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Characterization of the Pool of Amino Acids and Their Functional Significance in The Rat Brain

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Abstract

Amino acids (AA) play an important role in the metabolism and functioning of the brain. This is explained not only by their exceptional role as sources of synthesis of a large number of biologically important compounds (proteins, mediators, lipids, biologically active amines). Amino acids and their derivatives are involved in synaptic transmission as neurotransmitters and neuromodulators (glutamate, aspartate, glycine, GABA, taurine), and some AA are involved in the formation of nervous system mediators: methionine – acetylcholine, DOPA, dopamine; tyrosine – catecholamines; serine and cysteine – taurine; tryptophan – serotonin; histidine – histamine; L-arginine – NO; glutamic acid – glutamate.

Keywords: *glutamate; aspartate; glycine; GABA; taurine*

Introduction

Amino acids (AA) play an important role in the metabolism and functioning of the brain. This is explained not only by their exceptional role as sources of synthesis of a large number of biologically important compounds (proteins, mediators, lipids, biologically active amines). Amino acids and their derivatives are involved in synaptic transmission as neurotransmitters and neuromodulators (glutamate, aspartate, glycine, GABA, taurine), and some AA are involved in the formation of nervous system mediators: methionine – acetylcholine, DOPA, dopamine; tyrosine – catecholamines; serine and cysteine – taurine; tryptophan – serotonin; histidine – histamine; L-arginine – NO; glutamic acid – glutamate.

Their energy role is also significant, especially in conditions of hypoglycemia. Despite the use of glucose as the main energy source in the brain, amino acids are involved in energy metabolism through the formation of CoA, PAA, and other components of the tricarboxylic acid cycle (TCA), as well as cytochromes.

According to functional groups of AA in the brain, they can be classified:

Neurotransmitters: glycine, taurine, gamma-aminobutyric acid (GABA), glutamate, aspartate.

Sulfur-containing: cysteate, cystathionine, taurine, methionine, cysteine sulfinic acid.

Non-essential: Glycine, alanine, glutamine, glutamate, aspartate, asparagine, serine, tyrosine.

Essential: valine, isoleucine, leucine, methionine, lysine, histidine, threonine, tryptophan, phenylalanine.

Aromatic: tyrosine, tryptophan, phenylalanine.

Branched-chain amino acids (BCAAs): valine, isoleucine, leucine.

The amino acid fund of the brain averages 34 μmol per 1 g of tissue. Nervous tissue has a unique ability to maintain relatively constant AA levels under various physiological and even some pathological conditions.

The content of free AA in the brain is 8-10 times higher than their content in blood plasma and cerebrospinal fluid. The high concentration gradient

of AA between the blood and the brain is due to the selectivity of their active transfer through the blood-brain barrier (BBB). The transport of amino acids across the BBB is carried out by several carrier systems. The BBB has a higher permeability for essential AAs than for non-essential ones. The speed of AA transport is also due to their isomerism - L-isomers have a greater ability to pass through the BBB compared to D-isomers. In the brain, most (75% of the pool of free AAs) are glutamate, glutamine, aspartic, N-acetylaspartic acids and GABA, which act as mediators of the nervous system.

Despite the constancy of the total pool of AC of the brain, it is characteristic that there are differences in their content in different parts of the brain. The compartmentalization of the amino acid pool in various subcellular structures of nerve cells is characteristic, which reflects the morphological, physiological and functional heterogeneity of the brain. To the greatest extent, uneven distribution is characteristic of AAs with a neurotransmitter function (glutamic acid, taurine, GABA, glycine, etc.). The concentration of amino acids in the brain is determined by: their transport to and from the brain, the rate of metabolic transformations, inclusion in proteins and catabolism of the latter.

The structure of the free AA pool is stable under physiological conditions. Various organelles of neurons and glia of the brain receive amino acids with the expenditure of energy against concentration gradients. The transport of amino acids to the brain is a multi-step process. First of all, they pass through the BBB at the level of the brain capillaries. Then, transport from the extracellular fluid to the brain cells and then to the organelles takes place.

The transfer of amino acids against the concentration gradient is influenced by the energy potential, temperature and pH of the medium, inhibition by anaerobiosis and enzyme poisons, association with active membrane transport of Na+ ions, and competitive inhibition of membrane transport of some amino acids by others.

The level of specificity and power of transport systems for different amino acids is not the same. It is most significant for amino acid neurotransmitters (glycine, GABA, taurine, glutamic acid, etc.). Transport systems provide the plastic and energy needs of the cell, and are also important for the rapid decrease in the concentration of the neurotransmitter in the zone of the synaptic cleft. High selectivity of neurotransmitter uptake is carried out both by the presynaptic region and by glial cells.

The transport of amino acids into the cell is associated with the γ-glutamyl cycle. Its key enzyme is cell membrane-bound γ-glutamyl transpeptidase. The enzyme is able to transfer the γ-glutamyl group of glutathione located inside the cell to an amino acid localized on the outer side of the membrane and transporting the resulting dipeptide into the cell. Another cycle enzyme is γ-glutamyl cyclotransferase, whose function is to release the amino acid. The dipeptide cysteinylglycine is cleaved by the action of peptidase into two amino acids — cysteine and glycine. As a result of these reactions, one amino acid molecule is transferred into the cell (or intracellular structure). The following reactions ensure the regeneration of glutathione, so that the cycle is repeated many times. For the transport of one amino acid molecule into the cell with the participation of the γ-glutamyl cycle, 3 ATP molecules are spent. Under normal conditions, the rate of transport of amino acids does not directly limit their metabolism, since the rate of synthesis and degradation is less than the rate of transport. Therefore, amino acids are accumulated by the brain, forming a pool of free amino acids. However, without replenishment from the outside, the pool depletes rather quickly. Thus, the amount of amino acids used for the synthesis of brain proteins, neuropeptides and neurotransmitters within 30 minutes is equal to the total cerebral pool of most free amino acids. The activity of amino acid transport systems, as well as the composition of their pool, changes during brain development. Amino acids penetrate into the brain of young animals faster and reach higher concentrations earlier than in adults [3].

Thus, it is of interest to study the state of the amino acid pool of the rat brain in normal.

Purpose is to characterize the features of the pool of amino acids in the rat brain hippocampus.

Materials and methods of research

The experiments were performed on 10 male outbred white rats weighing 260 ± 20 g in compliance with the requirements of the Directive of the European Parliament and of the Council No. 2010/63/EU of 22.09.2010 on the protection of animals used for scientific purposes.

After extraction of the brain, a fragment of the hippocampus was taken, followed by freezing in liquid nitrogen.

Sample preparation 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.

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. Differences between groups were considered significant at p<0>

Results

When studying the amino acid pool of the hippocampus of rats, the following data were obtained (Table 1).

Table 1: Indicators of the pool of amino acids of the hippocampus of the rat brain, Me (LQ / UQ)

Amino acids	***Hippocampus***
Neurotransmitters	
Glycine	*174 (150/190)*
Taurine	*1032 (983/1125)*
GABA	*523 (485/665)*
Glutamate	*3375 (3146/3574)*
Aspartate	*1603 (1351/1768)*
Sulfur-containing	
Cysteate	*1,03 (0,278/1,69)*
Cystathionine	*37,7 (34,7/40,8)*
Taurine	*1032 (983/1125)*
Methionine	*19,3 (17,9/23,4)*
Cysteinsulfinic acid	*2,56 (1,24/4,05)*
Non-essential	
Glycine	*174 (150/190)*
Alanine	*318 (297/334)**
Glutamine	*1981 (1831/2172)*
Glutamate	*3375 (3146/3574)*
Aspartate	*1603 (1351/1768)*
Asparagine	*101 (92,5/105)*
Serine	*516 (496/552)*
Tyrosine	*49,3 (44,6/50,2)*
Ornithine	*11,2 (9,78/14,2)*
Essential	
Valine	*74,9 (70,8/79,1)*
Isoleucine	*33,2 (31,1/35,1)*
Leucine	*68,2 (64,8/72)*
Methionine	*19,3 (17,9/23,4)*
Lysine	*227 (179/259)*
Histidine	*17,7 (16,3/19)*
Threonine	*425 (345/567)*
Tryptophan	*29,8 (25,1/31,8)*
Phenylalanine	*31,6 (26/39,2)*
Amino Acid ratio Non-essential/Essential	
Non-essential/Essential	*8,36 (7,54/9,76)*
Aromatic	
Tyrosine	*49,3 (44,6/50,2)*
Tryptophan	*29,8 (25,1/31,8)*
Phenylalanine	*31,6 (26/39,2)*
BCAAs	
Valine	*74,9 (70,8/79,1)*
Isoleucine	*33,2 (31,1/35,1)*
Leucine	*68,2 (64,8/72)*
Amino Acid ratio BCAAs / Aromatic AAs	
BCAAs / Aromatic AAs	***1,56 (1,44/1,74)***

AAs with neurotransmitter properties are of primary importance in the brain. These include AAs with excitatory neurotransmitter properties (glutamate and aspartate) and AAs with inhibitory neurotransmitter properties (glycine, taurine and GABA).

The content of glutamate and aspartate in the hippocampus was the highest among all AAs.

Glutamate, or glutamic acid, is formed from α-

ketoglutarate and other amino acids in transamination reactions. With the participation of glutamate synthetase, glutamate is converted into glutamine, a compound that allows the removal of ammonia. A feature of glutamate metabolism in the nervous tissue is its close relationship with the intensively functioning CAC through the formation of its substrate α-ketoglutarate in transamination reactions, which allows us to consider glutamate as a component of energy metabolism. Thus, already 30 min after the injection of labeled glucose, more than 70% of the radioactivity of the soluble fraction falls on the share of glutamate and its derivatives. This is facilitated by the extremely rapid interconversion of glutamate and α-ketoglutarate in the CNS. The high percentage of incorporation of radioactivity from glucose into the amino acids of the brain was the basis for the assumption that the utilization of glucose in this organ to a large extent occurs through the metabolism of amino acids. In turn, α-ketoglutaric acid can be converted to α-glutamate by direct reductive amination with the participation of glutamate dehydrogenase or by transamination. In the brain, the glutamate dehydrogenase reaction is predominantly involved in the synthesis of glutamate from α-ketoglutaric acid, thereby ensuring the continuous utilization of free ammonia into the amino group of amino acids. The main pathway for glutamate oxidation in the brain is via transamination. During normal functioning of the CAC, the dehydrogenase pathway of glutamate oxidation is suppressed, while the transaminase pathway is active. With a decrease in the amount of macroergic compounds, for example, when an uncoupler of oxidative phosphorylation 2,4-dinitrophenol is added to mitochondria, the transaminase pathway is suppressed while the dehydrogenase pathway of glutamate oxidation is enhanced. Thus, glutamic acid performs an extremely important function in the energy supply of the brain, which consists in maintaining a high level of the CAC metabolite α-ketoglutarate, as well as in supplying mitochondrial synthetic processes with reducing equivalents. The formation of glutamine and asparagine from glutamate and aspartate, respectively, is an important mechanism for the detoxification of ammonium, the accumulation of which is detrimental to the CNS. In liver failure, the concentration of ammonium rises, which is the cause of hepatic coma, and its manifestations are mitigated by the introduction of glutamate. The main part of glutamine synthetase is localized in glial cells and only a small proportion of it is located in the nerve endings. Deamination of glutamine with the formation of α-glutamate is catalyzed by glutaminase, an enzyme that is most active in neurons, where it is localized in mitochondria. It is assumed that this enzyme is involved in the membrane transport of glutamate, and its activity in the brain is low. The reaction products – glutamic acid and ammonium – inhibit the activity of the enzyme. Biological membranes are more permeable to glutamine than to glutamate, and the conversion of blood glutamine into intracellular glutamate is realized with the help of glutaminase. The enzyme also plays an important role in regulating the content of glutamate in nerve endings. The fact that glutamine synthetase is localized mainly in glial cells, glutaminase is most active in neurons, and glutamine is the main precursor of glutamate and GABA, which perform a transmitter function, gives reason to assume the existence of a glutamine cycle. Glutamine serves as a glial-neuronal glutamate transporter. Glutamate, absorbed by glial cells, turns into glutamine in a synthetase reaction, the latter enters neurons, forming glutamic acid there. Another important function of glutamate is its participation in the synthesis of proteins and biologically active peptides. Glutamate and glutamine together make up 8-10% of the total amino acid residues in hydrolysed brain proteins. Glutamate is an integral part of a number of regulatory peptides in the brain, including glutathione and a number of γ-glutamyl dipeptides. Some neuropeptides (luliberin, thyroliberin, neurotensin, etc.) contain a cyclic glutamate derivative, pyroglutamate, as an N-terminal residue, which protects them from proteolysis. The introduction of glutamate into various areas of the brain leads to seizure activity. Glutamine has no such effect. When administered intravenously, glutamate can cause the death of brain neurons, especially in the region of the ventricles, where there is no BBB. The neurons of newborn animals, in which the BBB is not developed, are also very sensitive to the damaging effect of glutamate. Glutamate is known to be associated with the phenomenon of glutamate excitotoxicity during cerebral ischemia, which is a pathogenetic link in the biochemical cascade that initiates the formation of NO, oxidative stress, inflammation, and apoptosis. In addition, the negative role of glutamate excitotoxicity in the processes of neurodegeneration and demyelination in multiple sclerosis has been confirmed. After release of glutamate into the synaptic cleft, its reuptake is carried out with the participation of Na-dependent high-affinity carriers by neurons and, to a greater extent, by astrocytes. For the functioning of synapses with the participation of glutamate as a neurotransmitter, a constant replenishment of its pool

in nerve endings is necessary. The precursors of the transmitter pool of glutamate can be glucose and α-ketoglutarate. Glutamate can also be formed from ornithine and L-arginine (via glutamate semialdehyde). The main source is glutamine, which is synthesized mainly in astrocytes, where glutamine synthetase is localized. Further, it is easily transported through the astrocyte membrane and reaches the nerve endings with the help of active carriers. [11

Aspartate, or aspartic acid, is found in high concentrations in the brain along with glutamate. In mitochondria, up to 90% of glutamate undergoes transamination with the formation of aspartate. The enzyme that catalyzes transamination with OAA, aspartate aminotransferase, is the most powerful brain transaminase. Two aspartate aminotransferase isoenzymes localized in mitochondria and cytoplasm have been isolated. Their functional role is different. The mitochondrial fraction of the enzyme is mainly associated with the functioning of the CAC, the cytoplasmic fraction determines the intensity of gluconeogenesis. Aspartate excites neuromuscular endings on synaptosomes containing α-amino-3-hydroxy-5-methyl-4-isoxazolpropionic acid receptors (AMPA-receptors). This amino acid has several specific transport systems that are different in terms of kinetic parameters. Aspartate uptake by brain synaptosomes is inhibited after neuraminidase treatment, reflecting the involvement of glycosylated proteins in neurotransmitter binding. At rest, the accumulation of aspartic acid is detected only in the nerve endings of excitatory neurons. After excitation by potassium ions, a pool of aspartate accumulates in astrocytes in the form of a combined depot with glutamate. Along with the direct excitatory effects of dicarboxylic amino acids, their inhibitory effect on the hydrolysis of phosphoinositides was revealed. Some of the effects of aspartic acid on neural transmission may be at the level of second messengers. Along with glutamate, aspartate is also involved in the pathogenesis of brain damage during ischemia by affecting AMPA receptors. It is a glutamine mimetic. Causes reversible depolarization of spinal motor neurons [22].

The next AAs, in a significant amount represented in the brain, are inhibitory neurotransmitters: taurine, GABA and glycine.
Among the inhibitory mediators, taurine is contained in the largest amount.

As an inhibitory neuroactive amino acid, taurine activates receptors in nerve endings on neuronal membranes, causing partial depolarization of the cell membrane as a result of inactivation of Na+ channels. Taurine is involved in the regulation of hormone secretion, GABA and acetylcholine. Taurine is an inhibitor of GABA transaminase, a pyridoxal-dependent enzyme that catalyzes the breakdown of GABA, which contributes to an increase in the latter. As a glycine agonist, taurine reduces convulsive activity, i.e. it is a potential anticonvulsant. During the development of the brain, taurine affects cell migration, modulates neurotransmission in synapses. Along with GABA, taurine has neuroinhibitory properties and restores the concentration of intracellular ions during brain hypoxia. In addition, taurine, as an amino acid with mediator properties, has a number of other effects: it regulates osmotic pressure in the brain and has an antioxidant effect. Like other short-chain amino acids (glycine, β-alanine, GABA), taurine suppresses neuronal excitability, causing hyperpolarization. Endogenous synthesis of taurine occurs in the brain mainly through the decarboxylation of cysteine sulfinic acid (a product of the oxidation of cysteine) and hypotaurine, from serine, methionine, and also histidine. Inactivation of the amino acid in the brain synapses is carried out with the help of high-affinity reuptake. The uptake of taurine by glial cells is also described, which indicates the role of glia in the modulation of its mediator function. The effects of taurine are associated with the regulation of calcium transport in the nervous tissue. Taurine is a weak β-adrenergic agonist, it activates the K+-stimulated release of norepinephrine in the cerebral cortex. The release of taurine from the brain cells causes the release of adenosine into the cerebrospinal fluid, which indicates the involvement of taurine in the modulation of synaptic transmission. The transfer of taurine across cell membranes is associated with a change in cell volume. The release of taurine from cells is sensitive to Cl-channel blockers. Taurine transport is reduced by tyrosine kinase inhibitors and increased by tyrosine phosphatase inhibitors.

Gamma-aminobutyric acid (GABA).

One of the main components of the pool of free amino acids in the brain of various animals is γ-aminobutyric acid (GABA), a product of α-decarboxylation of glutamic acid. GABA is the most widely distributed inhibitory mediator in the nervous system. The cycle of GABA transformations in the brain includes three coupled enzymatic reactions, called the GABA shunt. The GABA shunt is a branch of the CAC from α-ketoglutarate to succinate. With the participation of the enzyme glutamate decarboxylase (GAD), the first carboxyl group of L-

glutamic acid is cleaved off with the formation of GABA. This enzyme is present only in the CNS, mainly in the gray matter of the brain, and is a marker of GABAergic synapses. The enzyme is synthesized in the perikarya of neurons and then rapidly transported along the axon. Like most other amino acid decarboxylases, GAD requires pyridoxal phosphate as a cofactor that is tightly bound to the enzyme. The rate of the GAD reaction is the limiting step in the formation of GABA. The level of GABA is regulated by the activity of GAD and does not significantly depend on the action of GABA degradation enzymes. Enzymes of GABA catabolism are isolated from GAD. GABA transaminase (GABA-T) is predominantly found in the gray matter of the brain, but is also found in other tissues. It contains pyridoxal phosphate as a cofactor and is strongly associated with it. GABA-T is located in mitochondria, while GAD and GABA are localized in synaptosomes. The final enzyme of the GABA shunt, succinic semialdehyde dehydrogenase, converts the latter into succinic acid, is cololiated with GABA-T in the mitochondria of CNS neurons, is specific for succinic semialdehyde and NAD+, and is activated by substances containing sulfhydryl groups [11].

Glycine

Is involved not only in protein synthesis, but also in other biosynthetic processes – the formation of porphyrins, cytochromes, creatine, choline, glutathione and is an inhibitory neurotransmitter in the spinal cord. It is also brain inhibitory neurotransmitter. It causes hyperpolarization of postsynaptic membranes by increasing the permeability for Cl- ions. Since the utilization of glycine in the nervous tissue is relatively large, and the intake from the blood is slow, a significant part of it is synthesized de novo in the brain. The main sources of glycine are glucose and serine. Synthesis of glycine de novo occurs in the nervous tissue by reversible methylenetetrahydrofolate-dependent transformation of serine with the participation of the enzyme serine hydroxymethyltransferase. In turn, serine can be formed from glucose through 3-phosphoglyceric acid and relatively quickly enters from the blood.

Aromatic amino acids

(tryptophan, phenylalanine and tyrosine) are important as precursors of mediators – 5-hydroxytryptamine (serotonin), methionine and catecholamines, which play an extremely important role in the functioning of the brain.

Tryptophan

Is an essential amino acid and is not synthesized in the human brain. From tryptophan, nicotinic acid (vitamin PP or niacin) is formed, which is a component of redox enzymes that play an important role in energy metabolism and a number of other metabolic transformations. In the organism, AA can be transaminated using oxaloacetic acid (OAA) as an amino group acceptor, and also decarboxylated to form serotonin and melatonin. The physiological significance of the first reaction is not recognized. About 5% of the total metabolism of tryptophan is used for the formation of the neurotransmitter's serotonin and melatonin. The content of tryptophan, and, consequently, serotonin in the brain is influenced by the nature of the food used; it increases with the intake of complete proteins and carbohydrate-rich food. Carbohydrates stimulate the release of insulin, which contributes to the entry into the muscles, and, consequently, the removal from the circulation of branched-chain amino acids – competitors of aromatic amino acids for the transport systems of the BBB of the brain. Thus, a decrease in the level of branched-chain amino acids in blood plasma leads to an increase in the transport of aromatic amino acids to the brain. In the regulation of tryptophan and serotonin levels in the brain, the kynurenine pathway of tryptophan catabolism, realized in the liver, plays an important role. This pathway is initiated by tryptophanpyrrolase, a liver enzyme that uses mainly tryptophan from food and is induced by both its substrate tryptophan and glucocorticoids. Growth hormone, in contrast, prevents the induction of tryptophan pyrrolase by tryptophan. Thus, liver tryptophan pyrrolase promotes the removal of excess tryptophan from blood plasma, which, in turn, minimizes changes in the tryptophan content in the brain [4, 16].

Phenylalanine

Is also an essential amino acid. It is transaminated and decarboxylated in the brain. The main metabolic pathway of this amino acid in the body is hydroxylation to tyrosine with the participation of the enzyme phenylalanine-4-hydroxylase, followed by the formation of the main catecholamine precursor dihydroxyphenylalanine (DOPA). With an enzyme deficiency observed in phenylketonuria, the conversion of phenylalanine occurs along the path of formation of phenylpyruvic and phenylacetic acids, which have a toxic effect on the brain [2, 14].

Tyrosine

Acts as a source of catecholamines in the brain. The conversion of tyrosine to catecholamines is the leading pathway for the metabolism of tyrosine in the brain. Under the action of the enzyme tyrosine-3-

hydroxylase, tyrosine is converted to 3,4-dihydroxyphenylalanine (DOPA). The main pathway for tyrosine degradation is via hydroxyphenylpyruvate, homogentisic acid, and aromatic ring cleavage. In the brain, active transamination of tyrosine occurs under the influence of the enzyme tyrosine-2-oxoglutarate aminotransferase. It is formed from phenylalanine; therefore, it is an essential amino acid in patients with phenylketonuria. Tyrosine also serves as a source of thyroid hormones, melanin, and affects the activity of nervous processes. It is also able to transform into a mediator with toxic properties – tyramine [3,6].

Sulfur-containing amino acids

(cysteine, cystothionine, methionine). Up to 20% of sulfur-containing amino acids are localized in synaptosomes. Cysteine, methionine are plastic materials.

Methionine

Is a neutral sulfur-containing AA, a donator of methyl groups. It enters the brain via active transport, like most neutral amino acids. The metabolism of methionine to cysteine begins with the formation of S-adenosylmethionine. The reaction is catalyzed by the enzyme methionine adenosyltransferase. S-adenosylmethionine is the main donor of methyl groups in the brain, necessary for the methylation of catecholamines, histamine, phosphatidylethanolamine, and nucleic acids. Methylation processes play an important role in signal transmission through the membrane, in the regulation of membrane fluidity, and in the formation of long-term memory. Methionine is a precursor of other sulfur-containing amino acids (cystathionine, cysteine), which have antioxidant properties, and glutathione, one of the main antioxidant molecules [6].

Homocysteine and cysteine

Are natural agonists of excitatory neurotransmitter amino acids [15].

Cysteine l

Is a non-essential amino acid synthesized from serine with the participation of methionine, ATP and vitamin B6. Acts as an inhibitory neurotransmitter. Cysteine has antioxidant properties and is a source for the formation of glutathione.

Cystathionine

Is a condensation product of homocysteine and serine with the participation of cystathionine synthase, is an intermediate product of the metabolism of sulfur-containing amino acids cysteine, methionine, participates in the synthesis of sulfatides and sulfated mucopolysaccharides. The content of cystathionine in the white matter of the brain is higher than in the gray matter [8].

In general, the main role in the functioning of the nervous system is played by AAs with the properties of neurotransmitters, aromatic and sulfur-containing AAs, which are sources of synthesis of a large number of biologically important compounds, and also participate in synaptic transmission as neurotransmitters and neuromodulators.

Thus, in connection with the multifunctionality of AA in the brain, it is important to study the shifts in the AA pool both in normal and pathological conditions, including as markers of various pathological processes.

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