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Possibilities of Magnetic Resonant Spectroscopy in the Diagnostics of Epilepsy in Patients with Cerebral Palsy

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Abstract Epilepsy is one of the most complex medical and social problems [2]. The high prevalence of the disease in the children's population of Uzbekistan (10 cases per 1000 population) determines the need to develop effective measures for early diagnosis, the search for new approaches to the correction of clinical manifestations and the prevention of complications of epilepsy [1]. MRI and CT are, in essence, representatives of structural neuroimaging, that is, they identify exclusively organic disorders, leaving any functional shifts beyond the boundaries of recognition. Meanwhile, it is functional disorders that are the area of special interest in epileptology [7]. The immense sensitivity of MRI allowed us to create a special type of MP studies capable of identifying significant changes in the functional state of the brain - primarily in aspects of regional cerebral blood flow and metabolic activity. This type of tomography is called functional MRI. Nuclear Magnetic Resonance Spectroscopy.

Keywords Magnetic resonance spectroscopy, Epilepsy, Cerebral palsy

1. Introduction

NMR spectroscopy is a spectroscopic method for studying chemical objects using the phenomenon of nuclear magnetic resonance. The most important for chemistry and practical applications are proton magnetic resonance spectroscopy (NMR spectroscopy), as well as NMR spectroscopy on carbon-13 nuclei (13C NMR spectroscopy), fluorine-19 (19F NMR spectroscopy), phosphorus-31 (31P NMR -spectroscopy). Like infrared spectroscopy, NMR reveals information about the molecular structure of chemicals. However, it provides more complete information than IP, making it possible to study dynamic processes in a sample — to determine the rate constants of chemical reactions and the magnitude of the energy barriers of intramolecular rotation [17].

Magnetic resonance spectroscopy (MR spectroscopy) makes it possible to non-invasively obtain information on metabolic changes in the brain. Proton lH - MR spectroscopy is based on a "chemical shift" - a change in the resonant frequency of protons that make up various chemical compounds. For the first time in science, spectroscopy was introduced by the scientist N. Ramsey in 1951 to indicate the difference between the frequencies of individual spectral peaks of various metabolites. The following metabolites and their chemical shift values, the peaks of which are determined in vivo in the proton MR spectrum, are mainly studied:

- NAA - N-acetyl aspartate (2.0 ppm);
- Cho - choline (3.2 ppm);
- Cr - creatine (3.03 and 3.94 ppm);
- mI - myoinositol (3.56 ppm);
- Glx - glutamate and glutamine (2.1 -2.5 ppm);
- Lac - lactate (1.32 ppm);
- Lip - lipid complex (0.8-1.2 ppm).

Mostly single-voxel and multivoxel (Chemical shift imaging) MR spectroscopy is used - a one-time determination of spectra from several parts of the brain. In single-voxel 1H-MR spectroscopy, only one region (voxel) of the brain is selected for analysis. Studying the composition of frequencies in the signal recorded from this voxel, we determine the distribution of peaks of various metabolites on the chemical shift scale (ppm). The ratio between the peaks of metabolites in the spectrum, a decrease or increase in the height of individual peaks of the spectrum, allows non-invasive assessment of biochemical processes occurring in tissues.

MRS is used as an additional mode to routine MR imaging. By comparing the relative concentrations of metabolites in the studied areas of the brain, one can assess the viability and energy metabolism of nerve tissue, proliferation and destruction of cell membranes, and necrotic transformation of the brain. The main focus is on proton MPC (^{1}H-MPC), since hydrogen is most common in the human body.

In the results, an MR spectrogram is a graphical representation of the peaks of various brain metabolites.

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MR spectrogram includes quantitative and qualitative indicators. Qualitative ones include the presence or absence of major metabolites. quantitative include the value of the integral peak area, the ratio of the amplitudes of the main metabolites.

Based on the foregoing, the aim of the study was to assess the information content of MRI spectroscopy in children with cerebral palsy with symptomatic epilepsy (SE).

The studies were conducted in 42 children, of which 26 children with cerebral palsy complicated by epilepsy (the main group) in which no structural changes were detected in MRI and CT studies. Also, for the control group, we studied the analysis of MR spectroscopy in 16 practically healthy children who did not have paroxysmal seizures, which were studied in the brain during other examinations. The age of children ranged from 1 to 14 years.

The debut of epileptic seizures was noted from the moment of birth to 14 years, the average age of the debut was 4.2 ±0.96 years. The duration of the disease averaged 3.2 ± 0.47 years. Patients underwent examination and treatment at the Department of Pediatric Neurology of the Bukhara Children's Regional Multidisciplinary Center from 2016 to 2018.

MRI and MRS studies were performed on a 1.5T Signa Excite HD (GE) scanner. To accurately localize the region of interest (OI) for recording 1H spectra in vivo, MR images were obtained in three orthogonal projections.

For quantitative and qualitative analysis of the peaks of the main metabolites, such as N-acetyl aspartate (NAA), creatinine (Cr), choline (Cho), lactate (Lac) was carried out in various areas of interest:

- white matter of the frontal lobes,
- the white matter of the temporal lobes,
- inner capsule,
- semi-oval center
- shell
- hippocampus

Statistical analysis for comparison groups was performed using the Statistica 6.0 software package (StatSoft, Inc., USA).

2. The Results of the Study

In our study, the peak ratio of the following metabolites was studied: N-acetyl aspartate (NAA), choline (Cho), creatine (Cr). When analyzing the obtained data, it was found that in the white matter of the frontal lobes, the ratio of NAA / choline metabolites (Cho) averaged 1.57 ± 0.12, in the temporal lobes this ratio was slightly increased and averaged 2.09 ±0. 13, the smallest values of 1.39 ±0.13 and 1.51 ± 0.14 were recorded in the thalamus, shell and inner capsule. In the hippocampus, the average values of this ratio were 1.72 ± 0.12 (Table 1). The ratio of the metabolites of NAA / creatine (Cr) were more increased compared to the ratio of NAA / choline (Cho). Especially high average values were recorded in the white matter of the temporal and occipital lobes (2.05 ±0.15 and 2.09 ±0.13, respectively). In the remaining parts of the cerebral hemispheres, this ratio was practically in the same ranges.

The severity of the average ratio of the metabolites of NAA / Cr + Cho was observed in the inner capsule and thalamus (1.59 ±0.14 and 1.49 ±0.11, respectively). In other departments, uniformity of indicators was recorded (Fig. 1).

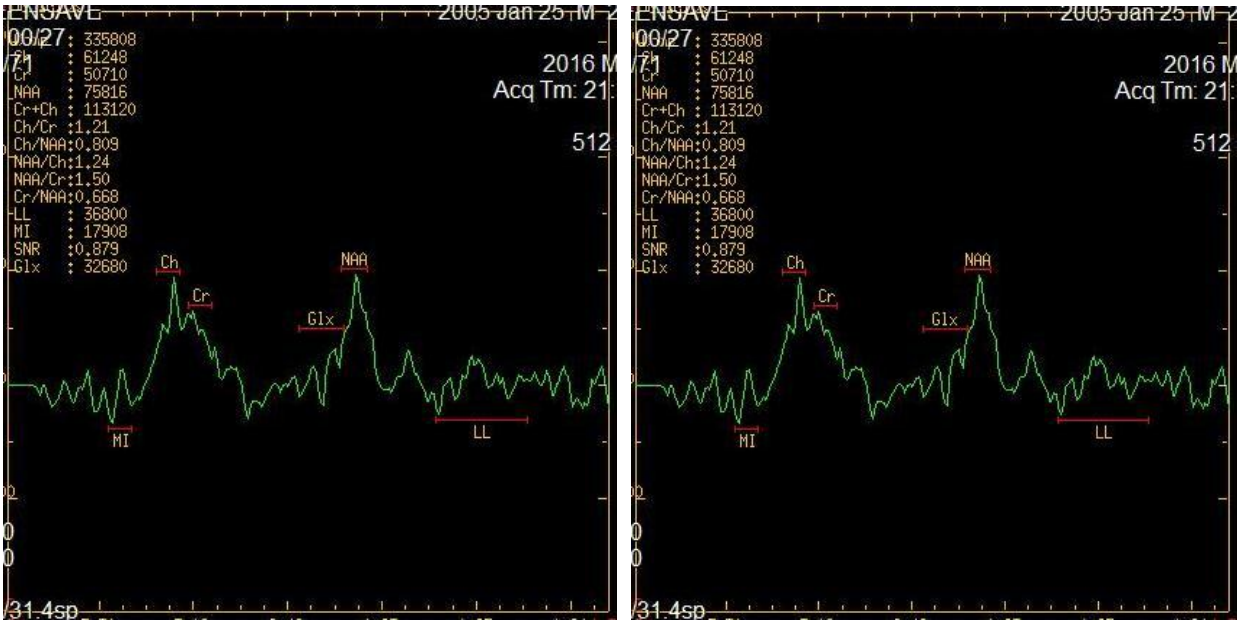

Figure 1. Child S., 7 years old. H^{1}-MRS - on a single-voxel spectrogram, the ratio of NAA (N-acetyl aspartate) and Cr (creatine) and Cho (choline) in the left temporal region is normal. Child A., 5 years old. H^{1}-MRS - on a single-voxel spectrogram, the ratio of NAA (N-acetyl aspartate) and Cr (creatine) and Cho (choline) in the projection of the internal capsule within the standard ratios

Table 1. Indices of the main brain metabolites in healthy children (n = 16) with MRI spectroscopy

Anatomical areas of the brain	NAA/ (Cr)	NAA/ (Cho)	NAA/Cr+Cho.
Frontallobe	1,74 ±0,18	1,57 ±0,12	1,22 ±0,15
Parietallobe	1,65 ±0,11	1,67 ±0,09	1,39 ±0,11
Temporallobe	2,05 ±0,15	2,09 ±0,13	1,43 ±0,12
Occipitallobe	2,09 ±0,15	1,89 ±0,13	1,07 ±0,10
Shell	1,45 ±0,25	1,39 ±0,13	1,12 ±0,15
Thalamus	1,68 ±0,12	1,51 ±0,14	1,49 ±0,11
Hippocampus	1,84 ±0,15	1,72 ±0,12	1,34 ±0,13
Innercapsule	1,77 ±0,25	1,45 ±0,13	1,59 ±0,12

For the epileptic focus, the only statistically significant change is a decrease in the level of N-acetyl aspartate (NAA), and more precisely, a decrease in the ratios of NAA / choline (Cho), NAA / creatine (Cr) and NAA / Cr + Cho. If a decrease in NAA contributes to a change in the NAA / Cho ratio in 100% of cases, then an increase in choline adds changes to these ratios in no more than 43% of cases.

Choline is an integral part of cell membranes and its level increases with damage to the membranes and cell death. In our studies, in patients of the main group, the concentration of N-acetylaspartate (NAA) increased from front to back, in the temporal lobes the concentration of the metabolite is greater than in the frontal, with maximum values in the islet cortex and basal nuclei (Table 2).

Table 2. Indicators of the main metabolites in the structures of the brain in children with cerebral palsy with single-voxel proton MR spectroscopy (n = 26)

Anatomical areas of the brain	NAA/ (Cr)	NAA/ (Cho)	NAA/Cr+Cho.
Frontallobe	1,51 ±0,12	1,33 ±0,22	1,12 ±0,11
Parietallobe	1,53 ±0,11	1,45 ±0,12	1,25 ±0,11
Temporallobe	1,91 ±0,14	1,74 ±0,13	1,11 ±0,12
Occipitallobe	1,84 ±0,10	1,83 ±0,12	1,02 ±0,1
Shell	1,43 ±0,25	1,45 ±0,13	1,12 ±0,12
Thalamus	1,49 ±0,10	1,40 ±0,14	1,13 ±0,11
Hippocampus	1,43 ±0,11	1,34 ±0,10	1,10 ±0,1
Innercapsule	1,64 ±0,15	1,72 ±0,12	1,12 ±0,1

Note: * - significance of differences in data compared with the control group (P <0.05).

The results of proton spectroscopy revealed a decrease in the most important ratio of NAA / Cr + Cho of less than 0.71 in the hippocampus in half of children with cerebral palsy on the side of the epileptogenic focus and in the other half on both sides. The concentration of neurometabolites in the external parts of the temporal lobes changed mainly on the side of the epileptogenic focus, determined according to the EEG results.

Choline has the same concentration in the gray and white substances of the brain. Its maximum concentration was determined in the islet cortex, hippocampus and basal nuclei. The ratio of NAA / choline metabolites (Cho) in children of the main group decreased compared with the control group. The most pronounced change was recorded in the white matter of the temporal and frontal lobes of the departments of the cerebral hemispheres - by 29.7% and 28.5%, respectively, as well as in the semi-oval center and hippocampus - 20% and 20.7%, respectively. Its smallest decrease was noted in the inner capsule - by 17.3%. The data obtained had significantly reduced values compared with the control group (P <0.05).

Creatine has a higher concentration in the cortex and basal nuclei. In 2 children, the creatinine concentration in the temporal lobe was higher than in the frontal lobe. In patients with cerebral palsy with SE, the ratio of NAA / creatine (Cr) was significantly reduced in all parts of the cerebral hemispheres (P <0.05). A particularly pronounced decrease was recorded in the inner capsule - by 24% compared with the control group. Its smallest decrease was recorded in the semi-oval center (by 11.2%).

A decrease in the NAA / Cr + Cho ratio in patients with cerebral palsy with SE in the hippocampus was recorded by 26.8%, as well as in the white matter of the frontal lobes - by 26.8%, these indicators significantly differed from the control group (P <0, 05). Although a significant decrease in the NAA / Cr + Cho ratio was recorded in other areas, the highest numbers were recorded in the semi-oval center.

A pronounced increase in the concentration of myo-inositol was also determined, with an increase in the ml / Cr ratio to 0.65. N-acetyl aspartate (NAA) has a higher concentration in the cerebral cortex and basal nuclei, the hippocampus, as compared to the white matter (Fig. 2).

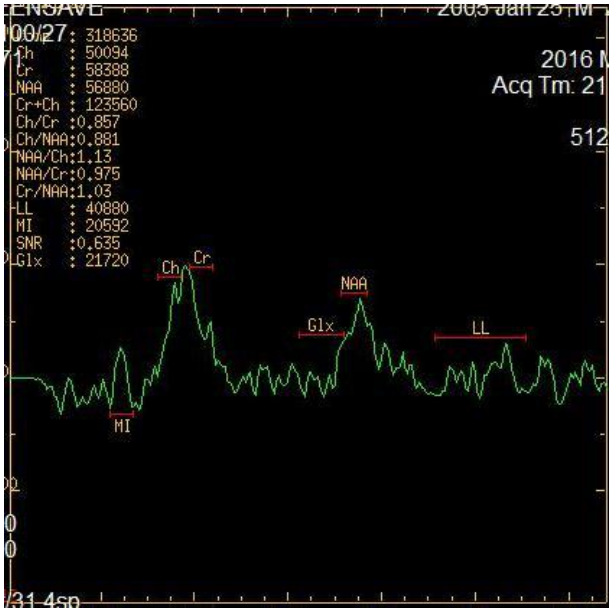

Figure 2. Patient A., 6 years old, with symptomatic focal epilepsy without structural changes in routine MRI. MRI spectroscopy: on a single-voxel spectrogram, a decrease in the level of NAA (N-acetyl aspartate) and an increase in the level of Cr (creatine) and Cho (choline) in the hippocampus on the right are determined

Thus, in spectral analysis (the frontal and temporal lobes are of interest), the following changes in the peak indices of

the main metabolites were established. A marked increase in choline level was noted with a moderate decrease in the concentration of N-acetyl aspartate (NAA) and a decrease in the concentration of the NAA / Cho ratio to 0.45 (Fig. 2).

According to the results of our studies, the ratio of the main neurometabolites in the studied areas of the brain showed a violation of the epiactivity site. A significant decrease in metabolic changes was observed in the external parts of the temporal lobes both on the contralateral side and on the side of epileptic activity, which had a multidirectional character.

A comprehensive study of the structural and functional methods of neuroimaging allows doctors to non-invasively identify and detect microstructural disorders at the metabolic level that are associated with epileptogenesis. One of the indicators of the course of the epileptic process is the state of cognitive functions. Structural and functional disorders are not always associated with the epileptic system.

Figure 3. Patient S., 9 years old, cerebral palsy with SE without structural changes according to the standard MRI protocol. H^1-MRS - on a single-voxel spectrogram, a decrease in the level of NAA (N-acetyl aspartate) and an increase in the level of Cr (creatine) and Cho (choline) in the temporal regions on both sides are determined

Identified microstructural changes outside the epileptic system require adequate management and treatment tactics. Compared with structural methods of research, functional methods of neuroimaging have high diagnostic value, but are not able to solve all the problems of diagnosing epilepsy.

3. Conclusions

As a result of the study, it was found that based on the obtained qualitative and quantitative indicators on MR spectroscopy, the anatomical localization of metabolic processes is determined, which characterizes the state of the white matter of the brain. The use of ^{1}H-MR spectroscopy is an addition to the standard MRI study, which characterizes the biochemical control of the main metabolites of the brain and the effectiveness of therapeutic measures, which is especially important in pediatric neuroradiology.

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