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INVESTIGATION OF INDIVIDUAL PARAMETERS OF CARBOHYDRATE METABOLISM IN THE EXPERIMENTAL MODEL OF VAT WITH SYMPTOMS OF ALZHEIMER'S DISEASE ON THE BACKGROUND OF HYPOTHYROISIS

Seit-Asan Lenara Serverovna
Chirchik State Pedagogical University
E-mail: seitasanlenara@gmail.com

Annotation
The effect of damage to brain structures in the AD model on carbohydrate metabolism testifies in favor of the common pathogenetic mechanisms of AD and DM-2. The presence of cognitive impairment may be accompanied by a change in the central regulation of energy metabolism. Thebasis of this work was the study of individual parameters of carbohydrate metabolism on an experimental model of a neurodegenerative state with symptoms of Alzheimer's disease (AH).

Key words: Alzheimer's disease, diabetes mellitus, thyroid hormones, thyroid gland, hypothyroidism.

Abstract
The influence of damage to brain structures in the AD model on carbohydrate metabolism testifies in favor of the commonality of the pathogenetic mechanisms of AD and DM-2. The presence of cognitive impairment may be accompanied by a change in the central regulation of energy metabolism. The aim of this work was to study individual parameters of carbohydrate metabolism in an experimental model of a neurodegenerative state with symptoms of Alzheimer's disease (MA).

Keywords: Alzheimer's disease, diabetes , thyroid hormones, thyroid gland, hypothyroidism.

The twentieth century was marked by the emergence of many drugs to combat infectious diseases, as a result of which the life expectancy of the population increased significantly. At the same time, a steady increase in the number of non-communicable diseases began to be observed [1]. Epidemics of the XXI century include both metabolic disorders (type 2 diabetes mellitus (type 2 diabetes mellitus), obesity), and Alzheimer's disease(BA). AD is a complex neurodegenerative disease, primarily

characterized by cognitive deficit, and at the pathomorphological level - progressive death of neurons and accumulation of senile plaques and neurofibrillary tangles in as a result of aggregation of β-amyloid. In recent years, numerous evidence of the relationship between AD and metabolic disorders has been accumulated. Disorders of insulin secretion and its signaling pathways are common mechanisms for AD and DM2 and provoke oxidative stress, inflammatoryprocesses and the accumulation of β-amyloid. However, it remains unclear whether AD is the direct cause of carbohydrate metabolism disorders or whether the association of dementia with the development of T2D is due to the combination of AD with classic risk factors for hyperglycemia, such as overweight and age of patients.

Table 1. Study of some biochemical parameters in the blood of animals with MA (M±m), n = 25

Group of animals	Weight of animals, g	Glucose level, mmol / l	Уровень HbA_{1c}, %
IT	250± 8	4,5±0,05	≤ 7
AK	400 ±7	7,0±0,07	≥7
MA	370 ±10	8,0±0,06	≥7

From the table it can be seen that against the background of an increase in the weight of animals, which occurs not only due to a high-calorie diet, but also for a hypothyroid state, there is an increase in the level of glucose and glycated hemoglobin, which is characteristic of metabolic syndrome (obesity) and type 2 diabetes mellitus. The content of lipid fractions also increases, which occurs not only in diabetes, but also in atherosclerotic damage to the vessels of the brain.

In the study, we tried to shape groups of animals in such a way that it was possible to share the contribution of weight gain on the one hand and degenerative brain changes typical of AD on the other. The age of the animals was the same, so the role of this factor was excluded. In our work, HCD led to pronounced metabolic disorders in animals - obesity and hyperglycemia.

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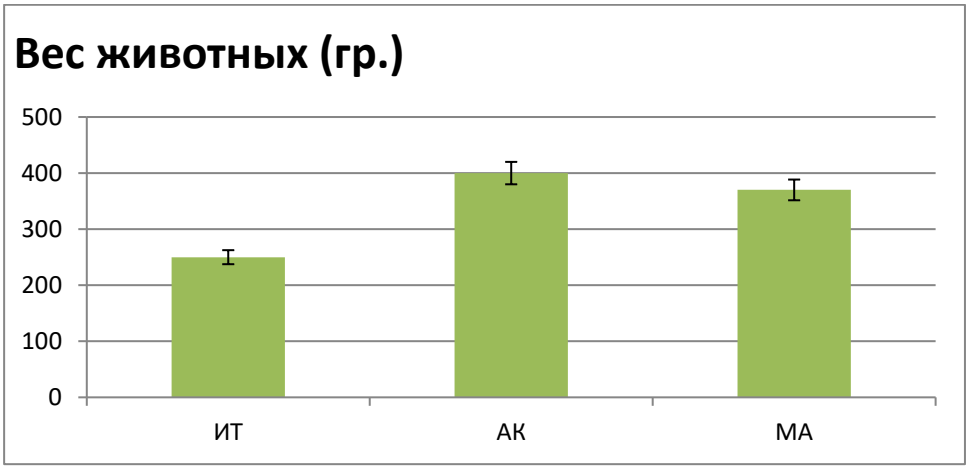
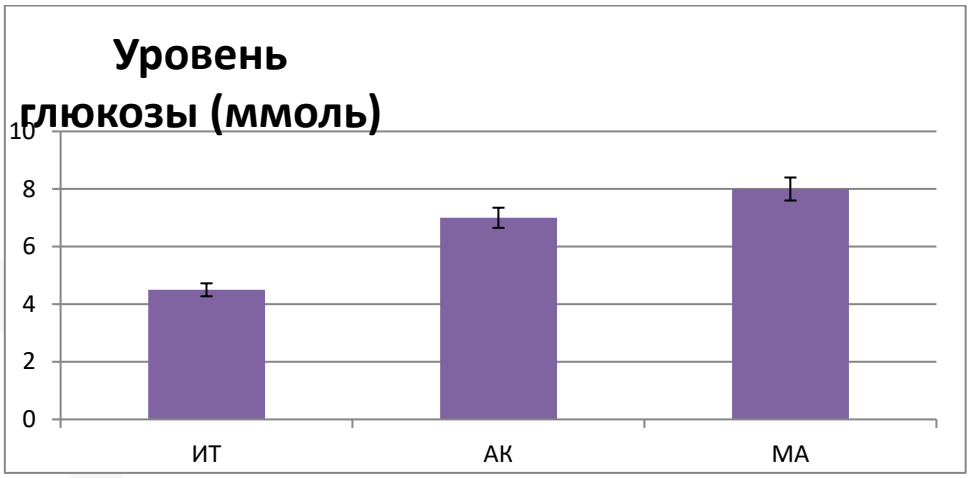
(A)



B)



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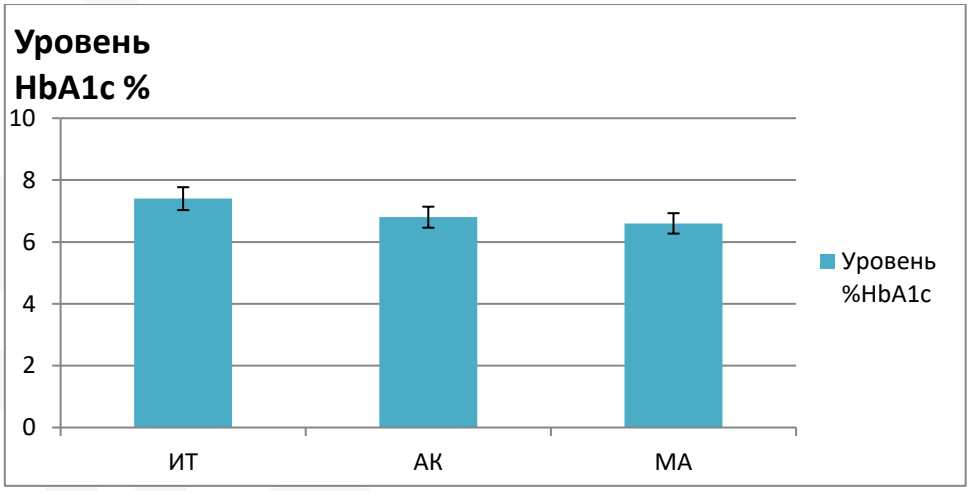

Figure 1. Study of the content of some biochemical parameters in the blood of animals with MA (M±m), n = 25:
a) Weight of animals, d b) Glucose level, mmol / l c) HbA level $_{1c}$, %

Morphologically, animals fed a high-fat diet naturally had a more pronounced ectopic accumulation of fat in liver and pancreatic tissue than animals on a norm-calorie diet. Experimentally, AD is modeled by intracerebral administration of STZ, which increases the aggregation of β-amyloid and leads to pathomorphological and behavioralchanges similar to AD [7]. At the same time, STZ is captured by a glucose transporter (GLUT2), exhibits high toxicity to pancreatic β cells and is used to induce diabetes in animals. It is known that with systemic administration of STZ,type 1 diabetes is caused in animals [1] Depending on the model, doses of CTZ vary from 30 to 100 mg / kg or more. A single systemic administration of CTZ in high doses (>50 mg / kg) causes almost complete death of pancreatic β cells and a decrease in insulin production to an undetectable concentration, while repeated systemic administration of small doses of CTZ is used to simulate moderate damage to β cells [1]. . It is important that a single administration of TSD at a dose of 35 mg / kg to rats in combination with a high-fat diet led to insulin resistance, disrupting insulin receptor signaling, while the same dose with a normocaloric diet did not cause significant changes [2]. In the same study, a dose of CSD of 25 mg / kg, regardless of diet, did not lead to changes in the basal concentration of glucose and insulin in the blood plasma. However, it is repeatedly shown that intracerebral administration of STZ, at doses of 1–3 mg/kg that do not cause diabetes, leads to cognitive deficits, local disruption of glucose metabolism, oxidative stress, and accumulation of amyloid β in brain structures, although the mechanisms of action of CTZ in the brain arenot fully understood [3].

But only STZ+NDC can be attributed to the isolated effects of STZ; in other words, this group was a model of obesity-free BA. Therefore, disorders of carbohydrate metabolism demonstrated in the STZ + NDC group could serve as confirmation of the effect of damage to brain structures on the metabolic status of animals.

According to the results of our study, a group of animals STZ + NDC showed an increase in the area under the glycemic curve compared to the control group LO + NDC, which indicates the involvement of the brain structures affected by STZ in the regulation of systemic glucose metabolism. We suggest that an important pathogenetic aspect of the FTZ-induced model of AD is damage to the structures of the hypothalamus. This assumption is confirmed by the degeneration we identified in the arcuate nucleus of the hypothalamus of tanititis, astroglia and dopamine neurons - cell populations that modulate the activity of hypothalamic neurons and are directlyinvolved in the sis dark energy homeostasis [5]. In the brain, β-amyloid appears to inhibit insulin signaling cascades at different levels . So, in transgenic mice, the expression of mutant APP (a precursor to β-amyloid) in the hypothalamus

caused a local decrease in glucose metabolism. It is important that the action of oligomers β-amyloid on the nuclei of the hypothalamus involved in energy metabolism causes peripheralglucose tolerance [6], in genetic models of AD there are also systemic metabolic disorders associated with dysfunction of the hypothalamus and musa. All this indicates the participation in the pathogenesis of AD not only local, intracerebral, but also systemic regulation of glucose metabolism.

Thus, the morphological changes in the structures of the hypothalamus in the STZ + NDC group demonstrated by us could independently lead to systemic disorders of carbohydrate metabolism.

However, we have not previously demonstrated the protective property of overweight on cognitive functions in sprague-Dawley rats in the current experiment. In our study, VCD did not lead to an improvement in the condition of the ventricular wall of the brain and adjacent hypothalamic structures damaged by the action of STZ. These contradictions are reflected in the works of other authors: there is evidence that that under the influence of a high-fat diet in genetic models of AD, the state of the blood-brain barrier improved and the accumulation of amyloid β in the hippocampus did not change, and in another study it was noted that a high-fat diet increases the accumulation of β-amyloid.

Thus, the direct effect of damage to brain structures in the AD model on carbohydrate metabolism shown in our work testifies in favor of the common pathogenetic mechanisms of AD and DM2. The presence of cognitive impairment may be accompanied by a change in the central regulation of energy metabolism.

References:

1. Alesenko A.V. The Potential Role of Sphingolipids in the Neuropathogenesis of Alzheimer's Disease.- Biomedical Chemistry, 2013, Volume 59, Vol. 1, P. 25-50.
2. Kudinova N.V., Berezov T. T., Kudinov A.R. Amyloid beta Alzheimer's disease and brain amyloidosis // Biochemistry. -1999. –T. 64. – S.752-757.
3. 18.Konoplyanko, V.A. Pathophysiological processes in hypothyroidism in experiment / V.A. Konoplyanko, R.D. Klebanov // Health and environment. – 2015. – Vol. 2, No 25. – P. 102-105, 140
4. Aksenov M. Y. et al. The expression of key oxidative stress-handling genes in different brain regions in Alzheimer’s disease //Journal of Molecular Neuroscience. 1998. Vol. 11. №. 2. P. 151-164.
5. Bijur G.N., Davis R.E., Jope R.S. Rapid activation of heat shock factor-1 DNA binding by H2O2 and modulation by glutathione in human neuroblastoma and Alzheimer’s disease cybrid cells // Mol. Brain Res. 1999. Vol. 71, № 1. P. 69–77.

6. Drachman D.A. The amyloid hypothesis, time to move on: Amyloid is the downstream result, not cause, of Alzheimer's disease // Alzheimer's Dement. Elsevier Ltd, 2014. Vol. 10, № 3. P. 372–380.
7. Mustafakulov Mukhammadjon, Tukhtaeva Sitora, Seit-Asan Lenara, Murodova Maftuna, Mustafakulova Nigora, Saatov Talat THE EFFECT OF NGF ON INDICATORS OF THE ANTIOXIDANT SYSTEM IN RAT BRAIN TISSUE // Universum: химия и биология. 2021. №9 (87).
8. Seit-Asan, L. S. (2022). STUDY OF THE LEVEL OF THYROID HORMONES IN AN EXPERIMENTAL MODEL OF ALZHEIMER'S AGAINST THE BACKGROUND OF HYPOTHYROIDISM. *INTERNATIONAL CONFERENCES*, *1*(10), 270–275. Retrieved from http://researchedu.org/index.php/cf/article/view/842