, theta-rhythm in O1 locus, entropy of PSD in T6 locus, deviation of alpha-rhythm as well as normal, but maximum for the sample levels of plasma potassium and blood T-helper lymphocytes.

Demarcation of cluster with **High Norm** BP, whose members are exclusively men, occurs along the axis of the third root. The bottommost position of patients reflects their **minimally decreased** level of *Bifidobacteria* in faeces and normal, but maximum for the sample levels of the PSD of beta-rhythm in T3 and T5 loci, on the one hand, while **minimum** for the sample lower border levels of the PSD of alpha-rhythm in Fp2 and T4 loci and deviation of delta-rhythm, as well as **maximally decreased** levels of circulating immune complexes, triiodothyronine and calcitonin.

Finally, along the axis of the fourth root, the top positions are occupied by cluster of patients with **AH I,** which reflects their normal, but maximum for the sample levels of the PSD of theta-rhythm in C4, F8 and P4 loci, entropy of PSD in T3 locus and plasma VLD LP cholesterol as well as **maximally increased** levels of plasma calcium, blood monocytes and Popovych's Strain Index of leukocytogram as marker of maladaptation [29]. The symmetry of the beta- rhythm is also characteristic, in contrast to its left-sided asymmetry in other clusters. On the other hand, such patients are characterized by normal, but **minimum** for the sample levels of cortisol and activity of phagocytosis of Staph. aureus by neutrophils as well as **maximally decreased** plasma levels of sodium, chloride and IgA.

Table 5. Correlations Variables-Canonical Roots, Means of Roots and Z-scores of Variables

Variables of Tensioregulome	Correlations Variables-Roots				Norm (16)	High N (13)	AH I (35)	Low N (13)	AH II (11)
Root 1 (55,2%)	R 1	R 2	R 3	R 4	+3,2	+2,4	+0,8	-2,7	-6,8
See Fig. 3									
Interleukin-6	-0,093	-0,046	0,087	-0,080	-0,44	+0,37	+0,27	+0,26	+2,16
Cholesterol total					-0,43	+0,13	+0,12	+0,05	+0,27
F7-α PSD	-0,062	-0,008	0,067	0,096	-0,63	-0,45	-0,03	-0,07	+0,09
O1-β PSD	-0,052	-0,071	0,199	-0,003	-0,70	-0,01	+0,12	-0,56	+0,37
Testosterone total					-0,35	+0,74	+0,37	-0,11	+0,84
Testosterone Male					-0,59	+0,74	+0,35	-0,50	+0,91

Testosterone Female					+0,37		+0,50	+0,13	**+0,71**
See Fig. 4									
Amplitude-θ	**0,034**	-0,030	-0,047	-0,086	**+0,57**	-0,02	+0,65	+0,30	-0,03
T3-δ PSD	**0,025**	0,033	**-0,207**	0,009	**+0,92**	-0,07	+0,06	+0,72	+0,01
Index-α	**0,022**	-0,008	**-0,123**	-0,028	**+0,42**	-0,12	-0,08	+0,09	-0,04
F4-α PSD	**0,016**	-0,011	-0,037	0,002	**+0,00**	-0,24	-0,16	-0,20	-0,26
Microb Cou St. aur.	**0,033**	0,057	-0,069	-0,026	**+0,26**	+0,16	-0,03	+0,23	-0,19
Root 2 (24,6%)	**R 1**	**R 2**	**R 3**	**R 4**	-1,1	+2,3	-1,15	**+4,0**	-2,1
See Fig. 4									
Age	-0,070	**-0,112**	0,110	-0,166	-0,18	+0,10	-0,04	**-0,52**	+0,92
LF PSD nu	0,037	**-0,154**	-0,056	-0,126	+1,28	+0,34	+0,51	**-0,34**	+0,68
Baevskiy's' Stress In					+1,26	-0,25	+0,75	**-0,62**	+1,51
C3-β PSD	0,002	**-0,099**	0,164	-0,067	-0,36	+0,11	+0,08	**-0,83**	+0,16
Entropy PSD F3	0,016	**-0,075**	0,134	0,109	-0,73	-0,48	+0,22	**-0,89**	-0,50
Entropy PSD T5	0,047	-0,059	0,016	0,060	-0,15	-0,45	+0,05	**-0,70**	-0,64
Entropy PSD P3	0,030	**-0,055**	0,020	-0,009	+0,16	+0,06	+0,17	**-0,26**	-0,02
$CD4^{+}CD25^{+}$ T-regs	0,046	**-0,090**	-0,013	0,047	+1,74	+1,07	+1,85	**+0,47**	+0,95
Phosphate Plasma	0,003	**-0,071**	0,127	-0,133	-0,98	-0,57	-0,89	**-1,49**	-0,58
Magnesium Plasma	-0,009	**-0,043**	-0,023	-0,181	-1,15	-1,21	-1,49	**-1,56**	-1,02
Potassium Excretion	0,004	**-0,047**	0,084	0,055	+0,05	+0,36	+0,80	**-0,11**	+0,43
Aldosterone					-0,24	-0,14	-0,20	**-0,37**	-0,28
Frolkis's NHSI					+0,46	+0,23	+0,23	**-0,10**	+0,54
Garkavi's NHSI					+0,41	+0,21	+0,22	**-0,01**	+0,49
See Fig. 5									
C3-δ PSD	-0,030	**0,115**	-0,033	0,030	+0,04	+0,33	-0,01	**+0,92**	+0,14
P3-δ PSD	-0,021	**0,079**	-0,026	0,095	-0,04	+0,03	+0,12	**+0,63**	-0,02
F4-δ PSD	-0,022	**0,041**	-0,093	-0,049	+0,48	+0,22	-0,05	**+0,66**	+0,45
O1-θ PSD	-0,041	**0,071**	0,013	0,066	-0,26	-0,01	-0,01	**+0,43**	+0,05
Deviation-α	-0,019	**0,071**	0,031	0,186	-0,39	-0,21	+0,17	**+0,39**	-0,29
Entropy PSD T6	0,008	**0,068**	0,032	0,143	-0,51	-0,22	+0,03	**+0,23**	-0,69
Electrokinetic Index					+0,56	+0,18	+0,38	**+0,89**	-0,90
Triangular Ind HRV					-0,40	-0,15	-0,04	**+1,03**	-1,13
Potassium Plasma					-0,70	-0,43	-0,69	**+0,35**	-0,12
$CD4^{+}$ T-helper Lym	-0,070	**0,145**	-0,076	0,168	-1,39	-0,99	-1,87	**-0,55**	-0,89
Root 3 (12,2%)	**R 1**	**R 2**	**R 3**	**R 4**	-2,3	**+2,0**	+0,7	-1,3	+0,1
See Fig. 6									
T3-β PSD	-0,017	0,075	**0,218**	-0,033	-0,79	**+0,55**	-0,15	-0,15	-0,15
T5-β PSD					-0,58	**+0,42**	+0,15	-0,26	-0,16
Bifidobacteria feces	0,030	-0,005	**0,065**	0,010	-1,25	**-1,02**	-1,10	-1,37	-1,39
See Fig. 7									
Sex Index	-0,099	0,097	**-0,235**	0,057	+0,05	**-0,54**	-0,27	+0,94	+0,32
Deviation-δ	-0,032	0,064	**-0,104**	0,177	-0,05	**-0,47**	-0,10	+0,67	-0,13
Fp2-α PSD	0,021	-0,007	**-0,085**	0,045	+0,09	**-0,39**	-0,11	-0,07	-0,34
T4-α PSD	-0,029	-0,076	**-0,005**	0,033	-0,15	**-0,48**	+0,02	-0,31	+0,18
Calcitonin total	-0,018	0,058	**-0,154**	0,047	-0,47	**-0,94**	-0,78	-0,12	-0,69
Calcitonin Male					-0,74	**-0,94**	-0,83	-0,70	-1,26
Calcitonin Female					+0,35		-0,37	+0,25	+0,32
Triiodothyronine					-0,06	**-0,95**	-0,50	+0,09	-0,60
CIC	-0,074	0,027	**-0,090**	0,036	-0,60	**-0,84**	-0,62	-0,11	-0,17
Root 4 (9,0%)	**R 1**	**R 2**	**R 3**	**R 4**	-0,95	-1,8	**+1,2**	+1,0	-1,4
See Fig. 8									
C4-θ PSD	0,010	-0,007	0,059	**0,250**	-0,29	-0,34	**+0,59**	+0,16	-0,36
F8-θ PSD	0,008	0,016	0,009	**0,212**	-0,35	-0,52	**+0,30**	0,14	-0,55
P4-θ PSD	-0,043	-0,024	0,050	**0,155**	-0,30	-0,32	**+0,31**	+0,12	+0,14

Entropy PSD T3	-0,014	-0,134	0,102	**0,192**	-0,70	-0,98	**+0,42**	-0,84	-0,21
Laterality-β	0,067	0,058	0,012	**0,195**	-0,37	-0,36	**-0,07**	-0,16	-0,97
Calcium Excretion	0,028	-0,010	0,127	**0,202**	-0,48	+0,54	**+1,92**	+0,47	-0,68
VLD LP Cholesterol					+0,16	-0,51	**+0,39**	-0,41	+0,19
Monocytes Blood					-0,62	+0,39	**+0,55**	-0,86	-0,96
Popovych's Strain-1					+1,18	+0,86	**+1,43**	+0,26	+0,18
See Fig. 9									
Cortisol	-0,033	0,008	0,043	**-0,131**	+0,15	+0,68	**+0,04**	+0,19	+0,89
Sodium Plasma	-0,093	0,049	-0,223	**-0,113**	+0,07	-0,93	**-1,05**	+0,65	+0,71
Chloride Plasma					+0,69	-0,54	**-0,67**	+1,38	+1,45
Phag. Ind. vs St. aur.	0,049	0,061	-0,042	**-0,131**	+0,53	+0,59	**+0,18**	+0,35	+0,14
IgA Serum					-0,31	+0,13	**-0,94**	+0,13	+0,50

In general, all clusters on the planes of four roots are clearly delineated, which is documented by calculating the Mahalanobis distances (Table 6).

Table 6. Squared Mahalanobis Distances between Blood Pressure Clusters, F-values (df=42,4) and p-levels

Blood Pressure Clusters	**High Norm**	**AH I**	**Norm**	**Low Norm**	**AH II**
High Norm	0	**24,8**	**31,2**	**47,9**	**108**
AH I	**2,83** 10^{-3}	0	**19,7**	**43,0**	**66,0**
Norm	**2,70** 10^{-3}	**2,60** 10^{-2}	0	**66,2**	**108**
Low Norm	**3,75** 10^{-4}	**4,91** 10^{-6}	**5,72** 10^{-6}	0	**62,0**
AH II	**7,73** 10^{-6}	**6,66** 10^{-6}	**8,49** 10^{-6}	**4,45** 10^{-5}	0

The same discriminant parameters can be used to identify the belonging of one or another person to one or another BP cluster. These functions are special linear combinations that maximize differences between groups and minimize dispersion within groups. The coefficients of the classifying functions are not standardized therefore they are not interpreted. An object belongs to a group with the maximum value of a function calculated by summing the products of the values of the variables by the coefficients of the classifying functions plus the constant (Table 7).

Table 7. Coefficients and Constants for Classification Functions for Blood Pressure Clusters

Blood Pressure Clusters	**High N**	**AH I**	**Norm**	**Low N**	**AH II**
Variables currently in the model	p=,148	p=,398	p=,182	p=,148	p=,125
Sex Index (M=1; F=2)	-298,9	-294,2	-288,7	-280,9	-282,3
Sodium Plasma, mM/L	-11,31	-11,10	-11,36	-10,26	-9,722
Entropy PSD T3	281,3	368,3	363,0	301,4	388,1
Age, years	1,877	1,642	1,774	1,550	1,315
Deviation-δ, Hz	-282,4	-270,4	-272,4	-257,8	-247,9
Phagocytic Index vs Staph. aureus, %	272,1	272,7	271,6	267,3	267,1
CD4$^+$ T-helper Lymphocytes, %	-5,945	-5,966	-6,270	-5,665	-4,916
LF PSD nu, %	0,514	0,731	0,937	0,369	0,476
T3-β PSD, %	3,683	3,076	3,391	3,460	2,050
P3-δ PSD, %	0,389	-0,094	-0,102	0,276	-0,490
F7-α PSD, %	6,536	6,820	6,272	7,033	7,540

O1-β PSD, %	-2,050	-1,694	-1,824	-1,716	-0,995
Laterality-β, %	0,595	0,414	0,329	0,643	0,332
Phosphate Plasma, mM/L	41,26	-13,73	7,844	-2,036	-60,62
Magnesium Plasma, mM/L	-134,1	-276,2	-225,6	-290,4	-372,4
Interleukin-6, ng/L	12,81	13,33	12,33	13,95	15,57
F8-θ PSD, %	7,509	8,516	9,002	6,578	7,331
Fp2-α PSD, %	1,550	1,521	1,999	1,169	0,638
Circulating Immune Complexes, units	-3,368	-3,435	-3,393	-3,130	-3,376
O1-θ PSD, %	-9,562	-10,52	-10,75	-8,570	-9,236
T3-δ PSD, %	2,814	2,929	3,116	2,926	2,521
Deviation-α, Hz	133,1	127,1	126,8	125,4	109,4
Calcium Excretion, mM/d	16,18	15,94	15,71	15,34	14,45
F4-α PSD, %	11,92	11,73	11,14	12,33	12,96
C4-θ PSD, %	30,31	28,63	28,49	29,24	26,76
Amplitude-θ, μV	-4,008	-2,987	-2,339	-4,932	-4,172
Index-α, %	2,889	2,686	2,586	2,902	2,466
P4-θ PSD, %	-14,93	-12,91	-15,13	-11,19	-8,149
Entropy PSD P3	311,7	258,6	296,2	267,7	205,4
Entropy PSD T6	-36,82	-74,55	-71,82	-61,75	-111,7
Entropy PSD F3	-322,8	-285,4	-325,8	-277,7	-184,2
$CD4^+CD25^+$ T-regulatory Lymph, %	25,38	25,76	25,42	24,75	25,92
Microbial Count for St. aur., Bac/Phag	-21,27	-21,23	-20,90	-20,96	-20,95
Cortisol, nM/L	-0,360	-0,364	-0,363	-0,355	-0,342
F4-δ PSD, %	7,874	8,218	7,627	8,357	9,544
T4-α PSD, %	4,799	5,161	4,577	5,385	6,373
C3-β PSD, %	21,85	22,60	20,93	22,97	24,94
C3-δ PSD, %	12,94	13,27	12,40	13,51	14,41
Calcitonin, Z	-14,91	-16,46	-13,93	-16,42	-20,37
Entropy PSD T5	-372,1	-388,9	-375,2	-399,5	-422,7
Bifidobacteria feces, lgCFU/g	-14,07	-15,15	-12,09	-16,29	-18,11
Potassium Excretion, mM/d	0,960	0,988	0,904	1,012	1,025
Constants	-13098	-13067	-12908	-12707	-12805

In this case, we can retrospectively recognize patients with high norm BP with two mistake and others patients **unmistakably**. Overall classification accuracy is 97,7% (Table 8).

Table 8. Classification Matrix for Blood Pressure Clusters

Group	Rows: Observed classifications Columns: Predicted classifications Percent Correct	High N p=,14773	AH I p=,39773	N p=,18182	Low N p=,14773	AH II p=,12500
High N	84,6	11	2	0	0	0
AH I	100,0	0	35	0	0	0
N	100,0	0	0	16	0	0
Low N	100,0	0	0	0	13	0
AH II	100,0	0	0	0	0	11
Total	97,7	11	37	16	13	11

At the next stage, an analysis of the correlations between the average Z-scores of systolic and diastolic BP, on the one hand, and the variables whose information is condensed in four discriminant roots, as well as not included in the model (see please Table 5), on the other hand, was performed.

Figures 3-10 illustrate that there are correlations between blood pressure and elements of the Tensioregulome, but they are non-linear and approximated by curves of only the second/third orders.

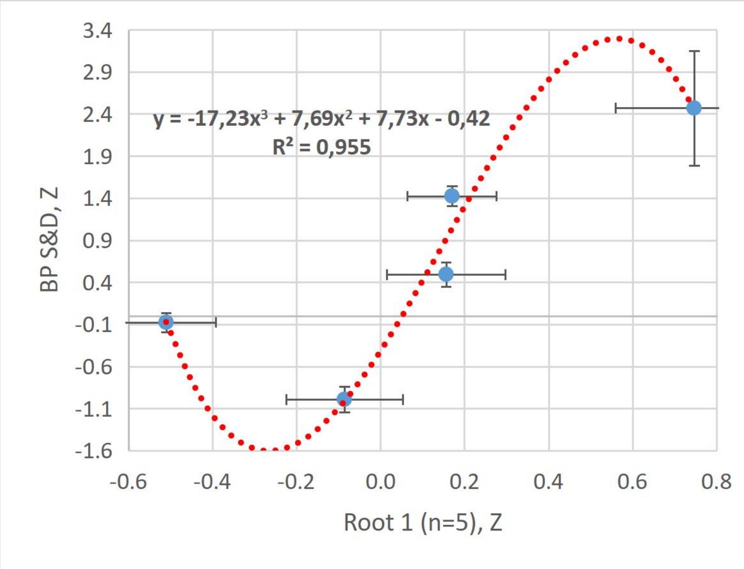

Fig. 3. Scatterplot of correlation between means of 5 variables of Root 1 (X-line) and means of systolic and diastolic blood pressure (Y-line)

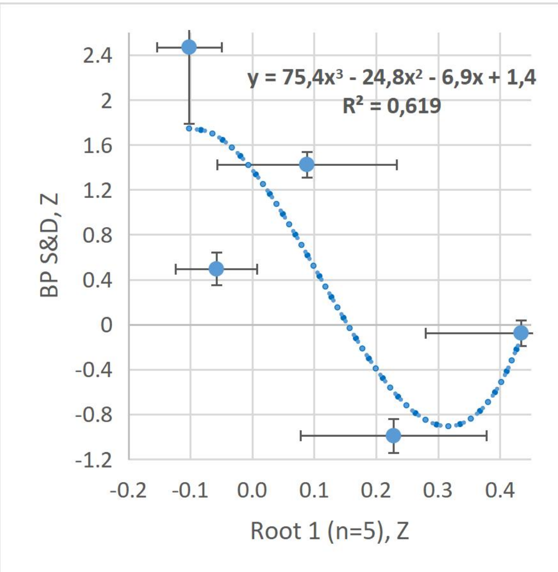

Fig. 4. Scatterplot of correlation between means of 5 variables of Root 1 (X-line) and means of systolic and diastolic blood pressure (Y-line)

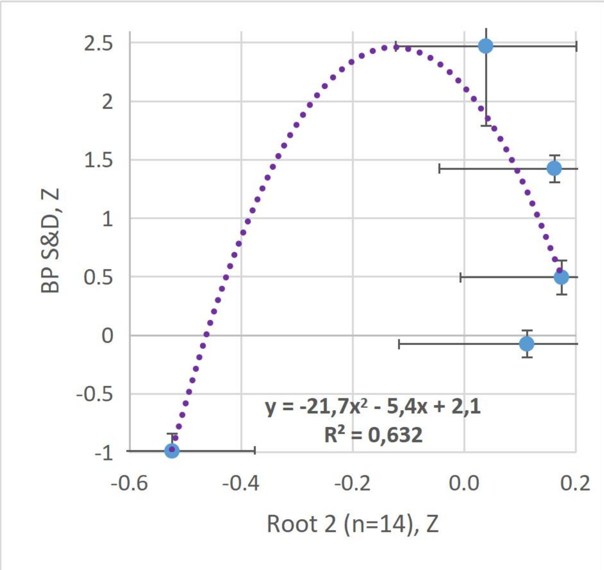

Fig. 5. Scatterplot of correlation between means of 14 variables of Root 2 (X-line) and means of systolic and diastolic blood pressure (Y-line)

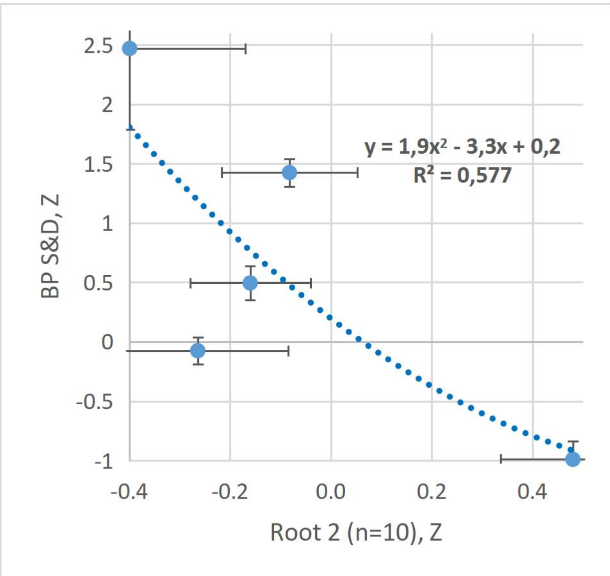

Fig. 6. Scatterplot of correlation between means of 10 variables of Root 2 (X-line) and means of systolic and diastolic blood pressure (Y-line)

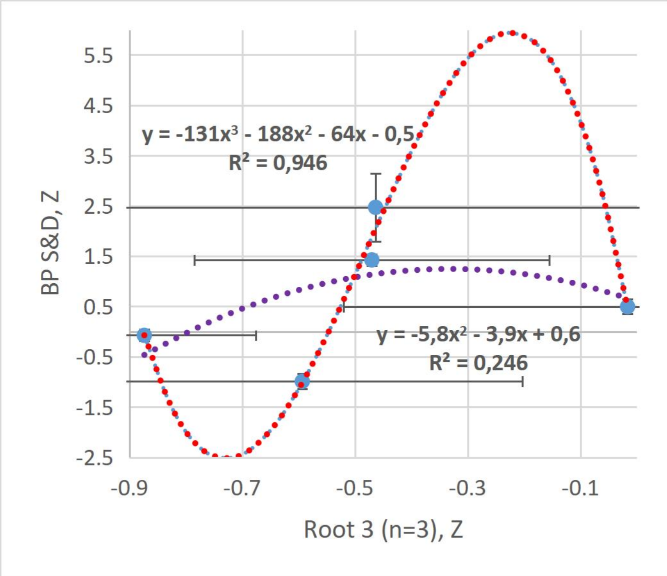

Fig. 7. Scatterplot of correlation between means of 3 variables of Root 3 (X-line) and means of systolic and diastolic blood pressure (Y-line)

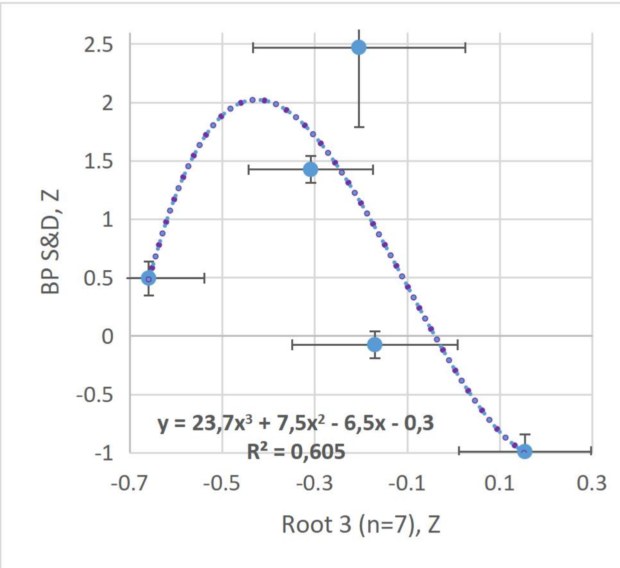

Fig. 8. Scatterplot of correlation between means of 7 variables of Root 3 (X-line) and means of systolic and diastolic blood pressure (Y-line)

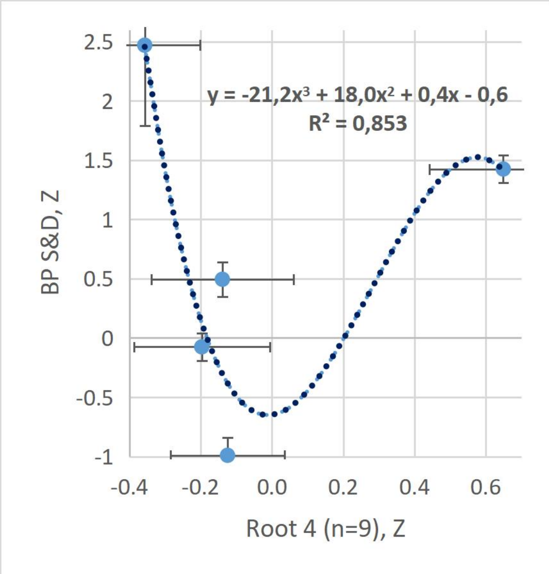

Fig. 9. Scatterplot of correlation between means of 9 variables of Root 4 (X-line) and means of systolic and diastolic blood pressure (Y-line)

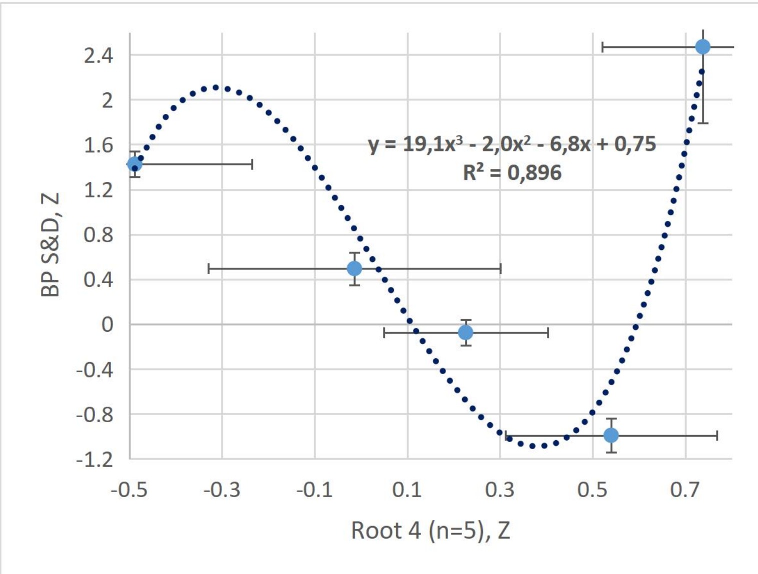

Fig. 10. Scatterplot of correlation between means of 5 variables of Root 4 (X-line) and means of systolic and diastolic blood pressure (Y-line)

CONCLUSION

Judging by the maximum structural coefficient (Variables-Roots correlation coefficient), the key element of Tensioregulome is the plasma level of IL-6. We have shown that the levels of this pro-inflammatory factor are normal in patients with normal BP, instead, it increase both when BP increases and decreases. It is known that the main sources of interleukins are monocytes/macrophages, as well as T- and B- lymphocytes, neutrophils, etc [34]. Both CR-mediated and FcγR-mediated phagocytosis increases levels of pro-inflammatory factors such as IL-6, TNF-α, IL-1β, and MMP-9 [1]. Cytokines released from immune cells, promote both renal and vascular dysfunction and damage, leading to enhanced sodium retention and increased systemic vascular resistance. Recent experiments have defined a link between oxidative stress and immune activation in hypertension [26]. Cells in innate immune system produce ROS, such as superoxide and hydrogen peroxide, which aimed at killing pathogens. Long-term inflammation process increases ROS production, causing oxidative stress which leads to endothelial dysfunction. Endothelial function is to regulate blood vessel tone and structure. When inflammation lasts, NO bioavailability decreases, disrupting its main function as vasodilator, so that blood vessels relaxation and vasodilatation are absent [2].

Recent laboratory evidence has defined a link between inflammation and the immune system in initiation and progression of hypertension. Moreover, cross-talk among natural killer cells, adaptive immune cells (T cells and B cells), and innate immune cells (i.e. monocytes, macrophages, neutrophils, and dendritic cells) contributes to end-cardiovasculature damage and dysfunction in hypertension [32,33,35]. It is important that the role of adaptive immunity is sex-specific with much more pronounced mechanisms in males than that in females [27]. Earlier, we discovered the same contingent sexual dimorphism in some psycho-neuro-endocrine parameters [12].

Our data are consistent with the classical notions of downregulation of BP by vagal tone and factors linked to female sex, instead of upregulation by factors linked to male sex and age, as well as by sympathetic tone and NaCl [10]. However, our data disagree with the concept that the hypertensive responses can be inhibited by T regulatory lymphocytes and their anti-inflammatory IL-10 [27,33].

In our humble opinion, what is new is the discovery of relationships between BP and EEG parameters, which, in turn, are related to immunity parameters [9,18,19,29,31].

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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 parent of 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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