



# CARDIOMETRY

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Space medicine:  
releasing return tickets  
for a human mission to Mars?

The background of the lower half of the cover features a space scene with Mars on the left, Earth on the right, and the Moon in the center. A red heart with a yellow ECG line is positioned between Mars and Earth. A solid red curved arrow points from the heart towards Mars, and a dashed white curved arrow points from the heart towards Earth, suggesting a cycle or a choice between the two destinations.

## Original research

# Glomus caroticus, environment, time parameters of cardiac and pathogenic mechanisms of formation of somatogenic depression and mixed encephalopathies on the methodological grounds of non-invasive hemogram analyzer

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## Aims

The aim is to determine interaction of risk factors (volume of ingested food and exogenous alcohol) and their effects on thermal regulation of a body due to the changed activity of biochemical reactions of neuromediator regulatory systems, related to the synthesis of endogenous alcohol.

## Materials and methods

Based on study of neurological status, biochemical and instrumental methods of precordial mapping, urine specific gravity and thermometry of five biologically active points, 1200 males were examined for pathogenic mechanisms of endogenous alcohol synthesis and formation of time parameters of cardiac and clinical manifestation of somatogenic depression.

## Results

The amount of endogenous alcohol determines disorders in the bradykinin-acetylcholine and dopamine-noradrenalin systems and formation of clinical syndromes in the continuum of somatogeny-psychogeny (according to the international classification of diseases (ICD-10)).

## Conclusion

Changes in thermal regulation were accompanied with changes of functional mechanisms of Glomus Caroticus, affecting erythrocyte and its receptors, related to atomic oxygen and hydrogen in atmosphere, with formation of relevant pH values of arterial and venous blood, amount of endogenous alcohol.

## Keywords

Non-invasive analyzer • Time parameters of cardiac • Encephalopathies

## Imprint

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## Introduction

In recent years, problems of pathogenesis of depressions and encephalopathies are indissolubly related to the issues of energy metabolism of a cell and vascular body homeostasis. These issues are a major focus of research clinical and experimental studies. They are based on defining symptoms on the ground of external manifestations of metabolic syndrome (MS), including a classic triad: overweight, high blood sugar level and elevated blood pressure. Alcoholic encephalopathies (due to alcohol abuse (AA)) are considered in terms of alcohol consumption and addition to alcohol without studying a connection between energy and metabolism aspect of this issue. In our opinion, studying of common pathogenic mechanisms of metabolic disorders, such as MS and AA should be based on scientific theoretical foundation of the present-day typology of metabolic disorders. These disorders include analysis of exogenous and endogenous risk factors in their connection to basic factors (genetic make-up of metabolism and blood circulation), reflected in continuum of somatogeny and psychogeny of continuum classification of P. Kielholz, 1969. Formation of somatogeny-psychogeny is syndromologically embodied in the ICD-10, chapter F-30-39, where connections in somatogeny-psychogeny system is established depending on etiologic factor.

Authors of continuum classification found the casual connection between AA and alcohol, but there is no connection between ingested food and MS.

MS and AA, as well as mechanisms of their development are considered in respective articles and monographs using various methodological approaches. Typically, there are no generalization of findings, reflecting common natural factors and mechanisms of influence of ingested food and exogenous alcohol on formation of energy metabolism and role of endogenous alcohol [1, 3, 8, 13, 14, 22, 24-26, 28-31, 33, 36, 38-40] in the structural and functional energy regulation of the central nervous system (CNS) at the neuromediator and hormone levels. Also, those papers lack analysis of temporal factors of interaction of the acetylcholine-, adren- and dopaminergic systems, based on relation of leptin with PPAR receptors (Peroxisome Proliferator Activated Receptor) [2, 10-12, 15, 16, 20, 21]. Practically, when studying energy metabolism, such papers lack data on effects of exogenous alcohol and ingested food (risk factors) on body temperature, pulse rate and respiration rate. There are no description of their relation to the energy supply for a reaction of lipid peroxidation (LPO) and metabolism of vitamins A, B and D.

LPO reaction occur at the different regulatory levels: CNS, gastro-intestinal tract (GIT), cardiorespiratory and renal systems, combined in a single regulatory mechanism by blood circulation. System of blood circulation regulation is based on receptor activity of skin and cells of hematopoietic and immunologic systems. Supposedly, these cells involve methanol in the

metabolism of enkephalines and regulatory neuropeptides at the neuromediator and hormone levels by changing activity of leptin, PPAR and insulin receptors. System of blood circulation regulation combines regulatory haemodynamic and metabolic mechanisms by changing activity of metalloenzyme systems (oxidases and catalases being a part of erythrocytes and blood cells). The latter determine metabolic regulatory connection at the level of neuromediator systems (synthesis and breakdown of acetylcholine, serotonin, dopamine and bradykinin, adrenaline and noradrenaline, insulin and glucagon, as well as icosanoids, which determine local blood flow in the brain and internal organs). Blood flow in the brain and internal organs determines thermometric and related energetic and metabolic specific features of regulation in the system pituitary-hypothalamic-hippocampal controlling mechanisms and definition of clinical, behavioral and emotional aspects of a personality [4, 17, 21-23, 25, 32, 34, 37-39].

### Goal of research

To determine interaction of risk factors (volume of ingested food and exogenous alcohol) and their effects on thermal regulation of a body due to the changed activity of biochemical reactions of neuromediator regulatory systems and changes in blood flow in the brain and internal organs, as well as synthesis of endogenous alcohol.

## Materials and methods

### Research tasks

1. Based on analysis of changes in thermal regulation due to food and alcohol ingestion, to determine limits of time range of interaction of choline- and serotonergic systems, which determine structural and functional potential initiating mechanisms of food factor and exogenous alcohol effect on genetic structures of the regulatory neuropeptides with determination of a volume of endogenous alcohol.
2. Based on analysis of changing of endogenous alcohol volume and its interrelation with time parameters of cardiac, to determine disorder of synthesis of enkephalines and endorphines, causing disorder of dopamine "turnover", which determines mental, emotional and organic neurological disturbances, typical for metabolic syndrome (ICD-10 F4 31,32,33) [6, 7]) and alcohol withdrawal syndrome of varying severity according to ICD-10 (F10.2.4.2.) with formation of clinical syndromes in the somatogeny-psychogeny system.



## Data for research

1200 males with AA, average age  $40 \pm 10$  years, average weight  $70 \pm 30$  kg, were studied on the clinical base of the 13-th Regional Psychiatric Hospital of Kharkov (Ukraine) for 10 years. Anamnesticly, it has been established that people, consuming more than 500 ml of alcohol per day, are admitted to hospital at least twice a year.

Control group (outpatient) consisted of 200 people, consuming up to 500 ml of alcohol per week and not having been admitted to hospital even once. A weight-to-age ratio and a relation between heart rate and accumulated temperature index in the carotid arteries have been determined in all examined subjects.

20 persons from control group at the age of  $25 \pm 5$  years with weight  $70 \pm 30$  kg (volunteers) consumed 450 ml of vodka (40%) during 2 hours with 40-minute interval (75 ml or 7 ml/kg on the average). The same group has been examined 24 hours after vodka consumption and 1 hour after food ingestion: 200 g pork, 2 patty cakes and 200 ml grape juice.

## Research methods

Clinico-neurological, instrumental, and biochemical (with blood sampling) for: alcohol, metalloenzymes, bilirubin, cholesterol, glucose, urea, proteins and creatinine. EKG was studied, as well as urine specific gravity, heart rate (HR) and respiratory rate (RR).

Thermometry was conducted 3 times per day for 5 points: 2 carotid arteries (in bifurcation region), 2 axillary points (in left and right armpits) and in abdominal region (near navel).

USPIH-based non-invasive blood formula analyzer was taken as a methodological foundation for studying alcohol metabolism in the body. USPIH software functioning is based on Dalton's law, Henry's law and fluid mosaic model of the structure of cell membranes (Singer S. Nicolson G., 1973), low-density lipoprotein model (M. Brown G. Goldstein, 1984) and organelle model [2-5]. Based on these methods, a temperature-dependent biotechnological model of correlation between temperature and lipid metabolism [29-32] was developed. This model is based on interaction of hemoglobin, bilirubin and cholesterol, occurring at the neuromediator, regulatory level (level of interaction of somatotrophic pituitary hormone (STPH), transforming growth factor (TGF), thyrotrophic pituitary hormone (TTPH), leu- and methionine-enkephalins, specialized ubiquitin-proteolytic system, and leptin). Along with retinol, rhodopsin and vitamins B<sub>1</sub> and D, these regulators change mass transport of hydrogen in the acetylcholine hydrolysis system with producing of choline and acetaldehyde. Such regulatory metabolic mechanism is associated with interaction system of the ratio between molar weights of adenosine triphosphoric acid (ATP), glucose, glutamic acid,  $\gamma$ -aminobutyric acid (GABA), palmitic acid, angiotensin converting enzyme (somatic), dopamine, and

adrenaline and molar weights of lactic acid, carnitine, serotonin, reproductive fragment of angiotensin converting enzyme, and noradrenaline. These weight ratios determine synthesis of endogenous alcohol and changes in the structure of cell membranes and organelles (peroxisomas, in particular), volume of incoming oxygen, related to the ratio between molar weight of glucose and lactic acid in cells.

The ratio between molar weight of glucose and lactic acid in cells is determined by regulatory function of limbic and hypothalamic systems, which is based on factor of the ration between acidic proteins and basic proteins, and constitutes 14.4. The ratio between this factor and molar weights of lactic acid and glucose determines basic value of arterial blood pH. pH value of arterial blood depends on the regulatory metabolic reactions of cholesterol, leptin and choline. In its turn, the ratio between molar weights of secretin, glucagon, insulin and dopamine and molar weights of ubiquitin, acetylcholine, gastrin and noradrenaline affect course of the regulatory metabolic reactions. Molar weight ratios determine  $H_2O_2$  synthesis and metabolic cost of peptide bond breaking in the cell membranes and peroxisomas.

The ratio between molar weight of acetylcholine and dopamine is regulated by PPAR receptors, which are connected with cell pore complexes (PC) and ratio between molar weights of acidic and basic proteins (factor 14.4).

This factor is associated with molar weight (115 kD; Gerondakis, 1998) of lymphocyte transcription factor NF- $\kappa$ B (consisting of two proteins with molar weight 50 kD and 65 kD, forming 15 dimmers), through a value of the ratio between molar weight of specialized protein ubiquitin and molar weight of leptin, as well as a value of the ration between molar weight of dopamine and molar weight of glucose and quantitative change of dopamine and glucose in one minute, value 7.424 (correlating with genetically determined pH value of venous blood).

The ratio between molar weights of phospholipids, forming a part of chylomicrons, and molar weight of amino acids is 5. The product of factor 14.4 by 5 equals a total accumulated temperature in two active points (in armpits).

Sequence of the regulatory biochemical processes is determined by the ratio of the above said factors and ratio of molar weights of intestinal synthetases, bilirubin, and cholesterol, and determines molar weight of ethyl alcohol, as well as total accumulated temperature in five active points and pH of arterial blood [5, 18, 18, 25, 27, 28-31, 35, 38, 39].

With regard to the above mentioned, a rate of interaction of major chemical environment components [28-31], occurring in the cell membranes, at the liquid-gaseous interface (alveoles) [4, 19, 25, 38, 39] takes place with obligatory involvement of bilirubin-hemoglobin complex, ethanol, E. coli synthetase (70% of membrane of which consists of phosphatidylethanolamine), vitamins A, B<sub>1</sub> and D, as well as with involvement of universal

proteolytic regulators of cholesterol and lipid metabolism (ubiquitin-proteolytic system,  $\alpha$ -trypsin, nitrogen oxide and calcium oxide) [19, 35, 9].

This structural and functional organization of biochemical reactions provides for the body thermal regulation, being implemented in thermometrical dependency of temperature factors of five points (2 carotid, 2 auxillary and 1 abdominal) [28-31]. Temperature component of these reactions is associated with neuromediator choline- and adrenergic systems, which are primarily connected with glomus caroticus [28-31], with formation of charge-carrying interaction at the level of thyroxin and imidazole protein receptor of erythrocytes, and PPAR (Shinizky, 1968). Along with erythrocytes, PPR forms pH value of arterial blood in accordance with temperature parameters of interaction of opiate receptors ( $\alpha$ ,  $\beta$ ,  $\gamma$ ) in the choline- and adrenergic regulatory mechanisms of endogenous alcohol synthesis, determined by interaction of the metabolic processes of cholesterol, vitamins B<sub>1</sub> and D, glucose, lactic acid, ubiquitin, intestinal synthetase and  $\alpha$ 1-trypsin.

Based on data, obtained using non-invasive Hemogram Analyzer and USPIH software, 1200 persons with AA and 200 persons from control group (consuming no alcohol or small amount of alcohol) were divided into three groups taking into account correlation of temperature indicators in various points:

1. group 1 (control group, 200 people) - total sum of temperature indicators of 5 points:  $168 \leq T_{\text{sum}} \leq 173$ , total sum of temperature indicators of 3 points (carotid and abdominal):  $102 \leq T_3 \leq 105$ , the ratio between total sum of temperature indicators of carotid arteries and abdominal temperature:  $2 < T_{\text{car/abd}} \leq 2.05$ .

2. group 2 (consuming up to 500ml alcohol) - total sum of temperature indicators of 5 points more than  $174 \leq T_{\text{sum}} \leq 178$ ; total sum of temperature indicators of 3 points  $100 \leq T_3 \leq 101$ ; the ratio between total sum of temperature indicators of carotid arteries and abdominal temperature:  $1.9 \leq T_{\text{car/abd}} \leq 2.00$ .

3. group 3 (consuming more than 500-1000 ml alcohol, when admitted to hospital) - total sum of temperature indicators of 5 points more than  $175 \leq T_{\text{sum}} \leq 180$ ; total sum of temperature indicators of 3 points  $102 \leq T_3 \leq 105$ ; the ratio between total sum of temperature indicators of carotid arteries and abdominal temperature less than  $T_{\text{car/abd}} < 1.9$ .

In the control group, the ratio between accumulated temperature of 5 points and abdominal temperature has made up  $5 \pm 0.05$ , and the ratio between accumulated temperature of two carotid arteries and abdominal temperature has made up  $2 \pm 0.05$ .

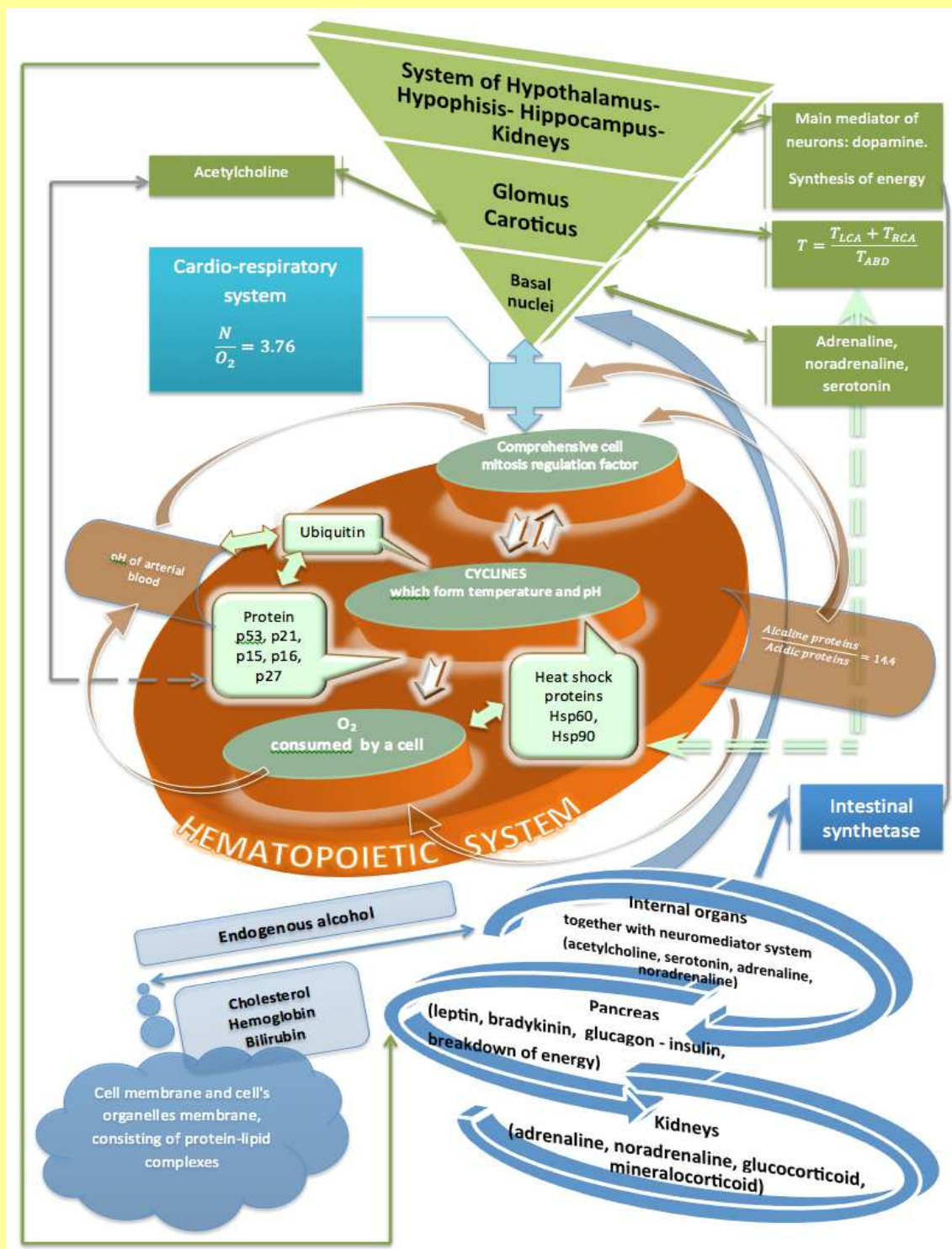
It has been proved on the volunteers, that intake of 100 g vodka causes changes in temperature of the right carotid artery in 15 minutes (increase by  $0.03^\circ\text{C}$ ), as well as decrease in temperature in the armpits by  $0.02^\circ\text{C}$  and increase in abdominal temperature by  $0.025^\circ\text{C}$ .

Accordingly, the ratio between accumulated temperature of the carotid arteries and abdominal temperature is changed ( $T_{car/abd} < 2$ ), and heart rate is elevated. by 10 heartbeats per 100 g alcohol. The said changes persist for 12-14 hours. With further alcohol consumption, abdominal temperature is increased by  $0.03^{\circ}\text{C}$ ; accordingly the ratio between accumulated temperature of the carotid arteries and abdominal temperature ( $T_{car/abd}$ ) is decreased.

As opposed to alcohol consumption, food ingestion increases temperature in the carotid arteries and abdominal region without changing the ratio between accumulated temperature of the carotid arteries and abdominal temperature ( $T_{car/abd}$ ) and heart rate. (See Table 1 and Figure 1).

Groups and temp. indicators	Ceruloplasmin, mg/dl	Transferrin g/l	$\text{pH}^* \frac{\text{pH}_a + \text{pH}_v}{\text{pH}_a - \text{pH}_v}$	Cholinesterase, mmol/l	LDH, mmol/l	Bilirubin, $\mu\text{mol/l}$	Endogenous Alcohol	Energy of peptide bond breaking
1 g - 200 ml. $\Sigma$ 168 $\pm$ 5	285.6 $\pm$ 1.16	2.5 $\pm$ 0.47	0.074 $\pm$ 0.025	307.02 $\pm$ 17.68	2.01 $\pm$ 0.17	12.08 $\pm$ 0.92	0.0260	1308.66 kJ/sec
2-group up to 500 $\Sigma$ 175.5 $\pm$ 2	439.2 $\pm$ 3.89	1.7 $\pm$ 0.61	0.082 $\pm$ 0.025	278.03 $\pm$ 21.19	2.47 $\pm$ 0.19	18.53 $\pm$ 1.49	0.0258	1302.55 kJ/sec
3 group $\geq$ 550 $\Sigma$ 178 $\pm$ 15	526.7 $\pm$ 4.77	1.4 $\pm$ 0.29	0.102 $\pm$ 0.025	229.61 $\pm$ 20.05	3.35 $\pm$ 0.27	31.06 $\pm$ 2.73	0.0256	1287.42 kJ/sec





**Figure 1.** Major Pathogenic Mechanisms of Metabolism and Hemodynamics Regulation.

Thus, obtained parameters of cerebrospinal fluid pressure by groups (1 gr -  $120 \pm 10$  mm Hg, 2 gr. -  $140 \pm 10$  mm Hg, 3 gr. -  $150 \pm 10$  mm Hg) enable to estimate pH values of arterial and venous blood, and accordingly, and accordingly arteriovenous difference by groups: 1 group- pH of arterial blood -  $7.35 \pm 0.04$ , pH of venous blood -  $7.424 \pm 0.03$ , arteriovenous difference -  $0.074 \pm 0.025$ ; 2 group - pH of arterial blood -  $7.32 \pm 0.025$ , pH of venous blood -  $7.4244 \pm 0.03$ , arteriovenous difference -  $0.082 \pm 0.025$ ; 3 group - pH of arterial blood -  $7.31 \pm 0.025$ , pH of venous blood -  $7.424 \pm 0.03$ , arteriovenous difference -  $0.102 \pm 0.02$ . (Table 1)

Important mechanisms of metabolic and hemodynamic aspects of regulation include energy processes, related to the ratio between age and weight, as well as the ratio between accumulated temperature in the carotid arteries and heart rate, and their changes per time unit. It has been established that value of arteriovenous pH difference is closely correlated with values of time intervals of QRS complex, PQ and urine specific gravity.

Quantitative indicators of basal glucose level depend on the interaction of various parameters, being defined as the ratio between product of molar weights of hemoglobin, dopamine, carnitine, atomic oxygen, sum of insulin subunits of receptors  $\alpha$  and  $\beta$  (located on the surface of membrane and transmembrane), ubiquitin and PC and product of molar weights of E.coli synthetase, glutamic acids, palmitic acid, PPAR-receptors, calatase and quantitative indicators of arteriovenous difference. Basal glucose level changes depending on the temperature indicators in five points, the ratio between temperature indicators of carotid and abdominal area, the ratio between accumulated temperature in axillary and abdominal, heart rate and respiratory rate (basal glucose levels at  $36,06^\circ\text{C}$  is  $4.09\text{mmol/l}$ ). Moreover, basal glucose level is affected by contents of cholinesterase.

Quantitative reference indicators of cholinesterase (E.Sh. Shatlina and V.V. Prikhozhan method), lactic acid, bilirubin, transferrin (by spectrophotometric method  $2.81 \pm 0.73$  g/l) and ceruloplasmin (by immunoturbometric method  $300 \pm 18$  mg/l) have been compared with quantitative data of glucose and endogenous alcohol, obtained by computational non-invasive method, using non-invasive blood formula analyzer, with further statistic analysis of correlation ratio, defined by means of Spearman's rank correlation coefficient. Spearman's rank correlation coefficient is in the range of 0.7-0.9, which indicates of high correlation ratio between the selected parameters: temperature in the left and right carotid arteries, age and weight, arteriovenous pH difference, level of cholinesterase and glucose, level of lactic acid and glucose, level of glutamic acid and  $\gamma$ -aminobutyric acid.

## Discussion and conclusions

1. General pathogenic mechanisms of formation of endogenous depressions and MS are related with the course of regulatory metabolic and hemodynamic LPO reactions. LPO reactions are related to the functioning of Glomus Caroticus and time parameters of cardiac, and regulated by the ratio between molar weights of transferrin and ceruloplasmin at the level of hepatocytes, angiotensin converting enzyme, PO and catalase, and difference of amino acids - components of gastrin and secretin (which is 14, since gastrin comprises 27 amino acids, and secretin consists of 13 amino acids), and factors 14.4 and 4.75 (ratio between molar weights of ubiquitin and leptin). These reactions result in temperature indicators in carotid arteries and abdominal region (sum of which makes up 102.36°C), pH of arterial blood (7.326) and pH of venous blood (7.351). Arteriovenous difference determines volume of endogenous alcohol (0.026).
2. Volume of endogenous alcohol is inversely related with energy of peptide bond breaking (1308 kJ/sec) and molar weight of lactic acid through the synthesis of leu-enkephalins (molar weight 554 mmol/l). Synthesis of methionine-enkephalins (molar weight 572 mmol/l) is determined by the same processes, but activity of synthesis is regulated by the ratio between molar weight of leptin and molar weight of ubiquitin and is related with amount of cholinesterase, atomic oxygen and the ratio between molar weight of glucose and molar weight of adrenaline. In its turn, the ratio between difference of molar weights of methionine- and leu-enkephalins with molar weight of glucose and volume of cholinesterase, leptin and ubiquitin determines activity of lactic dehydrogenases and oxygenases in the hemoglobin-bilirubin reaction at the level of PPAR-receptors and PO, as well as quantitative indicators of glucose level.
3. Reactions of atomic oxygen generation are important link in the PLO regulatory metabolic reactions and formation of time parameters of cardiac. Process of atomic oxygen production is regulated by the following interaction: the ratio between molar weights of  $\gamma$ -aminobutyric acid, transferrin, palmitic acid, carnitine with difference of molar weights of methionine- and leu-enkephalins and product of molar weight of ceruloplasmin, amount of amino acids and difference of molar weights of palmitic acid and carnitine. By affecting structure and molar weights of contractile proteins of the cell membranes and glycophorin (structural protein of an erythrocyte membrane), atomic oxygen determines necessary energy for breaking of chemical element bonds (H, C, O, NO, NH, N). Energy value is regulated by molar weight of catalase, pH of arterial blood, the ratio between molar weights of ubiquitin and leptin and factor 2.03 (the ratio of temperature indicators of carotid arteries to abdominal region temperature). This ratio is also related with thermal and temporal factors of interaction of LPO and PO, arteriovenous

pH difference, the ratio between molar weight of acetylcholine and pH of venous blood and molar weight of glutamic acid, factor 153.2, which is equal to molar weight of dopamine.

4. Initial mechanisms of somatogenic depressions, MS and encephalopathy pathogenesis are time relationship between bradykinin and acetylcholine, dopamine and serotonin, based on functioning of Glomus Caroticus. Glomus Caroticus functioning determines temperature indicators in five points, functions of surface cutaneous, muscle and PPAR receptors. Receptors are located in the cell membranes and intracellular compartment. They function synchronously with palmitin-carnitine complexes, signal temperature G-proteins, receptors of transforming growth factor (TGFB) and bone morphogenetic protein (BMP2). TGFB and BMP2 determine growth and growth inhibition of sympathetic neurons through photoreceptor molecule of retinol (286.5 g/mol), associated with metabolism of vitamins B1 and D (265.4 g/mol, 397.5 g/mol). Metabolism of vitamins determines thermal dependent function of  $\alpha$ - and  $\beta$ -adrenoreceptors with cholinoreceptors, included in their structure. Cholinoreceptors and  $\alpha$ - and  $\beta$ -adrenoreceptors are associated with calcium metabolism (calnexin, 88 kDa), calreticulin (46 kDa) and calmodulin (16.4 kDa). They combine regulatory mechanisms in one single structural and functional system by the course of LPO at the level of PPAR-receptors, related with temporal parameters of cardiac cycle.

5. MS and encephalopathy pathogenesis in AA is related with the course of reductive-oxidative proton-dependent proteolytic biochemical processes, occurring at the level of receptors of erythrocytes, monocytes, and lymphocytes, as well as in the extra cellular fluid compartment. Proton mechanisms determine time of acetylcholine hydrolysis and cholinesterase activity. Cholinesterase activity is associated with interaction reactions of serotonin, adrenaline and bradykinin. These reactions, occurring at the organ level, are related with functional activity of the brain, metabolism of regulatory neuropeptides and enkephalines, determining clinical syndromes, behavior, and emotions through regulatory functions of hypothalamo-pituitary-hippocampal-renal systems.

6. Pathogenic mechanisms of formation of clinical syndromes in MS and alcohol withdrawal in AA are related with disorders in biologic laws of cellular compartmentalization of the functions based on the phenomenon of targeted delivery of informational molecules to the cell membranes and organelles. Targeted delivery is based on the interaction mechanism of acidic and basic amino acids, thyrotrophin-releasing factor (TRF), growth hormones and transforming growth factor, gastrointestinal hormones, participating in the transmission of external signals through the cell membrane structures with the involvement of dopamine, NF- $\kappa$ B, specialized proteins rhodopsin and retinol, vitamins B1 and D, determining location of arginine in the 117th location of 7th chromosome and location of glutamic acid in the 292nd

position of 14th chromosome with formation of relevant pH values of arterial and venous blood, volume of endogenous alcohol and serotonin-dopamine and dopamine-noradrenalin interaction in the regulatory system of LPO reactions, related with PPAR function and insulin receptors by means of accumulated temperature indicator in five biologically active points.

7. Proton mechanism of formation of time parameters of cardiac, clinical syndromes of depressions and encephalopathies is associated with degenerative changes of nervous system, which are determined by disorders in the regulatory processes of formation of pH values of arterial and venous blood. Interaction of ATP and iodineperoxidase at the level of molar weights of TTF, photoperceptive protein - retinol, PO, mannose-6-phosphate, serotonin and dopamine, glucose, and TTPH is related with amount of endogenous alcohol, energy of peptide bond breaking, arteriovenous pH difference of the blood, correlating with temporal parameters of the QRS complex. In the somatogeny-psychogeny context, manifestation rate of clinical symptoms depends of the regulation of neuropeptides and enkephalines. The latter are related with activity of angiotensin converting enzyme, determined by arteriovenous pH difference, amount of endogenous alcohol, and the ratio between molar weight of glucose and molar weight of dopamine. Angiotensin converting enzyme and time relations between bradykinin and acetylcholine are the major ones in the formation of urine specific gravity, blood pressure, and greater lesser and circulation time, determining synthesis of enkephalines and dopamine.

### Statement on ethical issues

Research involving people and/or animals is in full compliance with current national and international ethical standards.

### Author contributions

A.M., N.M. and A.P. developed the concept, prepared the manuscript, analyzed the data and drafted the manuscript. All authors read and met the ICMJE criteria for authorship. All authors read and approved the final manuscript.

### Conflict of interest

None declared.

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