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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

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თანამშრომლობითა და მისი პატრონაჟით

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

ТБИЛИСИ - НЬЮ-ЙОРК

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board and The International Academy of Sciences, Education, Industry and Arts (U.S.A.) since 1994. **GMN** carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

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GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией и Международной академией наук, образования, искусств и естествознания (IASEIA) США с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения.

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GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

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При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

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2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

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ავტორთა საყურადღებოდ!

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1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

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5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

Содержание:

INTESTINAL MICROBIOTA IN ALZHEIMER'S DISEASE

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Over the past decades, the problem of cognitive impairment has confidently held one of the leading places in modern clinical medicine. This is especially true for the older age group. Moreover, the main cause of impaired functioning of higher cortical functions is Alzheimer's disease [3]. Cognitive impairment and dementia are currently among the most common causes of disability among patients of different ages. According to the WHO, there are currently 47 million dementia patients worldwide. This number will reach 75 million by 2030 and will almost triple by 2050 [31].

Analysis of literature on Alzheimer's disease pathogenesis has shown that the most common cause of cognitive impairment was mixed (vascular-neurodegenerative) brain lesions. One of the generally accepted hypotheses for the development of Alzheimer's disease is the amyloid hypothesis, according to which the cascade of the neurodegenerative process is triggered by a violation of the metabolism of the amyloid precursor protein (APP). A key link in this cascade is the formation and deposition of amyloid plaques in the brain parenchyma. In health, APP is cleaved by the enzyme alpha-secretase into polypeptides of equal size, which are not pathogenic, i.e., do not tend to aggregate. In early-onset genetically determined Alzheimer's disease, the process of cleavage of APP by α-secretase is disrupted. Cleavage of APP by β-secretase enzyme leads to the formation of an insoluble membrane protein with a higher molecular weight, the destruction of which by γ-secretase, in turn, leads to the formation of an abnormal isoform of amyloid protein (Aβ-42). Aβ-42 accumulates in the brain, leading to the formation of extracellular aggregates—amyloid plaques—and triggering a cascade of pathological processes leading to the development of neurofibrillary tangles and the progression of Alzheimer's disease [4].

The fate of amyloid protein in the brain is variable: it can aggregate and be deposited in the form of amyloid plaques, thereby disrupting the interaction between neurons and neurotransmitter transmission, which, in turn, causes cognitive deficits; can be utilized by cleavage by proteolytic enzymes such as neprilysin [15], chaperone molecules [16], lysosome and proteasome enzymes [7,21]. A small part of the protein can be excreted through the blood-brain barrier by interaction with the receptor-binding protein of low-density lipoproteins (LRP1) [34], as well as deposited in the walls of cerebral arteries of various sizes, leading to the formation of amyloid angiopathy, changing the architectonics of the vascular wall with the formation of fibrinoid necrosis, hyaline degeneration of vessels with obliteration of their lumen [27]. These changes are the initial mechanism of hypoxic-ischemic brain damage in Alzheimer's disease patients and the development of mixed dementia.

Over the past ten years, many researchers have found a link between gastrointestinal pathology and mental and neurological diseases such as depression, anxiety, autism, schizophrenia, and neurodegenerative disorders [24, 30]. Many scientists are skeptical about such studies since the complexity of interactions in a system called the gut-brain axis does not yet yield sufficient results for definitive conclusions about the molecular mechanisms of these interactions. However, the interest in such studies is steadily growing.

The main components of the microbiota-gut-brain axis are the central nervous system (CNS), neuroendocrine and neuroimmune systems, the sympathetic and parasympathetic autonomic nervous system, the intestinal nervous system, and, of course, the intestinal microbiota. These components interact with each other to form a complex multifactorial network. Through this network, signals from the brain can influence the motor, sensory and secretory activity of the intestine, and vice versa, visceral signals from the intestine, mediated by the microbiota, affect the brain function [23].

The classic signaling pathway of the intestinal microbiome and the CNS functions through the regulatory mechanisms of nutrition and satiety. Changes in diet can affect the availability of various nutrients for the intestinal microflora and, consequently, their qualitative and quantitative composition [30, 1]. It is known that the brain and, in particular, the hypothalamus, plays a key role in the regulation of energy metabolism and food intake. The hypothalamic-pituitary tract and brainstem are the main centers of the brain that control appetite. The gastrointestinal tract is closely connected with the hypothalamic-pituitary system through neuroendocrine and sensory signals from the intestine, in which peptides that control the brain's response are released. Food intake initiates a cascade of neural and hormonal responses that trigger a central nervous system response. The signal from mechanoreceptors is transmitted through afferent nerve impulses to the vagus nerve and the dorsal nucleus of the solitary tract, the neurons of which coordinate the motility of the gastrointestinal tract. The projections from the nuclei of the solitary tract enter the viscerosensory zone of the thalamus. Signals from the intestine are also critical for appetite control and energy balance regulation, glucose homeostasis, and fat metabolism. The intestinal microbiota can be considered an important element of the endocrine system. It carries out the enzymatic transformation of complex steroid compounds and nitrogen derivatives (the latter enter the body with food or are formed as a result of hydrolysis in the stomach or intestines by pancreatic enzymes) classified as prohormones. Food consumption induces the synthesis of various hormones in the intestine that stimulate (ghrelin) or suppress appetite (peptide-like glucagon, cholecystokinin, tyrosine-tyrosine peptide, pancreatic polypeptide, and oxyntomodulin). The binding of hormones to receptors in the hypothalamus leads to the synthesis of orexigenic or anorexigenic peptides [8].

The microbiota begins influencing the body from the moment of birth. External ascending signals from the intestinal microflora are important for early postnatal programming and brain development [10]. Heijtz et al. [11] established that colonization of intestinal microflora was essential for postnatal human brain development and mental health. During intrauterine development of the fetus, the brain forms at an increased rate. By the time of birth, the brain reaches full formation in terms of neurons, but the brain's development does not stop after birth [10]. One of the central mechanisms of interaction of the intestinal microflora and the CNS is the influence on the hypothalamic-pituitary-adrenal (HPA) system. Intestinal bacteria affect the functioning of the brain by modulating this axis. It has been shown that postnatal microbial colonization largely determined the development of the hypothalamic-pituitary-adrenal axis [25].

The intestinal microbiota can produce dopamine and its precursors from food substrates, and almost half of the dopamine in the body is produced in the gastrointestinal tract [29]. The microbiota also produces acetylcholine, serotonin, norepinephrine, and other biologically active substances [20, 29]. Another interesting fact is that some microbiota representatives of the macroorganism can activate glutamate receptors, which, in turn, are involved in the regulation of synaptic plasticity and cognitive functions [18].

The intestinal microbiota of the human body has multifactorial effects on homeostasis. The study of the microbiota functions in the human digestive tract and conditions leading to a violation of the microbiota's qualitative and quantitative composition is a challenging task. Its successful solution can lead to completely new therapeutic and preventive medicine strategies, the justified prescription of various drugs that positively affect microbiocenosis and human health in general.

The study aimed to assess the qualitative and quantitative composition of the intestinal microflora in Alzheimer's disease patients.

Material and methods. The intestinal microbiota was studied in Alzheimer's disease patients (n=37) aged 69±0.5 years. The qualitative and quantitative composition of microbiota was studied using the microbiological research method [6]; identification of microorganisms was carried out according to the scheme given in Bergey's Manual of Systematic Bacteriology [9].

The study included older adults (n 21) aged 72±0.3 years without Alzheimer's disease, diabetes mellitus, infectious pathologies as a control group (reference group) to compare all the studied parameters. The procedure for examining these individuals was following the standards of the ethics committee.

Adhesive properties of *Bifidumbacterium spp.* and *Lactobacillus spp.* were determined by the method of V. I. Brilis et al. [2]. The results were statistically processed using the Statistica 6.1 software package using the parametric Student's t-test.

Results and discussion. Analyzing the results of microbiological examination of feces of Alzheimer's disease patients, we found that 100% of the examined patients had various degrees of manifestation of qualitative and quantitative dysbiotic changes in the intestines: grade 1 dysbiosis was observed in 32.4±0.03% of cases; grade 2 – in 27.0±0.02% and grade 3 – in 40.6±0.04%.

According to the latest intestinal dysbiosis trends, a clinical and laboratory syndrome is understood as associated with changes in the qualitative and/or quantitative composition of the intestinal microbiota followed by the development of metabolic and immunological changes that lead to gastrointestinal disorders [32].

It should be noted that grade 1 dysbiotic disorders of the intestinal microbiota in Alzheimer's disease patients in 75.0±0.01% of cases were latent, compensated, which was characterized by insignificant quantitative changes in facultative aerobic and indigenous (*Bifidumbacterium spp*., *Lactobacillus spp*.) part of the intestinal microbiota, and the absence of intestinal dysfunctions according to the medical history. Other patients in this group (25.0±0.02%) had a history of intestinal dysfunction, which manifested itself in the form of infrequent diarrhea.

In patients with grade 2 dysbiosis (27.0±0.02%), subcompensated forms of dysbiotic disorders in the intestinal microbiota were recorded: qualitative changes (in parallel with quantitative ones) in the *Escherichia coli* population were observed (compared with the indicators of the reference group), namely, significant ($p<0.05$) increase in the degree of *Escherichia coli* colonization with low enzymatic activity (up to 7–10% of the total amount of E. coli) and a significant decrease ($p<0.05$) in the degree of colonization of the intestine with *Escherichia coli* with normal enzymatic activity up to lg 5.69 CFU/g. In addition to these changes in the intestinal microbiota of these patients, a significant ($p<0.05$) increase in the degree of colonization of the intestine with pathobionts (opportunistic microorganisms) of the *Enterobacteriaceae* family was observed: *Klebsiella spp*. up to lg 5.7 CFU/g (lg 4.0 CFU/g in the reference group); *Proteus spp*. up to lg 4.69 CFU/g (the reference group – ≤ lg 4.0 CFU/g); *Cirtobacter spp.* up to lg 4.47 CFU/g (the reference group – ≤ lg 3.0 CFU/g); in 60.0±0.02% of patients in this group, hemolytic species of staphylococci – *Staphylococcus aureus* were isolated in the amount of lg 3.0 – lg 4.69 CFU/g (reference group 0 – < log 2.0 CFU/g). All patients in this group had a history of gastrointestinal disorders.

A decompensated nature of dysbiotic disorders was observed in 40.6±0.04% cases with Alzheimer's disease patients, according to the results of the microbiological study. Such patients had a significant ($p < 0.05$), compared with the reference group, decrease in the degree of colonization of the intestine with obligate anaerobic pathobionts – *Bacteroides spp*., *Fusobacterium spp*., *Peptostreptococcus spp*. Moreover, these indicators were 2 – 3.5 times lower than those of the reference group. It should be noted that 66.7±0.04% of patients in this group had a significant ($p<0.05$) increase in the degree of intestinal colonization with *Clostridium spp*., namely *C. difficile* up to lg 6.47 CFU/g (the reference group – ≤ lg 5.0 CFU/g). The intestinal microbiota in patients of this group was characterized by a sharp qualitative and quantitative ($p<0.05$) decrease in *Escherichia coli* with normal enzymatic activity up to lg 4.3 CFU/g (reference group – lg 7.0 – lg 8.0 CFU/g) and quantitative dominance of pathobionts: *Klebsiella spp*.; *Proteus spp*.; *Cirtobacter spp*.; *Enterococcus spp*., *S. aureus*, *Morganella spp*., *Providencia spp*., *Hafnia spp*., *Candida spp*. – the total indicator was more than lg 8.47 CFU/g (the total indicator in the reference group was lg 7.0 CFU/g), and in 40.0±00.4% of the examined patients of this group, the intestinal microbiota contained *Pseudomonas spp*. (lg 4.54 CFU/g).

When studying the composition of the indigenous microbiota represented by obligate anaerobic bacteria – *Bifidumbacterium spp*. and aerotolerant anaerobes – *Lactobacillus spp*., which are representatives of the parietal microbiota and protect the mucous membrane from excessive colonization by potential pathogens, it was found that their quantitative composition was significantly lower ($p <0.05$) compared to the reference group. Moreover, the lowest quantitative indicators of *Lactobacillus spp.* were observed in patients with decompensated form lg 4.48 CFU/g, and *Bifidumbacterium spp.* – in patients with subcompensated form of dysbiosis (lg 3.7 CFU/g).

It should be noted that the international classification of diseases, tenth revision, does not contain independent nosological units – "dysbacteriosis" ("dysbiosis") and "bacterial overgrowth syndrome". However, given the fact that patients with subcompensated and decompensated forms of dysbiotic disorders of the intestinal microbiota have a significant decrease ($p<0.05$) in the quantitative composition of *Bifidumbacterium spp*. and *Lactobacillus spp*. against the background of qualitative and quantitative "shifts" in the composition of the opportunistic microbiota. This violation may be critical and, in our opinion, should be studied.

This is because pathogenic microorganisms and pathobionts of the gastrointestinal tract in health are under the control of the microorganism's immune system and the symbiotic microbiota. However, sometimes there is an increase in the number of pathogens and pathobionts and/or an increase in their metabolic activity, which can be associated with some diseases: diabetes mellitus, metabolic syndrome, obesity, autoimmune diseases, depression, some stress-induced and neurodegenerative diseas-

es, etc. [12,14]. Molecules of the walls of microorganisms, for example, lipopolysaccharides and amyloids, constantly activate the body's immune system, i.e., the macroorganism is under constant pressure from the products of microorganisms. Moreover, with age, when the permeability of the blood-brain barrier and the gastrointestinal tract barrier is disturbed, the destructive consequences of this pressure only increase [22].

Alzheimer's disease is characterized by an increased level of chronic inflammatory reactions. Activated microglia is a potent neuropathological stimulant leading to persistent inflammation in the brain [14,28]. These progressive pro-inflammatory and neurodegenerative processes are presumably stimulated by an abnormal response of the immune system [19], which, in turn, can be caused by acute or chronic infection, and by various products of the host microbiota [33], including intestinal pathobionts, which, under certain conditions, can cause etiopathogenesis.

There is evidence that most of the products and cell wall components secreted by the microbiota are a huge class of strong proinflammatory activators of the immune system, which can cause the release of proinflammatory cytokines, complement proteins, and activate microglia in the central nervous system of the host organism [33]. Pathogenic exposure to the microbiota can increase the gastrointestinal tract's permeability [17] and the blood-brain barrier [33], which also increases amyloid and other types of inflammatory reactions in the central nervous system. Violation of the blood-brain barrier's permeability may underlie the pathogenesis of such neurodegenerative diseases as Alzheimer's disease [28] and other diseases.

Analyzing the above information, it should be noted that the identified qualitative and quantitative changes in the composition of intestinal microbiota in Alzheimer's disease patients are serious and combined. An increase in the degree of intestinal contamination with conditionally pathogenic microorganisms against the background of a decrease in colonization resistance caused by *Lactobacillus spp*. and *Bifidumbacterium spp*. can complicate the course of Alzheimer's disease. Moreover, some pathobionts can cause other concomitant pathologies, for example, the fact that 66.7±0.04% of patients with a decompensated form of dysbiosis had a significant ($p<0.05$) increase in the degree of colonization of the intestine with C. difficile up to lg 6, 47 CFU/g against the background of a critical decrease in *Lactobacillus spp*. can lead to exacerbation of existing or the formation of ulcerative colitis caused by *C. difficile* (a history of ulcerative colitis was detected in 26.7±0.04% of patients in this group).

Considering the fact that the intestinal microbiota of patients with Alzheimer's disease showed a decrease in *Lactobacillus spp*., we studied the adhesive properties of isolates of these bacterial strains. Such *in vitro* tests were carried out in the aspect that the ability of microorganisms to take root in the gastrointestinal tract, creating an antagonistic effect against pathobionts, at the initial stage of colonization is due precisely to their adhesive properties. It was found that among all *Lactobacillus spp.* isolates 28.9±3.2% of the strains had low adhesive activity, 49.5±4.7% – average, and 21.6±5.3% – high adhesive activity.

Therefore, reducing the inflammatory response [26] and dysbiotic disorders of the intestinal microbiota can be an additional therapeutic method to manage Alzheimer's disease.

Probiotics, which include lactobacilli, are most often used to correct dysbiotic conditions [13]. It should be noted that the indicators of adhesive activity of *Lactobacillus spp.* isolates in the conditions of repeated micro-aeration on defatted milk [5] were higher by an average of 1.2 times ($P<0.05$), which may be a promising area in the development of personalized autobiotics for the correction of dysbiotic intestinal disorders in Alzheimer's disease and the creation of a bio-bank of cultures.

Conclusion.

1. Based on the data obtained during the microbiological study of the intestinal microbiota in Alzheimer's disease patients, various degrees of qualitative and quantitative dysbiotic changes in the intestines were revealed: in 32.4±0.03% of cases, grade 1 dysbacteriosis (latent form) was observed; in 27.0±0.02% – grade 2 (subcompensated dysbiosis) and in 40.6±0.04% – grade 3 (decompensated dysbiosis).

2. When studying the qualitative and quantitative composition of *Bifidumbacterium spp*. and *Lactobacillus spp*., as the main representatives of parietal microbiota and antagonists of colonization by potential pathogens and pathobionts, it was found that their quantitative composition was significantly lower ($p<0.05$) compared to the indicators of the reference group: the lowest quantitative indicators of *Lactobacillus spp*. were observed in patients with a decompensated form of dysbiosis lg 4.48 CFU/g, and *Bifidumbacterium spp*. – in patients with a subcompensated form of dysbiosis (lg 3.7 CFU/g).

3. Among all *Lactobacillus spp.* isolates from patients with Alzheimer's disease, 28.9±3.2% of the strains had low adhesive activity, 49.5±4.7% – average, and 21.6±5.3% – high adhesive activity.

4. Indicators of adhesive activity of *Lactobacillus spp.* isolates at repeated cultivation on defatted milk under micro-aeration conditions were 1.2 times higher on average ($p<0.05$), which may be a promising area in the development of personalized autobiotics for the correction of intestinal dysbiotic disorders in Alzheimer's disease.

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SUMMARY

INTESTINAL MICROBIOTA IN ALZHEIMER'S DISEASE

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The study aimed to assess the qualitative and quantitative composition of the intestinal microflora in Alzheimer's disease patients.

The paper presents the data obtained from a microbiological study of the intestinal microflora in Alzheimer's disease patients (n=37) aged 69±0.5 years. The analysis of the microbiological study of the feces of Alzheimer's disease patients found that the intestinal microflora of such patients had both qualitative and quantitative dysbiotic changes of various degrees of manifestation. The composition of the intestinal microflora of these patients showed a significant decrease in *Bifidumbacterium spp*. and *Lactobacillus spp*.: the lowest quantitative indicators of *Lactobacillus spp.* were observed in patients with a decompensated form of dysbiosis lg 4.48 CFU/g, and *Bifidumbacterium spp.* – in patients with a subcompensated form of dysbiosis (lg 3.7 CFU/g). Indicators of adhesive activity of *Lactobacillus spp.* isolates from Alzheimer's disease patients in the conditions of micro-aeration on defatted milk were higher by an average of 1.2 times ($P < 0.05$), which can be used in the development of additional therapeutic strategies – autobiotic therapy, which has a positive effect both on the microbiocenosis and the state of patients with Alzheimer's disease.

Keywords: Alzheimer's disease, intestinal microflora, amyloid inflammation, autobiotic therapy.

РЕЗЮМЕ

МИКРОБИОТА КИШЕЧНИКА ПРИ БОЛЕЗНИ АЛЬЦГЕЙМЕРА

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Цель исследования – оценка качественного и количественного состава микрофлоры кишечника у пациентов с болезнью Альцгеймера.

В статье изложены данные, полученные в результате микробиологического исследования состояния микрофлоры кишечника у пациентов с болезнью Альцгеймера (n=37) в возрасте 69±0,5 лет. Анализ данных микробиологического исследования испражнений пациентов с болезнью Альцгеймера выявил, что в микрофлоре кишечника пациентов присутствуют как качественные, так и количественные дисбиотические изменения различной степени. В составе микрофлоры кишечника выявлено достоверное снижение степени обсеменения *Bifidumbacterium spp*. и *Lactobacillus spp*.: наиболее низкие количественные показатели *Lactobacillus spp*. зарегистрированы у пациентов с декомпенсированной формой дисбиоза lg 4,48 КОЕ/г, а *Bifidumbacteium spp.* - у пациентов с субкомпенсированной формой дисбиоза (lg 3,7 КОЕ/г). Показатели адгезивной активности изолятов *Lactobacillus spp.* в условиях микроаэрации на обезжиренном молоке были выше, в среднем, в 1,2 раза ($p<0,05$), что может быть использовано в разработке дополнительных терапевтических стратегий, оказывающих позитивное влияние не только на микробиоценоз, но и на состояние пациентов с болезнью Альцгеймера.

რეზიუმე

ნაწლავის მიკრობიოტა ალცჰეიმერის დაავადების დროს

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კვლევის მიზანს წარმოადგენდა ნაწლავის მიკროფლორის შემადგენლობის თვისობრივი და რაოდენობრივი შეფასება პაციენტებში ალცჰეიმერის დაავადებით.

სტატიაში წარმოდგენილია მონაცემები, მიღებული ალცჰეიმერის დაავადებით (n=37), 69±0,5 ასაკის პაციენტების ნაწლავის მიკროფლორის მდგომარეობის მიკრობიოლოგიური კვლევით. პაციენტების ნაწლავების გამონაყოფის მიკრობიოლოგიური კვლევის შედეგების ანალიზმა გამოავლინა პაციენტების ნაწლავების მიკროფლორაში არსებული სხვადასხვა ხარისხის როგორც თვისობრივი, ასევე, რაოდენობრივი დისბიოტური ცვლილებები. მიკროფლორის შემადგენლობაში გამოვლინდა, ასევე *Bifidumbacterium spp*.- და *Lactobacillus spp*.-ით მოთესვიანობის ხარისხის სარწმუნო შემცირება: *Lactobacillus spp* -ის ყველაზე დაბალი რაოდენობრივი მაჩვენებლები დარეგისტრირდა პაციენტებში დისბიოზის დეკომპენსირებული ფორმით - lg 4,48 კწ/გ, ხოლო *Bifidumbacterium spp*.- ის – პაციენტებში დისბიოზის სუბკომპენსირებული ფორმით - lg 3,7 კწ/გ. *Lactobacillus spp* –ის იზოლატების ადჰეზიური აქტივობის მაჩვენებლები მიკროაერაციის პირობებში გაუცხიმოვნებულ რძეზე იყო, საშუალოდ, 1,2-ჯერ მეტი ($p<0,05$), რაც შესაძლოა გამოყენებული იყოს დამატებითი თერაპიული სტრატეგიების შემუშავებისათვის, რომელიც დადებით გავლენას მოახდენს არამარტო მიკრობიოცენოზზე, არამედ ალცჰეიმერის დაავადების მქონე პაციენტების მდგომარეობაზე.

ACTION OF SIMVASTATIN IN IMPROVING COGNITIVE FUNCTIONS IN VASCULAR DEMENTIA

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Dementia is a topical issue in the modern world, including Georgia. Statistically, the number of cases is increasing every year, with 2018 as many as 35 million people worldwide suffering from the disease. There were 805 cases of dementia in Georgia in 2014. Since then, these data have been increasing every year, and as of 2017, there have been 1,600 cases of dementia. 70% of these syndromes are caused by Alzheimer's disease, and 30% by vascular and other dementia [1]. More attention has been paid to such a sharp increase in statistical data. According to the WHO experts, a significant problem for older people is CNS disorders, in particular dementia [2,5,6], which is prevalent among individuals aged 75 and above, around 11.2-17.4%. Cardiovascular diseases are the second most common cause of dementia [7]. Vascular dementia encompasses a wide range of disorders and is diverse in both morphological substrates as well as pathophysiological mechanisms and clinical manifestations. The main forms of the disease are multi-infarct dementia, dementia caused by local infarcts of cognitive function zones, multi-infarct, brain hypoperfusion and haemorrhage [9]. Despite such morphological and pathochemical polymorphisms, the clinical picture of vascular dementia along with cognitive disorders is presented with certain neurological symptoms (paresis, static and coordination disorders, etc.). It is also noteworthy that the cerebral arteriosclerosis is among the most important pathophysiological mechanisms, which develops as a result of micro-atheromatosis and lipohyalinosis of the vascular wall and eventually leads to vascular remodelling, hypoperfusion and white matter damage to the brain. Disease risk factors include arterial hypertension, dyslipidemia, diabetes mellitus, ischemic heart disease, malformations, arrhythmias and more. A correlation is often observed between the listed diseases, which further worsens the prognosis. For instance, A number of studies have established a direct link between blood pressure levels and blood lipid concentrations, impaired lipid metabolism is consid-