RUSSIAN ACADEMY OF SCIENCES
SCIENTIFIC COUNCIL ON PROBLEMS OF BIOLOGICAL PHYSICS
INSTITUTE OF THEORETICAL AND EXPERIMENTAL BIOPHYSICS
INSTITUTE OF CELL BIOPHYSICS

BIOLOGICAL MOTILITY

Materials of International Symposium

Pushchino • 2016

treatment, which is consistent with our data mentioned above and concerning the mechanisms of ceramide accumulation in unloaded soleus muscle. Taking into account that muscle atrophy in AOS depends on the enhancing of protein degradation or limitation of protein synthesis, and based on the fact that mTOR system is one of the key regulators of intracellular protein synthesis we can assume that ceramide might be involved in the development of muscle disuse atrophy in weightlessness.

References

1. Bryndina I.G., Shalagina M.N., Ovechkin S.V., Ovchinina N.G. [Sphingolipids in skeletal muscles of C57B1/6 mice after short-term simulated microgravity]. Ross. Fiziol. Zh. Im. I.M. Sechenova. 2014.100(11):1280-6. Russian.
2. Mahfouz R., Khoury R., Blachnio-Zabielska A., Turban S. et al. Characterising the inhibitory actions of ceramide upon insulin signaling in different skeletal muscle cell models: a mechanistic insight. PLoS One. 2014. 9 (7):e101865.
3. Nikolova-Karakashian M. (2011) Sphingolipid metabolism, oxidant signaling, and contractile function of skeletal muscle. Antioxidants & Redox Signaling. 15, 2501-2517.

THE INFLUENCE OF 2-BENZAMIDO-2-(2-OXOINDOLIN-3-ILIDEN) ACETIC ACID DERIVATIVE ON RATS' INTEGRATIVE MOTILITY AFTER TRAUMATIC BRAIN INJURY

Yu.S. Bukataru[1], I.I. Zamorskii[1], S.V. Kolesnik[2]

[1]*Bukovinian State Medical University,*
Theatre Square, 2, Chernivtsi, 58002, Ukraine

[2]*National University of Pharmacy,*
Pushkinska str. 53, Kharkiv, 61002, Ukraine

Traumatic brain injury (TBI) is the most difficult and dangerous pathological condition in the structure of injuries. TBI continues to be the main cause of death (up to 60% among injured) and disability of population (25% of survived patients) in the age group of 20–40 years. As a rule main symptoms of closed TBI include the formation of muscle-tonic disorders resulting in disturbances of muscular tone, reflexes and coordination of complex motor acts. Among the neurogenic consequences blood circulatory and respiration disorders usually develop.

During the screening studies of the 24 2-benzamido-2-(2-oxoindolin-3-iliden) acetic acid derivatives an antihypoxic activity of certain compounds under the conditions of acute hypobaric hypoxia was established [3]. Among the studied derivatives the most significant antihypoxic activity was observed when using compound number 15 (ZNM), which suggests the neuroprotective properties of this substance.

The aim of the study was to establish the impact of 2-benzamido-2-(2-oxoindolin-3-iliden) acetic acid derivative ZNM on the course of experimental acute traumatic brain injury by the criteria of motor and exploratory activity, the state of muscle tone and coordination, physical endurance.

The research was conducted on 32 white nonlinear mature male rats weighting 180–200 g, divided into 4 groups (n = 8): the first group was injected

intraperitoneally the substance ZNM at a dose of 15 mg/kg in the form of an aqueous suspension stabilized by polysorbate 80 (Tween 80) prior the TBI of moderate severity modeling; the second group was administered prior the TBI the reference drug mexidol at a dose of 100 mg/kg; the third (control) group was administered an equivalent amount of solvent; the fourth group - intact control (ether anesthesia without TBI). TBI of moderate severity was modeled under the ether anesthesia with a standardized weight-drop device (49.5 g, 0.315 J) inducing a focal blunt injury over the unprotected parietal-occipital head area [2]. Drugs were administered during 3 days before (last injection – 30 min before TBI) and 2 days after TBI. With the help of an open-field test during the acute phase of injury (48 h after TBI modeling) the behavioral and neurological disorders in animals were evaluated by determination of the locomotor activity (number of crossed squares and reaching the central area of the open field), orienteering and exploratory activity (number of stands and examined holes), emotional reactions (number of grooming, defecation and urination acts). Physical endurance was determined in a swimming test with a 10% of body weight load, coordination of movements and muscle tone – by the rod test, rotating at 10 rev/min [1].

Statistical analysis of the results was performed using Statistica 10.0 and Microsoft Excel 2013. Statistical significance was evaluated using parametric Student's t-test (for normal distribution), Mann-Whitney U-test (for non-normal distribution) and angular Fisher transformation. The critical level of significance was accepted with $p \leq 0.05$.

As a result of the research was noted that in the first group of animals (use of substance ZNM on the background TBI) the number of crossed squares decreased by 38.3%, the number of reaching the central area of the open field increased by 11.3%, the number of stands increased by 6.8 % and examined holes – by 9.3%. Indicators of the emotional reactions and their vegetative maintenance decreased by the number of bowel movements and urination by 3.2 times compared to the control pathology group ($r \leq 0.05$). These data suggest the changing of locomotor activity profile of animals with increase of an orienteering and exploratory activity and reduction of emotionality after TBI on the background of treatment with substance ZNM.

In the rotating rod test indicators of muscle tone and coordination in the substance ZNM group and in the group of reference drug mexidol were the same: the number of animals fallen within period of 30 seconds – 2 (25%), 30 s – 1 min – 3 (37.5%), after 1 minute – 3 (37.5%), which is significantly higher than the intact control parameters ($p \leq 0.05$).

Physical endurance by the time of forced swimming with a load in the control pathology group significantly decreased by 30% ($p \leq 0.05$). ZNM drug and mexidol restored this index up to the level of intact animals.

Thus, according to the study results, the 2-benzamido-2-(2-oxoindolin-3-iliden) acetic acid derivative ZNM changes profile of the locomotor activity of animals with increase of an orienteering and exploratory activity and reduction of an emotionality of animals on the model of a closed craniocerebral injury of

moderate severity in the open-field test, increases physical endurance by swimming with the load test and improves coordination in the rotating rod test. The research results indicate a close profile in pharmacological activity of the substance ZNM and reference drug mexidol - specifically cerebroprotective, anxiolytic and sedative action.

References

1. Bures J., Buresova O., Huston J. P. Techniques and basic experiments for the study of brain and behaviour. Amsterdam, N.Y., Elsevier, 1983, 2nd ed. 326 pp.
2. El'skij V. N., Zyablicev S. V. Modelirovanie cherepno-mozgovoj travmy. Donetsk, Novyj mir, 2008. 139 pp.
3. Zamorskii I. I., Bukataru Yu. S., Kolesnik S. V. Activity definizione antihypoxants in derivati del 2-benzammide-2-(2-oksoindolin-3-ilidene)-vinegary acido in acuta ipossia iperbarica. Ital. Sci. Rev. 2016, Vol. 1, N 34, P. 79–83.

AMPK DOES NOT PLAY KEY ROLE IN REGULATION OF THE PPARGC1A GENE EXPRESSION IN HUMAN SKELETAL MUSCLE

A.D. Butkov, E.A. Lysenko, T.F. Vepkhvadze, D.V. Perfilov, D.V. Popov

Laboratory of Exercise Physiology, Institute of Biomedical Problems of Russian Academy of Sciences, 76A Khoroshevskoe Shosse, Moscow, 123007, Russia

The PPARGC1A (PGC-1α) is a principal regulator of mitochondrial biogenesis in skeletal muscle. The expression of *PGC-1α-b* mRNA via the alternative promoter plays a significant part in exercise-dependent expression of *PGC-1α* gene; probably the expression of *PGC-1α-b* mRNA is regulated by CREB1. Acute endurance exercise activates AMPK in skeletal muscle in intensity dependent manner. It is possible to suggest, that AMPK might be involved in mediating stimulus-induced phosphorylation of $CREB1^{Ser133}$ in human skeletal muscle. The purpose of the study was to evaluate a role of AMPK in regulation of *PGC-1α* gene expression via the alternative promoter.

For this goal, we analysed activation of AMPK and *PGC-1α* gene expression in skeletal muscle of amateur endurance-trained athletes (n=9) before and after exercise (45 min, 38% of $\dot{V}O_{2\,max}$), with or without administration of a single dose of acute metformin administration (2 g), well known AMPK activator. Biopsies from the vastus lateralis muscle were taken at baseline and at 2 min, 4 h, and 8 h after exercise in both control and metformin trials.

The phosphorylation level of $AMPK^{Thr172}$ did not change at 2 min after the exercise in either the metformin or placebo trials. However, $ACC^{Ser79/222}$ (the substrate of AMPK, i.e. a endogenous marker of AMPK activity) showed a 2.6-fold ($P < 0.01$) increase in phosphorylation level immediately after exercise in the metformin trial only. But post-exercise expression of *PGC-1α* gene via both the alternative and canonical promoters did not vary between trials. This study does not confirm a role of AMPK in regulation of *PGC-1α* gene expression in endurance-trained human skeletal muscle.