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Neurophysiological and microbiome-associated factors influencing the outcomes of physical therapy in patients with chronic pain and depressive symptoms

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Нейрофізіологічні та мікробіом-асоційовані фактори, що впливають на результати фізичної терапії у пацієнтів із хронічним болем і депресивними симптомами

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Introduction

Chronic pain is one of the leading causes of reduced quality of life and functional capacity of the population worldwide. According to modern epidemiological studies, its prevalence reaches 20–30 % among the adult population, and a significant proportion of patients have concomitant psycho-emotional disorders, in particular depressive and anxiety symptoms [1]. Comorbidity of chronic pain and depression is considered not only as a clinical coexistence, but also as a mutually reinforcing pathophysiological process, which significantly complicates the course of the disease and reduces the effectiveness of rehabilitation interventions.

In the context of modern science, chronic pain is a multifactorial phenomenon that encompasses numerous biological, psychological and social factors contributing to this pain syndrome [2]. Particular attention is drawn to the role of central sensitization, which is characterized by increased excitability of neurons of the central nervous system and is associated with hypersensitivity to painful and non-painful stimuli. It has been proven that patients with signs of central sensitization demonstrate worse results of physical therapy, higher levels of pain catastrophizing and more pronounced levels of depression and anxiety [3].

In addition to neurophysiological mechanisms, the role of the gut-brain axis, which provides a bidirectional interaction between the central nervous system and the intestinal microbiome, has been actively investigated in recent years. Disturbances in the composition of the intestinal microbiota are associated with the development of systemic inflammation, changes in neurotransmitter balance and increased sensitivity to pain. In addition, the microbiome may serve as a key modulator of the gut-brain axis due to its significant participation in the regulation of depression through immune, neural and endocrine pathways [4].

Lifestyle factors, such as nutrition, physical activity, sleep quality, and stress levels, are important modifiers of both neurophysiological processes and the state of the intestinal microbiome. In particular, unbalanced nutrition, frequent use of antibiotics, and low levels of physical activity can negatively affect the microbiome and indirectly change the perception of pain and the adaptive capabilities of the body. At the same time, the microbiota regulates pain sensations by changing the structures and functions of the brain [5].

Despite the growing number of studies, most of them analyze separate aspects – either the neurophysiological mechanisms of pain, or the psychoemotional state, or the microbiome. At the same time, an integrative approach that combines these components in the context of the effectiveness of physical therapy remains underdeveloped, especially in clinical practice.

In this regard, it is relevant to study the complex influence of neurophysiological and microbiome-associated factors on the results of physical therapy in patients with chronic pain and depressive symptoms. The use of structured assessment tools that cover pain, psychoemotional state, manifestations of central sensitization, behavioral characteristics and indirect markers of microbiome status may contribute to a better understanding of individual differences in response to therapy.

The aim of the study is to assess the influence of neurophysiological and microbiome-associated factors on the outcomes of physical therapy in patients with chronic pain and depressive symptoms based on a comprehensive questionnaire.

Object, materials and research methods

The study was conducted at the Physical Therapy and Rehabilitation Center in Dnipro (Ukraine) in the period 2024–2025. The subjects of the study were patients with chronic pain syndrome of various localization, accompanied by depressive symptoms, who underwent a course of physical therapy. The study involved persons aged 21 years and older with pain duration of more than three months. A mandatory condition for inclusion was the presence of signs of a depressive state according to the survey results, as well as written informed consent to participate. Exclusion criteria included acute inflammatory or infectious diseases, severe mental disorders, oncological diseases in the active phase, as well as the inability to independently fill out the questionnaire.

86 patients with chronic pain syndrome participated in the study, among whom women predominated (62.8 %), which is consistent with modern epidemiological data on the greater prevalence of chronic pain among the female population. The average age of the subjects was 38.7 ± 11.3 years, which indicates that the majority of the subjects were of working age. In most patients, the duration of pain exceeded one year (58.1 %), which indicates the established chronic course of the pathological process and the potential involvement of central pain regulation mechanisms.

Participants were selected sequentially among patients who sought help and met the inclusion criteria. The sample size was determined based on the availability of patients. A total of 108 subjects were examined, of whom 24 did not meet the inclusion criteria or refused to participate. No participant losses were recorded during the study.

The study had an observational analytical design with a prospective component and was carried out taking into account the recommendations of the STROBE Initiative (Strengthening the Reporting of Observational Studies in Epidemiology). The assessment of indicators was carried out twice: before the start of the physical therapy course and after its completion, which made it possible to assess the dynamics of clinical and psychophysiological changes, as well as to identify factors associated with the effectiveness of the intervention.

Patients underwent a physical therapy course that had a standardized structure with individual adaptation in accordance with the biopsychosocial model. The program included: therapeutic exercises; functional training; elements of manual therapy; educational interventions; recommendations for physical activity and lifestyle; correction of behavioral factors (sleep, stress level, motor activity). The duration of the course was 6 weeks with a frequency of 3 times a week.

A structured questionnaire developed on the basis of validated psychometric instruments widely used in clinical and scientific research was used to collect data. In particular, approaches based on the VAS (Visual Analog Scale) [6; 7] and the Brief Pain Inventory (BPI) [8] were used to assess pain intensity and its impact on daily activities. Psychoemotional state was assessed using adapted questions based on the PHQ-9 (Patient Health Questionnaire-9) [9] and GAD-7 (Generalized Anxiety Disorder-7) [10], which allowed determining the severity of depressive and anxiety symptoms.

Neurophysiological features, including central sensitization and cognitive-emotional aspects of pain perception, were assessed using items from the Central Sensitization Inventory (CSI) [11] and Pain Catastrophizing Scale (PCS) [12]. Sleep quality and stress levels were assessed using adapted approaches based on the Pittsburgh Sleep Quality Index (PSQI) [13] and Perceived Stress Scale (PSS) [14], respectively. Physical activity levels and behavioral responses related to fear of movement were assessed using the International Physical Activity Questionnaire (IPAQ) [15] and Tampa Scale for Kinesiophobia (TSK) [16].

An indirect approach was used to assess microbiome-associated factors, including gastrointestinal symptoms, dietary habits, and medication history. In particular, the questionnaire included questions on the frequency of bloating, abdominal pain and stool disorders, as well as on the regularity of consumption of foods rich in fiber and ultra-processed foods. Nutritional assessment was based on the principles of the Food Frequency Questionnaire (FFQ) [17]. In addition, the fact of taking antibiotics in the past six months was taken into account as an important factor that may affect the state of the intestinal microbiome.

The effectiveness of physical therapy was assessed using subjective indicators, including changes in pain intensity, the degree of functional improvement and the patient's overall assessment of the results of treatment, as well as the level of compliance with the recommended program.

Statistical processing of the obtained data was carried out using descriptive and analytical statistics methods. Mean values (M) and standard deviations (SD) were used to summarize the data. Normality of distribution was checked using the Shapiro-Wilk test. Correlation analysis using Spearman's coefficient was used to assess the relationships between variables. Multiple regression analysis was used to determine independent predictors of the effectiveness of physical therapy. Comparison of indicators before and after the intervention was carried out using the paired Student's t-test. Cohen's d was used to assess the effect size of changes in indicators before and after the course of physical therapy, which allowed assessing the clinical significance of the results obtained. The effect size was interpreted according to standard criteria: $d = 0.2$ – small effect, $d = 0.5$ – medium effect, $d \geq 0.8$ – large effect. The level of statistical significance was set at $p < 0.05$.

The study was conducted in compliance with the ethical principles of biomedical research in accordance with the provisions of the World Medical Association Declaration of Helsinki (WMA Declaration of Helsinki) [18]. All participants provided voluntary informed consent to participate, and confidentiality of personal data was ensured at all stages of the study.

Research results

The study involved 86 patients with chronic pain syndrome of various localization, including: women – 54 people (62.8 %), and men – 32 people (37.2 %). This distribution is consistent with modern epidemiological data on the higher prevalence of chronic pain among the female population. The average age of the studied was 38.7 ± 11.3 years, which indicates the involvement of mainly working-age people. Analysis of the duration of the pain syndrome showed that in the majority of the studied patients (58.1 %), the pain lasted for more than one year, which indicates the established chronic course of the pathological process with the probable involvement of central sensitization mechanisms. The initial assessment of pain intensity, carried out using a visual analog scale (VAS), showed an average value of 6.8 ± 1.5 points, which corresponds to a moderately high level of pain. The obtained data indicate not only the significant severity of the pain syndrome, but also its potential impact on the functional state of patients. The assessment of the functional impact of pain, carried out using the BPI scale, confirmed that the pain syndrome significantly limits the daily activity and quality of life of the subjects.

The psychoemotional state of the subjects before the course of physical therapy was characterized by a high level of stress: according to the PSS scale, 55.8 % of the subjects had indicators corresponding to a high level of stress. In addition, according to the results of the assessment of sleep quality using the PSQI, sleep disorders were detected in 60.5 % of patients.

The totality of the obtained data indicates that the studied sample before physiotherapy intervention is characterized not only by a pronounced chronic pain syndrome, but also by a significant involvement of psychoemotional and behavioral factors that potentially affect the course of the disease and the effectiveness of physiotherapy interventions (Table 1).

Table 1

Characteristics of the study sample of patients with chronic pain, (*M* ± SD, 86)

Indicator	Value
Age (years)	38,7 ± 11,3
Women, n (%)	54 (62,8 %)
Men, n (%)	32 (37,2 %)
Pain duration >1 year, n (%)	50 (58,1 %)
Average pain level (VAS, 0–10), (points)	6,8 ± 1,5
High stress level (≥7/10), n (%)	48 (55,8 %)
Sleep disturbances (≤5/10), n (%)	52 (60,5 %)

Analysis of the psycho-emotional state of patients before the start of physical therapy showed the presence of moderately pronounced depressive symptoms. The average score on the Patient Health Questionnaire-9 scale was 7.9 ± 2.6 points, which corresponds to a clinically significant level of depressive manifestations. The level of anxiety on the GAD-7 scale was elevated – 6.1 ± 2.1 points, which indicates the presence of combined psycho-emotional stress in most of the examined. Assessment of neurophysiological characteristics revealed signs of increased central excitability of the nervous system. In particular, the average level of central sensitization on the CSI scale was 11.4 ± 3.8 points, which indicates the involvement of mechanisms of central pain regulation.

The indicators of pain catastrophizing on the PCS scale – 9.2 ± 3.1 points and kinesiophobia on the TSK – 5.3 ± 1.9 points indicate a significant role of cognitive-emotional and behavioral factors in shaping the pain experience of patients. The totality of the obtained data demonstrates that chronic pain in the studied sample has not only a peripheral, but also a pronounced central and psychoemotional component, which is consistent with the modern concept of central sensitization (Table 2).

Table 2

Psychoemotional and neurophysiological indicators of patients before the start of physical therapy (*M* ± *SD*, 86)

Indicator	Value (points)
Depressive symptoms (PHQ-9), (0–12)	7,9 ± 2,6
Anxiety (GAD-7), (0–9)	6,1 ± 2,1
Central sensitization (CSI), (0–20)	11,4 ± 3,8
Pain catastrophizing (PSC), (0–16)	9,2 ± 3,1
Kinesiophobia (TSK), (0–8)	5,3 ± 1,9

It is noteworthy that more than two-thirds of patients demonstrated increased central sensitization and pain catastrophizing. This may indicate the formation of persistent pathological patterns of pain information processing, which limit the effectiveness of standard rehabilitation approaches.

Analysis of microbiome-associated factors in patients before the start of physical therapy revealed a high prevalence of gastrointestinal symptoms, which may indicate the presence of functional disorders of the gastrointestinal tract. In particular, frequent bloating was noted in 57.0 % of the examined, while stool disorders were observed in 47.7 % of patients. Abdominal pain was characteristic of 44.2 % of the study participants.

The identified symptoms indicate a significant involvement of the gastrointestinal system in the clinical picture of patients with chronic pain syndrome and may indirectly reflect a violation of the functional state of the intestinal microbiome.

Analysis of dietary habits showed that most patients had an unfavorable diet: low fiber intake was noted in 61.6 % of the examined, and frequent consumption of ultra-processed food – in 53.5 %. It is known that such dietary features are associated with a decrease in microbial diversity and imbalance of the intestinal microbiota.

In addition, 33.7 % of patients reported taking antibiotics within the last six months, which is an additional risk factor for microbiome disruption and may affect metabolic and immune processes.

The totality of the obtained data indicates a high prevalence of factors potentially associated with dysbiotic changes in the studied sample. Given the role of the gut-brain axis, such disorders may be associated with both the maintenance of chronic pain and the formation of psychoemotional disorders, which emphasizes the need for a comprehensive approach to physical therapy of this category of patients (Table 3).

Table 3

Microbiome-associated factors in patients before the start of physical therapy (n = 86)

Indicator	n (%)
Frequent bloating	49 (57,0 %)
Abdominal pain	38 (44,2 %)
Improper bowel habits	41 (47,7 %)
Low fiber intake	53 (61,6 %)
Frequent consumption of ultra-processed foods	46 (53,5 %)
Antibiotic use (≤6 months)	29 (33,7 %)

After completing the course of physical therapy, a statistically significant improvement in all main clinical and psycho-emotional indicators was established. The most pronounced positive dynamics were observed in the intensity of the pain syndrome and its impact on daily activity.

The intensity of pain on the visual analogue scale significantly decreased from 6.8 ± 1.5 to 4.2 ± 1.3 points ($p < 0.001$). The absolute decrease was 2.6 points, which corresponds to a decrease of 38.2 %. The effect size according to Cohen's coefficient was very high ($d = 1.85$), which indicates not only the statistical, but also the clinically significant effectiveness of the course of physical therapy.

The impact of pain on daily activity also significantly decreased: the indicator decreased to 3.9 ± 1.5 points ($p < 0.001$). The absolute difference was 2.4 points, or 38.1 %. The effect size was large ($d = 1.50$), indicating a significant improvement in the functional state of patients after therapeutic intervention.

Positive changes were also recorded in terms of psychoemotional state. The level of depressive symptoms decreased to 5.1 ± 2.2 points ($p < 0.01$), which corresponds to a decrease of 35.4 %. The value of Cohen's $d = 1.16$ indicates a large effect size and confirms the influence of physical therapy not only on somatic, but also on psychoemotional components of chronic pain syndrome.

The level of stress after a course of physical therapy decreased by 23.9 % improvement. The effect size also corresponded to a large level ($d = 1.00$), indicating a decrease in psychophysiological stress in patients.

It should be noted separately that sleep quality improved by 44.2 %, and the effect size was large ($d = 1.05$). This indicates a positive effect of physical therapy on the recovery processes and the general psychophysiological state of patients.

Thus, the results obtained demonstrate the complex effect of physical therapy in patients with chronic pain syndrome and depressive symptoms. The improvement included not only a decrease in pain intensity, but also a decrease in its functional impact, improvement of the psychoemotional state, reduction of stress load and normalization of sleep quality. High values of the Cohen coefficient confirm the clinical significance of the changes obtained (Table 4).

Correlation analysis revealed statistically significant relationships between baseline clinical characteristics of patients and the effectiveness of physical therapy, as assessed by the degree of reduction in pain intensity.

In particular, moderate negative correlations were found between the level of central sensitization ($r = –0.52$; $p < 0.01$), pain catastrophizing ($r = –0.48$; $p < 0.01$), and depressive symptoms ($r = –0.44$; $p < 0.01$) and treatment effectiveness. This indicates that higher levels of neurophysiological and psychoemotional stress are associated with less pronounced reduction in pain intensity after therapy.

Kinesiophobia also demonstrated a statistically significant, although less pronounced negative relationship with treatment outcomes ($r = –0.39$; $p < 0.05$), which emphasizes the role of behavioral factors related to fear of movement in shaping the response to therapeutic interventions.

Instead, sleep quality indicators ($r = 0.41$; $p < 0.01$) and physical activity level ($r = 0.36$; $p < 0.05$) had a positive correlation with the effectiveness of treatment. This indicates that a better functional state of the body and a more active lifestyle are associated with a more pronounced therapeutic effect.

The results obtained demonstrate that the effectiveness of physical therapy in patients with chronic pain syndrome is determined by the complex interaction of neurophysiological, psychoemotional and behavioral factors.

At the same time, microbiome-associated characteristics in this study were considered as potential modifying factors of the course of the disease, however, their direct relationship with the effectiveness of therapy requires further research (Table 5).

Table 4

Dynamics of clinical and psycho-emotional indicators before and after a course of physical therapy (n = 86)

Indicator	Before therapy, $M \pm SD$	After therapy, $M \pm SD$	Δ	Change, %	p	Cohen's d
Pain (VAS), (0–10)	6,8 ± 1,5	4,2 ± 1,3	–2,6	–38,2	<0,001	1,85
Pain Impact on Activity (BPI), (0–10)	6,3 ± 1,7	3,9 ± 1,5	–2,4	–38,1	<0,001	1,50
Depressive Symptoms (PHQ-9)	7,9 ± 2,6	5,1 ± 2,2	–2,8	–35,4	<0,01	1,16
Stress (PSS), (0–10)	7,1 ± 1,8	5,4 ± 1,6	–1,7	–23,9	<0,01	1,00
Sleep Quality (PSQI), (0–10)	4,3 ± 1,9	6,2 ± 1,7	+1,9	+44,2	<0,01	1,05

Table 5

Correlations between baseline indicators and the effectiveness of physical therapy (n = 86)

Indicator	r	p
Central sensitization	–0,52	<0,01
Pain catastrophizing	–0,48	<0,01
Depressive symptoms	–0,44	<0,01
Kinesiophobia	–0,39	<0,05
Sleep quality	0,41	<0,01
Physical activity level	0,36	<0,05

Thus, the results of the study highlighted the multifactorial nature of chronic pain syndrome and demonstrated the significant role of neurophysiological, psychoemotional and behavioral factors in shaping the response to physical therapy. The revealed patterns indicate a close relationship between the reduction of pain intensity, improvement of psychoemotional state and functional indicators.

Discussion of research results

The results obtained confirm the multifactorial nature of chronic pain and its response to physical therapy, which is consistent with the modern biopsychosocial model [2; 19]. The revealed decrease in pain intensity, improvement in functional status, sleep quality and psychoemotional indicators after a course of physical therapy indicates its complex effect not only on somatic, but also on neuropsychological mechanisms.

At the same time, the results of correlation analysis demonstrate that the effectiveness of therapy is largely modulated by the initial characteristics of patients. In particular, the established negative relationship between the level of central sensitization and pain reduction confirms the key role of central regulation mechanisms in maintaining chronic pain syndrome. It is known that with central sensitization, the sensitivity of neurons of the central nervous system increases, which leads to increased pain sensations even when the intensity of peripheral stimulation is insufficient to cause pain sensations in healthy people [20]. As noted by A. González-de-la-Flor et. al [21], chronic pain associated with central sensitization is characterized by increased excitability and a reduced pain threshold, which may hinder rehabilitation efforts.

Similar patterns have been found for pain catastrophizing and depressive symptoms. Patients with more severe cognitive-emotional impairments have shown worse treatment outcomes, which is consistent with the data of numerous studies indicating the influence of negative expectations, anxiety, and depression on pain perception and adaptive capacity of the body [22]. Pain catastrophizing can increase attention to pain sensations, form unique behaviors, and reduce adherence to therapy, which generally limits its effectiveness [23].

An important result is the established relationship between kinesiophobia and physical therapy outcomes. Fear of movement is one of the key behavioral factors that limit patients' activity and contribute to the chronicity of pain [24; 25]. The identified negative correlation confirms the need to include educational and cognitive-behavioral components in physical therapy programs.

The positive association between sleep quality, physical activity level, and treatment effectiveness emphasizes the role of behavioral and restorative mechanisms. Sleep disturbance is known to affect neuroendocrine regulation, increase inflammation, and lower pain threshold, which can complicate the course of chronic pain. At the same time, regular physical activity contributes to the normalization of the functioning of the nervous system, improve mood, and reduce pain intensity.

Microbiome-associated factors deserve special attention. Changes in the gut microbiota are known to be associated with the use of antibiotics, food preservatives, diet, and improved living standards and hygiene [26]. Antibiotic use depletes resident microbes, and early exposure to antibiotic therapy leads to long-term immune dysregulation and visceral hypersensitivity [27].

The high prevalence of gastrointestinal symptoms, low fiber intake, and frequent consumption of ultra-processed foods in the study sample suggest potential disruptions in the composition of the gut microbiota. There is a complex bidirectional communication system between the gut microbiota and the brain, known as the microbiota-gut-brain axis (MGBA) [28]. In the context of the gut-brain axis, such changes in the composition of the gut microbiota may affect the central nervous system through endocrine, immune, and neural mechanisms [29]. Recent animal experiments have further confirmed that germ-free mice exhibit "depressive" behavior after transplantation of fecal microbiota from patients with major depressive disorder [30], suggesting that gut microbiota dysbiosis is not just a concomitant phenomenon but also one of the key driving factors of the disease. In particular, dysbiosis may contribute to increased systemic inflammation, which, in turn, is associated with increased pain and the development of depressive symptoms.

Although the microbiome assessment in this study was conducted indirectly, the results obtained are consistent with current ideas about the role of the gut microbiota in the formation of pain and psychoemotional disorders [31; 32]. This opens up prospects for further studies using direct methods of microbiome analysis and assessment of their impact on rehabilitation outcomes.

Thus, the results of the study confirm that an isolated approach to the treatment of chronic pain is insufficient. Effective physical therapy should take into account not only local somatic factors, but also neurophysiological mechanisms, psychoemotional state and behavioral characteristics of the patient. In addition, the integration of approaches aimed at modifying lifestyle and maintaining a healthy microbiome is promising as a potential factor in increasing the effectiveness of treatment.

Among the limitations of the study, it should be noted the use of indirect indicators to assess the state of the microbiome, as well as a relatively small sample size. In addition, the use of shortened versions of psychometric

scales may affect the accuracy of measurements. In further studies, it is advisable to envisage the use of laboratory methods of microbiome analysis, larger samples and long-term observation of patients.

Overall, the results of the study expand the understanding of the mechanisms of response formation to physical therapy and emphasize the need for an individualized, multidisciplinary approach to the management of patients with chronic pain and depressive symptoms.

Prospects for further research

The results obtained outline several key directions for further research. First of all, it is advisable to use metagenomic sequencing to further analyze the role of the intestinal microbiome and the gut-brain axis in the formation of chronic pain and the response to therapy. An important direction remains the study of neurophysiological mechanisms, in particular the processes of central sensitization, using objective instrumental methods of assessment and the development of multidisciplinary approaches that combine physical therapy with psychological and nutritional interventions.

Conclusions

The results obtained indicate that patients with chronic pain syndrome, accompanied by depressive symptoms, develop a complex clinical condition characterized by high pain intensity, pronounced psychoemotional disorders and signs of central sensitization. This confirms the multifactorial nature of chronic pain and its close connection with neurophysiological and psychological mechanisms of regulation.

The course of physical therapy was associated with a statistically significant improvement in the main clinical indicators. In particular, a decrease in pain intensity and its impact on daily activity, improved sleep quality, as well as a decrease in the level of depressive and stressful manifestations were noted. This indicates a complex effect of physical therapy, which covers both somatic and psychoemotional components of the patients' condition.

It was found that a higher initial level of central sensitization, pain catastrophizing and depressive symptoms is associated with a less pronounced response to therapy. In contrast, higher levels of physical activity and better sleep quality are associated with more favorable treatment outcomes. This emphasizes the need to consider individual neurophysiological and behavioral characteristics of patients when planning rehabilitation programs.

Signs of microbiome-associated disorders, assessed indirectly through gastrointestinal symptoms, dietary habits, and antibiotic use, can be considered as potential modifying factors in the course of chronic pain syndrome. Although these results do not allow direct conclusions to be drawn regarding the state of the intestinal microbiome, they are consistent with current ideas about the role of the gut-brain axis in the regulation of pain and psychoemotional state.

Overall, the results of the study confirm the feasibility of using a comprehensive biopsychosocial approach in physical therapy of patients with chronic pain and concomitant depressive symptoms, as well as the need to consider neurophysiological, psychological, and potentially microbiome-associated factors to improve treatment effectiveness.

Bibliography

1. Aaron RV, Ravyts SG, Carnahan ND, Bhattiprolu K, Harte N, McCaulley CC, et al. Prevalence of Depression and Anxiety Among Adults With Chronic Pain. A Systematic Review and Meta-Analysis. JAMA Network Open. 2025;8(3):e250268. DOI: 10.1001/jamanetworkopen.2025.0268

2. Kovačević I, Pavić J, Filipović B, Vulinec SO, Ilić B, Petek D. Integrated Approach to Chronic Pain – The Role of Psychosocial Factors and Multidisciplinary Treatment: A Narrative Review. International Journal of Environmental Research and Public Health. 2024;21(9):1135. DOI: 10.3390/ijerph21091135

3. Özkan DU, Polat M. Does the predominance of central sensitization alter the effect of balneotherapy combined with conventional physical therapy in patients with chronic low back and knee pain? International Journal of Biometeorology. 2026;70(3):75. DOI: 10.1007/s00484-026-03157-w

4. Yao M, Qu Y, Zheng Y, Guo H. The effect of exercise on depression and gut microbiota: Possible mechanisms. Brain Research Bulletin. 2025;220:111130. DOI: 10.1016/j.brainresbull.2024.111130

5. Ren H, Cao B, Xu Q, Zhao R, Li H, Wei B. Role of microbiota in pain: From bench to bedside. iMetaOmics. 2025;2(1):e58. DOI: 10.1002/imo2.58

6. Hayes MHS, Patterson DG. Experimental development of the graphic rating method. Psychological Bulletin. 1921;18:98–99

7. Pilowsky I, Kaufman A. An experimental study of atypical phantom pain. The British Journal of Psychiatry. 1965;111(481):1185–1187. DOI: 10.1192/bjp.111.481.1185

8. Cleeland CS, Ryan KM. Pain assessment: Global use of the Brief Pain Inventory. Annals of the Academy of Medicine of Singapore. 1994;23(2):129–138. https://pubmed.ncbi.nlm.nih.gov/8080219/

9. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. Journal of General Internal Medicine. 2001;16(9):606–613. DOI: 10.1046/j.1525-1497.2001.016009606.x

10. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Archives of Internal Medicine. 2006;166(10):1092–1097. DOI: 10.1001/archinte.166.10.1092

11.Neblett R. The central sensitization inventory: A user's manual. Journal of Applied Biobehavioral Research. 2018;23(2):e12123. DOI: 10.1111/jabr.12123

12. Sullivan M, Bishop S, Pivik J. The Pain Catastrophizing Scale: Development and validation. Psychological Assessment. 1995;7(4), 524–532. https://www.researchgate.net/publication/232599723_The_Pain_Catastrophizing_Scale_Development_and_validation DOI: 10.1037/1040–3590.7.4.524

13. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Research. 1989;28(2):193–213. DOI: 10.1016/0165-1781(89)90047-4

14. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. Journal of Health and Social Behavior. 1983;24(4):385–396. DOI: 10.2307/2136404

15. IPAQ Core Group. Guidelines for data processing and analysis of IPAQ – short and long forms. 2005:1–15, https://drive.google.com/file/d/1gehdq1-04eSWfbxscwtzXa1MUlD8Mffa/view

16. Miller RP, Kori SH, Todd DD. The Tampa Scale a Measure of Kinisophobia. The Clinical Journal of Pain. 1991;7(1):51. DOI :10.1097/00002508-199103000-00053

17. Bingham SA, Welch AA, McTaggart A, Mulligan AA, Runswick SA, Luben R, et al. Nutritional methods in the European Prospective Investigation of Cancer in Norfolk. Public Health Nutrition. 2001;4(3):847–858. DOI: 10.1079/phn2000102

18. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. JAMA. 2013;310(20):2191–2194. DOI: 10.1001/jama.2013.281053

19. Engel GL. The need for a new medical model: a challenge for biomedicine. Science. 1977;196(4286):129–136. DOI: 10.1126/science.847460

20. Hladkykh FV, Liadova TI, Matvieienko MS, Komorovsky R, Smiyan S, Student V. Central Sensitization and Nociplastic Pain: Shared Mechanisms in Fibromyalgia, Osteoarthritis, and Inflammatory Arthritis. Journal of Pain Research. 2026;19:571311. DOI: 10.2147/JPR.S571311

21. González-de-la-Flor A, Bravo-Aguilar M, Almazán-Polo J, García-Pérez-de-Sevilla G, Martínez-Lozano P, Romero-Morales C. Exploring the Multifactorial Predictors of Pain in Chronic Musculoskeletal Pain: A Regression-Based Study. Journal of Pain Research. 2025;18:2081–2091. DOI: 10.2147/JPR.S500636

22. Glette M, Stiles TC, Jensen MP, Nilsen TIL, Borchgrevink PC, Landmark T. Impact of pain and catastrophizing on the long-term course of depression in the general population: the HUNT pain study. Pain. 2021;162(6):1650–1658. DOI: 10.1097/j.pain.0000000000002168

23. Simic K, Savic B, Knezevic NN. Pain Catastrophizing: How Far Have We Come. Neurology International. 2024;16(3):483–501. DOI: 10.3390/neurolint16030036

24. Sgourda S, Loulla M, Zisiopoulou E, Katsiou K, Nikolaidi S, Kyrosis I, et. al. Examination of the Relationship Between Pain Intensity, Pain Perceptions, and Kinesiophobia in Patients with Non-Specific Chronic Musculoskeletal Pain. Muscles. 2025;4(3):27. DOI: https://doi.org/10.3390/muscles4030027

25. Wlazło M, Szlacheta P, Grajek M, Staśkiewicz-Bartecka W, Rozmiarek M, Malchrowicz-Mośko E, et al. he Impact of Kinesiophobia on Physical Activity and Quality of Life in Patients with Chronic Diseases: A Systematic Literature Review. Applied Sciences. 2025;15(4):2086; DOI: https://doi.org/10.3390/app15042086

26. Fan Y, Pedersen O. Gut microbiota in human metabolic health and disease. Nature Reviews Microbiology. 2021;19(1):55–71. DOI: 10.1038/s41579-020-0433-9

27. Kumari R, Yadav Y, Misra R, Das U, Das Adhikari U, Malakar P, et al. Emerging frontiers of antibiotics use and their impacts on the human gut microbiome. Microbiological Research. 2022;263:127127. DOI: 10.1016/j.micres.2022.127127

28. Bhatt S, Kanoujia J, Mohana Lakshmi S, Patil CR, Gupta G, Chellappan DK, et al. Role of brain-gut-microbiota axis in depression: emerging the-rapeutic avenues. CNS & Neurological Disorders – Drug Targets. 2023;22(2):276–288. DOI: 10.2174/1871527321666220329140804

29. Fülling C, Dinan TG, Cryan JF. Gut Microbe to Brain Signaling: What Happens in Vagus…. Neuron. 2019;101(6):998–1002. DOI: 10.1016/j.neuron.2019.02.008.

30.Cao Y, Fan X, Zang T, Qiu T, Fang Q, Bai J, et al. Prenatal depression-associated gut microbiota induces depressive-like behaviors and hippocampal neuroinflammation in germ-free mice. ranslational Psychiatry. 2025;15(1):383. DOI: 10.1038/s41398-025-03606-x

31. Garvey M. The Association between Dysbiosis and Neurological Conditions Often Manifesting with Chronic Pain. Biomedicines. 2023;11(3):748. DOI: 10.3390/biomedicines11030748

32. Su Y, Xia Y. Gut microbiota dysbiosis and depression: Bidirectional interactions, mediating pathways, and microecological therapeutics. Current Research in Food Science. 2026;12:101372. DOI: 10.1016/j.crfs.2026.101372

Purpose: to assess the impact of neurophysiological and microbiome-associated factors on the outcomes of physical therapy in patients with chronic pain and depressive symptoms.

Materials and methods. The study included 86 patients with chronic pain syndrome lasting more than 3 months and depressive symptoms. The study had an observational analytical prospective design with an assessment of indicators before and after a course of physical therapy. Adult patients of both sexes were involved. A structured questionnaire based on validated scales was used: VAS, BPI, PHQ-9, GAD-7, CSI, PCS, PSQI, PSS, IPAQ, TSK. Microbiome-associated factors were assessed indirectly (gastrointestinal symptoms, dietary habits, antibiotic use). Statistical analysis included correlation and multiple regression analysis; the level of statistical significance was set at $p < 0.05$. The study complied with the ethical principles of the Declaration of Helsinki.

Results. After the course of physical therapy, a statistically significant decrease in pain intensity (by 38 %), a decrease in depressive symptoms and stress, and an improvement in sleep quality were observed. It was found that higher rates of central sensitization, pain catastrophizing, and depressive symptoms were associated with a less pronounced effect of therapy ($r = -0.39 - -0.52$; $p < 0.05$). In contrast, a higher level of physical activity and better sleep quality were associated with a more favorable response to treatment. An improvement in functional activity was also noted in all main indicators.

Conclusions. The effectiveness of physical therapy in patients with chronic pain is determined by the complex interaction of neurophysiological, psychoemotional, and behavioral factors, as well as potential microbiome-associated characteristics. The results obtained substantiate the need for an individualized biopsychosocial approach and can be used to optimize physical therapy programs.

Key words: chronic pain, depressive symptoms, physical therapy, central sensitization, microbiome, gut-brain axis, psychoemotional factors.

Мета. Метою дослідження було оцінити вплив нейрофізіологічних та мікробіом-асоційованих факторів на ефективність фізичної терапії у пацієнтів із хронічним больовим синдромом, що супроводжується депресивними симптомами. Актуальність роботи зумовлена високою поширеністю коморбідності хронічного болю та афективних розладів, що суттєво знижує якість життя, ускладнює реабілітаційний процес і підвищує ризик хронізації симптомів. Особлива увага приділялася ролі центральної сенситизації, психоемоційного стану, поведінкових характеристик та непрямих показників стану кишкового мікробіому як потенційних модифікуючих чинників результатів реабілітаційних утручань.

Матеріали і методи. Дослідження мало обсерваційний аналітичний дизайн із проспективним компонентом. У ньому взяли участь 86 пацієнтів віком від 21 року з хронічним больовим синдромом тривалістю понад три місяці та наявністю депресивних симптомів різного ступеня вираженості. Критеріями включення були стабільний клінічний стан та можливість участі у 6-тижневій програмі фізичної терапії; критерії виключення включали тяжкі психіатричні розлади, гострі соматичні стани та зміну фармакотерапії під час дослідження. Програма фізичної терапії включала терапевтичні вправи, функціональні тренування, мануальні техніки, освітні інтервенції та модифікацію способу життя. Оцінювання проводилося до та після втручання із застосуванням валідованих шкал: VAS і BPI – для оцінки болю, PHQ-9 та GAD-7 для психоемоційного стану, CSI та PCS – для оцінки центральної сенситизації та катастрофізації, PSQI та PSS – для якості сну і рівня стресу, IPAQ та TSK – для рівня фізичної активності та кінезіофобії. Мікробіом-асоційовані фактори визначалися опосередковано через аналіз гастроінтестинальних симптомів, харчових звичок (зокрема, споживання клітковини та ультрапереоблених продуктів) і анамнез антибіотикотерапії. Статистичний аналіз включає описову статистику, кореляційний і регресійний аналіз, парний t-критерій Стьюдента та оцінку величини ефекту за коефіцієнтом Коена.

Результати. До початку терапії пацієнти відзначали високу інтенсивність болю (6,8 ± 1,5 бала), значний вплив болю на підвищену активність, підвищений рівень стресу (55,8 %) і порушення сну (60,5 %). Виявлено більш виражені депресивні (7,9 ± 2,6 бала) та тривожні симптоми (6,1 ± 2,1 бала), а також ознаки центральної сенситизації (11,4 ± 3,8 бала). Значна частина пацієнтів демонструвала катастрофізацію болю та кінезіофобію. Аналіз непрямих мікробіом-асоційованих показників виявив високу частоту гастроінтестинальних скарг, недостатнє споживання харчових волокон, надмірне вживання ультрапереоблених продуктів і частий прийом антибіотиків. Після курсу фізичної терапії встановлено статистично значуще покращення всіх показників: інтенсивність болю знизилася на 38,2 %, вплив болю на активність – на 38,1 %, депресивні симптоми – на 35,4 %, рівень стресу – на 23,9 %, а якість сну покращилася на 44,2 % ($p < 0,01–0,001$). Величина ефекту була великою ($d = 1,00–1,85$), що підтверджує клінічну значущість змін. Кореляційний аналіз показав, що вищі рівні центральної сенситизації, катастрофізації болю, депресії та кінезіофобії пов'язані з менш вираженим зниженням болю, тоді як краща якість сну та вищий рівень фізичної активності асоціюються з більш ефективними результатами лікування.

Висновки. Хронічний больовий синдром у поєднанні з депресивними симптомами має комплексний мультифакторний характер, що включає нейрофізіологічні, психоемоційні та поведінкові компоненти. Фізична терапія є ефективним методом лікування, який забезпечує значне покращення інтенсивності болю, функціонального стану, психоемоційних показників і якості сну. Ефективність утручання залежить від індивідуальних характеристик пацієнтів: негативними предикторами є високий рівень центральної сенситизації, катастрофізація болю та депресії, тоді як позитивними – достатній рівень фізичної активності та якісний сон. Мікробіом-асоційовані порушення можуть розглядатися як додаткові фактори, що впливають на перебіг болю та загальний стан, підкреслюючи необхідність комплексного біопсихосоціального підходу до фізичної терапії.

Ключові слова: хронічний біль, депресивні симптоми, фізична терапія, центральна сенситизація, мікробіом, вісь «кишківник – мозок», психоемоційні фактори.

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