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THE INFLUENCE OF THE GUT MICROBIOME ON SYMPTOMS OF ANXIETY AND DEPRESSION

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Abstract

Background. The idea has evolved into what is known as the brain–gut–microbiota system—a more comprehensive framework that reflects the intricate interactions between the central nervous system, the endocrine signaling pathways, the immune system, gut microbes, metabolic processes, and the barrier functions of both the brain and the gut. The coordinated function of these systems is essential for maintaining overall health. When this balance is disrupted, it can contribute to a range of health issues, including mental health disorders such as depression.

Materials and methods. A total of 100 patients were selected. Inclusion and exclusion criteria were defined. The main group received a probiotic, the comparison group did not receive it. Non-parametric Mann–Whitney U tests were used for between-group analyses. The qualitative analysis was conducted by groups, anxiety and depression indicators were assessed in both groups, and frequencies were compared using the Pearson chi-square test.

Results. The results of the study confirm the fact of the influence of gut microbiota on mental health, specifically on the levels of anxiety and depression. The lack of correlation between the BAI and BDI scales and the GAD-7 and PHQ-9 require further research, probably the PHQ-9 and GAD-7 scales are more concise and less detailed than the BDI and BAI scales.

Conclusion. Extensive research has highlighted disturbances in intestinal microbiota and metabolites in depression. The potential benefits of probiotics, prebiotics, and psychobiotics in influencing brain function are indicated by both preclinical and clinical research.

Keywords: *gut microbiome, intestinal microbiota, brain–gut–microbiota axis, probiotics, prebiotics, psychobiotics, gut–brain interaction, mental health, anxiety, depression, mood disorders, gut dysbiosis.*

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Резюме

ВЛИЯНИЕ КИШЕЧНОГО МИКРОБИОМА НА СИМПТОМЫ ТРЕВОЖНОСТИ И ДЕПРЕССИИ

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Введение. Концепция «мозг-кишечник-микробиота» представляет собой целостную модель, учитывающую сложные взаимодействия между центральной нервной системой, эндокринной и иммунной системами, кишечной микробиотой, метаболическими процессами и барьерными функциями мозга и кишечника. Согласованная работа этих систем необходима для поддержания здоровья; её нарушение может способствовать развитию различных состояний, в том числе депрессивных расстройств.

Материалы и методы. В исследование было включено 100 пациентов. Были сформулированы критерии включения и исключения. Основная группа получала пробиотик; контрольная группа его не принимала. Для межгруппового анализа применялись непараметрические тесты Ман-Уитни (Mann–Whitney U). Качественный анализ проводился по группам, индикаторы тревоги и депрессии оценивались в обеих группах, частоты сравнивались с помощью критерия Пирсона (χ^2).

Результаты. Результаты исследования подтверждают факт влияния кишечной микробиоты на психическое здоровье, в частности на уровни тревоги и депрессии. Отсутствие корреляции между шкалами BAI и BDI и шкалами GAD-7 и PHQ-9 требует дальнейших исследований. Вероятно, шкалы PHQ-9 и GAD-7 являются более лаконичными и менее детализированными по сравнению с BDI и BAI.

Заключение. Обширные исследования подчеркивают нарушения кишечной микробиоты и метаболитов при депрессии. Применение пробиотиков, пребиотиков и психобиотиков потенциально может влиять на функции мозга, что доказано как доклиническими, так и клиническими исследованиями.

Ключевые слова: *Кишечный микробиом, кишечная микробиота, ось «мозг–кишечник–микробиота», пробиотики, пребиотики, психобиотики, взаимодействие кишечника и мозга, психическое здоровье, тревожность, депрессия, аффективные расстройства, дисбиоз кишечника.*

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Түйіндеме

ІШЕК МИКРОБИОМЫНЫҢ ҮРЕЙ ЖӘНЕ ДЕПРЕССИЯ БЕЛГІЛЕРІНЕ ӘСКРІ

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Кіріспе. «Ми–ішек–микробиота» тұжырымдамасы орталық жүйке жүйесі, эндокриндік және иммундық жүйелер, ішек микробиотасы, метаболикалық үдерістер мен ми және ішек тосқауылдық функциялары арасындағы күрделі өзара байланыстарды қамтитын тұтас модельді білдіреді. Бұл жүйелердің үйлесімді қызметі денсаулықты сақтауда маңызды рөл атқарады. Оның бұзылуы әртүрлі патологиялардың, соның ішінде депрессиялық бұзылыстардың дамуына ықпал етуі мүмкін.

Материалдар мен әдістер. Зерттеу барлығы 100 пациентті қамтыды. Қосылу және алынып тастау критерийлері анықталды. Негізгі топ пробиотик қабылдады, ал бақылау тобы қабылдамады. Топтар арасындағы айырмашылықтарды бағалау үшін Манн–Уитни (Mann–Whitney U) параметрлік емес тесттері қолданылды. Сапалық талдау топтар бойынша жүргізілді, мазасыздық пен депрессия көрсеткіштері екі топта да бағаланды, жиіліктер Пирсон (χ^2) критерийімен салыстырылды.

Нәтижелері. Зерттеу нәтижелері ішек микробиотасының психикалық денсаулыққа, атап айтқанда үрей мен депрессия деңгейлеріне әсер ететінін растайды. BAI және BDI шкалалары мен GAD-7 және PHQ-9 шкалалары арасындағы корреляцияның болмауы қосымша зерттеуді талап етеді. PHQ-9 және GAD-7 шкалалары BDI мен BAI-ға қарағанда қысқа және аз егжей-тегжейлі болып келуі мүмкін.

Қорытынды. Көптеген зерттеулерде депрессия кезінде ішек микробиотасы мен оның метаболиттерінің бұзылуы анықталған. Пребиотиктер, пробиотиктер және психобиотиктердің ми функциясына әсер ету және психикалық жағдайды жақсарту мүмкіндігі клиникаға дейінгі және клиникалық зерттеулерде дәлелденген.

Түйінді сөздер: *ішек микробиомы, ішек микробиотасы, «ми–ішек–микробиота» осі, пробиотиктер, пребиотиктер, психобиотиктер, ішек пен ми арасындағы өзара әрекеттесу, психикалық денсаулық, үрей, депрессия, аффективті бұзылыстар, ішек дисбиозы.*

Дәйексөз үшін:

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Introduction

The concept of the gut–brain axis was first introduced in 1980, following unexpected research findings that revealed how hormones produced by the gastrointestinal endocrine system could influence neurons and brain cells. In the decades since, this concept has been significantly expanded to include the role of the gut microbiome in the communication between the gut and the brain.

Today, the idea has evolved into what is known as the brain–gut–microbiota system—a more comprehensive framework that reflects the intricate interactions between the central nervous system (CNS), the endocrine signaling

pathways, the immune system, gut microbes, metabolic processes, and the barrier functions of both the brain and the gut.

The coordinated function of these systems is essential for maintaining overall health. When this balance is disrupted, it can contribute to a range of health issues, including mental health disorders such as depression [1,2,8].

Neural signal networks in the brain–gut–microbiota system are important and fast response routes, including the **enteric nervous system** (ENS), vagus nerves and spinal nerves. The ENS, which is also known as the "brain in the gut" or "second brain," controls the gut's external and internal environment. The complex regulation of the ENS serves a multifaceted role in modulating microbial composition, microbiota-related metabolites, **neurotransmitter** and immune signaling, and protection of the **intestinal barrier**. Thus, bidirectional communication between the CNS and ENS, as well as other signals, forms part of the network for the brain–gut–microbiota axis. The vagal pathway has been repeatedly identified as the most direct link for microflora signals to reach the brain. The vagus nerve plays a dual role in the body. On one hand, it helps regulate metabolic homeostasis and feeding behavior, including controlling gastrointestinal motility and secretion. On the other hand, it is actively involved in the body's inflammatory responses, linking the brain, gut, and other organs. Through its afferent and efferent pathways, the vagus nerve detects inflammatory cytokines via pattern recognition receptors such as toll-like receptors. The afferent signals carry this information to the brain, where it is processed. In response, the efferent arm of the vagus nerve regulates immune activity by suppressing the release of pro-inflammatory cytokines from the gut and other organs. This bidirectional communication forms the basis of the inflammatory reflex, a key mechanism in maintaining immune balance. In addition, acetylcholine receptors/ligands mediating the **cholinergic** anti-inflammatory pathway via the vagus nerve have also been proposed as an important immune modulator in the gut microbiota that communicates with the brain [1, 2, 8, 9].

Depression is described as a common mental disorder state, characterized by a continuous feeling of sadness and apathy lasting at least two weeks, as a result of interactions covering social, psychological, and biological factors, for example, significant changes in life, family matters, chronic health problems, or addiction. It is also a common cause of disability and a cause of suicide death. According to WHO, approximately 280 million people worldwide suffer from major depressive disorder (MDD) every year, and more than 700,000 people die from committing suicide. The data described many factors that link this mental disorder with the components of the intestinal microbiota, which was confirmed by *Naseribafrouei et al.* They have shown that the level of the Alistipes genus associated with inflammation and Oscillibacter, which has valeric acid involved in is associated with depression, was elevated in patients with MDD [4].

Zhang et al. [12] showed, using a mouse model, that microbiota dysbiosis was associated with greater intestinal permeability and systemic inflammation. As a result of endogenous melatonin reduction (EMR), the composition of the mice microbiota changed and consisted of a decrease in the relative abundance of Bacteroidetes, an alteration of the Firmicutes/Bacteroidetes ratio, and growth of the relative abundance of Lactobacillus. The study also revealed improved gut permeability (leaky gut) and systemic inflammation in EMR mice [4,6].

The determination of short chain fatty acids (SCFAs) content could be helpful in the analysis of the microbiota composition by patients with MDD. The study concerning the SCAFs profile conducted by *Skonieczna-Żydecka et al.* on a group of 116 women aged 52.0 (±4.7) years, in which 40.52% of them recognized depression, revealed a lower level of propionic acid and a higher content of isocaproic acid compared to healthy subjects [12]. However, because of the small sample size, it is not possible to definitively conclude that SCAFs contribute to the depressive phenotype. Research using animal models has demonstrated a link between the composition of the intestinal microbiota and behaviors or traits such as anxiety and depression. *Gan et al.* showed changes in the behavior of shy personalities of Mongolian gerbils (Meriones unguiculates) after transplantation of the gut microbiota of bold individuals. Shy gerbils often exhibited bold behavior after "bold fecal microbiota" transplantation, suggesting the association between the gut microbiota and the host's personality [4,6].

Communication between the gut and the brain occurs in both directions and utilizes multiple pathways, including neural, endocrine, and immune systems. The microbiota and their metabolites play a crucial role as modulators in this gut-brain communication, giving rise to the concept of the microbiota-gut-brain (MGB) axis. The role of the routes involved in the MGB axis in depression has been well delineated. The microbial composition and metabolites change in MDD patients results in a disrupted homeostasis of the gut microenvironment, affecting the function of the gut epithelium and causing intestinal barrier dysfunction and inflammatory responses. The increased systemic translocation of gut metabolites, microbial cell components, or even the microbiota via the damaged intestinal barrier (the "leaky gut") heightens systemic inflammatory responses (e.g., Th17/regulatory T cell (Th17/Treg) imbalance, interleukin [IL]-6, IL-1β, and tumor necrosis factor-alpha) that have been implicated in the pathogenesis of depression. The ENS, referred to as the "second brain", has been reported to be involved in the development of brain disorders. Abnormal ENS activity arising from intestinal pathology aggravates depression-related pathological changes by altering gut secretion, immune defenses, motility, and permeability. Besides the ENS, the vagus nerve also plays an important role in transmitting microbial signals from the gut to the brain in depression. Preclinical studies have verified that subdiaphragmatic vagotomy blocked the development of depression-like behaviors in rodents after lipopolysaccharide (LPS) injection or fecal microbiota transplantation from Chrna7 knock-out mice with depression-like behaviors. In clinical, vagus nerve stimulation has long been approved for treatment-resistant depression. The microbial cell components, e.g., LPS produced by gram-negative bacteria, and peripheral inflammatory signals reach the brain by crossing the blood–brain barrier resulting in neuroinflammation, subsequently induce neuropathological changes through chronic

activating specific cells, including synaptic defects, demyelination, abnormal neurogenesis and neurotransmitters release, that are involved in the pathogenesis of depression. Microbial signals, pathological neurobiological changes, and depressive emotions can activate the hypothalamic-pituitary-adrenal axis, increasing the synthesis and release of cortisol. As a part of the brain-gut axis, excessive levels of cortisol promote gut pathology by modulating intestinal barrier function and inflammatory responses, resulting in a leaky gut; this process is a key component of the MGB axis in depression. Beyond these routes, various signal transduction systems and metabolic pathways are also implicated in the MGB-based pathogenesis of depression, such as the endocannabinoid system, CAMKII-CREB and MAPK signaling, and glycerophospholipid metabolism. Moreover, mitochondria are reported to be potential key mediators of the gut microbiota dysbiosis and depression relationship. The various pathways involved in gut-brain bidirectional communication create a complex network of mechanisms, and their interactions make it challenging to study how gut microbiota regulate depression [6,7,12].

In Kazakhstan, the association between gut microbiota and heart failure, insulin resistance and cognitive functions, including the association gut dysbiosis with Alzheimer's disease, were investigated. However, researches related to the influence of microbiota on anxiety and depression were not covered. This issue is relevant throughout the world, especially in Kazakhstan, because the Republic of Kazakhstan has great potential for the development of such investigations, taking into account the characteristics of the national diet with the consumption of dairy products.

Materials and methods

A total of 100 patients were selected. Inclusion criteria: Age over 18 years; Diagnosis of heart failure in accordance with internationally recognized guidelines and class I-IV according to NYHA, stage A-C according to the ACC/AHA heart failure classification. Clinically stable condition and optimally selected; drug therapy for CHF at least 4 weeks ago in accordance with current recommendations; Consent to participate in the study. Exclusion criteria: Age under 18 years; Refusal to undergo diagnostic procedures defined by the study protocol; Terminal stage of CHF (stage D according to ANA/ACC); Coronary or peripheral revascularization procedures, valve procedures or any major surgical procedure within 3 months prior to inclusion in the study; Use of antibiotics, cytostatic therapy and pro- or prebiotics less than 1 month before the baseline visit; Oncological and autoimmune diseases (diseases of connective tissue, intestines, skin, etc.). Any acute illness or active infection; Individual intolerance to the nutrients taken (probiotics); The presence of other anatomical or concomitant diseases, or other medical, social or psychological conditions that, in the opinion of the investigator, may limit the ability of the subject to participate in the clinical trial or to comply with the requirements of follow-up, or affect the scientific validity of the results of the clinical trial. Patients in both groups underwent a complete ultrasound examination of the heart.

The main group received a probiotic, the comparison group did not receive it. The multicomponent probiotic contains strains of live lyophilized bifido- and lactobacilli identical to human microflora, with high viability: resistant to gastric juice, digestive enzymes and bile acids. These strains are characterized by a high ability to adhere and colonize on the intestinal mucosa, which creates optimal conditions for the growth of normal microflora. Patients took the probiotic in a sachet for three months before the survey, one sachet twice a day before meals. The laboratory tests were performed but not applicable in this study.

Patients were interviewed on four questionnaires. Anxiety level was assessed on two tests: Beck Anxiety Inventory (BAI) – this scale is a self-report measure of anxiety and General Anxiety Disorder-7 (GAD-7) – this initial screening tool for generalized anxiety disorder. The level of depression was also assessed by two tests: Beck Depression Inventory (BDI) – this self-report rating inventory that measures characteristic attitudes and symptoms of depression and Patient Health Questionnaire (PHQ-9) – this depression symptom scale. All questionnaires are validated and widely used in medicine.

Ethics statement

This study was approved by the Local Ethics Committee No. 2023/01-009.

Statistical analysis

As almost all were not normally distributed, non-parametric Mann–Whitney U tests were used for between-group analyses. The qualitative analysis was conducted by two groups, anxiety and depression indicators were assessed in both groups, and frequencies were compared using the chi-square tests: Pearson chi-square, likelihood ratio, linear-by-linear association and number of valid cases.

Results

Comparisons of groups were performed in both tables using the Mann-Whitney test. As we can see in Table 1, both groups are comparable according to the main criteria: age, body mass index, ejection fraction, valve sizes.

Table 1.

Comparability of groups, comparisons of groups using the Mann-Whitney test.

	Control group M±SD n=44	Study group M±SD n=97	p
age	57,48±14,76	58,24±12,09	0,815
BMI (kg/m2)	28,76±5,24	30,42±5,43	0,124
EF, %	54,17±8,61	46,62±11,06	0,001
MV	0,90±0,84	1,03±0,96	0,553
TV	1,19±0,94	0,81±0,91	0,012
Vmax TR	2,35±0,21	1,92±0,79	0,315
PASP (mm.Hg)	33,51±15,34	29,17±8,40	0,353
AV	0,27±0,40	0,25±0,50	0,317
PV	0,13±0,27	0,05±0,22	0,021

BMI - Body Mass Index, EF - ejection fraction, MV- mitral valve, TV- tricuspid valve, Vmax TR - maximum velocity of the blood flow during tricuspid regurgitation, PASP-pulmonary artery systolic pressure, AV - aortic valve, PV- pulmonary valve.

In table 2 comparisons of groups using the Mann-Whitney test, with median-quartiles, the distribution differs from the normal one due to the asymmetry, especially at the expense of the last columns.

Table 2.

Comparisons of groups using the Mann-Whitney test, with median-quartiles.

	Control group Me(Q1-Q3) n=44	Study group Me(Q1-Q3) n=97	p
EDV (ml)	81,00 (66,50-96,08)	116,00 (87,00-152,00)	<0,001
Index. EDV (ml)	46,44 (39,64-51,60)	59,64 (46,51-78,89)	<0,001
ESV (ml)	35,65 (25,70-43,35)	63,00 (36,30-94,10)	<0,001
Index. ESV (ml)	20,25 (14,42-23,29)	34,75 (19,96-47,82)	<0,001
EDD (cm)	4,50 (4,03-4,98)	5,20 (4,60-5,70)	<0,001
Index. EDD (cm)	2,54 (2,19-2,82)	2,69 (2,41-3,02)	0,024
ESD (cm)	3,15 (2,60-3,50)	4,10 (3,30-4,70)	<0,001
Index. ESD (cm)	1,75 (1,42-1,99)	2,06 (1,74-2,46)	0,001
LA V (ml)	55,55 (43,25-75,48)	74,00 (58,00-102,00)	<0,001
Index. LA V (ml)	31,22 (25,00-39,43)	38,08 (29,87-53,62)	0,003
BAI	11,00 (6,00-22,00)	7,00 (3,00-12,00)	0,001
BDI	8,00 (4,00-13,50)	2,50 (0,00-8,00)	<0,001
GAD-7	4,00 (0,00-6,00)	3,00 (0,00-6,00)	0,481
PHQ-9	6,00 (4,00-8,75)	6,00 (4,00-8,00)	0,869

Table 3.

Qualitative analysis of the results of the BAI.

		Control group		Study group	
		Абс.	%	Абс.	%
BAI	,0			6	6%
	1,0	1	2%	3	3%
	2,0	1	2%	8	8%
	3,0	3	7%	14	14%
	4,0	2	5%	5	5%
	5,0	2	5%	5	5%
	6,0	3	7%	7	7%
	7,0	3	7%	7	7%
	8,0			3	3%
	9,0	2	5%	8	8%
	10,0	1	2%	2	2%
	11,0	4	9%	3	3%
	12,0	1	2%	3	3%
	13,0	2	5%	3	3%
	14,0	1	2%	1	1%
	15,0	1	2%	3	3%
	16,0	1	2%	2	2%
	17,0	2	5%	3	3%
	18,0	1	2%	3	3%
	19,0			1	1%
	20,0			1	1%
	21,0	1	2%		
	22,0	2	5%		
	23,0	4	9%	2	2%
	26,0			2	2%
	27,0			1	1%
	29,0	1	2%		
	30,0	1	2%		
	32,0	1	2%		
	33,0	1	2%		
	35,0			1	1%
	51,0	1	2%		

BAI - Beck Anxiety Inventory.

EDV - end-diastolic volume, Index. EDV – index end-diastolic volume, ESV - end-systolic volume, Index. ESV – index end-systolic volume, EDD - end-diastolic diameter, Index. EDD – index End-diastolic diameter, ESD - end systolic diameter, Index. ESD – index end systolic diameter, LA V - left atrial volume, Index. LA V – index left atrial volume, BAI - Beck Anxiety Inventory, BDI - Beck Depression Inventory, GAD-7 - Generalized Anxiety Disorder and PHQ-9 Patient Health Questionnaire-9.

As a result of statistical analysis, we obtained a statistical difference in the following parameters: end-diastolic volume, index end-diastolic volume, end-systolic volume, index end-systolic volume, end-diastolic diameter, index End-diastolic diameter, end systolic diameter, index end systolic diameter, left atrial volume, index left atrial volume, BAI, BDI. There was no statistical difference between the studied groups on the PHQ-9 and GAD-7 scales.

A qualitative analysis was conducted, where the results of depression and anxiety tests were selected as the analyzed features. Tables 3,5,7,9 provide a qualitative analysis of the analyzed features. The tables 4,6,8,10 show several chi-square tests of the analyzed features respectively.

Table 4.

Chi-Square tests for BAI.

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	35,221[a]	31	0,275
Likelihood Ratio	40,321	31	0,122
Linear-by-Linear Association	13,160	1	0,000
N of Valid Cases	140		

df - Degrees of Freedom, Asymp. Sig. (2-sided) - Asymptotic Significance (2-sided). a - in this table have expected count less than 5, and the minimum expected count is 0,31.

There is a statistical difference between the studied groups on the scale BAI.

Table 5. **Qualitative analysis of the results of the BDI.**

		Control group		Study group	
		Абс.	%	Абс.	%
BDI	,0	2	5%	29	30%
	1,0	2	5%	7	7%
	2,0	2	5%	12	13%
	3,0	2	5%	8	8%
	4,0	5	12%	3	3%
	5,0	3	7%	3	3%
	6,0			3	3%
	7,0	2	5%	5	5%
	8,0	3	7%	6	6%
	9,0	1	2%	3	3%
	10,0	1	2%	3	3%
	11,0	3	7%	1	1%
	12,0	2	5%	1	1%
	13,0	3	7%		
	14,0	1	2%	2	2%
	15,0	2	5%	3	3%
	16,0	1	2%	2	2%
	17,0	1	2%	1	1%
	18,0			1	1%
	19,0	2	5%	1	1%
	20,0			1	1%
	22,0			1	1%
	24,0	1	2%		
	26,0	1	2%		
	29,0	1	2%		

BDI – Beck Depression Inventory.

Table 6. **Chi-Square tests for BDI.**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	40,861[a]	24	0,017
Likelihood Ratio	44,339	24	0,007
Linear-by-Linear Association	15,703	1	0,000
N of Valid Cases	137		

df - Degrees of Freedom, Asymp. Sig. (2-sided) - Asymptotic Significance (2-sided). a – in this table have expected count less than 5, and the minimum expected count is 0,30.

There is a statistical difference between the studied groups on the scale BDI.

Table 7. **Qualitative analysis of the results of the GAD – 7.**

		Control group		Study group	
		Абс.	%	Абс.	%
GAD-7	,0	12	27%	26	27%
	1,0	3	7%	7	7%
	2,0	4	9%	13	13%
	3,0	1	2%	6	6%
	4,0	3	7%	10	10%
	5,0	6	14%	7	7%
	6,0	5	11%	11	11%
	7,0	2	5%	7	7%
	8,0	1	2%	2	2%
	9,0	3	7%	2	2%
	10,0	1	2%	2	2%
	11,0	1	2%	1	1%
	12,0			2	2%
	13,0	1	2%		
	16,0	1	2%		
	18,0			1	1%

GAD-7 **–** General Anxiety Disorder Questionnaire – 7.

Table 8. **Chi-Square tests for GAD-7.**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	1,544[a]	5	,713
Likelihood Ratio	2,600	5	,633
Linear-by-Linear Association	,871		,351
N of Valid Cases	41		

df - Degrees of Freedom, Asymp. Sig. (2-sided) - Asymptotic Significance (2-sided). a - in this table have expected count less than 5, and the minimum expected count is 0,31.

According to the results of the calculations of the GAD-7 scale, there is no statistical difference in the groups.

Table 9. **Qualitative analysis of the results of the PHQ–9.**

		Control group		Study group	
		Абс.	%	Абс.	%
PHQ-9	,0			2	2%
	1,0	1	2%	2	2%
	2,0	3	7%	9	9%
	3,0	5	11%	4	4%
	4,0	7	16%	8	8%
	5,0	4	9%	14	15%
	6,0	8	18%	15	16%
	7,0	2	5%	16	17%
	8,0	3	7%	11	11%
	9,0	5	11%	8	8%
	10,0	2	5%	2	2%
	11,0	2	5%		
	12,0			1	1%
	13,0	1	2%	1	1%
	14,0			1	1%
	15,0			1	1%
	17,0	1	2%		
	18,0			1	1%

PHQ-9 – Patient Health Questionnaire-9.

Table 10. **Chi-Square tests for PHQ-9.**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	19,762[a]	17	0,287
Likelihood Ratio	22,351	17	0,172
Linear-by-Linear Association	0,020	1	0,888
N of Valid Cases	140		

df - Degrees of Freedom, Asymp. Sig. (2-sided) - Asymptotic Significance (2-sided). a - in this table have expected count less than 5, and the minimum expected count is 0,31.

According to the results of the calculations of the PHQ-9 scale, there is no statistical difference in the groups.

From the tables above we can judge the statistically significant difference between the anxiety and depression levels in the probiotic groups and the control group. The p-value is less than 0,05 when comparing the groups between themselves on the scales: BAI, BDI, GAD-7. The result of comparison on the PHQ-9 scale is very different, because there is no statistical difference**.**

Discussion

In this research, both groups were studied, selected according to the inclusion and exclusion criteria, which were

comparable in terms of the main indicators. A survey was conducted on anxiety and depression scales, ultrasound examination of the heart. According to the results of the study, a statistically significant difference was revealed in some indicators of ultrasound examination of the heart and the results of the BAI and BDI. An unexpected result was the absence of a statistical difference in the GAD-7 and PHQ-9 scales. The results of statistical analysis according to the Mann-Whitney and chi-square criteria were correlated with each other.

The results of the study confirm the fact of the influence of gut microbiota on mental health, specifically on the levels of anxiety and depression. The lack of correlation between the BAI and BDI scales and the GAD-7 and PHQ-9 require further research, probably the PHQ-9 and GAD-7 scales are more concise and less detailed than the BDI and BAI scales. The identified difference in some indicators of ultrasound of the heart also requires further research in the direction of the influence of gut microbiota on heart failure. In general, the study conducted on the Kazakhstani population is quite ambiguous in its results and deserves the attention of the scientific community.

Extensive research has highlighted disturbances in intestinal microbiota and metabolites in depression [3,11]. Traditional treatments targeting neurotransmitter reuptake have demonstrated limited efficacy, prompting the exploration of novel mechanisms focusing on the gut-brain axis. One study provides compelling evidence for a mechanism of depression involving altered gut microbiota leading to depleted catecholamine neurotransmitter metabolites. The substrates of HVA were tyrosinecontaining compounds, and tyrosine-rich foods such as lean meat, fish, dairy products, and nuts had the mood-regulating effects [12].

The purpose of this work was to enhance our understanding of the role of microbiota and nutrition in the communication between the intestine and the brain. The vast array of microbes residing in and on the human body appears to influence mental health and disease by affecting this communication pathway [5,10]. Clinical studies suggest that the diversity and richness of microbiota contribute to resilience, helping to maintain a balanced microbial composition that may facilitate effective interactions between the gut and the brain. Additionally, the potential benefits of probiotics, prebiotics, and psychobiotics in influencing brain function are indicated by both preclinical and clinical research. Nutrition may play a role in supporting microbial balance and influencing the gut-brain axis as it relates to mood and cognition. However, establishing direct correlations between these observations remains challenging due to the complex nature of psychiatric disorders and the variability of individual microbial profiles. Future extensive clinical trials in humans could provide valuable insights into the potential for microbiota-based approaches in the treatment and prevention of psychiatric disorders, possibly offering alternatives to traditional pharmacological methods [3].

Dietary interventions targeting the gut microbiota to alleviate depression and improve mental health offer promising therapeutic avenues. Further clinical studies are needed to confirm the therapeutic effect of dietary interventions targeting the gut microbiota. And the development of reliable, individualized treatment strategies for mental disorders is also needed [3].

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