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MICROSTRUCTURAL AND FUNCTIONAL NEUROVISUALIZATION METHODS FOR VASCULAR MIND DAMAGES IN ADOLESCENTS

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Abstract: Vascular brain lesions in adolescents represent a heterogeneous group of diseases characterized by complex pathophysiological mechanisms and diverse clinical manifestations. The characteristics of the anatomical and physiological development of the nervous system during puberty, including myelination, synaptogenesis, and vascularization processes, determine the specific course of cerebrovascular pathology and require the application of highly sensitive diagnostic methods.

Keywords: nzeural imaging, diffusion-tensor MRI, functional MRI, perfusion MRI, vascular brain lesions, adolescents, white matter microstructure, functional connectivity

Introduction. Traditional structural neuroimaging methods, such as computed tomography and standard magnetic resonance imaging, do not always allow for the early detection of pathological changes in brain tissues, especially in the subclinical stage of the disease. In this regard, the use of modern microstructural and functional neuroimaging methods capable of detecting subtle disruptions in white matter integrity, changes in cerebral perfusion, and functional connectivity of neural networks is becoming particularly relevant. Diffusion-tensor magnetic resonance imaging (DT-MRI) allows for the quantitative assessment of the microstructural organization of the brain's white matter, the identification of areas with impaired diffusion, and the tracking of changes in the tractographic characteristics of the conduction pathways. Functional MRI at rest (fMRI-PS) provides an opportunity to study the spontaneous neural activity and functional connectivity of various brain networks, which is especially important for understanding compensation mechanisms in vascular lesions. Perfusion MRI and MR spectroscopy complement the diagnostic arsenal, allowing for the assessment of cerebral blood flow, metabolic processes in nerve tissue, and the identification of areas of hypoperfusion or metabolic dysfunction[1,2,3,4]. The integration of data from various neural imaging methods provides a comprehensive characterization of pathological processes and contributes to more accurate diagnosis, prognosis of the disease course, and monitoring of therapeutic intervention effectiveness.

Neurovascular pathology in adolescence remains one of the least studied and at the same time clinically significant issues in modern neurology. Despite the relatively low frequency of acute cerebrovascular events compared to the adult population, functional and subclinical vascular disorders in adolescents occur significantly more frequently and are often masked by autonomic dysfunction, migraine-like conditions, and cognitive overstrain. Thus, in conditions of increasing functional neurovascular disorders in the adolescent population and the limitation of standard neuroimaging, a need arises for a comprehensive clinical and neuroimaging approach using modern quantitative MR technologies[5,6]. The integration of clinical data with parameters of perfusion, microstructure, and vascular wall allows not only to clarify pathogenetic mechanisms but also to increase the diagnostic

accuracy of early forms of neurovascular pathology.

The aim of the study is to study and identify the clinical and neuroimaging features of neurovascular pathology in adolescents in order to early verify functional vascular disorders.

Research material and method. The study was conducted at the Multidisciplinary Clinic of Samarkand State Medical University in the departments of pediatric neurology, general neurology, and therapeutic units between 2024 and 2025. The study included adolescents aged 16 to 19. The main group consisted of 33 patients with clinically verified neurovascular pathology (100%). The control group consisted of 31 practically healthy adolescents of comparable age and gender who underwent a preventive examination at the SamSMU MC polyclinic. In the main group, girls accounted for 18 people (54.5%), while boys accounted for 15 people (45.5%). In the control group, there were 16 girls (51.6%) and 15 boys (48.4%). The gender distribution did not differ statistically ($p>0.05$), and the percentage difference between the groups did not exceed 2.9%. Age structure of the main group: 16 and 17 years - 14 patients (42.4%); 18 and 19 years - 19 patients (57.6%). In the control group, 16 and 17 years, 13 people (41.9%); 18 and 19 years - 18 people (58.1%). No differences in age stratification were identified between the groups ($p>0.05$); the percentage difference was less than 1%. Distribution by type of neurovascular pathology in the main group (ICD-10) was as follows: secondary neurovascular conditions against the background of arterial hypertension (I10–I15) accounted for 15 patients (45.5%); congenital cerebral vascular anomalies (Q28.0–Q28.3) accounted for 9 patients (27.3%); and patients with other cerebrovascular diseases (I67) accounted for 9 patients (27.3%). Thus, the hypertensive-associated variant among patients was 18.2% more frequent than each of the other variants of the pathology. The average duration of clinical manifestations in the main group was 2.3 ± 0.8 years. In 19 adolescents (57.6%), the duration of symptoms exceeded 2 years, which is 57.6% longer compared to the control group, where chronic neurological symptoms were absent. The sampling was conducted taking into account inclusion and exclusion criteria, which ensure group comparability and the reliability of clinical and neuroimaging analysis. Clinical examination was conducted in all adolescents of the primary and control groups and included a detailed clinical-neurological examination with an assessment of complaints, neurological status, the nature of cephaltic syndrome, autonomic manifestations, coordination and sensory disorders, as well as signs of astheno-neurosis. Particular attention was paid to the duration of symptoms, trigger factors, family history of vascular pathology, and the presence of arterial hypertension.

Neuroimaging studies were performed on adolescents in the primary group at the Multidisciplinary Clinic of Samarkand State Medical University in the Department of Radiology and Radiology, as well as at private diagnostic centers in the city of Samarkand—"MedExpert" and "Miroz." The examination was conducted using high-field magnetic resonance imagers (1.5–3.0 T) using standard and expanded protocols. The standard protocol included T1, T2, FLAIR, and TOF angiography to assess structural changes in brain matter and vascular anatomy. The expanded protocol included modern quantitative methods: arterial spin marking (ASL) to assess regional cerebral blood flow, diffusion-tensor tomography (DTI) to analyze white matter microstructure, SWI to identify microangiopathic changes and evaluate the venous component, and vessel wall imaging to evaluate structural changes in the arterial wall. Analysis of neuroimaging data was conducted by comparing clinical symptoms and the type of neurovascular pathology according to ICD-10, which allowed for an assessment of the correlation between functional vascular disorders and identified MR signs. The expanded protocol was aimed at identifying functional and microstructural changes that were not detectable during standard MRI. The arterial spin marking (ASL) method was used to quantitatively assess regional cerebral blood flow (CBF, ml/100 g/min). Analysis was conducted in the cortical and subcortical zones, primarily in the frontal, temporal, and temporal regions, as well as in the basins of the anterior and middle cerebral arteries. The average CBF values, interhemispheric asymmetry of perfusion, and the presence of relative hypoperfusion zones were evaluated. Diffusion-tensor tomography (DTI) was used to analyze the microstructure of the white matter. Fractional anisotropy (FA), average diffusion (MD), as well as radial (RD) and axial diffusion (AD) were calculated. Parameters were assessed in the projection of the conduction pathways, primarily in the areas of the frontal striate tract, the corpus callosum, and the periventricular zones. A decrease in FA and an increase in MD were interpreted as

signs of microstructural disorganization and the disruption of axonal fiber integrity.

The SWI (susceptibility-weighted imaging) sequence was used to identify microangiopathic changes, microhemorrhages, and features of the venous pattern. The severity of venous visualization, the presence of hypointensive foci, and signs of venous congestion were analyzed. Vascular wall imaging (vessel wall imaging, black-blood) was used to assess the thickness and homogeneity of the arterial wall, signs of remodeling, and subclinical inflammation. The symmetry of the signal and local thickening of the walls of the main intracranial arteries were evaluated. In a number of cases, resting-state fMRI was additionally performed to analyze functional connectivity and evaluate the integration of neural networks in a state of rest. Signal synchronization indicators within frontoparietal and default-mode networks were evaluated. Quantitative analysis of MR parameters was conducted using embedded post-processing software packages. The obtained data were compared with clinical symptoms, the type of neurovascular pathology according to ICD-10, and the age stratification of adolescents. Statistical processing of the results was carried out using a package of applied programs on a personal computer.

The quantitative indicators are presented as the arithmetic mean and standard deviation (M ± SD). The verification of data distribution was carried out using the Shapiro-Wilk criterion. Comparison of quantitative parameters between the primary and control groups was conducted using Student's t-test for normal distribution or the non-parametric Mann-Whitney test for deviation from normal. Pearson's $\chi 2$-criterion was used for the analysis of qualitative traits. Correlation analysis was performed using Pearson (r) or Spearman (rs) coefficients to evaluate the relationship between clinical indicators and perfusion parameters (CBF), diffusion (FA, MD, RD, AD), and other neuroimaging characteristics. To determine the diagnostic significance of MR indicators, ROC analysis was conducted to calculate the area under the curve (AUC), sensitivity, and specificity. The optimal cut-off point was determined by the Yuden index. The differences were considered statistically significant at a level of $p < 0.05$.

Research Results. The result of clinical and neurological analysis showed that neurovascular pathology in patients aged 16 and 19 years is primarily formed as a functional-regulatory syndrome with a combination of general cerebral, vegetative, and cognitive manifestations. In the main group (n=33), headache was noted in 26 patients (78.8%), which was 59.4% higher than the control group (19.4%; p<0.001). Dizziness was recorded in 60.6% of patients in the main group, compared to 9.7% in the control group, where the difference was 50.9% (p<0.001). At the same time, increased fatigue was observed in 72.7% of patients with a difference of 46.9% (p<0.001), while a decrease in attention was noted in 66.7% with a difference of 50.6% (p<0.001). The level of stratification in the age aspect of patients showed an increase in symptoms in the older age category from 18 to 19 years (n=19), headache was recorded in 84.2% of patients, compared to 71.4% of patients aged 16 and 17 years (n=14), where the difference corresponds to 12.8% (p=0.18). The fatigue indicator in the main group of patients was found in 78.9% of cases in older age groups, compared to 64.3% in younger age groups, representing a difference of 14.6% (p=0.16). Although the differences did not reach strict statistical significance, there was a tendency for functional manifestations to increase with age, associated with an increase in cognitive and psycho-emotional stress[7,8]. Analysis of the study results by disease types revealed the most pronounced clinical manifestations in the hypertensive-associated variant (I10–I15, n=15), with the headache frequency reaching 86.7%, which is 19.4% higher than in congenital vascular anomalies (Q28.0–Q28.3, n=9) and 22.2% higher than in other cerebrovascular diseases (I67, n=9) (p=0.03). The duration of symptoms for more than 2 years was recorded in 66.7% of patients with ICD 10 code (I10–I15), which was 22.3% higher than in other subgroups (p=0.04) [9].

Despite the pronounced clinical picture, standard MRI (T1, T2, FLAIR) did not reveal structural changes in 26 patients (78.8%). Single subcortical foci of gliosis were identified in 5 patients (15.2%), and moderate expansion of perivascular spaces was noted in only 2 (6.0%). Thus, in 4 out of 5 cases, standard neuroimaging failed to explain the clinical symptoms. The use of neural imaging using the ASL method demonstrated a significant decrease in regional cerebral blood flow, where the average level of CBF in the frontal lobes was 42.6±6.3 ml/100 g/min in the main group, while in the control group it was 51.8±5.9 ml/100 g/min, a decrease in this case was 17.8% (p<0.001). Among patients aged 18 and 19, the CBF level was lower at 40.9±5.8 ml/100 g/min compared to 44.8±6.1 ml/100 g/min in patients aged 16 and 17, with a difference of 8.7% (p=0.04). Hypoperfusion zones were

recorded in 60.6% of patients in the main group, while in 70% of cases, previously conducted studies showed no structural changes according to standard MRI. When comparing patients depending on the disease type, in the ICD-10 (I10–I15) code variant, the decrease in the CBF indicator reached 20.3% compared to the control group ($p<0.001$), whereas in the Q28.0–Q28.3 code disease type, this percentage corresponded to 13.1% ($p=0.02$), and in the disease code (I67) patients, it was 14.8% ($p=0.01$). Thus, the most pronounced perfusion disorders were noted in the hypertensive variant. Diffusion-tensor tomography of the study revealed microstructural changes in the white matter in patients of the main group, where the average level of FA was 0.39±0.03 compared to 0.44±0.04 in the control group, with a decrease of 11.4% accordingly ($p=0.001$). The MD indicator increased by 9.6% ($p=0.002$). Furthermore, in patients aged 18 and 19, FA indicators decreased to 0.37±0.02, which is 5.1% lower compared to 16 and 17 years ($p=0.03$). Analysis of patients by disease type showed that in patients with ICD-10 code (I10–I15), the decrease in FA reached 13.5% ($p=0.002$), whereas in patients with disease code Q28.0–Q28.3, the percentage corresponded to 8.4% ($p=0.04$). At the same time, the increase in MD data for the hypertensive variant of the disease was 12.1% compared to the control group ($p=0.003$)[10,11]. Correlation analysis between data indicators in comparative groups demonstrated a significant correlation between perfusion and microstructural indicators, as the CBF level correlated positively with FA data ($r=0.49$; $p=0.003$), while a decrease in FA was associated with disease duration ($r=-0.46$; $p=0.006$), and the severity of cephaltic syndrome had a negative correlation with CBF level ($r=-0.48$; $p=0.004$) and FA indicator ($r=-0.42$; $p=0.01$). Thus, the identified changes are predominantly functional-microstructural in nature and are significantly correlated with clinical manifestations in the examined patients.

Discussion. To assess the diagnostic significance of quantitative MRI parameters in differentiating patients with neurovascular pathology from healthy individuals, ROC analysis was performed. Group membership was used as the binary outcome. The ROC model considered two predictors: the CBF level from ASL (ml/100 g/min) and the FA level from DTI. The ROC curve was constructed by sequentially varying the classification threshold (cut-off) and calculating sensitivity (Sensitivity, TPR) and 1-specificity (1-Specificity, FPR) at each threshold. The area under the curve (AUC) was interpreted as an integral measure of discriminatory power (values closer to 1.0 indicate high diagnostic accuracy). The Youden's index was used to select the optimal cut-off point. An integrative analysis was used for the combined CBF and FA model. The AUCs of the individual parameters were compared with that of the combined model to evaluate the added diagnostic value of integrating perfusion and microstructural markers[12,13].

To improve diagnostic accuracy, quantitative parameters of perfusion (CBF from ASL) and white matter microstructural integrity (FA from DTI) were combined into an integrated diagnostic indicator. The rationale for this combination was that both parameters reflect different links in the same process: the CBF level characterizes the hemodynamic component of neurovascular insufficiency, whereas the FA level reflects the degree of microstructural changes in the conducting pathways[14,15]. To construct the ROC curve for the integrated indicator, values were used where low CBF and FA values increase the probability of belonging to the main group; the cut-off threshold was then sequentially varied, and sensitivity and specificity were calculated.The combined model (CBF and FA) demonstrates higher diagnostic accuracy compared to each parameter individually, which reflects the advantage of integrating hemodynamic and microstructural markers for the early verification of functional vascular disorders in patients.

Conclusions:

1. In patients aged 16 and 19, neurovascular pathology primarily manifests as a functional-regulatory clinical syndrome with a predominance of cephalgic, vestibulo-asthenic, and cognitive components, which are more pronounced in the hypertension-associated variant of the disease and in the older age group.

2. Standard MRI does not reveal structural changes in most cases, whereas quantitative ASL and DTI methods allow for the detection of significant perfusion and microstructural impairments that are in direct correlation with clinical symptoms.

3. An integrative assessment of CBF and FA parameters increases the diagnostic accuracy of early

verification of neurovascular insufficiency (AUC >0.85), which justifies the need to include modern quantitative neuroimaging techniques in the examination algorithm for adolescents with suspected vascular dysregulation.

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