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Opinion Article

Amino Acids that Play an Important Role in the Functioning of the Nervous System Review

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Abstract:

The purpose of this review is to summarize and systematize literature data on metabolism, functions, amino acids in the brain, as well as on their structure and classification. Amino acids play an important role in the metabolism and functioning of the brain. This is explained not only by the exceptional role of amino acids as sources of synthesis of a large number of biologically important compounds, such as neuropeptides and hormones, but also by their participation in synaptic transmission as neurotransmitters and neuromodulators, involvement in energy metabolism through the formation of components of the cycle of tricarboxylic acids and cytochromes. Brain-specific amino acids are noted: N-acetylaspartic acid, which performs the function of synthesizing proteins and peptides of the brain, and gamma-aminobutyric acid, which acts as a mediator of inhibition in the nervous system. A characteristic feature is the heterogeneity of the distribution of amino acids in different parts of the brain, with the most unevenly distributed neutrotransmitters (glutamic acid, taurine, glycine, gamma-aminobutyric acid). Determination of the activity of the enzyme systems of their metabolism can serve as an important diagnostic marker of the reaction of the central nervous system to damage in various cerebral and other pathologies. Also important is their energy value, especially in hypoglycemia. Despite the fact that glucose is used as the main source of energy in the brain, amino acids, in particular glutamic acid, are consumed in energy metabolism through the formation of Coenzyme A, oxaloacetic acid and other components of the tricarboxylic acid cycle, as well as cytochromes.

Keywords: amino acids; brain;enzyme systems

Introduction

Amino acids (AA) play an important role in the functioning and metabolism of the brain. They act as a source for the synthesis of a significant number of biological compounds, such as proteins, biologically active amines, lipids and mediators. But this is not their only role. Amino acids and their derivatives are involved in synaptic transmission as neurotransmitters and neuromodulators (glutamate, aspartate, glycine, GABA, taurine). Some AAs are involved in the formation of neurotransmitters of the nervous system: tyrosine - catecholamines; methionine - acetylcholine, DOPA, dopamine; serine and cysteine - taurine; histidine - histamine; tryptophan - serotonin; L-arginine - NO; glutamic acid – glutamate [3].

Research methods. Analysis and systematization of literature data on brain amino acids.

Research results. Essential AAs include: phenylalanine, valine, isoleucine, histidine, lysine, leucine, methionine, threonine, tryptophan, arginine; and to replaceable: alanine, aspartate, asparagine, glutamine, glycine, glutamate, serine, proline, tyrosine and cysteine [3].

Classification of AA by functional groups:

Aliphatic AAs are the largest group:

- monocarboxylic AAs (isoleucine, leucine, glycine, alanine and valine);
- hydroxyamino acids (serine and threonine);
- monoaminodicarboxylic AA, having a negative charge, due to the additional carboxyl group (aspartate and glutamate);
- diaminomonocarboxylic AAs (lysine and arginine);
- amides of monoaminodicarboxylic AAs (asparagine and glutamine);
- sulfur-containing AAs (methionine and cysteine).

Aromatic amino acids have a distinctive feature - a closed aromatic ring (Phenylalanine, tyrosine, tryptophan, histidine).

Heterocyclic AAs contain carbon cycles with other atoms (tryptophan, histidine, proline).

Imino acids (proline).

Some AAs belong to different groups. This is explained by their structure; it can simultaneously include both an aromatic ring and a heterocycle. Sulfur-containing AAs (serine, cysteine, cystathionine, taurine, methionine) protect

cell membranes from oxidative stress factors, as they have antioxidant activity. An important component of the antioxidant system of the cell is formed from glutathione - methionine. Cell membrane lipids, namely phospholipids, sphingolipids and lecithin, are formed from serine. Some AAs act as a substrate for vitamins: valine - pantothenic acid, tryptophan - nicotinic acid. AA metabolites are involved in the regulation of osmotic pressure in the brain - taurine, in the formation of circadian rhythms - tryptophan as a source of melatonin and histidine as a source of histamine. Some AA are involved in the storage and implementation of genetic information, as they are part of the nitrogenous bases of DNA nucleotides (aspartic acid - pyrimidine, glutamine - purine, serine - pyrimidine and purine) and histone proteins (glutamine). Some other AAs are involved in the formation of other amino acids. For example, glutamate is involved in the synthesis of glutamine, aspartate - alanine and asparagine, methionine - cysteine, cysteine - serine and taurine [4-8].

In brain tissue, on average, there are 34 mcM of amino acids per gram of tissue. It is able to maintain a relatively constant level of AA under various physiological and pathological conditions. The amount of free AA in the brain is much higher than their amount in the cerebrospinal fluid and blood plasma by 8-10 times. AAs are actively transported across the blood-brain barrier (BBB). This is due to the high concentration gradient of AA between the blood and the brain. The penetration of AA through the BBB is due to several systems of carriers. Irreplaceable AAs are more easily transported across the BBB than replaceable ones. Also, the rate of AA transport depends on isomerism - L-isomers have a greater ability to be transported through the BBB than D-isomers.

In the brain, a significant part (75% of free AAs) is glutamate, GABA, glutamine, N-acetylaspartic acids, aspartic acids, which act as mediators of the nervous system. In different parts of the brain, the content of AA varies, but the total amount of AA in the brain invariably remains constant. Compartmentalization of the pool of amino acids in various subcellular structures of nerve cells is characteristic, which reflects the morphological, physiological, and functional heterogeneity of the brain. Uneven distribution is more characteristic of AA with the function of a neurotransmitter (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, their incorporation into proteins, and their catabolism. The composition of free AA is stable under physiological conditions. Various organelles and glial neurons in the brain receive AA at an energy expenditure against a concentration gradient. Transportation of AA to the brain is a multi-step process. First, they penetrate through the BBB at the level of cerebral capillaries, and then they are transported from the extracellular fluid to brain cells and, finally, to organelles [10].

The transport of AA against the concentration gradient is affected by: energy potential, pH of the medium and temperature, connection of Na + ions with active membrane transport, inhibition by anaerobiosis and enzymatic poisons, competitive inhibition of AA transport through the membrane by other AAs.

For different AAs, the degree of specificity of transport systems, as well as the power, differ. More important is the specificity for amino acid neurotransmitters (GABA, glycine, glutamic acid, taurine, etc.). Transport systems are responsible for meeting the needs for energy and plastic material of the cell, as well as for the instantaneous decrease in the concentration of the neurotransmitter in the synaptic cleft. The presynaptic region and glial cells are highly selective for neurotransmitter uptake. [10-21].

The transport of AA into the cell is associated with the γ-glutamyl cycle. The leading enzyme is γ-glutamyl transpeptidase associated with the cell membrane. The enzyme can transfer a γ-glutamyl group from glutathione (inside the cell) to an amino acid (outside the membrane) and transfer the resulting dipeptide into the cell. The second cycle enzyme, γ-glutamyl cyclotransferase, releases AA. The cysteinylglycine dipeptide is cleaved into two amino acids by the action of peptidase - cysteine and glycine. Eventually, the amino acid molecule is transferred into the cell (or intracellular structure).

In subsequent reactions, glutathione is regenerated, so the cycle is repeated several times. The energy value of the transport of an AA molecule into the cell with the participation of the γ-glutamyl cycle is 3 ATP molecules. Under normal conditions, the rate of AA transport does not directly limit metabolism. Due to the speed of synthesis and decomposition, which are less than the speed of transportation. Because of this, AA accumulates in the brain and forms a pool of free AA. If you do not replenish the pool from the outside, it will quickly run out. The amount of AA used in the brain for the synthesis of proteins, neuropeptides and neurotransmitters in 30 minutes will be equal to the total pool of most free AAs in the brain. During brain development, the activity of AA transport systems changes, as does the composition of their pool. In young organisms, AA enter the brain more quickly and reach the highest concentrations earlier than in adults [23, 24].

Metabolism of dicarboxylic amino acids and glutamine

In the spinal cord and brain, glutamate and its derivatives make up more than 67% of the amino nitrogen in AA. Brain contains more N-acetylaspartate, glutamine and glutamate than peripheral NS. The content of GABA in the peripheral NS is insignificant, we can say that it is practically absent.

Glutamate (glutamic acid)

Glutamic acid is formed from α-ketoglutarate and other amino acids by a transamination reaction. Glutamine is a compound that allows you to remove ammonia, is formed with the participation of glutamate synthetase from glutamate. Glutamate is also a component of energy metabolism, since glutamate metabolism is associated with TAC through the formation of its substrate α-ketoglutarate in transamination reactions. If we conduct an experiment with injection of labeled glucose, then after 30 minutes a portion of glutamate and its derivatives will be responsible for more than 70% of the radioactivity. In the central nervous system, glutamate and α-ketoglutarate are rapidly converted into each other. It is assumed that the use of glucose in the brain occurs mainly due to the metabolism of AA. This assumption is associated with a high percentage of radioactivity transfer from glucose to AA. This assumption comes from the high percentage of radioactivity transfer from glucose to AA. The reaction of direct reductive amination with the participation of glutamate dehydrogenase or by transamination of α-ketoglutaric acid forms α-glutamate. The synthesis of glutamate (from α-ketoglutaric acid) in the brain tissue is carried out by the glutamate dehydrogenase reaction, which will cause the constant utilization of free ammonia in the amino groups of AAS. Transamination is the main pathway of glutamate oxidation in the brain**.** When TAC works adequately, the transaminase pathway is active, while the dehydrogenase pathway is inactive. When 2,4-dinitrophenol (an uncoupler of oxidative phosphorylation) is added to mitochondria, the number of macroergic compounds decreases, the transaminase pathway is inhibited, and the oxidation of glutamate along the duhydrogenase pathway is simultaneously activated. As a result, glutamate maintains α-ketoglutarate (TAC metabolite) at the proper level and supplies the reducing elements of synthetic processes in mitochondria. This ensures the important role of glutamate in providing the brain with energy. 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 central nervous system. In hepatic insufficiency, the concentration of ammonium increases, which causes hepatic coma, and its symptoms are alleviated by the administration of glutamate. The main part of glutamine synthetase is found in glial cells, and only a small part is found in nerve endings. The deamination of glutamine to form α-glutamate is catalyzed by glutaminase, the most active enzyme in neurons, where it resides in mitochondria. It is believed that this enzyme is involved in the transport of glutamate across the membrane and its activity in the brain is low. The reaction products - glutamic acid and ammonium - inhibit the activity of enzymes. Biological membranes are more permeable to glutamine than to glutamate, and the conversion of glutamine in the blood to intracellular glutamate is carried out by glutaminase. The enzyme also plays an important role in regulating the content of glutamate in nerve endings. The fact that glutamine synthetase is mainly found in glial cells, glutaminase is more active in neurons, and glutamine, the main precursor of glutamate and GABA, which acts as a messenger, suggests the existence of a glutamine

cycle. Glutamine acts as a glutamate transporter in glial neurons. Glutamate taken up by glial cells is converted to glutamine by a synthetase reaction, which enters neurons to form glutamic acid. Another important function of glutamate is participation in the synthesis of biologically active proteins and peptides. Together, glutamate and glutamine make up about 10% of all AA residues in the brain protein hydrolyzate. Glutamate is an integral part of many regulatory peptides in the brain, including glutathione and various 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. Administration of glutamate to various areas of the brain results in seizure activity. Glutamine, on the other hand, has no such effect. When administered intravenously, glutamate can cause neuronal death in the brain, especially in the ventricular region, where there is no BBB. Neurons in the neonatal period that do not develop a BBB are also very sensitive to the damaging effects of glutamate. It is known that glutamate is 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. Once glutamate is released from the synaptic cleft, its uptake is mediated by high-affinity Na-dependent transporters for neurons and, to a greater extent, for astrocytes. For the work of synapses with the participation of glutamate as a neurotransmitter, it is necessary to constantly replace its reserve in nerve endings. Glucose and α-ketoglutarate may be precursors to the glutamate transmitter pool. In addition, glutamate can be formed from ornithine and L-arginine (via glutamate semialdehyde). The main source is glutamine, most of which is synthesized in astrocytes containing glutamine synthetase. In addition, it easily penetrates the astrocyte membrane and, with the help of active transporters, reaches the nerve endings. [1-18].

Aspartic acid (aspartate).

It is found in high concentrations in cerebral along with glutamate. In its mitochondria, up to 90% of glutamate will undergo transamination and, as a result, aspartate will be synthesized. Aspartate aminotransferase (AST) is an enzyme that catalyzes transamination with the help of oxaloacetic acid, it is a strong transaminase in cerebral. Two AST isoenzymes are localized in the cytoplasm and mitochondria. Their functionality is different. The cytoplasmic fraction of the enzyme predetermines the intensity of gluconeogenesis, and the mitochondrial fraction is associated with the work of the TAC. Aspartate excites synaptic neuromuscular endings containing α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors (AMPA receptors). This amino acid has several specific transport systems that differ in 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 found only in the nerve endings of excitatory neurons. After excitation by potassium ions, the pool of aspartate accumulates in astrocytes as a precipitate in combination with glutamate. Along with the direct excitatory effect of dicarboxylic amino acids, their inhibitory effect on the hydrolysis of phosphoinositides was revealed. Some effects of aspartic acid on nerve transmission can be realized at the level of second messengers. Along with glutamate, aspartate is also involved in the pathogenesis of ischemic brain damage by acting on AMPA receptors. It is a glutamine mimetic. Causes reversible depolarization of spinal motor neurons [23].

N-acetylaspartic acid.

One of the main components of the pool of free amino acids in the brain is N-acetylaspartic acid (AcA). It is present in higher concentrations in the gray matter of the brain and spinal cord, it is also present in the peripheral nervous system, in the retina. Its concentration is low at birth and increases as the body develops. AcA is formed with the participation of acetyl-CoA. The function of AcA in the brain is not fully understood, but it is believed that it is part of the intracellular fixed pool of anions or acetyl group depots, and is also a source of N-acetylated end groups for the synthesis of certain proteins and peptides in the brain. The acetyl groups of exogenous AcA are a source of carbon for the synthesis of fatty acids in the developing brain [13-20].

Gamma-aminobutyric acid (GABA).

This is one of the main components of the free AA pool in the brain of various organisms. It is the most popular inhibitory mediator of the NS. It is a product of α-decarboxylation of glutamic acid. The metabolism of GABA in the brain consists of 3 enzymatic reactions and is combined in a cycle called the GABA shunt. It is a branch of TAC from α-ketoglutarate to succinate. The first carboxyl group of L-glutamic acid is cleaved off by the enzyme GAD (glutamic acid decarboxylase) to form GABA. The enzyme is found only in the CNS, predominantly in the gray matter, and will be a marker of GABAergic synapses. Its formation occurs in the perikarya of neurons and then its rapid transport along the axon occurs. Pyridoxal phosphate is required as a cofactor. In the formation of GABA, this process will be limited by the rate of GAD synthesis. The level of GABA is highly independent of the effects of enzymes that break it down. GABA catabolism enzymes are secreted from GAD. GABA transaminase (GABA-T) is localized predominantly in the gray matter of the brain, but it is also found in other tissues. It is strongly associated with pyridoxal phosphate, which is its cofactor. GAD and GABA are found in synaptosomes, while GABA-T is found in mitochondria. The terminal enzyme of the GABA shunt is succinic semialdehyde dehydrogenase, converts it to succinic acid, is grouped in mitochondria of CNS neurons with GABA-T, is characteristic of succinic semialdehyde and NAD+, and is activated by substances containing sulfhydryl groups [3].

Glycine

takes part in the formation of porphyrins, creatine, cytochromes, glutathione, choline. It is an inhibitory neurotransmitter of brain and spinal cord. Increases the permeability of the postsynaptic membrane for Cl- and thereby leads to hyperpolarization of the membrane. The consumption of glycine in the brain tissue is large, and its transport from the bloodstream is slow, so most of it will be formed directly in the brain tissue de novo. Serine and glucose are the main sources of glycine. De novo formation is carried out in the NS through a reversible methylenetetrahydrofolate-dependent transformation of serine by the enzyme serine hydroxymethyltransferase. Serine, on the other hand, is also formed from glucose through 3-phosphoglyceric acid and rather quickly enters from the bloodstream [4-23].

Arginine

is involved in protein formation and the synthesis of non-essential amino acids. L-arginine is a nitric oxide (NO) donor. The latter is an endothelium-relaxing factor formed with the participation of the enzyme NO-synthase. NO is involved in the regulation of cerebral blood flow as a vasodilator, performs mediator functions, and is able to exhibit antiaggregant, antioxidant, and anti-inflammatory properties [18-20].

Ornithine

is a diamino acid. It is also a precursor of polyamines, which perform a set of regulatory functions in the CNS [23, 24].

Taurine

is an amino acid with mediator properties. In addition, it has a number of other effects: regulation of osmotic pressure in the brain, antioxidant action. Like other short chain amino acids (glycine, β-alanine, GABA), taurine is involved in the suppression of neuronal excitability, causing hyperpolarization. Endogenous synthesis of this amino acid occurs in the brain mainly through the decarboxylation reaction of cysteine sulfinic acid (a product formed during the oxidation of cysteine) and hypotaurine, from serine, methionine, and also histidine. Inactivation of the amino acid in the brain synapses occurs with the help of high-affinity reuptake. The description of taurine uptake by glial cells 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, as a weak β-adrenergic agonist, activates K+ - stimulated release of norepinephrine in the cerebral cortex. Due to the release of taurine from the brain cells, adenosine is released into the cerebrospinal fluid, thereby indicating the involvement of taurine in the modulation of synaptic transmission. Taurine is found in high concentrations in the developing brain tissue and retina. The transfer of this amino acid across cell membranes affects the 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. In the hypothalamus, the protective effect of taurine

is realized through the adenylate cyclase mechanism. As an inhibitory neuroactive amino acid, taurine takes part in the activation of receptors in nerve endings on the membranes of neurohypophysis cells, thereby 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. In the neurohypophysis, it stimulates the release of vasopressin and oxytocin. Taurine is an inhibitor of GABA transaminase, a pyridoxal-dependent enzyme that catalyzes the breakdown of GABA, which increases the latter. As a glycine agonist, taurine reduces seizure activity, being a potential anticonvulsant. During brain development, taurine influences cell migration and modulates neurotransmission at synapses. Along with GABA, it has neuroinhibitory properties and restores the concentration of intracellular ions during brain hypoxia. In hepatic encephalopathy, a decrease in the content of taurine in the brain may be one of the causes of its edema [3, 4].

β-Alanine

provides inhibitory neurotransmitter functions in the brain (cerebellum and brain stem), as well as in some ganglia of the peripheral NS.

Sulfur containing amino acids.

Their representatives are methionine, cysteine and cystothionine. Approximately 20% of these AAs will be located in synaptosomes. The plastic material will be cysteine and methionine.

Methionine

is a neutral AA, contains sulfur in the structure, a donor of methyl groups. Like many neutral AAs, methionine enters the brain via active transport. Under the action of the enzyme methionine adenosyltransferase, AA metabolizes to cysteine and S-adenosylmethionine is formed - the most important donor of methyl groups in the brain tissue, which will be needed for the methylation reaction of catecholamines, phosphatidylethanolamine, histamine and nucleic acids. The latter reactions are important for the action of a signal across the membrane, the formation of long-term memory, and in the regulation of membrane fluidity. This AA also acts as a precursor to other AAs that also contain sulfur, such as serine, cysteine, and methionine. The last good antioxidants. Cysteine and homocysteine act as natural agonists of excitatory neurotransmitter AKs. If methionine metabolism is disturbed, accumulation of homocysteine will occur, which is a pathological metabolite characteristic of homocysteinemia. The causes of the pathological condition will be:

1. Deficiency of cyanocobalamin, pyridoxine and folic acid. They must bind to enzymes such as cystathionine synthase and methionine synthase. The latter play a major role in the metabolism of homocysteine and methionine.
2. Hereditary deficiency of the above enzymes. Dissolved in blood plasma, homocysteine activates lipid peroxidation in lipoproteins and traumatizes apoproteins, and, consequently, they are retained in the blood due to a violation of their adhesion to receptors. This is strongly pronounced for LDL, when the latter are oxidized, they are absorbed by macrophages in the intima of the vessels and subsequently leads to atherosclerosis. Homocysteine activates platelet aggregation and leads to injury of the endothelial layer of the vessel, activating the formation of thrombosis.

Cysteine

is a non-essential AA, which is formed from serine with the participation of methionine, adermin (vitamin B6) and ATP. It is an inhibitory neurotransmitter. Cysteine will be a source for the synthesis of glutathione. It also has antioxidant properties.

Cystathionine

is synthesized using cystathionine synthase from serine and homocysteine in a condensation reaction, it takes part in the synthesis of sulfatides and sulfated mucopolysaccharides and is an intermediate product of the metabolism of sulfur-containing AAs. The concentration of cystathionine in brain in the white matter is greater than in the gray matter. Its level in rat brain tissue decreases during development, while in humans it increases. Its concentration in the brain can increase under the influence of neurotoxic substances, as well as in certain mental disorders. [16, 17].

Aromatic amino acids

such as phenylalanine, tryptophan, and tyrosine play a large role as precursors for serotonin (5-hydroxytryptamine), catecholamines, and methionine, which play a major role in brain function.

Tryptophan is an essential amino acid that is not produced in the brain. Due to the discrepancy between the minimum nutritional requirements in the diet, protein synthesis disorders may appear. A component of redox enzymes that are involved in energy metabolism and other metabolic reactions - nicotinic acid, is synthesized from tryptophan. With the help of oxaloacetic acid (amino group acceptor), tryptophan is transaminated and can be decarboxylated, resulting in the synthesis of methionine and serotonin. Only 5% goes to the metabolism of tryptophan for the synthesis of neurotransmitters (melatonin, serotonin). When the diet is rich in complete proteins and carbohydrates, the content of tryptophan in brain tissue is higher. And from this we can conclude that the content of serotonin is also greater. Carbohydrates activate the release of insulin, which contributes to the entry into the muscles, and, consequently, the removal of branched chains of AA - competitors of aromatic amino acids for the transport systems of the BBB of the brain. A decrease in the concentration of branched AAs in plasma causes an increase in the transport of aromatic AAs into the brain tissue. In the liver, the kynurenine pathway of riptofan catabolism occurs; it plays an important role in the regulation of the level of serotonin and tryptophan in the brain tissue. The pathway is activated by the hepatic enzyme tryptophan pyrrolase, which utilizes dietary tryptophan and is induced by both its substrate tryptophan and glucocorticoids. The activation of the enzyme is inhibited by somatotropic hormone. Thanks to tryptophanpyrrolase of the liver, excess tryptophan is removed from the blood, and this makes changes in the concentration of tryptophan in the brain tissue minimal [2-4].

Phenylalanine is an essential AA. Its decarboxylation and transamination occur in the brain tissue. Under the action of the enzyme phenylalanine-4-hydroxylase, it is hydroxylated to tyrosine and then DOPA is formed - this is the main metabolic chain. In conditions of enzyme deficiency in pathological conditions, such as phenylketonuria, the change in phenylalanine is carried out along the path of synthesis of phenylacetic and phenylpyruvic acid. The latter have a toxic effect on brain tissue [3-16].

Tyrosine is a source of catecholamines such as epinephrine and norepinephrine. It is metabolized in the brain tissue by the formation of catecholamines, which is the main pathway of tyrosine metabolism. When exposed to the enzyme tyrosine-3-hydroxylase, 3,4-dihydroxyphenylalanine (DOPA) is formed from the latter. The predominant pathway for tyrosine degradation occurs via homogentisic acid, hydroxyphenylpyruvate, and ring cleavage. Its intensive transamination occurs in the brain tissue under the action of the enzyme tyrosine-2-oxoglutarateamine transferase. In a pathological condition such as phenylketonuria, it is an indispensable AA, since it is synthesized from phenylalanine. The formation of thymine mediator from tyrosine is possible. The latter acts as a source of thyroid hormones and affects the activity of processes in the brain tissue. [2].

Histidine is an irreplaceable AA, which is a precursor of the histamine neurotransmitter, metabolism occurs under the action of non-specific aromatic AA decarboxylase. Synthesis of histidine does not occur in the brain; however, its active synthesis occurs in the BBB. Metabolism goes to the TAC, is involved in it through α-ketoglutarate, which is synthesized from glutamate [3- 6].

Lysine is an irreplaceable AA, with insufficiently studied functions. Its catabolism occurs in the brain with the transformation into pipecolic acid. If there is a failure of lysine metabolism in other tissues, then the NS reacts to this with severe demyelination and destructive processes, which is accompanied by mental retardation [15- 24].

Summing up, we can say that AA play an important role in the metabolism and brain function. AA act not only as a source of synthesis of biologically important substances, but also as neurotransmitters and neuromodulators, thereby participating in synaptic transmission. Through the synthesis of TAC components and cytochromes, they are also involved in energy metabolism.

Acts as a significant marker in the diagnosis of various cerebral and other disorders by finding the activity of the metabolism of enzyme systems.

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