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PSYCHOPHYSIOLOGICAL CHARACTERISTICS OF THE HEALTH STATUS OF INDIVIDUALS WITH CHRONIC HEPATOPATHIES

165.01. HUMAN AND ANIMAL PHYSIOLOGY

Summary of the doctoral thesis in biological sciences

CHIȘINĂU, 2025

The thesis was developed within the Institute of Physiology and Sanocreatology of the Moldova State University, the Gastroenterology Laboratory of the "Nicolae Testemițanu" State University of Medicine and Pharmacy, Doctoral School of Natural Sciences, Moldova State University.

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The defense will take place on July 1, 2025, at 2 PM, during the Meeting of the Public Defense Committee of the Doctoral Thesis within the Doctoral School of Natural Sciences, MSU. Headquarters – Moldova State University (http://www.usm.md), 65A M. Kogâlniceanu str., block 3, room 332, MD-2009, Chisinau, Republic of Moldova.

The doctoral thesis and the abstract can be consulted at the National Library of the Republic of Moldova, the Central Library of the State University of Moldova (MD 2009, Chisinau, Alexei Mateevici 60), on the ANACEC website (http://www.anacec.md) and on the MSU website (http://www.usm.md).

The abstract was sent on "____"_____ 2025

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GENERAL CHARACTERISTICS OF THE WORK

Relevance of the study. The study of human health remains one of the priority tasks of modern physiology, psychology, sanocreatology, and medicine. Information stress, the psychologically traumatic rhythm of life, and the global problems of the modern world have a negative impact on society, causing dissonogenic emotions and exacerbating human health problems.

In recent years, serious attention has been paid to the mental sphere, especially human mental health. However, most scientific work in this area focuses on the study of psychopathology, whereas mental health rarely becomes the subject of fundamental and clinical research [1].

Somatic diseases, including chronic hepatopathies (CHPs), are often accompanied by mental health disorders. The interrelation between mental and somatic spheres presents a complex and insufficiently studied problem of modern medicine. CHPs are characterized by a wide range of extrahepatic manifestations, including psycho-emotional disorders, which require special attention in the diagnosis and clinical correction of the disease [3].

In turn, CHPs represent one of the most pressing issues in modern medicine. Since the second half of the 20th century, there has been a steady global increase in the prevalence of liver diseases, which in recent decades has taken on the form of a pandemic. According to the World Health Organization (WHO), every 12th person in the world lives with chronic viral hepatitis. At the same time, CHPs caused by metabolic disorders and obesity, leading to the development of fatty liver disease, are coming to the forefront, deteriorating the quality of life of patients and contributing to the chronic nature of hepatic processes, influencing the progression of the disease with the potential formation of liver cirrhosis. Liver pathology is one of the leading causes of mortality worldwide, with approximately 1.4 million people dying annually due to acute viral infection, liver failure, cirrhosis, and liver cancer [3, 4].

Since the end of the 20th century, the Republic of Moldova has ranked high in European statistics for chronic liver pathology incidence. For several decades, the country has consistently been among the top ten countries in the world for mortality from liver diseases [5]. In recent decades, liver diseases have ranked third among the causes of adult mortality in Moldova [6]. Thus, CHPs are among the most serious and urgent medical-social problems of our time.

Despite significant progress in studying chronic hepatopathies (their etiology, immunopathogenesis, methods of diagnosis, prevention, pathogenetic and etiological therapy), the problem of effective management of patients with CHPs remains unresolved. Although a review of bibliographic sources from recent decades shows an increase in publications dedicated to the relationship between psychophysiological functioning and somatic manifestations in various chronic pathologies, many authors have noted in their studies that mental health disorders are common and significant issues for most individuals with chronic liver diseases, affecting both the patient and their close environment [7, 8, 9].

There is also a high frequency of mental health deviations amid somatic manifestations in patients with chronic liver pathology. Researchers believe that the awareness of one’s illness leads to changes in various aspects of patients’ lives, accompanied by disruptions in habitual social behavior [10, 11, 12]. Many researchers report that a diagnosis of "chronic liver disease" strongly influences an individual's social functioning. Stigmatization by family, friends, employers, and society at large contributes to social isolation and reduced intimacy in relationships. Stigma, perceived as discrimination, hinders adaptation to the diagnosis and can be a cause of anxiety and depression in people with CHPs [10, 11, 13].

At the same time, specialists often fail to give due attention to timely assessment of the mental state of individuals with chronic liver pathology. According to bibliographic data, a very limited number of studies have been conducted in the Republic of Moldova on the mental health and quality of life of patients with CHPs [2, 14, 15]. Hence, there is a pressing need to study mental health in order to identify the psychophysiological features of individuals with chronic liver

diseases, as these may change due to direct neurotoxic effects of hepatotropic viruses, metabolic factors [3], chronic stress, and psychosocial influences such as awareness of disease severity and stigmatization [10, 11]. Treatment effectiveness largely depends on identifying individual characteristics and selecting a personalized approach for timely compensation and correction of mental disorders [10, 16].

One of the causes of psychophysiological dysfunctions in chronic hepatopathies may be an imbalance in the spectrum of neurotransmitter amino acids, which regulate all key nervous processes: excitation and inhibition, alertness and sleep, aggression and anxiety, synaptic plasticity, emotions, behavior, memory, somato-vegetative functions, and more. Currently, the role of neurotransmitter amino acids in regulating central nervous system functions, particularly behavioral reactions, emotions, memory, and others, is considered indisputable [17, 18].

Amino acids are the building blocks of proteins and essential substrates for synthesizing many low-molecular-weight and psycho-functional substances with significant physiological importance for the body [19]. Physiological concentrations of amino acids and their metabolites are necessary for maintaining vital bodily functions. An imbalance in their levels is one of the causes of pathological processes that disrupt the nervous, adaptive, emotional, and cognitive systems, contributing to the development of neurological and psychiatric disorders, oxidative stress, and more. An optimal amino acid balance, both in diet and blood serum, is crucial for maintaining overall homeostasis [20]. Considering the liver's central role in amino acid metabolism, individuals with chronic liver disease exhibit imbalances in amino acid concentrations in bodily fluids and tissues [21]. A correlation has been noted between serum levels of essential amino acids and affective changes in patients [22]. Additionally, amino acid metabolism disturbances are believed to trigger depression, and abnormalities in their metabolism in the brain have been linked to increased vulnerability to stress [23].

Thus, it can be concluded that CHPs represent a significant pathology globally and in Moldova. Changes in mental health are frequently associated with liver pathology and form an integral part of the clinical picture of chronic liver diseases. To enhance treatment effectiveness and improve the psychological and social adaptation of patients with CHPs, it is essential to thoroughly study the causes and psychophysiological characteristics of this group's health status.

Theoretical Justification, Objective, Tasks, and Hypothesis of the Research

Based on the theoretical premises drawn from the literature review on the physiopathological and psychosomatic changes in individuals with CHPs, including those caused by chronic viral infection and lipid metabolism disorders, the objective, tasks, and research hypothesis were formulated.

The purpose of the work: to identify the psychophysiological characteristics of the health status of individuals with chronic hepatopathies and to clarify the influence of liver pathology on their psychophysiological state.

Objectives:

1. To establish the specifics of the physiological status in individuals with mild forms of chronic hepatopathies using clinical, laboratory, and instrumental methods; to characterise clinical and paraclinical findings, serological markers of viral hepatitis, serum metabolism of free amino acids, Kerdo autonomic index, and indicators of protein, carbohydrate, and lipid metabolism;
2. To determine parameters that characterize the quality of life of individuals with chronic hepatopathies;
3. To identify the most typical indicators of psychological dissonance in individuals with mild forms of chronic hepatopathies;
4. To study biochemical indicators and the spectrum of free amino acids, including neurotransmitter and other metabolites, in individuals with chronic hepatopathies;

5. To conduct a correlation analysis of emotional and asthenic components and quality of life indicators with biochemical data and serum amino acid concentrations in individuals with chronic hepatopathies;

6. To develop a method for collecting information on psycho-emotional status and a set of psychometric tests that improve the diagnosis of psychophysiological conditions in individuals with chronic hepatopathies.

Research Hypothesis:

Psychophysiological characteristics of the health status of individuals with chronic hepatopathies are determined by a complex of physiological, biochemical (including the concentration of free amino acids in the blood serum), clinical and some indicators of the psychoemotional sphere.

Scientific Novelty of the Study:

For the first time, it was demonstrated that psychophysiological impairments in the health status of individuals with chronic hepatopathies are driven by the diagnosis semantics, imbalances in free amino acids, lipid and carbohydrate metabolism disorders, all of which determine the deterioration of overall health throughout the disease. New data were obtained on the changes in the spectrum and quantitative content of neurotransmitter amino acids in individuals with chronic HBV infection and fatty liver disease associated with metabolic dysfunctions. An original contribution includes the correlation analysis between emotional indicators and quality of life (QoL) with physiological, metabolic disturbances and serum amino acid content in individuals with chronic hepatopathies. A new integrative perspective was established on the interconnection of psychophysiological, metabolic, and somatic factors in health status, which can be utilized both in daily medical practice and in expanding scientific research in this field.

The results obtained by the author contribute to the solution of an important scientific problem:

Revealing physiological and psychoemotional interrelationships in people with chronic liver diseases caused by viral and metabolic etiology, using physiological, psychometric, biochemical, clinical and routine paraclinical methods in order to determine specific characteristics for these pathologies.

Fundamentally New Results for Science and Practice:

Previously unknown positive correlations were identified between asthenia indicators and the Kerdo autonomic index (KAI), and negative correlations between depression levels and KAI, between asthenia and levels of albumin and urea in individuals with chronic hepatitis B virus (HBV) infection. Additionally, a positive correlation was observed between body mass index (BMI) and indicators of asthenia, disruptions in carbohydrate and lipid metabolism, and a negative correlation between physical quality of life and markers of carbohydrate and lipid metabolism, components of quality of life, and elevated levels of neurotransmitter amino acids in individuals with fatty liver disease associated with metabolic dysfunctions.

Theoretical Significance of the Study:

The findings deepen and broaden scientific understanding of the body's dissonogenic responses in chronic hepatopathies, of the psychophysiological characteristics of health status from the standpoint of a new perspective on the relationships between the central nervous system (CNS) and liver, the impact of chronic hepatopathies on quality of life, and the correlations between metabolic parameters, concentrations of inhibitory and excitatory neurotransmitter amino acids, and psychophysiological status in individuals with chronic liver diseases.

Practical Significance:

An indigenous specialized questionnaire was developed, tested, and implemented for forming control groups in scientific studies in gastroenterology, hepatology, and internal medicine. This can be used for further research in the field. A diagnostic method for assessing mental health in people with chronic hepatopathies was created and applied, including a set of psychometric

tests. Psychophysiological characteristics of the body's response to chronic stress were identified, which may serve as the basis for future strategies to improve the QoL of people with CHPs. Models of psychophysiometabolomic phenotypes in patients with various forms of CHPs were developed, which can be applied for differential diagnosis, educational purposes for students and professionals, and personalized approaches to management.

Implementation of Scientific Results:

The results were implemented into scientific-practical and didactic activities within the "Gastroenterology" course of the Department of Internal Medicine, Faculty of Medicine No. 1 at the Nicolae Testemitanu State University of Medicine and Pharmacy. Achievements include: 5 authorship certificates, 6 innovation certificates, and 1 act of innovation implementation.

Author's Personal Contribution:

The dissertation is based on research into the psychophysiological characteristics of the physiological and psycho-emotional health of individuals with chronic hepatopathies. Studies were conducted by the author from 2019 to 2023. Together with Academician T. Furdui, Professor V.-T. Dumbrava and Associate Professor Iu. Lupasco, the scientific problem, objectives, tasks, and hypothesis were formulated. An indigenous questionnaire for assessing health in control group participants was developed and implemented; a complex psychological assessment method for participants was created and applied; research groups were formed; methodology and study design were developed. The author conducted psychometric testing, measured physiological parameters, performed statistical analysis and correlation of results, interpreted findings, and formulated general conclusions and practical recommendations.

Work Approbation.

The main provisions and results of the research were repeatedly discussed at meetings of the Gastroenterology Laboratory of the Nicolae Testemitanu State University of Medicine and Pharmacy. The dissertation materials were presented at the following international conferences: Meeting of the Romanian Society of Neurogastroenterology (Romania, Iași, 2019), "26th Russian Gastroenterological Week" (Russia, Moscow, 2020); at national scientific conferences with international participation: "Integrare prin cercetare și inovare" (Chișinău: 2020, 2022, 2023), "Natural Sciences in the Dialogue of Generations", National Conference with International Participation, Edition VI (Chișinău, 2023), "Natural Sciences in the Dialogue of Generations", National Conference with International Participation, Edition VII (Chișinău, 2024), 8th Congress of Physiologists of the Republic of Moldova with International Participation "Fiziologia şi sănătatea" (Chișinău, 2024); at national conferences: Scientific-practical online conference "Chronic Hepatic and Pancreatic Diseases: Nutritional and Surgical Aspects", 2020 Edition (Chișinău, 2020), National Scientific Doctoral Conference "Contemporary Research and Evaluation Methodologies" (Chișinău, 2021), Annual Scientific Conference "Research in Biomedicine and Health: Quality, Excellence, and Performance" (Chișinău, 2021), Multidisciplinary scientific-practical online conference "Chronic Hepatic and Pancreatic Diseases: Nutritional, Psychosomatic and Ethical Aspects" (Chișinău, 2021), Scientific-practical conference "Concepts in Gastroenterology: Aspects of Chronic Hepatobiliary, Pancreatic, Nutritional, and Psychosomatic Pathologies" (Rezina, 2022), Scientific-practical conference "Gastroenterological Discourse: Aspects of Chronic Hepatobiliary, Pancreatic, Nutritional, and Psychosomatic Pathologies" (Soroca, 2022), Scientific-practical online conference "Chronic Hepatic and Pancreatic Diseases: Nutritional and Multidisciplinary Aspects", 2022 Edition (Chișinău, 2022), National Conference "Health and the Phenomenon of Antimicrobial Resistance in Low- and Middle-Income Countries in Eastern Europe" (Chișinău, 2024).

Publications Related to the Dissertation Topic

A total of 22 scientific and methodological works were published on the topic of the dissertation (including 4 without co-authors): articles in scientific journals indexed in Web of Science – 2, articles in journals from the National Register of Profiled Journals – 5, publications

in proceedings of international scientific conferences – 1, publications in national scientific conferences with international participation – 5, articles in national scientific conference proceedings – 2, abstracts in scientific journals indexed in SCOPUS – 3, co-author of 3 specialty books; author's certificates (issued by AGEPI) – 5, innovation certificates – 6, innovation implementation act – 3.

Volume and Structure of the Dissertation:

The dissertation is presented on 118 pages of main text, which includes: an introduction, 4 chapters, general conclusions and practical recommendations, an abstract (in Russian, Romanian, and English), and 6 appendices. The dissertation contains 7 tables, 46 figures, and a bibliography of 279 sources.

Keywords: chronic hepatopathies, chronic HBV viral infection, fatty liver disease associated with metabolic dysfunctions, psychophysiological characteristics, depression, anxiety, asthenia, amino acids.

CONTENT OF THE DISSERTATION

Introduction

The introduction highlights the relevance of the problem, as well as the scientific and practical significance of studying the psychophysiological characteristics of health in people with CHPs. It outlines the objectives, tasks, hypothesis, and defense propositions, indicates the scientific novelty, and describes the theoretical and practical significance of the study, the author's contribution, implementation, and approbation of the work.

1. THE PROBLEM OF MENTAL AND PHYSIOLOGICAL CHARACTERISTICS OF HEALTH IN INDIVIDUALS WITH CHRONIC HEPATOPATHIES AS A SUBJECT OF SCIENTIFIC ANALYSIS IN MODERN LITERATURE

This chapter contains a summarized analysis of modern scientific publications and synthesizes accumulated knowledge in the fields of mental and physiological health research, chronic liver diseases, studies on amino acid content indicators and their significance for mental health diagnostics and chronic liver pathology, as well as the peculiarities of comorbidity between CHPs and mental health disorders.

2. MATERIALS AND RESEARCH METHODS

The chapter presents the concept and design of the study, as well as a detailed description of each of the four stages aimed at proving the existence of certain psychophysiological traits in individuals with CHPs and determining the impact of liver pathology on their psychophysiological condition. The research subjects were adults who visited a gastroenterologist-hepatologist in outpatient or inpatient settings. A total of 59 individuals aged 18 to 75 with CHPs were examined. A control group (CG) of 26 practically healthy adults was also formed to determine the degree of influence of CHPs on the studied parameters. The liver pathology diagnosis was established jointly with a gastroenterologist-hepatologist. Inclusion and exclusion criteria were determined. All participants provided written informed consent.

Diagnosis of CHPs was performed using classical clinical and paraclinical methods. For comparative research, the participants were divided into 2 groups based on the etiological factor: Group I: 34 adults with chronic HBV infection (CHVI-HBV), without signs of active chronic hepatitis: serological tests (HBsAg and HBeAg negative, anti-HBc positive, anti-HBs and anti-HBe positive or negative); undetectable or low levels of viremia (HBV DNA < 2000 IU/mL); normal bilirubin levels, alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT) within normal limits, absence of hepatic steatosis on ultrasound; Group II: 25 individuals with steatotic liver disease associated with metabolic dysfunctions (SLDAMD): serological tests negative for HBsAg, HBeAg, anti-HBc, and anti-HBe; anti-HBs negative or positive post-vaccination; undetectable HBV DNA; total cholesterol, LDL, triglycerides normal or elevated; HDL decreased or normal; serum glucose elevated or normal; ultrasound signs of hepatic steatosis.

Research Methodology

For all study participants, clinical and physiological parameters were recorded, including age, sex, body weight (BW), height, pulse rate (PR), systolic (SBP) and diastolic (DBP) blood pressure. Based on these data, the Body Mass Index (BMI) and Kerdo's autonomic index (KAI) were calculated [24, 25].

Assessment of mental health included evaluations of health-related quality of life (QoL), levels of anxiety, depression, and asthenia. Several validated psychometric instruments were employed: 1) Quality of life: The SF-36 questionnaire was used [26], which includes 8 subscales – PF (Physical functioning), RF-P (Role-physical functioning), BP (Bodily pain), GH (General health), VT Vitality), SF (Social functioning), RF-E (Role-emotional functioning), MH-2 (Mental health 2) – and 2 summary indices: Physical Health (PH) and Mental Health (MH) [12]. This tool has been previously validated in Moldova, Romania, and Russia [27, 28, 29]. 2) Depression and Anxiety: The Zung Self-Rating Depression Scale (SDS) and the Zung Self-Rating Anxiety Scale (SAS) were applied [30, 31]. Both are recommended tools for assessing depression and anxiety levels in the Republic of Moldova [32, 33]. 3) Asthenia: The Multidimensional Fatigue Inventory (MFI-20) was used to evaluate five subscales of fatigue: general fatigue (GF), physical fatigue (PFat), reduced motivation (RM), reduced activity (RA), and mental fatigue (MF). The tool has demonstrated good validity and reliability [34]. All tests were available in both Romanian and Russian languages, with the language selected according to the participant's preference.

To identify metabolic disorders, levels of certain inhibitory (glycine, taurine, gamma-aminobutyric acid (GABA)) and excitatory (glutamic acid, aspartic acid, and tryptophan) neurotransmitter amino acids were measured. The ratio of inhibitory to excitatory neurotransmitters was calculated, along with levels of ornithine, urea, and ammonia in serum. The analysis of free amino acids in blood serum was performed using ion-exchange liquid chromatography [35].

To confirm diagnoses and identify syndromes typical of CHPs in patients with liver pathology, biochemical analysis results were assessed, including indicators of cytolysis (ALAT, ASAT), cholestasis (bilirubin and its fractions, alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGTP)), hepatodepressive syndrome, protein (total protein, albumin, prothrombin index by Quick), carbohydrate (glucose), and lipid metabolism (total cholesterol, HDL, LDL, non-HDL cholesterol, atherogenic index (AI), and triglycerides). For detecting viral hepatitis markers (HBV, HCV, HDV), ELISA tests with specialized equipment were used. HBV/HCV/HDV DNA or RNA was assessed qualitatively/quantitatively using PCR (the polymerase chain reaction**)**. SLDAMD was diagnosed by ultrasound.

Reliability of Research Results and Conclusions was based on fundamental principles of psychological and laboratory research methodology. Quantitative analysis of data included various statistical criteria, particularly the Student's *t*-test, Mann-Whitney *U* test, Pearson and Spearman correlation coefficients. Statistical analysis was conducted using built-in functions and the Data Analysis tool in Excel 365.

3. PSYCHOPHYSIOLOGICAL CHARACTERISTICS OF HEALTH IN INDIVIDUALS WITH CHRONIC HEPATOPATHIES

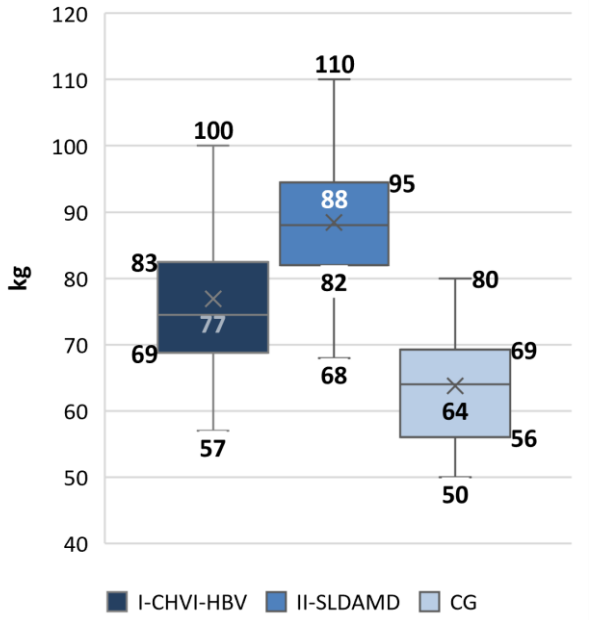
3.1. Characteristics of the Physiological Status in Individuals with Chronic Hepatopathies

In the studied groups, the gender and age distribution was as follows: in Group I (34 individuals), males accounted for 44.1 % and females 55.9 %, with an average age of 48.5 ± 2.3 years; in Group II (25 individuals), males accounted for 64 %, females 36 %, and the average age was 49.9 ± 3.4 years; the Control Group (CG) (26 individuals) consisted of 26.9 % males and 73.1 % females, with an average age of 38.03 ± 2.04 years.

The highest average height was observed in Group II at 1.75 ± 0.02 m, which was statistically significantly higher than Group I (1.70 ± 0.02 m; p(I/II)<0.05) and the CG (1.66 ± 0.01 m; p(II/CG)<0.01).

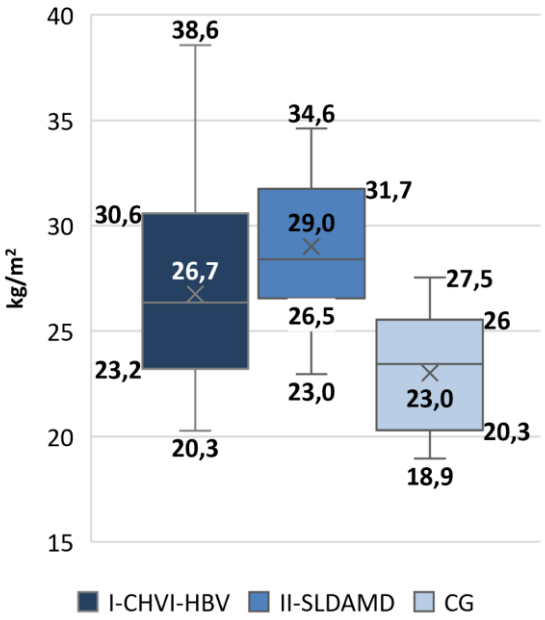
It was found that individuals with chronic pancreatitis (CP) had an average body weight (BW) of 81.79 ± 1.7 kg. The highest BW (Figure 3.1) was observed in individuals with SLDAMD – 88.44 ± 1.89 kg. In the group with chronic HBV infection, the BW was lower – 76.91 ± 2.27 kg (p(I/II) < 0.001), and in the control group – 63.79 ± 1.79 kg (p(I/CG) < 0.001; p(II/CG) < 0.001).

The body mass index (BMI) in CP was 27.71 ± 0.54. The highest BMI values (Figure 3.2) were also found in individuals with SLDAMD – 29.02 ± 0.64. In the group with chronic HBV infection, this indicator was significantly lower – 26.75 ± 0.78 (p(I/II) < 0.01), and the lowest values were recorded in the CG – 23.01 ± 0.56, with the differences statistically significant compared to both the first and second groups (p(I/CG) < 0.001; p(II/CG) < 0.001).



p(I/II)< 0,001; p(I/CG) < 0,001; P(II/CG)< 0,001

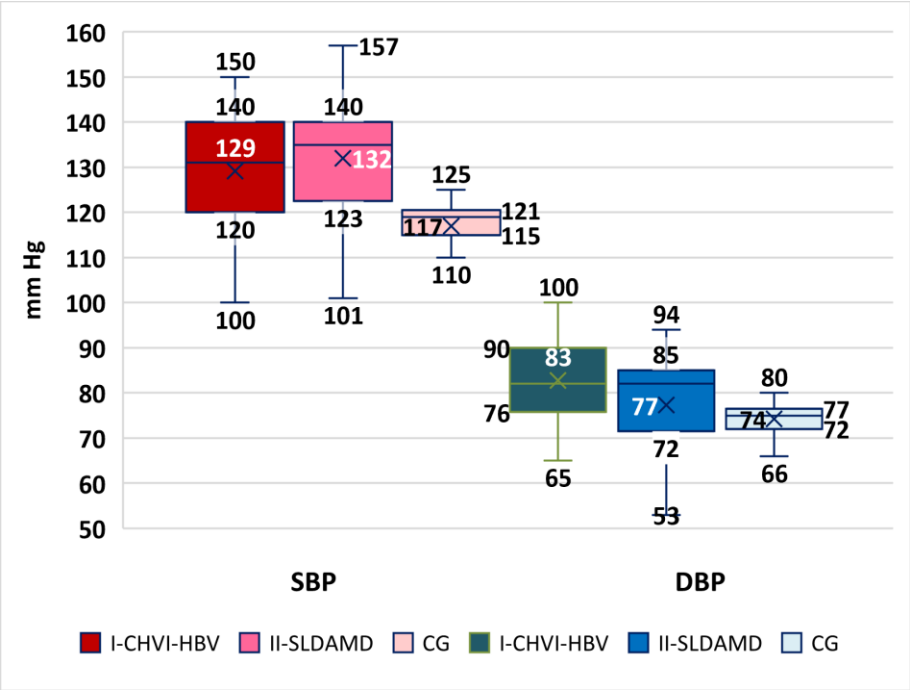
Figure 3.1. Body weight values in the study groups



P(I/II)< 0,01; P(I/CG) < 0,001; P(II/CG)< 0,001

Figure 3.2. Body mass index values in the study groups

The highest systolic blood pressure (SBP) values (Figure 3.3) were also observed in the group with SLDAMD, where the mean value was 131.96 ± 2.42 mmHg. In individuals with chronic HBV infection, the mean SBP was slightly lower – 129.12 ± 2.37 mmHg (p(I/II) > 0.05). In the CG, this value was significantly lower – 116.92 ± 1.44 mmHg (p(I/CG) < 0.001; p(II/CG) < 0.001). The highest diastolic blood pressure (DBP) values were also observed in Group I, where the mean was 82.66 ± 1.66 mmHg. In Group II, it was 77.28 ± 2.38 mmHg (p(I/II) > 0.05). In the control group, the value was significantly lower – 74.23 ± 1.05 mmHg (p(I/CG) < 0.001; p(II/CG) < 0.001).

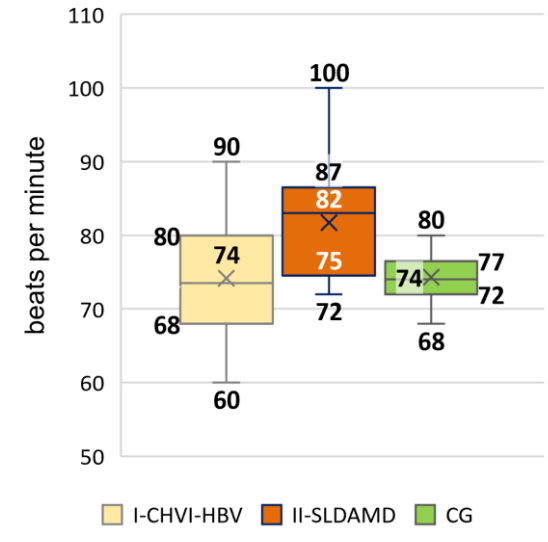


SBP:
P(I/II)> 0,05;
P(I/CG)< 0,001;
P(II/CG)< 0,001

DBP:
P(I/II)> 0,05;
P(I/CG)< 0,001;
P(II/CG)< 0,001

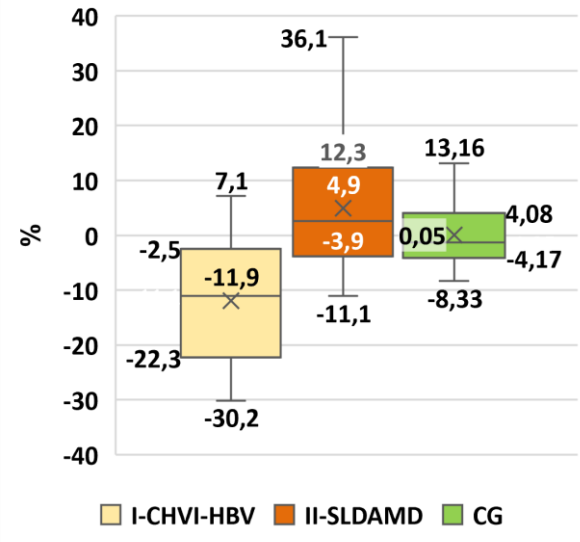
Figure 3.3 Systolic (SBP) and diastolic (DBP) blood pressure values in the study groups

Pulse rate values (Figure 3.4) were highest in Group II: 81.7 ± 1.7 beats per minute, which was significantly higher than in Group I and the control group, where this parameter was 74.2 ± 1.3 and 74.3 ± 0.9 beats per minute respectively (p(I/II) < 0.001; p(I/CG) > 0.05; p(II/CG) < 0.001). When analysing the results for the KAI (Figure 3.5), it should be noted that vagotonia predominated among subjects with HBV infection: the mean KAI was (-11.93) ± 1.87 % In individuals with SLDAMD and in the control group, normotonia was observed, with values of 4.93 ± 2.52 % and 0.05 ± 1.04 % respectively (p(I/II) < 0.01; p(I/CG) < 0.01; p(II/CG) > 0.05).



p(I/II)< 0,001; p(I/CG)> 0,05; p(II/CG)< 0,001

Figure 3.4 Pulse rate values in the study groups



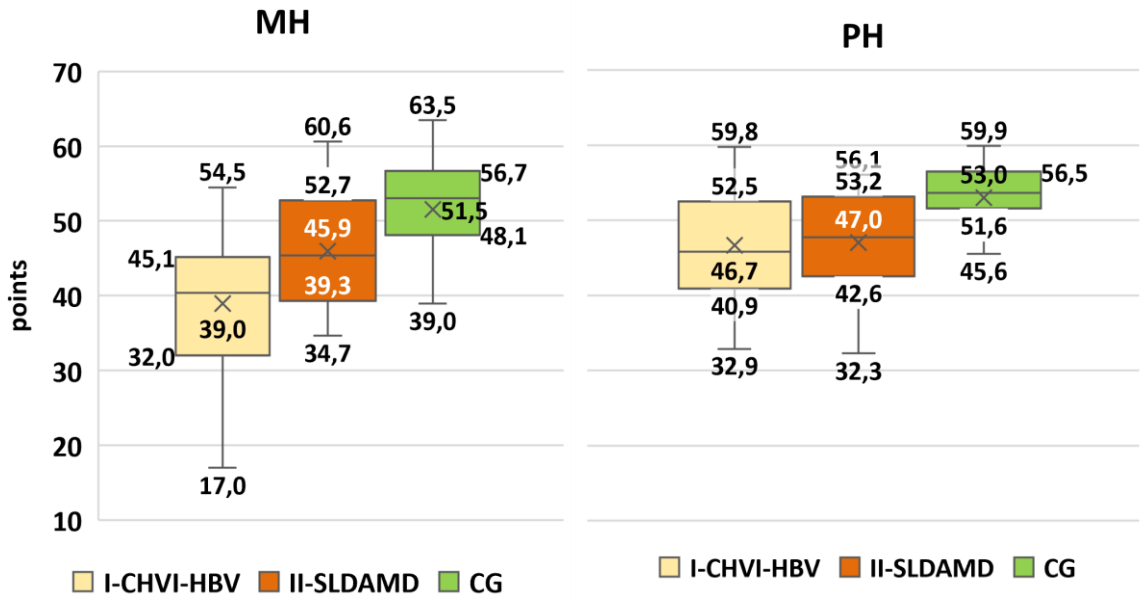
p(I/II)< 0,01; p(I/CG) < 0,01; p(II/CG)> 0,05

Figure 3.5 Kerdo's autonomic index (KAI) in the study groups

Thus, in the assessment of physiological status, it was found that the highest average values for body weight, BMI, systolic blood pressure, and pulse rate were observed in individuals with SLDAMD. Furthermore, vagotonia predominated in those with chronic HBV infection, while a tendency towards sympathicotonia was identified in individuals with SLDAMD

3.2. Mental Health Characteristics in Individuals with Chronic Hepatopathies Quality of Life in Individuals with Chronic Hepatopathies.

Analysis of QoL diagnostic results (Figure 3.6) revealed a decline across all QoL components in individuals with CHPs, particularly within the Mental Health (MH) component, with an average score of 41.91 ± 1.19 points. The Physical Health (PH) component averaged 46.83 ± 0.9 points.



p(I/II)< 0,01; p(I/CG) < 0,01; p(II/CG)< 0,01 p(I/II)> 0,05; p(I/CG) < 0,01; p(II/CG)< 0,01

Figure 3.6 Results of assessing the physical (PH) and mental (MH) components of quality of life in the study groups

The lowest mean values for both components of quality of life (QoL) were observed in Group I, with PH at 46.69 ± 1.22 points and MH at 38.97 ± 1.56 points. In Group II, these values were 47.02 ± 1.37 and 45.91 ± 1.55 points respectively. In the control group, the mean PH was 53.01 ± 0.91 and MH – 51.51 ± 1.50 points. The significance of differences for PH was: p(I/II) > 0.05; p(I/CG) < 0.01; p(II/CG) < 0.01, and for MH: p(I/II) < 0.01; p(I/CG) < 0.01; p(II/CG) < 0.01.

When analysing subscale results (Figure 3.7), a consistent trend towards lower values across all parameters in Group I was noted. The lowest scores were recorded for the RF-E subscale (part of the MH component of QoL): 37.25 ± 4.83 points in Group I, 66.67 ± 7.45 in Group II, and 93.59 ± 3.71 points in the control group (p(I/II) < 0.01; p(I/CG) < 0.01; p(II/CG) < 0.01).

The PH component subscales showed less pronounced declines (Figure 3.7). The greatest reduction was observed in the RF-P subscale, with values of 52.94 ± 5.76 points in Group I, 68.00 ± 5.69 in Group II, and 89.42 ± 3.45 points in the control group (p(I/II) < 0.05; p(I/CG) < 0.01; p(II/CG) < 0.01). Both CP groups showed a marked decrease in the GH subscale: 52.32 ± 2.84 in Group I and 53.88 ± 3.50 points in Group II, while in the control group the value was 70.54 ± 3.05 points (p(I/CG) < 0.01; p(II/CG) < 0.01).

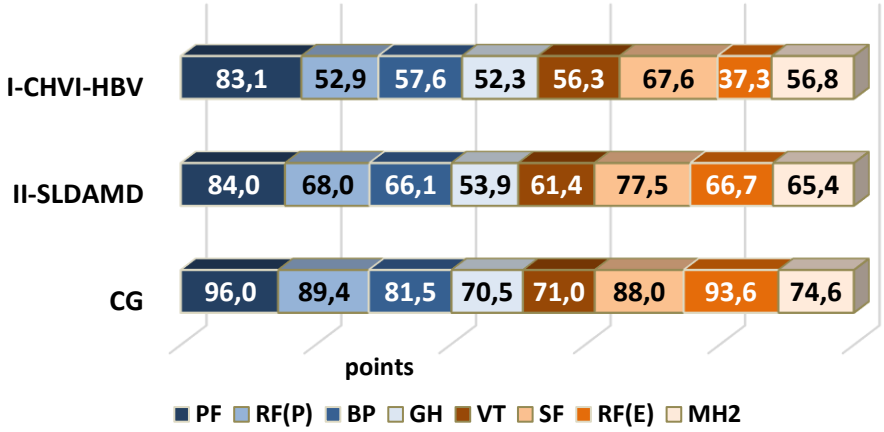


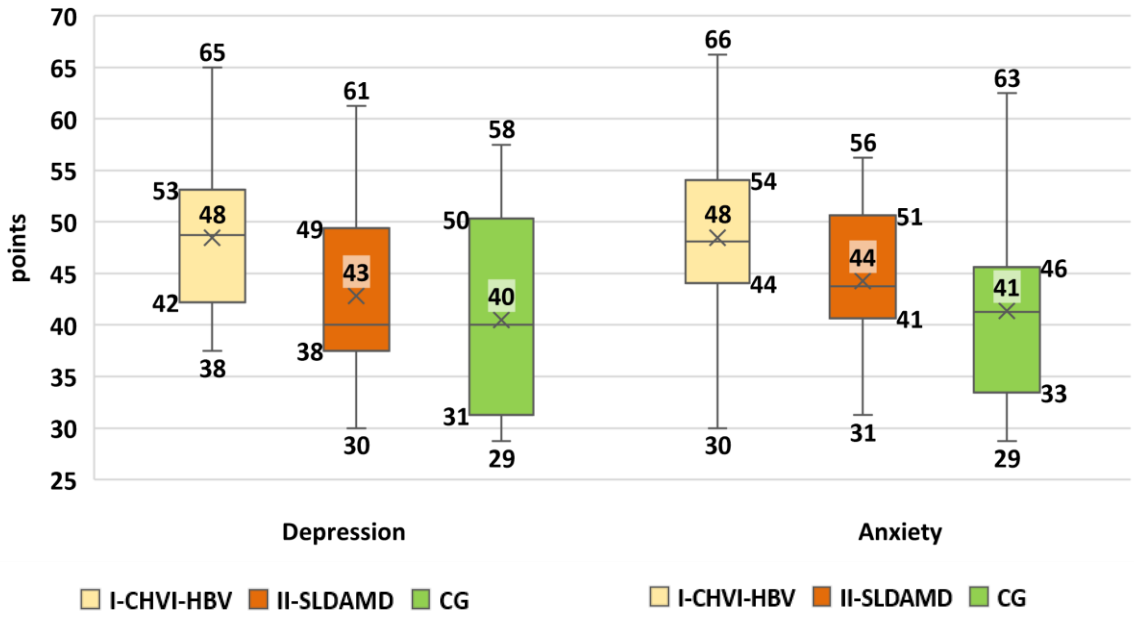
Figure 3.7 Results of the SF-36 questionnaire subscales in the study groups

Thus, it can be concluded that QoL declines in the presence of liver pathology. The mental component of QoL is more significantly affected in individuals with CHPs, and QoL is most severely impaired in cases of chronic viral disease.

Levels of depression and anxiety in individuals with chronic hepatopathies. The mean values for depression and anxiety levels obtained in the study are presented in Figure 3.8. The highest average values for both indicators were observed in Group I, where the depression level was 48.46 ± 1.15 points, and the anxiety level was 48.49 ± 1.49 points. In Group II, these values were significantly lower: 42.8 ± 1.6 points and 44.25 ± 1.36 points, respectively. In the control group, the depression level was 40.05 ± 1.84 points and the anxiety level – 40.9 ± 1.73 points.

The statistical significance of differences for depression levels was: p(I/II) < 0.01; p(I/CG) < 0.01; p(II/CG) > 0.05, and for anxiety levels: p(I/II) < 0.05; p(I/CG) < 0.01; p(II/CG) < 0.05.

Thus, it should be noted that chronic hepatopathies, anxiety, and depression are interconnected through multiple mechanisms of interaction.



P(I/II)< 0,01; P(I/CG)< 0,01; P(II/CG)> 0,05

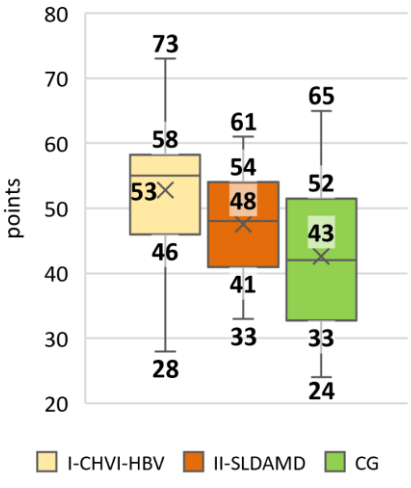
P(I/II)< 0,05; P(I/CG)< 0,01; P(II/CG)< 0,05

Figure 3.8 Results of depression and anxiety assessment in the study groups

Assessment of asthenia levels in individuals with chronic hepatopathies. The highest mean asthenia scores (Figure 3.9) were also observed in individuals from Group I – 52.79 ± 1.63

points. In Group II, the asthenia level was significantly lower – 47.52 ± 1.57 points (p(I/II) < 0.01). The lowest value was recorded in the control group – 42.58 ± 2.03 points (p(I/CG) < 0.01; p(II/CG) < 0.05).

When analysing the results by questionnaire subscales (Figure 3.10), it should be noted that the general asthenia (GA) scale proved the most indicative. The highest scores were observed in the group with chronic HBV infection – 12.88 ± 0.42 points, compared to 11.76 ± 0.46 points in those with SLDAMD and 10.15 ± 0.53 in the control group (p(I/II) < 0.05; p(I/CG) < 0.05; p(II/CG) < 0.05). On the PFat scale, higher values were recorded in individuals with CHPs from both groups: 11.15 ± 0.47 points in Group I and 10.40 ± 0.65 points in Group II, compared to 7.85 ± 0.47 points in the control group (p(I/CG) < 0.01; p(II/CG) < 0.01).



P(I/II)<0,05; P(I/CG)<0,01; P(II/CG)<0,05

Figure 3.9 Asthenia level in the study groups

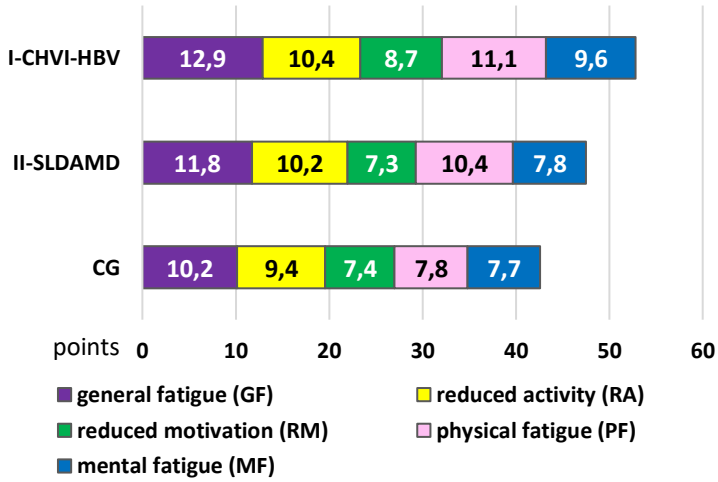


Figure 3.10 Asthenia component scores in the study groups

Changes in the MF and PFat subscales were most pronounced in individuals with chronic HBV infection, who had mean scores of 8.74 ± 0.38 and 9.59 ± 0.36 points respectively, compared to individuals with SLDAMD (7.32 ± 0.44 and 7.84 ± 0.45 points) and the control group (7.42 ± 0.58 and 7.73 ± 0.41 points). Statistical significance for the MF scale was: p(I/II) < 0.05; p(I/CG) < 0.05; p(II/CG) > 0.05. For the PFat scale: p(I/II) < 0.01; p(I/CG) < 0.01; p(II/CG) > 0.05.

The assessment results showed that all components of QoL were significantly reduced in individuals with CHPs, with the mental component being most affected. QoL was most severely impaired in those with chronic HBV infection. Participants with CHPs experienced depressive, anxious, and asthenic disorders significantly more often, with the highest severity of emotional and asthenic disturbances also recorded in those with chronic HBV infection.

3.3. Metabolomic Features in Individuals with Chronic Hepatopathies

To assess the metabolic state in individuals with hepatopathies and practically healthy subjects, our study measured serum levels of glycine (Gly), taurine (Tau), tryptophan (Trp), glutamic acid (Glu), aspartic acid (Asp), γ-aminobutyric acid (GABA), as well as ornithine (Orn), urea, and ammonia.

Free inhibitory neurotransmitter amino acid levels in individuals with chronic hepatopathies

Taurine. In most individuals with CHPs, taurine levels remained within the age- and region-specific normal range (2.9–17.6 μmol/dL) [35]. The mean taurine levels were significantly higher in individuals with CHPs (11.00 ± 1.35 μmol/dL) compared to the control group (8.26 ±

1.35 µmol/dL). The highest mean levels (Figure 3.11) were observed in individuals with SLDAMD – 12.87 ± 1.80 µmol/dL, while in the HBV group, the values were considerably lower – 9.12 ± 1.18 µmol/dL. Statistical significance of the differences: p(I/II) > 0.05; p(I/CG) > 0.05; p(II/CG) < 0.05.

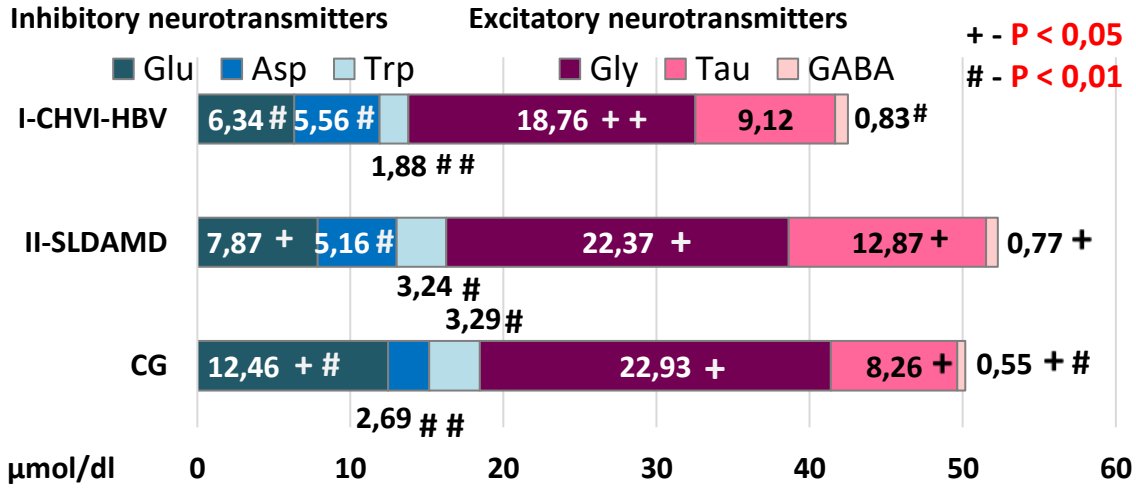


Figure 3.11 Levels of free neurotransmitter amino acids in the blood serum of study participants

Glycine. In CHPs, the glycine level was 20.56 ± 0.92 µmol/dL, which did not exceed the regional norm of 12.0–28.2 µmol/dL [35]. Glycine levels were significantly lower in individuals with chronic HBV infection (Figure 3.11), at 18.76 ± 1.45 µmol/dL, compared both with the SLDAMD group (22.37 ± 0.91 µmol/dL) and the control group (22.93 ± 2.21 µmol/dL), with statistical significance: p(I/II) < 0.05; p(I/CG) < 0.05; p(II/CG) > 0.05.

γ-Aminobutyric acid (GABA). In individuals with CHPs, the mean GABA levels exceeded the regional norm of 0.09–0.53 µmol/dL [35]. GABA levels in the CHPs groups averaged 0.80 ± 0.03 µmol/dL, higher than in the control group. The highest mean GABA values were observed in Group I (Figure 3.11): 0.83 ± 0.06 µmol/dL, compared with 0.77 ± 0.03 µmol/dL in Group II and 0.55 ± 0.06 µmol/dL in the control group. Statistical significance: p(I/II) > 0.05; p(I/CG) < 0.01; p(II/CG) < 0.05.

Thus, in individuals with CHPs, GABA levels exceeded regional and age norms, while taurine and glycine remained within normal limits across all groups. CHPs was associated with higher GABA and taurine levels than in healthy controls. The highest taurine levels were found in SLDAMD, and the highest GABA levels in CHVI-HBV. Glycine levels were lower in CHVI-HBV.

Excitatory neurotransmitter amino acid levels in individuals with chronic hepatopathies

Aspartic acid (Asp). Most individuals with CHP had Asp levels within the regional norm (2.5–5.9 µmol/dL) [35]. The mean Asp level in CHPs was 5.36 ± 0.60 µmol/dL. Serum levels were 5.56 ± 0.97 µmol/dL in Group I and 5.16 ± 0.74 µmol/dL in Group II, compared with 2.69 ± 0.45 µmol/dL in the control group (Figure 3.11). Statistical significance: p(I/II) > 0.05; p(I/CG) < 0.01; p(II/CG) < 0.01.

Glutamic acid (Glu). Mean Glu levels in CHP patients were 7.11 ± 0.81 µmol/dL, significantly lower than the regional norm (13.8–26.3 µmol/dL) [35]. Serum Glu levels (Figure 3.11) were 6.34 ± 0.70 µmol/dL in the HBV group and 7.87 ± 1.47 µmol/dL in the SLDAMD group, compared with 12.46 ± 1.92 µmol/dL in the CG. Statistical significance: p(I/II) > 0.05; p(I/CG) < 0.01; p(II/CG) < 0.05.

Tryptophan (Trp). Tryptophan levels in CHPs patients were 2.50 ± 0.26 µmol/dL, within the regional norm (1.0–5.9 µmol/dL) [35]. The lowest levels were observed in Group I – 1.88 ±

0.18 µmol/dL, compared to 3.24 ± 0.44 µmol/dL in Group II and 3.29 ± 0.45 µmol/dL in the CG. Statistical significance: p(I/II) < 0.01; p(I/CG) < 0.01; p(II/CG) > 0.05.

In summary, individuals with CHPs exhibited reduced glutamate levels, especially in CHVI-HBV. Other excitatory neurotransmitters (aspartate and tryptophan) were within regional and age norms. However, in CHVI-HBV, tryptophan levels were lower than in SLDAMD and the control group. Aspartate levels were elevated in both CHPs groups, particularly in CHVI-HBV.

Thus, CHPs is associated with a neurotransmitter amino acid imbalance – significantly reduced glutamate (excitatory) and increased GABA (inhibitory). This imbalance may affect mental health, particularly emotional status, even in mild disease. More profound neurotransmitter changes were observed in CHVI-HBV.

Ratio of inhibitory to excitatory neurotransmitters This was calculated using the formula [35]: **Xn-t= Σ (inhibitory) / Σ (excitatory),** where inhibitory neurotransmitters = Tau, Gly, GABA, and excitatory neurotransmitters = Asp, Glu, Trp.

This ratio was particularly informative in CHPs: in the CHVI-HBV group: 2.21 ± 0.16; in the SLDAMD group: 2.34 ± 0.10, which is significantly higher than mean in the CG: 2.02 ± 0.36. Statistical significance: p(I/II) > 0.05; p(I/CG) < 0.05; p(II/CG) < 0.05.

These results suggest that emotional disturbances in CHPs may be related to neurotransmitter imbalance, which could explain the increased prevalence of asthenia, depression, and anxiety revealed in our psychometric assessments.

Content of ornithine, urea, and ammonia levels in individuals with chronic hepatopathies

Ornithine. Mean serum Orn levels in CHP patients were 4.84 ± 0.60 µmol/dL, significantly lower than in controls (8.08 ± 0.99 µmol/dL). In Group I (Figure 3.12), Orn was 3.79 ± 0.63 µmol/dL, below the regional norm (4.1–12.6 µmol/dL) \[35] and lower than in Group II (5.90 ± 0.96 µmol/dL) and controls. Statistical significance: p(I/II) < 0.05; p(I/CG) < 0.01; p(II/CG) > 0.05.

Urea. Urea levels in CHP patients (Figure 3.12) were significantly below the regional norm (276.85–565.83 µmol/dL) [35] and below those in controls (375.16 ± 61.59 µmol/dL). The lowest urea levels were observed in the HBV group: 96.12 ± 9.75 µmol/dL, versus 122.28 ± 17.09 µmol/dL in the SLDAMD group. Statistical significance: p(I/II) > 0.05; p(I/CG) < 0.01; p(II/CG) < 0.05.

Ammonia. Ammonia levels in CHP patients (Figure 3.12) were significantly above both age and regional norms (7.05–39.81 µmol/dL) [35] and higher than in controls (53.67 ± 9.88 µmol/dL). The highest levels were in the SLDAMD group (166.27 ± 25.76 µmol/dL), slightly lower in the HBV group (159.35 ± 19.65 µmol/dL). Statistical significance: p(I/II) > 0.05; p(I/CG) < 0.01; p(II/CG) < 0.01.

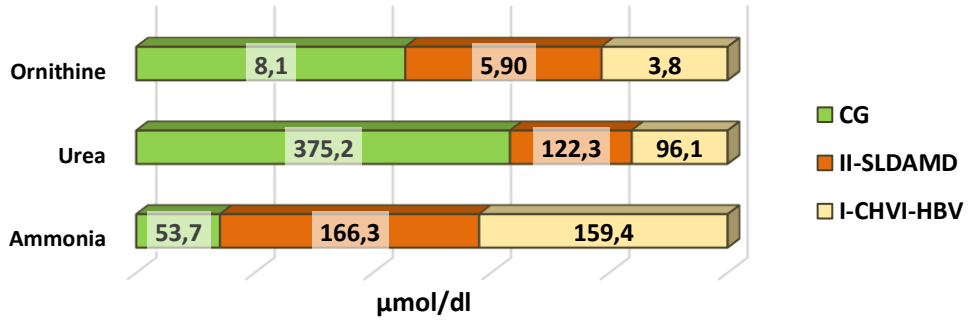


Figure 3.12 Content of ornithine, urea, and ammonia in the blood serum

Thus, characteristic metabolic features were identified in individuals CHPs, and it was determined that these individuals exhibited elevated levels of aspartate and GABA, as well as a decrease in glutamate levels. Additionally, for individuals with SLDAMD, an increase in taurine levels was observed, while individuals with CHVI-HBV exhibited the most profound changes in the composition of neuroactive amino acids, namely, the highest levels of GABA and the lowest levels of glutamate, glycine, and tryptophan. The results obtained, combined with the analysis of contemporary scientific literature, suggest that the imbalance in neuroactive amino acids, even in individuals with mild forms of CHPs, may affect their mental functioning and responses to stressors. Moreover, according to the findings, a decrease in urea levels and an increase in ammonia levels in the blood serum may be used for detecting and predicting the progression of liver disease.

3.4. Characteristic Biochemical Markers of Liver and Metabolic Syndromes in Individuals with Chronic Hepatopathies

Cytolysis Syndrome

Alanine aminotransferase and aspartate aminotransferase. Both study groups showed upper-normal average values for ALAT: in the group with CHVI-HBV, this indicator was 29.14 ± 1.88 U/l, in the group with SLDAMD, it was slightly lower at 28.61 ± 1.78 U/l (P(I/II) > 0.05). The average ASAT level was also slightly higher in the CHVI-HBV group at 23.81 ± 1.34 U/l, while in the SLDAMD group, it was 23.13 ± 1.31 U/l (P(I/II) > 0.05).

Cholestasis Syndrome

Gamma-glutamyltranspeptidase and alkaline phosphatase. The average level of GGTP was higher in the group with SLDAMD (37.79 ± 6.86 U/l), while in the CHVI-HBV group, it was slightly lower at 31.82 ± 3.12 U/l (P > 0.05). The average level of ALP was also higher in the II group, 80.94 ± 10.68 U/l, while in the I group, it was lower at 62.38 ± 3.55 U/l (P > 0.05).

Total Bilirubin. The average level of total bilirubin was higher in the II group, where it was 15.67 ± 1.49 μmol/l, while in the I group, it was 14.91 ± 0.88 μmol/l (P > 0.05). It should be noted that 44 % of individuals with SLDAMD and 35.3 % of those with CHVI-HBV had total bilirubin levels exceeding reference values, indicating a higher proportion of individuals with elevated total bilirubin levels in the SLDAMD group.

Direct Bilirubin. The average level of direct (conjugated) bilirubin in the SLDAMD group was 4.58 ± 0.58 μmol/l, while in the CHVI-HBV group, it was 3.70 ± 0.43 μmol/l (P < 0.05).

Indirect Bilirubin. The average level of indirect (unconjugated) bilirubin was higher in the SLDAMD group, at 11.45 ± 1.12 μmol/l, while in the CHVI-HBV group, it was 11.20 ± 0.72 μmol/l (P > 0.05).

Protein Metabolism and Hepatodepressive Syndrome

Total Protein. The average values of protein metabolism indicators were within normal limits. However, the average level of total protein was higher in the CHVI-HBV group (71.75 ± 1.01 g/l), and slightly lower in the SLDAMD group at 14.91 ± 0.88 g/l (P > 0.05).

Serum Albumin. The average level of serum albumin was higher in the SLDAMD group at 44.56 ± 0.77 g/l, while in the CHVI-HBV group, it was slightly lower at 42.86 ± 0.60 g/l (P > 0.05).

Prothrombin Index (Quick's Method). The average prothrombin index was higher in the II group (91.73 ± 2.18 %), while in the I group, it was 89.20 ± 2.09 % (P > 0.05).

Lipid Metabolism

Total Cholesterol. The average level of total cholesterol (Figure 3.13) was significantly higher in the II group (5.97 ± 0.25 mmol/l), while in the I group, it was 5.16 ± 0.20 mmol/l (P < 0.05).

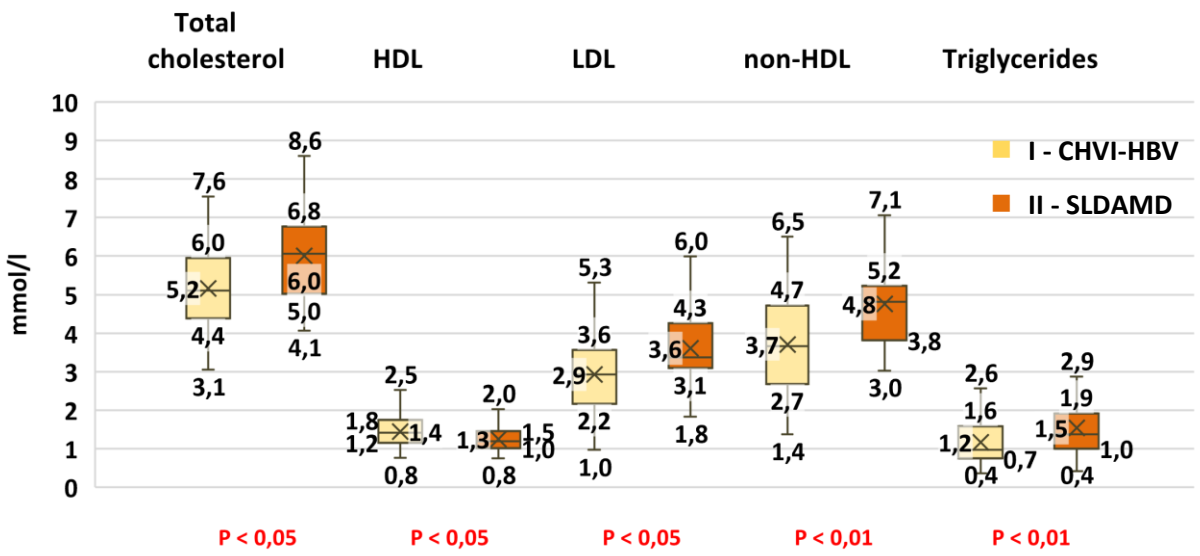


Figure 3.13 Total cholesterol, its fractions (HDL, LDL), non-HDL cholesterol and triglycerides in individuals with chronic hepatopathies

HDL, LDL, and non-HDL Cholesterol. The average HDL level (Figure 3.13) was significantly lower in individuals with SLDAMD (1.25 ± 0.06 mmol/l), while in the group with CHVI-HBV, it was 1.45 ± 0.06 mmol/l ($P < 0.05$). The average LDL level was significantly higher in individuals with SLDAMD, where it was 3.65 ± 0.22 mmol/l, while in the CHVI-HBV group, it was 2.93 ± 0.19 mmol/l ($P < 0.05$). The average non-HDL level was also significantly higher in individuals with SLDAMD (4.72 ± 0.23 mmol/l), while in the CHVI-HBV group, it was 3.71 ± 0.22 mmol/l ($P < 0.01$).

Triglycerides. The average triglyceride level was also significantly higher in individuals with SLDAMD, at 1.54 ± 0.14 mmol/l, while in the CHVI-HBV group, it was 1.17 ± 0.16 mmol/l ($P < 0.05$).

Atherogenic and Index (AI). The average atherogenic index (Figure 3.14) was significantly higher in individuals with SLDAMD (3.94 ± 0.24 CU), while in the CHVI-HBV group, it was 2.86 ± 0.26 CU ($p < 0.01$).

Thus, individuals with SLDAMD exhibited a significant increase in total cholesterol, LDL, non-HDL cholesterol, and the atherogenic index, but had lower HDL levels compared to patients with CHV-HBV.

Carbohydrate Metabolism

Blood Glucose. The average blood glucose level in the group with SLDAMD exceeded the normal range (3.3–5.5 mmol/l) and was 6.16 ± 0.45 mmol/l (Figure 3.15). In the group with CHVI-HBV, the average glucose level was significantly lower and did not exceed normal values (5.34 ± 0.12 mmol/l). The statistical significance of the differences between Group I and Group II was 95 % ($p < 0.05$).

Thus, it can be concluded that individuals with chronic hepatopathies experience impaired urea genesis, with decreased levels of ornithine and urea and increased ammonia levels in the serum. The most pronounced changes in these parameters were observed in individuals with CHVI-HBV. Additionally, both groups of individuals with CHPs exhibited upper-normal levels of transaminases. The obtained results and analysis of the current scientific literature suggest that an upper-normal level of ALAT in individuals with CHVI-HBV could serve as an adverse prognostic sign. Furthermore, it should be noted that individuals with SLDAMD exhibited a tendency toward increased levels of carbohydrate and lipid metabolism markers, which can be considered significant predictors of SLDAMD development.

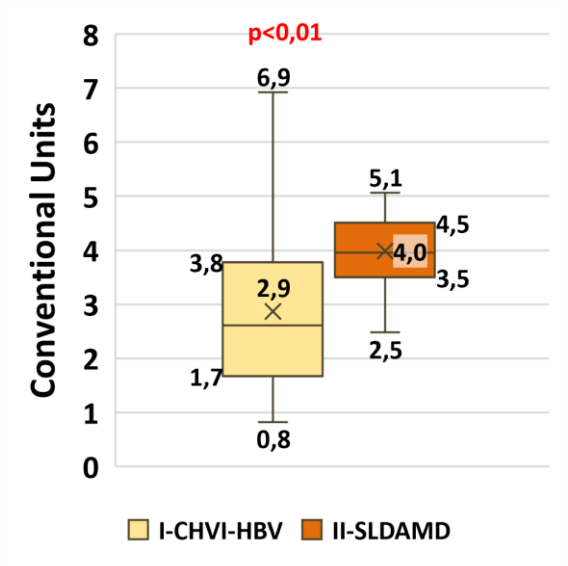


Figure 3.14 Atherogenic index in individuals with chronic hepatopathies

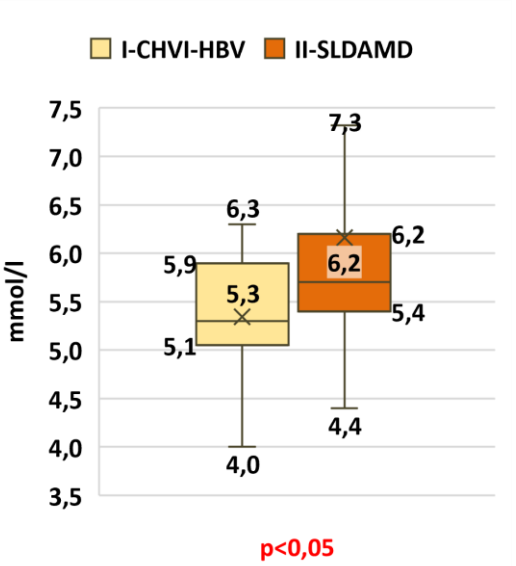


Figure 3.15 Blood glucose levels in the serum of individuals with chronic hepatopathies

4. CORRELATIONAL RELATIONSHIPS BETWEEN PSYCHOPHYSIOLOGICAL CHARACTERISTICS AND BIOCHEMICAL AND METABOLOMIC PARAMETERS. THE SIGNIFICANCE OF PSYCHOPHYSIOLOGICAL PARTICULARITIES OF HEALTH STATUS IN CHRONIC HEPATOPATHIES

An analysis of the correlational relationships between the psychophysiological characteristics of individuals with CHPs and their biochemical and metabolomic parameters revealed several significant correlations.

For instance, BMI showed a significant negative correlation with the subscale scores reflecting the state of physical health (SF-36): with the PF scale (r_p = -0.22, $p < 0.05$) and the GH scale (r_p = -0.23, $p < 0.05$), indicating a connection between excessive body mass and increased BMI, leading to a decline in physical well-being, with limitations in physical activity, reduced range of achievable physical activities, and physical health indicators. Additionally, anthropometric indicators demonstrated a significant positive correlation with lipid metabolism markers: total cholesterol (r_p = 0.29, $p < 0.01$ – for weight and r_p = 0.53, $p < 0.01$ – for BMI), LDL (r_p = 0.30, $p < 0.01$ – for weight and rp = 0.49, $p < 0.01$ – for BMI), triglycerides (r_p = 0.51, $p < 0.01$ – for both parameters), non-HDL cholesterol (r_p = 0.36, $p < 0.01$ – for weight and r_p = 0.56, $p < 0.01$ –for BMI), and atherogenic index (r_p = 0.41, $p < 0.01$ – for weight and r_p = 0.49, $p < 0.01$ –for BMI), as well as a significant negative correlation with HDL levels (r_p = -0.34, $p < 0.01$ – for weight and r_p = -0.23, $p < 0.05$ – for BMI). Additionally, in individuals with chronic hepatopathy, there was a significant positive correlation between BMI and amino acid levels: GABA (r_p = 0.40, $p < 0.01$), Tau (r_p = 0.30, $p < 0.05$), and Glu (r_p = 0.29, $p < 0.05$), indicating an increased risk of metabolic disturbances and heightened imbalance in neurotransmitter amino acids with increased body weight.

Furthermore, a significant negative correlation was found between SBP and the GH scale of the QoL questionnaire (r_p = -0.23, $p < 0.05$), a significant positive correlation between SBP and triglyceride levels (r_p = 0.43, $p < 0.01$), non-HDL cholesterol (r_p = 0.32, $p < 0.01$), and AI (r_p = 0.37, $p < 0.01$). Thus, a direct relationship was observed between increased SBP and worsening QoL components, lipid metabolism disturbances, as well as the fact that non-HDL cholesterol and atherogenic index indices are more informative than routine lipid metabolism markers in

individuals with chronic hepatopathy. Moreover, significant correlations between biochemical markers and heart rate were identified: a positive relationship with liver cholestasis markers (r_p = 0.32, $p < 0.01$ – GGTP and rp = 0.40, $p < 0.01$ – ALP) and lipid and carbohydrate metabolism indicators such as total cholesterol ($r_p = 0.25$, $p < 0.01$), LDL ($r_p = 0.26$, $p < 0.01$), triglycerides ($r_p = 0.41$, $p < 0.01$), non-HDL cholesterol ($r_p = 0.26$, $p < 0.01$), and glucose levels ($r_p = 0.27$, $p < 0.01$). These results indicate a direct relationship between increased heart rate and liver cholestasis, as well as disturbances in lipid and carbohydrate metabolism.

Among individuals with chronic hepatopathy, a number of correlations were found regarding the MH component of the QoL: a significant positive correlation with scales reflecting the mental health subcomponents of the quality of life: SF ($r_p = 0.25$, $p < 0.05$), RF-E ($r_p = 0.28$, $p < 0.01$), and the RA scale of the MFI-20 questionnaire (rp = 0.23, $p < 0.05$), and a significant negative correlation with depression levels ($r_p = -0.27$, $p < 0.01$), confirming the relationship between increased KAI and the rise of asthenic symptoms, more often manifesting as decreased activity, and the association between increased vagotonia and an increased risk of depression, worsening social interaction, and emotional functioning in individuals with chronic hepatopathy. In addition, a significant number of correlations between sympathetic tone and cholestasis markers, lipid, and carbohydrate metabolism disorders were found: a significant positive correlation with ALP levels ($r_p = 0.32$, $p < 0.01$), total cholesterol (rp = 0.34, $p < 0.01$), non-HDL cholesterol ($r_p = 0.32$, $p < 0.01$), and glucose levels ($r_p = 0.26$, $p < 0.01$). This suggests a direct relationship between increased sympathetic tone and the severity of lipid, carbohydrate metabolism disturbances, and the development of cholestasis symptoms in individuals with chronic hepatopathy.

A significant correlation was also found between the parameters of QoL and the levels of carbohydrate and lipid metabolism indicators, including a positive relationship between the glucose level and the integral indicator MH ($r_p = 0.21$, $p<0.05$), a negative relationship with the integral indicator PH ($r_p = -0.26$, $p<0.01$) and with the subscales GH ($r_p = -0.21$, $p<0.05$) and PF ($r_p = -0.34$, $p<0.01$); as well as a significant negative relationship between the subscale GH (QoL) and lipid metabolism indicators: total cholesterol ($r_p = -0.21$, $p<0.05$), LDL ($r_p = -0.23$, $p<0.05$), non-HDL cholesterol index ($r_p = -0.25$, $p<0.01$) and AI ($r_p = -0.24$, $p<0.05$). This may indicate a direct interconnection between the deterioration of QoL and the increased levels of carbohydrate and lipid profile indicators in individuals with chronic liver diseases.

Furthermore, a significant negative correlation was noted between the albumin level and the level of asthenia (MFI-20) $r_p = -0.33$, $p<0.01$ and its subscales GF ($r_p = -0.33$, $p<0.01$) and PF ($r_p = -0.41$, $p<0.01$). A significant negative correlation was also observed between the indicators of asthenia and the level of urea: the total asthenia indicator (MFI-20) $r_p = -0.34$, $p<0.05$ and its subscales GF and PFat ($r_p = -0.36$, $p<0.05$ for both subscales). These data confirm a direct relationship between the disturbance of protein and urea metabolism and the formation and exacerbation of asthenic syndrome in chronic liver diseases.

In individuals with chronic liver diseases, significant correlations were observed between the MH indicators of QoL indicators and the levels of neurotransmitter amino acids: a moderate positive relationship between the integral MH indicator and the RF-E subscale with the Trp level: rp = 0.30 ($p<0.05$) and rp = 0.38 ($p<0.01$) respectively, and a moderate negative relationship between the SF subscale and the Gly level: rp = -0.33 ($p<0.05$). This indicates opposite correlations between the changes in the concentration of neurotransmitter amino acids and the mental component of QoL in individuals with chronic liver diseases, meaning that practical doctors should be cautious and take an individual approach when prescribing medications and food supplements containing neurotransmitter amino acids to patients with chronic liver diseases, especially when metabolic disturbances are present.

Additionally, the correlation analysis demonstrated that problems related to the reduction of quality of life, disturbances in the emotional and asthenic spectra, were interconnected and of a complex nature.

The correlation analysis in the studied groups of individuals with CHPs revealed specific interrelationships for individual conditions. Thus, in individuals with CHVI-HBV, the following were observed:

- A significant negative correlation between BMI and the PH index of QoL ($rp = -0.28$, $p<0.05$), with the subscales of QoL: RF-P ($rp = -0.26$, $p<0.05$) and GH ($rp = -0.34$, $p<0.01$), as well as a significant positive correlation with the GF scale of the asthenia questionnaire ($rp = 0.29$, $p<0.05$). Therefore, an increase in BMI corresponds with a reduction in physical functioning and the progression of asthenia in individuals with CHVI-HBV.
- A negative correlation between the MH index (QoL) and the levels of glycine ($rp = -0.59$, $p<0.01$), taurine ($rp = -0.48$, $p<0.05$), and tryptophan ($rp = -0.46$, $p<0.05$), while PH (QoL) negatively correlated with the GABA level ($rp = -0.45$, $p<0.01$). These correlations may indicate interrelationships between the levels of inhibitory and excitatory neurotransmitters and changes in the mental and physical components of QoL in individuals with CHVI-HBV.
- A moderate negative correlation between the ornithine level and indicators of depression ($rp = -0.46$, $p<0.05$), anxiety ($rp = -0.51$, $p<0.05$), and asthenia ($rp = -0.48$, $p<0.05$), as well as with the subscales of the MFI-20 questionnaire: RA ($rp = -0.51$, $p<0.05$), RM ($rp = -0.47$, $p<0.05$), and PFat ($rp = -0.48$, $p<0.05$). These correlations confirm the existence of interrelationships between a decrease in the ornithine level and the intensification of anxiety, depression, and asthenia manifestations. A low ornithine level in individuals with CHVI-HBV may be accompanied by a decrease in urea levels and an increase in ammonia levels, typically due to a deterioration in liver detoxification function.
- A moderate positive correlation between the levels of depressive disorders and the indicators of cholestasis syndrome – total bilirubin ($rs = 0.34$, $p<0.05$) and its free fraction ($rp = 0.31$, $p<0.05$), as well as a moderate negative correlation between albumin levels and asthenia indicators – GF ($rp = -0.39$, $p<0.01$; $rs = -0.41$, $p<0.05$) and PFat ($rp = -0.32$, $p<0.05$). Thus, increased bilirubin levels are associated with the development of depressive disorders, while a decrease in serum albumin levels is associated with an intensification of asthenia in individuals with CHVI-HBV.
- A significant positive correlation between KAI and the indicators of asthenia: RM ($rp = 0.27$, $p<0.05$) and RA ($rp = 0.41$, $p<0.01$; $rs = 0.47$, $p<0.01$), indicating interrelationships between the progression of sympathetic tone and the worsening of asthenic disturbances in individuals with chronic HBV infection.
- A moderate negative correlation between sympathetic tone (KAI) and the levels of glycine ($rp = -0.41$, $p<0.05$) and ornithine ($rp = -0.41$, $p<0.05$), confirming a relationship between an increase in vagotonia and elevated glycine and ornithine levels.

Similarly, in individuals with SLDAMD, several significant correlations were identified:

- A positive correlation between BMI and SBP parameters ($rp = 0.32$, $p<0.05$; $rs = 0.38$, $p<0.01$), the PFat scale of the MFI-20 questionnaire ($rp = 0.41$, $p<0.01$; $rs = 0.38$, $p<0.01$), levels of ASAT ($rp = 0.36$, $p<0.01$; $rs = 0.33$, $p<0.05$), GGTP ($rp = 0.50$, $p<0.01$; $rs = 0.41$, $p<0.05$), total cholesterol ($rp = 0.43$, $p<0.01$; $rs = 0.48$, $p<0.05$), LDL ($rp = 0.33$, $p<0.05$; $rs = 0.30$, $p<0.05$); triglycerides ($rp = 0.47$, $p<0.01$; $rs = 0.52$, $p<0.01$), non-HDL cholesterol ($rp = 0.46$, $p<0.01$; $rs = 0.49$, $p<0.05$), AI ($rp = 0.34$, $p<0.05$; $rs = 0.32$, $p<0.05$), and the glutamate level ($rp = 0.50$, $p<0.05$), as well as a high negative correlation with tryptophan levels ($rs = 0.82$, $p<0.01$). These data may suggest a relationship between an increased BMI and the development of hypertension, physical asthenia, lipid metabolism disturbances, intensified cytolysis and cholestasis syndromes, as well as neurotransmitter amino acid concentration abnormalities in individuals with SLDAMD.

- A significant positive correlation was observed between the KAI and the levels of GGTP ($rs = 0.41$, $p<0.05$), ALP ($rp = 0.35$, $p<0.01$; $rs = 0.46$, $p<0.05$), glucose ($rp = 0.31$, $p<0.05$), non-HDL cholesterol ($rp = 0.55$, $p<0.01$; $rs = 0.52$, $p<0.01$), and Atherogenic Index ($rp = 0.53$, $p<0.01$; $rs = 0.44$, $p<0.05$), as well as a significant negative correlation with the level of depression ($rp = -0.33$, $p<0.05$) and glycine content ($rp = -0.54$, $p<0.01$). This demonstrates consistent changes, including increased sympathetic tone, disorders of lipid and carbohydrate metabolism, the development of cholestasis syndrome and/or reduced glycine levels. An increase in vagal tone, in turn, correlates with a higher risk of depression in individuals with SLDAMD.
- A significant positive correlation was found between ALAT levels and depression ($rp = 0.47$, $p<0.01$; $rs = 0.42$, $p<0.05$), as well as anxiety ($rp = 0.40$, $p<0.01$; $rs = 0.42$, $p<0.05$), and a significant negative correlation with QoL subscale indicators: RF-P ($rp = -0.54$, $p<0.01$), SF ($rp = -0.43$, $p<0.01$; $rs = -0.40$, $p<0.05$). These findings indicate a relationship between elevated ALT levels and the development of anxiety and depressive disorders, and impaired social and physical functioning in individuals with SLDAMD.
- A significant positive correlation was found between glucose levels and the asthenia score ($rp = 0.41$, $p<0.01$) and the MFI-20 subscales: GF ($rp = 0.40$, $p<0.01$), RA ($rp = 0.49$, $p<0.01$) and PFat ($rs = 0.50$, $p<0.05$), as well as a significant negative correlation with the PH subscales of QoL: PF ($rp = -0.47$, $p<0.01$; $rs = -0.59$, $p<0.01$), GH ($rp = -0.37$, $p<0.01$; $rs = -0.44$, $p<0.05$) and PH ($rp = -0.44$, $p<0.01$; $rs = -0.41$, $p<0.05$). These results indicate a consistent association between increased glucose levels and the development of asthenic disorders or impaired physical functioning in individuals with SLDAMD.
- A number of subscales of the MH component of QOL were found to be negatively correlated with lipid profile indicators: MH with LDL levels ($rp = -0.31$, $p<0.05$); VT subscale with total cholesterol ($rp = -0.37$, $p<0.01$; $rs = -0.44$, $p<0.01$), LDL ($rp = -0.59$, $p<0.01$; $rs = -0.58$, $p<0.01$), and non-HDL cholesterol index ($rp = -0.37$, $p<0.01$; $rs = -0.50$, $p<0.05$); RF(E) subscale with triglycerides levels ($rp = -0.35$, $p<0.01$). Additionally, a significant positive correlation was found between indicators of asthenic disorders (MFI-20) and total cholesterol ($rp = 0.45$, $p<0.01$; $rs = 0.41$, $p<0.05$), LDL ($rp = 0.43$, $p<0.01$; $rs = 0.41$, $p<0.05$), and non-HDL cholesterol ($rp = 0.45$, $p<0.01$; $rs = 0.44$, $p<0.05$). A significant negative correlation was also found between asthenia indicators and serum albumin levels ($rp = -0.30$, $p<0.05$; $rs = 0.39$, $p<0.05$). This fact indicates the existence of a relationship between the progression of metabolic disorders (decreased albumin levels, increased lipid metabolism indicators) and the intensification of asthenia and/or reduction in the mental component of QoL in individuals with SLDAMD.
- A direct correlation was observed between the Glu level and the PFat score (MFI-20): $rp = 0.54$, $p<0.01$; $rs = 0.63$, $p<0.05$, and an inverse correlation with the MH (QoL) score: $rp = -0.48$, $p<0.05$, and RA (MFI-20): $rp = -0.48$ ($p<0.05$), indicating a consistent association between increased Glu levels and suppression of the mental QoL component, and/or increased activity and/or intensification of physical asthenia. Glycine level showed a moderate negative correlation with the RF-E subscale (SF-36): $rp = -0.40$ ($p<0.05$), $rs = -0.62$ ($p<0.05$), demonstrating an inverse relationship between the level of the inhibitory neurotransmitter Gly and the emotional functioning of individuals with SLDAMD. A moderate direct correlation was found between tryptophan levels and MF ($rp = 0.59$, $p<0.01$), indicating a consistent association between increased tryptophan content and the progression of mental asthenia in individuals with SLDAMD.

Thus, the conducted correlation analysis revealed significant and multifaceted involvement of psychophysiological factors in shaping the clinical picture and evolution of various nosological forms of chronic hepatopathies. This served as a basis for developing criteria for psychophysiometabolomic phenotypes in individuals with chronic HBV infection and those with SLDAMD. These phenotypes are based on characteristic physiological, psychological, biochemical, and metabolomic changes specific to each type of chronic liver pathology. The formulated psychophysiometabolomic phenotypes can be recommended for use by general

practitioners, gastroenterologists, and hepatologists for the differential diagnosis of chronic liver diseases, as well as for forming an individualised approach and personalised management strategy for patients with CHPs.

GENERAL CONCLUSIONS

1. During the study, it was established that the health condition of individuals with chronic hepatopathies, characterised by a complex of various specific clinical and paraclinical psychophysiological disorders along the "liver–CNS" axis, worsens their overall health status.

2. Among individuals with chronic hepatopathies, a number of physiological changes were identified, including increased body weight, body mass index, systolic and diastolic blood pressure, and pulse rate. These were most pronounced in individuals with steatotic liver disease associated with metabolic dysfunctions, while vagotonia predominated in those with chronic HBV infection.

3. In the groups of individuals with chronic hepatopathies, all components of quality of life were found to be reduced, with a predominance of deterioration in psycho-emotional status, most intensely expressed in individuals with chronic HBV infection.

4. The most common indicators of impaired mental health were depression, anxiety, and asthenia, which were more frequently observed and more pronounced in individuals with chronic HBV infection.

5. The effects of chronic hepatopathies impact protein metabolism: the analysis of free amino acids in blood serum revealed altered spectra and concentrations of glutamate and ornithine, along with increased levels of GABA and aspartate in individuals with chronic hepatopathies. In individuals with steatotic liver disease associated with metabolic dysfunctions, increased taurine was typical, whereas those with chronic HBV infection exhibited reduced levels of ornithine, glycine, and tryptophan.

6. Changes in the spectrum and concentration of neurotransmitter amino acids in individuals with chronic hepatopathies were specific and included elevated GABA and decreased glutamate. A distinctive marker was the increased total of inhibitory over excitatory neurotransmitters, which may explain the more frequent manifestation of asthenia, depression, and anxiety found in our psychometric assessments.

7. Characteristic biochemical changes in individuals with steatotic liver disease associated with metabolic dysfunctions included increased total cholesterol, LDL, non-HDL cholesterol, triglycerides, and atherogenic index, accompanied by decreased HDL and increased glucose levels in the blood serum.

8. In individuals with chronic hepatopathies, a number of significant correlations were established between emotional and asthenic indicators, quality of life measures, and anthropometric, physiological, biochemical, and metabolomic parameters. Positive correlations were found between levels of asthenia and the mental component of quality of life with body weight and the Kerdo vegetative index. Negative correlations were observed between asthenia and albumin levels, between anxiety and depression levels and the Kerdo index, between the Physical Health summary index and carbohydrate and lipid metabolism parameters, and between the Mental Health summary index component and its subscales and amino acid levels.

9. Disruption of psychophysiological health indicators – manifested as elevated levels of anxiety, depression, asthenia, reduced mental quality of life, and altered amino acid profiles in serum, with phenotype-specific patterns for chronic HBV infection and steatotic liver disease associated with metabolic dysfunctions – accompanied by a decrease in quality of life, indicate the necessity of additional psycho-emotional therapy for individuals with chronic hepatopathies to prevent potential complications.

PRACTICAL RECOMMENDATIONS

- The "Questionnaire for assessing the condition of apparently healthy individuals for control group formation in scientific studies," developed during this work, can be used as a tool for evaluating the health status of self-reported healthy individuals for selection and formation of control groups in research in gastroenterology, hepatology, and internal medicine.
- The application of a set of psychometric tools for assessing quality of life, depression, anxiety, and asthenia can be employed by practitioners for individuals with chronic hepatopathies.
- Detection of reduced urea alongside elevated ammonia levels can be used in clinical practice as an unfavourable prognostic marker in individuals with chronic hepatopathies, indicating increased cytolysis, decreased liver detoxification function, and disturbances in lipid and carbohydrate metabolism.
- Altered levels of amino acid neurotransmitters can serve as additional indicators of protein, lipid, and carbohydrate metabolic disorders; reduced ornithine may serve as an additional indicator of impaired liver detoxification function.
- The identified specific amino acid patterns– characterised by elevated aspartate and glutamate, and reduced glycine and ornithine – may be used for the early detection of chronic hepatopathies.
- The proposed psychophysiometabolomic phenotypes of individuals with chronic HBV infection and those with steatotic liver disease associated with metabolic dysfunctions may be used by clinicians for differential diagnosis of chronic hepatopathies, as well as for forming an individualised and personalised management strategy.
- When prescribing amino acid-containing preparations to patients with chronic hepatopathies, clinicians are advised to adopt an individualised approach, taking into account the diagnosis and baseline amino acid levels prior to treatment, followed by post-treatment monitoring.

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European Meeting", 16-18 March 2017, Iasi, Romania. Bologna (Italy): Filodiritto Editore – Proceedings, 2017, pp. 190-195. ISBN 978-88-95922-89-8. https://www.webofscience.com/wos/woscc/full-record/WOS:000406422100036.

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21. **BEREZOVSCAIA, E.** Comorbiditatea hepatopatiilor cronice și tulburărilor mintale. În: *Tendințe contemporane ale dezvoltării științei: viziuni ale tinerilor cercetători*. Ediția IX. Chișinău: Tipogr. „Biotehdesign", 2020, Ediția 9, Vol. 1, pp. 92-97. ISBN 978-9975-108-66-9. https://ibn.idsi.md/ro/vizualizare_articol/112747.
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25. **БЕРЕЗОВСКАЯ, Е.**, ЛУПАШКО, Ю., ДУМБРАВА, В.-Т. и др. Изменение содержания некоторых нейромедиаторных аминокислот у пациентов с хроническими гепатопатиями. În: *Integrare prin cercetare și inovare. Ştiinţe ale naturii și exacte*. Chișinău: CEP al USM, 2023, pp. 76-82. ISBN 978-9975-62-690-3. https://ibn.idsi.md/ro/vizualizare_articol/200664.
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5. Patents and other intellectual property objects (IPO)

5.2. issued by the State Agency for Intellectual Property

- ***Author's note***

1. LUPAŞCO, Iu., DUMBRAVA, V.-T., VENGHER, I., TARAN, N., **BEREZOVSCAIA, E.** și al. Adeverința privind înscrierea obiectelor dreptului de autor și ale drepturilor conexe cu titlul: „*Compendiul Repere esențiale în patologia hepato-biliară cu elemente de nutriție*", Seria OȘ Nr. 7520 din 11.05.2023. https://www.db.agepi.md//opere/Details.aspx?RealID=6875&lang=ro.
2. LUPAȘCO, Iu., VENGHER, I., TARAN, N., **BEREZOVSCAIA, E.** și al. Adeverința privind înscrierea obiectelor dreptului de autor și ale drepturilor conexe cu titlul: „*Ghidul practic. Algoritme diagnostice și de tratament în hepatopatii cronice*", Seria OȘ Nr. 8014 din 02.10.2024. https://www.db.agepi.md//opere/Details.aspx?RealID=7392&lang=ro.
3. **BEREZOVSCAIA, E.**, LUPAȘCO, Iu. Adeverința privind înscrierea obiectelor dreptului de autor și ale drepturilor conexe cu titlul: „*Evaluarea stării de sănătate a persoanelor practic sănătoase prin elaborarea, expertizarea și implementarea chestionarului specializat autohton pentru formarea unui lot de control de cercetare științifică în domeniu gastroenterologiei, hepatologiei și medicinei interne"*, Seria OȘ Nr. 8036 din 28.11.2024. https://www.db.agepi.md//opere/Details.aspx?RealID=7419&lang=ro.
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11. **BEREZOVSCAIA, E.**, LUPAȘCO, Iu. *Aplicarea chestionarului „Chestionar de evaluare a persoanelor practic sănătoase pentru formarea lotului de control în cercetarea științitică”*. Certificat de inovator Nr 6265 din 26.06.2024.

- ***Innovation implementation acts***

12. LUPAŞCO, Iu., VENGHER, I., TARAN, N., **BEREZOVSCAIA, E.** et al. *Aplicarea ghidului practic. „Algoritme diagnostice și de tratament în hepatopatii cronice”*. Actul de implementare a inovației în procesul științifico-didactic în cadrul USMF ”Nicolae Testemițanu” Nr 101 din 02 iulie 2024.
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14. **BEREZOVSCAIA, E.**, LUPAȘCO, Iu. *Aplicarea chestionarului. „Chestionar de evaluare a persoanelor practic sănătoase pentru formarea lotului de control în cercetare științitică”*. Actul de implementare a inovației în procesul științifico-practic/științifico-didactic în cadrul USMF „Nicolae Testemițanu”, Nr. 106 din 18 octombrie 2024.

АННОТАЦИЯ

Березовская Елена. «Психофизиологические особенности состояния здоровья лиц с хроническими гепатопатиями». Диссертация на соискание ученой степени доктора биологических наук. Кишинев, 2025.

Структура диссертации: введение, четыре главы, общие выводы и рекомендации, библиография из 279 источников, 6 приложений; 118 стр. основного текста, 46 рисунков, 7 таблиц. Полученные результаты опубликованы в 22 научных работах.

Ключевые слова: хронические гепатопатии (ХГП), хроническая инфекция HBV (ХВИ-HBV), стеатозная болезнь печени ассоциированная с метаболическими дисфункциями (СБПАМД), психофизиологические особенности, качество жизни (КЖ), депрессия, тревога, астения, аминокислоты (АК).

Цель работы: выявление психофизиологических особенностей состояния здоровья лиц с хроническими гепатопатиями и выяснение влияния патологии печени на их психофизиологическое состояние.

Задачи исследования: 1) установить специфику физиологического статуса у лиц с легкими формами хронических гепатопатий клиническими, лабораторными и инструментальными методами, клиническую и параклиническую картину, серологические маркеры вирусного гепатита, метаболизм свободных аминокислот в сыворотке крови, вегетативный индекс Кердо, показатели белкового, углеводного и липидного обменов; 2) выявить параметры, характеризующие качество жизни лиц с хроническими гепатопатиями; 3) установить наиболее характерные показатели психической диссаногенности у лиц с легкими формами хронических гепатопатий; 4) исследовать биохимические показатели и спектр свободных аминокислот, включительно медиаторных, и других метаболитов у лиц с хроническими гепатопатиями; 5) провести корреляционный анализ показателей эмоционального, астенического компонентов и качества жизни с биохимическими показателями и содержанием аминокислот в сыворотке крови у лиц с хроническими гепатопатиями; 6) разработать метод сбора информации о психоэмоциональном статусе и комплекс психометрических тестов, улучшающие диагностику психофизиологического состояния у лиц с хроническими гепатопатиями.

Научная новизна и оригинальность: было продемонстрировано, что психофизиологические нарушения состояния здоровья у лиц с ХГП, обусловленные семантикой диагноза, дисбалансом свободных АК, углеводного и липидного обменов, детерминируют ухудшение общего состояния человека; получены новые данные об изменении спектра и содержания нейромедиаторных АК у лиц с ХГП; был проведен корреляционный анализ показателей эмоционального компонента и КЖ с физиологическими и метаболическими параметрами и содержанием АК при ХГП; создано новое комплексное видение взаимосвязи психофизиологических, метаболических и соматических факторов состояния здоровья.

Полученные автором результаты, способствующие решению важной научной проблемы: выявление физиологических и психоэмоциональных взаимосвязей у лиц с хроническими заболеваниями печени вирусной и метаболической этиологии с использованием физиологических, психометрических, биохимических, клинических и рутинных параклинических методов с целью определения специфических особенностей данной патологии.

Теоретическое значение: полученные результаты углубляют и расширяют научные представления об особенностях диссаногении организма при ХГП, о психофизиологических особенностях состояния здоровья с точки зрения взаимоотношений ЦНС и печени; влияния ХГП на снижение КЖ и взаимосвязи метаболических показателей, содержания нейромедиаторных АК с психофизиологическим статусом у лиц с ХГП.

Прикладное значение: была создана комплексная методика для изучения ментального здоровья лиц с ХГП; выявлены психофизиологические особенности реакции на хронический стресс; выявленные психофизиологические характеристики могут быть положены в основу улучшения КЖ людей с ХГП.

Внедрение научных результатов: Результаты диссертации были внедрены в Лаборатории гастроэнтерологии при ГУМФ им. Николае Тестемицану. Получены: 3 свидетельства о внедрении результатов и 5 сертификатов об авторском праве.

ADNOTARE

Berezovscaia Elena. „Particularităţi psihofiziologice ale stării sănătăţii persoanelor cu hepatopatii cronice". Teză de doctor în ştiinţe biologice. Chişinău, 2025.

Structura tezei: introducere, patru capitole, concluzii generale şi recomandări, bibliografia constă din 279 de surse, 6 anexe, 118 p. prezintă textul de bază, 46 de figuri, 7 tabele. Rezultatele obţinute au fost publicate în 22 de lucrări ştiinţifice.

Cuvinte-cheie: hepatopatii cronice (HPC), infecția cronică HBV (ICV-HBV), boala ficatului steatotic asociată cu disfuncții metabolice (BFSADM), particularităţi psihofiziologice, calitatea vieții (QoL), depresie, anxietate, astenie, aminoacizi (AA).

Scopul lucrării: identificarea particularităților psihofiziologice ale stării sănătății persoanelor cu hepatopatii cronice și elucidarea efectelor patologiei hepatice asupra stării psihofiziologice.

Obiectivele cercetării: 1) aprecierea specificității statutului fiziologic al persoanelor cu forme ușoare de hepatopatii cronice cu ajutorul metodelor clinice, de laborator și instrumentale, a tabloului clinic și paraclinic, a markerilor serologici ai virusului hepatic, metabolismul aminoacizilor liberi în serul sangvin, indicele vegetativ Kerdo, parametrii metabolismului proteic, glucidic și lipidic; 2) identificarea parametrilor ce caracterizează calitatea vieții persoanelor cu hepatopatii cronice; 3) evidențierea parametrilor specifici ce caracterizează dissanogenia psihică a persoanelor cu forme ușoare de hepatopatii cronice; 4) determinarea indicilor biochimici, spectrului aminoacizilor liberi și a celor mediatori, cât și a altor metaboliți la persoanele cu hepatopatii cronice; 5) efectuarea analizei corelative a parametrilor componentei emoționale, astenice și a calității vieții cu parametrii biochimici și a conținutului aminoacizilor în ser la persoanele cu hepatopatii cronice; 6) elaborarea metodei de colectare a informației despre statutul psihoemoțional și a complexului testelor psihometrice ce facilitează diagnosticul statutului psihofiziologic al persoanelor cu hepatopatii cronice.

Noutatea şi originalitatea ştiinţifică: s-a demonstrat că tulburările psihofiziologice ale sănătății la subiecții cu HPC, cauzate de semantica diagnosticului, dezechilibrul AA liberi, metabolismului glucidic și lipidic, determină deteriorarea stării generale a unei persoane; au fost obținute date noi privind modificările în spectrul și conținutul AA neurotransmițători la subiecții cu HPC; a fost efectuată o analiză a corelației indicatorilor componentei emoționale și QoL cu parametrii atât fiziologici cât și celor metabolici și a conținutului de AA în HPC; a fost creată o nouă viziune cuprinzătoare asupra relației dintre factorii psihofiziologici, metabolici și somatici ai sănătății.

Rezultatele obținute de autor, care au contribuit la soluționarea unei probleme științifice importante: dezvăluirea interrelațiilor fiziologice și psihoemoționale la persoanele cu hepatopatii cronice cauzate de etiologia virală și metabolică, utilizând metode fiziologice, psihometrice, biochimice, clinice și paraclinice de rutină în scopul determinării caracteristicilor specifice pentru aceste patologii.

Semnificaţia teoretică: rezultatele obținute aprofundează și extind înțelegerea științifică a caracteristicilor dissanogeniei organismului în HPC; despre particularitățile psihofiziologice ale stării de sănătate din punctul de vedere ai relației dintre SNC și ficat; influența HPC asupra reducerii QoL și a relației dintre parametrii metabolici, conținutul de AA neurotransmițători și starea psihofiziologică la persoanele cu HPC.

Valoarea aplicativă: a fost creată o metodologie complexă, pentru studierea sănătății mintale a persoanelor cu HPC; au fost identificate caracteristici psihofiziologice ale reacției la stresul cronic; caracteristicile psihofiziologice identificate pot fi folosite ca bază, pentru îmbunătățirea QoL a persoanelor cu HPC.

Implementarea rezultatelor ştiinţifice: rezultatele tezei au fost implementate în cadrul subdiviziunii USMF „Nicolae Testemitanu", Laboratorul de Gastroenterologie. Au fost obținute:3 certificate de implementare a rezultatelor și 5 certificate de drepturi de autor.

ANNOTATION

Berezovscaia Elena, "Psychophysiological Characteristics of the Health Status of Individuals with Chronic Hepatopathies", PhD thesis in Biological Sciences, Chișinău, 2025.

Thesis structure: introduction, four chapters, general conclusions and recommendations, bibliography (279 sources), six appendices; 118 pages of main text, 46 figures, and seven tables. The results obtained have been published in 22 scientific papers.

Keywords: chronic hepatopathies (CHPs), chronic HBV infection (CHVI-HBV), steatotic liver disease associated with metabolic dysfunctions (SLDAMD), psychophysiological characteristics, quality of life (QoL), depression, anxiety, asthenia, amino acids (AAs).

The purpose of the work: to identify the psychophysiological characteristics of the health status of individuals with chronic hepatopathies and to clarify the influence of liver pathology on their psychophysiological state.

Objectives: 1) to establish the specifics of the physiological status in individuals with mild forms of chronic hepatopathies using clinical, laboratory, and instrumental methods; to characterise clinical and paraclinical findings, serological markers of viral hepatitis, serum metabolism of free amino acids, Kerdo autonomic index, and indicators of protein, carbohydrate, and lipid metabolism; 2) to determine parameters that characterize the quality of life of individuals with chronic hepatopathies; 3) to identify the most typical indicators of psychological dissonance in individuals with mild forms of chronic hepatopathies; 4) to study biochemical indicators and the spectrum of free amino acids, including neurotransmitter and other metabolites, in individuals with chronic hepatopathies; 5) to conduct a corelation analysis of emotional and asthenic components and quality of life indicators with biochemical data and serum amino acid concentrations in individuals with chronic hepatopathies; 6) to develop a method for collecting information on psycho-emotional status and a set of psychometric tests that improve the diagnosis of psychophysiological conditions in individuals with chronic hepatopathies.

Scientific Novelty and Originality. This research demonstrates that psychophysiological disorders of health in individuals with CHPs are influenced by the semantics of the diagnosis, imbalances in free AAs, carbohydrate, and lipid metabolism indices, leading to a deterioration in overall condition of a person. New data on changes in the spectrum and levels of neurotransmitter AAs in individuals with CHPs have been obtained. A corelation analysis was performed between emotional components, QoL, physiological and metabolic parameters, and AAs levels in CHPs. The study presents a new, integrated perspective on the relationship between psychophysiological, metabolic, and somatic health factors.

The results obtained by the author contribute to the solution of an important scientific problem. Revealing physiological and psychoemotional interrelationships in people with chronic liver diseases caused by viral and metabolic etiology, using physiological, psychometric, biochemical, clinical and routine paraclinical methods in order to determine specific characteristics for these pathologies.

Theoretical Significance. The findings deepen and expand the scientific understanding of dyssanogeny in individuals body with CHPs, the psychophysiological aspects of health in relation to CNS-liver interactions, the impact of CHPs on QoL, and the relationships between metabolic indicators, neurotransmitter AAs levels, and psychophysiological status.

Practical Significance. A comprehensive methodology for studying the mental health of individuals with CHP has been developed. Psychophysiological characteristics of reactions to chronic stress have been identified. These findings may serve as a basis for improving the QoL of individuals with CHPs.

Implementation of Scientific Results. The dissertation results have been implemented at the Laboratory of Gastroenterology at the Nicolae Testemitanu State University of Medicine and Pharmacy. Received: 3 certificates of implementation of results and 5 copyright certificates.

BEREZOVSCAIA ELENA

PSYCHOPHYSIOLOGICAL CHARACTERISTICS OF THE HEALTH STATUS OF INDIVIDUALS WITH CHRONIC HEPATOPATHIES

165.01 HUMAN AND ANIMAL PHYSIOLOGY

Summary of the doctoral thesis in biological sciences

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