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EFFECTS OF TRANSCUTANEOUS ELECTRICAL STIMULATION WITH THE DEVICE "VEB" ® ON THE HUMAN BODY

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Abstract

Background. In 2015, a generator for electrotherapy and stimulation oh human nerve centers was created, called “VEB-1”®. Preliminary observation of volunteers revealed a modulating effect of a four-day course of electrical stimulation on the parameters of electroencephalogram, metabolism, as well as gas-discharge visualization (GDV). In this message, we present the results of the approbation of the device on an expanded contingent of volunteers with the use of additional research methods and a new modification of the device. **Material and research methods.** The object of observation were employees of the sanatorium “Moldova”, patients with chronic cholecystitis: 19 women 30-62 y and 19 men 25-63 y. In the morning registered HRV (“CardioLab+HRV”, “KhAI-Medica”, Kharkiv, UA), EEG (“NeuroCom Standard”, “KhAI-Medica”, Kharkiv, UA), kirlianogram by the method of GDV (“GDV Chamber”, “Biotechprogress”, SPb, RF), electroconductivity of skin in three pairs of points of acupuncture (“Medissa”), electrokinetic index of buccal epithelium ("Biotest", Kharkiv State University), as well as some endocrine, immune and metabolic parameters. After the initial testing, an transcutaneous electrical stimulation session was performed with a “VEB-1”® or a “VEB-2” devices. The next morning after completing the four-day course, retesting was performed. **Results.** Electrical stimulation causes a sympathotonic shift in the sympatho-vagal balance and an increase in PSD of delta-rhythm generating neurons combined with a decrease in PSD of beta- and theta-rhythm generating neurons. This is accompanied by increase in phagocytosis and favorable changes in immune, biochemical and biophysical parameters as well as increase in testosterone level in men only. The integral effects on the constellation of registered body parameters of both device modifications do not differ significantly. **Conclusion**. The "VEB" device exerts an adaptogenic effect on the body through transcutaneous electrical stimulation of neurons.

Keywords: "VEB" device, transcutaneous electrical stimulation, EEG, HRV, GDV, Immunity, Metabolism.

INTRODUCTION

In 2015, a generator for electrotherapy and stimulation oh human nerve centers was created (**Babelyuk VE, Dobrovolsky YG, Korsunskyi IH)**, called “VEB-1”®. Conceiving and creating our device, we were based on the following provisions. The influence of impulses of a rectangular shape (range 7-18 Hz) made it possible to fix the frequency ranges of each basic nerve node. Low frequency had minimal effects of stimulation on the corresponding nerve node, while high frequency - the maximum. For the effective excitation of nerve centers, the frequency beat method is used. It consists in obtaining oscillations with close frequencies. To obtain the effect of the frequency beats are generated by pulses of rectangular shape to two signal channels. The channels differ in frequency, which is the beat frequency. For example, for obtaining a beat frequency 6 Hz, forming pulses in a first channel to a carrier frequency of 30 Hz, a second channel at a frequency of 36 Hz. When the first pulse is formed on both channels with a phase shift of 0^o, we obtain an absolute zero current in the output (Figure 1).

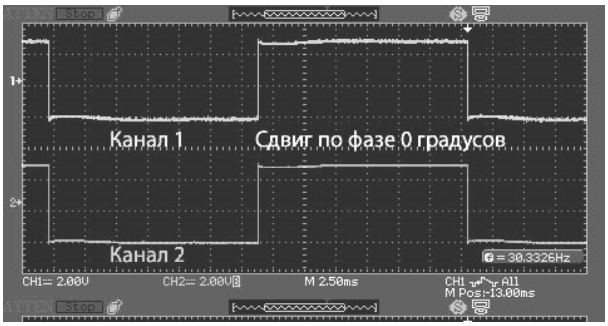

Fig. 1. Oscillogram of the first clock pulse

Figure 2 shows a periodic signal generated by frequency beats voltage in the two channels to form a common output signal (a). Also in Figure 2 is a graph of the current of the output signal (б). Such effect creates a shock wave through the object at the desired frequency. He also spins an electromagnetic field in the object.

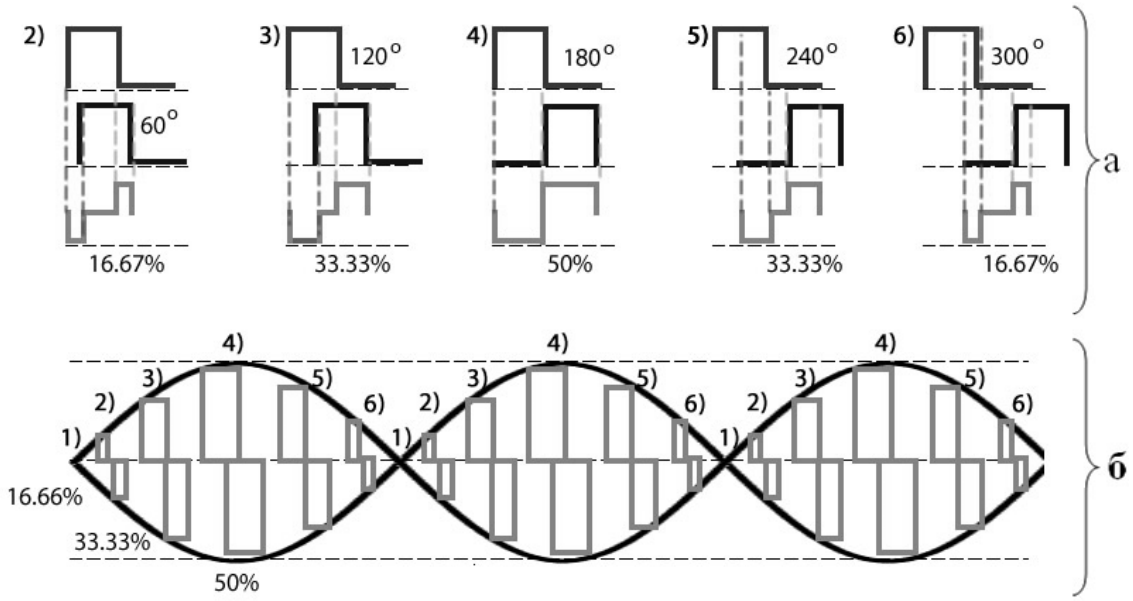

Fig. 2. Received by frequency beats a periodic signal (a) and a current diagram of the generated output signal (б)

The generator is assembled on the basis of the patent of Ukraine for utility model 105875 “Portable device for electrotherapy and stimulation” [1]. Its operation is described [7,9].

The generator is assembled on the basis of a two-channel circuit using two frequency synthesizers, amplifiers, each of which generates its own frequency.

Figure 3 shows a block diagram of the device indicating the movement of electric current.

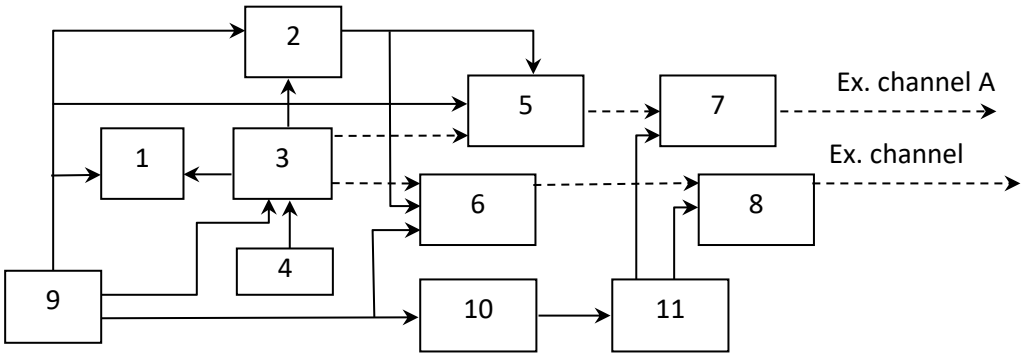

Fig. 3. A block diagram of the generator VEB-1

1 - display; 2 - synthesizer of the signal with a sampling frequency up to 0,001 Hz; 3 - micro-controller; 4 - the encoder; 5 - channel A signal synthesizer; 6 - synthesizer of the channel B signal; 7 - channel A signal amplifier; 8 - the amplifier of a signal of the channel B; 9 - battery 5 V; 10 - voltage converter 5-24 V; 11 - voltage regulator; 12 - amplitude control of the output signal.

Transmission of the electrical signal to the patient is carried out by means of contact copper electrodes through the wires. The generator operates as follows. Instrument software sets the operating frequency of the pulse beats 0,01-100 Hz with steps on each channel is not more than 0,001 Hz. Discreteness in each channel is not more than 0,001 Hz is provided by a clock synthesizer (2). It forms the frequency corresponding to the number of filling of the thirty two-bit synthesizer frequency (5,6) divided by 1000.

The appearance of the generator with a set of necessary equipment is shown in Figure 4.

Fig. 4. The appearance of the generator with a set of necessary equipment

1 - generator VEB-1; 2 - two cords with JACK connectors and terminal clamps for connection to OUT-A and OUT-B outputs; 3 - contact pads or tubes; 4 - power cable with connectors USB-B and USB-A; 5 - battery 5 V.

Table 1. The technical characteristics of the generator

Parameter	Parameter norm
The maximum power consumption, W	1,2
Output signal level by amplitude, V	3,6-16,2
The maximum amplitude of the output signal, V	16,2
The maximum possible current impact mA	25
Ripping protection when current exceeds 25 mA	yes
Operating current, mA	8-18
The shape of the output signal	Meander
Frequency range of action, Hz	144-1120
Power battery voltage, V	4,8-5,3
Continuous operation time, hours	8

Preliminary observation of volunteers, among whom was also the authors, revealed a modulating effect of electrical stimulation (during 21 min four days in a row) on the parameters of electroencephalogram (EEG), metabolism, as well as gas-discharge visualization (GDV) [2-6,14,25].

Recently designed device “VEB-2”. In contrast to the device “VEB-1”, designed to stimulate nerve centers, the electrostimulator “VEB-2” (Fig. 5) implemented an additional channel for input of information impulses into the body - channel C, whose task is the local concentration of the field, which is formed by two signal channels (A and B) to the point and body of the person as close as possible to the organ affected (heart, liver, spleen, right and left kidneys) at frequencies that contribute to the maximum recovery of the organ.

The first part of the program for adjusting the level of the output signal lasts 20 seconds, after which the main part of the program (generation of pulse current of alternating frequency in the range from 144 Hz to 1120 Hz) lasts for 21 (“VEB-1”) or 26 (“VEB-2”) minutes.

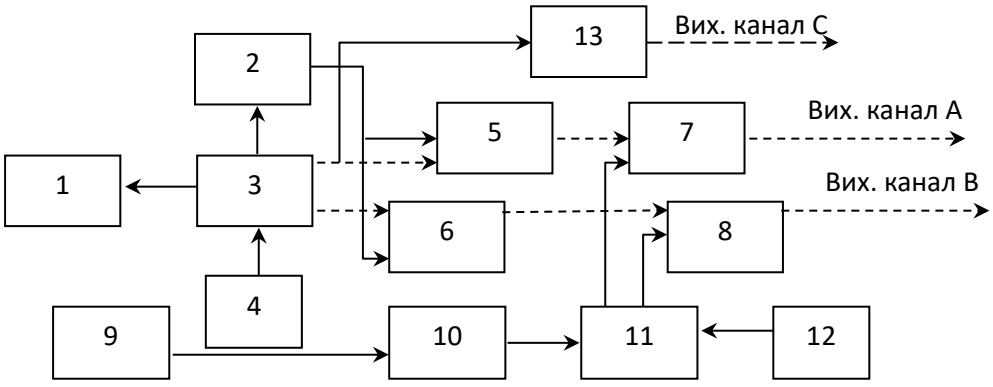

Fig. 5. A block diagram of the generator VEB-2

1 - display; 2 - clock signal synthesizer; 3 - controller; 4 - encoder; 5 - signal synthesizer channel A; 6 - signal synthesizer channel B; 7 - signal amplifier channel A; 8 - signal amplifier channel B; 9 - 5 V battery; 10 - voltage converter 5-24 V; 11 - voltage regulator; 12 - regulator of the amplitude of the output signal; 13 - channel filter C

It is known about the functional relationships between EEG and HRV parameters [41,44,49] as well as neuroimmunomodulation [27,28,36,42,43,45-48]. From here we hypothesized that changes in EEG parameters may be accompanied by a change in HRV and immune parameters.

The foregoing led to the selection of a battery of tests.

MATERIAL AND RESEARCH METHODS

The object of observation were employees of the sanatorium “Moldova”, patients with chronic cholecystitis: 19 women 30-62 y and 19 men 25-63 y.

In the morning in basal condition registered (**Dubkova GI**) kirlianogram by the method of GDV by the device of “GDV Chamber” (“Biotechprogress”, SPb, RF). Method of GDV, essence of which consists in registration of photoelectronic emission of skin, induced by high-frequency electromagnetic impulses, allows to estimate integrated psycho-somatic state of organism. The first base parameter of GDV is area of gas discharge image (GDI) in Right, Frontal and Left projections registered both with and without polyethylene filter. The second base parameter is a coefficient of shape (ratio of square of length of external contour of GDI toward his area), which characterizes the measure of serration/fractality of external contour. The third base parameter of GDI is entropy, id est measure of chaos. It is considered that GDI, taken off without filter, characterizes the functional changes of organism, and with a filter characterizes organic changes. Program estimates also Energy and Asymmetry of virtual Chakras [29-31].

As the attitude to the GDV method is ambiguous, our laboratory conducted studies that proved its relevance [8,10-13,15-19].

Then recorded (**Korolyshyn TA**) simultaneosly electrocardiogram (ECG) and electroencephalogram (EEG). ECG recorded during 7 min in II lead to assess the parameters of heart rate variability (HRV) (hardware-software complex "CardioLab+HRV" production "KhAI-Medica", Kharkiv, Ukraine). For further analysis the following parameters HRV were selected. Temporal parameters (Time Domain Methods): heart rate (HR), 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 then 50 ms (pNN_{50}), triangular index (TNN). Spectral parameters (Frequency Domain Methods): spectral power 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 ultra low-frequency (ULF, range 0,015÷0,003 Hz) [HRV,1996; Berntson GG et al, 1997]. We calculated classical indexes: LF/HF, LFnu=100%•LF/(LF+HF), Centralization Index (CI)=(VLF+LF)/HF), Baevskiy’s Stress Index and Activity Regulatory Systems Index (BARSI) [20,21,23].

EEG recorded during 25 sec 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.

Among the options considered the average EEG amplitude (μV), average frequency (Hz), frequency deviation (Hz), index (%), coefficient of asymmetry (%), 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 Laterality Index (LI) for PSD each Rhythm using formula [37]:

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

We calculated for HRV and each locus EEG the Entropy (h) of normalized PSD using Popovych's IL formulas [40] based on classic Shannon's CE formulas:

$$hHRV = -[SPHF \bullet \log_2 SPHF + SPLF \bullet \log_2 SPLF + SPVLF \bullet \log_2 SPVLF + SPULF \bullet \log_2 SPULF]/\log_2 4$$

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

Electroconductivity recorded (**Hubyts'kyi VY**) in follow points of acupuncture: Pg(ND), TR(X) and MC(AVL) at Right and Left side, which represents the nervous, endocrine and immune systems respectively [24]. Used complex "Medissa". For each pair, the Laterality Index was calculated according to the already mentioned formula.

Parameters of phagocytic function of neutrophils estimated as described by Douglas SD and Quie PG [22] with our (**Kovbasnyuk MM**) moderately modification [42].

For phenotyping subpopulations of lymphocytes used the methods of rosette formation with sheep erythrocytes on which adsorbed monoclonal antibodies against receptors CD3, CD4, CD25, CD8, 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 classes G, A, M (ELISA, analyser "Immunochem", USA) and circulating immune complexes (by polyethylene glycol precipitation method) [35].

We calculated also the Entropy of Immunocytogram (ICG) and Leukocytogram (LCG) as well as Popovych's Leukocytary Strain Indexes (PSI-1 and PSI-2) using formulas [40]:

$$hICG = -[CD4 \bullet \log_2 CD4 + CD8 \bullet \log_2 CD8 + CD22 \bullet \log_2 CD22 + CD56 \bullet \log_2 CD56]/\log_2 4$$

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

$$PSI\text{-}1 = [(Eosinoph/3{,}5\text{-}1)^2 + (StubNeutroph/3{,}5\text{-}1)^2 + (Monoc/5{,}5\text{-}1)^2 + (Leukocyt/5\text{-}1)^2]/4$$

$$PSI\text{-}2 = [(Eosinoph/2{,}75\text{-}1)^2 + (StubNeutroph/4{,}25\text{-}1)^2 + (Monoc/6\text{-}1)^2 + (Leukocyt/5\text{-}1)^2]/4$$

Next determined (**Musiyenko VY and Kyrylenko IG**) the Elektrokinetic Index (EKI) as rate of electronegative nuclei of buccal epithelium by intracellular microelectrophoresis on the device "Biotest" (Kharkiv State University), according to the method described [32-34].

At last in portion of venous blood determined (**Kikhtan VV**) plasma levels of IL-1, IL-6 and C-reactive protein (by the ELISA with the use of analyzer "RT-2100C"), total cholesterol (by a direct method after the classic reaction by Zlatkis-Zack) and content of him in composition of high-density lipoproteins (by the enzyme method) as well as routine biochemical parameters according to instructions with the use of analyzers "Reflotron" (BRD) and "Pointe-180" (USA) and corresponding sets of reagents.

After the initial testing, an transcutaneous electrical stimulation session was performed with the "VEB-1"® (21 patients) or the "VEB-2" (17 patients) devices. The next morning after completing the four-day course, retesting was performed.

Reference values are taken from the database of our laboratory.

Results processed (**Popovych IL**) using the software package "Statistica 64".

RESULTS AND DISCUSSION

According to the algorithm of the Truskavetsian Scientific School, to enable a correct comparison of parameters expressed in different units and with different variability, which

determines the “physiological price” of parameter changes (the most striking examples: changes by 1% of glomerular filtration and tubular reabsorption or by 0,1 unit of urine and blood pH), registered parameters-variables (V) were transformed into Z-score according to the formula:

Z = (V-N)/SD = (V/N-1)/Cv, where

N is average norm, SD is standard deviation, Cv is coefficient of variation in norm.

Profiles of their Z-scores before and after a course of transcutaneous electrical stimulation were created as a result of screening for statistically significant (according to the Student's criterion) changes in registered parameters. Running ahead of the train, we note that the profile also included several of those variables that nevertheless appeared in the discriminant model despite insignificant changes (while a number of parameters with significant dynamics were left out of the model).

Since the width of the page does not allow to reproduce the panorama, it is forcibly divided into downregulating (Figs. 6 and 7) and upregulating (Figs. 8 and 9) effects of electrical stimulation.

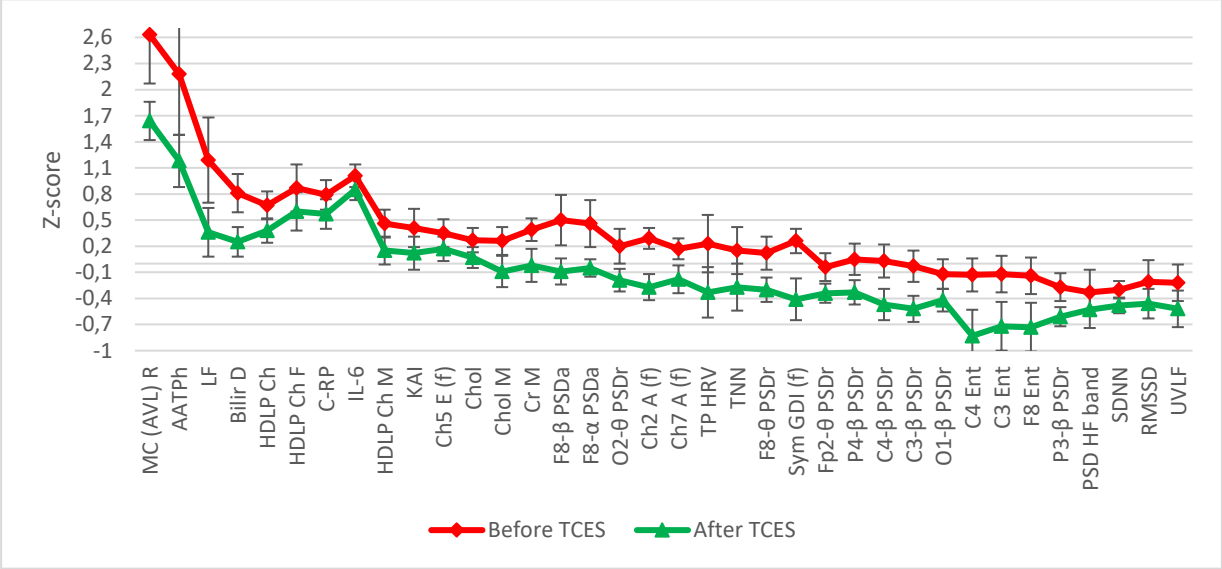

Fig. 6. Profiles of parameters whose levels decreased under the influence of transcutaneous electrical stimulation

The sequence of placement of parameters in fig. 7 was modified in such a way that the changes in HRV/EEG parameters, which we accepted as causal/factorial, preceded the parameters of acupuncture, biophotonics, immunity, and metabolism, which we accepted as consequential/resultative.

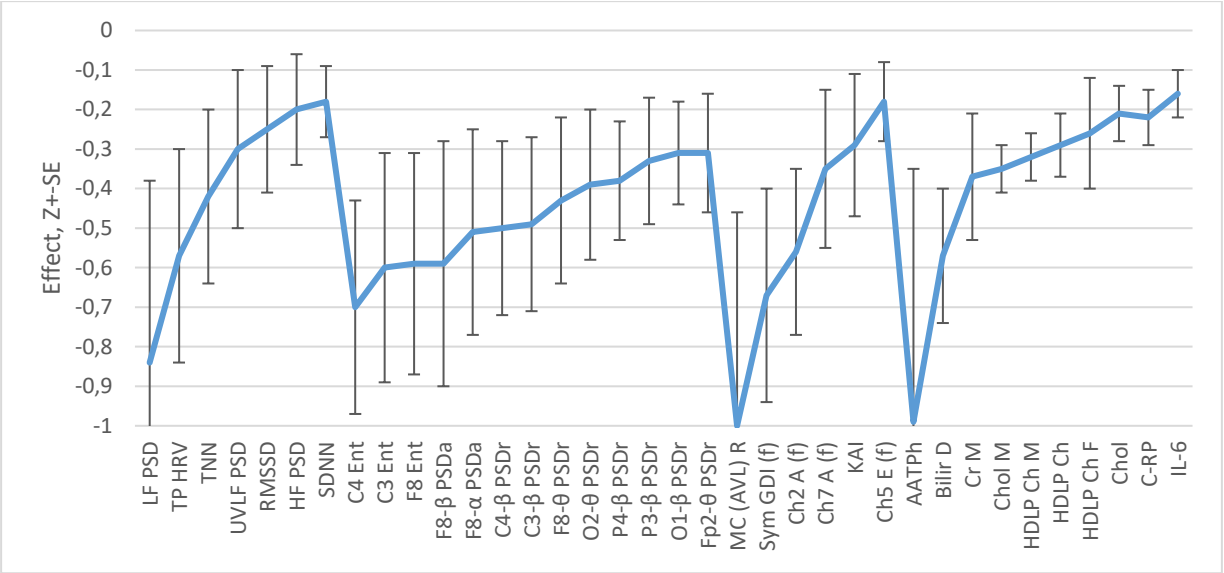

Fig. 7. Inhibitory/downregulating effects of transcutaneous electrical stimulation

As can be seen, electrical stimulation reduces to a greater or lesser extent the level of 7 HRV-markers of vagal tone, PSD of beta-rhythm in 6 loci, theta-rhythm in 3 loci, alpha-rhythm in locus F8 as well as PSD entropy in 3 loci. Such changes in the electrical activity of the brain are accompanied by a decrease, first of all, in the electrical conductivity of AP MC(AVL) Right and 5 parameters of GDV, levels in the blood of asparagine transferase, direct bilirubin, creatinine, cholesterol in general and in the composition of high-density lipoproteins, as well as markers of inflammation: C-RP and IL-6.

On the other hand (Figs. 8 and 9), electrical stimulation causes a drastic increase in PSD of delta-rhythm in 4 loci and less pronounced in the other 5 loci, as well as PSD of theta-rhythm in locus F3, combined with a sympathotonic shift of HRV-markers of sympatho-vagal balance. Such changes in the electrical activity of the brain are accompanied by a increase, first of all, in Strain Index of leukocytogram and 6 parameters of phagocytosis of Gram-positive and Gram-negative bacteria by neutrophils, blood levels of $CD3^{+}CD25^{+}$ T-lymphocytes and CIC as well as in 2 GDV parameters. Separately, a moderate increase in testosterone levels should be noted, but only in men.

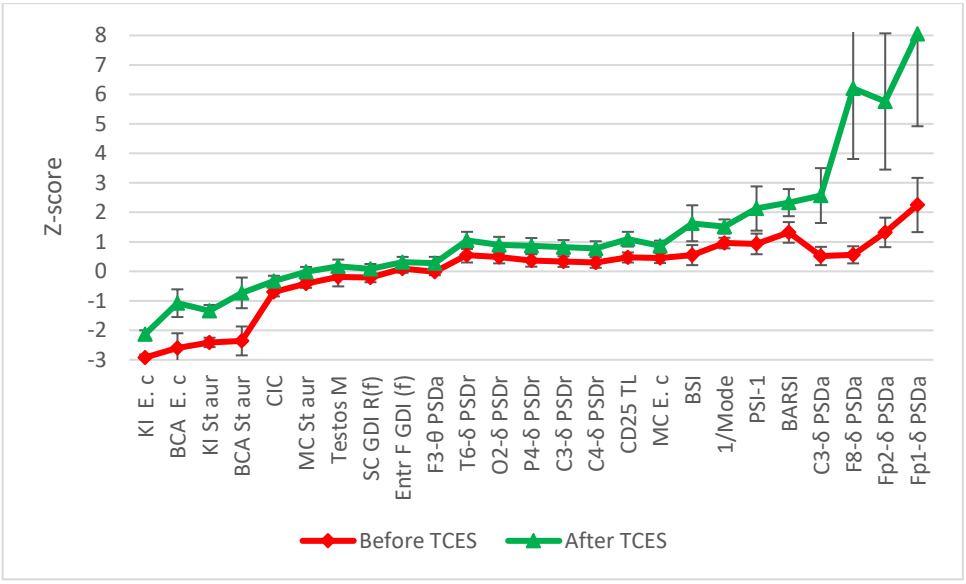

Fig. 8. Profiles of parameters whose levels increased under the influence of transcutaneous electrical stimulation

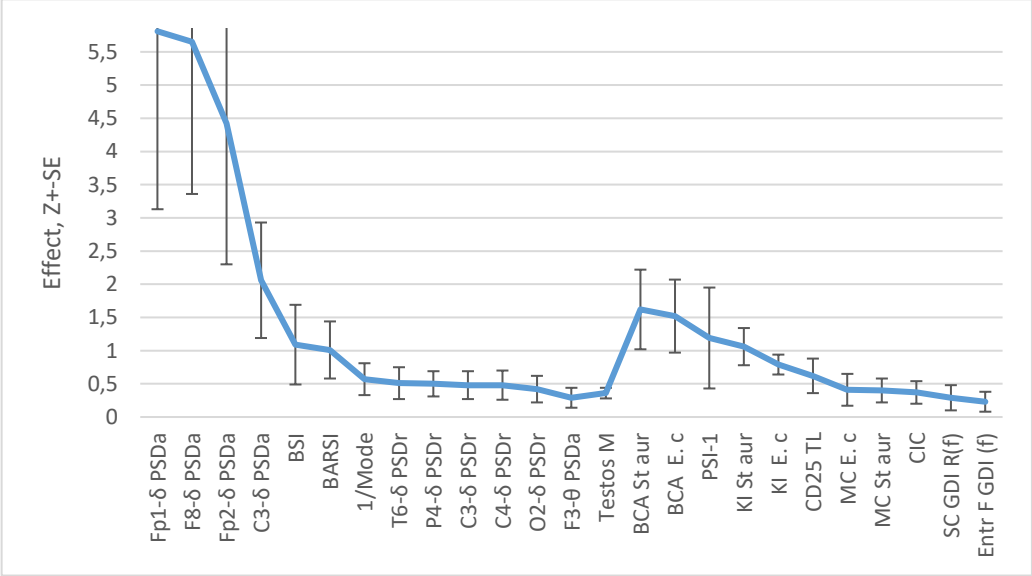

Fig. 9. Enhancing/upregulating effects of transcutaneous electrical stimulation

As a result of the discriminant analysis [26], the forward stepwise program included only 24 variables in the model, including 3 HRV, 10 EEG (reflected **δ-, θ-, α-, β**-rhythms and **entropy**), 3 **biophysical** (AP and GDV), 3 immune as well as 5 metabolic (Tables 2 and 3).

Table 2. Discriminant Function Analysis Summary

Step 24, N of vars in model: 24; Grouping: 2 grps;
Wilks' Lambda: 0,2439; approx. $F_{(25)}=6,6$; $p<10^{-6}$

Variables currently in the model	Groups (n) and Means±SE			Parameters of Wilks' Statistics					
	Before ES (38)	After ES (38)	*Effect of ES (38)*	Wilks' Λ	Partial Λ	F-remove (1,51)	p-level	Tolerancy	Refer Cv SD
Mode HRV, msec	772 18	715 25	*-57* *24*	0,264	0,925	4,14	0,047	0,620	869 0,116
PSD LF band, msec²	1093 164	813 105	*-280* *137*	0,294	0,830	10,45	0,002	0,225	690 0,482
PSD HF band, msec²	292 70	214 42	*-78* *48*	0,267	0,915	4,75	0,034	0,243	382 0,713
O2-δ PSD, %	30,7 3,5	37,6 4,4	*+6,9* *3,4*	0,261	0,933	3,63	0,062	0,473	22,8 0,720
Fp2-δ PSD, μV²/Hz	213 50	660 232	*+447* *214*	0,258	0,944	3,01	0,089	0,169	74 1,260
Fp1-δ PSD, μV²/Hz	205 60	584 204	*+379* *175*	0,253	0,965	1,87	0,178	0,190	58 1,132
F8-θ PSD, %	10,4 0,9	8,4 0,7	*-2,1* *1,0*	0,300	0,812	11,83	0,001	0,459	9,8 0,492
O2-θ PSD, %	7,9 0,8	6,3 0,5	*-1,54* *0,73*	0,313	0,779	14,51	10^{-3}	0,555	7,1 0,554
F8-α PSD, μV²/Hz	65 14	39 5	*-25,3* *13,2*	0,249	0,980	1,02	0,317	0,423	41,6 1,202
F8-β PSD, μV²/Hz	62 10	41 5	*-20* *10*	0,274	0,889	6,36	0,015	0,527	44 0,771
P4-β PSD, %	23,4 2,1	19,1 1,6	*-4,3* *1,7*	0,249	0,981	0,96	0,331	0,405	22,8 0,503
P3-β PSD, %	23,4 2,2	18,7 1,6	*-4,6* *2,2*	0,252	0,969	1,65	0,204	0,361	22,7 0,514
C4 PSD Entropy	0,854 0,018	0,788 0,029	*-0,066* *0,025*	0,302	0,809	12,07	0,001	0,549	0,867 0,109
AP MC (AVL) Right EC, un	63,2 1,1	61,3 0,4	*-2,0* *1,0*	0,278	0,876	7,22	0,010	0,488	58,0 0,034
Symmetry GDI (f), %	93,57 0,20	92,63 0,33	*-0,94* *0,34*	0,322	0,758	16,32	10^{-4}	0,407	93,2 0,015
Chakra 2 Asymmetry (f)	-0,01 0,04	-0,18 0,05	*-0,17* *0,06*	0,253	0,964	1,88	0,176	0,677	-0,10 **0,31**
Killing Index vs E. coli, %	33,7 1,0	41,4 1,3	*+7,7* *1,4*	0,342	0,713	20,48	10^{-4}	0,550	62,0 0,156
$CD3^+CD25^+$ T-Lymphocyt, %	17,6 0,4	19,1 0,6	*+1,6* *0,7*	0,266	0,918	4,54	0,038	0,378	16,4 0,153
Interleukin-6, ng/L	5,63 0,18	5,41 0,17	*-0,22* *0,08*	0,257	0,947	2,83	0,099	0,016	4,25 0,324
Bilirubin direct, μM/L	2,39 0,19	1,91 0,15	*-0,48* *0,14*	0,248	0,983	0,89	0,351	0,718	1,70 0,500
Creatinine, μM/L	91,8 2,4	89,2 1,9	*-2,9* *1,8*	0,270	0,904	5,39	0,024	0,672	83,9 0,157

Total Cholesterol, mM/L	5,68 0,16	5,48 0,16	*-0,21* *0,07*	0,270	0,903	5,46	0,023	0,013	5,39 0,193
HDLP Cholesterol, mM/L	1,66 0,06	1,54 0,06	*-0,12* *0,03*	0,286	0,852	8,87	0,004	0,108	1,39 0,298
Asparagine ATPh, µKat/L	33,9 4,5	27,5 1,9	*-6,3* *4,0*	0,269	0,908	5,14	0,028	0,379	20,0 0,318

Notes. In each column, the first line is the average, the second – SE. In norm column - the average and Cv or ***SD***. The "*Effect*" and "*Norm*" columns are not the result of discriminant analysis

Table 3. Summary of stepwise analysis of discriminant variables ranked by criterion Λ

Variables currently in the model	F to enter	p-level	**Λ**	F-value	p-level
Killing Index vs E. coli, %	22,6	10^{-5}	0,766	22,6	10^{-5}
Mode HRV, msec	6,81	0,011	0,700	15,6	10^{-5}
Chakra 2 Asymmetry (f)	4,72	0,033	0,657	12,5	10^{-6}
C4 PSD Entropy	5,30	0,024	0,612	11,3	10^{-6}
F8-θ PSD, %	5,73	0,019	0,565	10,8	10^{-6}
F8-β PSD, µV²/Hz	4,25	0,043	0,533	10,1	10^{-6}
PSD LF band, msec²	4,18	0,045	0,502	9,64	10^{-6}
Bilirubin direct, µM/L	3,58	0,063	0,476	9,21	10^{-6}
O2-θ PSD, %	3,28	0,075	0,454	8,82	10^{-6}
PSD HF band, msec²	3,24	0,077	0,432	8,54	10^{-6}
Creatinine, µM/L	3,04	0,086	0,413	8,28	10^{-6}
Symmetry GDI (f), %	3,24	0,077	0,393	8,13	10^{-6}
$CD3^+CD25^+$ T-Lymphocytes, %	2,47	0,121	0,377	7,86	10^{-6}
HDLP Cholesterol, mM/L	4,10	0,047	0,354	7,96	10^{-6}
Total Cholesterol, mM/L	3,18	0,080	0,336	7,91	10^{-6}
O2-δ PSD, %	2,64	0,110	0,322	7,78	10^{-6}
AP MC (AVL) Right EC, un	1,87	0,177	0,312	7,54	10^{-6}
P4-β PSD, %	2,35	0,131	0,299	7,42	10^{-6}
Asparagine ATPh, µKat/L	3,07	0,085	0,284	7,44	10^{-6}
Interleukin-6, ng/L	1,98	0,166	0,274	7,29	10^{-6}
P3-β PSD, %	1,38	0,245	0,267	7,06	10^{-6}
F8-α PSD, µV²/Hz	1,77	0,189	0,258	6,92	10^{-6}
Fp2-δ PSD, µV²/Hz	1,13	0,294	0,253	6,68	10^{-6}
Fp1-δ PSD, µV²/Hz	1,87	0,178	0,244	6,59	10^{-6}

Other variables, despite their recognizable properties, were outside the discriminant model, apparently due to duplication and/or redundancy of information (Tables 4-6).

Table 4. HRV variables currently not in the discriminant model

Variables currently not in the model	Groups (n) and Means±SE			Parameters of Wilks' Statistics					
	Before ES (38)	After ES (38)	*Effect of ES (38)*	Wilks' Λ	Partial Λ	F to enter	p-level	Tolerancy	Refer Cv SD
Baevskiy's ARS Index, un	2,74 0,32	3,68 0,43	*+0,95* *0,41*	0,240	0,983	0,89	0,351	0,608	1,50 0,625
Baevskiy's Stress Index HRV, units	166 21	226 35	*+60* *34*	0,240	0,995	0,24	0,397	0,139	133 0,417
HRV Total Power, msec^2	2679 385	2040 262	*-636* *278*	0,240	0,986	0,73	0,397	0,149	2405 0,402
PSD UVLF band, msec^2	1294 212	1012 66	*-282* *166*	0,243	0,995	0,24	0,629	0,421	1443 0,572
SDNN HRV, msec	47,9 3,3	42,3 2,8	*-5,6* *2,5*	0,241	0,990	0,51	0,479	0,193	56,2 0,516
RMSSD HRV, msec	25,7 2,9	21,6 1,9	*-4,1* *1,9*	0,244	1,000	0,00	0,952	0,139	30,0 0,486
TNN HRV, units	11,6 0,7	10,6 0,7	*-1,0* *0,5*	0,242	0,992	0,42	0,518	0,435	11,2 0,217

Table 5. EEG variables currently not in the discriminant model

Variables currently not in the model	Groups (n) and Means±SE			Parameters of Wilks' Statistics					
	Before ES (38)	After ES (38)	*Effect of ES (38)*	Wilks' Λ	Partial Λ	F to enter	p-level	Tolerancy	Refer Cv SD
F8-δ PSD, μV^2/Hz	177 44	1030 363	*+853* *346*	0,243	0,995	0,26	0,614	0,118	92 1,642
C3-δ PSD, %	33,6 3,1	41,8 4,1	*+8,1* *3,6*	0,243	0,997	0,15	0,704	0,305	28,0 0,602
C3-δ PSD, μV^2/Hz	151 26	323 78	*+172* *73*	0,243	0,998	0,12	0,733	0,413	108 0,774
C4-δ PSD, %	33,4 3,1	41,7 4,1	*+8,3* *3,8*	0,243	0,995	0,25	0,619	0,344	28,2 0,613
T6-δ PSD, %	35,0 4,1	43,3 4,7	*+8,3* *4,0*	0,242	0,993	0,33	0,569	0,275	26,1 0,626
P4-δ PSD, %	29,1 3,1	36,5 3,8	*+7,3* *2,9*	0,243	0,998	0,11	0,740	0,233	23,6 0,626
Fp2-θ PSD, %	9,7 1,0	7,8 0,7	*-1,9* *0,9*	0,242	0,993	0,33	0,567	0,423	9,9 0,620
F3-θ PSD, μV^2/Hz	39,4 5,3	52,3 9,3	*+12,8* *6,6*	0,240	0,985	0,76	0,387	0,460	40,0 1,101
C3-β PSD, %	25,1 1,9	19,9 1,6	*-5,2* *2,1*	0,243	0,996	0,22	0,639	0,260	25,45 0,420
C4-β PSD, %	26,2 1,9	21,0 1,9	*-5,2* *2,3*	0,241	0,987	0,66	0,419	0,336	25,9 0,405
O1-β PSD, %	24,6 2,4	20,2 1,8	*-4,4* *1,9*	0,243	0,996	0,18	0,677	0,216	26,3 0,542
F8 PSD Entropy	0,792 0,034	0,694 0,047	*-0,098* *0,046*	0,243	0,998	0,22	0,419	0,344	0,815 0,202
C3 PSD Entropy	0,850 0,020	0,790 0,028	*-0,060* *0,028*	0,244	0,998	0,08	0,782	0,450	0,862 0,115

Table 6. Immune and GDV variables currently not in the discriminant model

Variables currently not in the model	Groups (n) and Means±SE			Parameters of Wilks' Statistics					
	Before ES (38)	After ES (38)	*Effect of ES (38)*	Wilks' Λ	Partial Λ	F to enter	p-level	Tolerancy	Refer Cv **SD**
Microb Count vs E. coli, B/Ph	59,5 1,8	63,9 1,8	*+4,4* *2,5*	0,242	0,990	0,48	0,490	0,703	54,7 0,194
Bactericidity vs E. coli, 10^9 B/L	73 5	88 5	*+15* *5*	0,243	0,998	0,12	0,731	0,491	99 0,100
Killing Index vs Staph. aur., %	38,8 1,3	47,7 1,6	*+8,9*	0,243	0,997	0,16	0,688	0,456	58,9 0,142
Microb Count vs St. aur, B/Ph	57,5 1,4	61,5 1,7	*+3,9* *1,8*	0,243	0,997	0,16	0,695	0,497	61,6 0,160
Bactericidity vs St. aur, 10^9 B/L	81 5	98 6	*+17* *6*	0,243	0,997	0,16	0,691	0,478	106 0,100
CIC, units	32,8 2,6	39,3 3,1	*+6,5* *3,0*	0,243	0,997	0,13	0,725	0,386	45,0 0,389
Popovych's Strain Ind-1, un	0,15 0,02	0,21 0,04	*+0,06* *0,04*	0,244	1,000	0,00	0,971	0,603	0,097 0,559
C-reactive Protein, µg/L	2,74 0,12	2,58 0,12	*-0,15* *0,05*	0,243	0,983	0,89	0,351	0,608	2,18 0,324
Korotkov's Activation Ind GDI	1,75 0,24	1,44 0,21	*-0,31* *0,20*	0,243	0,997	0,16	0,688	0,491	1,31 0,824
Entropy Frontal GDI (f)	3,65 0,02	3,68 0,02	*+0,03* *0,02*	0,243	0,995	0,50	0,612	0,350	3,64 0,038
Chakra 5 Energy (f)	+0,19 0,06	+0,12 0,05	*-0,07* *0,04*	0,243	0,997	0,18	0,677	0,497	+0,06 **0,37**
Chakra 7 Asymmetry (f)	-0,01 0,03	-0,11 0,04	*-0,09* *0,05*	0,244	0,999	0,07	0,798	0,287	-0,06 **0,27**

Calculating the value of the discriminant root for each patient as the sum of the products of non-standardized (raw) coefficients on the individual values of discriminant variables together with the constant (Table 7) allows visualization of each patient in the information space of the root (Fig. 10).

Table 7. Standardized and raw coefficients and constant for discriminant variables

	Coefficients	
Variables	**Standardized**	**Raw**
Killing Index vs E. coli, %	-0,830	-0,118
Mode HRV, msec	0,400	0,003
Chakra 2 Asymmetry (f)	0,264	0,995
C4 PSD Entropy	0,679	0,056
F8-θ PSD, %	0,736	0,148
F8-β PSD, $\mu V^2/Hz$	0,527	0,011
PSD LF band, $msec^2$	0,999	0,001
Bilirubin direct, µM/L	0,177	0,170
O2-θ PSD, %	0,727	1,115
PSD HF band, $msec^2$	-0,681	-0,002
Creatinine, µM/L	0,434	0,033
Symmetry GDI (f), %	0,888	0,532
$CD3^+CD25^+$ T-Lymphocytes, %	0,535	0,160
HDLP Cholesterol, mM/L	1,350	3,669
Total Cholesterol, mM/L	-3,130	-3,207
O2-δ PSD, %	0,431	0,018
AP MC (AVL) Right EC, units	0,580	0,112
P4-β PSD, %	0,246	0,022
Asparagine ATPh, µKat/L	-0,566	-0,027
Interleukin-6, ng/L	2,079	1,911
P3-β PSD, %	0,339	0,028
F8-α PSD, $\mu V^2/Hz$	0,248	0,004
Fp2-δ PSD, $\mu V^2/Hz$	-0,661	-0,001
Fp1-δ PSD, $\mu V^2/Hz$	0,497	0,001
	Constant	-177,8
	Eigenvalue	**3,10**
Squared Mahalanobis Distance=12,1; $F_{(24)}$=6,6; $p<10^{-6}$		
Canonical R=0,870; Wilks' Λ=0,2439; $\chi^2_{(24)}$=87; $p<10^{-6}$		

As we can see, the reaction to electrical stimulation takes place in all participants without exception, although the severity of the reaction has significant individual differences, which is quite natural.

No significant differences were found either for both device models or for both sexes (Figs. 11 and 12).

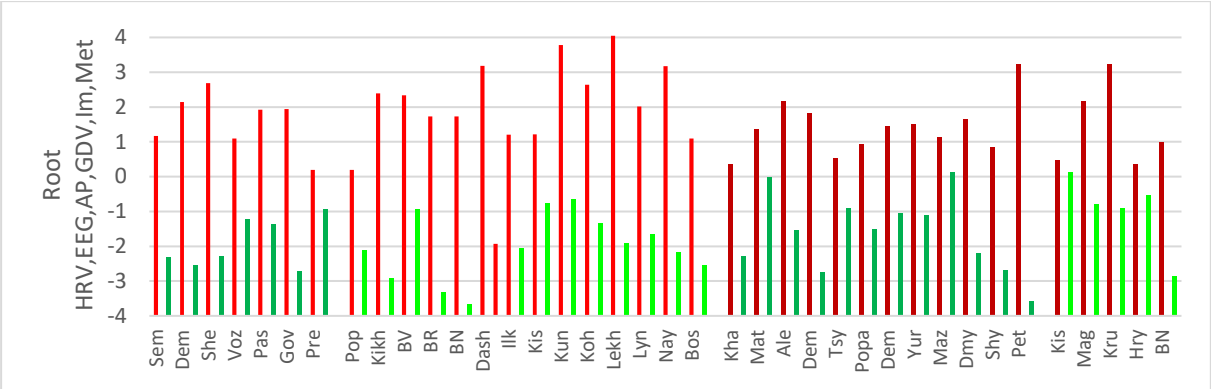

Fig. 10. Individual integral reactions to the course of electrical stimulation with the "VEB-1" and "VEB-2" devices of women and men

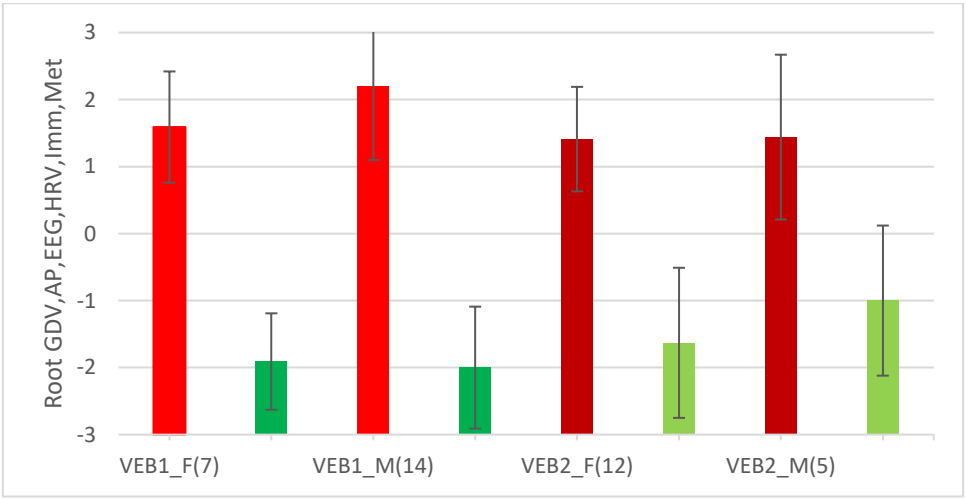

Fig. 11. Average values (Mean±SD) of the discriminant root before and after course of electrostimulation by "VEB-1" or "VEB-2" devices at Female and Male

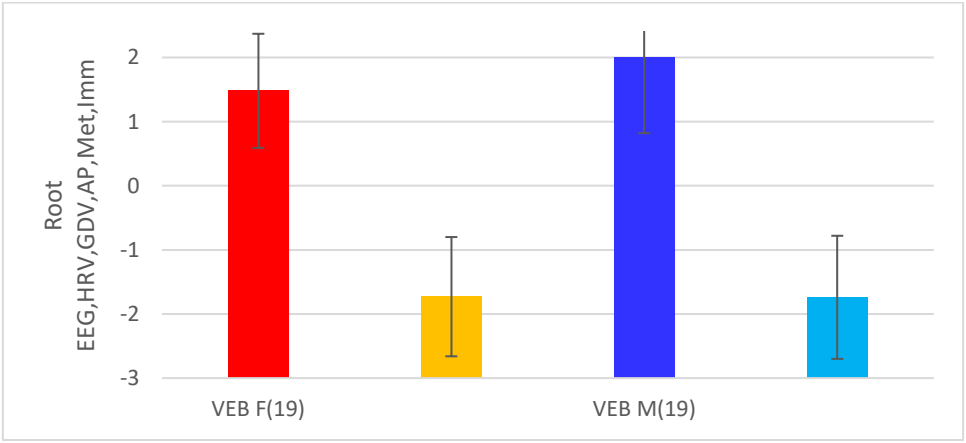

Fig. 12. Average values (Mean±SD) of the discriminant root before and after course of electrostimulation by VEB at Female and Male

Retrospective recognition of the integral state of patients by calculating the classification functions according to the coefficients and constants given in the table. 8, with respect to the initial state is error-free, and with respect to the final state – with only two errors (Table 9).

Table 8. Coefficients and constants of classification functions

Clusters	Before ES	After ES
Variables	p=,500	p=,500
Killing Index vs E. coli, %	-12,16	-11,75
Mode HRV, msec	0,735	0,724
Chakra 2 Asymmetry (f)	-24,12	-27,57
C4 PSD Entropy	7579	7384
F8-θ PSD, %	24,10	23,59
F8-β PSD, $\mu V^2/Hz$	2,506	2,468
PSD LF band, $msec^2$	0,307	0,303
Bilirubin direct, µM/L	-7,629	-8,218
O2-θ PSD, %	56,2	52,3
PSD HF band, $msec^2$	-0,710	-0,703
Creatinine, µM/L	9,174	9,059
Symmetry GDI (f), %	181,4	179,6
$CD3^+CD25^+$ T-Lymphocytes, %	52,75	52,19
HDLP Cholesterol, mM/L	834,4	821,7
Total Cholesterol, mM/L	-290,9	-279,8
O2-δ PSD, %	3,625	3,564
AP MC (AVL) Right EC, units	23,91	23,52
P4-β PSD, %	6,301	6,226
Asparagine ATPh, µKat/L	-6,224	-6,131
Interleukin-6, ng/L	35,33	28,69
P3-β PSD, %	1,293	1,195
F8-α PSD, $\mu V^2/Hz$	-0,388	-0,402
Fp2-δ PSD, $\mu V^2/Hz$	-0,145	-0,143
Fp1-δ PSD, $\mu V^2/Hz$	0,152	0,150
Constants	-36931	-36313

Table 9. Classification Matrix

	Rows: Observed classifications Columns: Predicted classifications		
Group	Percent Correct	Before p=,50000	After p=,50000
Before	100,0	38	0
After	94,7	2	36
Total	97,4	40	36

Although a significant number of variabless, despite significant responses to electrical stimulation, were outside the discriminant model, we decided to analyze them together with those included in the model (Table 10).

The validity of this approach is confirmed by the harmonious combination of model (with structural coefficients R) and non-model variables in the structure of clusters selected from the profiles (Fig. 13).

Table 10. Clusters of effects of transcutaneus electrical stimulation

Clusters and Variables	R	Before ES (38)	After ES (38)	*Effect of ES (38)*
B++/A+++ (5)				
Fp1-δ PSDa	-0,117	2,25±0,92	8,05±3,13	5,81±2,68
Fp2-δ PSDa	-0,124	1,32±0,50	5,76±2,31	4,42±2,12
F8-δ PSDa		0,56±0,29	6,21±2,40	5,65±2,29
Baevskiy's ARS Index HRV		1,32±0,35	2,33±0,46	1,01±0,43
Popovych's Strain Index-1 LCG		0,93±0,35	2,13±0,75	1,19±0,76
B+/A++ (10)				
C3-δ PSDa		0,52±0,31	2,57±0,93	2,06±0,87
T6-δ PSDr		0,55±0,25	1,05±0,29	0,51±0,24
P4-δ PSDr		0,37±0,21	0,87±0,26	0,50±0,19
C3-δ PSDr		0,33±0,18	0,82±0,24	0,48±0,21
C4-δ PSDr		0,30±0,18	0,78±0,24	0,48±0,22
O2-δ PSDr	-0,080	0,48±0,21	0,90±0,27	0,42±0,20
1/Mode HRV	-0,122	0,96±0,18	1,52±0,24	0,57±0,24
Baevskiy's Stress Index HRV		0,55±0,34	1,63±0,61	1,09±0,60
$CD3^+CD25^+$ T-Lymphocytes	-0,134	0,47±0,17	1,09±0,25	0,62±0,26
Microb Count vs E. coli		0,45±0,17	0,87±0,17	0,41±0,24
B--/A- (10)				
F3-θ PSDa		-0,01±0,12	0,28±0,21	0,29±0,15
Testosterone Male		-0,19±0,32	0,17±0,23	0,36±0,08
Entropy Frontal GDI (f)		0,09±0,14	0,31±0,18	0,23±0,15
Shape Coefficient GDI R(f)		-0,21±0,16	0,08±0,17	0,29±0,19
Microb Count vs St. aureus		-0,42±0,14	-0,02±0,17	0,40±0,18
CIC		-0,70±0,15	-0,33±0,18	0,37±0,17
Killing Index vs E. coli	-0,314	-2,92±0,10	-2,13±0,13	0,79±0,15
Killing Index vs Staph. aureus		-2,41±0,16	-1,34±0,20	1,06±0,28
Bactericidity vs E. coli		-2,60±0,50	-1,08±0,47	1,52±0,55
Bactericidity vs St. aureus		-2,36±0,49	-0,73±0,52	1,62±0,60
B++/A+ (8)				
PSD LF band	0,095	1,19±0,49	0,36±0,28	-0,84±0,46
AP MC (AVL) Right EC	0,105	2,63±0,56	1,64±0,22	-1,00±0,54
Asparagine ATPh	0,085	2,18±0,70	1,18±0,30	-0,99±0,64
Bilirubin direct	0,130	0,81±0,22	0,25±0,17	-0,57±0,17
HDLP Cholesterol M&F	0,093	0,67±0,16	0,38±0,14	-0,29±0,08
HDLP Cholesterol Female	0,093	0,87±0,27	0,60±0,22	-0,26±0,14
C-reactive Protein		0,79±0,17	0,57±0,17	-0,22±0,07
Interleukin-6	0,059	1,01±0,13	0,85±0,12	-0,16±0,06
B+/A0 (10)				
F8-β PSDa	0,120	0,50±0,29	-0,09±0,15	-0,59±0,31
F8-α PSDa	0,114	0,46±0,27	-0,05±0,10	-0,51±0,26
O2-θ PSDr	0,098	0,20±0,20	-0,19±0,13	-0,39±0,19
Chakra 7 Asymmetry (f)		0,17±0,12	-0,18±0,16	-0,35±0,20
Korotkov's Activation Ind GDI		0,41±0,22	0,12±0,19	-0,29±0,18
Chakra 5 Energy (f)		0,35±0,16	0,17±0,14	-0,18±0,10
Creatinine Male	0,054	0,39±0,13	-0,02±0,19	-0,37±0,16
Total Cholesterol Male	0,061	0,26±0,16	-0,09±0,18	-0,35±0,06
HDLP Cholesterol Male	0,093	0,46±0,16	0,15±0,16	-0,32±0,06

Total Cholesterol M&F	0,061	0,27±0,14	0,07±0,12	-0,21±0,07
B0/A- (18)				
C4 PSD Entropy	0,138	-0,13±0,19	-0,83±0,30	-0,70±0,27
C3 PSD Entropy		-0,12±0,21	-0,72±0,28	-0,60±0,29
F8 PSD Entropy		-0,14±0,21	-0,73±0,28	-0,59±0,28
C4-β PSDr		0,03±0,19	-0,47±0,18	-0,50±0,22
C3-β PSDr		-0,03±0,18	-0,52±0,15	-0,49±0,22
F8-θ PSDr	0,119	0,12±0,19	-0,30±0,14	-0,43±0,21
P4-β PSDr	0,109	0,05±0,18	-0,33±0,14	-0,38±0,15
P3-β PSDr	0,111	-0,27±0,16	-0,61±0,11	-0,33±0,16
O1-β PSDr		-0,12±0,17	-0,42±0,13	-0,31±0,13
Fp2-θ PSDr		-0,04±0,16	-0,34±0,11	-0,31±0,15
Total Power HRV		0,23±0,33	-0,33±0,29	-0,57±0,27
TNN HRV		0,15±0,27	-0,27±0,27	-0,42±0,22
PSD UVLF band		-0,22±0,21	-0,52±0,21	-0,30±0,20
RMSSD HRV		-0,21±0,25	-0,46±0,17	-0,25±0,16
PSD HF band	0,063	-0,33±0,26	-0,53±0,21	-0,20±0,14
SDNN HRV		-0,30±0,10	-0,48±0,09	-0,18±0,09
Symmetry GDI (f)	0,162	0,26±0,14	-0,41±0,24	-0,67±0,27
Chakra 2 Asymmetry (f)	0,188	0,29±0,12	-0,27±0,15	-0,56±0,21
Without change				
Creatinine M&F	0,054	0,63±0,17	0,44±0,14	-0,19±0,17
Creatinine Female	0,054	0,87±0,30	0,84±0,17	-0,02±0,22
Total Cholesterol Female		0,29±0,22	0,22±0,17	-0,07±0,09
Testosterone Female		1,61±0,67	1,54±0,62	-0,08±0,24

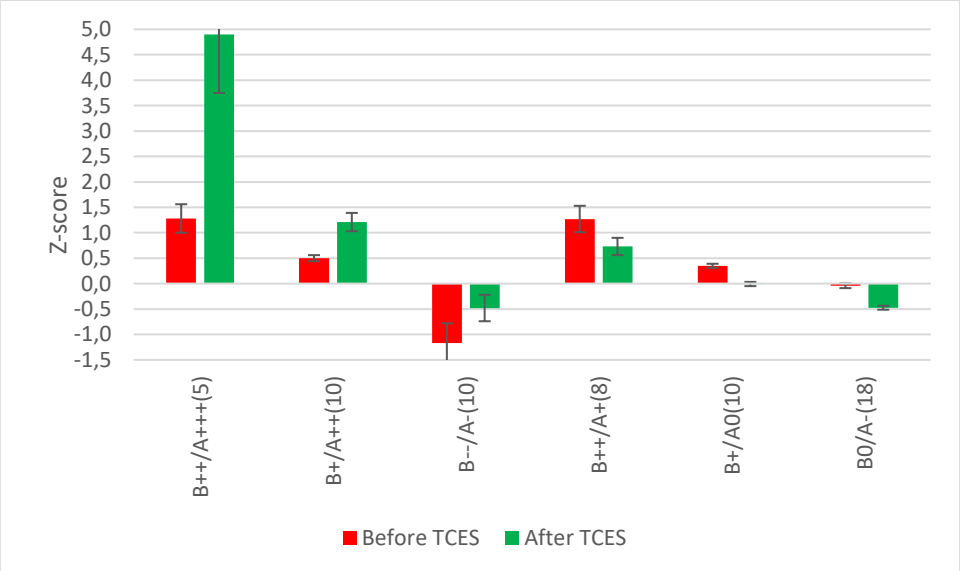

Fig. 13. Clusters (n) of effects of transcutaneous electrical stimulation

At first glance at Fig. 13 gives the impression that the main effect of electrical stimulation is a drastic increase in the PSD of the delta-rhythm in the prefrontal loci, which is accompanied by an increase in Baevskiy's ARS Index (as HRV-marker of **strain**) and Popovych's Strain Index (as leukocytary marker of **strain**). The next cluster reflects a smaller but still significant increase in PSD delta-rhythm at other loci, which is accompanied by an increase in Baevskiy's Stress Index and a decrease in Mode HRV (reflecting an increase in circulating catecholamines). Taken together, both clusters reflect electrostimulation-initiated stress, or rather **eustress**. This identification of the stress reaction is supported by the accompanying further increase in the intensity of phagocytosis and the level of $CD3^+CD25^+$ T-lymphocytes in the blood, as well as the reduction of the suppression of other parameters of phagocytosis and the level of CIC in the next cluster of variables.

The other three clusters reflect the opposite, downregulating effects of electrical stimulation. However, they are also physiologically beneficial. In particular, the fourth cluster reflects a decrease in elevated levels of markers of cytolysis, intoxication, and inflammation against the background of a decrease in PSD LF band HRV (in this context, a vagal marker). The fifth cluster reflects a decrease in creatinine and cholesterol levels against the background of a decrease in PSD in three loci. The last cluster reflects a decrease in HRV-markers of vagal tone against the background of a decrease in the PSD of the beta rhythm.

As a conclusion, we quote that at low and normal doses, adaptogens act as mild stress mimetics, increasing the homeostatic range and resulting in increased resistance to stress [38]. Electrical stimulation with the "VEB" device, judging by the results obtained, acts as an adaptogen.

A more detailed analysis of the cause-and-effect relationships of EEG/HRV parameters with parameters of immunity, metabolism and GDV will be presented in the next article.

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ACCORDANCE TO ETHICS STANDARDS

Tests in patients are carried out 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.

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