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Review Article

Characteristics of Changes in The Pool of Amino Acids in the Brain of Rats with Subtotal Cerebral Ischemia Against the Background of The Introduction of Omega-3 Polyunsaturated Acids

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Abstract

Amino acids and their derivatives are involved in synaptic transmission as neurotransmitters and neuromodulators, and some of them are involved in the formation of neurotransmitters of the nervous system. Therefore, the study of the state of the amino acid pool in simultaneous cerebral ischemia plays a significant role.

The aim of the study was to study the effect of the introduction of polyunsaturated fatty acids on the amino acid pool of the brain of rats with cerebral ischemia. The administration of Omega-3 polyunsaturated acids at a dose of 5 g/kg of body weight for a week to rats with SCI did not have a corrective effect on the levels of amino acids of taurine, methionine, L-arginine, and lysine, which changed during ischemia.

Key Words: amino acid; neurons; ischemia; omega-3 polyunsaturated acids

Introduction

As is known, one of the directions for detailing the mechanisms of development of damage and adaptation of the brain during its ischemia is the study of changes in the pool of amino acids [18].

Amino acids and their derivatives play an important role in the functioning of the brain, both in normal and pathological conditions, participating in the biosynthesis of membrane and signal protein and peptide molecules, some lipids, vitamins, hormones and biogenic amines, and are also directly involved in the implementation of neurotransmitter functions, regulation of the activity of excitation and inhibition processes (glutamate, aspartate, GABA) [16]. Aromatic amino acids (phenylalanine, tyrosine, tryptophan, histidine) are of particular importance as precursors of catecholamines and serotonin [1,3,6,9,15]. The study of the pool of amino acids is important for detailing the mechanisms of brain damage in cerebral ischemia.

Changes in the pool of amino acids in rats with ischemic brain injury of varying severity were studied with partial (one-sided ligation of the common carotid artery, CCA), subtotal (simultaneous bilateral ligation of both CCAs), stepwise subtotal (alternate ligation of both CCAs at different time intervals) and total (complete cessation of cerebral blood flow) CI [21, 34, 35].

Due to the important role of Omega-3 acids in the functioning of ion channels, the regulation of physiological processes through the synthesis of lipid mediators, impulse transmission, the functioning of receptors that affect the fluidity of cell membranes, as well as the presence of corrective properties in relation to morphological changes in the hippocampus in rats with subtotal cerebral ischemia (SCI) [34,38,39] studied their effect on the state of the pool of amino acids in the cerebral cortex of rats with cerebral ischemia [37].

The introduction of the drug Omega-3 acids "Omegamed" has a corrective effect on the structures of the hippocampus in conditions of subtotal cerebral ischemia, reducing the number of shadow cells and hyperchromic wrinkled neurons, while not affecting the size and shape of neurons in the parietal cortex of the brain and contributing to a lesser severity manifestation of neurological deficit. The study of the characteristics of the energy exchange of neurons in the brain of rats with subtotal cerebral ischemia against the background of the administration of Omega-3 acids showed a significant improvement in the parameters of mitochondrial respiration and an increase in the content of ATP synthase in hippocampal neurons in animals with SCI [38,20,30,31,36].

In addition, against the background of the introduction of Omega-3 PUFA, correction of the parameters of antioxidant protection of brain neurons was noted, which was manifested by an increase in the content of total SH-groups of proteins and glutathione [2,39,32,33].

The study of the pool of amino acids was carried out in prepared homogenates of the studied structures of the brain of experimental animals, isolated 1 hour after ischemia modeling. To do this, after removing the brain, a fragment of the parietal cortex and hippocampus was taken, followed by freezing in liquid nitrogen.

Preparation of samples for the study included homogenization in a 10-fold volume of 0.2 M perchloric acid, centrifugation for 15 min. at 13000 g at 4°C, followed by collection of the supernatant. Amino acids were analyzed by reversed-phase chromatography with pre-column derivatization with o-phthalaldehyde and 3-mercaptopropionic acid in Na-borate buffer on an Agilent 1100 chromatograph [29]. To prevent a systematic measurement error, brain samples from the compared control and experimental groups of animals were studied under the same conditions.

Statistical processing. As a result of the research, quantitative continuous data were obtained. Since the experiment used small samples that had a non-normal distribution, the analysis was performed by nonparametric statistics using the licensed computer program Statistica 10.0 for Windows (StatSoft, Inc., USA). The data are presented as Me (LQ; UQ), where Me is the median, LQ is the value of the lower quartile; UQ is the value of the upper quartile.

When the applicability conditions were met (normality of the samples and homogeneity of the variances), parametric analysis of variance was used with a posteriori comparison of the selected contrasts; A study was made of the features of the pool of amino acids in the parietal lobe and hippocampus of the brain of rats with one-hour subtotal cerebral ischemia against the background of the administration of Omega-3 PUFA at a dose of 5 g/kg of body weight during the week (Table 1) [26].

Parietal lobe				**Hippocampus**		
	Groups of animals			**Groups of animals**		
Amino acids	**Control**	**SCI 1 hour**	**SCI+Omega-3 PUFA**	**Control**	**SCI 1 hour**	**SCI+Omega-3 PUFA**
Neurotransmitters						
Glycine	**176 (161/201)**	**209 (180/211)**	**176 (172/187)**	**174 (150/190)**	**191 (176/214)**	**181 (158/212)**
Glutamate	**3137 (3040/3277)**	**2829 (2166/3130)**	**3341 (2991/3689)**	**3375 (3146/3574)**	**3265 (2947/3429)**	**3668 (3648/4040)**
Aspartate	**1653 (1501/1820)**	**1489 (1260/1766)**	**1315 (1243/1422)**	**1603 (1351/1768)**	**1663 (1398/1952)**	**1556 (1378/1724)**
Taurine	**1035 (909/1120)**	**1134 (1076/1265)**	**1326 (1283/1347)***	**1032 (983/1125)**	**1129 (1038/1194)***	**1160 (1116/1326)**
GABA	**481 (446/534)**	**1102 (704/1515)**	**1075 (824/1432)**	**523 (485/665)**	**857 (749/1097)**	**1059 (727/1320)**
Endogenous NMDA receptor antagonist						
a-aminoadipate	**21.5 (20.2/24)**	**14.6 (11.2/19.8)***	**16.6 (15.1/21.7)**	**13 (11,5/14,1)**	**5,08 (4,63/6,51)***	**6,34 (5,21/6,72)**
Sulfur containing						
Cysteate	**1.66 (0.767/2.16)**	**1.2 (0.657/1.59)***	**1.64 (1.1/1.87)**	**1,03 (0,278/1,69)**	**2,19 (1,73/2,72)***	**1,99 (1,51/2,09)**
Cystathionine	**36.7 (30.3/40.2)**	**43.9 (35.7/57.7)**	**30.4 (24.7/38.5)**	**37,7 (34,7/40,8)**	**46,5 (34,2/52,7)**	**39,2 (29,2/59,6)**
Taurine	**1035 (909/1120)**	**1134 (1076/1265)**	**1326 (1283/1347)**	**1032 (983/1125)**	**1129 (1038/1194)**	**1160 (1116/1326)**
Methionine	**16.7 (15.6/20.3)**	**14.8 (13.7/15.4)***	**13.5 (12.8/14.8)***	**19,3 (17,9/23,4)**	**15,9 (15/16,5)**	**14,3 (11,4/15,5)**
Cysteinsulfinic acid	**1.27 (0.757/3.07)**	**2.59 (1.49/4.23)**	**2.77 (1.35/3.41)**	**2,56 (1,24/4,05)**	**2,35 (1,41/2,87)**	**3,11 (2,68/6,53)**
Glycogenic						
Aspartate	**1653 (1501/1820)**	**1489 (1260/1766)**	**1315 (1243/1422)**	**1603 (1351/1768)**	**1663 (1398/1952)**	**1556 (1378/1724)**

Asparagine	**92.3 (87.8/98.1)**	**101 (97.2/116)**	**132 (119/147)**	**101 (92,5/105)**	**106 (102/111)**	**109 (101/122)**
Threonine	**330 (282/443)**	**252 (233/265)**	**275 (207/332)**	**425 (345/567)**	**253 (226/317)**	**281 (267/365)**
Serine	**566 (535/580)**	**526 (433/543)**	**604 (572/674)**	**516 (496/552)**	**505 (452/528)**	**567 (537/589)**
Glutamine	**1937 (1600/2084)**	**1834 (1743/1953)**	**2058 (1898/2139)**	**1981 (1831/2172)**	**1740 (1645/1960)**	**1827 (1616/2025)**

Table 1 - Indicators of the pool of amino acids of the cerebral hemispheres of rats with subtotal cerebral ischemia against the background of the introduction of omega-3 polyunsaturated fatty acids, nmol / g; Me (LQ; UQ)

Glycine	**176 (161/201)**	**209 (180/211)**	**176 (172/187)**	**174 (150/190)**	**191 (176/214)**	**181 (158/212)**
Alanine	**264 (251/276)**	**389 (297/436)**	**426 (409/452)***	**318 (297/334)**	**456 (446/487)**	**497 (433/547)***
Valine	**61.1 (54.8/78.3)**	**48.4 (45.9/56.9)**	**50.9 (49.7/54.8)***	**74,9 (70,8/79,1)**	**52,4 (49,3/64,2)**	**51,7 (49,4/59,8)***
Methionine	**16.7 (15.6/20.3)**	**14.8 (13.7/15.4)***	**13.5 (12.8/14.8)***	**19,3 (17,9/23,4)**	**15,9 (15/16,5)**	**14,3 (11,4/15,5)**
Histidine	**19.9 (16.2/21.4)**	**18.6 (17.7/20.5)**	**21.3 (19.4/22.8)**	**17,7 (16,3/19)**	**16,7 (16,5/18,2)**	**16,9 (15/20,8)**
Arginine	**32.1 (30.5/33.5)**	**44.7 (36/51.4)***	**37.4 (34.6/41.7)***	**27,8 (21,2/32,4)**	**43,4 (32,1/48,6)**	**43,6 (39,8/47,7)***
Citrulline	**12.5 (11.6/13.8)**	**14.3 (12.1/17.5)**	**14.5 (12.4/16.7)***	**11,5 (10,5/12,5)**	**11,9 (10,7/12,5)**	**16 (14,6/17)**
Ketogenic						
Lysine	**160 (129/191)**	**112 (98.1/130)**	**80.2 (69.7/113)***	**227 (179/259)**	**134 (117/187)**	**129 (113/150)***
Leucine	**56.7 (49.8/67.2)**	**52.3 (50/54.2)**	**50.2 (48/52.8)**	**68,2 (64,8/72)**	**56,3 (51,8/67,9)**	**49,4 (48,5/60,7)**
Histidine derivative						
3-methylhistidine	**5.57 (4.96/5.9)**	**5.77 (4.85/6.03)**	**5.53 (4.83/6.18)**	**4,65 (4,37/5,84)**	**5,56 (5,23/5,8)**	**5,47 (4,61/6,2)**
Nonessential						
Glycine	**176 (161/201)**	**209 (180/211)**	**176 (172/187)**	**174 (150/190)**	**191 (176/214)**	**181 (158/212)**
Alanine	**264 (251/276)**	**389 (297/436)**	**426 (409/452)***	**318 (297/334)**	**456 (446/487)**	**497 (433/547)***
Glutamine	**1937 (1600/2084)**	**1834 (1743/1953)**	**2058 (1898/2139)**	**1981 (1831/2172)**	**1740 (1645/1960)**	**1827 (1616/2025)**
Glutamate	**3137 (3040/3277)**	**2829 (2166/3130)**	**3341 (2991/3689)**	**3375 (3146/3574)**	**3265 (2947/3429)**	**3668 (3648/4040)**
Aspartate	**1653 (1501/1820)**	**1489 (1260/1766)**	**1315 (1243/1422)**	**1603 (1351/1768)**	**1663 (1398/1952)**	**1556 (1378/1724)**
Asparagine	**92.3 (87.8/98.1)**	**101 (97.2/116)**	**132 (119/147)**	**101 (92,5/105)**	**106 (102/111)**	**109 (101/122)**
Serine	**566 (535/580)**	**526 (433/543)**	**604 (572/674)**	**516 (496/552)**	**505 (452/528)**	**567 (537/589)**
Tyrosine	**46.2 (40.1/50.1)**	**47.9 (43.8/50.7)**	**54.4 (47.7/59.5)**	**49,3 (44,6/50,2)**	**50,3 (46,1/54)**	**55,8 (46,3/61,3)**
Ornithine	**10.6 (8.89/13.4)**	**10.3 (10.2/13.5)**	**12 (10.9/12.7)**	**11,2 (9,78/14,2)**	**15,8 (12,8/20,2)**	**15,6 (14,8/18,7)**

Continuation of table 3.3.1

Essential						
Valine	**61.1 (54.8/78.3)**	**48.4 (45.9/56.9)**	**50.9 (49.7/54.8)***	**74,9 (70,8/79,1)**	**52,4 (49,3/64,2)**	**51,7 (49,4/59,8)***
Isoleucine	**29.7 (26.2/34.4)**	**30.1 (26.1/32.8)**	**26.1 (23.5/28)**	**33,2 (31,1/35,1)**	**26,5 (25,1/32,1)**	**25,7 (22,2/31,7)**
Leucine	**56.7 (49.8/67.2)**	**52.3 (50/54.2)**	**50.2 (48/52.8)**	**68,2 (64,8/72)**	**56,3 (51,8/67,9)**	**49,4 (48,5/60,7)**

Methionine	**16.7 (15.6/20.3)**	**14.8 (13.7/15.4)***	**13.5 (12.8/14.8)***	**19,3 (17,9/23,4)**	**15,9 (15/16,5)***	**14,3 (11,4/15,5)***
Lysine	**160 (129/191)**	**112 (98.1/130)**	**80.2 (69.7/113)***	**227 (179/259)**	**134 (117/187)**	**129 (113/150)***
Histidine	**19.9 (16.2/21.4)**	**18.6 (17.7/20.5)**	**21.3 (19.4/22.8)**	**17,7 (16,3/19)**	**16,7 (16,5/18,2)**	**16,9 (15/20,8)**
Threonine	**330 (282/443)**	**252 (233/265)**	**275 (207/332)**	**425 (345/567)**	**253 (226/317)**	**281 (267/365)**
Tryptophan	**27.7 (24.6/32)**	**19.8 (17.3/24.5)**	**20.9 (20/22.3)**	**29,8 (25,1/31,8)**	**22,7 (21,5/27,8)**	**22,8 (21,5/24)**
Phenylalanine	**29.4 (24.6/33.7)**	**30.3 (28.5/34)**	**28.1 (25.7/30.6)**	**31,6 (26/39,2)**	**31,3 (30,5/32,4)**	**30,8 (24,5/34,1)**
Aromatic						
Tyrosine	**46.2 (40.1/50.1)**	**47.9 (43.8/50.7)**	**54.4 (47.7/59.5)**	**49,3 (44,6/50,2)**	**50,3 (46,1/54)**	**55,8 (46,3/61,3)**
Tryptophan	**27.7 (24.6/32)**	**19.8 (17.3/24.5)**	**20.9 (20/22.3)**	**29,8 (25,1/31,8)**	**22,7 (21,5/27,8)**	**22,8 (21,5/24)**
Phenylalanine	**29.4 (24.6/33.7)**	**30.3 (28.5/34)**	**28.1 (25.7/30.6)**	**31,6 (26/39,2)**	**31,3 (30,5/32,4)**	**30,8 (24,5/34,1)**
BHAA						
Valine	**61.1 (54.8/78.3)**	**48.4 (45.9/56.9)**	**50.9 (49.7/54.8)***	**74,9 (70,8/79,1)**	**52,4 (49,3/64,2)**	**51,7 (49,4/59,8)***
Isoleucine	**29.7 (26.2/34.4)**	**30.1 (26.1/32.8)**	**26.1 (23.5/28)**	**33,2 (31,1/35,1)**	**26,5 (25,1/32,1)**	**25,7 (22,2/31,7)**
Phenylalanine	**29.4 (24.6/33.7)**	**30.3 (28.5/34)**	**28.1 (25.7/30.6)**	**31,6 (26/39,2)**	**31,3 (30,5/32,4)**	**30,8 (24,5/34,1)**

Continuation of table 3.3.1
* - p<0.05 compared with the control group

It was found that subtotal cerebral ischemia (SCI) leads to a change in a number of amino acids in the brain: an increase in the content of L-arginine and taurine, as well as a decrease in the content of methionine, cysteate and lysine [4,5,8,14,17,24 ,25].

Compared with the indicators in the control group, in rats with SCI after the introduction of Omega-3 PUFAs, an increase in the content of L-arginine by 14% in PL (p<0.05) and by 36% in HP (p<0 .05), alanine - by 38% in PL (p<0.05) and by 36% - in HP (p<0.05) and a decrease in the content of valine as a branched hydrocarbon amino acid (BHAA) by 6% - in PL (p<0.05) and by 31% in HP (p<0.05). Also, the content of lysine remained less than in the control by 50% - in PL (p<0.05) and by 43% - in HP (p<0.05), and the sulfur-containing AA "methionine" - by 19% (p<0.05) and by 26%, respectively (p<0.05) [7,10,19, 22,23,29].

At the same time, compared with the SCI group, after the introduction of Omega-3 PUFAs, there were no differences in the content of AA (p>0.05) [11,12,13,27,28].

Thus, the administration of Omega-3 PUFAs at a dose of 5 g/kg of body weight for a week to rats with SCI did not have a corrective effect on the levels of AA of taurine, methionine, L-arginine, and lysine, which changed during SCI.

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