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Inhaber: Marina Kisiliuk

Tel.: + 49 51519191533

Fax.: + 49 5151 919 2560

Email: info@dwherold.de

Internet: www.dwherold.de

Chefredakteur/Editor-in-chief:

Marina Kisiliuk

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Theraphy, Belarus
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n.kanunnikova@grsu.by

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Giedrius.Vanagas@lsmuni.lt

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Neurofiziologija, Lithuania
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meyramow@mail.ru

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Ais.shahlol@sebhau.edu.ly

Edmundas Kadusevicius, MD, PharmD, PhD, Prof.
Pharmacology, Lithuania
Edmundas.Kadusevicius@lsmuni.lt

Ivo Grabchev, Prof., PhD.
Chemistry, Bulgaria
i.grabchev@chem.uni-sofia.bg
grabchev@mail.bg

Mariyana Ivanova Lyubenova, Prof., PhD.
Ecology, Bulgaria
ryann@abv.bg
ryana_1@yahoo.com

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Biologv. Bulgaria
tmarinova@yahoo.com

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Biology. Bulgaria
evgueni_ananiev@yahoo.com

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Biology, Bulgaria
mitovplamen@gmail.com

Atanas Dimov Arnaudov, Ph.D.
Physiology, Bulgaria
arny87@yahoo.co.uk

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Ecology, Bulgaria
anivel@abv.bg

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Biology, Turkey
osdemir@cu.edu.tr

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Neurogenetics, India
Indijharnaray@gmail.com

Marián Halás doc. RNDr, Ph.D.
Human geography, Czech
marian.halas@upol.cz

Ayfer Pazarbasi Prof.Dr.
Biology, Turkey
payfer@cu.edu.tr

Tusharkanti Ghosh Prof.
Physiology, India
tusharkantighosh53@yahoo.in

Khudaverdi Gambarov Gambarov, Prof.
Microbiology, Azerbaijan
khuda1949@mail.ru

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hrovshan@hotmail.com

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Samuel M.Johnson, Prof.Dr.phil.
Theology, Wells, Maine, USA
djtjohnson@earthlink.net

Satanovsky Leon MD/PhD.
Perio-odontologie, Israel
satleonid@gmail.com

Lists of references are given according to the Vancouver style

**Galagdina A.A.,
Dmytrenko R.R.,
Bambuliak A.V.**

Department of Surgical and Pediatric Dentistry, Higher State Educational Establishment of Ukraine "Bukovinian State Medical University", Chernivtsi, Ukraine

DIAGNOSTICS OF ISCHEMIC-REPERFUSION DAMAGE OF THE BRAIN IN RATS AFFLICTED WITH DIABETES MELLITUS

Abstract. *Diagnosics of ischemic-reperfusion damage of the brain in rats in case of diabetes mellitus is made under conditions of ischemia-reperfusion of the brain against the ground of three-month diabetes mellitus by collagenolysis. Bilateral carotid ischemia-reperfusion against the ground of three-month diabetes mellitus inhibits collagenolysis on the frontal cortex and hippocampus of the brain in rats. Application of the method suggested has enabled to determine the criteria to assess the development of ischemic-reperfusion damage of the brain with diabetes mellitus in rats which will promote further studies concerning the cerebral tissue state under conditions of comorbid pathology.*

Key words: *collagenolysis, diabetes mellitus, ischemia-reperfusion.*

Introduction. Cerebrovascular pathology is known to be one of the most topical issues of modern medicine which is caused by an increased occurrence of vascular diseases. Ischemic damages of the brain attract special attention. They constitute more than 2/3 of all the cerebrovascular diseases. Therefore, the process of cerebral ischemia is much determinable concerning the level of health and life span [1]. Acute stroke remains one of the leading problems in modern medicine, first of all due to high disability and mortality of the adult population of the planet [2]. Nowadays the existence of cause-and-effect relations between diabetes mellitus available and a high risk of cerebral circulation disorders including dyscirculatory encephalopathy and vascular dementia does not give rise to any doubt [3]. According to the WHO definition diabetes mellitus has become non-infectious epidemic. Today there are 240 million people on the globe suffering from diabetes mellitus, and till 2030 this number will increase to 330 or probably to 500 million of people. In 01.01.2007 in Ukraine 1048375 diabetic patients were registered, which was 2242,6 cases per 100 000 of population. Due to this fact the issues of increased occurrence of chronic complications of diabetes mellitus, investigation of the mechanism of its development, diagnostic peculiarities and elaboration of effective means of treatment and prevention are of great importance

[4,5,6].

Objective: to improve the diagnostics of cerebral damage in case of bilateral carotid ischemia-reperfusion against the ground of three-month diabetes mellitus by collagenolysis in the frontal cortex and hippocampus of rats.

Materials and methods. Diabetes mellitus was simulated by means of a single intraperitoneal injection of streptozotocin (Sigma, Aldrich) in the dose of 60 mg/kg given to male rats at the age of two months. Duration of diabetes was three months. To make bilateral carotid ischemia-reperfusion both general carotid arteries were isolated under intraperitoneal narcosis (calipsol, 75 mg/kg) by means of the anterior cervical access. The arteries were clipped for 20 minutes, afterwards the clips were removed for reperfusion during 1 hours. The animals were killed by means of decapitation under calipsol narcosis. After fixation of the brain in liquid nitrogen, using the atlas of stereotaxic coordinates, the cortex of the frontal lobe and CA1, CA2 and CA3 fields of the hippocampus were taken for examination. Tissue proteolytic activity was studied homogenates of the structures indicated.

The study was conducted on 13 male non-linear rats of four groups: control rats, rats after bilateral carotid ischemia-reperfusion, rats with diabetes mellitus and rats with diabetes mellitus exposed to carotid ischemia-reperfusion.

Results and discussion. The peculiarities of stroke are determined by pre-stroke (underlying) condition of the cerebral metabolism, its energy requirements and status and response of the nervous-immune-endocrine system of the body. Among underlying diseases against the ground of which cerebral ischemia develops diabetes mellitus is one of the most spread. Diabetes mellitus increases the risk of development of ischemic lesions of the brain in several times. Such complications of diabetes mellitus as coma are of special importance, as they result in the development of incomplete global ischemia of the brain with further reperfusion, and which is additional complication of energy disorders of the

nerve cells and glia. In the complex of topical responses occurring in case of ischemia-reperfusion changes in the tissue proteolysis systems play an important role, which is a marker of tissue response to stress. Condition of the tissue proteolysis determines pathogenesis of ischemic-reperfusion changes, degree of cellular damage, adaptation and survival of the afflicted cerebral tissue very much.

To examine proteolytic activity collagenolysis was investigated. The results of the study are presented in Table 1.

The indices of all the structures of the brain studied responded to diabetes mellitus and bilateral carotid ischemia-reperfusion in one

Table 1

Effect of ischemia-reperfusion on the indices of tissue proteolysis in the frontal cortex and different fields of the hippocampus of male rats under conditions of diabetes mellitus (M±T,n=11)

	Group of the study	Collagenolysis (mkg azocol/g of tissue per hour)
Cortex of the frontal lobe	Control	5,10±0,131
	Ischemia-reperfusion	5,70±0,151 P1<0,01
	Diabetes mellitus	6,10±0,533
	Diabetes mellitus and ischemia-reperfusion	3,89±0,549 p2<0,01 p3<0,01
Field CA1	Control	6,06±0,180
	Ischemia-reperfusion	6,58±0,310
	Diabetes mellitus	7,33±0,825
	Diabetes mellitus and ischemia-reperfusion	4,67±0,581 pr<0,05 p3<0,05
Field CA2	Control	5,71 ±0,133
	Ischemia-reperfusion	7,92±0,382 pi<0,001
	Diabetes mellitus	7,76±0,550 Pi<0,01
	Diabetes mellitus and ischemia-reperfusion	5,60±0,573 p2<0,05 pi<0,01
Field CA3	Control	4,86±0,126
	Ischemia-reperfusion	6,63±0,112 pi<0,001
	Diabetes mellitus	7,33±0,642 pi<0,01
	Diabetes mellitus and ischemia-reperfusion	5,04±0,441 p2<0,01 pi <0,01

Notes: difference probability in comparison with: pi - control, p2 - diabetes, p3 – ischemia-reperfusion.

direction or did not respond, thus discordant changes were absent.

A peculiar feature of changes in the tissue proteolysis in response to combination of bilateral carotid ischemia-reperfusion and three-month diabetes mellitus is decreased collagenolysis in all the structures examined.

Conclusion. Diagnostics of ischemic-reperfusion damage of the brain in rats in case of diabetes mellitus is made under conditions of ischemia-reperfusion of the brain against the ground of three-month diabetes mellitus by collagenolysis. Bilateral carotid ischemia-reperfusion against the ground of three-month diabetes mellitus inhibits collagenolysis on the frontal cortex and hippocampus of the brain in rats. Application of the method suggested has enabled to determine the criteria to assess the development of ischemic-reperfusion damage of the brain with diabetes mellitus in rats which will promote further studies concerning the cerebral tissue state under conditions of comorbid pathology.

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