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MULTIVOXEL MAGNETIC RESONANCE SPECTROSCOPY IN THE DIAGNOSIS OF BRAIN TUMORS

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Abstract:

To study the possibilities of multivoxel magnetic resonance spectroscopy (MRS), patients with brain tumors were examined. Verification of the tumor was carried out by histological examination of the surgical material. Hydrogen MR spectroscopy revealed significant differences in the content of metabolites between tumor types. Compared to tumors of the neuroectodermal tissue, tumors of the meningovascular series were characterized by minimal values of the proportion of N-acetylaspartate and the presence of alanine metabolite. Glial tumors were characterized by intermediate values of the shares of N-acetylaspartate, creatine, as well as the absence of alanine content. The use of MRS is advisable not only for the purpose of differential diagnosis of various types of tumors, but also in situations where the data of conventional MRI do not correspond to the obtained clinical manifestations, as well as to clarify the degree of anaplasia of glial tumors.

Keywords: Magnetic resonance spectroscopy, brain, glial tumors, meningiomas.

INTRODUCTION:

Technological progress, improvement of the hardware base and development of software have made it possible to make significant progress in understanding the etiology and pathogenesis of many diseases, as well as significantly improve the results of treatment. In many ways, these changes became possible only with the advent of new high-tech methods of radiation diagnostics. In the last few decades, there has been a rapid development of the diagnostic field of medicine. The possibility of non-invasive study of morphological changes occurring in the patient's body has radically changed a number of medical specialties.

Modern neurosurgery and neurology are currently unthinkable without magnetic resonance imaging (MRI). However, it should be recognized that, as a rule, according to MRI data, only macroscopic morphological changes can be detected, while functional changes that lie at the biochemical level often turn out to be unrecognized. In this regard, magnetic resonance spectroscopy (MRS) is promising in this regard, which makes it possible to noninvasively determine the biochemical composition of the tissues of the examined organism in vivo.

With the introduction of MRS into clinical practice, it became possible to rethink the existing diagnostic algorithms. The use of MRS for the purpose of differential diagnosis of brain tumors is of paramount importance for a number of complex diagnostic tasks. The most common brain tumors in adults are gliomas. Although their incidence is low in relation to other malignant diseases, their mortality is high .

THE PURPOSE OF THE STUDY

Was to evaluate MRS data in the differentiation of brain tumors.

MATERIAL AND RESEARCH METHODS.

An examination was carried out on an Optima MR450w GEM 1.5T magnetic resonance tomograph. The MRS technique is based on two physical phenomena — nuclear magnetic resonance and chemical shift of the resonant frequency. To study the possibilities of proton MRS in the diagnosis of brain tumors, we examined 48 patients.Verification of the diagnoseswas carried out during the operation, followed by a histological examination of the surgical material.

RESEARCH RESULTS:

Analysis of the MRI characteristics of brain tumors was performed according to the following parameters: change in the intensity of the MR signal; assessment of the structure of the tumor (homogeneity, heterogeneity), the presence or absence of per focal edema, the presence or absence of dislocation of the ventricular system, the presence of hemorrhage, cysts and calcifications, the nature of the accumulation of the contrast agent.

The study group included patients with the most common types of brain tumors: glial brain

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tumors - 33 (68.8%), meningiomas 10 (20.8%), brain metastases 5 (10.4%).

To compare the data obtained by hydrogen MR spectroscopy with morphological changes, according to the results of histological analysis, 33 patients with glial brain tumors were divided into 3 subgroups depending on the degree of anaplasia (Grade):

Subgroup I - 8 patients with Grade II neuroectodermal tissue tumors (fibrillar-protoplasmic astrocytoma, oligodendroglioma);

subgroup II - 14 patients with Grade III neuroectodermal tissue tumors (anaplastic astrocytoma);

Subgroup III - 11 patients with tumors of the neuroectodermal tissue Grade IV (glioblastoma).

On native MR tomograms, astrocytomas with a low degree of anaplasia (Grade II) were characterized by a reduced MR signal on T1-WI, increased on T2-WI, a predominantly homogeneous structure, without perifocal edema, necrosis, and hemorrhage. Accumulation of paramagnetic contrast agent in tumors was not detected in approximately 88% of cases. Mandatory signs in most cases were the deformation of the ventricular system and the displacement of the median structures.

On MRI scans, anaplastic astrocytomas (Grade III) were formations with a pronounced heterogeneous signal on both T1 and T2 WI, with fuzzy and uneven contours. On T1-WI, pathological areas of mixed iso- and hypointensity of the MR signal were detected. On T2-WI, anaplastic astrocytomaswere characterized by a heterogeneous increase in the intensity of the MR signal: a brighter signal was determined from foci of cystic degeneration, a less bright one, from the solid part of the tumor. Perifocal edema in varying degrees of severity was detected in all patients with anaplastic astrocytomas. "Mass effect" in the form of displacement and deformation of the median structures was also observed in all patients. Contrast enhancement was observed in 79% of patients. Contrast in anaplastic astrocytomas on MRI was more often diffuse-focal in nature, less often of an "annular" type.

Glioblastoma (Grade IV) on MRI was characterized by the presence of a formation with a heterogeneous change in the intensity of the MR signal (iso-, hypo-, hyperintense signal in T1-WI, iso- and hyperintense signal in T2-WI). Glioblastomas are characterized by the presence of multiple areas of necrosis, hemorrhage, richly vascularized stroma and perifocal edema, deformation of the ventricular system, and displacement of midline structures. Typical for glioblastoma was the absence of boundaries between the tumor, the zone of perifocal edema and the normal brain matter. When contrasting on T1-WI, all patients visualized extensive areas of pathological accumulation of the contrast agent according to the "ring-shaped" or "diffuse-focal" type.

Hydrogen MRS was performed in all patients immediately after conventional MRI. Depending on the location and size of the tumor, multivoxel spectroscopy was used. Voxels containing only tumor tissue (without areas of necrosis, hemorrhage and edema) were evaluated, their number ranged from one to eight and averaged three voxels. The obtained spectra were compared with the spectra of the contralateral side from the unchanged brain substance. After obtaining the spectra and processing the data, for more objective information about the characteristics of the tumor, the values of all voxels in each case were averaged.

Tumor invasion into surrounding normal tissues, intravasation and extravasation of tumor cells are largely provided by a wide range of proteases expressed by tumor cells - enzymes that cause degradation of the extracellular matrix. By proteolytically destroying various structures of the extracellular matrix — basement membranes and interstitial stroma, proteases "pave the way" for migrating tumor cells deep into surrounding tissues.

N-acetylaspartate (NAA) is a derivative of amino acids synthesized in neurons and further transported along axons. In glial tumors of the brain, axons, neurons, and dendrites are destroyed, with the development of an insufficiency of the enzyme system involved in aspartate acetylation, which leads to a decrease in its content. Substituted choline phosphates are the structural basis of phospholipids, the most important building material of basement membranes. With glial tumors of the brain, cell membranes are destroyed, with the release of choline (Cho), as a result of which its content increases.

The resulting amount of ATP is not enough to cover the energy needs during active cell proliferation of tumors. Therefore, in addition to oxidative phosphorylation (the Krebs cycle), additional ways of obtaining ATP are formed - anaerobic glycolysis and serinolysis (serine is first converted into 3-phosphoglycerate, and then into pyruvate and lactate with the formation of ATP) with the formation of the final product - lactate (Lac).

As a result, the most significant changes in patients with glial brain tumors in comparison with the unchanged brain substance of the contralateral side

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were: a decrease in the proportion of NAA, an increase in the proportion of Cho and Lac (Table 1).

With an increase in the degree of anaplasia and cell proliferation, a more active proteolytic destruction of the basement membranes of presynaptic cell endings occurs, with a break in the connection of choline with proteins and the registration of its increased content in the spectrum.

Cell proliferation is a process that requires a lot of energy. The higher the degree of anaplasia and the rate of cell proliferation, the more active are additional processes for obtaining energy - anaerobic glycolysis and serinolysis with the formation of lactate. In addition, in highly malignant tumors, areas of necrosis make the largest contribution of lactate

Table 1
Comparison of MRS indicators in glial tumors

	Glialtumors Me (25 %; 75 %)	**Unalteredbrainmatter Me (25 %; 75 %)**
shareNAA	12,59 (7,34; 19,31)	44,13 (41,17; 47,07)
shareCho	43,91 (39,89; 47,71)	28,21 (26,67; 30,0)
shareCr	21,04 (14,13; 31,16)	27,54 (25,15; 28,97)
shareLac	19,55 (13,8; 24,42)	0,0 (0,0; 0,23)

Analyzing the results, it was noted that the higher the degree of anaplasia of the brain glial tumor (Grade II-Grade IV), the significantly higher the values of the Cho/Cr and Lac/Cr ratios (Fig. 1, Fig. 2).

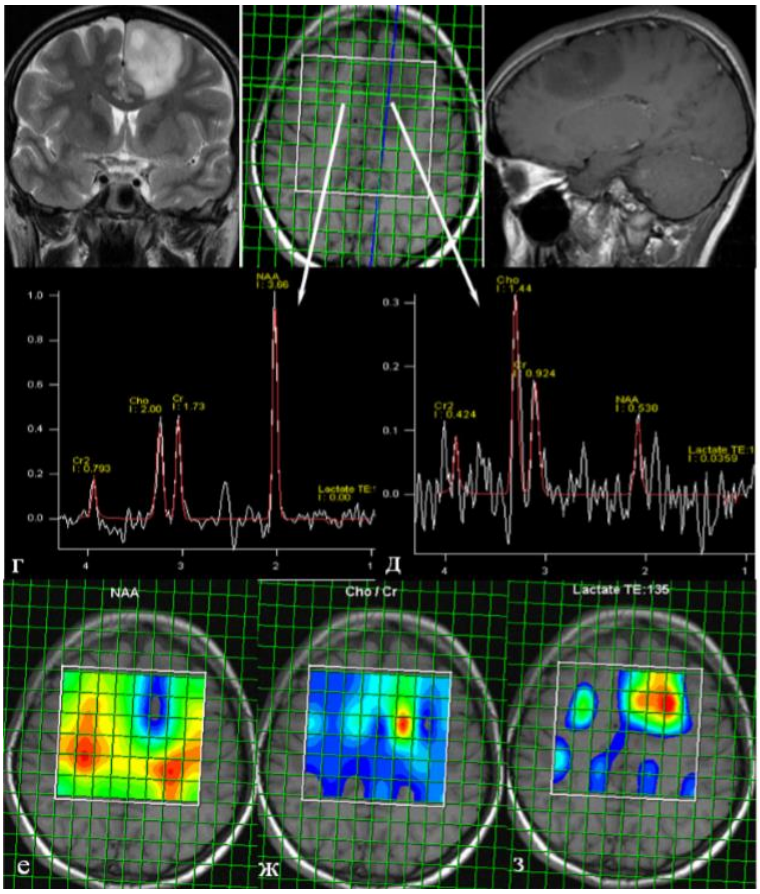

Figure 1 (a, b, c, d, e, f, g, h). Patient I., 29 years old. Fibrillar-protoplasmic astrocytoma of the left frontal lobe.

On MR tomograms (Fig. 1) in the left frontal lobe, a formation is determined, characterized by a hypointense MR signal on T1-WI (b) and a hyperintense signal on T2-WI (a). On post-contrast T1-WI (c), the intensity of the MR signal from the formation did not change. On the spectrum and color mapping images (e, f, g, h) for fibrillar-protoplasmic astrocytoma, compared with the spectrum from the

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unchanged brain substance of the contralateral side (d), the following is characteristic:

- decrease in the content of N-acetylaspartate (NAA);
- a slight decrease in the content of creatine (Cr);
- decrease in NAA/Cr ratios (0.58);
- the appearance of lactate (Lac);
- an increase in the Cho/Cr (1.56) and Lac/Cr (0.51) ratios.

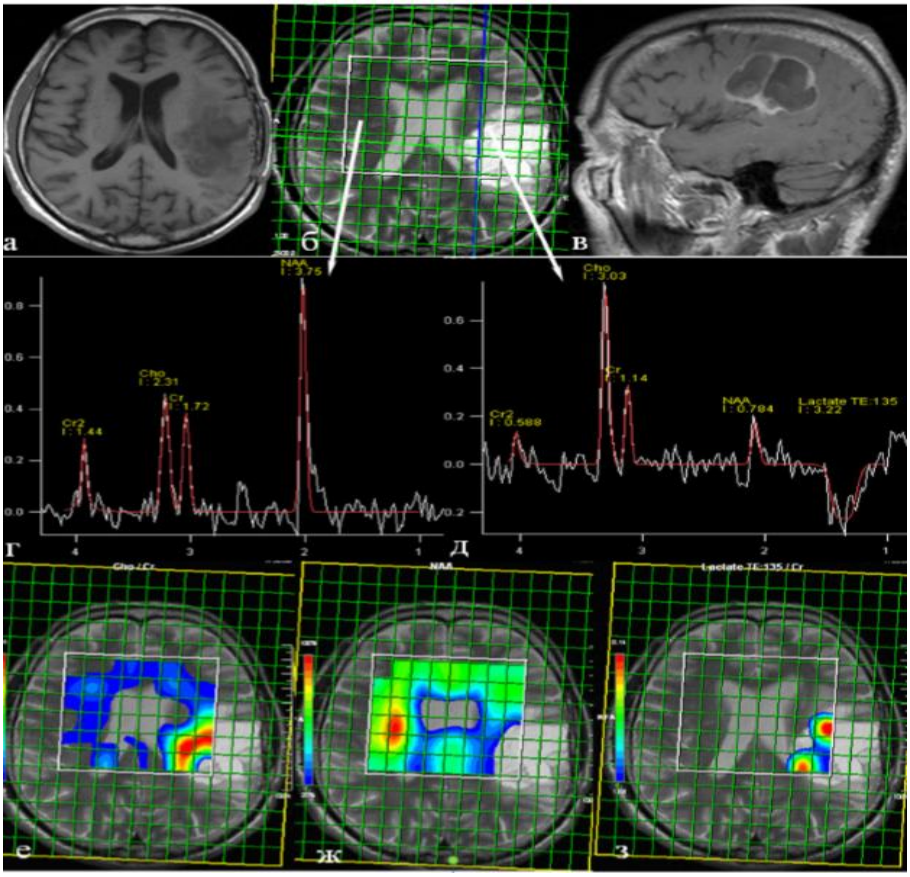

Figure 2 (a, b, c, d, e, f, g, h). Patient D., 55 yearsold. Glioblastoma

On MR tomograms (Fig. 2): in the left parietal lobe, the formation of a heterogeneous structure is determined, iso- and hyperintense on T2-WI (b) and hypointense on T1-WI (a, c). On post-contrast T1-WI (c), there is an uneven (mainly along the periphery) increase in the intensity of the MR signal from the formation. On the spectrum and color mapping images (e, f, g, h) for glioblastoma, compared with the spectrum from the unchanged brain substance from the contralateral side (d), it is characteristic:

- decrease in the content of N-acetylaspartate (NAA);
- a slight decrease in the content of creatine (Cr);
- a significant increase in the content of lactate (Lac);
- decrease in the NAA/Cr ratio (0.68);
- increase in the Cho/Cr ratio (2.7);
- increase in the Lac/Cr ratio (2.82)

Tumors of the meningovascular series, detected in 10 (20.8%) patients, are formed from the arachnoid, less often the pia mater, or from the stroma of the choroid plexus. From the characteristic signs of meningiomas on MRI, the following were distinguished: a wide base of the tumor, adjacent to the dura mater; the presence of a site of hyperostosis or germination of the bone by a tumor. Meningiomasare usually characterized by a homogeneous structure. However, in the presence of foci of calcification or hemorrhages, multiple small feeding vessels, cystic cavities, a heterogeneous structure of meningiomaswas sometimes observed. Most meningiomas were characterized by an isointense or moderately hyperintense signal on T2-WI, and an isointense or hypointense signal on T1-WI.

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Malignant meningiomaswere characterized by the absence of clear contours between the tumor and brain tissue, heterogeneity of the structure and intensity of the MR signal, with the presence of multiple cystic areas, small areas of hemorrhagic impregnation along the periphery, and uneven accumulation of a contrast agent.

Vessels in the tumor stroma and on its capsule were visualized as dotted or linear, tortuous areas of reduced MR signal intensity on T1 and T2-WI. However, they are better seen on T2-weighted image, against the background of a bright signal from perifocal edema. With large sizes of meningiomas, MRI scans revealed branches of the feeding arteries located both in the stroma and on the surface of the tumor. On T1 and T2-WI, they were visualized as areas of decreased intensity of the MR signal of a tortuous, linear shape, coming in the form of rays from the tumor matrix.

In many cases, there was a combination of the presence of vessels on the tumor capsule and cerebrospinal fluid between its capsule and brain tissue, which significantly changed the nature of the visualization of the border of the meningioma with the adjacent medulla in MRI. The dividing line, the border between meningioma and brain tissue on MRI is clearly detected in the majority (60%) of patients.

It should be emphasized that clear margins on MRI are not specific to meningiomas. They are also observed in metastases, glioblastomas, neuromas and other tumors. As a rule, with meningiomas, the presence of perifocal edema is noted, which has a pronounced hyperintense MR signal on T2-WI.

When using the technique of contrast enhancement with intravenous administration of a paramagnetic substance, almost all meningiomaswere characterized by homogeneous and intense accumulation of contrast. Their heterogeneity in MRI after amplification is due to the presence of calcifications, small cysts, and vessels. In meningiomas, as well as in glial tumors, during active proliferative processes of the tumor tissue, the basement membranes of cells are damaged by proteolytic enzymes and choline is released, the increased content of which was recorded in the MR spectrum. The content of NAA in tumors of the meningovascular series was minimal or absent, since this compound is present mainly in glial tissues, in motor nerve endings, and only in minimal concentration can be found in other tissues. In meningiomas, under conditions of sufficient oxygenation, a glucose-alanine cycle is formed, during which alanine and α-ketoglutarate are formed from pyruvic acid by transamination with glutamate.

Regarding the total number of metabolites detected, among the most significant changes, a significantly pronounced decrease in the proportion of NAA, an increase in the proportion of Cho, and the presence of alanine can be noted (table 2).

Table 2
Comparison of MRS indicators in meningovascular tumors

	Tumors of the meningovascular series Me (25%; 75%)	**Unalteredbrainmatter Me (25%; 75%)**
shareNAA	1,29 (0,52; 2,22)	44,13 (41,17; 47,07)
shareCho	48,27 (35,63; 58,79)	28,21 (26,67; 30,0)
shareAla	17,63 (12,28; 22,48)	0,0 (0,0;0,0)
shareCr	21,31 (13,73; 26,54)	27,54 (25,15; 28,97)
shareLac	0,06 (0,02; 0,67)	0,0 (0,0; 0,23)

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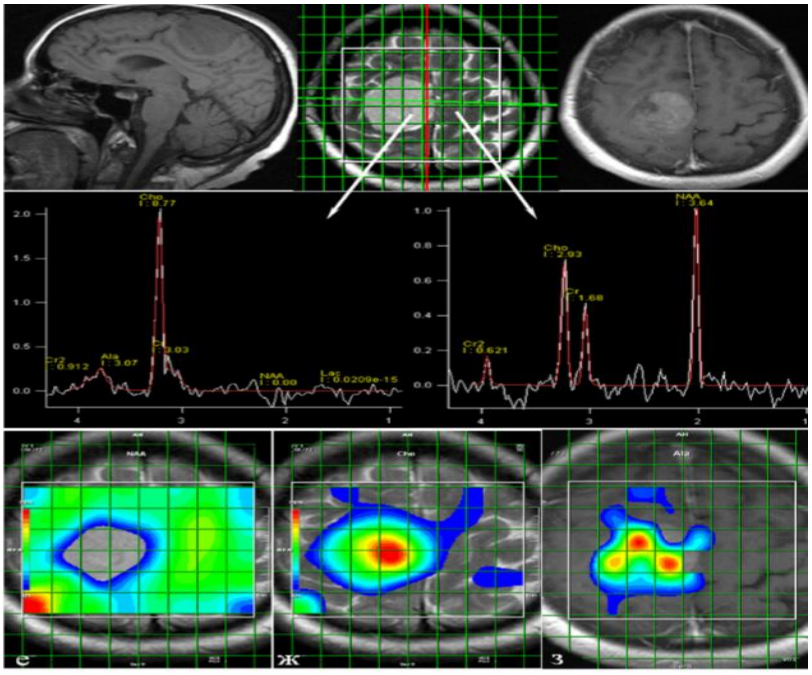

Figure 3 (a, b, c, d, e, f, g, h). Patient I., 40 years old. Meningioma of the right parietal lobe.

The metabolite alanine, according to our observations, was detected in meningovascular tumors in 92% of cases, and was not detected in glial brain tumors (Fig. 3). On MR tomograms: in the right parietal lobe, a formation is determined, with a wide base adjacent to the dura mater, having a hyperintense MR signal in T2 (b), a hypointense MR signal in T1 (a) VI. On post-contrast T1-WI (c), there is an uneven pronounced increase in the intensity of the MR signal from the formation. On the spectrum and color mapping images (d, f, g, h) for meningioma, compared with the spectrum from the unchanged brain substance from the contralateral side (e), it is characteristic:

- no N-acetylaspartate (NAA) content;
- an increase in the content of choline (Cho),
- increase in the Cho/Cr ratio (up to 2.89);
- the appearance of alanine (Ala).

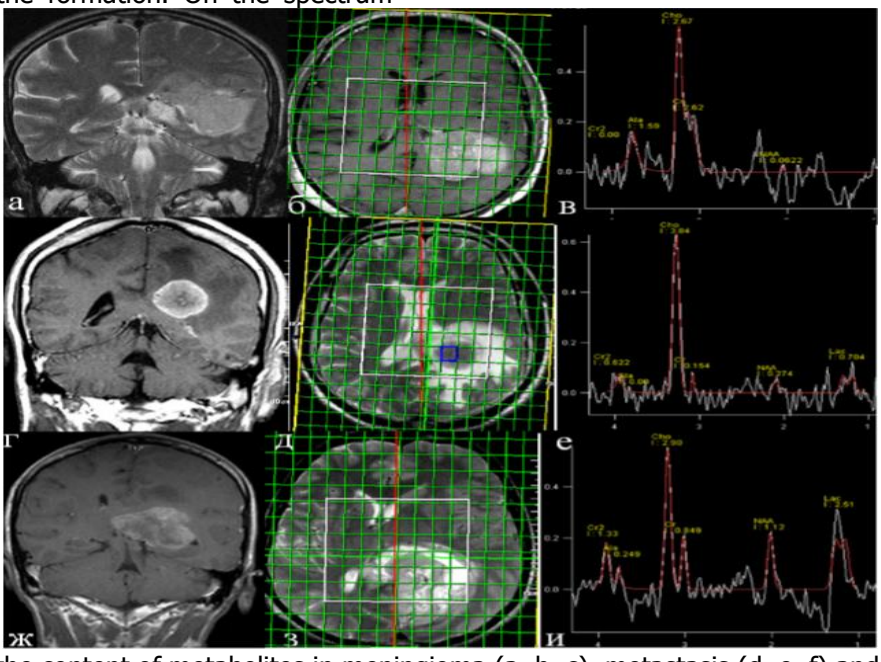

Figure 4. Changes in the content of metabolites in meningioma (a, b, c), metastasis (d, e, f) and glioblastoma (g, h, i)

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Malignant meningiomas, in contrast to benign ones, were characterized by a moderately pronounced or pronounced increase in lactate content and variable alanine content (the alanine peak was not determined in 40% of cases). In contrast to tumors of the glial series, in meningiomas, a pronounced decrease in the proportion of N-acetylaspartate to 1-2% (with glial tumors 8-18%), the appearance of an alanine peak is revealed.

Comparative characteristics of changes in the content of metabolites in meningioma, metastasis and glioblastoma are shown in Fig. 4, from which it can be seen that meningiomas (Fig. 4, a, b, c) are characterized by the absence of N-acetylaspartate (NAA), an increase in the content of choline (Cho) , the appearance of an alanine (Ala) peak; for metastases (d, e, f) - the minimum content of N-acetylaspartate (NAA) and creatine (Cr), a significant increase in the content of choline (Cho); for glioblastomas (g, h, i) a significant decrease in N-acetylaspartate (NAA), a moderate decrease in creatine (Cr), a significant increase in the content of choline (Cho) and lactate (Lac) are pathognomonic.

DISCUSSION OF THE RESEARCH RESULTS.

After statistical analysis of the data obtained by hydrogen MR spectroscopy in patients with brain tumors, significant differences in the content of metabolites between tumor types were determined. Tumors of the meningovascular series were characterized by minimal values of the proportion of N-acetylaspartate in comparison with tumors of the neuroectodermal tissue. For tumors of the meningovascular series, in contrast to tumors of the neuroectodermal tissue, the presence of alanine metabolite is characteristic. Tumors of the glial series are characterized by intermediate values of the shares of NAA, Cr, as well as the absence of Ala content.

The results of our study suggest that the use of hydrogen MR spectroscopy is appropriate in the diagnostic algorithm for examining patients with brain tumors, not only for the purpose of differential diagnosis of various types of tumors, but also in dubious diagnostic situations when the data of traditional MRI do not correspond to the obtained clinical data. manifestations, as well as to clarify the degree of anaplasia of glial tumors.

Using multivoxel proton MRS,it is possible to determine the zone with the highest proliferation in the tumor, which is characterized by the highest Cho content and the Cho/Cr ratio, which is important when choosing a biopsy site.

Follow-up MRI spectroscopic studies may be useful in monitoring the progression of glioma. Tumor progression is characterized by an increase in the level of Cho by more than 45%. In tumors that do not progress, Cho levels decrease, remain unchanged, or increase by less than 35%.

CONCLUSIONS.

Thus, the study of brain tumors using multi-voxel MR spectroscopy in comparison with the histological features of brain tumors will improve the quality of differential diagnosis at the stage of preoperative examination of patients. The 3D MRS method is of high relevance and its purposeful study will provide new data on the tumor structure in terms of developing new approaches to treatment and prognosis.

The use of the MRS technique serves as an important addition to solving problems in the field of differential diagnosis of almost all major groups of tumors of the brain and adjacent tissues. This technique opens up the possibility of a non-invasive way to control the course of the disease at the biochemical level. This information can be used both to determine the site of a biopsy, and to determine the goals of radiation therapy and monitor its effectiveness. Special hopes are inspired by the use of MRS in relation to the problem of continued growth and recurrence of tumors after therapy.

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