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**THE EFFECT OF HEMIC HYPOXIA THAT OCCURRED IN RATS WITH NITRITE-INDUCED DEMENTIA ON THE DYNAMICS OF BIOCHEMICAL INDICATORS OF ENERGY METABOLISM IN BRAINS****Pavlova O.O.***d.t.s., prof.*

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**Abstract.** *Have been considered the role of hemic hypoxia, which arose against the background of nitrite-induced dementia of the Alzheimer type in rats on the dynamics in biochemical indicators of energy metabolism, the degree of hypoxia, the content of acetylcholine in the brain tissue homogenate in comparison to the control, where it was found: a decrease in the synthesis and transport of acetylcholine, the intensity of energy exchange, an integral indicator of the decrease in the level of which is the ATP content. The level of cholinodeficiency, hypoxia, and tissue energy supply (ATP) was almost the same between the Nitr-14 and Nitr-28 groups, but the level of cardiolipin in brain homogenates decreased proportionally with increasing duration of sodium nitrite administration.*

**Keywords:** *nitrite-induced dementia Alzheimer type, brain tissue homogenate, energy metabolism, cholinodeficiency*

Alzheimer's disease is a multifactorial progressive neurodegenerative disease characterized by a violation of protein conformation with subsequent protein aggregation and loss of brain neurons [1,2]. An important role in its progression is played by cerebrovascular and cardiovascular diseases, which cause brain hypoxia [3]. It is known that nerve cells of the brain are very sensitive to hypoxia and energy deficit [4]. In mitochondria, as the main "synthesizers" of ATP, under the influence of hypoxia during the transfer of electrons from the respiratory chain, reactive oxygen species (ROS) are formed due to an excess of which damage to cells and tissues is possible [5,6]. Thus, the issue of the dynamics of changes in biochemical indicators of energy metabolism, and the degree of hypoxia that occurs against the background of nitrite-induced dementia is an actual link of pathogenesis and requires further clarification.

The aim of the study was to determine the effect of hemic hypoxia that occurred in rats with nitrite-induced dementia of the Alzheimer type on the dynamics of biochemical indicators of energy metabolism, the degree of hypoxia, and the content of acetylcholine in brain homogenates.

The study involved 24 male rats from the WAG population, weighing between 180-230g. They were divided into 3 groups, each comprising of 8 rats. The experiment utilized a non-transgenic nitrite-induced model to simulate dementia of the Alzheimer type. The control group (group C) received intraperitoneal injections of 0.5 ml of 0.9% aqueous sodium chloride solution for 14 and 28 days. Nitrite-induced dementia was modeled by administering an aqueous solution of sodium nitrite (Nitr) at a dose of 50 mg/kg per rat daily. Mitochondria were isolated from the brain using the method of differential centrifugation. Separation of lipids into

fractions was carried out by the method of thin-layer chromatography on silica gel plates Silufol (Czech Republic)[7]. To identify the lipids, we exposed them to iodine vapors and compared them to a standard. To determine the cardiolipin content (nmol/mg protein), we used Bartlett G.'s method. We measured the acetylcholine (AC) content ( $\mu\text{g/g}$ ) and ATP ( $\mu\text{mol/g}$ ) content in brain homogenates using spectrophotometric methods. We evaluated the normality of the sample distribution using the Shapiro-Wilk test and used non-parametric tests to compare independent groups of variables based on the results.

**The results of the study and their discussion** In animals with nitrite-induced dementia, there were noticeable changes in the level of ATP in the rat brain tissue compared to the control group. The level of ATP significantly decreased after 14-day (1.2-fold) and 28-day (1.4-fold) administration of nitrite sodium. Additionally, the concentration of cardiolipin, a crucial lipid in mitochondrial membranes that coordinates the work of oxidative complexes in the respiratory chain, decreased in all studied groups. The most significant decrease was observed in the rats of the Nitr-28 group, with a decrease of 2.3 times (Table 1).

**Table 1. Biochemical indicators of energy metabolism, degree of hypoxia, acetylcholine content in rats with nitrite-induced dementia of the Alzheimer type**

Indicators	Control group (C)	Group Nitr-14	Group Nitr-28	Група Nit-28
AC, $\mu\text{g/g}$	2,54 $\pm$ 0,17 (2) *	2,17 $\pm$ 0,07	2,3 $\pm$ 0,03 (2) *	2,17 $\pm$ 0,03
ATP	2,83 $\pm$ 0,01 (1) *	2,3 $\pm$ 0,01 (C) *	2,03 $\pm$ 0,02 (C) *	2,3 $\pm$ 0,01
Cardiolipin nmol/mg protein	51,94 $\pm$ 0,06 (1) *	26,66 $\pm$ 0,1 (C) *	21,84 $\pm$ 0,09 (C) *	26,66 $\pm$ 0,1

The data is displayed as the mean values and standard error of the mean.

\* $p < 0.05$  - indicates that there is a significant difference between the data of the groups (in parentheses), statistical significance (Kruskal-Wallis analysis of variance and Dunn's multiple comparisons test).

The introduction of sodium nitrite resulted in a decrease in the level of acetylcholine in the brains of rats in the Nitr-14 and Nitr-28 groups, as compared to the control group (Table 1). These changes in biochemical parameters were significant after 14 and 28 days of sodium nitrite administration. It is worth noting that the levels of cholinodeficiency, hypoxia, and ATP in the Nitr-14 and Nitr-28 groups were similar. However, there was a decrease in the level of cardiolipin in brain homogenates as the duration of sodium nitrite increased.

**Conclusions.** Based on the experimental data gathered, it has been found that the addition of sodium nitrite plays a crucial role in altering the biochemical indicators of energy metabolism and causing brain hypoxia in rats and is considered to be a relevant link that contributes to the development of Alzheimer's disease.

**CONTENTS****Innovative engineering, technology and industry**

<https://www.proconference.org/index.php/usc/article/view/usc18-01-005> 3

PROSPECTS OF THE USE AND ANALYSIS OF BIOMASS TYPES OF THE POLTAVA REGION AS SOURCES OF ELECTRICAL ENERGY

*Basova Y.O., Levchenko Y.V., Suprovych O.S.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-016> 7

PERSPECTIVES OF THE SOLAR ENERGY DEVELOPMENT AND ITS EFFECT ON THE OPERATION OF ELECTRICAL ENERGY SYSTEMS

*Buslova N., Dmitriyev V.*

**Computer science, cybernetics and automatics**

<https://www.proconference.org/index.php/usc/article/view/usc18-01-029> 12

THE ES\_RFCHD EXPERT SYSTEM FOR THE ANDROID PLATFORM

*Burdaev V.P.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-034> 16

HARTLEY AMPLITUDE MODULATION

*Kokhanov A.B., Startsev V.I., Yemelianov S.V.  
Dereviagin Y.V., Pascu D.G., Barabanjv N. A.*

**Architecture and construction**

<https://www.proconference.org/index.php/usc/article/view/usc18-01-015> 21

PHYSICS OF FLUCTUATIONS IN SPACE-TIME DIMENSIONS OF THE DEVELOPMENT OF URBANIZED TERRITORIES AS ECOLOGIC-URBAN PLANNING SYSTEMS

*Ustinova I.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-022> 28

CONSRUCTION OF INCLUSIVE URBAN SPACE BY MEANS OF LANDSCAPE ARCHITECTURE

*Ustinova I., Matsokha A.*

**Physics and mathematics**

<https://www.proconference.org/index.php/usc/article/view/usc18-01-010> 34

ASPECTS OF MULTI-CRITERION SELECTION OF ADMINISTRATIVE DECISIONS

*Mormul M. F., Shchyotov D. M.  
Shchyotov O. M., Rudyanova T. M.*

**Chemistry and pharmaceuticals**

<https://www.proconference.org/index.php/usc/article/view/usc18-01-003> 41

ABOUT THE POSSIBILITY OF USING THE RED SLUDGE IN THE SYNTHESIS OF INORGANIC PIGMENTS COFFE-BROWN COLOUR

*Ivanyuk E.V., Suprunchuk V.I.*

**Medicine and health care**

<https://www.proconference.org/index.php/usc/article/view/usc18-01-011> 45

CORRELATION OF CERVICAL TEETH INJURIES WITH DENTIN HYPERAESTHESIA IN YOUNG PEOPLE

*Zabolotna I.I., Bogdanova T.L.  
Komlev A.A., Yurina L.M.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-026> 50

IMPLEMENTATION OF STATE SOCIAL AND HYGIENE MONITORING – THE MAIN TASK OF THE CENTERS FOR DISEASE CONTROL AND PREVENTION

*Zaitsev V.V.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-027> 53

THE EFFECT OF HEMIC HYPOXIA THAT OCCURRED IN RATS WITH NITRITE-INDUCED DEMENTIA ON THE DYNAMICS OF BIOCHEMICAL INDICATORS OF ENERGY METABOLISM IN BRAINS

*Pavlova O.O., Lukyanova Y.M.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-032> 56

MOTIVATION FOR TRAINING FUTURE PHARMACISTS

*Chornenka Zh.*

**Agriculture, forestry, fishery and water management**

<https://www.proconference.org/index.php/usc/article/view/usc18-01-012> 58

PROBLEMS OF PLANTATION GROWING OF ST. JOHN'S WORT (*Hypericum perforatum* L.)

*Pospelov S.V., Pospelova G.D., Semenko M.V.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-017> 61

KHARKIV SCHOOL OF FOREST TYPOLOGY, ITS SIGNIFICANCE IN THE MODERN EDUCATIONAL PROCESS

*Pozniakova S.I.*

**Economy and trade**

<https://www.proconference.org/index.php/usc/article/view/usc18-01-018> 66

UKRAINIAN EDUCATIONAL INSTITUTIONS ABROAD AND THEIR INFLUENCE ON THE DEVELOPMENT OF THE ACCOUNTING SPHERE IN THE SYSTEM OF UKRAINIAN COOPERATION OF EASTERN HALICHINA IN THE FIRST HALF OF THE 20TH CENTURY: THE TRANSNATIONAL DIMENSION

*Lemishovska O.S.*

**Management and marketing**

<https://www.proconference.org/index.php/usc/article/view/usc18-01-025> 71

METRICS AND INDICATORS IN ADAPTATION PROCESS OF EMPLOYEES AT SOCIAL ENTERPRISES

*Yurchenko H.M.*

**Education and pedagogy**

<https://www.proconference.org/index.php/usc/article/view/usc18-01-006> 76

THE STRUCTURE OF ARTISTIC ABILITIES OF YOUNGER STUDENTS: MOTIVATIONAL COMPONENT

*Ren Wei*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-013> 79

THE ROLE OF SCANNING FOR TEACHING READING TECHNICAL UNIVERSITY STUDENTS

*Shalova N.S., Khymai N.I., Zarivna O.T.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-020> 82

FORMATION OF THE COMPETENCE OF PEDAGOGICAL PARTNERSHIP BETWEEN TEACHERS AND PARENTS OF STUDENTS ON COURSES OF IMPROVING PEDAGOGICAL QUALIFICATIONS

*Shopina M.O., Yakunin Y.Y.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-023> 85

CRITERIA AND PERFORMANCE INDICATORS OF THE ORGANIZATION OF SELF-EDUCATION ACTIVITIES IN THE INFORMATION AND EDUCATIONAL ENVIRONMENT OF MEDICAL INSTITUTIONS OF HIGHER EDUCATION

*Barjadze R.V.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-030> 88

MASS-MEDIA AS A FACTOR OF FORMING NEW COMMON REALITY

*Samoilenko O. V., Kornieieva O. M.*



<https://www.proconference.org/index.php/usc/article/view/usc18-01-031> 90

SCOPE AND FORMS OF AESTHETIC EDUCATION OF STUDENTS  
IN THE SYSTEM OF OUT-OF-SCHOOL EDUCATION INSTITUTIONS  
OF UKRAINE

*Varnavska L.I., Viktorova M.V., Serhieieva V. M.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-033> 96

TEACHING FOREIGN LANGUAGE TO FUTURE AGRONOMISTS:  
POINTS TO CONSIDER

*Holovko I.O.*

**Physical education and sport**

<https://www.proconference.org/index.php/usc/article/view/usc18-01-002> 101

THE EFFECT OF SWIMMING ON THE ABILITY TO RESIST HYPOXIA  
IN CHILDREN AGED 11-15 YEARS WITH THE CONSEQUENCES OF  
BRONCHOPULMONARY DISEASES

*Salnykova S.V., Puzdymir M.I., Holovkina V.V.*

**Philology, linguistics and literary studies**

<https://www.proconference.org/index.php/usc/article/view/usc18-01-001> 106

THE RELEVANCE OF TEACHING THE UKRAINIAN LANGUAGE  
AS A FOREIGN LANGUAGE UNDER THE CONDITIONS OF  
MARITAL STATE

*Vekua O.V.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-008> 109

A LOOK AT THE HISTORY OF PHRASEOLOGY

*Halazdra S.I., Pidvysotska G.V.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-019> 112

THE FUNCTION OF ORNITHONYMS IN “TALES OF THE PECULIAR”  
BY RANSOM RIGGS

*Aleksenko V. F.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-024> 115

LINGUAL AND PHILOSOPHICAL FUNDAMENTALS OF THE  
CATEGORY OF REFERENCE (BASED ON ENGLISH, UKRAINIAN  
AND RUSSIAN)

*Terekhova S.I.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-028> 119

ON INTERPRETING THE USE OF ZOONYMS IN FICTION

*Slobodiak S.I.*

**History**

<https://www.proconference.org/index.php/usc/article/view/usc18-01-004>

122

RELIGIOUS POLICY OF THE RUSSIAN EMPIRE IN GALICIA  
ON THE EVE OF THE FIRST WORLD WAR

*Baran. I. V.*

**Art history and culture**

<https://www.proconference.org/index.php/usc/article/view/usc18-01-007>

125

FORMATION OF CULTURAL AND SPIRITUAL VALUES IN  
THE MODERN YOUTH ENVIRONMENT

*Ryzheva N.A., Marynchenko H.M.*

<https://www.proconference.org/index.php/usc/article/view/usc18-01-014>

129

PAINTING PORTRAIT OF MYKOLA KOSTOMAROV WITH  
THE BRUSH OF IVAN TRUSH: PROVENANCE, ATTRIBUTION  
AND EXPERTISE

*Yamash Y. V.*

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