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ECONOMIC SCIENCES

MODERN FINANCIAL CRISES - CAUSES, CONSEQUENCES, CONCLUSIONS

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Abstract

The increasing frequency of financial crises in recent decades has sparked research interest in elucidating their emergence, genesis, and development. In this article, we briefly review the leading views on contemporary financial crises and the causes behind them.

Keywords: crisis, finance, banking.

Financial crises are catastrophic events for any economy, as they lead to the collapse of the financial system, which in turn leads to the collapse of the real economy. As Gorton and Ordonez note, financial crises occur in all market economies, both emerging market economies and developed economies, regardless of whether they have a central bank and whether they have introduced deposit insurance, thus the authors consider them to be an inherent characteristic of market economies and an inherent flaw in their financial markets. (Gorton, Ordonez, 2023). As a number of other studies have shown, the frequency of crises is the same in high- and middle-income countries (Reinhart and Rogoff (2009, 2013), Kindleberger and Aliber (2005)).

The increased frequency of crises, especially in the 21st century (Global Financial Crisis of 2007, Eurozone Sovereign Debt Crisis of 2010, COVID-19 crisis), combined with the increased instability of the modern global financial system (over-indebted countries, high real estate prices, volatile capital flows) has raised concerns among financial circles (Bandt, Drumetz, Pfister, 2021). Recent financial crises have become increasingly widespread and devastating, affecting the core of the global economic system, affecting economies that generate a significant share of the world's economic output, and generating significant long-term instabilities (Yilmaz, 2021).

All these crises lead some authors (Hsu, 2017) to argue that the contemporary global financial system, which is based on the efficient markets hypothesis, i.e. that financial markets, as self-correcting and symmetric, automatically reflect all available information about assets through changes in their prices, has suffered a total failure and requires a rethinking of the economic foundations of the financial management of the economy. Even the former chairman of the US Federal Reserve, Alan Greenspan, admits that he was wrong to approach monetary policy from the ideology of the free market, since instead of reaching equilibrium, markets can stagnate without active measures from regulators.

This also necessitates rethinking the nature and systematic nature of financial crises, with some authors in recent years advocating the thesis that financial crises are transforming from a "black swan" phenomenon, i.e. as a rare and completely unpredictable, but massive

event, into a "white swan" phenomenon, i.e. considering that crises are the result of a simple, repetitive and predictable process (Yilmaz, 2021).

If we look at the impact of the Global Financial Crisis, its impact was not limited to a narrowly defined market - geographical or asset class, but rather gave rise to a global breakdown of trust between financial institutions, which very quickly affected the real economies of countries, regardless of their participation in the affected financial markets Mazzola, P. (2022). Financial globalization, deregulation, liberalization, unregulated expansion of financial markets, the introduction of new and innovative financial instruments led to the development of the so-called shadow banking and increasingly risky speculation in financial markets and the transformation of the global financial system (Marichal, 2009). This corresponds to the change in the nature of financial crises noted by Grytten and Koilo, which have transformed from those caused by banking panics and credit crashes into financial crises caused by stock market crashes, bursting financial bubbles, currency crises and defaults by countries (Grytten, Koilo, 2019).

It is worth noting here that in the late 19th and early 20th centuries, financial crises were most often caused by bank runs and bank failures. The problems in the banking sector, which at that time was dominant in the financial sector of countries, very quickly transferred to the real economy, disrupting the normal relationship between economic agents seeking and offering resources, which in turn led to a contraction of the activities of enterprises, respectively, a decrease in the volume of production and the number of people employed in them. The resulting inflation and stagnation of the economy led to a decrease in consumer demand for goods and services, as a result of reduced disposable income and a lower standard of living, which in turn further reduced industrial production as a result of reduced solvent demand (Copolovitch, Singer, 2020).

Typically, a banking panic, which can later develop into a financial crisis, is triggered by a key event that makes depositors question the ability to convert their deposits or other short-term banking and/or financial obligations into cash. During the panic, banking institutions find themselves unable to fulfill their contractual obligations, and since there are no economic agents

willing to buy part of the bank's assets in order to recapitalize the institution, the latter falls into a state of insolvency (Gordon, Tallman, 2018).

As a number of authors point out, the main reason for the insolvency of the banking institution lies in the classic banking business model in which banks attract short-term loans (deposits of depositors) and at the same time provide long-term credit resources to their borrowers, which creates a significant imbalance between the maturity structure of the bank's assets and liabilities (Bojinov, 2013a, 2013b). This imbalance is dictated both by the purely commercial interest of banking institutions to generate income, but at the same time it is also of interest to society and the economy, as it consolidates the free funds of small individual depositors, directing them to the development of the economy and business, thus transforming liquidity into a socially productive function (Moro, Beker, 2016).

When this event goes beyond the scope of the individual banking and/or financial institution and covers multiple institutions or the entire financial system, the banking panic becomes systemic, and the crisis becomes a systemic financial crisis. This process is usually realized through the so-called contagion process, in which the risk of insolvency is transferred from one bank to another, especially when these banks have interbank exposures to the distressed bank, common asset exposure or through the domino effect due to counterparty risk (Gordon, Tallman, 2018, Moro, Beker, 2016).

It is worth noting here that in recent financial crises, especially the Global Financial Crisis of 2007, banks played a much more modest role in their emergence and development. For example, at the root of the 2007 crisis, it was precisely the problems with short-term financial debt instruments that gave rise to the financial panic, and as Ben Bernanke pointed out in his testimony before the Commission to Inquire into the Financial Crisis in the United States (2011), twelve of the thirteen most important financial institutions in the United States were on the verge of failure within a week or two after the bankruptcy of Lehman Brothers (Gordon, Tallman, 2018).

As Moro and Becker (2016) point out, the 2007–2009 US financial crisis was not a classic banking crisis, but a securities-based financial crisis, triggered by the enormous development of securities and derivatives. They emphasize that the modern securities-based financial system has significant advantages, related both to the possibility of almost unlimited geographical expansion of issuers, significantly expanding the potential market for their securities, and to the existence of a secondary market, allowing investors to trade their securities before their maturity. In this way, the modern financial system, by analogy with the banking institution, allows, through the securities market, to aggregate various investors with diversifiable short-term liquidity needs in order to provide long-term resources (debt and equity in the form of bonds and shares) for production purposes, while trading on the secondary market provides a significantly higher degree of operability and mobility of the attracted and invested financial re-

sources, and through the use of various derivative financial instruments, the possibilities for hedging and risk-taking for all participants have increased (Moro, Beker, 2016).

Insofar as practically all financial intermediaries, banks and non-bank institutions hold securities of varying degrees of liquidity on their balance sheets, they are also exposed to the risk of changes in the prices of these securities on the financial markets. The financial crisis caused by the securities market has exactly the same economic logic as the banking panic: investors' concern about the prices of the securities they hold can make them want to transform them into more liquid assets in the form of other securities or cash. The excessive supply of securities, in turn, causes a decline in their prices and the issuer or trader's refusal to buy them at a given price or at par. In turn, this refusal further depresses the prices of securities and, by analogy with financial contagion, is capable of negatively affecting a similar class of securities, even though their issuers do not have liquidity problems. As Giovannini (2010) points out, the securities market fails to function and provide liquidity services both when market participants themselves are unable to value the securities being traded and when participants lose confidence in the ability of other market participants to settle their obligations in the market (Giovannini, 2010).

As Shenai (2018) points out, shadow banking is based on transactions in two main types of securities: asset-backed commercial paper (ABCP) and repurchase agreements ("repos"), which are a kind of short-term "deposits" in the shadow banking system. In turn, shadow banks use the proceeds from ABCP and repos to purchase long-term securitized assets: asset-backed securities (ABS), or bonds backed by cash flows from pooled loans from sectors such as housing, credit card and auto loans, and other types of underlying collateral, thus making the security counterparties in the ABS loan portfolios a kind of "borrowers" (see Fig. 1.2) (Shenai, 2018).

As Gorton (2010) points out, unlike traditional regulated banks, shadow banks are significantly more exposed to the risk of runs, as they do not have government guarantees for the funds and securities invested in them (Gorton, 2010). The economic boom in the US since the early 2000s, combined with rising housing prices, further boosted the development of shadow banking, as their transactions mainly through ABCP, repos and securitization created systemic vulnerability in the system to falling housing prices, which was manifested in a full-scale flight of investors from the shadow banking system, especially after the bankruptcy of the investment bank Lehman Brothers (Shenai, 2018).

And if we can argue that the root of the Global Financial Crisis is imperfections and distortions in the financial markets, then the sources of the recession after the emergence of the COVID-19 pandemic are mainly due to the administrative measures taken to limit the spread of the disease, which also reflected on the normal implementation of business activities in the economy. The termination of a significant part of production and services requiring the physical presence of people

led to a kind of "freezing of the economy", a decline and change in the profile of consumer demand, as well as disruption of global supply chains (International Monetary Fund, 2020). All this led to a drastic reduction in cash flows to both consumers and companies, reflecting on a significant increase in the risk of non-service of granted corporate and consumer loans, which in turn increased the risks of problems in banking institutions and the financial sector as a whole. The lockdowns imposed on the global economy led to a depreciation of assets on capital markets and a sharp increase in the risks associated with them, causing subsequent liquidity problems and a contraction in the granting of new loans by banks. And although governments adopted and implemented significant anti-crisis support measures for the entire economy, including the financial sector, the shock to the global economy triggered a supply-driven recession, combined with accelerating inflation, an energy crisis and disruption of supply chains.

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STUDY ON THE IMPACT OF DEMOGRAPHIC TRANSFORMATION ON CHINAS ECONOMIC GROWTH

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Abstract

This study aims to delve into the impact of demographic transformation on Chinas economic growth. Through a multi-dimensional analysis of population age structure, urban-rural structure, and educational structure, the economic effects of demographic changes on labor supply, consumption patterns, technological innovation, and industrial restructuring are revealed. The research finds that demographic transformation has both opportunities and challenges for Chinas economic growth. On the one hand, population aging leads to a reduction in labor supply and rising labor costs, posing certain pressures on economic growth. On the other hand, the improvement of population quality and optimization of the educational structure provide strong support for economic transformation and upgrading and innovation-driven development. Additionally, changes in the urban-rural population structure have also promoted the coordinated development of regional economies to a certain extent. This study provides theoretical support and practical guidance for China to formulate more targeted population and economic policies.

Keywords: Demographic transformation; Economic growth; Labor supply; Consumption patterns; Technological innovation.

Chapter I Analysis of the Current situation of Population Transformation in China

Chinas population transformation process is complex and unique, undergoing a process from free migration to restricted migration, and then to full free migration. With the deepening of the reform and opening up and the development of the economy and society, Chinas population transformation presents a new characteristics of the current situation, which has had a profound impact on the economic growth. This section will provide an in-depth analysis of the current situation of the population transition in China to better understand its impact on economic growth.

1. Population migration and flow are highly active

Since the reform and opening up, Chinas population migration and flow has entered a new stage of development. A large number of people have moved from rural areas to urban areas and from less developed areas to developed areas, seeking better employment opportunities and living conditions. This migration flow not only accelerates the urbanization process, but also promotes the optimal allocation of the labor market. However, this has also brought about a series of problems, such as the gap between urban and rural areas, regional development imbalance and so on.

2. The scale of the floating population continues to expand

With the acceleration of urbanization, the scale of the floating population in urban areas continues to expand. These floating population mainly come from rural areas and underdeveloped areas, and they have made great contributions to the economic and social development of the cities. However, due to the restrictions of the household registration system and social security system, the floating population still has many difficulties in enjoying urban public services, social security and other aspects.

3. The population is aging

The aging trend of the population in China is increasing, and the proportion of the elderly population is increasing. This is mainly attributed to the implementation of the family planning policy and the improvement of medical and health conditions. The aging of the population has many effects on economic growth, including the reduction of labor supply, the change of consumer demand structure, and the increasing burden of social security.

4. The quality dividend of the population is gradually emerging

Although Chinas demographic dividend is gradually disappearing, the demographic quality dividend is gradually emerging. With the improvement of education level and the improvement of talent training mechanism, the quality of Chinas labor force has been constantly improved. This makes China more competitive in high-end manufacturing, services and other sectors. At the same time, with the improvement of scientific and technological innovation ability, China is gradually changing from demographic dividend to talent dividend.

5. The impact of the population policy adjustment

In recent years, China has made a series of adjustments to its population policy, including the full implementation of the two-child policy and the gradual liberalization of the three-child policy. The implementation of these policies has had a positive impact on the population transformation, and has helped to alleviate the pressure of population aging and optimize the population structure. However, the policy adjustment also brings some new challenges, such as the decline of fertility intention and the imbalance of sex ratio at birth.

6. Population changes are closely related to economic development

Chinas population changes are closely related to its economic development. On the one hand, the migra-

tion flow promotes the optimal allocation of labor market and urbanization; on the other hand, the aging population and demographic quality dividend have a profound impact on economic growth. Therefore, when formulating economic policy and population policy, we need to take full account of population changes in order to achieve sustainable economic development.

Vii. Population changes show regional differences

Chinas population changes show obvious differences in different regions. The southern and southeast coastal provinces attract more developed economy and more employment opportunities, while some economically underdeveloped provinces face population outflow. This trend of population mobility reflects the pattern of Chinas economy strong in the south and weak in the north, and also has different effects on the economic development of different regions.

VIII. The Impact of new urbanization on population transformation

New urbanization is one of the important strategies for Chinas future development, which has had an important impact on the population transformation. The new type of urbanization emphasizes putting people first and improving the quality and life of the urban population and towns. This helps to attract more people to the cities and promote urbanization, and also improve the living conditions of the migrants and their social integration.

To sum up, the current situation of population transformation in China is characterized by highly active population, continuous expansion of scale, intensified aging trend, emergence of quality dividend, significant impact of policy adjustment, close relationship with economic development and obvious regional differences. These characteristics have had a profound impact on economic growth, bringing both opportunities and challenges. Therefore, in the process of promoting economic growth, it is necessary to fully consider the factors of population transformation and formulate reasonable population policies and economic policies in order to realize the sustainable development of economy and society.

Chapter 2: Coping Strategies and Policy Suggestions

Section 1 Economic Growth Strategies for a Population Transformation

As a complex and profound social and economic phenomenon, the population transformation has had a profound impact on Chinas economic growth. In the face of profound demographic changes, we need to develop and implement a series of effective response strategies to alleviate the pressure of population transformation and promote sustained and healthy economic growth.

1. We will improve population policies and promote balanced population development

In view of the characteristics of Chinas population transformation, the population policy needs to adjust and optimize timely. On the one hand, we should continue to implement a positive birth policy and encourage school-age couples to have children, so as to improve the birth rate and alleviate the pressure of population aging. On the other hand, it is also necessary to

pay attention to the optimization of the quality and structure of the population, improve the quality of the labor force, and promote the coordinated development of the population and the economy by improving the level of education and strengthening vocational training.

2. We will deepen economic restructuring and energize economic growth

The challenges posed by population transformation need to be addressed by deepening economic restructuring. This includes improving the market economy system, optimizing the allocation of resources and improving economic efficiency, strengthening innovation drive, promoting industrial upgrading and transformation, and cultivating new economic growth points, deepening the reform of the household registration system, promoting the integration of urban and rural areas, releasing the potential of rural labor force and providing new impetus for economic growth.

3. We will strengthen the social security system to ensure peoples wellbeing

Population transformation has put forward higher requirements for the social security system. Therefore, it is necessary to further improve the social security system, expand the coverage, and improve the level of security. At the same time, a multi-level and diversified pension service system should also be established to meet the pension needs of the elderly population at different levels and with different needs. In addition, we should also pay attention to the vulnerable groups and intensify poverty alleviation efforts to ensure social equity and stability.

4. We will promote coordinated development among regions and improve the spatial distribution of the population

Population transformation also poses new challenges to the coordinated regional development. In order to realize the spatial balance between population and economy, it is necessary to promote the implementation of regional coordinated development strategy. On the one hand, the infrastructure construction and industrial development in the central and western regions should be strengthened to attract the flow of population to these regions; on the other hand, the population size and spatial distribution of big cities should be optimized to alleviate the problem of "big city disease".

5. Strengthen international cooperation and exchanges to jointly address population challenges

Population transformation is a global challenge that needs to be addressed by all countries. Therefore, China should strengthen cooperation and exchanges with other countries in the field of population, jointly study the law and influence of population transformation, and share experience and practices in dealing with population transformation. Through international cooperation, we can learn from the successful experience of other countries and improve Chinas ability and level to cope with population transformation.

To sum up, the economic growth strategy to deal with the population transformation is a complex and systematic project, which requires us to formulate comprehensive policies and measures from many aspects.

By optimizing the population policy, deepening the reform of economic system, strengthen the construction of social security system, promote regional coordinated development, strengthen international cooperation and exchanges, promote scientific and technological innovation, strengthening the construction of cultural education and improve the implementation of the labor market system, we can effectively meet the challenge of population transformation, promote Chinas economy to achieve sustained and healthy growth.

Section 2 Relevant policy Suggestions and measures

In the face of multiple challenges brought by population transformation to Chinas economic growth, the government needs to adopt a series of targeted policies and measures to alleviate the negative impact of population change on economic growth and find new growth drivers. This section will put forward relevant policy suggestions and measures from several aspects.

1. We will improve the family planning policy and promote balanced population development

First, the birth policy should be further optimized to create a social environment conducive to the balanced development of population. On the basis of maintaining the stability of the current birth policy, the relevant supporting measures should be gradually adjusted and improved, such as improving the level of birth security, expanding the parenting holidays, and reducing the burden of family parenting, so as to encourage school-age couples to have children according to the policy. At the same time, strengthen publicity and education, improve the fertility willingness and fertility level of the whole society, and realize the coordinated development of population and economy, society, resources and environment.

2. Strengthen education and training to improve the quality of human resources

In the face of the decrease of labor force and the trend of aging, improving the quality of human resources has become the key. The government should increase the investment in education, optimize the allocation of educational resources, and improve the quality of education. At the same time, we will strengthen vocational education and skill training to improve workers skills and their competitiveness in employment. In addition, enterprises should also be encouraged to strengthen staff training, improve the comprehensive quality and innovation ability of employees, and provide strong human resources support for economic development.

3. We will deepen reform and opening up and stimulate new drivers of economic growth

Reform and opening-up is an important driving force for Chinas economic growth. Facing the challenge of population transformation, we should further deepen reform and opening up and unleash market vitality and social creativity. To be specific, we can accelerate market-oriented reform, improve market mechanisms, optimize the business environment, and stimulate the vitality and innovation of market entities. At the same time, we will step up opening up, actively

participate in global economic cooperation and competition, and expand the external space for economic growth.

4. We will implement a prudent monetary policy and maintain financial stability

A prudent monetary policy is an important means to maintain steady economic growth. In the process of meeting the challenge of population transformation, we should implement a prudent monetary policy to maintain the reasonable growth of the money supply and maintain the stability of the financial market. At the same time, we will strengthen financial supervision and risk prevention to ensure the healthy operation of the financial system.

To sum up, facing the challenges brought by the population transformation to Chinas economic growth, the government needs to take various policies and measures to deal with them. By optimizing the birth policy, strengthen education training, deepen the reform and opening up, promote innovation driven development, improve the social security system, strengthen the regional coordinated development, the implementation of proactive fiscal policy and prudent monetary policy, can effectively alleviate the negative impact of population change on economic growth, and promote Chinas economy to achieve sustainable and healthy development.

Chapter III Study Conclusion

This study is dedicated to the deep discussion of the impact of population transformation on Chinas economic growth, and draws a series of important conclusions through the combing of historical data, the construction of theoretical models and empirical analysis. Below is a summary of the main conclusions of this study.

1. Population transformation has remarkable characteristics and has a multidimensional impact on economic growth

This study first provides a systematic review of the characteristics of Chinese population transition. The results show that Chinas population structure has undergone significant changes in recent years, including the decline of population growth rate, the decrease of labor supply, the increasing trend of population aging and the adjustment of urban and rural population distribution. These changes have not only changed the potential growth drivers of Chinas economy, but also had a profound impact on the speed and quality of Chinas economic growth.

2. The impact of changes in labor supply on economic growth is complex

Labor force is one of the most important factors of production for economic growth. This study found that with the advancement of population transformation, Chinas labor supply gradually tightened, with a complex impact on economic growth. On the one hand, the decrease of labor supply leads to rising labor cost, which puts pressure on enterprise profitability; on the other hand, the change of labor market also promotes technological innovation and industrial upgrading, which promotes the optimization of economic structure.

3. The aging of the population faces both challenges and opportunities for economic growth

Population aging is one of the important features of population transition, and this study analyzes its impact on economic growth. The study found that the aging population has brought challenges to China's economic growth, such as the rising social dependency ratio and the increasing pressure on pension expenditure. But at the same time, the aging population has also brought opportunities such as the upgrading of consumption structure and the development of healthy industry, providing new impetus for economic growth.

4. The adjustment of urban and rural population distribution has a significant spatial effect on economic growth

With the advancement of urbanization process, the distribution of urban and rural population in China has changed significantly. This study found that the spatial effect of this change on economic growth was significant. On the one hand, urbanization brings population aggregation and scale effect, which promotes the rapid growth of urban economy; on the other hand, the transfer of rural population to the city also promotes the development of rural economy and the coordinated development of urban and rural economy.

Through this study, we are deeply aware of the profound impact of population transformation on China's economic growth. In the future, with the continuous promotion of population transformation and the continuous change of the economic development environment, we need to continue to pay attention to the relationship between population transformation and economic growth, and constantly adjust and improve the policies and measures to adapt to the new development situation and challenges. At the same time, we also need to strengthen international cooperation and exchanges, draw lessons from the successful experience of other countries, and jointly promote global economic prosperity and development.

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MEDICAL SCIENCES

ДИФЕРЕНЦИАЛНО – ДИАГНОСТИЧЕН ПОДХОД НА КИШЛИЦАТА ПРИ ДЕЦА

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DIFFERENTIAL – DIAGNOSTIC APPROACH TO COUGH IN CHILDREN

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Резюме

Кашлицата е съпътстващ симптом на широк спектър от болестни състояния в детска възраст (ДВ) и е едно от най – честите оплаквания, за които родителите водят децата си при лекар. И представлява защитен рефлекс, който помага за изчистване на дихателните пътища (ДП) от различни инхалирани химични, механични и биологични дразнители, които активират рецепторите на кашлицата, разположени в мукозата на ДП от ларинкс до респираторните бронхиоли, също така има и екстрапулмонални рецептори, намиращи се в параназалните синуси, външния слухов канал и тимпаничната мембрана, хранопровода, диафрагмата, париеталната плевра и перикарда, които реагират основно на механични стимули. Тези рецептори са нервни окончания на вагусовите аферентни нерви, които изпращат сигнали обратно към центъра на кашлицата в продълговатия мозък, който задейства последователност от събития, които предизвикват кашлица. Подходите за контрол на кашлицата трябва да се фокусират върху характеризирането на кашлицата чрез клинична оценка за да се идентифицира точно нейната етиология. Подробната анамнеза и физикалният преглед са крайногелните камъни на оценката на дете с кашлица. При диференциалната диагноза на острата кашлица е съществено да не се пропуснат потенциално животозастрашаващи състояния като белодробен тромбемболизъм и остра сърдечна недостатъчност. Тази статия има за цел да представи подробен диференциално – диатностичен подход на кашлицата в ДВ.

Abstract

Cough is a concomitant symptom of a wide range of childhood (CH) diseases and is one of the most common complaints for which parents take their children to a doctor. It is a protective reflex that helps to clear the airways (AW) from various inhaled chemical, mechanical and biological irritants that activate cough receptors located in the mucosa of the AW from the larynx to the respiratory bronchioles, there are also extrapulmonary receptors located in the paranasal sinuses, external auditory canal and tympanic membrane, esophagus, diaphragm, parietal pleura, and pericardium that respond primarily to mechanical stimuli. These receptors are nerve endings of the vagus afferent nerves that send signals back to the cough center in the medulla oblongata, which triggers a sequence of events that cause cough. Approaches to cough control should focus on characterizing the cough through clinical evaluation to accurately identify its etiology. A detailed history and physical examination are the cornerstones of the evaluation of a child with cough. In the differential diagnosis of acute cough, it is essential not to miss potentially life-threatening conditions such as pulmonary thromboembolism and acute heart failure. This article aims to present a detailed differential-diagnostic approach to cough in the CH.

Ключови думи: Етиология, диагностика, деца, диференциална диагноза, кашлица.

Keywords: Etiology, diagnosis, children, differential diagnosis, cough.

Introduction

Cough is the most common symptom seen in outpatient clinics in many countries, and persistent cough (> 2 weeks) is one of the most common reasons for referral of children to a pediatrician or pediatric pulmonologist. Researchers have found that 35 – 40% of school - aged children continue to cough 10 days after the onset of the common cold, which is a common viral infection of the upper respiratory tract, and 10% of pre-school children continue to cough up to 25 days after a respiratory tract infection. A healthy child may normally cough up to 11 times a day, including in winter when returning home from playing outside in the cold. Cough may also be due to compression of the trachea or n. vagus by enlarged lymph nodes or by mediastinal tumors. The most common cause of acute cough in

childhood is a viral upper respiratory tract (URT) infection, while the most common causes of chronic cough are bronchial asthma, gastroesophageal reflux disease (GERD), and postnasal drip (often secondary to allergic rhinosinusitis). The definition of chronic cough varies across guidelines. It is defined as a persistent and continuous cough lasting more than 4 weeks in the 2020 CHEST consensus, and the British Thoracic Society guideline defines chronic cough in children as one that lasts more than 8 weeks, while also recognizing sub-acute cough that lasts 4–8 weeks.[2][4][5][6][7][8][11][12][13]

Cough classification

Cough is usually classified based on its duration, quality, or etiology. These indicators are important for the differential diagnosis (DD) of cough, (Tables 1, 2).

Cough is classified by its sound pattern as either dry (unproductive) or wet (productive) in nature. Parents are usually able to describe the cough sound pattern or provide recordings of their child's cough. The physician can determine the cough sound pattern when the child coughs spontaneously during examination or by asking her/ him to cough, therefore determining the sound pattern can help to indicate the etiology of the cough. A wet cough suggests mucous hypersecretion or impaired mucociliary clearance as the underlying cause, whereas a dry cough suggests airway irritation or inflammation or a non-airway etiology. In addition, clinicians should be aware that dry cough can become wet when AW secretions increase.[10] Cough is classified by duration as acute (up to 2 weeks), subacute/persistent (up to 4 weeks), or chronic (>4 weeks). Cough is classified by etiology as specific (SC) and nonspecific coughs (NSC). NSC is a dry cough in an unidentified respiratory disease with a known etiology. Most cases of NSC are due to non-serious causes - e.g. post-viral cough, and/or increased sensitivity of cough receptors, which may resolve spontaneously. Whereas SC is associated with other symptoms and signs suggesting an underlying problem.[3][4][5][6] Indicators of the presence of SC are[18]:

- Sudden cough with an episode of shortness of breath
- Progressive cough
- Difficulty breathing chronically or during physical exertion
- Delay in physical development
- Hypoxemia
- Constitutional symptoms
- “Club fingers” and “watch glass” nails
- Hemoptysis
- Chest wall abnormalities

• Noisy breathing and/or unusual auscultatory pulmonary rales

- Cough with a history of recurrent pneumonia
- Cough with onset in the neonatal period
- Difficulty swallowing
- Craniofacial anomaly
- Neuromuscular disease
- Wet cough, lasting more than 3 - 4 weeks.

DD of common causes of cough in children according to its duration.

1. Acute cough (<2 weeks):

• Classic recognizable cough: Barking cough in laryngotracheobronchitis; Staccato cough in chlamydial infection; Paroxysmal in case of pertussis (whooping cough) and parapertussis; psychogenic cough (dry/barking, absent at night, without clear etiology)

- Infection of upper/lower respiratory tract
- Foreign body aspiration (FBA)
- Bronchial asthma (BA)

• Inhalation injury in case of acute exposure to smoke or volatile substances.

- Embolic hemorrhage (rare)

2. Subacute (2-4 weeks) - examples are: postviral cough and acute bronchitis.

3. Chronic (> 4 weeks):

• Nonspecific cough: Postviral; Increased receptor sensitivity; Bronchial asthma; GERD; Chronic process in the upper respiratory tract;

- Subacute bronchitis

• Bronchiectasis and persistent pneumonia: cystic fibrosis; ciliary dyskinesia; immunodeficiency; congenital lung lesions

- Aspiration

• Chronic infections: tuberculosis; nontuberculous mycobacteria; mycoses

- Interstitial lung disease (e.g. rheumatic disease)

- Cardiac etiology.

Table 1.

Common causes of chronic cough by age (according to Haya Alsubaie et al, 2015)

Young children (<5 years)	Older children (>5 years)
Infections	Bronchial asthma
Postviral hyperreactivity of the Airway	Infections – such as tuberculosis, mycoses, nontuberculous mycobacteria
GERD	Postnasal drip
Congenital malformations of the AW	Recurrent pneumonia
Bronchial asthma	Protracted bacterial bronchitis
Protracted bacterial bronchitis	Passive smoking
Passive smoking	Bronchiectasis
Foreign body aspiration	Psychogenic cough

Table 2.

Classification of classically recognizable cough based on its sound qualities (according to Chang et al, 2006)

Cough characteristic	Possible etiology
Paroxysmal (with or without "whoop") with urge to vomit	Pertussis/pertussis-like syndrome
Dry/barking, laryngeal cough	Acute croup, tracheomalacia, habitual/psychogenic
Staccato cough in infants and young children	Chlamydial infection
Wet/ productive	Protracted bacterial bronchitis, pneumonia, primary ciliary dyskinesia
Morning chronic wet cough	Purulent lung diseases

Differential diagnostic algorithm for cough in childhood.

History and physical examination. A precise history and a thorough physical examination are essential

for the correct preparation of a differential diagnostic plan and subsequent establishment of an accurate etiological diagnosis.

The history should focus on identifying:

- Duration, quality, provoking factors, progression and daily/seasonal variations of the cough, accompanying symptoms, neonatal and family history, history of exposure to harmful environmental factors (passive smoking and air pollutants), medication intake and family and personal history of allergic diseases (BA, allergic rhinitis, allergic rhinosinusitis, atopic dermatitis, etc.). Parents and relatives of children from 6 months to 6 years of age should be asked about the possibility of aspiration of foreign bodies (small toys, small objects, consumption of peanuts, grapes, etc.), the entry of a foreign body into the respiratory tract is often accompanied by the so-called "respiratory choking": during feeding (usually when crying, laughing, playing) a painful attack of coughing suddenly occurs, sometimes with cyanosis and short-term apnea.

- The medical history should include recent respiratory infections, recurrent pneumonia, and questions about risk factors for tuberculosis (TB) - contact with a person who is proven or suspected to have tuberculosis, risk groups for TB are those at higher risk of exposure (have traveled to or immigrated from countries with endemic TB, live in poor conditions or do not have access to health services, such as homeless people, drug addicts, alcoholics).

- Psychogenic cough is characterized by its absence at night and during play and is not accompanied by fever and other symptoms. Paroxysmal cough in case of pertussis (whooping cough) is characterized by a prolonged series of coughing fits, followed by deep and noisy inhalation (whoop) with the release of sticky mucus, sometimes with vomiting.

- Gastroesophageal reflux disease (GERD) in infants and young children is characterized by a history of spitting up after eating, irritability during eating, paroxysmal dystonic postures including torticollis and opisthotonus (Sandifer syndrome), growth retardation, recurrent wheezing or pneumonia, and in older children GERD is characterized by chest pain or heartburn after eating and lying down, night cough, hoarseness, halitosis, abdominal pain and regurgitation.

The physical examination should be directed at the general condition of the child and should include determination of:

- Vital signs and growth parameters, detailed examination of the respiratory system, including ENT status

- Inspection of the chest wall for signs of hyperinflation and deformities

- Inspection for edema, cyanosis, the presence of "Club fingers" and "watch glass" nails, and for recurrent/persistent auscultatory physical findings, indicating chronic lung infections, that occur in children with bronchiectasis, cystic fibrosis, pulmonary congenital anomaly, or lung abscess

- Persistent exudative physical findings on pulmonary auscultation in the same location for months and years are indicative of irreversible morphological changes and are pathognomonic for the presence of

bronchiectasis. Auscultatory findings of crepitations, rhonchi and crackles, indicating pneumonia, bronchiolitis or bronchial obstruction, and bilateral "wheezing" breathing indicates asthma, but may be associated with vascular ring, cystic fibrosis, etc. Persistent unilateral "wheezing" breathing is highly suspicious for FBA. The presence of inspiratory stridor and low or lack of respiratory sounds with or without cyanosis, indicate Croup syndrome.

- Hemoptysis can be observed in bronchiectasis, pulmonary hemosiderosis, hemorrhagic pneumonia in newborns, severe congestion in the small circle of blood circulation in case of left ventricular failure, mitral or aortic valve disease, parasitosis, mycoses, pneumonia, cystic fibrosis, tuberculosis and endobronchial processes.

Investigations.

Investigations that aid in the diagnosis of cough include:

- CBC, differential CBC, ESR, and CRP

- Collection of a sample of the sputum for rapid antigen testing or culture

- Chest radiography may provide information about pulmonary infiltrates/consolidations, pneumothorax, hyperinflation, atelectasis, and chronic pulmonary changes. Lateral or anteroposterior neck radiography is necessary in some unclear cases of croup

- Functional respiratory testing (spirometry) in cooperative children over 6 years of age. This test aids in the diagnosis of restrictive and obstructive lung disease (including it aids in the diagnosis of asthma)

- Mantoux tuberculin skin test as a screening test for tuberculosis infection

- GERD can be proven by pH-metry, sometimes fibroesophagogastroscope is performed to diagnose anatomical causes of obstruction in the upper parts of the gastroesophageal tract. But in most cases the diagnosis is clinical, and a diagnostic and therapeutic attempt is made with positional treatment and the use of H₂ - inhibitors or proton pump inhibitors.

- Bronchoscopy (or fibrobronchoscopy) allows for assessment of the anatomical structure of the tracheobronchial tree (detection of congenital anomalies, tumors, granulations, foreign bodies); assessment of the condition of the bronchial mucosa (hyperemia, bleeding, erosions); assessment of bronchial secretions - purulent, serous, hemorrhagic, these symptoms are suspicious for bronchiectasis; detection and removal of foreign bodies in the respiratory tract; performing diagnostic and therapeutic bronchoalveolar lavage [2]

- Sweat chloride test in case of clinical and radiological data of cystic fibrosis

- Computed tomography (CT) in case of suspected data of bronchiectasis, tumors, vascular "ring" anomaly and congenital lung malformations (lung sequestration, etc.)

- In case of chronic wet cough, an attempt can be made to expectorate and examine sputum for cytological, cultural examination and microbial sensitivity, includingly for acid-fast bacilli (AFB)

- Allergy tests: skin allergy tests or specific RAST tests

- Attempt of treatment with antiasthmatic drugs in case of chronic wet cough in young children for a period of 6-8 weeks, after which the same treatment can be discontinued[9].

Recommendations for cases of cough in a child, for which a mandatory consultation with a pediatric pulmonologist is required:

- Chronic wet cough, not responding to antimicrobial therapy
- Cough of unclear etiology and duration of more than 4 weeks
- Chronic cough, accompanied by a lag in physical development and/or associated with persistent hypoxemia
- Cough with a history of recurrent pneumonia
- Cough with persistent pulmonary wheezing
- Cough, accompanied by hemoptysis pointing to an underlying disease, for example, bronchiectasis, pulmonary hemosiderosis, hemorrhagic pneumonia, cystic fibrosis, tuberculosis and endobronchial processes
- Chronic cough associated with bronchial asthma, not responding to maintenance anti-asthmatic therapy.

In conclusion, cases of cough of unclear etiology and duration of more than 4 weeks should be referred for consultation with a pediatric pulmonologist and children with cough should be treated according to disease-specific guidelines. In the differential diagnosis of acute cough, it is essential not to miss potentially life-threatening conditions such as pulmonary thromboembolism, acute heart failure and foreign body aspiration. The treatment of cough in kids to be based on its etiology.

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COMPARATIVE EFFECTIVENESS OF PROSTHETICS WITH CLASP AND PARTIALLY REMOVABLE LAMELLAR DENTURES

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Abstract

Clasp dentures have become widespread due to the widespread introduction of casting technology for various metal alloys into dental institutions. These prostheses differ significantly in design and method of distributing the load on supporting tissues from other prostheses used to eliminate defects in the dentition. They rest on the teeth and the toothless area of the alveolar process or alveolar part. At the same time, they transmit chewing pressure to two biologically different structures: the periodontium of the supporting teeth and the mucous membrane of the alveolar ridge.

Keywords: partial loss of teeth, clasp dentures, plate dentures.

The purpose of the study is to increase the effectiveness of orthopedic treatment using various designs of removable dentures in patients with partial absence of teeth.

Material and methods. A total of 20 patients with partial absence of teeth were examined and received orthopedic treatment during the year. Depending on the orthopedic treatment plan, two groups of patients were identified. In the 1st group (n=10) clasp dentures with a clasp fixation system were made, and in the 2nd group (n=10) partial removable laminar dentures with wire retaining clasps were made. The criteria for inclusion of patients in the study were: partial absence of teeth, indications for removable dentures, absence of somatic diseases in the acute stage, diseases of the mucous membrane [1.2.3]. To assess the severity of inflammation of the soft tissues and the state of epithelization of the prosthetic bed, a Schiller test was performed, modified by Yu. Pisarev, by treating the oral mucosa with a potassium iodide solution [4.5.6]. To assess the subjective feelings of patients when using partial removable dentures, a questionnaire was used, in which the patient, answering five questions, ranked the answer in points from 1 to 5 [7.8]. The questions concerned the assessment of the restoration of five functions: 1. Restoration of chewing function; 2. Restoration of the act of swallowing; 3. No pain associated with the prosthesis in the oral cavity; 4. Restoration of diction; 5. Restoration of salivation. With a total score of 18 or more, the result was considered good; from 14 to 17 points - satisfactory; 13 points or less - unsatisfactory

Results.

Thus, in patients of group 1, moderate inflammation predominated before prosthetics and after 3 months, 69 and 85%, respectively. After 6 months, the indicators improved towards mild inflammation and amounted to 93%. Group 2 patients were characterized by moderate inflammation throughout the study. Thus, the highest rates were after 6 months - 85%. After 6 months they decreased to 82%, but still remained at an

elevated level. In group 1, patients noted shorter periods and higher quality of restoration of chewing function, swallowing, diction, salivation, and also experienced less pain associated with the use of dentures in less quantity and intensity. From this we can conclude that the scoring of the effectiveness of prostheses, taking into account subjective sensations, in patients of group 2 compared with group 1 was lower in the immediate period after prosthetics by 14%, after 3 months - by 15%, after 6 months - by 22%. A comparative analysis of the data obtained revealed that when patients with dentition defects used partial removable laminar dentures compared to clasp dentures, the performance parameters of orthopedic structures were objectively lower. When patients were fitted with partial removable plate dentures, chewing efficiency was lower—chewing time was prolonged, the quality of grinding solid food was reduced, and the adaptation period of getting used to the dentures was lengthened. From the above data we can conclude that when providing prosthetics for patients with partial absence of teeth, clasp dentures function with greater efficiency compared to partial removable plate dentures in almost all evaluation parameters. This circumstance allows us to recommend clasp dentures for prosthetics of patients in the treatment of dentition defects.

Conclusion.

In total, 20 patients with partial absence of teeth were examined and received orthopedic treatment and 2 groups were identified: in one, clasp dentures were made, in the second, partial removable laminar dentures were made. In the immediate period after prosthetics, as well as 3 and 6 months after orthopedic treatment, the condition of the supporting teeth and tissues of the prosthetic bed was examined. Thus, the work established that when providing prosthetics for patients with dentition defects, partial removable lamellar dentures have a more pronounced effect on the tissues of the prosthetic bed and supporting teeth than clasp dentures. Moderate inflammation predominated (82%),

with intense inflammation of the gums present in 7.5%. Moderate gingivitis predominated (75%), with severe gingivitis present in 13.4%. The average degree of inflammatory-destructive processes in the periodontium predominated (78%). When assessing the effectiveness of prosthetics for partial loss of teeth, patients with clasp dentures noted that the quality of restoration of chewing function, swallowing, diction, and the normal volume of salivation was higher, and the recovery time was lower; in addition, they experienced less pain associated with the use of dentures: through 6 months chewing efficiency is lower in group 2 (56% versus 84%) by 27%; The score for the effectiveness of partial removable dentures, taking into account subjective sensations, is also lower than the 2nd group after 6 months - by 22%. Thus, the conducted study of the results of orthopedic treatment of patients with partial absence of teeth indicates the advantage of using clasp dentures over partial removable laminar dentures, based on the condition of periodontal tissues, the prosthetic bed, the results of functional tests and a qualitative assessment of the results of the operation of the dentures and the level of dental health.

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CLINICAL AND MICROBIOLOGICAL FACTORS FOR BACTERIA IN BLOOD AND BILE AMONG PATIENTS WITH ACUTE CHOLANGITIS**Fuss J.,***PhD, St.Paraskeva medical center***Voloboyeva A.,***Communal Municipal Clinical Hospital 8, Lviv***Polovyj V.***Doctor of medical science,**Bukovinian State Medical University, Chernovtsy*DOI: [10.5281/zenodo.14707896](https://doi.org/10.5281/zenodo.14707896)**Abstract****Background.** Acute cholangitis is a clinical syndrome caused by bacterial infection in the biliary system.**Methods.** Patients with acute cholangitis admitted to hospital between January 2018 and December 2023. The diagnostic criteria for acute cholangitis were based on Tokyo Guidelines 18.**Results.** A total of 250 patients had bacterial growth in bile. Alanine aminotransferase concentration and duration of antibiotic use correlated with bacteria in bile.**Conclusion.** The commonly isolated bacteria from bile samples in patients with acute cholangitis were *E.coli*, *Kl.pneumoniae*, and *E.faecalis*. Age, C-reactive protein, duration of antibiotic usage, alanine aminotransferase level were independent risk factors, and the predictive model could efficiently identify the patients with a high risk of bacteria in bile when invasive operations are conducted.**Keywords:** acute cholangitis, bacteria, blood culture, bile culture.

Introduction. Acute cholangitis, the most common hepatobiliary system disease, is an infectious condition caused by partial or complete obstruction of the biliary system and can have life-threatening consequences if not given timely treatment [1,2]. Fever, abdominal pain, and jaundice are typical clinical manifestations of patients with acute cholangitis and obstruction of the bile duct is the main cause biliary obstruction [3].

Controlling biliary infections and obstruction release are the most common two important strategies in the clinical management of acute cholangitis. Treatment methods include intravenous fluid, antibiotics administration, and biliary drainage [4,5]. The presents of bacteria in bile increased the risk of entering the circulation system when invasive operations were conducted to remove the stone in the biliary duct system, consequently resulting in systemic infections [6]. However, there is limited data on risk factors related to positive culture results in bile specimens before bile drainage. Therefore, bile samples were collected to analyze the distribution of bacteria that remains in patients with acute cholangitis after antibiotic treatment. Clinical manifestations and laboratory tests upon admission were reviewed to predict the presence of bacteria in bile when bile drainage was conducted [7,8].

Material and methods. This was a retrospective study. Patients with acute cholangitis admitted to a

St.Paraskeva medical center, Communal Clinical hospital 8, department of surgery Pustomy Hospital between January 2018 and December 2023. The diagnostic criteria for acute cholangitis were based on Tokyo Guidelines 18. Data were collected retrospectively by local investigators using electronic case report forms (eCRF) then centralized and anonymized. The following data were collected: age, gender, cardiovascular diseases (coronary artery diseases or chronic heart failure), hypertension, other comorbidities (e.g. diabetes mellitus, cancer, immune deficiency, cirrhosis, chronic renal failure), clinical symptoms (abdominal pain, jaundice, diarrhea, chills) at ICU admission. Laboratory examinations of blood cell components and other analyses were collected within 24h during hospitalization.

Results. According to the bile culture results, 322 patients with acute cholangitis were divided into the following group: bacteria in bile – group I (212) and control (110) groups – group II.

The median age was 66 years with a twofold higher incidence of men (65%). Patient characteristics are summarized in Table 1. Commodities were frequent, notably diabetes ($n = 96$, 45%), cardiovascular diseases ($n = 156$, 73%) and active solid tumors ($n = 45$, 21%). Abdominal pain (93%) and jaundice (85%), which are classical clinical signs of AC, were frequently observed but fever (defined by a temperature $> 38^{\circ}\text{C}$) was only reported in 135 patients (64%).

Table 1

General characteristics of patients			
Characteristics		Group I (n=212)	Group II (n=110)
Gender			
	Male	146	68
	Female	66	42
Age (years)		72 (60-84)	66 (46-74)
Commodities	Diabetes	96 (45%)	58 (53%)
	Hypertension	112 (53%)	64 (58%)
	Cardiovascular disease	156 (73%)	98 (89%)
	Chronic kidney disease	30 (14%)	20 (18%)
	Cirrhosis	20 (9,5%)	8 (7%)
	Cancer and hematologic malignancies	45 (21%)	23 (21%)
Biliary drainage procedure	Percutaneous derivation	22 (10%)	18 (16%)
	ERCP	198 (93%)	92 (84%)
	Surgery	12 (5,7%)	8 (7%)
Complications after ERCP	Bleeding	35 (16,5%)	22 (20%)
	Gastrointestinal perforation	27 (13%)	15 (14%)
	Pancreatitis	31 (15%)	17 (15,5%)

At ICU admission, patients with AC had severe disease, with sepsis (), septic shock () and a high SOFA score (). A high proportion of patients had renal (□) failure, coagulopathy and lactic acidosis. Finally, in ICU

mortality reached 18%, half of the death occurring within the first 10 days of ICU admission (table 2).

Table 2

Clinical and biological parameters of patients with acute cholangitis				
Characteristic		Group I (n=212)	Group II (n=110)	p-value
Clinical signs	Abdominal pain	198 (93%)	89 (81%)	
	jaundice	180 (85%)	78 (71%)	
	chills	124 (59%)	64 (58%)	
	Temperature >38	135 (64%)	85 (77%)	
Biological parameters	Leukocytes (*10 ⁹ /L)	0,84 (0,42-1,34)	1,07 (0,7-1,5)	<0,001
	Platelets (*10 ⁹ /L)	10,00 (9,0-10,8)	10,00 (9,0-10,8)	0,942
	Alanine aminotransferase (U/l)	107,00 (45,00-220,00)	190,00 (80,00-350,00)	<0,001
	Aspartate aminotransferase (U/l)	95,00 (40,00-250,00)	150,00 (50,00-300,00)	0,001
	Total blood bilirubin (μM)	44,00 (18,50-80,50)	45,50 (22,00-80,50)	0,406
	Serum creatinine (μM)	65,00 (54,00-84,00)	61,00 (50,00-76,00)	0,018
	C-reactive protein (mg/l)	25,00 (5,00-70,00)	8,5 (2,50-44,50)	<0,001

Positive blood culture was frequently reported in patients with AC (n=240/322). Bile culture was only performed in 145/322 and was positive in 75% of the cases (250). microbiological data are summarized in Table 3. in blood or bile culture, the most frequently identified bacteria were gram-negative bacilli (82%)

and gram positive (17%). The most frequently identified bacteria were Escherichia coli (47%), Kl.pneumonia (11%), Enterococcus faecalis (7%), Enterobacter cloacae (6,5%) and Pseudomonas aeruginosa (4,5%). finally, an infection caused by Extended spectrum beta lactamase (ESBL) – producing bacteria was observed in 35 AC patients.

Table 3

Microbiological data in blood and bile culture

Germes	Blood	Bile
Positive culture	240 (75%)	145 (45%)
Total pathogens	318 (98%)	250 (78%)
Gram negative bacilli	264 (82%)	196 (61%)
<i>Escherichia coli</i>	152 (47%)	82 (25%)
<i>Kl.pneumonia</i>	35 (11%)	20 (6%)
<i>Enterobacter cloacae</i>	21 (6,5%)	16 (5%)
<i>Kl. oxytoca</i>	15 (4,5%)	8 (2,5%)
<i>Ps.aeruginosa</i>	15 (4,5%)	18 (5,6%)
ESBL	35 (11%)	30 (9,3%)
Gram positive bacilli	54 (17%)	54 (17%)
<i>Enterococcus faecium</i>	23 (7%)	25 (7,8%)
<i>Streptococcus spp.</i>	19 (6%)	6 (1,9%)
<i>Enterococcus faecalis</i>	16 (5%)	38 (12%)
<i>Staphylococcus aureus</i>	4 (1,3%)	6 (1,9%)
Other GP	13 (4%)	11 (3,5%)

Discussion. Infection of biliary system causes acute cholangitis, a clinical condition that may result in death if not treated appropriately. Biliary obstruction, followed by bacteria ascending into the bile duct, is an important factor in the pathogenesis of acute cholangitis [9,10]. However, bacteria can remain in the bile despite antibiotic usage. In the study, the distribution of bacteria in the bile was determined, and multiple indicators of the first laboratory examination during hospitalization were analyzed to determine the risk factors for bacteria in the bile for patients with cholangitis [11].

It was found that age was independent risk factor for bacterial bile in patients with acute cholangitis, which might be attributed to a decline in defense response immunity with aging, and the body's weakened resistance to pathogens [12]. Furthermore, the incidence of acute cholangitis is higher in older people than in younger people. As a diagnostic indicator of acute cholangitis, elevated C-protein level suggest bacterial infection. However, the results of this study demonstrated that only a substantially elevated level could be indicative of the presence of bacteria in bile specimens based on the limited contribution [13].

Conclusion. The commonly isolated bacteria from bile samples in patients with acute cholangitis were *E.coli*, *Kl.pneumoniae*, and *E.faecalis*. Age, C-reactive protein, duration of antibiotic usage, alanine aminotransferase level were independent risk factors, and the predictive model could efficiently identify the patients with a high risk of bacteria in bile when invasive operations are conducted.

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ВИВЧЕННЯ ЗОРОВОГО НАВАНТАЖЕННЯ СЕРЕД СТУДЕНТІВ

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Анотація

Проведено анкетування 412 здобувачів освіти Івано-Франківського національного медичного університету з метою вивчення стану зорового навантаження та чинників, які впливають на нього. Було встановлено, що найбільш частими причинами зниження зору у здобувачів освіти є тривале безперервне використання гаджетів, недостатнє освітлення робочого місця, а також було виявлено, що тривалий стрес та спадкова схильність мали вплив на розвиток порушень зору у студентів. Враховуючи рекомендації МОЗ України щодо профілактики стану зору, такі як вправа “20-20-20”, регулярно перевіряти гостроту зору в офтальмолога, можуть допомогти суттєво знизити негативний вплив надмірного зорового навантаження.

Abstract

A survey of 412 students of Ivano-Frankivsk National Medical University was conducted to study the state of visual load and factors that affect it. It was found that the most common causes of vision loss in students are prolonged continuous use of gadgets, insufficient lighting of the workplace, and it was also found that prolonged stress and hereditary predisposition had an impact on the development of vision disorders in students. Taking into account the recommendations of the Ministry of Health of Ukraine on the prevention of vision, such as the “20-20-20” exercise, regularly checking visual acuity at an ophthalmologist can help significantly reduce the negative impact of excessive visual load.

Ключові слова: зорове навантаження, студенти, анкетування.

Keywords: visual load, students, survey.

Актуальність теми. У сучасному світі цифрових технологій та інформаційного перенасичення люди стикаються зі значним зоровим навантаженням, яке пов'язане з використанням смартфонів, комп'ютерів та інших гаджетів. За даними Всесвітньої організації охорони здоров'я, близько 2,2 мільярда людей у світі мають порушення зору, частина з яких спричинена підвищеним зоровим навантаженням.

Школярі та студенти в сучасному світі частіше користуються електронними носіями інформації, порівняно із друкованими в процесі навчання. Постійне зорове навантаження може призводити до таких явищ, як астенопія, підвищена втомлюваність очей, головний біль, порушення сну, а також погіршення психоемоційного стану.

Вивчення факторів, що впливають на зорове навантаження, є важливим для розробки рекомендацій щодо оптимізації режиму роботи студентів з електронними пристроями, профілактики зорових порушень та збереження їхнього загального здоров'я. Це особливо актуально для сьогодення в Україні, оскільки часто проводиться навчання в дистанційному режимі.

Таким чином, актуальним є вивчення стану зорової системи та факторів впливу на неї, оскільки результати такого дослідження можуть сприяти підвищенню ефективності навчального процесу, покращенню якості життя студентів та зниженню ризиків, пов'язаних із надмірним зоровим навантаженням.

Мета дослідження: Вивчити стан зорового навантаження та чинників, які впливають на нього серед студентів Івано-Франківського національного медичного університету.

Матеріали і методи дослідження. Нами було розроблено анкету із 27 запитань. Анонімно опитано 412 здобувачів освіти Івано-Франківського національного медичного університету від першого по шостий курс. Анкетування проводилось онлайн протягом п'яти днів.

Результати дослідження та їх обговорення.

Перший розділ анкети включав загальні питання про вік, рік навчання та стать. Серед опитуваних, найбільшу групу, 105 студентів, склали студенти, яким виповнилось 17 років, 63 – 18 років, 64 – 19 років, 54 студентам – 20 років, 52 – 21 років, 54 студентам – 22, 13 студентам – 23 років і 3 студентам на час проходження анкетування було 24 роки.

Найбільше студентів, які взяли участь в анкетуванні були студенти 1 курсу, що становить 36 % від усіх опитаних, другого курсу - 10 %, третього – 20%, четвертого – 14% та 20 % інших. Серед респондентів значну частину, а це 80 %, склали особи жіночої статі.

Наступний блок запитань стосувався стану зору. На запитання: «Чи носите ви окуляри або контактні лінзи?» - 156 (38%) опитуваних відповіли, що носять. Серед них 55 (18%) студентів вказали, що носять окуляри через хворобу, 198 (66%) – через поганий зір, а 48 (16%) студентів - не знають з якої причини використовують окуляри. Через порушення рефракції, такі як астигматизм, окуляри носять 14 студентів, міопію – 33 осіб і гіперметропію – 3 осіб. Також, серед причин, які зумовили використання окулярів чи контактних лінз були вказані: попередньо перенесений хімічний опік рогівки, ускладнення від кору, а також через перенапруження органу зору через навчання. Загалом, 33% студентів оцінюють свій зір як хороший, середнім свій зір вважають 24% студентів, поганим – 21%, дуже поганим – 5% і 17% - зазначають, що їхній зір є дуже хорошим. Тобто, 50 % серед опитаних мають проблеми з зором, однак тільки 38% користуються окулярами або контактними лінзами. Тим самим некорегована рефракція провокує погіршення стану очей, розвитку астенії, швидкої втоми дратівливості, що в свою чергу може викликати погіршення успішності студентів. Важливим запитанням у нашому дослідженні було встановити зміни зору за період навчання в університеті. Так, 59% опитаних зазначили, що їхній зір суттєво погіршився за останній рік. У таких випадках рекомендується звернутися до офтальмолога для діагностики зору та при потребі підбору окулярів.

Наступним блоком запитань було встановлення інформації щодо користування гаджетами. Ми виявили, що 35% опитуваних студентів проводять за гаджетами 6-8 годин на день, а 29% - проводять більше 8 годин, 27% - 4-6 годин і 9% студентів - зазначили, що використовують гаджети менше 4 годин на день. У зв'язку із діджиталізацією та необхідністю тривалій час працювати за комп'ютером можна скористатися правилом 20-20-20 (після 20-ти хвилин зорового навантаження перевести погляд на 20 секунд на предмет, який знаходиться на відстані 20 футів (6 метрів))[1],[4].

Найчастіше гаджетами користуються ввечері з 18:00 до 22:00 (41%), вдень (12:00-18:00) гаджетами користуються 29% студентів, 20% - користуються вночі (після 22:00), найрідше користуються гаджетами зранку (6:00-12:00) – всього 11%. Кожного дня, перед сном 86% студентів використовують гаджети. Зазвичай 48% опитуваних зменшують яскравість екрана у темряві вручну, ще 36% використовують «нічний режим», а 12% не змінюють налаштування взагалі. Тобто більшість студентів використовують гаджети протягом довгого періоду часу впродовж доби, у таких випадках рекомендовано робити перерви, переводити погляд вдалину, робити вправи для очей, щоб зменшити втому.[2]

Цікавий факт, що 45% студентів витрачає близько 1-3 години на читання друкованих книг, конспектів, текстів впродовж доби, інші 27% - витрачають 3-5 годин, 16% - менше 1 години і 11% - більше 5 годин. Найчастіше читають ввечері – 47%, трохи рідше вдень – 32%, 14% - вночі і 7% - зранку. 41% опитаних студентів зазначає, що зрідка читають при слабкому освітленні, час від часу – 32%, 17% - ніколи не читає при поганому освітленні і 9% - часто. 87% студентів вказали, що використовують електронні книги або PDF-файли для читання. Кілька разів на тиждень 33% опитаних людей читають з екрана гаджета в темряві, 32% - щодня і 30% - зрідка. Загалом, із відповідей студентів можна зробити висновки, що, як правило студенти, працюють із друкованими підручниками і конспектами при достатньому освітленні і тільки зрідка при слабкому. Проте при роботі з гаджетами майже третина студентів все ж таки читає при поганому освітленні.

Під час анкетування половина студентів зазначила, що в аудиторіях під час занять завжди достатньою світла, а половина, що іноді може бути недостатньою. 52% добре оцінює освітлення у своєму місці проживання, 31% - дуже добре, 14% - середнє.

Спадковість є базовим компонентом нашого розвитку. Тому, нам було цікаво дізнатись чи мали родичі опитуваних проблеми з зором. У 58% опитаних студентів є родичі з порушенням зору, найчастіше це бабусі і дідусі – 32%, 25% - мати, 20% - батько і 18% - брати або сестри. Переважно проблеми із зором у цих родичів почалися уже в дорослому віці (після 18 років) – 42%, 28% студентів не знає коли саме у їхніх родичів почалися проблеми із зором, 16% стверджує, що проблеми почалися у дитинстві і 14% - у підлітковому віці. Найпоширеніші проблеми у цих родичів - це міопія – 42%, далі гіперметропія – 26%, у 14% - астигматизм, 11% - катаракта. Отже, у значної частини студентів які відзначають у себе порушення зору були генетичні передумови, так як вони відзначили, що у їхніх батьків є порушення зору, які пов'язані із вадами рефракції, але як ми бачимо, із попередніх відповідей, вони самі, в певній мірі, посприяли погіршенню зору в себе, тому що перенапружували зору в себе, читали при поганому освітленні.

На жаль, сьогодні кожен українець живе у стресовому середовищі зумовленому війною. Стрес або тривожний стан негативно впливає на зір. Тому, нами було опитано студентів, щодо цих факторів. Встановлено, що 41% респондентів часто відчуває тривогу чи стрес, 36% - іноді, 14% - постійно і 9% - майже ніколи. 64 студента оцінили свій рівень тривоги на 8 балів за 10-ти бальною шкалою, 61 – оцінили на 5, 57 – на 7, від 1-3 балів в середньому по 30 студентів, 52 – на 6, на 9 – 27 студентів і на 10 – 11 студентів. Стрес може викликати: чутливість до світла та рухів, посмикування очей, їх сухість, нечіткий зір. Переважно, проблеми із зором викликані стресом швидко минають після закінчення дії стресу. Проте варто звернутися до офтальмолога, якщо помітили проблеми. [3]

На думку більше половини опитаних студентів (51%) на стан їхнього зору найбільше впливають гаджети, на думку 17% - тривале читання, 13% вважають тривогу і стрес основним фактором погіршення зору, 12% - недостатнє освітлення.

На запитання: «Які заходи, на вашу думку, допомогли б покращити ваш зір або зменшити навантаження?», - більшість студентів відповіли, що потрібно зменшити час користування гаджетами, інші студенти вважають, що потрібно зменшити навантаження на студентів в університетах, також популярними відповідями є: зменшити час читання, проводити вправи для очей, більше гуляти на свіжому повітрі, покращити освітлення при читанні, постаратись зменшити емоційну напругу, регулярно відвідувати офтальмолога, робити перерви в читанні або роботі з гаджетом, вживати вітаміни та здоровий сон. Студенти які взяли участь у опитуванні запропонували ряд пропозицій, які на їхню думку можуть покращити зір. Ці пропозиції перекликаються із рекомендаціями МОЗ України. Зокрема МОЗ рекомендує для збереження здоров'я очей: носити захисні окуляри під час занять спортом та будівельних робіт, використовувати сонцезахисні окуляри, щоб захистити очі від дії ультрафіолету, адже згубний вплив ультрафіолету може спровокувати розвиток катаракти і пошкодження

рогівки ока, а також давати очам відпочити при тривалому зоровому навантаженні.[4]

Висновки. Враховуючи достатньо велику вибірку студентів (412 осіб), які прийняли участь у анкетуванні, можна зробити наступні висновки: найбільш частими причинами зниження зору у здобувачів освіти є тривале безперервне використання гаджетів, недостатнє освітлення робочого місця, а також було виявлено, що тривалий стрес та спадкова схильність мали вплив на розвиток порушень зору у студентів. Враховуючи рекомендації МОЗ України щодо профілактики стану зору, такі як вправа "20-20-20", регулярно перевіряти гостроту зору в офтальмолога, можуть допомогти суттєво знизити негативний вплив надмірного зорового навантаження.

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РОЛЬ НЕКОТОРЫХ ПОЛИМОРФИЗМОВ В ТЕЧЕНИИ ИШЕМИЧЕСКОЙ БОЛЕЗНИ СЕРДЦА, АССОЦИИРОВАННОЙ С САХАРНЫМ ДИАБЕТОМ 2 ТИПА

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THE ROLE OF SOME POLYMORPHISMS IN THE COURSE OF ISCHEMIC HEART DISEASE ASSOCIATED WITH TYPE 2 DIABETES MELLITUS

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Аннотация

Определение локуса ишемической болезни сердца (ИБС) стало знаковым открытием в генетике сердечно-сосудистых заболеваний. Как и многие другие важные достижения в науке, оно было обусловлено достижениями в области технологий, в данном случае доступностью плотных генных массивов. Эти массивы сделали возможным изучение генетической изменчивости на уровне всего генома с разумным охватом.

Это позволило использовать безгипотезные подходы к изучению генетических компонентов заболеваний с использованием исследований ассоциаций по всему геному (GWAS). На сегодняшний день GWAS оказались чрезвычайно успешными в выявлении новых генетических факторов для многих признаков заболеваний

Abstract

The identification of the coronary heart disease (CHD) locus was a landmark discovery in the genetics of cardiovascular disease. Like many other important advances in science, it was facilitated by advances in technology, in this case the availability of dense gene arrays. These arrays have made it possible to study genetic variation at the genome-wide level with reasonable coverage.

This has enabled hypothesis-free approaches to studying the genetic components of disease using genome-wide association studies (GWAS). To date, GWAS have been extremely successful in identifying new genetic factors for many disease traits

Ключевые слова: полиморфизм, ишемическая болезнь сердца, сахарный диабет 2 типа, ADIPOQ, CDKN2B-AS1

Keywords: polymorphism, coronary heart disease, type 2 diabetes mellitus, ADIPOQ, CDKN2B-AS1.

Локус Chr9p21 представляет собой набор гаплотипов, содержащий множество однонуклеотидных полиморфизмов, находящихся в тесном неравновесии по сцеплению, и охватывающий участок ДНК длиной около 50 кб. Аллель риска встречается часто, его частота составляет 50%. Передаваемое увеличение риска ИБС составляет около 30 % и 60 % для носителей 1 и 2 аллелей, соответственно. Интересно, что риск не зависит от обычных факторов риска ИБС, таких как гипертония или гиперлипидемия. В этом контексте важно также отметить, что локус Chr9p21 действует независимо от близко расположенного локуса сахарного диабета. Последний расположен в соседнем блоке гаплотипов на хромосоме 9p21, более удаленном от области ИБС. В совокупности эти результаты позволяют предположить, что Chr9p21 может влиять на атеросклероз через совершенно новый механизм.

Образование бляшек – патогномичный признак атеросклероза, вызванного нарушением работы эндотелиальных клеток, которые, как было показано, регулируются длинными некодирующими РНК (lncRNAs). LncRNA состоят более чем из 200 нуклеотидов, и в последнее время появились исследования, подчеркивающие их ключевую роль в различных сердечно-сосудистых заболеваниях и опухолях. LncRNA cyclin-dependent kinase inhibitor 2B antisense RNA 1 (CDKN2B-AS1), также известная как ANRIL, экспрессируется преимущественно в тканях, ассоциированных с ишемической болезнью сердца, включая кардиомиоциты, эндотелиальные клетки сосудов и человеческие моноцитарные макрофаги. Имеются данные, свидетельствующие о том, что варианты lncRNA CDKN2B-AS1 играют критическую роль в развитии различных заболеваний, включая атеросклероз, диабет и некоторые виды рака. В частности как результат взаимодействия между lncRNA CDKN2B-AS1 и дезинтегрином и металлопротеазой 10 (ADAM10), которое было определено с помощью первоначальной метилирование-специфической ПЦР (MS-PCR) с последующим подтверждением анализом иммунопреципитации хроматина (CHIP). ADAMs – это мембраносвязанные ферменты, которые могут отщеплять или расщеплять различные молекулы клеточной поверхности, такие как молекулы адгезии, цитокины/хемокины и факторы роста, что может свидетельствовать о причастности ADAM к различным метаболическим и воспалительным заболеваниям, таким как атеросклероз, диабет, ревматоидный артрит.

Как член семейства белков с доменом интегринов и металлопротеиназ, была выявлена тесная взаимосвязь между ADAM10 и нейровоспалительным ответом. С другой стороны, ДНК-метилтрансфераза 1 (DNMT1) принадлежит к семейству ДНК-метилтрансфераз, которые могут регулировать метилирование ДНК. Более того, прогрессирование атеросклероза тесно связано с провоспалительной активацией макрофагов, т.е. регулируется DNMT1. Существующие литературные данные свидетельствуют о том, что ADAM10, медиатор функции эндотелиальных клеток, регулируемый фактором роста эндотелия сосудов, тесно связан с развитием атеросклероза. Основные наблюдения показали, что сверхэкспрессированная CDKN2B-AS1 потенциально может способствовать оттоку холестерина при атеросклерозе путем снижения регуляции ADAM10 через DNMT1-опосредованное метилирование ДНК ADAM10.

В исследованиях было показано, что уровень CDKN2B-AS1 снижен в тканях атеросклеротической бляшки и в макрофагах THP-1, подвергшихся воздействию окси-ЛПНП. Было показано, что некоторые lncRNA играют важнейшую роль в развитии и прогрессировании сердечно-сосудистых заболеваний, таких как инфаркт миокарда и атеросклероз. Например, варианты в lncRNA CDKN2B-AS1 были связаны с развитием ишемической болезни сердца. Были получены данные, подтверждающие наличие низкой экспрессии CDKN2B-AS1 в тканях клинических атеросклеротических бляшек, а также выяснена потенциальная антиатерогенная роль CDKN2B-AS1. В соответствии с результатами исследования, сообщалось, что предрасположенность к коронарному атеросклерозу и прогноз прогрессирования заболевания связаны с метаболизмом внеклеточного матрикса и фиброгенезом, в которых CDKN2B-AS1 играет важную роль. Кроме того, результаты текущего исследования показали, что ADAM10 высоко экспрессируется в тканях атеросклеротической бляшки и в макрофагах THP-1, подвергшихся воздействию окси-ЛПНП. Многие ADAM были связаны как с ранними, так и с поздними стадиями атеросклероза, и, например, повышение уровня ADAM10 было обнаружено в тканях нестабильных атеросклеротических бляшек.

Согласно результатам предыдущего исследования, аномальная экспрессия ADAM10 играет важную роль в прогрессировании атеросклероза, а также в воспалительном процессе макрофагов.

Данные, полученные в ходе исследования, позволили выявить взаимосвязь, при которой сверхэкспрессия lncRNA CDKN2B-AS1 индуцировала метилирование гена ADAM10 для подавления его экспрессии, что указывает на основной механизм регуляции CDKN2B-AS1 при атеросклерозе. lncRNA CDKN2B-AS1 привлекала DNMT1 в промоторную область ADAM10, инициировала метилирование и подавляла экспрессию ADAM10, тем самым уменьшая атеросклероз и способствуя оттоку холестерина. ADAM10 в лейкоцитах ассоциируется с воспалением, тем самым оказывая влияние на уменьшение рекрутирования воспалительных клеток. Сверхэкспрессия CDKN2B-AS1 привела к снижению экспрессии ADAM10, а восстановление ADAM10 отменило эффект ингибирования, вызванный CDKN2B-AS1, на уровне ТГ и ЛПНП, что указывает на то, что CDKN2B-AS1 может подавлять атеросклероз путем ингибирования экспрессии ADAM10.

Кроме того, было показано, что IL-1 β и TNF- α являются провоспалительными медиаторами, играющими важную роль в развитии атеросклеротических поражений. Одновременно с этим уровни IL-1 β и TNF- α в группе CDKN2B-AS1 значительно снизились, что свидетельствует о том, что CDKN2B-AS1 может подавлять атеросклеротический воспалительный ответ. В то же время развитие атеросклероза тесно связано с иммунной системой, в которой важную роль играют как мПНК, так и lncRNA. Имеются данные о том, что lncRNA способны регулировать функцию стенки сосудов, липидный обмен, активацию макрофагов, а также воспалительный ответ. С другой стороны, широкогеномные исследования ассоциаций показали, что CDKN2B-AS1 содержит множество маркеров ишемической болезни сердца, а также сообщения о разрушении гена CDKN2B в опухолях, что подчеркивает его жизненно важную роль в регуляции клеточного цикла. В соответствии с вышеупомянутыми литературными данными, в нашем исследовании было установлено, что сверхэкспрессия CDKN2B-AS1 может снижать экспрессию ADAM10, тормозит прогрессирование атеросклероза и способствовать оттоку холестерина через связывание с DNMT1.

В дополнение к модифицируемым факторам риска, генетические факторы также могут предрасполагать людей к сердечно-сосудистым заболеваниям. Ген адипонектина человека, известный как ADIPOQ, ранее называемый Acrp 30 (белок, связанный с комплементом адипоцитов, 30 кДа), APM1 (наиболее распространенный генетический транскрипт жировой ткани) и GBP28 (желатинсвязывающий белок, 28 кДа), расположен в хромосоме 3q27, имеет структурную гомологию с коллагеном VII и IX, фактором комплемента C1q и семейством ФНО. Наиболее широко изученным полиморфизмом в гене адипонектина является вариант Adipoq +276G>T (rs1501299), расположенный в интроне 2 и являющийся результатом замены G на T. Было обнаружено, что варианты адипогена связаны с ожирением, маркерами метаболического синдрома и

сердечно-сосудистыми заболеваниями. Только в нескольких предыдущих исследованиях изучалась связь полиморфизма AdipoQ (rs1501299) с сопутствующим наличием сердечно-сосудистых заболеваний. Исследования также показали связь полиморфизма AdipoQ с сахарным диабетом 2 типа.

Переокисление липидов и окисление ЛПНП, индуцируемые активными формами кислорода, являются ранним событием в формировании атеросклеротических поражений. Малоновый диальдегид (MDA), который является одним из продуктов перекисного окисления липидов, был наиболее широко изученным маркером. Его повышенный уровень указывает на индекс оценки окислительного стресса. Соответственно, в настоящем исследовании наблюдалась значительная разница в средних уровнях MDA как маркера окислительной модификации липидов, когда случаи сравнивались с контрольными. Аналогичным образом, значительное повышение уровней MDA также наблюдалось Sowmya et al.. В другом исследовании Bhargava et al. сообщалось о повышенных уровнях MDA у пациентов с ИБС и ССЗ с гипергомоцистемией.

Для другого изученного прооксидантного карбонилпротеина ЛПНП значительная разница в средних уровнях вновь наблюдалась у субъектов с ССЗ по сравнению с субъектами без ССЗ. Аналогичным образом, повышенные уровни карбонильного белка также наблюдались у пациентов с сердечно-сосудистыми заболеваниями в исследовании, проведенном Lopes et al.. В другом исследовании, проведенном Джавалекаром и соавт. сообщалось об увеличении содержания карбонила белка в экстракте эритроцитов у пациентов с ИБС, АГ и цереброваскулярными заболеваниями по сравнению с контрольной группой. Это говорит о том, что повышенный уровень карбонильного белка может быть связан с клиническими осложнениями. Внеклеточная супероксиддисмутаза (СОД) является секретирующим гликопротеином и мощным антиоксидантом, уровень которого в кровеносных сосудах находится на высоком уровне, что позволяет подавлять окислительный стресс в нормальных условиях. Результаты настоящего исследования подтверждают эту теорию, поскольку было обнаружено, что повышенное переокисление липидов было связано со снижением активности эндогенного антиоксидантного фермента СОД. Настоящее исследование выявило снижение средних уровней СОД у испытуемых с ССЗ по сравнению с испытуемыми без ССЗ. Это снижение активности СОД может быть связано с воздействием на СОД повышенного количества свободных радикалов, образующихся из кислорода. Потому что супероксиданион, который является основной формой кислорода, вступает в реакцию с радикалом оксида азота, образуя пероксинитрит – свободный радикал, вызывающий окислительный стресс и повреждение клеток. Гуманова и др. в своем исследовании обнаружили, что более высокие уровни оксида азота (NO) в значительной степени связаны с поражениями коронарных артерий, хотя в некоторых

исследованиях сообщалось о повышенной активности СОД у пациентов с ишемической болезнью сердца. С другой стороны, другие исследования, аналогичные нашему, выявили снижение активности СОД. Сравнение частоты аллелей полиморфизма AdipoQ(1501299) с другими популяциями мира показало, что в нынешней популяции пенджабцев частота минорных аллелей гена ADIPOQ, о которой сообщалось, была довольно схожей (29,5%) с частотой, о которой сообщалось в японской популяции (29,7%); у греческих женщин (28%); и у китайских подростков (30,6%). Согласно анализу рецессивной модели, полиморфизм ТТ генотипа ADIPOQ(rs1501299) обеспечивал значительный риск, в 9 раз превышающий предрасположенность к ССЗ.

В настоящей исследуемой популяции с ССЗ частота носительства аллеля Т была выше по сравнению с субъектами без ССЗ. Филиппи и соавт. наблюдали повышенный риск развития ИБС с этим аллелем в итальянской популяции. Исследование, проведенное Ghattas et al., также показало, что генотип ТТ полиморфизма AdipoQ(rs1501299) был связан с повышенным риском развития ИБС в египетской популяции. В другом исследовании Tong et al., посвященном населению Китая, вариант AdipoQ (rs1501299) также был положительно связан с повышенным риском ИБС. Мохам-Мадзаде и др. выявили на изученной ими популяции иранцев, что как генотипы GT, так и генотип ТТ с аллелем Т SNP rs1501299 были связаны с повышенным риском ИБС. Кроме того, они также наблюдали, что частота аллеля Т у пациенток с САД была значительно выше, чем у контрольных субъектов. Напротив, Qi et al. сообщили, что rs1501299 был достоверно связан со снижением риска сердечно-сосудистых заболеваний у женщин на 45% по результатам исследования здоровья медсестер. Снижение риска у гомозиготных носителей аллеля Tallele по сравнению с носителями аллеля G также наблюдалось в кавказской популяции Васси и соавт.. Широко сообщалось об ассоциациях различных генов-кандидатов с предрасположенностью к ССЗ, и полиморфизм во множестве генов был связан с дифференциальными эффектами липидного обмена при этом заболевании. Адипонектин ослабляет экспрессию рецептора-поглотителя класса А в макрофагах человека и ингибирует трансформацию макрофагов в пенистые клетки. Модифицированные частицы ЛПНП не связываются непосредственно с эндогенным рецептором ЛПНП и, следовательно, не выводятся из кровообращения с помощью этого механизма. Они легче проникают в интиму артерий и легче окисляются, вероятно, потому, что обладают меньшей антиоксидантной защитой. Окисленные ЛПНП состоят из многочисленных модифицированных липидных и белковых молекул. Таким образом, они поглощаются макрофагальными рецепторами-поглотителями, ускоряющими образование пенистых клеток. В настоящем исследовании, когда испытуемые были разделены в соответствии с липидемическим статусом на лиц с нормолипиде-

мией и гиперлипидемией, распространенность Таллеле была выше в этих случаях по сравнению с контрольной группой. Интересно, что носители Т нормолипидемических гомозигот с ССЗ по рецессивной модели имели больший риск (≈ 11 раз) в отношении предрасположенности к ССЗ по сравнению с гиперлипидемическими (≈ 8 раз) субъектами с ССЗ по сравнению с контрольной группой. Это указывает на то, что развитие сердечно-сосудистых заболеваний начинается раньше, даже когда липиды в норме, что указывает на вовлечение окислительного стресса как раннего события в атеросклеротический процесс, что также доказано другими исследованиями. Amrita, Jyot, et al. отмечает что, не только гиперлипидемические ТТ-гомозиготы, но и нормолипидемические ТТ-гомозиготы были связаны с повышенным риском сердечно-сосудистых заболеваний. Окислительный стресс является основным регулятором различных систем передачи сигналов, участвующих в атеросклеротическом сосудистом воспалении и на протяжении всего процесса образования жировых прожилок и поражений, прогрессирующих до окончательного разрыва бляшки. На клеточном и молекулярном уровнях адипонектин выполняет противовоспалительную, антиоксидантную и антиапоптотическую функции, тем самым смягчая ключевые механизмы, лежащие в основе патогенеза сердечно-сосудистых заболеваний. Повышенный окислительный стресс и снижение антиоксидантной активности или и то, и другое вместе являются основными механизмами, участвующими в патогенезе сердечно-сосудистых заболеваний. Свободные радикалы кислорода образуются особенно на ранних стадиях ИМ, и снижение активности СОД может быть связано с эффектом увеличения содержания свободных радикалов, образующихся из кислорода, в СОД. Таким образом, эти результаты позволяют предположить, что окислительный стресс может влиять на инициацию и прогрессирование атерогенеза у пациентов с ССЗ.

Нынешний процесс перехода к рациональному питанию способствует дальнейшему ускорению возникновения метаболических нарушений, как и ряд факторов окружающей среды, которые приводят к диагностике хронических заболеваний, поскольку диета с низкой питательной ценностью, возможно, связана с распространенностью метаболического синдрома. В дополнение к этим факторам метаболический синдром также может быть связан с генетическими факторами, полиморфизм ADIPOQ + 45T> G был связан с уровнем адипонектина в сыворотке крови, чувствительностью к инсулину и ожирением, которое влияет на уровень адипонектина, выступающего в качестве защитного фактора от сердечно-сосудистых заболеваний.

Адипонектин является наиболее распространенным в количественном отношении адипокином, секретируемым адипоцитами, который, как известно, регулирует чувствительность к инсулину и метаболизм глюкозы, а концентрация адипонектина снижается у лиц с ожирением.

Активность адипонектина в эндотелиальных клетках сосудов, клетках гладкой мускулатуры,

макрофагах и метаболизме липидов, а также глюкозы обеспечивает защиту от метаболического синдрома и ожирения.

Адипонектин кодируется геном, содержащим адипонектин C1Q и коллагеновый домен (ADIPOQ), который расположен на хромосоме 3q27. Синтез адипонектина имеет сильный генетический компонент, наследуемость которого оценивается выше 70%.

Наиболее распространенным однонуклеотидным полиморфизмом (SNP) этого гена является rs266729(-11,377C>G), он расположен в проксимальной промоторной области гена ADIPOQ. Литературные данные указывают на то, что полиморфизм ADIPOQ rs266729 функционально регулирует активность промотора адипонектина и уровни адипонектина. Более того, было обнаружено, что ADIPOQ rs266729 коррелирует с уровнем циркулирующего адипонектина при ожирении. Было идентифицировано, что этот вариант ADIPOQ связан с высоким индексом массы тела, инсулинорезистентностью и диабетической нефропатией. Влияние снижения веса или диетических вмешательств на метаболическую реакцию с учетом этого SNP в литературе мало. Например, финское исследование по профилактике диабета (европеоидная популяция) показало, что генетический вариант гена ADIPOQ rs266729 способствует изменению массы тела и концентрации адипонектина в сыворотке крови. Hsiao et al. показывают, что этот генетический вариант может способствовать снижению веса в ответ на прием противоопухолевого препарата, такого как сибутрамин. Недавнее исследование 10 продемонстрировало, что аллель этого генетического варианта является предиктором улучшения липидного профиля после снижения веса после бариатрической операции.

Не носители G-аллеля показали лучшую реакцию на уровни глюкозы, HOMA-IR, инсулина, общего холестерина, холестерина ЛПНП и адипонектина, чем носители G-аллеля после обеих диет.

Таким образом, впервые было сообщено обнадеживающее открытие, заключающееся в том, что этот вариант гена ADIPOQ может играть важную роль в модулировании результатов лечения с помощью диетических вмешательств. Есть несколько исследований, показывающих связь между rs266729 и ожирением и связанными с ним патологиями, такими как сахарный диабет 2 типа и метаболический синдром, но существует мало данных о влиянии потери веса на эту связь при разработке интервенционных программ. В литературе описано пять вариантов вмешательства, два исследования были проведены с нехирургическим вмешательством и три после бариатрической операции. Первое нехирургическое исследование было проведено с использованием препарата против ожирения (сибутрамин). Сяо и соавт. сообщили о значительно большей потере веса для ADIPOQ rs266729 Генотип CC по сравнению с группой плацебо в течение 12-недельного периода. В это исследование были включены пациенты неевропеоидного происхождения: 44 в группе плацебо и 87 в группе сибутрамина

с 10 мг в день. Фактически, исследуемая популяция отличалась от нашей схемы, и снижение веса было выше (на 7,9 кг), чем наши данные. Авторы показали, что носители аллеля G имели более высокий вес после 4-летнего наблюдения, а аллель C был связан с повышенным риском развития сахарного диабета 2 типа. Этот любопытный результат, ассоциация более высокой массы тела после лечения и более низкого уровня сахарного диабета, таким образом, позволяет предположить, что влияние этого варианта ADIPOQ на метаболизм глюкозы не зависит от его влияния на массу тела.

Первое хирургическое интервенционное исследование было проведено с использованием Рука и гастроэнтеростомия. В рамках проекта 60 пациентов с патологическим ожирением были обследованы через 32 месяца, лица с Аллель C был более склонен к снижению уровня холестерина ЛПНП (-43%) после бариатрической операции по сравнению с (-18%) у носителей аллеля G. Снижение уровня холестерина ЛПНП в этом исследовании было выше, чем наши результаты (5%), возможно, связано с большей потерей веса после бариатрической операции (35%), чем в нашей работе с вмешательством в питание (5%). В этом хирургическом вмешательстве, потеря веса была одинаковой у обоих генотипов после бариатрической операции, как показало наше диетическое исследование. Более того, в этих трех предыдущих исследованиях уровень адипонектина не измерялся после потери веса.

Первое исследование, в котором оценивалось влияние этого полиморфизма и потери веса на уровни адипонектина, было проведено Poitou et al. Эти авторы сообщили, что вариант rs266729 не оказал существенного влияния на концентрацию циркулирующего адипонектина у 65 пациентов с ожирением перенес операцию по бандажированию желудка через 12 месяцев. Однако липидный профиль и метаболизм глюкозы в этом исследовании не измерялись. Де Луис и соавт. провели другое исследование, в котором оценивали уровни адипонектина. В этом трехлетнем интервенционном исследовании с билиопанкреатическим отведением концентрация адипонектина увеличилась после снижения веса у пациентов с CC, чего не наблюдалось у носителей аллеля G.

Кроме того, у пациентов с генотипом CC также наблюдалось лучшее улучшение липидного профиля, уровня инсулина и HOMA-IR, чем у носителей G-аллеля. Потенциальные физиологические механизмы, объясняющие зависимость эффекта потери веса между этими генетическими вариантами и метаболическими параметрами, остаются неизвестными. ADIPOQ кодирует адипонектин, экспрессируемый исключительно как в коричневой, так и в белой жировой ткани. Недавние результаты показали, что аллель G изменяет последовательность для одного сайта связывания белка, стимулирующего транскрипцию, и вторично снижает активность промотора адипонектина. Кроме того, некоторые исследования показали, что существует связь между адипонектином и массой жировой

ткани и предположил, что секреция адипонектина и его циркулирующие уровни были обратно пропорциональны количеству жира в организме(65). Возможно, какой-то молекулярный путь связывает этот генетический вариант ADIPOQ ген, отвечающий за адипогенез и секрецию адипокинов. Второй потенциальной гипотезой, объясняющей эти ассоциации, является взаимодействие генов и питательных веществ. Фергюссон и др. продемонстрировали, что аллель G для этого SNPs был идентифицирован как имеющий степень резистентности к инсулину и был высоко чувствителен к различиям в насыщенных жирных кислотах плазмы. В других исследованиях сообщалось о взаимодействии гена и питательных веществ между вариантом rs266729 гена ADIPOQ и процентным содержанием энергии, получаемой из пищевых жиров в рационе. Возможно, пищевые жирные кислоты могли бы модулировать вовлечение гена адипонектина и его рецепторов в нижестоящие пути.

Некоторые однонуклеотидные полиморфизмы (SNP) были связаны с уровнями адипонектина в сыворотке. Однако существует противоречие между ассоциацией этих генетических вариантов и уровнями адипонектина. Эти расхождения могут быть связаны с взаимодействием между этими генетическими вариантами и питательными веществами. В частности, неоднородность реакции на жирные кислоты рыбьего жира в разных группах пациентов была объяснена генетическими вариациями(8).

Более того, ненасыщенные жирные кислоты (полиненасыщенные и мононенасыщенные) являются важными лигандами для фактора транскрипции PPAR- γ 16, который усиливает экспрессию гена ADIPOQ 17 и повышает уровень адипонектина. Таким образом, на уровень адипонектина может влиять взаимодействие между SNP ADIPOQ, (и) потреблением с пищей полиненасыщенных жирных кислот (ПНЖК)18 и мононенасыщенных жирных кислот (MUFAs). Однако другие компоненты рациона, такие как пищевые волокна из цельнозерновых продуктов, продукты с низким гликемическим индексом, ограничение калорийности и соотношение соотношения между ненасыщенными жирами и низким содержанием углеводов может влиять на уровень адипонектина.

Жировая ткань выделяет различные про- и противовоспалительные адипокины, которые регулируют воспаление и инсулинорезистентность; индуцированная ожирением инсулинорезистентность и сахарный диабет 2 типа могут частично быть результатом дисбаланса в экспрессии анти- и провоспалительных адипокинов. Адипонектин - это противовоспалительный гормон, который, как было показано, повышает чувствительность к инсулину за счет усиления окисления жирных кислот и ингибирования метаболизма глюкозы в печени.

Было оценено влияние других стратегий снижения веса с использованием эффектов гена ADIPOQ на метаболические параметры. Например, генотип GG у пациентов с патологическим ожирением связан с повышением уровня адипонектина и более выраженным снижением уровня HOMA-IR и

инсулина после массивной потери веса с помощью операции по удалению билиопанкреатической артерии и 3-летнего наблюдения. Точные молекулярные механизмы, ответственные за взаимодействие между потреблением с пищей различных профилей ненасыщенных жирных кислот и этот генетический вариант (rs1501299) оставался неясным. D.A. de Luis et al. (была высказана гипотеза об активации PPAR- γ ненасыщенными жирными кислотами, этот факт увеличивает экспрессию гена ADIPOQ и уровни адипонектина в сыворотке крови, а также (а) неизвестное нарушение равновесия связи между элементом ответа пролифератора пероксисом и геном ADIPOQ. Во-вторых, возможно, этот SNP может непосредственно влиять на метаболическую реакцию, некоторые исследования показали связь этого SNP с уровнями холестерина ЛПНП40,41 и кровяным давлением. В-третьих, аллель T гена ADIPOQ rs1501299 может изменять последовательность одного из сайтов связывания белка, стимулирующего транскрипцию, и снижают активность промотора адипонектина.

Способ расширения жировой ткани (увеличение размеров, гипертрофия и/или количества клеток, гиперплазия) может регулировать синтез и секрецию адипонектина. Дроле и соавт. продемонстрировали обратную зависимость между средним диаметром адипоцитов и секрецией адипонектина. Гипертрофия жировой ткани приводит к состоянию гипоксии адипоцитов, приводящему к высвобождению воспалительных цитокинов и ингибированию мРНК адипонектина. Кроме того, было показано, что активность промотора гена APN подавлялась гипоксией и TNF- α .

Адипонектин играет важную роль в регулировании уровня глюкозы и окисления жирных кислот. Многочисленные исследования оценивали связь между полиморфизмом rs2241766 в гене адипонектина (ADIPOQ) и предрасположенностью к ожирению.

Ген ADIPOQ рассматривался как единственный основной ген адипонектина плазмы. Адипонектин секретируется главным образом жировой тканью и, как полагают, опосредует повышенное фосфорилирование и активность активируемой AMP протеинкиназы (AMPK), а также активность рецептора, активируемого пролифератором пероксисом (PPAR α), путем связывания с рецепторами адипонектина (AdipoR1 и AdipoR2), активируя окисление жирных кислот и поглощение глюкозы как в скелетных и сердечных мышцах. Мыши с дефицитом адипонектина проявляют инсулинорезистентность, и сообщалось, что замена адипонектина у людей является многообещающим методом профилактики и/или лечения ожирения и сахарного диабета 2 типа. Интересно, что уровень адипонектина в плазме крови был ниже у лиц с ожирением, чем у худощавых испытуемых, и мог быть значительно повышен при потере веса. Эти исследования предполагают, что адипонектин участвует в развитии ожирения.

Уровни адипонектина в плазме показали высокую наследуемость, и мета-анализ GWAS определил, что только локус ADIPOQ оказывает важное влияние на уровни адипонектина в плазме. Сообщалось, что вариант ADIPOQ-rs2241766 G/T связан с уровнем адипонектина. Исследования показали, что эта синонимичная мутация может влиять на устойчивые уровни мРНК, изменяя сплайсинг или стабильность РНК, что позволяет предположить аллель-специфичную дифференциальную экспрессию адипонектина. Стационарные уровни мРНК, транскрибируемые аллелем G, были выше, чем уровни, транскрибируемые аллелем T в жировой ткани гетерозиготных субъектов, и многомерный линейный регрессионный анализ с поправкой на возраст и пол показал, что доза аллеля G была связана со снижением ИМТ примерно на 1,12 кг/м² население на Тайване. Таким образом, предположение о том, что полиморфизм ADIPOQ-rs2241766 G/T может быть связан с ожирением, является обоснованным.

Аллель G, по-видимому, является одним из генетических факторов риска предрасположенности к ожирению в общих исследованиях, особенно в китайских исследованиях. Адипонектин также рассматривался в качестве маркера метаболического синдрома (MetS). Мета-анализ, включающий 13 исследований с 2684 случаями и 2864 контрольными группами в китайской популяции, был проведен для выявления ассоциации варианта rs2241766 с метаболическим синдромом, и результаты подтвердили, что частота аллеля G у пациентов с метаболическим синдромом была значительно выше, чем у контрольной группы (29,8% против 23,3%, или $p = 0,033$).

В китайской погруппе по данным Wu J et al. значимой связи обнаружить не удалось.

ФНО- α генерирует набор реакций либо самостоятельно, либо посредством взаимодействия с другими физиологически активными молекулами.

Повышенные уровни ФНО- α в плазме и тканях, наблюдаемые при ожирении приводят к установлению постоянного воспалительного состояния. Считается, что АПН обладает благоприятными противоопухолевыми эффектами, которые, как полагают, обусловлены антипролиферативными, противовоспалительными эффектами, наряду с противодействием резистентности к инсулину.

Однако уровень циркулирующего АПН обратно пропорционален массе тела. АПН присутствует в кровообращении здоровых людей в высоких концентрациях. Сниженные уровни адипонектина в сыворотке крови коррелируют с развитием и прогрессированием опухоли и являются обратно пропорционально связаны с маркерами воспаления. В частности, адипонектин уменьшает индуцированное ФНО- α воздействие на пролиферацию и миграцию клеток. Исследования *in vitro* показывают, что ФНО- α , уровень которого повышен при ожирении, может быть частично ответственен за снижение выработки адипонектина при ожирении. Уровни адипонектина имеют сильный генетический компонент.

Среди сообщенных вариаций гена ADIPOQ было показано, что SNP rs266729, обнаруженный в промоторной области, в значительной степени связан с уровнем адипонектина. Адипонектин был предложен в качестве определяющего фактора в этиологии метаболического синдрома из-за его важного регулирующего действия на чувствительность к инсулину и воспаление. Таким образом, полиморфизм в гене ADIPOQ может играть определенную роль в патогенезе метаболического синдрома.

Увеличение веса связано со снижением АПН циркулирующие уровни и накопление висцерального жира могут продуцировать ингибирующие факторы, такие как TNF- α для синтеза или секреция АПН.

Доказательства того, что гипертрофия адипоцитов и чрезмерное накопление жировой ткани могут способствовать патогенным эффектам на адипоциты и жировую ткань, привели к формулированию концепции “адипозопатии”, определяемой как дисфункция адипоцитов и жировой ткани.

Адипозопатия, наряду с другими факторами (уровень ТГ, снижение уровня холестерина ЛПВП, высокое кровяное давление или нарушение метаболизма глюкозы), способствует инициации ишемической болезни сердца, сахарного диабета 2 типа, метаболического синдрома. Причины и патофизиологические механизмы, вызывающие воспалительное состояние, связанное с ожирением, до конца не известны. Однако адипокины могут представлять собой биохимическую связь между ишемической болезнью сердца, воспалением и метаболическим синдромом.

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ASSOCIATION OF VITAMIN D AND MENTAL HEALTH

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ORCID: <https://orcid.org/0009-0000-4237-1158>DOI: [10.5281/zenodo.14707918](https://doi.org/10.5281/zenodo.14707918)**Abstract**

Depression and anxiety are mood disorders that affect health and therefore quality of life and increase the global burden of disease. One of the possible mechanisms in the pathophysiology of these mood disorders has been reported as oxidative stress and inflammation. In the light of this information, it is important to determine the relationship between antioxidant nutrients (such as vitamin D) and these diseases. There are points where the brain regions involved in the pathophysiology of depression and anxiety and vitamin D metabolism intersect.

Low vitamin D levels are associated with increased symptoms of depression and anxiety. For this reason, vitamin D screening should be performed in the prevention and treatment planning of these mood disorders.

Vitamin D, which has antioxidant properties and activity in brain tissue, is important for mood disorders preventions or treatments but serum levels must be followed.

Keywords: Depression, Anxiety, Mood disorders, Vitamin D, Antioxidant, Cholecalciferol.

Introduction

Depression and anxiety are mood disorders that affect individuals' daily lives and health status with their social and economic dimensions, which are frequently observed. Identifying the factors that cause these mood disorders is a cornerstone to prevent or delay their occurrence. It is important to provide disease management for individuals diagnosed with mood disorders.

It has been determined that oxidative stress and inflammation are involved in the pathophysiology of these mood disorders along with many diseases (1). Thereupon, the relationship between antioxidant and immunomodulatory nutrients and these diseases was examined. In this review, it is aimed to explain the place of vitamin D in the pathophysiology of depression and anxiety, the effect of vitamin D supplementation, and its interactions with the drugs used.

Vitamin D

Vitamin D is a fat-soluble vitamin that has been reported to have efficacy in many tissues, as well as its effects on calcium-phosphate homeostasis and bone health. Approximately one-fifth of vitamin D is provided by dietary intake, and the remaining 80% is synthesized from 7-dehydrocholesterol in the skin by ultraviolet rays (2). Then, calcidiol, which is the serum form of the vitamin, is hydroxylated in the liver with the enzyme 25-hydroxylase (CYP2R1), and calcidiol is re-hydroxylated in the kidney and brain with the enzyme 1- α -hydroxylase (CYP27B1) and turns into 1,25 (OH)₂ cholecalciferol, also called calcitriol, which is the active form of the vitamin (3). Vitamin D synthesis and active form formation stages. This active form binds to vitamin D receptors located on cell membranes of many tissues to mediate gene transcription and non-genomic reactions (2).

Serum 25(OH) cholecalciferol (calcidiol) level is taken into account to evaluate the sufficiency status for vitamin D. However, there is no international consensus on the cut-off points of this parameter for proficiency/inability. The cut-off points determined by different authorities vary.

When the causes of vitamin D deficiency are examined, it may be caused by decreased exposure to sunlight, decreased endogenous synthesis with the deterioration in liver-kidney functions, malabsorption (cystic fibrosis, short bowel syndrome, gastric bypass, chronic pancreatic insufficiency, etc.), the drugs used (phenobarbital, carbamazepine, dexamethasone, nifedipine, spironolactone, clotrimazole, and rifampin), increased catabolism, and genetic resistance to vitamin D (4).

Adequate intake of vitamin D is particularly dependent on sunlight. Synthesis occurs with short-term (15–20 min) direct exposure to sunlight. In longer exposure to sunlight, compounds called lumesterol and which do not show vitamin D activity are formed. However, vitamin D synthesis levels in exposure to sunlight are affected by various factors such as skin pigmentation, sunscreen use, latitude, season, and age, and dietary or supplemental intake does not directly contribute to 25(OH) cholecalciferol levels. It is emphasized that factors such as body mass index, body fat percentage, and calcium intake are also effective on serum vitamin D levels (5). When the prevalence of vitamin D insufficiency is examined, it is reported that 40% of Europe has vitamin D insufficiency, and 13% of them have severe insufficiency (6).

Vitamin D receptors located in many tissues are also located in the brain specifically in the prefrontal cortex, hippocampus, cingulate gyrus, thalamus, hypo-

thalamus, and substantia nigra. These regions are of extra importance for this research as they are defined in the pathophysiology of depression (7). It has also been determined that the vitamin D activating enzyme 1- α -hydroxylase (CYP27B1) is widely distributed in many different cell types of many brain regions, especially in neurons in the amygdala and glial cells in the hypothalamus. This distribution strengthens the relationship between vitamin D and neuropsychiatric diseases. It is reported that the active form of vitamin D can cross the blood-brain barrier, which increases the possibility of vitamin D being directly or indirectly involved in brain and cognitive functions (8).

There are many studies in the literature reporting that vitamin D deficiency was associated with symptoms of depression and anxiety (9-13). Although the cause and effect relationship of vitamin D and related diseases has not been clarified, it has been reported that vitamin D deficiency exacerbates the symptoms specific to these diseases [9]. Therefore, it is important to detect vitamin D deficiency and to plan appropriate treatments.

Depression

The global burden of the disease is generally assessed by the World Health Organization (WHO) based on disability-adjusted life years (DALY). From this point of view, mood disorders are reported to be at the top of the global disease burden (14). Depression, one of the mood disorders, results from the complex interaction of social, psychological, and biological factors and is a common disease globally. According to 2019 data, it is reported that 5.0% of adults, 5.7% of individuals over the age of 60, and 3.8% of the global population suffer from depression (15, 16). Although depression is different from the usual mood swings and short-term emotional reactions to the difficulties in daily life, it can deeply affect the lives of individuals, especially with the accompanying major depression (15).

The presence of five or more symptoms over a 2-week period is essential for the diagnosis of a major depressive episode according to DSM-5 criteria. At least one of the symptoms must be depressed mood or anhedonia, and secondarily, it may include appetite or bodyweight changes, sleep difficulties, psychomotor agitation, fatigue, decreased cognitive abilities, feelings of worthlessness, and extreme guilt. These symptoms are rated as always (1) or never (0) (17). DSM-V assumes that depression can be accepted as one-dimensional and suggests that major depression can be determined by the sum of these degrees of change. However, it has been reported that depression may have different dimensions. It is stated that grouping the changes determined by DSM-V and mentioned above as somatic (insomnia, changes in appetite or body weight, decreased cognitive abilities, fatigue, and psychomotor agitation) and non-somatic (depressed mood, anhedonia, feelings of worthlessness, and suicidal thoughts) changes is the best representative. No correlation has been identified between the number of changes and the severity of depression. Scales are used for the severity of depression, and it has been reported that the most frequently used one is the Hamilton Depression Scale (HDS) (18).

Depression can lead to cardiovascular events and stroke due to these changes that affect daily life and lifestyle changes, and as a result, it can increase mortality and morbidity (19). In addition, depression can extend to suicide, and it has been reported that the fourth cause of death for individuals aged 15–29 is suicide (15, 18). When all these are evaluated together, the prevention, diagnosis, and treatment of depression are important. The WHO highlights the steps needed to provide appropriate interventions for many mental disorders, including depression, in the Mental Health Action Plan 2013–2030 (20).

The underlying biological mechanisms for depression have not been fully elucidated. However, some possible pathways are indicated. It mainly focuses on 3 hypotheses, including the effects of vitamin D on neurotrophs, monoamine neurotransmission, and immunomodulation (8, 19, 21).

It has been stated that the determination of the role of inflammation in the pathophysiology of depression may provide hope for anti-inflammatory agents for this mood disorder. Changes involving oxidative stress and neuroinflammation may cause activation of peripheral macrophages and central microglia, dysfunction of the hypothalamus–pituitary–adrenal (HPA) axis, and hypercortisolemia. As a result of all these, dendritic growth, synaptic plasticity, and deterioration in synaptic communication can be seen. It has been stated that the effect of vitamin D on the pathophysiology of depression may also be due to its immunomodulatory properties (5). It is reported that with this feature, it can show a neuroprotective effect by preventing the abnormal function of the immune system (19, 21). However, it was emphasized that these results were not at the level of evidence that could be used in clinical guidelines (5).

It is thought that increased expression of region-specific vitamin D receptors (VDR) in brain regions known to play an important role in mood regulation (such as prefrontal and cingulate cortices) may be effective on the progression of depression (19, 21). Because the hippocampal structure can control memory, emotional functions in other brain regions, and limbic structure atrophy, it has been determined that individuals with disorders in this hippocampal structure suffer from chronic depression. After detecting the presence of VDR in the hippocampus, the activity of vitamin D in this structure was examined, and it was revealed that vitamin D is a potent modulator of the expression of neurotrophic agents such as nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), and neurotrophin (NT)-3. Neurotrophic factors are necessary for the viability, growth, and migration of neurons that display their biological functions by combining with cognate tropomyosin-related kinase (Trk) receptors, and vitamin D can increase the expression of these neurotrophic factors. It is emphasized that neurons that secrete neurotransmitters, and therefore neurogenesis, are important in depression and that vitamin D has an important role in maintaining the vitality of neurons (8).

Calcitriol, also called neurosteroid hormone due to its immunomodulatory and neurotrophic roles, is effective

tive in the synthesis of neurotransmitters (serotonin, dopamine, noradrenaline, adrenaline) that play a role in the pathophysiology of mood disorders by activating the gene expression of the tyrosine hydroxylase enzyme, reported as the rate-limiting step in catecholamine synthesis (13, 22). Vitamin D both protects serotonergic neuron health with its neurotrophic effect and supports serotonin synthesis by providing gene expression of enzymes that are active in synthesis. Alteration of serotonin synthesis in case of vitamin D deficiency is also evident (21). In addition to the synthesis, it is also stated that vitamin D takes part in the metabolism of these neurotransmitters and prevents their depletion (13, 19). Vitamin D is also thought to be a factor in the onset of depression with its potential roles in correcting this calcium and glutamate- γ -aminobutyric acid (GABA) imbalance by regulating intracellular calcium stores and cellular signals (21). Considering all this, it is reported that vitamin D provides modulation of the HPA axis (19). It is emphasized that vitamin D is neuroprotective for neurons that secrete neurotransmitters (especially dopamine), but it may show neurotoxic effects when plasma levels exceed the threshold value (22).

The results of preclinical studies examining the relationship between vitamin D and depression were found to be inconsistent. It was determined that high-dose vitamin D administration (5 mg/kg/day) for 14 days in ovariectomized rats ($n = 96$) showed antidepressant-like behavior in depression caused by ovariectomy (23). Low levels of vitamin D have also been observed in the offspring ($n = 15$) of mothers exposed to low levels of vitamin D from pre-pregnancy to the end of the lactation period. In addition, low vitamin D levels were found to cause anhedonia, an important marker of depression in offspring (24). It has been reported that the administration of vitamin D3 for 7 days effectively prevents depressive-like behavior caused by corticosteroid exposure and brain oxidative stress markers, and this antidepressant effect may also be due to oxidative stress modulation (25). Another study showed that intraperitoneal treatment with 1,25(OH) $_2$ vitamin D3 (5, 10 μ g/kg, twice a week) for 5 weeks effectively ameliorated anhedonia with chronic mild stress (26). However, there is also a study in the literature reporting that vitamin D deficiency does not affect the proliferation or survival of neurons in rats (27).

When the epidemiological and clinical studies were examined, cross-sectional and cohort studies were encountered that revealed an inverse relationship between plasma 25(OH)D $_3$ and depression symptoms and major depressive disorder (28-32). In these studies, the cut-off points considered for vitamin D adequacy, insufficiency, and deficiency, the group in which the study was conducted and the scale used to determine depressive symptoms, show heterogeneity. However, it is emphasized in all studies that individuals with high vitamin D levels are less likely to develop depressive symptoms/depression. In a 4-year follow-up cohort study, which was planned especially in a large sample and aimed to reveal the causality between vitamin D and depression, it was determined that individuals with vitamin D deficiency were 75% more likely to develop

depression when compared to individuals with adequate levels (28).

There are also studies evaluating the polymorphism, reporting that the relationship between plasma vitamin D levels and depression is not significant (33, 34). Although these studies were planned as case control, vitamin D classification was not made, and interpretations were made on the averages of plasma 25 (OH) vitamin D levels.

In addition to these studies, there are also studies in which vitamin D therapy has been used as a therapeutic agent alone or as an adjuvant to classical pharmacotherapy in major depressive disorder (13, 36-42]. In a cell culture study examining the effect of vitamin D on serotonin reuptake transporters (SERT), which is the target of serotonin reuptake inhibitors (SSRI) used in the treatment of depression, and monoamine oxidase (MAO), which catalyzes the destruction of serotonin, it was determined that 10 nmol vitamin D application could suppress the expression of SERT and MAO (59%, 51%, respectively). However, it was also emphasized that there was no statistically significant difference for other doses (1 nmol/100 nmol) (13). Epidemiological studies in which vitamin D supplementation was carried out were conducted on the effect of depressive symptoms observed due to the presence of chronic diseases such as diabetes, ulcerative colitis, and Chron's rather than individuals with a diagnosis of depression. Therefore, it was thought that the positive outcomes of vitamin D supplementation obtained from studies on depressive symptoms may be related to its effect on metabolic and inflammatory markers as an immunomodulator. In a placebo-controlled double-blind randomized clinical study evaluating the effect of vitamin D supplementation (50,000 IU for 2 weeks) on plasma 25 (OH) vitamin D levels and some neurotransmitters in individuals ($n = 56$) with mild and moderate depression, it was reported that serum 25 (OH) vitamin D levels increased significantly in the intervention group, and the severity of depression decreased. In the same study, it was reported that no significant change was observed in platelet serotonin levels (12). In the meta-analysis of 25 studies ($n = 7534$) evaluating the effectiveness of vitamin D supplementation on depression, it was reported that vitamin D was effective in individuals with major depressive disorder and plasma 25(OH)D levels ≤ 50 nmol/L and this effect was achieved with supplements less than 4000 IU for ≥ 8 weeks (10). However, there is also a study in the literature that vitamin D supplementation does not affect depressive symptoms.

Anxiety

Anxiety disorders (generalized anxiety disorder, phobia, panic disorder, and others) are defined as a negative, uncertain, and unpleasant emotional state resulting from the anticipation of a potential danger with multifactorial causes. It represents a group of common mental health disorders that negatively affect daily life and well-being. Anxiety disorders involve excessive and persistent fear, worry, and/or avoidance of perceived threats in the external (e.g., social situations) or internal (e.g., bodily sensations) environment, often accompanied by panic attacks. Anxiety and depression or

other mental health disorders can also be observed together (5). Although the developmental ages of the subtypes of anxiety disorders vary, it is reported that they are mostly onset in childhood and adolescence. It has been reported that DSM-V and ICD-10 criteria are used in the classification of anxiety disorders, and these two classifications are similar.

In the meta-analysis study on the global prevalence of anxiety, it was reported that the prevalence of anxiety in Asia was 32.9% (13 studies), while the prevalence of anxiety in Europe was 23.8% (3 studies). However, this current study is given depending on the COVID-19 process. Anxiety, like depression, is among the mental disorders that affect the quality of life and therefore daily life and health costs. It has been determined that anxiety is in the second place in terms of DALY burden. Although anxiety, which is attributed to the 4.2% burden in DALY, is observed to be low, this burden increases with comorbidity depression. Therefore, the prevention and treatment of anxiety disorders are important.

Some hypotheses have been defined in anxiety disorders. In the hypothesis defined for the neural circuit, it is reported that fear and anxiety are regulated by a mixture of bidirectional connections in the amygdala, ventromedial prefrontal hypothalamus, and anterior cingulate cortex with the functional effect of the hippocampus. It is emphasized that the discord between these centers plays a role in anxiety disorders (hyperactivation in the amygdala, decreased activation in the ventromedial prefrontal hypothalamus). It has been reported that amygdala hyperactivation, especially in response to a threat, is associated with the risk of developing anxiety in later years. Another hypothesis is a defect in the HPA axis, which is also involved in the pathophysiology of depression. Vitamin D activity should be considered due to the increased expression of the vitamin D receptor in these regions and the presence of the 1- α -hydroxylase enzyme. It has been reported that there are irregularities in the HPA axis in vitamin D deficiency (12). This information supports the relationship between vitamin D and anxiety. It is stated that the deficiency of substrates such as dopamine, serotonin, and norepinephrine is also involved in the pathophysiology, but it is generally associated with reduced inhibitory signalling by GABA or hyperexcitability caused by increased excitatory glutaminergic neurotransmission. In addition, it is thought that vitamin D may also be a factor in anxiety due to oxidative stress and inflammation in the pathophysiology (5).

In a study on ovariectomized rats ($n = 96$), in which anxiety was evaluated as well as depression, it was found that low-dose vitamin D administration (1 mg/kg/day) for 14 days had an anti-anxiolytic effect, in contrast to depression (23).

The results of epidemiological studies conducted to determine the relationship between anxiety and vitamin D show a negative correlation similar to depression (9, 11). In a study evaluating the relationship between vitamin D levels and anxiety in individuals with rheumatoid arthritis ($n = 161$), it was concluded that there was an inverse relationship between vitamin D levels

and the presence of anxiety (29). In the systematic review of fourteen studies published by Fallah et al., it was determined that 10 studies reported a direct relationship between vitamin D levels and anxiety, and one study reported an indirect relationship.

In a randomized controlled clinical study evaluating the efficacy of vitamin D supplementation on anxiety, it was reported that the administration of 1600 mg of vitamin D for 6 months improved anxiety symptoms. In the study in which different vitamin D supplements applied to individuals ($n = 34$) in the remission stage of Crohn's disease were examined, it was reported that only high-dose (10,000 IU) vitamin D supplementation significantly increased serum vitamin D levels, but both doses improved the symptoms of depression and anxiety.

Conclusion and recommendations

In conclusion, vitamin D has immunomodulatory, neuroprotective, and neurotrophic properties and may affect the brain tissues involved in the pathophysiology of depression and anxiety. The results of studies in the literature on the relationship of vitamin D levels with supplementation, depression, and anxiety are inconsistent. It is thought that the reason for the inconsistency in studies examining vitamin D levels may be due to the use of different cut-off points regarding vitamin D adequacy, the differences in the groups in which the studies were conducted, and the differences in the tools used to determine depression and anxiety. It is thought that many factors may have contributed to the inconsistency in the studies in which vitamin D supplementation was evaluated, including the difference between the groups applied, the severity of depressive symptoms, the presence of comorbidities, initial 25(OH)D3 level, vitamin D supplement dose, supplement form, and duration. In addition, studies in the literature include not only individuals with symptoms of major depression or anxiety but also individuals with chronic inflammatory diseases such as ulcerative colitis, Crohn's, and diabetes. Therefore, positive outcomes in individuals with these diseases can be associated with the effect of vitamin D as an immunomodulator on metabolic and inflammatory markers. Although the cause and effect relationship of vitamin D with depression and anxiety has not been clarified in the literature, it is emphasized that low vitamin D levels cause an increase in the symptoms of these diseases. It is important to screen for vitamin D deficiencies regarding mood disorders, to plan appropriate treatments, and to determine the optimal dose. Because although there are studies in the literature reporting that the level of side effects and toxicity of vitamin D is low, it is also reported that the course of vitamin D levels above the threshold value is neurotoxic. Therefore, the necessity of monitoring vitamin D levels in planned vitamin D supplements is also clear. Besides, vitamin D is not included in the guidelines in the literature on mood disorders. For this disease group, cohort studies are needed to determine the effectiveness of vitamin D levels, supplement dose, and form.

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ASSOCIATION OF VITAMIN D AND SKIN HEALTH

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The "sunshine" vitamin is a hot topic that attracted ample attention over the past decades, specially that a considerable proportion of the worldwide population are deficient in this essential nutrient. Vitamin D was primarily acknowledged for its importance in bone formation, however; increasing evidence point to its interference with the proper function of nearly every tissue in our bodies including brain, heart, muscles, immune system and skin. Thereby its deficiency has been incriminated in a long panel of diseases including cancers, autoimmune diseases, cardiovascular and neurological disorders. Its involvement in the pathogenesis of different dermatological diseases is no exception and has been the subject of much research over the recent years. In the current review, we will throw light on this highly disputed vitamin that is creating a significant concern from a dermatological perspective. Furthermore, the consequences of its deficiency on the skin will be in focus.

Keywords: Vitamin D, Deficiency, Dermatology, Immunological

Introduction

It is somewhat ironic that vitamin D, through a historical accident, became classified as a 'vitamin', owing to the fact that vitamin is conventionally defined as 'essential item needed in the diet'. The paradox with 'vitamin D' is that diet per se is usually poor in vitamin D except for cod or other fish oils or food fortified with this vitamin (1).

Vitamin D is actually a fat-soluble prohormone steroid that has endocrine, paracrine and autocrine functions (2). The endocrine effects of vitamin D are mainly involved in serum calcium homeostasis. Vitamin D and calcium are often used in the same sentence because they work closely together, vitamin D's primary role is to control the levels of calcium found in the bloodstream by constantly allowing calcium and phosphate absorption from the intestine or taking calcium from bones. Furthermore, vitamin D is an enabling agent that, when present in optimal concentrations, has no perceptible effect on calcium absorption in its own right; however, it permits or facilitates flexible physiologic response to varying calcium need (3).

The paracrine and autocrine effects of vitamin D depend on genetic transcription, unique to the type of cell expressing nuclear vitamin D receptors. These potential effects include inhibition of cell proliferation, promotion of cell differentiation, and apoptosis which may in turn have roles in cancer, immunity, and many organ systems (4-8). The potential myriad effects of this vitamin in human health and disease have led to an

escalating interest in vitamin D inadequacy and the best methods to normalize suboptimal levels.

Sources of vitamin D

There are only 3 known sources of vitamin D; sunlight, diet, and vitamin D supplements (2, 9, 10).

Vitamin D and the skin

The skin is unique in being not only the source of vitamin D for the body but also in being capable of responding to the active metabolite of vitamin D, 1,25(OH)₂D. Both 1,25(OH)₂D and its receptor (VDR) play essential roles in the skin.

Skin differentiation and proliferation

Both calcium and 1,25(OH)₂D perform important and interacting functions in regulating the skin differentiation process. 1,25(OH)₂D increases the expression of involucrin, transglutaminase, loricrin, and filaggrin and increases keratinocyte cornified envelope formation while inhibiting proliferation (9, 10). These actions are due to, at least in part, the ability of 1,25(OH)₂D to increase intracellular calcium levels achieved by induction of the calcium receptor (11), and the phospholipase C (12) that are critical for the ability of calcium to stimulate keratinocyte differentiation (13,14). Mice lacking the VDR show defective epidermal differentiation manifesting as reduced levels of involucrin and loricrin and loss of keratohyaline granules (15, 16).

Cutaneous antimicrobial effects

1,25(OH)₂D and its receptor regulate the processing of the long chain glycosylceramides that are

critical for the skin barrier formation (17) which is crucial in defending the skin. Furthermore, they induce toll like receptor 2 (TLR2) and its coreceptor CD14, that initiate the innate immune response in skin (18). Activation of these receptors leads to the induction of CYP27B1, which in turn induces cathelicidin resulting in the killing of invasive organisms (18, 19). Mice lacking the VDR or the enzyme (CYP27B1) show decreased lipid content of the lamellar bodies leading to a defective permeability barrier, and a defective response of the innate immune system to invading infections.

Vitamin D and cutaneous innate immunity

The historical link between vitamin D and innate immune function stemmed initially from the use of cod liver oil as treatment for tuberculosis (TB). More recent work has focused on the cellular and molecular machinery that underpins the actions of vitamin D on the pathogen that causes TB, *Mycobacterium tuberculosis* (M. TB). In the first of these studies, carried out 25 years ago, active 1,25(OH)₂D was shown to reduce the proliferation of M. TB in macrophages with this effect being enhanced by the cytokine interferon γ (IFN γ), a known stimulator of macrophages (20). However, the major advance in our understanding of how vitamin D directs antibacterial responses in TB arose from much more recent studies aiming at defining the way by which monocytes and macrophages, key cells in directing bacterial killing, respond to an encounter with M. TB (21). These data suggested that monocytes promote localized activation of vitamin D in response to M. TB, with the resulting 1,25(OH)₂D binding to endogenous VDR. In this way, vitamin D can act to modulate gene expression in response to M. TB immune challenge – a classical intracrine mechanism (22, 23). Functional analyses showed that 25OHD-mediated induction of cathelicidin is coincident with enhanced killing of M. TB in monocytes. Naturally occurring variations in serum 25OHD have been shown to correlate with induction of monocyte cathelicidin expression (24). The conclusion from these studies was that individuals with low serum 25OHD will be less able to support monocyte induction of antibacterial activity and may therefore be at greater risk of infection. Conversely, supplementation of vitamin D-insufficient individuals *in vivo* has been shown to improve TLR-mediated induction of monocyte cathelicidin (25) and may therefore help to protect against infection.

Studies have shown that T-cell cytokines play a pivotal role in both amplifying and attenuating vitamin D-mediated cathelicidin production (26). Indeed, cytokine production by monocytes themselves may be central to the intracrine metabolism of vitamin D in this cell type (27, 28). Thus, it seems likely that the ability to mount an appropriate response to infection will be highly dependent on the availability of vitamin D, with additional tuning of this response by other components of the normal human immune response.

Vitamin D can also influence innate immune responses to pathogens via effects on antigen presentation by macrophages or dendritic cells (DCs). These cells are known to express VDR (29), and treatment

with 1,25(OH)₂D has been shown to inhibit DC maturation, suppress antigen presentation and promote a tolerogenic T-cell response (30, 31).

Conclusions

In conclusion one could clearly sense the unique relationship that entangles vitamin D to dermatology. On one hand, our skin is one source for this important vitamin and on the other hand all available data point to its important impact on the health of our skin and the involvement of its deficiency in the pathway of many dermatological diseases. Several factors are responsible for maintaining it in optimum levels; therefore sunny climates are by far not a guarantee for providing a “comfort zone” regarding the possibility of this vitamin deficiency, a concern documented by several epidemiological studies carried out in areas close to the equator (32–35). On the basis of currently available data, it is clear that supplemental vitamin D should be the preferred recommendation toward achieving its normal serum levels, thereby avoiding the deleterious effects accompanied by its deficiency. Still more research is needed to unravel its complicated ties to dermatological diseases and create clear guidelines and recommendations for its supplementation.

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PHYSICAL SCIENCES

SCIENTIFIC VALUE OF RESEARCHES OF ASTROPHYSICAL PORTALS¹

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Abstract

The article claims that the version of the special theory of relativity studied in all physics textbooks is incorrect and sets out the main provisions of its corrected version. And from the relativistic formulas of the corrected version of SRT it follows that in nature, in addition to our visible universe, there are mutually invisible universes and anti-universes that are connected to each other by a large number of portals. At the same time, the entrances to the portals are supposedly the so-called anomalous zones, which people avoid visiting, since it is very difficult to get out of them. However, scientific research of portals by unmanned robotic complexes is possible and necessary. Such scientific research will allow solving a number of very important scientific problems - proving the existence of mutually invisible universes adjacent to our visible universe, explaining the Fermi paradox, proving the possibility of traveling not only in the space of the hidden Multiverse, but also in time, etc.

Keywords: imaginary numbers; special theory of relativity, invisible universes and antiuniverses, hidden Multiverse, Hyperverse, portals, anomal zones.

1. The version of SRT taught in all physics textbooks is incorrect

Although Albert Einstein became famous as the author of the special and general theories of relativity, who was nominated for the Nobel Prize 66 times, he received it in 1921 not for the theory of relativity, but for the study of the photoelectric effect. And he never received the Nobel Prize for the special theory of relativity (SRT) because SRT had no experimental confirmation. In other words, SRT was actually called a theory incorrectly, since it was only a hypothesis. And therefore, according to the Nobel Committee, sooner or later it could be experimentally refuted.

And the Nobel Committee turned out to be right - now it has already been experimentally refuted.

First, in 1934, it was refuted by the discovery of Cherenkov radiation [1], which was created by the movement of electrically charged particles in a transparent medium with a refractive index $n > 1$ at a speed exceeding the phase velocity of light in this medium. For this discovery, P.A. Cherenkov, I.E. Tamm and I.M. Frank even received the Nobel Prize in 1958. But the SRT was then corrected and survived.

Then, in 2011, the OPERA collaboration tried to disprove it at the Large Hadron Collider, expecting to receive the Nobel Prize for this. And they even published a message about their success [2]. But six months later, in 2012, at the same Large Hadron Collider, the ICARUS collaboration found an error in the OPERA experiment and disproved it [3].

And in the 21st century, the generally accepted version of SRT has already been confidently refuted by the existence of radio technology, the existence of tsunamis, the existence of pianos and other musical instruments, and even the existence of suspended swings on playgrounds, as well as many other experiments [4]-[15]. But throughout the 20th century, relativistic phys-

icists could not figure this out. And even now, the authors of physics textbooks do not understand this. And therefore, these textbooks still present the incorrect version of SRT created in the 20th century [16]-[45], according to which relativistic formulas have the form (see Fig. 1a, b, c)

$$m = m_0 / \sqrt{1 - (\frac{v}{c})^2} \quad (1)$$

$$\Delta t = \Delta t_0 \sqrt{1 - (\frac{v}{c})^2} \quad (2)$$

$$l = l_0 \sqrt{1 - (\frac{v}{c})^2} \quad (3)$$

in which m_0 – rest mass of a moving body;

m – relativistic mass of a moving body;

Δt_0 – rest time of a moving body;

Δt – relativistic time of a moving body;

l_0 – rest length of a moving body;

l – relativistic length of a moving body;

v – speed of motion of a body;

c – speed of light.

And these formulas in textbooks are explainable only in the range of subluminal speeds $v < c$, in which the quantities m , Δt and l take on values measured by real numbers. But in the range of superluminal speeds $v > c$, these quantities m , Δt and l already take on values measured by imaginary numbers discovered by Scipione Del Ferro, Niccolo Fontana Tartaglia, Gerolamo Cardano, Lodovico Ferrari and Rafael Bombelli [46] 400 years before the creation of the SRT, the physical meaning of which, however, was not explained by them. But, perhaps, even earlier than them, imaginary numbers were discovered by Paolo Valmes [47], who was burned alive at the stake for this by the sentence of the inquisitor Thomas de Torquemada. The creators of

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the SRT also could not explain this. And the physical meaning of imaginary numbers in physics textbooks has not been explained to this day.

Moreover, the graph of the function $m(v)$ in the range of speeds $v > c$ (see Fig. 1a) corresponds to a physically unstable process, which cannot exist in nature at all. Therefore, all formulas (1)-(3) are completely incorrect. But since such a theory, which even its authors could not explain, was of no use to anyone, a postulate was introduced into it, called the principle of not exceeding the speed of light, the meaning of

which is clear from its name. And the SRT was preserved, since it claimed that in nature processes confirming the physical reality of imaginary numbers allegedly do not exist. And in the 20th century, no one objected to this. And therefore, despite the above-mentioned experiments refuting the SRT, it is sometimes even claimed that Albert Einstein understood that nothing in the Universe can move faster than the speed of light. And that the speed of light is not just a number, but a physical limit. The same as, for example, absolute zero at a temperature of minus 273.15 degrees Celsius.

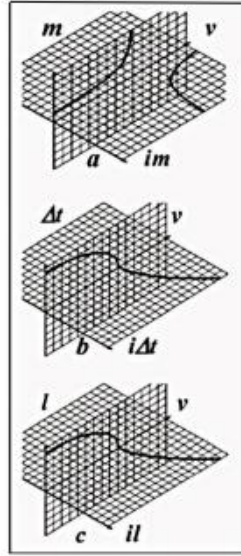


Fig. 1. Graphs of functions $m(v)$, $\Delta t(v)$ and $l(v)$ corresponding to the existing versions of the SRT in the subluminal $v < c$ and superluminal $v > c$ ranges

But the version of SRT that is still studied in all physics textbooks is incorrect [16]-[45], because:

- the relativistic formulas obtained in it are incorrect;
- the relativistic formulas obtained in it were incorrectly explained using the incorrect principle of not exceeding the speed of light;
- from these incorrect relativistic formulas, incorrect conclusions were made about the physical unreality of imaginary numbers and about the existence in nature of our only visible universe, in which everything is measured only by real numbers.

2. Corrected version of SRT

But not all scientists share the opinion set out in the version of SRT given in physics textbooks that, in accordance with the principle of not exceeding the speed of light, imaginary numbers are physically unreal and that in nature there is only one visible universe, ours, since both of these statements are refuted experimentally.

And the relativistic formulas of the corrected version of SRT have the form [48]-[56]

$$m(q, r, s) = \frac{m_0 i_1^q i_2^r i_3^s}{\sqrt{1 - [\frac{v}{c} - (q + r + s)]^2}} \quad (4)$$

$$\Delta t(q, r, s) = \Delta t_0 i_1^q i_2^r i_3^s \sqrt{1 - [\frac{v}{c} - (q + r + s)]^2} \quad (5)$$

$$l(q, r, s) = l_0 i_1^q i_2^r i_3^s \sqrt{1 - [\frac{v}{c} - (q + r + s)]^2} \quad (6)$$

in which $q(v) = [v/c]$ is the “floor” function of discrete mathematics of the argument

v/c , which is the fourth spatial dimension (Fig. 2);

$r(v) = [v/c]$ is the “floor” function of discrete mathematics of the argument v/c , which is the fifth spatial dimension (Fig. 2);

$s(v) = [v/c]$ is the “floor” function of discrete mathematics of the argument v/c , which is the sixth spatial dimension (Fig. 2).

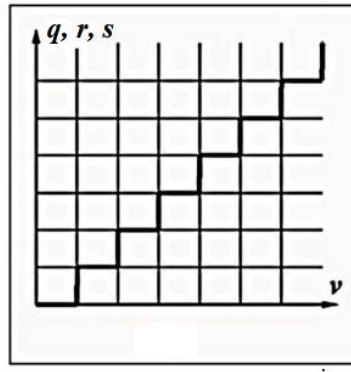


Fig. 2. Graphs of functions $q(v)$, $r(v)$, $s(v)$, illustrating the meaning of the “floor” function of discrete mathematics

That is, our Multiverse is six-dimensional – each universe has three dimensions x, y, z and three more dimensions q, r, s have coordinates of these universes in the Multiverse (Fig. 3) – and is described by quaternions $f_{q,r,s}(x, y, z) + i_1 q + i_2 r + i_3 s$, the number of which is equal to the number of universes in the Multiverse. This is exactly what Lisa Randall predicted: “We could be living in a three-dimensional pocket of higher dimensional space.”

In this case, the three imaginary units i_1, i_2, i_3 in quaternions are related by the relations

$$i_1^2 = i_2^2 = i_3^2 = -1 \quad (7)$$

$$i_1 i_2 i_3 = i_2 i_3 i_1 = i_3 i_1 i_2 = -1 \quad (8)$$

$$i_1 i_3 i_2 = i_2 i_1 i_3 = i_3 i_2 i_1 = 1 \quad (9)$$

In the mathematics of hypercomplex numbers, the function $i_1^q i_2^r i_3^s$ can be calculated only for integer values q, r, s , but can take both positive and negative values and both real and imaginary values. But we have already proven that imaginary numbers are physically real and therefore we must also explain them. Therefore, let us now consider the values $m(v)$, $\Delta t(v)$ and $l(v)$ of the quantities, and in the range of velocities $V > C$ for successive values of the argument $q + r + s$ equal to 0, 1, 2, 3, 4, 5, ... Then for our visible universe with coordinates $q=0, r=0, s=0$,

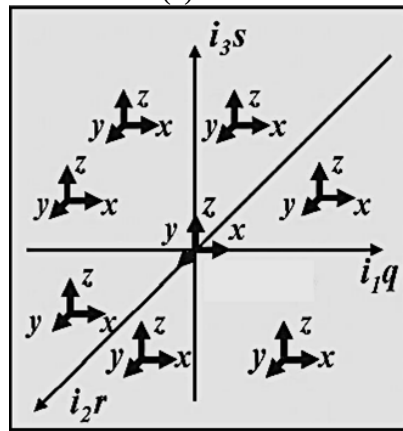


Fig. 3. Six-dimensional space of the hidden Multiverse, where q, r, s are the coordinates of invisible parallel universes, and x, y, z are the coordinates of the matter content in each parallel universe

i.e. located at the origin, we obtain $i_1^q i_2^r i_3^s = 1$. For definiteness, we will call it the tardyon universe. For the value $q + r + s = 1$ in the range of velocities $V > C$, we obtain $i_1^q i_2^r i_3^s = +i$. This situation corresponds to the invisible universe, since it is located beyond the event horizon. For definiteness, we will call it the tachyon universe. For the value $q + r + s = 2$ in the velocity range $V > C$ we get $i_1^q i_2^r i_3^s = -1$. This situation also corresponds to an invisible universe, since it is located beyond the event horizon. We will call it a tardyon antiuniverse. For the value $q + r + s = 3$ in the

velocity range $V > C$ we get $i_1^q i_2^r i_3^s = -i$. This situation also corresponds to an invisible universe, since it is also located beyond the event horizon. We will call it a tachyon antiuniverse. For the value $q + r + s = 4$ in the velocity range $V > C$ we get $i_1^q i_2^r i_3^s = +1$. This situation also corresponds to an invisible tardyon universe (but a different one), since it is also located beyond the event horizon. For the value $q + r + s = 5$ in the velocity range $V > C$ we get $i_1^q i_2^r i_3^s = +i$. This situation also corresponds to an invisible tachyon universe (but a different one), since it is also located beyond the event horizon. Thus, all universes except ours

are invisible. Therefore, we will call our Multiverse hidden. And the hidden Multiverse has a helical structure.

An example of a possible structure of the hidden Multiverse is shown in Fig. 4. As can be seen, in such a structure of the hidden Multiverse, it is possible to move to the tardion antiuniverse from the tardion universe and to the tardion universe from the tardion antiuniverse in different ways, but not arbitrarily, but only in such a way, in which the value will successively take the values $+1, +\dot{i}_1 \oplus +\dot{i}_2 \oplus +\dot{i}_3, -1, -\dot{i}_1 \oplus -\dot{i}_2 \oplus -\dot{i}_3, +1, \dots$ etc., where $\oplus$ is the symbol of the logical operation of discrete mathematics 'exclusive OR'. In this case, different trajectories of movement from one universe (or antiuniverse) to another can differ only due to substitution of some tachyon universes from $\dot{i}_1, \dot{i}_2, \dot{i}_3$ with

others and some tachyon antiuniverses from $\dot{i}_1, \dot{i}_2, \dot{i}_3$ with others. Consequently, the tachyon universes $\dot{i}_1, \dot{i}_2, \dot{i}_3$ in the hidden Multiverse are located parallel to each other. The tachyon antiuniverses $\dot{i}_1, \dot{i}_2, \dot{i}_3$ for the same reasons are also placed parallel to each other. And therefore, in the hidden Multiverse, when moving from any tardyon universe to a tardyon antiuniverse and then to another tardyon universe, parallel universes and antiuniverses must alternate in the following sequence – 'tardyon universe', 'one of the tachyon universes', 'tardyon antiuniverse', 'one of the tachyon antiuniverses', 'tardyon universe', 'one of the tachyon universes', etc.

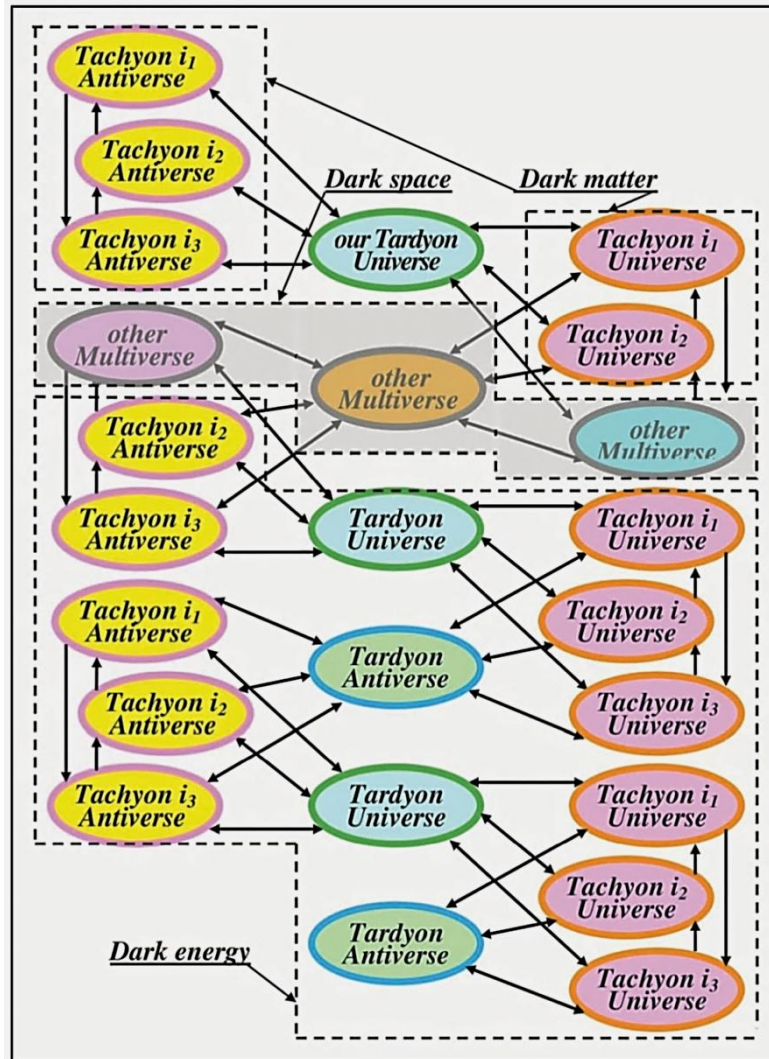


Fig. 4. Possible quaternion structure of the hidden Multiverse containing twenty-two parallel universes, including six invisible universes adjacent to our visible universe

Moreover, naturally, the movement from our tardion universe to the tardion antiuniverse through some tachyon universe - for example, $\dot{i}_1$ - does not necessarily have to proceed further through the tachyon anti-

universes $\dot{i}_2$ and $\dot{i}_3$. The same reservation applies to the situation if the movement from the tardion universe

to the tardion antiuniverse begins through tachyon universes $\dot{l}_2$ or $\dot{l}_3$.

All these transitions are shown in Fig. 4. Moreover, since all such hidden Multiverses correspond to its open screw structures, united through the corresponding portals with other Multiverses, then all together they form the Hyper-universe. In this case, the invisible universes adjacent to our visible universe give rise to the phenomenon of dark matter, the remaining invisible universes of the hidden Multiverse give rise to the phenomenon of dark energy, and the invisible universes located outside the hidden Multiverse give rise to the phenomenon of dark space.

3. Portals research

Numerous universes actually existing in space - if they exist - forming a hidden Multiverse, drift and touch, slightly immersing themselves in each other. And these zones of mutual immersion of neighboring universes, through which it is possible to pass from one universe to another, are called portals [57], [58]. And portals exist (and this still needs to be experimentally proven - see below) only if there exist at least two parallel universes, between which the portals are located.

The entrances and exits to portals are called anomalous zones [59]-[62], since incomprehensible phenomena occur in them. In particular, people disappear in them, since the paths from the entrance to the exit in

portals are invisible labyrinths, from which it is almost impossible to escape. Because of this, people avoid visiting anomalous zones. And there are more than two hundred thousand anomalous zones on Earth.

But portals are of great scientific interest. And they can be studied without visiting, using unmanned vehicles.

3.1. How to see invisible universes?

The question of whether mutually invisible universes and portals between them exist in nature is fundamental. The answer to it determines whether the version of SRT presented in textbooks is correct or not. But since scientists, despite long theoretical debates, have not yet come to a consensus, the truth can be revealed by an experiment. Moreover, it is quite simple and clear.

And for this, it is not at all necessary to visit other universes. It is enough to at least look at them. As in order to be convinced that in addition to the room visible to us, in which we are now, there is a neighboring invisible room, it is enough to look from the corridor connecting these rooms into the neighboring room. The corridors connecting neighboring universes are portals [57], [58].

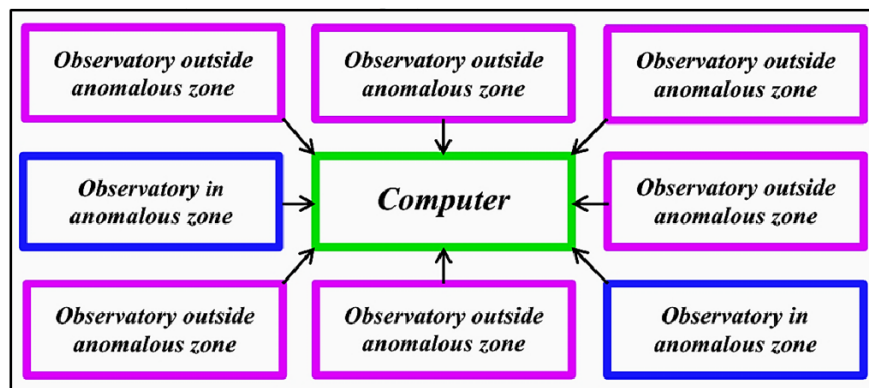


Fig. 5. Scheme of an astronomical experiment to detect invisible universes

And in order to be convinced, while in the portals, that you are no longer in our universe, but on the way to the neighboring universe, you need to look from the portal through a telescope at the starry sky and see other constellations on it [63]-[68]. This is a very reliable experiment, since you can't draw constellations in the sky.

3.2. The Arrow of Time

Here are some quotes on this topic.

"Time is the most frequently used word in English and the third most frequently used word in Russian. It is in every other language, too, because synchronizing actions in time is as important as coordinating them in space. Without knowing the exact time, it is impossible to organize your life and plan it in advance. If in ancient times you could rely on natural cycles and an internal sense of time, then in our days you need to constantly have a watch or a phone with you. Time is the most important of the abstract concepts that we pronounce every day. Every thinking person has thought

about the problem of time at least once in their life, and a huge amount of philosophical and scientific literature has been written on this topic. However, no one will say for sure what time is. Or prove that time is irreversible. Or maybe it only seems that way to us?" [70]

Here is what Stephen Hawking writes: *"We can see a cup fall off a table and break into pieces, but we never see the cup put back together from those pieces and return to the table. The increase in disorder, or entropy, makes it possible to distinguish the past from the future and thus gives time a definite direction."*

This phenomenon, known as the arrow of time, is one of the most amazing mysteries of physics. And the name "arrow of time" for this phenomenon was proposed at the beginning of the 20th century by the British physicist Sir Arthur Stanley Eddington.

And it would seem that one cannot argue with such statements.

3.3. Anti-time

But we will nevertheless try to show that the concept of the arrow of time, used in the generally recognized incorrect version of the SRT, is refutable in its corrected version. To do this, let us return to Fig. 4. And note something unusual in it. A hypothetical journey along the structural diagram of the hidden Multiverse shown in the figure is, according to formulas (4)-(6), a journey not only in space, but also in time. Since the transition from our visible tardion universe to one of the neighboring tachyon universes or antiuniverses is accompanied by their movement not only in space, but also in time, since time in them is different.

And this can be proven using various routes of such movements. Let us cite one of the simplest. Let us assume that we moved through a portal from our visible tardion universe - using for this purpose some anomalous zone on the surface of the Earth - in a short time (for example, one day) to one of the neighboring tachyon universes or antiuniverses. And at the same time,

naturally, we disappeared from the sight of our colleagues who saw us off at the edge of the anomalous zone. But we did not disappear anywhere in this neighboring tachyon universe or antiuniverse and carried out some research on it for a couple of months. Then, having carried out the planned research, we again in a short time (for example, one more day) through the same portal safely returned to Earth. And since on Earth, relative to the neighboring invisible tachyon universe or antiuniverse, time flows (into the future or into the past) in a direction perpendicular to earthly time, then on Earth it seems to have stopped. Therefore, it seemed to our colleagues who met us on Earth that we had been absent not for two months, but only for two days. But we showed our unshaven beards for two months and thus proved that we had ended up in the past, since our colleagues who saw us off had moved into the future for two months. And in this past, we were beardless two months ago.

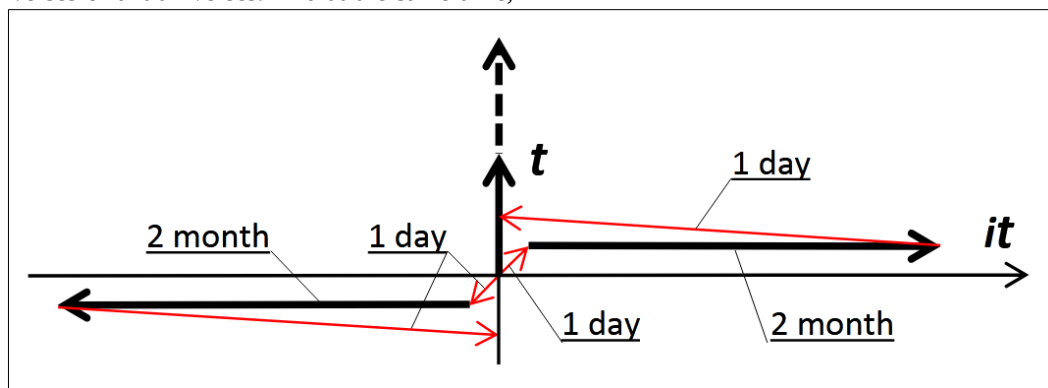


Fig. 7. The vertical solid arrow t is the real time axis (in our visible tardyon universe). Horizontal thin arrow it is the axis of imaginary time (in the neighboring invisible tachyon universe and antiverse). Vertical dotted arrow - coordinate of the scientists' position 2 months after they, being at the beginning of the coordinates, sent two expeditions through the portals to the tachyon universe and the antiverse. Big horizontal arrows correspond to stay of scientists in tachyon universe and antiverse. And red arrows show transitions through portals.

Of course, we won't be able to contradict Stephen Hawking with such an experiment and see the process of restoring a broken cup from its fragments. But the fictional travelers from our visible tardion universe to neighboring invisible tachion universes or anti-universes and back, nevertheless made a journey through time. And due to this, having returned to the past, they nevertheless turned the arrow of time by 180° .

And for those who are not convinced by this hypothetical experiment, below it is explained how to make it really physically feasible.

3.4 Geophysical research of portals

Oddly enough, geophysical studies of portals [71]-[80] can be much more productive in space exploration than astronomical studies of the visible starry sky. Indeed, astronomical observations allow us to study only our visible universe. And geophysical studies of portals, which are transitions to neighboring invisible universes, allow us to study invisible universes neighboring our visible universe. Moreover, as can be seen from Fig. 4, they allow us to study invisible universes, even those located outside the hidden Multiverse. They also allow, since there are more than two hundred thousand anomalous zones on Earth that are supposedly entrances to portals, having studied the portals, to perform

the most detailed classification of invisible universes antiuniverses neighboring our visible universe. And to identify, and then even study some characteristics of invisible universes and antiverses, even those located outside the boundaries of the hidden Multiverse. Which will allow us to understand why they are not part of the hidden Multiverse. And it is possible that several other Multiverses neighboring our hidden Multiverse will be discovered.

And with all this, geophysical research of space is much cheaper than astronomical research.

Moreover, geophysical research of portals will allow attempts to create time machines [81], with the help of which the research described in the previous section 4.3 can be transformed from hypothetical into real astrophysical ones.

3.5. Fermi paradox

The Fermi paradox is a statement of a seemingly paradoxical situation in which, on the one hand, it is known that there are many stellar systems in space suitable for life, but on the other hand, despite all the efforts of scientists, no signs of life have been found in this space. And it would seem very strange [82]-[84].

But in fact, there is nothing strange about it [85]-[97]. After all, what are we looking for? What signs of

life do we expect to see? The same as now on Earth? For the same radio stations to work as on Earth, which, when transmitting signals, spend most of their energy on transmitting signals to nowhere due to an imperfect radiation pattern? For the inhabitants of supercivilizations to detonate atomic and hydrogen bombs? And so on.

But first of all, these are all defects of our imperfect civilization, which supercivilizations got rid of long ago. And therefore they are invisible. And secondly, why not assume that we do not see their ships in space also because they have different logistics as a result of using their super knowledge. Even on Earth, on the way to work in large cities, people now often use the subway. And therefore, such their movement from space is also invisible.

And then their activity can be proven by comparing two texts:

1. "Our contemporaries – **people of the Earth** – begin their working day, leaving **their homes**, by visiting the nearest **metro station "A"**. Then, invisible from space, they **travel in the tunnel "Aa"** underground to the transfer point **"ab" on our planet Earth**. After that, they travel through another **underground tunnel "bB"** to another **underground station "B"**, leaving which they rise to the **surface of the Earth** in the place they need."

2. "Our contemporaries – **inhabitants of supercivilizations** – begin their working day, leaving **their invisible home built using superstealth technology**, by visiting the nearest **anomalous zone "A"**. Then, invisible from space, they **move through the portal "Aa"** to the transfer point **"ab" in the neighboring universe**. After which, through **another portal "bB"**, they move to another **neighboring universe "B"** and exit the portal in the **anomalous zone** in the place they need.

As you can see, the same thing happens in both situations – invisible movement in space, with the replacement of terms of our civilization currently existing on Earth with similar terms in supercivilizations:

- "people of the Earth" with "inhabitants of supercivilizations";
- "housing" with "invisible housing built using superstealth technology";
- "metro station "A" with "anomalous zone "A";
- "riding in tunnel "Aa" with "moving through portal "Aa";
- "ab" on our planet Earth" with "ab" in the neighboring universe";
- "underground tunnel "bB" with "portal "bB";
- "underground station "B" with "neighboring universe "B";
- "the surface of the Earth" with "in the anomalous zone".

That is, in order for the movement of inhabitants of supercivilizations in space to become invisible, it is only necessary that they move between universes through portals, and that planets in star systems serve as transfer stations from one portal to another. And therefore, this circumstance will need to be taken into account during geophysical studies of portals.

And the Fermi paradox must be recognized as yet another proof of the existence of portals and mutually

invisible parallel universes, and, consequently, the incorrectness of the version of SRT studied in all physics textbooks.

4. Conclusion.

Thus, the article experimentally proves and theoretically explains that the version of SRT, created in the 20th century, which is still studied in all physics textbooks, is incorrect, because:

- the relativistic formulas obtained in it are incorrect;
- these formulas are incorrectly explained using an incorrect postulate called the principle of not exceeding the speed of light;
- incorrect conclusions are made from these formulas about the physical unreality of imaginary numbers and the existence in nature of our only visible universe, in which everything is measured only by real numbers.

But in the corrected version of SRT, from the relativistic formulas obtained in it, it follows that in nature, in addition to our visible universe, there are many other mutually invisible universes and anti-universes. And they, drifting in space, touch each other, even slightly plunging into each other and forming transition zones called portals. Moreover, through portals, neighboring universes and anti-universes exchange their material contents according to the law of communicating vessels.

However, people avoid visiting portals, as they are invisible labyrinths. Therefore, if you accidentally get into them, it is almost impossible to get out of them. At the same time, portals are of significant scientific interest, as as a result of their astro-geophysical research, unlike astronomical research, they allow us to prove the existence of neighboring invisible universes and anti-universes and to obtain some information about them that cannot be obtained otherwise. They also allow us to carry out other interesting research - to prove the possibility of traveling in the Multiverse not only in space, but also in time and thereby prove the existence of anti-time, etc.

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SOCIAL SCIENCES

ПЕРЕПЛЕТЕНИЕ КУЛЬТУРЫ И КОГНИЦИИ: ПЕРЕВОД И ИНТЕРПРЕТАЦИЯ МЕТАФОР КИТАЙСКИХ ПОСЛОВИЦ В РОССИЙСКИХ СМИ

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THE INTERWEAVING OF CULTURE AND COGNITION: TRANSLATION AND INTERPRETATION OF CHINESE PROVERBS IN RUSSIAN MEDIA

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Аннотация

С углублением глобализации межкультурное общение становится всё более частым. Китай и Россия имеют значительные различия в языке, культуре и когнитивных моделях, при этом пословицы, являясь носителями культуры, часто играют важную роль в межъязыковом и межкультурном общении. В данной статье анализируется перевод и интерпретация китайских пословиц и метафор в российских СМИ, а также исследуется взаимодействие между культурой и когницией. Используя теории когнитивной лингвистики и межкультурной коммуникации, статья рассматривает культурный контекст метафор в китайских пословицах, когнитивные модели, а также возможные трудности, возникающие при переводе. На основе конкретных примеров раскрываются стратегии перевода китайских пословиц и метафор в российских СМИ, а также их культурное значение и преобразования, подчёркивая глубокое влияние культурных и когнитивных рамок на восприятие метафор.

Abstract

With the deepening of globalization, intercultural communication is becoming increasingly frequent. China and Russia have significant differences in language, culture, and cognitive models, and proverbs, as carriers of culture, often play an important role in interlingual and intercultural communication. This article analyzes the translation and interpretation of Chinese proverbs and metaphors in Russian media, as well as the interaction between culture and cognition. Using theories of cognitive linguistics and intercultural communication, the article examines the cultural context of metaphors in Chinese proverbs, cognitive models, and the possible difficulties that arise in translation. Based on specific examples, it reveals translation strategies for Chinese proverbs and metaphors in Russian media, their cultural significance, and transformations, emphasizing the profound impact of cultural and cognitive frameworks on the perception of metaphors.

Ключевые слова: культура и когниция, метафора, пословица, перевод, российские СМИ, межкультурное общение.

Keywords: culture and cognition, metaphor, proverb, translation, Russian media, intercultural communication.

С углублением китайско-российских отношений, обмен языками и культурами становится всё более важным. Китайские пословицы, являясь одной из основ китайской культуры, содержат в себе глубокую мудрость и отражают уникальное мировоззрение и способы мышления китайского народа. Однако перевод пословиц часто сталкивается с большими трудностями, особенно когда речь идет о различиях в метафорах, культурных контекстах и когнитивных моделях. В российских СМИ перевод китайских пословиц — это не только вопрос языковой трансформации, но и проявление культурных и когнитивных различий. Целью данной статьи является исследование влияния переплетения культуры и когниции на перевод метафор китайских пословиц, а также анализ их распространения и интерпретации в российских СМИ. Конкретно, мы применим теории когнитивной лингвистики и межкультурной коммуникации для анализа

когнитивной структуры метафор китайских пословиц и их переводческих стратегий в российском контексте. Через эмпирические примеры статья исследует различные способы восприятия и воспроизведения метафор в разных культурных контекстах, а также выявляет значимость культуры и когниции в межкультурной коммуникации.

В данной статье были использованы следующие основные методологические подходы: теория когнитивной лингвистики, теория межкультурной коммуникации и теория перевода метафор (Вежбицкая А., 1990; Кириллова, Н.С., 2010, 2012; Варшавская, И.М., 2015; Кун, И., 1990; Куликова, Т. В. и т.д.).

Когнитивная лингвистика подчеркивает тесную связь между языком и мышлением, считая язык не только инструментом выражения мыслей, но и отражением способов мышления. В книге «Метафоры, которыми мы живем» утверждается,

что метафора — это не просто риторическое средство языка, но и основная составляющая человеческого познания (Лакофф, Джонсон, 1980). Через метафоры человек может преобразовывать абстрактные концепты в конкретные, осязаемые переживания, формируя восприятие мира.

Теория межкультурной коммуникации акцентирует внимание на языковом обмене и понимании в условиях различных культурных контекстов. Хофстед (2001) утверждает, что различные культуры значительно различаются в когнитивных, поведенческих и эмоциональных выражениях, и что перевод и культурная коммуникация — это не только преобразование языка, но и перенос ценностей и способов мышления. Таким образом, в процессе межкультурной коммуникации культурные различия могут оказывать влияние на передачу, восприятие и понимание информации. Теория перевода метафор фокусируется на том, как точно передать значение метафоры в процессе перевода, поэтому при переводе метафор необходимо учитывать их культурный контекст и ситуацию.

Материалы в данной статье составляют фрагменты, включающие китайские пословицы с 2020-го года по 2024 год в таких Российских СМИ, как РИА Новости, Российская газета, Факты и Аргументы, Новая Газета, Известия и т.д.

На многих новостных сайтах, журналисты и переводчики иногда используют китайские пословицы для объяснения китайских и глобальных социальных явлений. Также в статьях на китайские темы нередко встречаются китайские пословицы или устойчивые выражения, которые подвергаются переводу. Примером может служить использование пословиц в контексте экономических или политических новостей, где эти выражения добавляют культурный контекст для российской аудитории.

Метафора — это не только риторический инструмент языка, но и важный носитель когнитивных и культурных значений. Она через повседневные выражения позволяет абстрактным мыслям, эмоциям и переживаниям становиться конкретными и осязаемыми, предоставляя индивидууму способ понимания мира и своей идентичности. Метафора эффективно соединяет когнитивный и эмоциональный миры людей, превращая сложные философские, психологические или социальные явления в конкретный, воспринимаемый в повседневной жизни опыт. Этот процесс преобразования способствует не только углублению познания индивида, но и создаёт основу для общения и взаимопонимания в социальных группах. Особенно в условиях глобализации и культурного разнообразия важность межкультурных исследований метафор становится всё более очевидной. Анализ моделей использования метафор в разных культурах позволяет нам не только лучше понять ценности и социальные структуры каждой из них, но и способствует межкультурному пониманию и диалогу.

Например, «в Китае есть пословица “Триста шестьдесят профессий, в каждой можно стать мастером”, смысл которой в том, что, прилагая уси-

лия, можно добиться успеха в любом деле. Традиционное представление “навыки менее важны, чем диплом” постепенно ломается.” (Российская газета, 20.11.2024).

Метафорическое значение этой пословицы “Триста шестьдесят профессий, в каждой можно стать мастером” заключается в том, что она использует слово «профессия» как представление конкретных областей деятельности, намекая на то, что в каждой сфере есть выдающиеся и талантливые люди. Здесь «мастер» (жуаньюань) означает не только первого кандидата в традиционном китайском экзамене на ученую степень, но и символизирует выдающихся людей, которые могут быть найдены в любой профессии или области. Метафора, в которой число «триста шестьдесят профессий» представляет все профессии, подчёркивает, что различные профессии в обществе имеют свою ценность и возможности для достижения успеха, призывая людей стремиться к высокому мастерству в любой сфере, независимо от того, чем они занимаются. С метафорической точки зрения, эта пословица передает идею «равенства возможностей», утверждая, что успех не принадлежит только некоторым профессиям или отраслям, но является доступным в любой сфере, и каждый человек может стать «жуаньюанем» в своей области.

Более того, метафоры китайских пословиц в российских СМИ играют важную роль в эмоциональном выражении и передаче ценностей, углубляют эмоциональное восприятие читателем, усиливают впечатление и улучшают визуализацию у читателя. Через яркие описания и образные сравнения метафоры превращают абстрактные концепции в конкретные образы, помогая читателю создавать яркие картины в своем воображении. Например: “Слежу за питанием. Не переедаю, не совмещаю белки с углеводами. Присмотрелся к тому, что мой кишечник принимает. Потому кашу ем не густую, а с молоком. Люблю манную, делаю её себе раз в месяц. Перешёл с кофе на цикорий. В нём много витаминов. Плюс добавляю в него ложечку элеутерококка. И усталость пропадает. Обычный чай заменил иван-чаем. Кстати, есть хорошая китайская пословица: «Воду надо кушать, а пищу надо пить». Пережевываю пищу так, что она в водичку превращается, а воду задерживаю во рту.” (Аргументы и факты, 12.04.2024).

Однако в реальных условиях новостных СМИ эквивалентность перевода напрямую влияет на построение метафоры, особенно в контексте межкультурного общения. Перевод китайских пословиц с метафорами становится сложным и тонким процессом. Переводчик должен не только точно передать буквальное значение исходного текста, но и глубже проникнуть в его культурное содержание и когнитивные особенности. В этом процессе ключевую роль играют как культурная осведомленность переводчика, так и его языковые навыки. Необходимо сохранить нюансы метафоры оригинала, при этом найти способ выражения, который будет понятен и принят читателями целевой культуры.

Только в этом случае метафора китайской пословицы сможет быть эффективно передана и интерпретирована в межкультурном контексте, что обеспечит подлинный культурный обмен и интеграцию.

В процессе перевода также могут возникать ошибки или недочеты, особенно когда речь идет о китайских пословицах, насыщенных культурными и метафорическими значениями. Эти ошибки могут быть вызваны недостаточным пониманием исходного текста переводчиком или различиями в культуре целевого языка, что создает препятствия для точного выражения. Например, метафоры и символические значения в некоторых китайских пословицах могут не иметь прямых аналогов в русской культуре, и переводчик должен прибегать к творческим преобразованиям, чтобы найти наиболее подходящий русский эквивалент. Однако такие преобразования нелегки, и малейшая ошибка может привести к потере или искажению метафорического смысла, что негативно скажется на восприятии оригинала и его принятии читателем.

Встречается такая пословица в российском медийном пространстве — «при встрече близких людей и тысячи бокалов мало» (Аргументы и факты, 09.02.2024). Эта пословица связана с китайской культурой питья.

Метафора вышесказанной пословицы отражает глубокую дружбу и эмоциональное единение между людьми. Буквальное значение таково: когда пьешь с другом, даже если выпить тысячу чашек, это будет мало. Здесь выражение «тысяча чашек мало» не просто указывает на количество алкоголя, а с помощью гиперболы передает мысль, что в истинной дружбе и душевном согласии даже полные чашки не могут быть достаточными, что намекает на глубокие чувства и бесконечное общение между людьми.

Эта метафора передает эмоциональный слой, который выходит далеко за пределы самого алкоголя. Она выражает радость и наслаждение от совместного времени с другом, а также отражает важность межличностных отношений и эмоционального общения в китайской культуре. В данном контексте алкоголь становится посредником для передачи эмоций и дружбы, символизируя некую гармонию и глубокую эмоциональную связь между двумя людьми.

Таким образом, эта метафора не ограничивается только буквальным значением «алкоголь». Через этот символ она передает искренность, резонанс и бесконечное общение в межличностных отношениях, что придает пословице глубокий эмоциональный и культурный смысл.

В российской культуре «дружба» обычно ассоциируется с глубокими эмоциональными связями, тогда как в контексте культуры России алкоголь чаще является символом встреч и общения. Поэтому при переводе эту идею можно адаптировать в форму, подобную: «С другом каждый момент — это ценность, и ни одна встреча не может быть слишком долгой», что ближе отражает уважение к дружбе и времени в российской культуре.

А также «Учителя только открывают двери, дальше вы идете сами» (Аргументы и факты, 12.07.2022)—это китайская пословица с глубоким метафорическим значением. Буквальный перевод: учитель ведет ученика к порогу, но в конце концов успех и достижения ученика зависят от его собственных усилий. Эта метафора передает основную идею: хотя наставник может предоставить ученику руководство и вдохновение, в конечном итоге успех и прогресс зависят от усилий, настойчивости и таланта самого человека.

В этой метафоре «учителя только открывают двери» символизирует внешнюю помощь и наставничество, представляя передачу знаний, опыта и направлений, тогда как «дальше вы идете сами» подчеркивает личную ответственность и инициативу. Она говорит о том, что независимо от того, насколько велика поддержка и ресурсы извне, достижения зависят от того, как человек будет их практиковать, трудиться, учиться и преодолевать трудности.

Эту метафору можно также интерпретировать как призыв к личному развитию, напоминая людям, что, даже получив первоначальное руководство и помощь, истинный прорыв и успех все равно требуют постоянных усилий. В более широком контексте она отражает баланс между уважением к «учительскому пути» и «личным усилием», что является важной частью китайской культуры, которая высоко ценит личные усилия и самосовершенствование.

В российской культуре также существует уважение к ремесленному мастерству и профессиональным способностям, что выражается, например, в выражении «мастер своего дела». Поэтому перевод этой пословицы может быть таким: «В каждой профессии есть свои мастера, и каждая из них ценна по-своему». Хотя структура языка может отличаться, основная идея — уважение к разным профессиям и восхищение профессиональными навыками — схожа в обеих культурах.

Анализируя китайские классические пословицы в контексте российских медиа, можно заметить, что при переводе и интерпретации этих пословиц в российских источниках сталкиваются с трудностями, связанными с культурными различиями в восприятии и передаче метафор. Успешный перевод требует не только точных языковых навыков, но и глубокого понимания культурного контекста, чтобы, передавая исходное значение, создать резонанс у читателей целевой культуры. Только через тщательную культурную адаптацию и преобразование метафор, эти пословицы могут быть правильно и значимо переданы в другой культуре.

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TECHNICAL SCIENCES

PARTICIPATION OF AGGREGATORS IN ELECTRICITY MARKETS OF LOCAL ELECTRICITY SYSTEM

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Abstract

The local electricity system is a decentralized network. To achieve effective interaction between suppliers and consumers in the operation of local systems in electricity markets, a load aggregator is needed. The goal of the aggregator is to maximize its profit in the day-ahead energy market. The article examines the features of the participation of load aggregators in day-ahead electricity markets and presents an analysis of the aggregator's operation with forecasted load schedules when applying different demand response programs. The daily load schedule and 4 load change strategies (Load Curtailment, Load Shifting, Flexible Load Shape, Energy Arbitrage, Utilizing Onsite Generation, Utilizing ES System) for a local electricity system consisting of a centralized grid, an energy storage system, and a solar generator are considered. An analysis of the impact of different load change strategies on the total daily cost of electricity showed that all strategies will lead to a decrease in cost. The best results were shown by Load Curtailment strategies and Energy Arbitrage.

Keywords: local electricity system, aggregator, electricity market, demand response.

The integration of distributed energy resources and new technological resources into the existing energy system and energy markets poses a number of challenges, as operators usually do not have adequate monitoring or control mechanisms for low-voltage networks.

Demand response (DR) is a mechanism that allows electricity consumers to adjust their consumption in response to changes in electricity prices or to signals from the electricity grid operator. The purpose of this adjustment is to ensure a balance between supply and demand in the electricity grid, which can help reduce the need for expensive and polluting peaking power plants and improve the reliability and efficiency of the electricity system [1].

An aggregator is an important link in dispatching, as it manages the capacity of distributed facilities, consumption, generation, and storage of energy. For market participants, this provides an opportunity to generate additional revenues, and for the transmission system operator, more balancing capacity and a simplified dispatching structure.

Aggregators that are designed to work with specific distributed energy technologies usually do not participate in the same markets. Aggregators that operate and are defined in the context of renewable energy, such as wind turbine or small solar power plant owners, sell electricity in long-term bilateral contract markets or short-term markets. RES are inflexible sources of electricity, as they depend on the stochasticity of wind and sun, so they cannot be used as providers of flexibility

in balancing markets. Distributed storage or electric vehicles require the operation of an aggregator operating in short-term markets or offering its flexibility in balancing markets [1-14].

The following general models of aggregation implementation can be distinguished [2, 3]:

1. Supplier/aggregator: one business entity provides work in different markets, suppliers simultaneously provide electricity supply and aggregation services to ensure additional flexibility.

2. Independent aggregator: the consumer uses the services of two market entities, where the supplier provides electricity supply, the aggregator separately provides system flexibility.

Two groups of such models can also be distinguished [4]:

- Without balance responsibility: the aggregator is not responsible for the balance and is not obliged to send day-ahead plans to the system operator.

- With balance responsibility: the aggregator must be the responsible party, and it is obliged to send day-ahead plans to the system operator. In this case, services can be provided without imbalance correction. The aggregator does not compensate the supplier for the imbalance caused. Thus, it is exempted from payments for imbalance. Aggregation model with imbalance correction. In this case, the aggregator is responsible for the imbalance caused by the supplier and compensates for it.

The advantages of the supplier/aggregator models are easy integration into the current market model and balancing scheme with minimal regulatory changes.

On the other hand, markets with a small number of retail companies will not experience significant changes when it comes to increasing liquidity and competitiveness. The main part of the revenues for such companies will still come from energy supply.

The advantages of the independent aggregator model for small markets are increased market competition and the development of new business models in terms of technologies and services. Specialized companies for aggregation and flexibility of distributed energy resources will also appear, which can lead to more efficient operation of the system and the market. The main disadvantage is the need for a comprehensive change in legislation and the market model.

The main advantage of an independent aggregator, which is not responsible for imbalances, is the simplic-

ity and low costs of entering the market as a new participant, but, on the other hand, it complicates the balancing scheme, which can lead to economic losses for some market participants.

An independent aggregator with responsibility for imbalance but without its correction can also be quite simple to implement. However, if the aggregator has to pay the system operator for the imbalance it causes, it will have no economic motivation to enter the market, which makes this model unstable.

An independent aggregator with balance responsibility and imbalance correction, on the contrary, has an economic motivation to enter the market, but the main disadvantage of such an aggregator model is the calculation of compensation costs between the aggregator and the supplier. The question also arises as to how imbalances will be settled if the aggregator and the supplier are in two different balancing groups.

A schematic distribution of aggregation models is shown in Figure 1 [4].

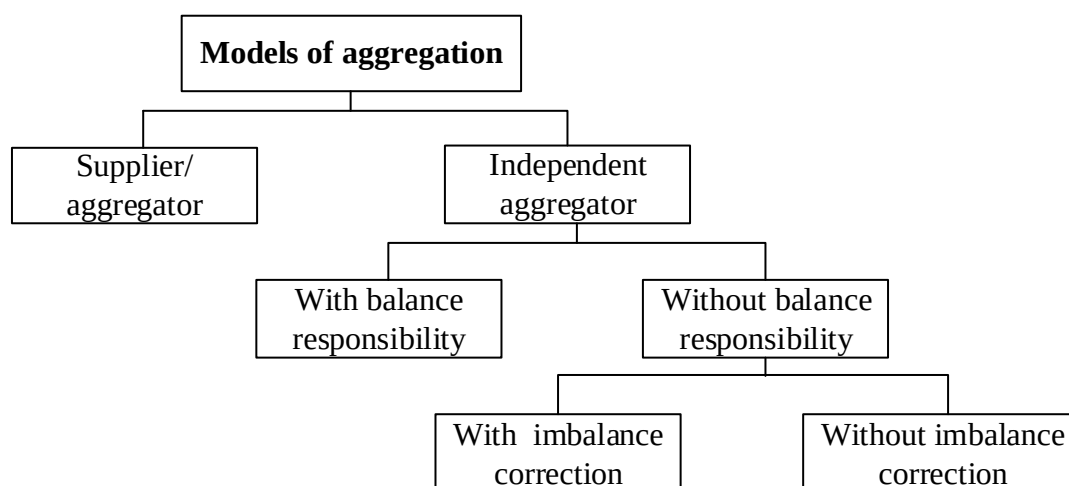


Figure 1. Possible models for implementing aggregation

The wide range of DRG technologies leads to a wide range of definitions of aggregators (Fig. 1). When aggregators are defined in the context of renewable energy generation (RES), such as small photovoltaics or wind turbines, they sell their electricity on long-term markets or on short-term ones. Since renewables are inherently inflexible (dependent on wind and sun), they are not used as flexibility providers in balancing markets or as flexibility sinks in intraday markets. Distributed energy storage, stationary DR or electric vehicles (EVs) require an aggregator that can efficiently buy/sell

energy on short-term markets or offer its flexibility on balancing markets as an ancillary service. Traditional suppliers buy electricity from their inflexible customers on long-term markets. If consumers C integrate demand response, generation or storage into their technologies, they become active consumers (AC). Such consumers have the ability to feed power into the grid and respond to grid/market signals, so they also need an aggregator that can offer such flexibility for energy exchange [4].

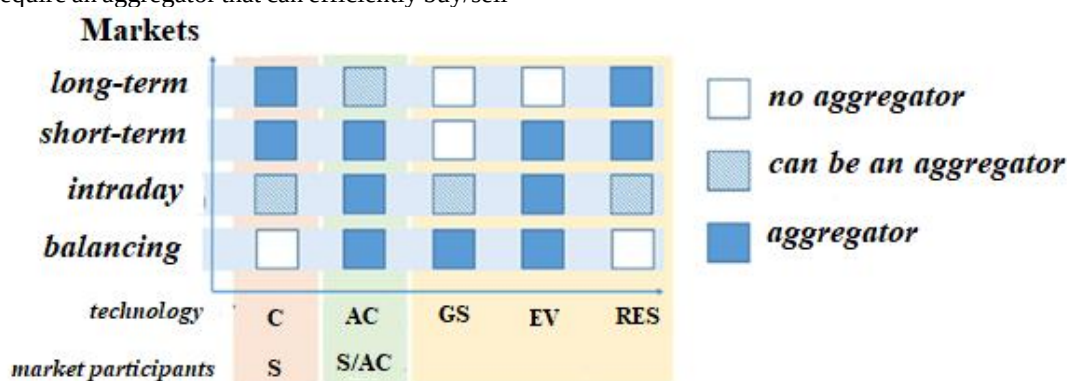


Figure 2. Aggregators in electricity markets

Demand-side management of electricity is usually a shift of consumption from peak to off-peak hours. In turn, energy efficiency is a gradual reduction in electricity consumption, which is achieved by introducing more efficient and economical equipment and gradually abandoning less efficient equipment without reducing functionality. Energy efficiency measures depending on the hours of use of energy-efficient equipment can reduce peak consumption. In turn, demand management can affect total electricity consumption. Although in general demand management does not have a significant impact on total consumption in terms of the day, some demand management programs can even increase consumption during off-peak hours and in some cases increase total electricity consumption. In this case, the increase in consumption must be justified from an economic point of view by reducing the cost of off-peak electricity or reducing fuel costs. In European markets, joint optimization of demand-side management and energy efficiency programs for maximum combined effect is widespread [5, 6]. Suppliers have the ability to act as load aggregators, organize their own demand management programs, and encourage independent aggregators to participate in their own programs.

The purpose of the article is to consider the features of the participation of load aggregators in day-ahead electricity markets and analyze the operation of the aggregator with forecasted load schedules when applying various demand response programs.

The essence of dynamic pricing is to offer monetary benefits to consumers (using the aggregator) for redistributing their load consumption and balancing demand in the electricity network. DR with the aggregator enabled should guarantee a reduction in the total cost of consumption by shifting the load of consumers taking into account the preferences of consumers.

For example, consumers report their load characteristics to the aggregator the day before consumption, and prices are calculated one day-ahead.

Aggregators need to forecast mandatory prices to determine energy consumption for the current time interval and future time intervals. The overall goal is to develop stable and coordinated strategies for dynamic pricing and demand response in electricity networks.

The interaction between the aggregator and the consumer can be divided into the following types:

- Direct load control – the traditional demand management method, according to which the load is controlled by the aggregator at all times, but the consumer is not rewarded at all.

- Price-based control. Currently, many aggregators provide their consumers with manual or automatic price-based programs. With this strategy, the consumer can be rewarded in many different ways, for example, the consumer will receive a fixed price for reducing the load. On the other hand, most aggregators offer a dynamic pricing mechanism, and therefore the consumer will be rewarded with a price based on the real-time electricity market.

- An incentive-based pricing mechanism allows consumers to directly interact with the energy market by betting against having their electricity disconnected.

Similarly, contracts between consumers and the aggregator can be bilateral or unilateral. If it is a bilateral contract, then it is an agreement in which the aggregator promises to pay an incentive to the consumer, and in return, the consumer promises to disconnect or regulate the shared loads to reduce the required consumption. However, if it is a unilateral contract, then only the aggregator promises to pay the incentive to the consumer if he disconnects or regulates his load. This means that the consumer does not control the load, and the aggregator must pay the incentive to the consumer if he disconnects the load.

Consider a generalized model of a local electricity system load aggregator with all possible demand response options for day-ahead market participation. Six load shifting strategies [7-16]:

- 1) Load Curtailment (LC). The LC strategy reduces the total electricity consumption in the scheduled DR program without shifting the load to any other time period.

- 2) Load Shifting (LS). In the LS strategy, customers change their electricity consumption schedule to other hours. For example, a customer may postpone the operation of their appliances to later hours of the day, or an industrial enterprise may shift the batch production process to other hours of the day or other days of the week.

- 3) Flexible Load Shape (FLS) is an advanced level that controls the overall shape of load demand through system scheduling.

- 4) Energy Arbitrage (EA) is a DSM strategy that is achieved by saving energy during periods of lower energy costs versus periods of higher energy costs. Energy arbitrage is mainly achieved through energy storage devices such as batteries, supercapacitors and electric vehicles.

- 5) Utilizing Onsite Generation (OG): In the OG strategy, customers reduce their load by switching on a local or backup generator to supply some or all of their own electricity loads. Although participants may experience a minor interruption in their electricity consumption, their net load will be reduced in the DR program. Therefore, using off-site generation is equivalent to reducing the customer's load from the perspective of the power system, although on-site generation may have its own technical limitations for the customer to participate in DR.

- 6) Utilizing ES System (ES). In the ES system strategy, customers use their ES system to supply some or all of their electricity needs during the DR program. The ES can be a large modular storage device or an aggregated capacity of small distributed storage systems. By using ES, the net load of DR participants will be reduced as ES is discharged and will increase as ES is accrued in energy markets.

The considered load-shifting strategies help aggregators to coordinate local electricity systems in a more comprehensive way. Aggregators use the monitoring, measurement and verification processes that are necessary for the implementation of response programs in electricity markets.

The goal of the aggregator is to maximize its profit (total revenue minus costs) in the day-ahead energy

market. The aggregator makes a profit by offering (selling) a demand response strategy in the energy market and paying the response program participants for hourly/daily load changes. The incentive for aggregation is the difference between the prices of the response

$$\sum_{t \in N_T} \left[\rho_t (LR_t^{LC} + LR_t^{LS} + LR_t^{FLS} + LR_t^{EA} + LR_t^{OG} + LR_t^{EC}) - (CLR_t^{LC} + CLR_t^{LS} + CLR_t^{FLS} + CLR_t^{EA} + CLR_t^{OG} + CLR_t^{EC}) \right] \rightarrow \max,$$

where N_T – the time range of the next day, equal to 24, ρ_t – the market price, LR – the load change according to the CLR strategy, CLR – the cost of this change.

The first part in the objective function is the revenue from the sale of the combined volumes of the six load reduction strategies, and the second part are the costs of paying contract customers for load reduction.

Consider the daily load schedule and 4 load change strategies (Fig. 3-4) for a local electricity system consisting of a grid, an energy storage system, and a solar generator. Strategy 5 has a similar schedule to

programs in contracts with consumers and the hourly market prices of electricity.

The objective function for the aggregator's self-scheduling is maximized as follows, taking into account the 6 strategies considered above:

strategy 1, the consumer decides whether to cover the load reduction with his own needs. Strategy 6 is similar in strategy to 4 for the system under consideration, the consumer's battery can be charged from the local network at low prices during the day, and discharged for his own needs at night. Therefore, it was chosen as an example of the application of the first four considered strategies.

Figure 3 b shows a graph of the predicted value of the cost of electricity per hour for the daily schedule (Fig. 3 a) and offered by the aggregator, taking into account the limitations of the application of strategy 1 (LC) and the consumer's ability to change the load.

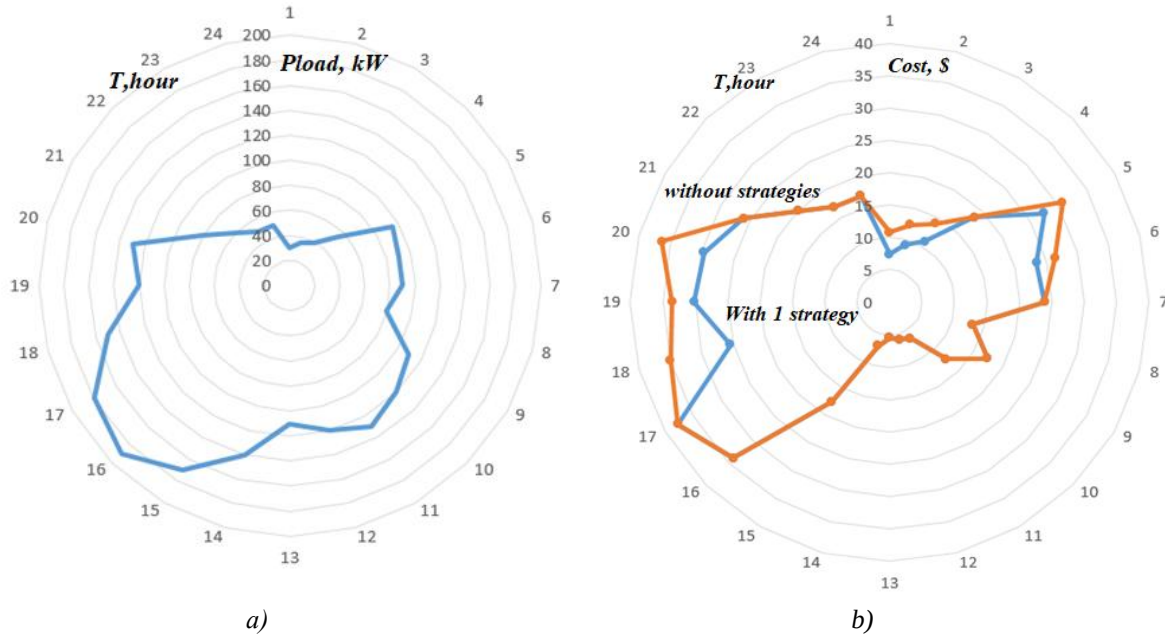


Figure 3 Research results: daily power schedule (a), cost schedule (b)

Similarly, Figure 2 shows the application of strategies 2-4 (LS, FLS, EA).

The aggregator offers consumers 4 load-shifting options, based on four different load-shedding strategies, and seeks to maximize its day-ahead profit

through price-based planning for forecasted load schedules.

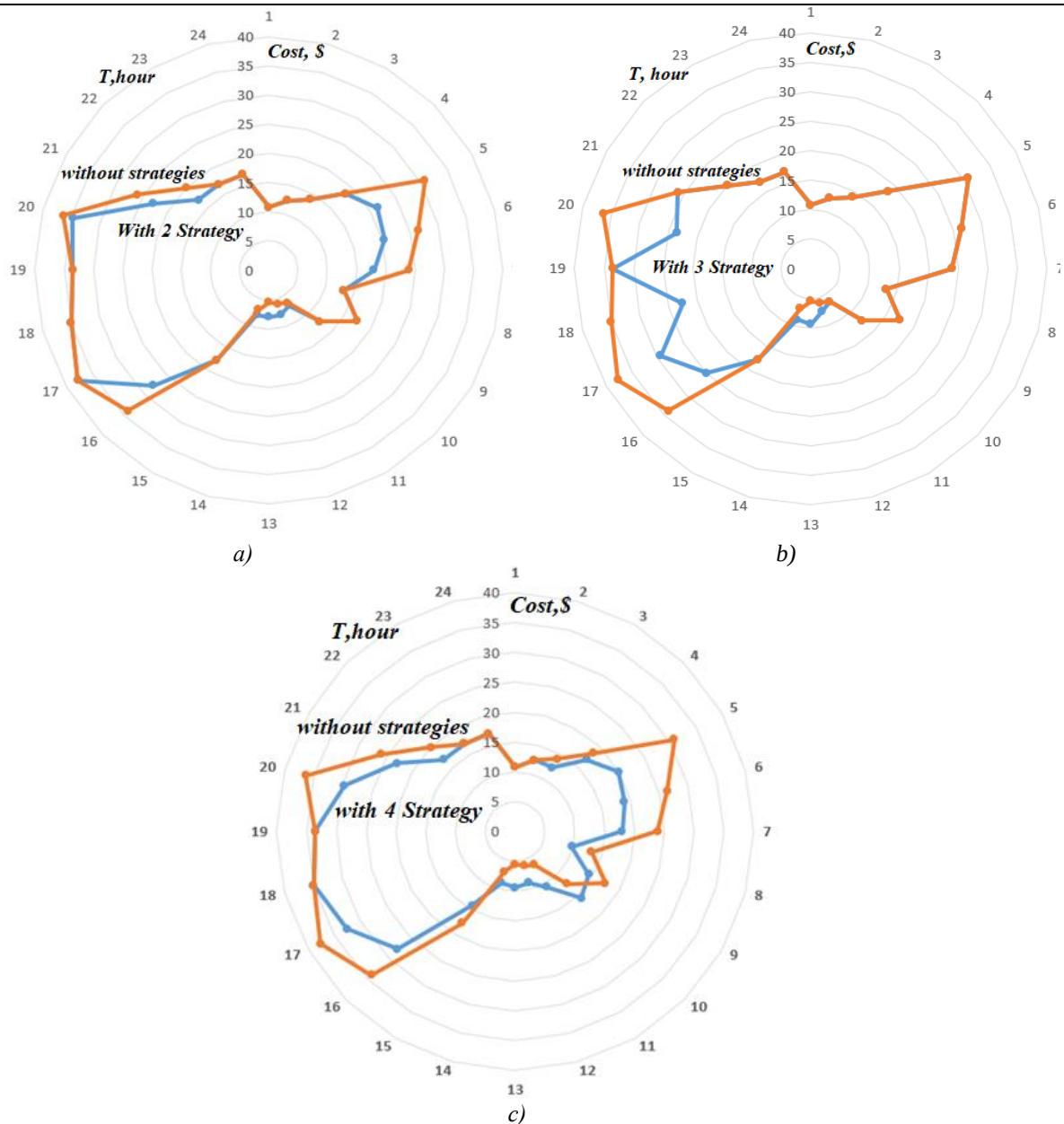


Figure 4 Research results

Table 1 shows the indicators obtained when modeling the operation of the aggregator. When calculating the cost, values were taken from sources [17].

The best results are achieved when reducing the load. But in reality this is achieved by the fact that the

consumer consumed less. With the same consumer power, energy arbitrage is the best for the considered case.

Table1.

Research results				
	Average power, kW	Maximum power, kW	Minimum power, kW	Total cost per day \$
Without DR	100	190	30	478
LS	95	190	20	443
LC	100	190	30	444
FLS	100	180	30	450
EA	100	190	30	434

Conclusions.

Aggregation of distributed energy resources is a necessity for an energy-efficient and ecological energy

system. Using the DR program provides benefits to both consumers and the grid.

The features of the participation of load aggregators in day-ahead electricity markets are considered.

The aggregator controls the load of consumers, developing a control and monitoring strategy to maximize its own income, minimize the supplier's costs and provide incentives for consumers.

The work of the aggregator with forecasted load schedules when applying various demand response programs is analyzed.

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