ISSN: 2754-4737

Journal of Neurology Research Reviews & Reports

Research Article Open Access

Neuroglial Cells Have Liver Function for the Brain

Nugzar G Aleksidze

GEOMEDI University, Georgia

Abstract

Recently, the noteworthy results have been published regarding the uptake and degradation of biologically active substances, neurotransmitters, amino acids and carbohydrates by neuroglial cells and their inactivation as it takes place in the liver of living organisms. Based on the above-said, an assumption was made that the neuroglial cells in the brain, presented in biologically active glial-synaptic and neuron-neuroglial regions, should perform a similar function as the liver does. The functions of the liver are well known and determined by the excess accumulation of metabolic and physiologically active substances in the organism by means of inactivation, degradation and detoxication. For this purpose, the neurolectins existing in glial cells were specially studied. Based on the preliminary data, by means of them, the inhibition of agglutination of blood trypsinized erythrocytes took place via biologically active substances, neurotransmitters and aminoacids. This indicates that by means of neuroglial cells it is possible to uptake the above-said substances and then their degradation and inactivation in the cell. Based on the obtained data, it should be recognized that the neuroglial cells in glial-synaptic and neuron-neuroglial regions, the neuroglia should be considered as a structural formation having liver function in the brain.

Corresponding author: Nugzar G Aleksidze, GEOMEDI University, Georgia. Email: aleksidze.nugzar@yahoo.com

Received: February 28; **Accepted**: March 09, 2020; **Published:** March 15, 2020

Keywords: Neuroglial Cells, Liver Function, Brain

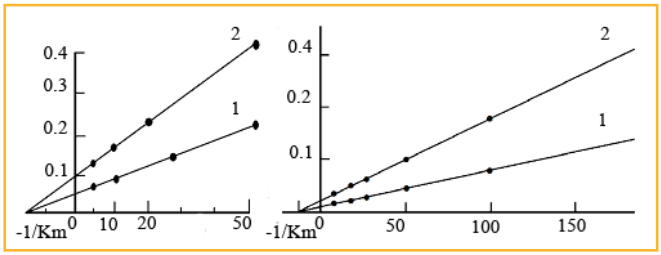
Introduction

The uptake and the inactivation of biologically active substances intensively take place at the level of glial cells plasma membrane and intracellular [1]. The example of the first way of the inactivation is a hydrolytic decay of excitatory neurotransmitter acetylcholine by glial cells at the level of plasma membrane. It has been established that glial cells membrane are characterized by a high acetyl- and butyrylcholinesterase activity [2]. Which facilitates an extraneuronal inactivation of hydrolysis of acetylcholine excess accumulated in presynaptic sites. For the inactivation of biologically active substances, their preliminary uptake is necessary. The mechanisms of uptake were studied using the methods of kinetic analysis, which gave us the opportunity to establish that 75% of neurotransmitters released in synaptic regions were absorbed by means of reverse uptake via nerve endings by a high affinity to the substrate (uptake I). Extraneuronally, their absorption took place to a extent

(uptake II) by glial cells [1].

Results

The uptake of neurotransmitters, biologically active substances and aminoacids has widely been studied for this purpose. On the below Figure the uptake of serotonin-C^{14} and dopamine-H^3 (0.25 mg protein 1 ml) by neuroglial cells and synaptosomes is presented in the following incubation media: 100 mM- NaCI, 6 mM - KCI, 2 mM - $CaCI_2$, 3 mM - $MgCI_2$, 10 mM – glucose, 100 mM – saccharose in 30 mM triphosphate buffer, pH 7.4 [3, 4]. The results are given on the Figure 1.



A B

Figurre 1: The kinetics of serotonin-C^{14} uptake by synaptosomes (A, 1) and neuroglial cells (A, 2), and dopamine-H^3 – by synaptosomes (B, 1) and neuroglial cells (B, 2) of rabbit cerebral cortex. (Linewiver-Burke schedule, data of 5-7 experiments).

In case of serotonin, Km of the uptake by synaptosomes and glial cells equals to 0.083±0.002 mkM. As it turned out, in case of dopamine uptake by glial cells occurred with a high affinity [3-4]. As well as an uptake of γ-aminobutyric acid by glial cells (Km - 31 mkM [5]. However, as compared to neurons, uptake of γ-aminobutyric acid by neuroglial cells takes place 100 times more intensively. It has been established that the uptake processes are regulated by ATP and potassium concentration [6-9].

The inactivation of catechol indolamines occurs by means of their uptake and intracellular catechol methiltransferase via methylation or monoamine oxidase by oxidative deamination [10]. After the discovery of the neurolectins of rat brain glial cells [11-12]. We undertook the experiments to study the mechanisms of their possible participation in the uptake and inactivation of neuro¬transmitters, biologically active substances and amino acids. For this purpose, the brain glial cells enriched fraction was prepared according to Rose method, modified by us [2-13].

The extraction of neurolectins from the enriched fraction of glial cells was performed with 0, 5 мМ Triton X-100. After homogenization, the mixture was centrifuged (10000 g/30 min.). The supernatant was fractionated with ammonium sulfate of various saturations (40, 60, and 80%) and then again centrifuged (10000 g/30 min.). The precipitate was dissolved in an agglutinating solution (0.9 % NaCI/ 40 mM potassium phospat buffer (pH 7.4) and after dialysis, the activity of neurolectin was determined visually using micro titration method by Takachi [14]. It has been established that neurolectins isolated from glial cells enriched fractions showed a carbohydrate specificity for D-fructose (16.2 mM), D-xylose (16.2 mM), N-acetyl-D-galactosamine (9.3 mM) and inositol (4.6 mM) and was designated as glial lectins GL-FXAI. After the detection of carbohydrate specificity of lectins by the hapten-inhibitory method [15]. The neurolectins were purified by affinity chromatography on a column of tris-acryl-inositol and tris-acryl-galactose to obtain glial lectins with the highest lectin activity. The specific activity of neurolectins of neuroglia made up 71.3±1.12 units on an average [11-12].

The molecular masses of the obtained neurolectins were measured using the HPL chromatograph system (Millipore-Waters, USA). The molecular mass of glial lectins made up respectively 11.5 kDa on an average. Glial lectins appeared to be glycoproteins; the content of carbohydrate residues was 26-28±0.5%. It should be noted that neurolectin GL-FXAI contains the following amino acids: leucine, isoleucine, valine, phenylalanine, tryptophan, glutamic acid, threonine, glycine, serine, glutamine, asparagine, arginine, praline and tyrosine [11-12]. At the same time, the presence of SH-groups was noted in glial neurolectins, which was established by the Ellman method and the method developed by us [16-17].

The number of SH-groups per mg/ protein for GL-FXAI was 12-15x10-4 M on an average. Glial neurolectins showed a particular sensitivity to Ca^{2+} ions and were maximally inhibited in the presence of 0.2 mM Ca^{2+} of EGTA chelator [11-12]. Taking into account a strategic role of glial cells in the uptake and inactivation of neurotransmitters, biologically active compounds and amino acids, based on the presented material, the determination of the orientation of GL-FXAI lectins active center on the membrane of glial cells was of great interest. The first duty an attempt was made to study the effect of neuroglial cells on the hemagglutination of trypsin zed rabbit erythrocytes. Using the hapten-inhibitory method, it has experimentally been shown that the inhibitory

effect of neurolectins sensitive to haptens of D-fructose, D-xylose, N-acetyl-galactose and inositol (GL-FXAI) on hemagglutination of trypsin zed rabbit erythrocytes is blocked by amino acids at the appropriate concentrations: L-arginine (37.5 mM), L-serine (18.7 mM), L-glutamine (9.4 mM), tyrosine (37.5 mM), acetylcholine (0.62 mM), β-alanine (0.156 mM), serotonin (0.32 mM), adrenaline (1.25 mM), norepinephrine (0.62 mM), dopamine (0.156 mM), tyramine (0.63 mM), hydroxytyramine (0.156 mM), choline bromide (0.08 mM) and hydroxytryptamine (1.25 mM). It is important to note that a number of other biologically active substances also had an inhibitory effect on the activity of GL-FXAI neurolectins, but only at a relatively high concentration [11-12]. The results of these experiments indicate that glial cell neurolectins can be involved in the uptake and inactivation of a number of biologically active substances, neu¬rotransmitters and amino acids.

First of all, it has been shown that native glial cells cause the agglutination of trypsinized rabbit erythrocytes. The agglutination of trypsinized rabbit erythrocytes by neuroglia was completely inhibited by amino acids and biogenic amines: L-arginine, L-serine, L-glutamine, tyrosine, acetylcholine, β-alanine, serotonin, adrenaline, norepinephrine, dopamine, tyramine, hydroxytyramine, choline bromide, hydroxytryptamine and inositol. This suggested that the GL- FXAI active center on the membrane of glial cells is oriented toward the outer side of the membrane in the direction of the intercellular space [11-12].

The question arises regarding the role of GL-FXAI neurolectins, which are oriented to the outer side of the glial cell membrane. It is more likely that after finding the fact that neuro¬transmitters, amino acids, and biologically active substances have an inhibitory effect of neuroglia on agglutination of trypsinized rabbit erythrocytes by the use of hapten-inhibitory method, it has been suggested that GL-FXAI neurolectin can actively participate in the uptake and transport of neurotransmitters, amino acids, and biologically active substances excess in the glial-synaptic and neuron-neuroglial regions and their metabolism and inactivation. It was previously shown that in conditions of an excess of neurotransmitters in the neuron-neuroglia-synaptic region, an active inactivation of acetylcholine and uptake of serotonin, dopamine and γ-aminobutyric acid by glial cells occur. It is worth noting that the uptake of serotonin by glial cells and their inactivation actively occurs by conjugation with glucuronic acid, resulting in the formation of a biologically inactive compound glucuronide-serotonin [18]. The uptake of dopamine, serotonin and γ-aminobutyric acid by glial cells of the rabbit cerebral cortex also occurs in the same way [3-4].

After detecting the pulsation of glial cells [20], the idea of the presence of non-muscle contractile proteins arose, which, in our opinion, should participate in the processes of uptake of neurotransmitters, biologically active substances and amino acids. Later, based on the properties of pulsation of glial cells, first a non-muscle contractile protein was separated, which was named gliostenin [20-22]. Based on the kinetic characteristics, gliostenin appeared to be a non-muscle contractile protein of allosteric nature. It has been proved that a non-muscle contractile protein gliostenin, identified and purified by us, participates in the mechanisms of pulsation of glial cells, which is well shown on the below Figure 2.

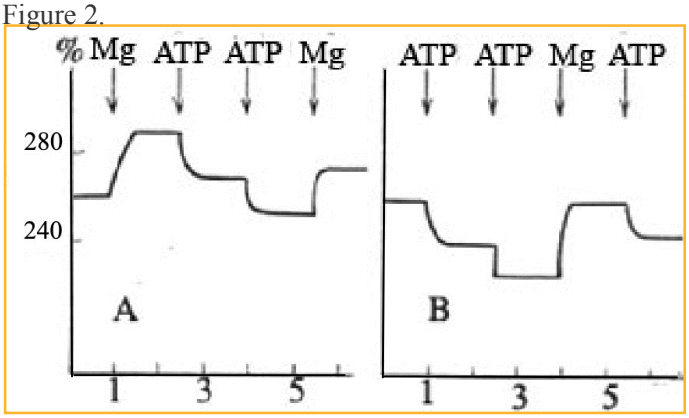


Figure 2: Contraction-relaxation of gliostenin in the conditions of permanent addition of Mg ions and ATP. Gliostenin concentration (47 mkg/ml) was dissolved in 0.1 M KCl solution, in the presence of 30 mM tris HCl coexistence (pH 7.4). On the abscissa - wave length in nm, below - time in minutes. On the ordinate – optic density in 240-280 nm extinction.

As seen from the above Figure 2, based on light scattering, the reaction of contractile protein gliostenin association (contraction – at Mg addition) and dissociation (relaxation – at ATP addition) was observed. The maximum spectrum of uptake is 260-280 nm. A characteristic sign of gliostenin is a specific reaction while adding Mg ion and ATP. At the addition of Mg, a light scattering enhances, which indicates the polymerization and aggregation of gliostenin subfraction. On the contrary, when adding ATP, a reduction of light scattering takes place, which indicates a dissociation of gliostenin. Initially, it was electrophoretic ally proved that in conditions of ATP addition to gliostenin, a decay of

gliostenin into actin and myosin was noted. It is noteworthy that gliostenin has been found to have Na+-K+ ATP-ase and Ca+-ATP-ase activity. By means of them, the rocesses contraction and relaxation are actively accomplished [23-24].

Conclusion

It has been shown that at an excess accumulation of neurotransmitters, biogenic amines, amino acids, and biologically active substances in brain neuroglial-synaptic and neuron-neuroglial physiologically active regions, their active uptake by neuroglial cells occurrs. Non-muscle contractile protein – gliostenin by means of pulsation actively participates in the uptake of neurotransmitters, and biogenic amines, and stimulates their metabolism and detoxication. Thus, we can conclude that the neuroglial cells can be recognized, as a cellular structural unit having liver function for brain.

References

1. Aleksidze N (1988) Molecular and cellular mechanisms of integative activity of the brain. Tbilisi State University 500 p.
2. Aleksidze N, Akhalkatsi R, Balavadze M (1974) Comparative Study of AChE and BHE activity of the brain cortex, enriched fractions of glial and neuronal cells. Bull. Acad. 56-60.
3. Bakhanashvili TA, Maysov NI, Aleksidze NG, Raevsky KS (1978) Uptake of tryptophan by glia cells and synaptosomes of the rabbit cortex. Bull. Of expert. Biol. and med. 85: 172-175.
4. Bakhanashvili TA, Maisov NI, Aleksidze NG (1980) Uptake of dopamine-H3 by glial cells and synaptosomes of rabbit cerebral cortex. Bull. Georg. Acad. Sci., Ser. Biol. 6:273-276
5. Maysov NI, Raevsky KC, Aleksidze NG, Bakhanashvili T (1977) the capture of gamma-aminobutyric acid by glial cells and synaptosomes of the rat brain during the action of psychotropic substances. Bull. Of expert. Biol. and med 5:56-59.
6. Aleksidze N, Meshvelishvili D (1969) on acetylcholine regulation of the level of inhibitory mediator of gamma-aminobutyric acid in cuts of the brain. Academy of Sciences of the GSSR, 56:213-217.
7. Machiyama Y, Balazs R, Hammond BJ, Julian T, Richter D (1970) the metabolism of γ-aminobutirate and glucose in potassium ion-stimulated brain tissue in vitro. Biochem 116:469-474.
8. Henn FA, Hamberger S (1971) Glial cell function: uptake of transmitter substances. Proc. Nat. Acad. Sci. (USA) 68:2686-2695.
9. Shon F, Kelly JS (1974) the characterization of [3H] GABA uptake into the satellite glial cells of rat sensory ganglia. Brain res 66:289-296.
10. Mak Ilvein G (1962) Biochemistry and central nervous system. London.
11. Koshoridze NI (2001) Biochemical characteristics of neurolectins of subcellular fractions of nerve cells of embryonic and mature chickens 46.
12. Lekishvili T, Koshoridze N, Aleksidze G, Aleksidze N (1999) Biochemical charac¬teri¬zation of brain glial cells lectin. Bull. Acad. Sci. Georg 159:337-339.
13. Rose S (1967) Preparation of enriched fractions from cerebral cortex containing metabolically active neuronal and glial cells. Biochem 102: 33-43.
14. Takatsy G (1967) Lectins as molecules and tools. Symp. Series Immunobiol. Standard. 4: 275-280.
15. Liener I (1976) Hapten inhibitory techniques. Ann. Rev. Plant Physiol. 27:291-319.
16. Ellman GL, Kcourtney YD, Andres V, Feather-Stone RM (1961) Rapid Colorimetric determination of acetylcholinesteraze activity. Biochem. Pharmacol 7:88-95.
17. Aleksidze N, Koshoridze N (1980) Determination of sulfhydryl groups by laboratory titrator T-201. Bull. Experimental Biology and Medicine 6: 66-68.
18. 18. Aleksidze T, Khanashvili T, Goguadze R, Balavadze MK (1983) the issue of inactivation of serotonin in the cells of the world in the blood with a glucose card slot. Сообщ. АН ГССР, 8: 621-624.
19. Chang JJ, Hild W (1959) Contractile responses to electrical stimulation of glial cells from the mamm¬alian central nervous system cultivated in vitro. J. Cell Comp. Physiol. 53: 139-144.
20. Sandalov YG, Glebov RN, Kryzhanovski GN, Chipashvili MD, Beletskaya RP, et al.(1977) Actomyosin-like protein isolation from the bovine brain cells and its properties. Bull. Exp 8: 280-282.
21. Chipashvili MD, Aphadze MG, Beletskaya RP, Aleksidze NG (1980) Unders¬tanding biochemical identity of actomyosin-like proteins of neuronal and glial origin. Bull. Georg. Acad 100: 681-684.
22. Davitashvili E, Chipasvili M, Menabde K, Aleksidze N (1999) the glycoprotein nature of rat's brain actomyosin-like protein. Bull. Georg. Acad 159: 498-502.
23. Koshoridze NI, Menabde KO, Surguladze NB, Vardiashvili TM, Solomonia RO, et al. (1999) Effects

of endogenous lectins on HCO3-ATPase activity of the brain glia cells. Ukr. Bioch. J., 79:12-18.

24. Vardiashvili T, Koshoridze N, Menabde K, Aleksidze N (2006) HCO3-ATPase of bovine brain. Proc. Georgian Acad 32: 465-471.