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RELATIONSHIP OF THE ISCHEMIC STROKE RISK IN YOUNG AGE WITH THE CONCENTRATION OF BRAIN NEUROTROPHIC FACTOR

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ABSTRACT. We were aimed to study the role of brain-derived neurotrophic factor in the development of ischemic stroke in young people. **Materials and methods:** a comparative analysis of the results of quantitative determination of the level of BDNF by enzyme immunoassay in the blood serum of patients of the main group (n=83) with the results of examination of the control group (n=54), which included practically healthy individuals of comparable age and sex, was carried out. The level of biomarker concentration in patients of the main group was determined on the 1st day from the moment of admission. **Results.** When comparing serum BDNF indices in the main group, differences were established depending on the severity of neurological disorders, as well as in various types of ischemic stroke. When studying the concentration of brain-derived neurotrophic factor, an inversely proportional relationship with the severity of clinical manifestations was established: the lower the level of BDNF, the more pronounced the neurological deficit was. **Conclusion.** This fact makes it possible to assume that a low level of BDNF in the blood serum could affect the development and aggravation of the ischemic process of the brain in the patients we examined.

Keywords: ischemic stroke, young age, brain-derived neurotrophic factor.

Neurotrophicity is a natural reaction manifested by proliferation, migration, differentiation and survival of cells and is characterized by regeneration processes[1]. In these neurotrophic processes, the main role is assigned to neurotrophins, which are regulatory proteins of the nervous tissue. Neurotrophins determine the plasticity of neuronal tissue and form the mechanisms involved in the restoration of impaired neurological functions, being a powerful stimulator of neurogenesis [2-4]. Brain-Derived Neurotrophic Factor (BDNF), which is a key

mediator of survival and recovery of neurons, is currently of the greatest interest for us among all neurotrophins [5-7].

With a decrease in the concentration of circulating BDNF, the development of stroke increases, and a decrease in the level of serum BDNF in the acute period of ischemic stroke is considered a factor in bad forecast, which was confirmed by Stanne et al. (2016) [4,6,8].

Recently, we are increasingly faced with the problem of determining the main cause of the development of acute ischemic brain damage due to the simultaneous impact of several provoking factors, as we could see earlier [9-11]. At the same time, according to a number of authors, in 29% of all cases of ischemic stroke, its genesis cannot be established, which causes an urgent need for a thorough search for possible biomarkers of the risk of ischemic stroke [12,13].

In connection with the above, we were aimed to study the role of brain-derived neurotrophic factor in the development of ischemic stroke in young people.

Materials and methods. a comparative analysis of the results of quantitative determination of the level of BDNF by enzyme immunoassay in the blood serum of patients of the main group (n=83) with the results of examination of the control group (n=54), which included practically healthy individuals of comparable age and sex, was carried out. The level of biomarker concentration in patients of the main group was determined on the 1st day from the moment of admission.

The concentration of BDNF was determined by the enzyme-linked immunosorbent assay "sandwich" type. The biomarker level was expressed in pg/ml, while the reference values were taken as determined by the manufacturer of the Quantikine ELISA laboratory kit from R&D Systems (USA). Given that the content of brain-derived neurotrophic factor was determined in serum, the blood was subjected to centrifugation for 15 minutes. The resulting serum was diluted with a special dilution solution included in the laboratory kit. The sensitivity of the method, determined by the manufacturer, was 20 pg/ml.

To prepare a standard solution (4000 pg/ml BDNF) by mixing 2 ml of standard diluent with a BDNF standard. After that, working solutions were prepared with the following concentration of the studied biomarker: in the 1st tube - 2000 pg/ml, in the 2nd tube - 1000 pg/ml, in the 3rd tube - 500 pg/ml, in the 4th tube - 250 pg/ml, in the 5th tube - 125 pg/ml and in the 6th tube - 62.5 pg/ml.

After obtaining working solutions, 100 µl of the diluent and 50 µl of previously diluted blood serum samples of the examined persons were added to each well of a special microplate, then the wells were closed and sent to the incubator.

After 2 hours, 100 µl of BDNF-conjugate was added to the samples, the wells were closed and placed back in the incubator for 1 hour at room temperature. After the time allotted for incubation, the wells were washed with a buffer solution and 200 µl of the prepared substrate were applied, then they were again placed in the incubator for 30 minutes after the preliminary addition of 50 µl of stop solution.

The optical density of the samples was recorded on a vertical photometer StatFax 3200 (Awareness). (USA).

The BDNF concentration was determined from the calibration curve (Fig. 1).

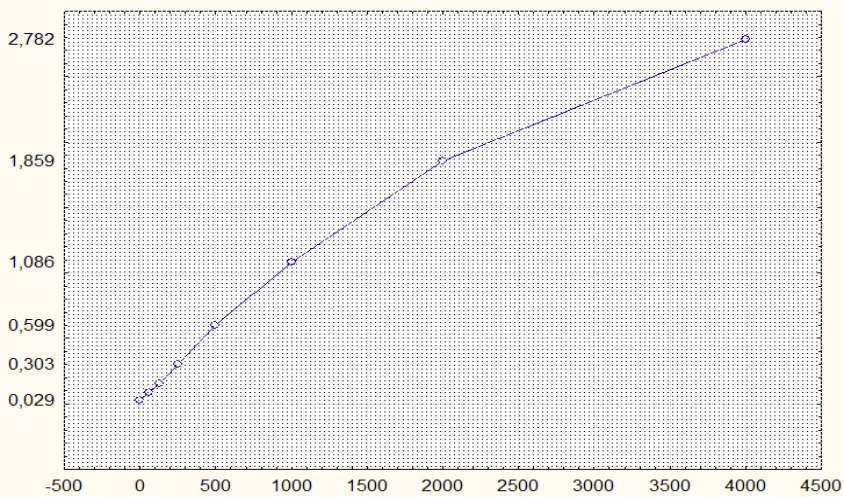

Fig.1. Calibration plot for the quantitative determination of the concentration of brain-derived neurotrophic factor

Results and discussion. When comparing serum BDNF levels in individuals of the main group, we tried to establish differences depending on the severity of neurological disorders (Table 1), as well as in various types of ischemic stroke (Table 2). At the same time, in the examined persons of the control group, the average level of this biomarker was 2954.3 pg / ml (3758.9-2157.0), which indicates the risk of developing cerebrovascular pathology, in particular acute cerebrovascular accident.

Table 1

Levels of serum brain-derived neurotrophic factor in the acute period of IS, depending on the severity of neurological deficit according to the NIHSS scale

The severity of neurological deficit	**BDNF,** pg/ml (M±m)		**veracity**
	Main group (n=83) Q1-Q2	**Control group (n=54)** Q1-Q2	
mild	1946,46±513,48 [2532,1-1234,5]	2954,3±403,24 [3758,9; 2157,0]	p=0,97
average	1564,7±483,91 [2347,7-1161,0]		
severe	1285,67±607,21 [1349,6-1145,3]		
extremely severe	1275,98±592,75 [1807,3-1145,0]		

When studying the concentration of brain-derived neurotrophic factor, an inversely proportional relationship with the severity of clinical manifestations was established: the lower the BDNF level, the more pronounced the neurological deficit was. So, with a mild degree of neurological disorders, the average concentration of the molecular biomarker was 1946.46±513.48 pg/ml; with an average degree - 1564.7 ± 483.91 pg / ml; with a severe degree - 1285.67±607.21 pg/ml, with an extremely severe degree - 1275.98±592.75 pg/ml.

In this case, we observed a slight difference in the average. The average level of BDNF in the blood serum of patients of the main group with a mild degree of neurological deficit in atherothrombotic variant of ischemic stroke was

2028.0±583.79 pg/ml, in lacunar variant - 1991.3±623.08 pg/ml, in hemodynamic stroke – 1791.1±592.33 pg/ml.

Table 2

Serum BDNF levels (pg/ml) in the acute period of ischemic stroke depending on the subtype

Sub type	The severity of neurological deficit according to the NIHSS scale			
	mild	average	severe	extremely severe
ATS	**2028,2±583,79** [2532,1-1546,2]	**1586,9±605,31** [1876,4-1297,4]	**1307,0±491,57** [1349,6-1264,5]	**1179,5± 511,43** [1243,2-1146,5]
CES	-	-	**1347,5±412,23** [1257,4-1237,6]	**1134,7±397,01** [1807,3-1145,0]
LS	**1991,3±623,08** [2413,2-1579,0]	**1538,0±429,36** [1647,3-1207,1]	**1392,1±489,13** [1436,8-1347,4]	-
HDS	**1791,1± 592,33** [2371,0-1234,5]	**1526,9±493,21** [1914,5-1240,0]	**1320,1±511,61** [1436,8-1347,4]	**1147,6± 397,10** [1197,6-1172,7]
	p=2,01	p=2,01	p=2,44	p=2,44

In patients with moderate neurological disorders, its concentration in atherothrombotic subtype was 1586.9±605.31 pg/ml, in lacunar - 1538.0±429.36 pg/ml, in hemodynamic stroke - 1526.9±493.21 pg/ml; with a severe degree in atherothrombotic stroke was equal to 1307.0±491.57 pg/ml, in cardioembolic - 1347.5±412.23 pg/ml, in lacunar - 1392.1±489.13 pg/ml, in hemodynamic stroke 1320.1±511.61 pg/ml with an extremely severe degree in atherothrombotic lesions was equal to 1179.5±511.43 pg/ml, in the cardioembolic variant - 1134.7±397.01 pg/ml, and in hemodynamic stroke - 1147.6±397.10 pg/ml.

A careful study of the data presented in the above table revealed an inverse correlation between the biomarker concentration and the severity of the disease and the severity of neurological symptoms. So, in patients with mild neurological disorders according to the NIHSS scale, we observed a high concentration of serum BDNF and, conversely, a decrease in its level was determined in patients with an extremely severe degree of neurological deficit. ($r=-0,137$, $p<0,05$).

Thus, when conducting an intragroup analysis of the quantitative determination of serum BDNF in patients, depending on the pathogenetic subtype of ischemic stroke, a relationship was established between the level of neurotrophin and the severity of neurological disorders, while the lowest level of this biomarker was observed in patients with hemodynamic stroke. This fact makes it possible to assume that a low level of BDNF in the blood serum could affect the development and aggravation of the ischemic process in the brain of the patients we examined.

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