

Research Article

Perspectives on the use of electrostimulation with the device “VEB”[®] in the management of disorders related to COVID-19

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Background. One of the symptoms of COVID-19 is the so-called "cytokine storm". Its pathogenesis is that the initial release by lymphocytes and macrophages of proinflammatory cytokines in the classical immune response to SARS-CoV-2 is significantly enhanced and maintained due to excessive adrenergic stimulation of the immune cells. The proinflammatory adrenergic mechanism of the "cytokine storm" can be offset by the activation of the anti-inflammatory cholinergic mechanism by non-invasive stimulation of the vagus nerve. In 2015, a generator for electrotherapy and stimulation of 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). We hypothesized that changes in EEG parameters may be accompanied by a vagotonic shift of the sympatho-vagus balance, favorable for calming the “cytokine storm”. The main purpose of this study was to find out. In addition, concomitant changes in EEG, immunity, GDV, etc. due to the use of the devices “VEB-1”[®] and recently designed “VEB-2” had to be detected. **Material and research methods.** The object of observation were 18 volunteers: 11 women 33–62 y and 7 men 29–62 y (Mean±SD: 51±12 y) without clinical diagnose but with dysfunction of neuro-endocrine-immune complex and metabolism. In the morning registered HRV (“CardioLab+HRV”, “KhAI-Medica”, Kharkiv, UA), EEG (“NeuroCom Standard”, “KhAI-Medica”, Kharkiv, UA), kirlionogram 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 parameters of immunity and metabolism. After the initial testing, an 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.** The effects of electrical stimulation can be divided into the following networks. Regarding EEG, this is a leveling of right-hand lateralization and normalizing decrease in the increased of the amplitude of the θ -rhythm and its spectral power density (SPD) at the loci F3, F7, F8, T3, T4, T6, P3, O1 and O2; further increase of SPD of δ -rhythm in loci F3, F4, T6, P3 and O1 as well as further decrease of SPD F4- α ; reversion of the increased level of entropy in loci Fp1, F4, C3 and P3 to the lowered level. Regarding HRV, it is a vagotonic shift of sympatho-vagus balance due to a decrease in elevated levels of sympathetic tone markers and an increase in decreased levels of vagus tone markers, but without normalization. Neurotropic effects are accompanied by favorable changes in a number of immune parameters and a tendency to decrease the level of C-Reactive Protein. Regarding GDV, it is almost complete normalization of the initially increased GDI Area in the frontal projection and third Chakra Energy; normalizing decrease in the initially increased Energy of second and seventh Chakras; normalizing right-hand shift of more or less pronounced left-sided Asymmetry of first and third Chakra. These effects should be clearly interpreted as physiologically beneficial. The effects on these parameters are almost equally pronounced in people of both sexes when using both devices. **Conclusion.** Vagotonic and immunotropic effects of our device give us a reason to offer it for further research on the leveling of “cytokine storm” in patients with COVID-19.

Perspectives on the use of electrostimulation with the device “VEB”[®] in the management of disorders related to COVID-19

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Abstract

Background. One of the symptoms of COVID-19 is the so-called "cytokine storm". Its pathogenesis is that the initial release by lymphocytes and macrophages of proinflammatory cytokines in the classical immune response to SARS-CoV-2 is significantly enhanced and maintained due to excessive adrenergic stimulation of the immune cells. The proinflammatory adrenergic mechanism of the "cytokine storm" can be offset by the activation of the anti-inflammatory cholinergic mechanism by non-invasive stimulation of the vagus nerve. In 2015, a generator for electrotherapy and stimulation of 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). We hypothesized that changes in EEG parameters may be accompanied by a vagotonic shift of the sympatho-vagus balance, favorable for calming the "cytokine storm". The main purpose of this study was to find out. In addition, concomitant changes in EEG, immunity, GDV, etc. due to the use of the devices "VEB-1"[®] and recently designed "VEB-2" had to be detected. Material and research methods. The object of observation were 18 volunteers: 11 women 33-62 y and 7 men 29-62 y (Mean±SD: 51±12 y) without clinical diagnose but with dysfunction of neuro-endocrine-immune complex and metabolism. In the morning registered HRV ("CardioLab+HRV", "KhAI-Medica", Kharkiv, UA), EEG ("NeuroCom Standard", "KhAI-Medica", Kharkiv, UA), kirlionogram 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 parameters of immunity and metabolism. After the initial testing, an 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. The effects of electrical stimulation can be divided into the following networks. Regarding EEG, this is a leveling of right-hand lateralization and normalizing decrease in the increased of the amplitude of the θ -rhythm and its spectral power density (SPD) at the loci F3, F7, F8, T3, T4, T6, P3, O1 and O2; further increase of SPD of δ -rhythm in loci F3, F4, T6, P3 and O1 as well as further decrease of SPD F4- α ; reversion of the increased level of entropy in loci Fp1, F4, C3 and P3 to the lowered level. Regarding HRV, it is a vagotonic shift of sympatho-vagus balance due to a decrease in elevated levels of sympathetic tone markers and an increase in decreased levels of vagus tone markers, but without normalization. Neurotropic effects are accompanied by favorable changes in a number of immune parameters and a tendency to decrease the level of C-Reactive Protein. Regarding GDV, it is almost complete normalization of the initially increased GDI Area in the frontal projection and third Chakra Energy; normalizing decrease in the initially increased Energy of second and seventh Chakras; normalizing right-hand shift of more or less pronounced left-sided Asymmetry of first and third Chakra. These effects should be clearly interpreted as physiologically beneficial. The effects on these parameters are almost equally pronounced in people of both sexes when using both devices. Conclusion. Vagotonic and immunotropic effects of our device give us a reason to offer it for further research on the leveling of "cytokine storm" in patients with COVID-19.

Key words: device "VEB-1"; device "VEB-2"; electrostimulation; EEG; HRV; gas-discharge visualization; immunity; cytokine storm; cytokine cascade; cytokine release syndrome; cytokine storm syndrome; CSS; hypercytokinemia; proinflammatory adrenergic mechanism; COVID-19; SARS-CoV-2; ACE2 receptors; stimulation of the vagus nuclei; VNS; Chakras; spectral power density.

INTRODUCTION

One of the symptoms of COVID-19 is the so-called "cytokine storm". Its pathogenesis is that the initial release by lymphocytes and macrophages of proinflammatory cytokines in the classical immune response to SARS-CoV-2 contact with ACE2 receptors of the nasal mucosa, pharynx, conjunctiva, etc. is significantly enhanced and maintained due to excessive adrenergic stimulation of the immune cells, in turn, caused by the direct effect of SARS-CoV-2 on the sympathetic nuclei of the brain, where it penetrates through the afferent fibers of the vagus and olfactory nerves [Baptista AF et al, 2020].

The proinflammatory adrenergic mechanism of the "cytokine storm" can be offset by the activation of the anti-inflammatory cholinergic mechanism [Borovikova LV et al, 2000; Tracey KJ, 2007,2010; Chavan SS et al, 2017,2017a; Pavlov VA et al, 2018] by non-invasive vagus nerve stimulation (VNS). Direct VNS is realized by electrical stimulation of the nerve endings of the skin through procedures of transcutaneous auricular vagus nerve stimulation (taVNS) or cervical vagus nerve stimulation (nVNS). Indirect VNS is realized by electrical stimulation of the scalp in the locus F3, which is projected left dorsolateral prefrontal cortex, the neurons of which, in turn, activate the nuclei of the vagus [Baptista AF et al, 2020;

Bikson M et al, 2020; Fudium M et al, 2020; Staats P et al, 2020; Tornero C et al, 2020). Hyoju SK et al [2020] offer to achieve the same goal to dampen the sympathetic influences on immune response.

In 2015, a generator for electrotherapy and stimulation of human nerve centers was created (Babelyuk VE, Dobrovolsky YG, Korsunsky 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°, 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" [Babeluk VE, 2016]. Its operation is described in [Babeluk VY et al, 2017].

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.

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

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.

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) [Babalyuk NV et al, 2015,2016,2016a,2018; Babalyuk VYe et al, 2018; Kindzer BM et al, 2019].

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 [Ohtake Y et al, 2007; Tang Yi-Y et al, 2009; Tolkunov D et al, 2010; Subhani AR et al, 2012; Prinsloo GE et al, 2013; Popovych IL et al, 2013,2014; Vanneste S, De Ridder D, 2013] as well as neuroimmunomodulation [Korneva EA, 1993; Sternberg EM, 2006; Nance DM, Sanders VM, 2007; Tracey KJ, 2007,2010; Popovych IL, 2008; Thayer JF, Sternberg EM, 2010; Kul'chyns'kyi AB et al, 2017; Popovych IL et al, 2017,2018a,2020; Popadynets' OO et al, 2020]. From here we hypothesized that changes in EEG parameters may be accompanied by a vagotonic shift of the sympatho-vagus balance, favorable for calming the "cytokine storm". The main purpose of this study was to find out. In addition, concomitant changes in EEG, immunity, GDV, etc. due to the use of the devices "VEB-1"® and recently designed "VEB-2" had to be detected.

MATERIAL AND RESEARCH METHODS

The object of observation were 18 volunteers: 11 women 33-62 y and 7 men 29-62 y (Mean±SD: 51±12 y) without clinical diagnose but with dysfunction of neuro-endocrine-immune complex and metabolism documented previously.

In the morning on an empty stomach registered (Dubkova GI) first 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 [Korotkov KG, 2001,2007,2014].

As the attitude to the GDV method is ambiguous, our laboratory conducted studies that proved its relevance [Popovych IL et al, 2010; Babelyuk VY, 2013; Babelyuk VY et al, 2017b,2018].

In addition, the response of GDV parameters to the course of use of bioactive water Naftusya [Gozhenko AI et al, 2016], the course of rehabilitation by Kozyavkin's method [Babelyuk VY et al, 2018a; Popovych IL et al, 2018; Kozyavkina OV et al, 2018,2018a], as well as the immediate response to Katas of Kyokushin Karate operator [Babelyuk VY et al, 2017a] were demonstrated.

Then recorded (Korolyshyn TA) simultaneously 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 (pNN50), triangulary index (TNN). Spectral parameters (Frequency Domain Methods): spectral power density (SPD) bands of HRV: high-frequency (HF, range 0,4÷0,15 Hz), low-frequency (LF, range 0,15÷0,04 Hz), very low-frequency (VLF, range 0,04÷0,015 Hz) and ultra low-frequency (ULF, range 0,015÷0,003 Hz) [HRV,1996; Berntson GG et al, 1997]. Baevskiy's parameters: mode (Mo), the amplitude of mode (AMo), variational sweep (MxDmN) [Baevskiy RM et al, 2001]. We calculated classical indexes: LF/HF, LFnu=100%·LF/(LF+HF), Centralization Index (CI=(VLF+LF)/HF), Baevskiy's Stress Index (BSI=AMo/2·Mo·MxDmN).

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 (μ V), average frequency (Hz), frequency deviation (Hz), index (%), coefficient of asymmetry (%), absolute (μ V/Hz) and relative (%) SPD of basic rhythms: β (35±13 Hz), α (13±8 Hz), θ (8±4 Hz) and δ (4±0,5 Hz) in all loci, according to the instructions of the device. In addition, calculated Laterality Index (LI) for SPD each Rhythm using formula [Newberg AB et al, 2001]:

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

We calculated for HRV and each locus EEG the Entropy (h) of normalized SPD using formulas [Popadynets' OO et al, 2019] based on classic Shannon's CE [1963] formula:

$$hHRV = -[\text{SPHF} \cdot \log_2 \text{SPHF} + \text{SPLF} \cdot \log_2 \text{SPLF} + \text{SPVLF} \cdot \log_2 \text{SPVLF} + \text{SPULF} \cdot \log_2 \text{SPULF}] / \log_2 4$$

$$hEEG = -[\text{SPD}\alpha \cdot \log_2 \text{SPD}\alpha + \text{SPD}\beta \cdot \log_2 \text{SPD}\beta + \text{SPD}\theta \cdot \log_2 \text{SPD}\theta + \text{SPD}\delta \cdot \log_2 \text{SPD}\delta] / \log_2 4$$

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 [Hubyts'kyi VY et al, 2013]. 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 [1981] with our (Kovbasnyuk MM) moderately modification. 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 40C. 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 shaken and placed in thermostat at 370C 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 Papanheim. Microscoped during immersion lens h90, x10 eyepiece. Take into account the following parameters of phagocytosis: activity (percentage of neutrophils, in which found microbes - Hamburger's Phagocytic Index), intensity (number of microbes absorbed one phagocytes - Microbial Count or Right's Index) and completeness (percentage of dead microbes - Killing Index). Microbial number and index their digestion is determined for each phagocyte and fixed in phagocytic frame.

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 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) [Lapovets' LYE, Lutsyk BD, 2002].

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

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

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

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

Then determined (Musiyenko VY and Kyrlyenko IG) the Electrokinetic Index as rate of electronegative nuclei of buccal epithelium by intracellular microelectrophoresis on the device "Biotest" (Kharkiv State University), according to the method described [Shakhbazov VG, 2000].

At last in portion of venous blood determined (Kikhtan VV) plasma level of 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) according to instructions with the use of analyzers "Reflotron" (BRD) and "Pointe-180" (USA) and corresponding sets of reagents.

Reference values are taken from the database of our laboratory.

Results processed (Popovych IL) using the software package "Statistica 8.0".

RESULTS AND DISCUSSION

Obviously, the presentation of results should begin with changes in EEG parameters. According to the results of screening of direct differences between the values of the parameters after and before electrical stimulation, 41 were found to be significant. Of these, the discriminant analysis program (forward stepwise method) included only 23 in the model, and other parameters (variables) were outside the discriminant model, apparently as carriers of redundant discriminatory information (Tables 1 and 2).

Pseudo-staining gives the visual impression that the most numerous set of EEG parameters that are subject to electrical stimulation are θ -rhythm parameters, the other two networks form δ -rhythm and entropy parameters, while α -rhythm is represented by only two parameters, and β -rhythm was not subject to significant effects of electrical stimulation.

Table 1. Discriminant Function Analysis Summary for EEG Variables

Step 23, N of vars in model: 23; Grouping: Before and After Electrostimulation

Wilks' Lambda: 0,048; approx. F(23,1)=10,4; p<10⁻⁴

Reference value (122)

Average value

Wilks' statistics parameters

Variables

currently in the model

Before

(18)

After

(18)

Wilks'

Λ

Partial

Λ

F-

remove

p-

level

Tolerance

rancy

θ rhythm Laterality Index, %

-3

14

-4

0,197

0,243

37,32

$<10^{-4}$

0,046

F3- θ SPD, %

9,6

11,5

9,7

0,203

0,237

38,66

$<10^{-4}$

0,011

F8- θ SPD, %

8,4

12,5

9,0

0,068

0,701

5,11

0,043
0,071
T3-0 SPD, %
8,5
10,1
8,5
0,146
0,328
24,54
<10-3
0,026
T6-0 SPD, %
7,2
9,8
7,5
0,075
0,642
6,70
0,024
0,062
F8-0 SPD, $\mu\text{V}^2/\text{Hz}$
19
48
28
0,051
0,936
0,82
0,382
0,119
P3-0 SPD, %
7,8
10,3
8,4
0,052
0,914
1,12
0,310
0,100

θ rhythm Amplitude, μV

7,4

10,9

9,5

0,230

0,209

45,46

<10-4

0,007

O1-θ SPD, %

6,7

10,1

8,3

0,067

0,719

4,68

0,051

0,048

F7-θ SPD, %

7,9

11,5

8,9

0,056

0,860

1,95

0,188

0,061

O2-θ SPD, %

6,0

9,6

7,2

0,054

0,890

1,48

0,248

0,038

T4-θ SPD, %

8,7

10,3

8,2

0,335

0,143

71,84

<10⁻⁵

0,011

Fp1 SPD Entropy

0,81

0,85

0,77

0,073

0,658

6,23

0,028

0,080

C3 SPD Entropy

0,83

0,87

0,77

0,087

0,552

9,73

0,009

0,059

F4 SPD Entropy

0,82

0,85

0,76

0,072

0,671

5,89

0,032

0,026

P3 SPD Entropy

0,80

0,80

0,72

0,362
0,132
78,62
<10⁻⁶
0,016
F3-δ SPD, μV2/Hz
213
222
751
0,164
0,293
28,96
<10⁻³
0,008
F4-δ SPD, μV2/Hz
155
183
592
0,098
0,489
12,53
0,004
0,030
T6-δ SPD, %
30,5
35,7
45,4
0,127
0,378
19,77
<10⁻³
0,035
T6-δ SPD, μV2/Hz
276
204
621
0,078
0,611

7,63
0,017
0,011
P3- δ SPD, %
26,5
31,2
43,0
0,141
0,341
23,21
<10⁻³
0,026
O1- δ SPD, %
26,7
31,8
42,0
0,232
0,207
46,04
<10⁻⁴
0,011
F4- α SPD, %
32,7
25,9
22,3
0,197
0,243
37,32
<10⁻⁴
0,020
Variables
currently not in the model
Refer
value
Before
After
Wilks'
 Λ

Partial

Λ

F to

enter

p-

level

Tole-

rancy

C3-θ SPD, %

9,6

12,9

9,5

0,046

0,967

0,37

0,554

0,046

C4-θ SPD, %

9,7

11,9

8,9

0,044

0,926

0,88

0,369

0,044

Fp2-θ SPD, %

8,3

10,7

7,6

0,047

0,981

0,21

0,658

0,047

F4-θ SPD, %

10,1

12,3

8,7

0,047

0,977

0,26

0,623

0,047

F3 SPD Entropy

0,81

0,84

0,75

0,047

0,984

0,18

0,678

0,047

F8 SPD Entropy

0,75

0,81

0,73

0,046

0,966

0,38

0,549

0,046

T3 SPD Entropy

0,81

0,84

0,76

0,048

0,999

0,01

0,929

0,048

C4 SPD Entropy

0,84

0,88

0,76

0,046

0,957

0,49

0,499

0,046

O2 SPD Entropy

0,73

0,81

0,75

0,048

0,996

0,04

0,840

0,042

P4 SPD Entropy

0,79

0,81

0,76

0,047

0,969

0,35

0,567

0,054

Fp2 SPD Entropy

0,80

0,80

0,74

0,048

0,998

0,02

0,891

0,048

C3-δ SPD, %

29,3

22,5

44,0

0,048

0,991

0,10

0,758
0,048
C3- δ SPD, μ V2/Hz
139
135
351
0,047
0,980
0,23
0,641
0,047
C4- δ SPD, %
29,9
33,3
44,9
0,047
0,983
0,20
0,667
0,047
F4- δ SPD, %
32,7
36,9
47,1
0,046
0,957
0,49
0,499
0,046
P4- δ SPD, %
27,1
32,7
39,7
0,048
0,998
0,02
0,896
0,058

O2- δ SPD, %

25,9

30,0

39,1

0,047

0,989

0,12

0,737

0,056

F4- α SPD, μ V2/Hz

128

64

41

0,047

0,977

0,25

0,624

0,047

Table 2. Summary of Stepwise Analysis for EEG Variables (ranked by criterion Lambda)

Variables currently in the model

F to

enter

p-

level

Lambda

F-

value

p-

level

C3 SPD Entropy

4,72

0,037

0,878

4,72

0,037

F8- θ SPD, %

2,90

0,098

0,807
3,94
0,029
F3- θ SPD, %
2,08
0,159
0,758
3,41
0,029
P3 SPD Entropy
1,59
0,217
0,721
3,00
0,033
P3- θ SPD, %
2,63
0,115
0,663
3,05
0,024
 θ rhythm Amplitude, μ V
3,78
0,062
0,586
3,41
0,011
O1- θ SPD, %
4,66
0,040
0,503
3,96
0,004
F3- δ SPD, μ V²/Hz
1,88
0,182
0,470
3,81

0,004
O1- δ SPD, %
1,79
0,193
0,440
3,68
0,004
T4- θ SPD, %
2,53
0,124
0,399
3,76
0,003
F8- θ SPD, μ V2/Hz
2,97
0,098
0,355
3,96
0,002
 θ rhythm Laterality Index, %
3,13
0,090
0,313
4,21
0,002
T3- θ SPD, %
2,75
0,112
0,278
4,39
0,001
P3- δ SPD, %
1,73
0,202
0,257
4,34
0,001
F4- α SPD, %

2,17
0,156
0,232
4,42
0,001
F4- δ SPD, μ V²/Hz
3,40
0,081
0,197
4,85
<10⁻³
T6- δ SPD, %
6,20
0,023
0,146
6,18
<10⁻³
T6- δ SPD, μ V²/Hz
4,57
0,047
0,115
7,25
<10⁻⁴
Fp1 SPD Entropy
2,34
0,146
0,101
7,53
<10⁻⁴
T6- θ SPD, %
2,43
0,140
0,087
7,92
<10⁻⁴
F7- θ SPD, %
2,49
0,137

0,073

8,41

<10⁻⁴

F4 SPD Entropy

4,72

0,049

0,054

10,4

<10⁻⁴

O2-θ SPD, %

1,48

0,248

0,048

10,3

<10⁻⁴

r*=0,976; Wilks' Λ=0,048; χ²(23)=68,3; p<10⁻⁵

Squared Mahalanobis Distance=79; F=10; p<10⁻⁴

Recognition information is condensed in the canonical discriminant root, which, judging by the Structural coefficients, reflects 17 variables directly and 6 inversely (Table 3). The same table also shows the Raw coefficients, the sum of the products of which on the individual values of discriminant variables together with the Constant gives the individual values of the root before and after the course of electrical stimulation (Fig. 6).

Table 3. Standardized, Structural and Raw Coefficients and Constant for EEG Variables (ranked by Structural coefficient)

Coefficients

Variables

currently in the model

Standardized

Structural

Raw

C3 SPD Entropy

2,829

0,084

20,56

F8-θ SPD, μV2/Hz

2,109

0,075

0,385

T6-θ SPD, %

-2,463

0,070

-0,652
P3 SPD Entropy
7,549
0,062
47,58
F8- θ SPD, %
0,753
0,061
0,020
O2- θ SPD, %
1,729
0,059
0,361
F4 SPD Entropy
-3,639
0,059
-20,69
 θ rhythm Laterality Index, %
4,156
0,058
0,111
Fp1 SPD Entropy
2,125
0,055
12,17
F7- θ SPD, %
-1,553
0,053
-0,271
T4- θ SPD, %
-9,213
0,052
-1,974
T3- θ SPD, %
5,164
0,050
1,428
F3- θ SPD, %

-8,569
0,040
-0,137
P3- θ SPD, %
-0,950
0,036
-0,152
O1- θ SPD, %
-2,474
0,032
-0,373
 θ rhythm Amplitude, μ V
10,914
0,028
1,951
F4- α SPD, %
6,236
0,026
0,387
T6- δ SPD, μ V2/Hz
-5,986
-0,057
-0,007
P3- δ SPD, %
5,175
-0,056
0,214
F4- δ SPD, μ V2/Hz
4,218
-0,056
0,005
O1- δ SPD, %
-8,847
-0,051
-0,382
F3- δ SPD, μ V2/Hz
9,721
-0,048

0,008
 T6- δ SPD, %
 4,344
 -0,042
 0,161
 Eigenvalue
 19,84
 Constant
 -60,62

Fig. 6. Individual values of the canonical discriminant EEGs root before and after four-day electrostimulation course with the devices "VEB-1" and "VEB-2" at females and males. Below the columns are the codes of the volunteers

Therefore, the characteristic manifestations of the effect of electrical stimulation are: leveling of right-hand Lateralization and normalizing decrease in the increased of the Amplitude of the θ -rhythm and its SPD at the loci F3, F7, F8, T3, T4, T6, P3, O1 and O2; further increase of SPD of δ -rhythm in loci F3, F4, T6, P3 and O1 as well as further decrease of SPD F4- α ; reversion of the increased level of Entropy in loci Fp1, F4, C3 and P3 to the lowered level.

Retrospective clustering of volunteers by gender and applied modification of the device indicates the absence of significant differences in the set of discriminant EEG parameters between women and men both before and after the course of electrical stimulation of both devices (Fig. 7).

Fig. 7. Average values (Mean \pm SE) of the canonical discriminant root EEG before and after four-day electrostimulation course with the devices "VEB-1" and "VEB-2" at women (F) and men (M)

The application of the parameters of classification functions (Table 4) makes it possible to unmistakably recognize retrospectively when the EEG was registered: before or after the course of electrical stimulation.

Table 4. Coefficients and Constants for Classification Functions

Variables
 currently in the model
 Before
 After
 C3 SPD Entropy
 1333
 1155
 F8- θ SPD, %
 0,408
 0,234
 F3- θ SPD, %
 -9,983
 -8,797
 P3 SPD Entropy
 3150
 2738
 P3- θ SPD, %

-3,320
-2,003
θ rhythm Amplitude, μV
145,6
128,8
O1-θ SPD, %
-21,45
-18,23
F3-δ SPD, μV2/Hz
0,539
0,472
O1-δ SPD, %
-26,89
-23,58
T4-θ SPD, %
-134,9
-117,9
F8-θ SPD, μV2/Hz
25,01
21,68
θ rhythm Laterality Index, %
7,393
6,431
T3-θ SPD, %
105,3
92,98
P3-δ SPD, %
16,42
14,56
F4-α SPD, %
27,94
24,60
F4-δ SPD, μV2/Hz
0,409
0,366
T6-δ SPD, %
10,954
9,557

T6- δ SPD, μ V2/Hz

-0,425

-0,364

Ep1 SPD Entropy

1100

994,7

T6- θ SPD, %

-41,57

-35,93

F7- θ SPD, %

-25,74

-23,39

F4 SPD Entropy

-929,2

-750,1

O2- θ SPD, %

9,516

6,388

Constants

-2531

-2006

Secondly, we will consider significant or noteworthy changes in HRV parameters, as well as immune, biophysical and metabolic (Tables 5 and 6).

Regarding HRV the characteristic manifestations of the effect of electrical stimulation are: a decrease in elevated levels of sympathetic tone markers (LFnu and AMo) and an increase in decreased levels of vagus tone markers (RMSSD, HF, TNN and pNN50), that is vagotonic shift of sympatho-vagus balance indicex (LF/HF, Bayevsiy's SI, Centralization Index), but without normalization. This is accompanied by a normalizing increase in the reduced entropy of the HRV spectrum.

Among the biophysical parameters revealed a insignificant increase in Electrokinetic Index and significant decrease in the increased electrical conductivity of the skin at the point of acupuncture MC (AVL) on the right, which led to the reversion of its Lateralization.

The Electrokinetic Index reflects the integral state of the organism [Shakhbazov VG, 2000], which is documented by its relationships with the parameters of EEG, HRV, Immunity, Metabolism, etc. [Kyrylenko IG, 2018,2018a]. The point of acupuncture MC (AVL) reflects the state of Immunity [Hubyts'kyi VY et al, 2013]. Therefore, favorable changes in the parameters of Immunity, especially an increase in the Killing Index of Neutrophils versus both Escherichia coli and Staphylococcus aureus, as well as level of CIC and T-killers, are quite expected for us.

Table 5. Discriminant Function Analysis Summary for HRV, Immune, Biophysic&Metabolic Variables

Step 9, N of vars in model: 9; Grouping: 2 grps

Wilks' Lambda: 0,467; approx. F(9,3)=3,3; p=0,008

Referen-

ce value

(36)

Average value

Wilks' statistics parameters

Variables currently in the model

Before

(18)

After

(18)

Wilks'

Λ

Partial

Λ

F-

remove

p-

level

Tolerance-

rancy

Killing Index vs Escherichia coli, %

62,0

34,7

40,0

0,670

0,697

11,3

0,002

0,542

Popovych's Leukocytary Strain Index

0,07

0,15

0,25

0,532

0,878

3,60

0,069

0,622

Klimov's Atherogenicity Coefficient

2,97

2,45

2,65

0,486

0,961

1,04

0,316

0,736

Spectral Power of LFnu, %

65,4

84,0

76,8

0,575

0,813

6,00

0,021

0,310

LF/HF ratio HRV

2,87

7,09

4,49

0,517

0,905

2,74

0,110

0,288

EC AP MC (AVL) Right, units

58,0

63,3

61,2

0,518

0,902

2,82

0,105

0,591

Amplitude of Mode HRV, %

38,9

52,3

47,6

0,544

0,859

4,26

0,049

0,111

Bayevskiy's Stress Index, ln units

4,90

5,21

5,07

0,516

0,906

2,70

0,113

0,100

EC AP MC(AVL) Laterality Index, %

0

0,2

-0,3

0,508

0,920

2,26

0,145

0,636

Variables currently not in the model

Before

After

Wilks'

Λ

Partial

Λ

F to

enter

p-

level

Tolerance

rancy

RMSSD HRV, msec

27,3

17,4

22,0

0,461

0,986

0,35

0,562

0,380

Entropy of HRV

0,798

0,710

0,775

0,463

0,991

0,24

0,632

0,643

Spectral Power of HF band, %

13,8

7,4

11,3

0,464

0,994

0,16

0,692

0,414

Spectral Power of HF band, msec2

346

134

209

0,464

0,994

0,15

0,700

0,452

Triangular Index HRV, units

11,2

9,7

10,7

0,465

0,994

0,14

0,710

0,076

pNN50, %

9,8

1,94

3,72

0,465

0,995

0,13

0,726

0,529

Electrokinetic Index, %

41,3

41,3

42,5

0,466

0,997

0,06

0,804

0,594

CD8+CD3+ T-Lymphocytes, %

23,5

20,5

21,9

0,466

0,997

0,06

0,802

0,564

Circulating Immune Complicex, units

45

33

41

0,467

0,999

0,02

0,888

0,750

Killing Index vs Staphyloc. aureus, %

58,9

41,1

49,3

0,467

1,000

0,00

0,963

0,587

(VLF+LF)/HF as Centralization Index

7,0

16,8

10,3

0,456

0,977

0,60

0,446

0,302

High Density LP Cholesterol, mM/L

1,40

1,75

1,61

0,465

0,996

0,11

0,741

0,396

C-Reactive Protein, mg/L

2,18

2,90

2,79

0,466

0,998

0,06

0,809

0,711

Table 6. Summary of Stepwise Analysis for HRV, Immune, Biophysic&Metabolic Variables (ranked by criterion Lambda)

Variables currently in the model

F to

enter

p-

level

Lambda

F-

value

p-

level

Killing Index vs Escherichia coli, %

7,55

0,010

0,818

7,55

0,009

Spectral Power of LFnu, %

5,82

0,022

0,696

7,22

0,003

Popovych's Leukocytary Strain Index

2,36

0,135

0,648

5,79

0,003

Amplitude of Mode HRV, %

1,25

0,272

0,623

4,69

0,004

Bayevskiy's Stress Index, ln units

2,61

0,117

0,573

4,47

0,004

LF/HF ratio HRV

1,86

0,184

0,539

4,14

0,004

EC AP MC(AVL) Right, units

1,15

0,293

0,517

3,73

0,006

EC AP MC(AVL) Laterality Index, %

1,74

0,198

0,486

3,57

0,006

Klimov's Atherogenicity Coefficient

1,04

0,316

0,467

3,29

0,008

$r^*=0,730$; Wilks' $\Lambda=0,467$; $\chi^2(9)=22,4$; $p=0,008$

Squared Mahalanobis Distance= $4,56$; $F=3,29$; $p=0,008$

Under the identified circumstances, we consider further increase of the Popovych's Leukocyary Strain Index to be favorable. And the increase within the norm of reduced Klimov's Atherogenicity Coefficient due to the decrease within the norm of the increased level of High Density LP Cholesterol we interpret as at least neutral.

Unfortunately, due to lack of funding, we could not determine the level of pro-inflammatory cytokines. Therefore, it is hoped that the tendency to decrease the level of C-Reactive Protein is a predictor of the anti-inflammatory effect of electrical stimulation.

Leaving without comments Tables 7 and 8, we emphasize that the parameters included in the discriminant model when using classification functions allow to retrospectively recognize the initial state of the organism with an accuracy of 88,9% (2 errors), and the final even less (83,3%, 3 errors) against the background of error-free recognition by EEG parameters.

Table 7. Standardized, Structural and Raw Coefficients and Constant for for HRV, Immune, Biophysic&Metabolic Variables (ranked by Structural coefficient)

Coefficients

Variables currently in the model

Standardized

Structural

Raw

Killing Index vs Escherichia coli, %

1,024

0,441

0,175

Popovych's Leukocytary Strain Index

0,606

0,228

2,724

Klimov's Atherogenicity Coefficient

0,314

0,228

0,712

Spectral Power of LFnu, %

-1,066

-0,369

-0,114

LF/HF ratio HRV

0,788

-0,286

0,179

EC AP MC(AVL) Right, units

-0,558

-0,177

-0,095

Amplitude of Mode HRV, %

-1,544

-0,157

-0,106

Bayevskiy's Stress Index, ln units

1,331

-0,106

2,093

EC AP MC(AVL) Laterality Index, %

0,486

-0,062

13,840

Eigenvalue

1,14

Constant

-0,348

Table 8. Coefficients and Constants for Classification Functions for HRV, Immune, Biophysic&Metabolic Variables

Variables currently in the model

Before

After

Killing Index vs Escherichia coli, %

-0,753

-0,391

Spectral Power of LFnu, %

2,333

2,098

Popovych's Leukocytary Strain Index

44,35

50,01

Amplitude of Mode HRV, %

-2,041

-2,261

Bayevskiy's Stress Index, ln units

65,38

69,73

LF/HF ratio HRV

-4,592

-4,219

EC AP MC(AVL) Right, units

1,531

1,334

EC AP MC(AVL) Laterality Index, %

-92,00

-63,28

Klimov's Atherogenicity Coefficient

24,44

25,92

Constants

-267,7

-268,4

If the GDV parameters are offered for the program from the information field, the discriminant model will absorb 10 of them, which will displace a number parameters of HRV, Immunity and Metabolism from the previous model (Tables 9-12), but will provide an error-free retrospective classification (Table 13).

Table 9. Discriminant Function Analysis Summary for GDV, HRV, Immune, Biophysic and Metabolic Variables

Step 16, N of vars in model: 9; Grouping: Before&After electrostimulation

Wilks' Lambda: 0,114; approx. $F(16,2)=9,2$; $p<10^{-5}$

Refer

value

(36)

Average value

Wilks' statistics parameters

Variables currently in the model

Before

(18)

After

(18)

Wilks'

Λ

Partial

Λ

F-

remove

p-

level

Tolerance

rancy

Killing Index vs Escher. coli, %

62,0

34,7

40,0

0,142

0,806

4,57

0,046

0,375

Spectral Power of LFnu, %

65,4

84,0

76,8

0,167

0,684

8,78

0,008

0,244

Chakra 3 Asymmetry (f)

0,01

-0,05

0,04

0,180

0,636

10,86

0,004

0,262

RMSSD HRV, msec

27,3

17,4

22,0

0,208

0,551

15,50

<10⁻³

0,293

Chakra 2 Asymmetry (f)

0,02

-0,04

-0,14

0,226

0,505

18,59

<10⁻³

0,307

Chakra 2 Energy

-0,07

0,13

-0,01

0,126

0,908

1,94

0,180

0,038

Chakra 7 Energy (f)

0,02

0,07

0,11

0,227

0,503

18,78

<10⁻³

0,054

Area GDI Frontal, kpixels

24,9

26,2

25,0

0,187

0,610

12,15

0,003

0,067

Entropy GDI Left

3,93

3,82

3,74

0,216

0,529

16,91

<10⁻³

0,252

Symmetry GDI (f), %

94,7

93,4

92,6

0,121

0,945

1,12

0,304

0,237

Chakra 7 Energy

-0,11

0,08

-0,03

0,150

0,763

5,91

0,025

0,036

Chakra 4 Asymmetry

0,03

-0,05

0,10

0,144

0,793

4,95

0,039

0,393

Chakra 1 Asymmetry (f)

-0,01

-0,17

-0,07

0,140

0,819

4,21

0,054

0,275

EC AP MC(AVL) Lateral. Ind, %

0,0

0,2

-0,3

0,121

0,948

1,05

0,318

0,613

LF/HF ratio HRV

2,87

7,09

4,49

0,127

0,897

2,18

0,156

0,243

GDI Shape Coefficient Left (f)

11,5

13,0

13,6

0,124

0,925

1,55

0,228

0,099

Variables currently not in the model

Before

After

Wilks'

Λ

Partial

Λ

F to

enter

p-

level

Tolerance

variance

Klimov's Atherogenicity Coefficient

2,97

2,45

2,65

0,113

0,992

0,15

0,703

0,517

Bayevskiy's Stress Index, ln units

4,90

5,21

5,07

0,114

0,999

0,02

0,893

0,334

Spectral Power of HF band, msec2

346

134

209

0,114

0,999

0,03

0,875

0,168

EC AP MC(AVL) Right, units

58,0

63,3

61,2

0,111

0,969

0,58

0,455

0,461

Popovych's Leukocyt Strain Index

0,07

0,15

0,25

0,114

0,999

0,01

0,918
0,583
Entropy of GDI Right
3,85
3,80
3,76
0,110
0,961
0,74
0,402
0,550
Chakra 3 Energy
-0,09
0,03
-0,07
0,112
0,977
0,43
0,522
0,154
Amplitude of Mode HRV, %
38,9
52,3
47,6
0,111
0,998
0,57
0,450
0,460

Table 10. Summary of Stepwise Analysis for GDV, HRV, Immune, Biophysic and Metabolic Variables (ranked by criterion Lambda)

Variables currently in the model

F to

enter

p-

level

Lambda

F-

value

p-

level

Killing Index vs Escherichia coli, %

7,55

0,010

0,818

7,55

0,010

Spectral Power of LFnu, %

5,82

0,022

0,696

7,22

0,003

Chakra 3 Asymmetry (f)

5,98

0,020

0,586

7,53

<10⁻³

RMSSD HRV, msec

3,56

0,069

0,526

6,99

<10⁻³

Chakra 2 Asymmetry (f)

2,93

0,098

0,479

6,52

<10⁻³

Chakra 2 Energy

3,34

0,078

0,430

6,42

<10⁻³

Chakra 7 Energy (f)

5,63

0,025

0,358

7,18

<10⁻⁴

Area GDI Frontal, kpixels

7,48

0,011

0,280

8,67

<10⁻⁵

Entropy GDI Left

2,99

0,096

0,251

8,61

<10⁻⁵

Symmetry GDI (f), %

5,40

0,029

0,207

9,60

<10⁻⁵

Chakra 7 Energy

2,78

0,108

0,185

9,61

<10⁻⁵

Chakra 4 Asymmetry

4,01

0,057

0,158

10,2

<10⁻⁶

Chakra 1 Asymmetry (f)

2,12

0,159

0,144

10,1

<10⁻⁵

EC AP MC(AVL) Laterality Index, %

1,72

0,204

0,133

9,79

<10⁻⁵

LF/HF ratio HRV

1,48

0,237

0,124

9,44

<10⁻⁵

GDI Shape Coefficient Left (f)

1,55

0,228

0,114

9,20

<10⁻⁵

$r^*=0,941$; Wilks' $\Lambda=0,114$; $\chi^2(16)=56,4$; $p<10^{-5}$

Squared Mahalanobis Distance=31,0; $F=9,2$; $p<10^{-5}$

Table 11. Standardized, Structural and Raw Coefficients and Constant for GDV, HRV, Immune, Biophysic and Metabolic Variables (ranked by Structural coefficient)

Coefficients

Variables currently in the model

Standardized

Structural

Raw

Killing Index vs Escherichia coli, %

0,764

0,169

0,130

RMSSD HRV, msec

1,316

0,103

0,161
Chakra 3 Asymmetry (f)
1,252
0,097
7,907
Chakra 1 Asymmetry (f)
-0,863
0,080
-3,588
Chakra 4 Asymmetry
0,770
0,072
1,996
GDI Shape Coefficient Left (f)
0,926
0,074
0,688
Chakra 7 Energy (f)
3,233
0,030
12,67
Spectral Power of LFn_u, %
-1,211
-0,141
-0,129
LF/HF ratio HRV
0,692
-0,110
0,157
Entropy GDI Left
-1,452
-0,086
-9,356
Symmetry GDI (f), %
-0,514
-0,083
-0,278
Chakra 2 Asymmetry (f)

-1,349

-0,070

-5,311

Chakra 2 Energy

-1,664

-0,059

-3,882

Chakra 7 Energy

-2,728

-0,050

-7,100

Area GDI Frontal, kpixels

2,564

-0,048

0,56

EC AP MC(AVL) Laterality Index, %

0,311

-0,024

8,847

Eigenvalue

7,744

Constant

37,47

Table 12. Coefficients and Constants for Classification Functions for GDV, HRV, Immune, Biophysic and Metabolic Variables

Variables currently in the model

Before

After

Killing Index vs Escherichia coli, %

-2,415

-1,709

Spectral Power of LFnu, %

5,603

4,904

Chakra 3 Asymmetry (f)

-139,1

-96,35

RMSSD HRV, msec

-6,233

-5,360
Chakra 2 Asymmetry (f)
-112,3
-141,0
Chakra 2 Energy
-282,4
-303,4
Chakra 7 Energy (f)
407,6
476,2
Area GDI Frontal, kpixels
12,01
15,02
Entropy GDI Left
835,6
785,0
Symmetry GDI (f), %
154,5
153,0
Chakra 7 Energy
590,2
551,8
Chakra 4 Asymmetry
-54,27
-43,481
Chakra 1 Asymmetry (f)
-187,8
-207,2
EC AP MC(AVL) Laterality Index, %
-1406
-1358
LF/HF ratio HRV
8,316
9,167
GDI Shape Coefficient Left (f)
214,2
217,8
Constants

-10577

-10375

Table 13. Classification Matrix

Rows: Observed classifications

Columns: Predicted classifications

Percent

correct

Before

After

Before

100

18

0

After

100

0

18

Total

100

18

18

If the biophysical (Area and Shape of GDI and its Symmetry) and informational (GDI Entropy) GDV parameters are more or less tolerantly perceived by scientists who follow the paradigm of Western medicine, then for the Chakras, which are almost the main attribute of Eastern medicine, we risk further obstruction.

According to existent paradigm, Chakras are power centers, related to the endocrine glands and neural plexus as well as to some organs. In particular, the first Chakra is related to the testicles and sacral plexus, second Chakra to the ovaries, adrenals and kidneys, third Chakra to spleen, liver and solar plexus, fourth Chakra to thymus, heart and cardiac plexus, fifth Chakra to thyroid and parathyroid glands, sixth Chakra to pituitary gland and brain, seven Chakra to pineal gland [Puchko LG, 2004].

The method we use evaluates the Energy and Asymmetry of the virtual Chakras, calculated by the program based on the GDV parameters of the skin of ten fingers.

The effects of electrical stimulation can be divided into the following networks. First, it is almost complete normalization of the initially increased GDI Area in the Frontal projection and Chakra 3 (Spleen!) Energy. Second, it is a normalizing decrease in the initially increased Energy of Chakra 2 (Steroides!) and Chakra 7(f). Third, it is a normalizing right-hand shift of more or less pronounced left-sided Asymmetry of Chakra 1(f) and Chakra 3(f). These effects should be clearly interpreted as physiologically beneficial.

The second set is created by quasi-normal (Chakra 4 (Thymus!) Asymmetry, Chakra 7 Energy(f) and elevated (Shape Coefficient Left,f) parameters, which increase after electrical stimulation, the physiological assessment of changes of which we will leave without comment.

The third set is formed by initially reduced levels of GDI Entropy in the Right and Left projections, which continue to decrease after electrical stimulation, as well as quasi-symmetric Chakra 2(f), which is transformed into left-asymmetric. If the decrease in Entropy can still be assessed positively, then the price change of the latter parameters will wait.

Fig. 8 demonstrates that more or less pronounced changes in these parameters occur in all volunteers without exception.

Fig. 8. Individual values of the canonical discriminant root of GDV, HRV&Immune parameters before and after four-day electrostimulation course with the devices "VEB-1" and "VEB-2" at females and males

The effects on the set of GDV, HRV and Immune parameters are almost equally pronounced in people of both sexes when using both devices (Fig. 9).

Fig. 9. Average values (Mean±SE) of the canonical discriminant root of GDV, HRV&Immune parameters before and after four-day electrostimulation course with the devices "VEB-1" and "VEB-2" at women (F) and men (M)

We consider it necessary to return to the Tracey's KJ [2007] scheme of immunological homunculus by which the neural structures that are projected onto definite loci responsible for certain immune functions, that is the immune compartment cytokines release (F3 and/or F4), activation of memory B cells (Fp1 and/or Fp2), dendritic cells maturation (T3 and/or T4), regulation of T cells (T5 and/or T6), clonal expansion (P3 and/or P4) and late cytokine release (P? or O?).

It is believed that a hippocampus is projected at the C3 and C4 loci, and the T3 and T4 loci reflect the activity of the amygdala [Romodanov AP, 1993]. The prefrontal loci record the activity of anterior cingulate [Cahn BR, Polish J., 2006] as well as orbito-frontal cortex. It is shown that the cortical thickness of an area within these regions positively correlated with two HRV-markers of parasympathetic activity both HF [Winkelmann T et al, 20107] and RMSSD [Yoo HJ et al, 2016]. It is shown significantly positive correlations between HFnu and Fz- θ , FCz- θ and Cz- θ [Tang et al, 2009]. Previously we [Popovych IL et al, 2013,2014] also found correlations between HFnu and F4- θ and P4- θ , between HF relative and Fp1- θ and P4- θ also between RMSSD and P4- θ . Prinsloo GE et al [2013] found that less pronounced changes in HRV, due to work-related stress, accompanied by higher relative SPD Fz- θ , Pz- θ and Cz- θ , lower fronto-central relative β power and higher θ/β ratio. It is also perfectly consistent with our [Popovych IL et al, 2013,2014] data on a negative correlation LFnu, LFr and LF/HF with F4- θ , P4- θ , F7- θ , F8- θ and positive - with F7- β and F8- β - on the one hand, and a positive correlation HFr with Fp1- θ and P4- θ and negative - with P4- β - on the other side.

We hope that our results complement and specify the concept according to which the hippocampus and amygdala are limbic brain structures that process experiences by interfacing with lower vegetative brain areas, such as the hypothalamus and brainstem, and higher cortical areas, particularly within the prefrontal cortex. Cortical structures providing inhibitory control over limbic and brainstem sympathoexcitatory circuits, indeed, disruption of prefrontal activity leads to disinhibition of sympathoexcitatory circuits, with a resultant decrease in vagally-mediated HRV [Carnevali L et al, 2018]. In particular, we found that electrostimulation-induced vagotonic shift of sympatho-vagus balance is associated with activation of neurons that generate δ -rhythm, whereas the activity of generating θ -rhythm neurons that are projected at the same EEG loci, is reduced.

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ACCORDANCE TO ETHICS STANDARDS

Tests in volunteers 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.

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