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### **NON-STRABISMIC ANOMALIES OF THE EYES IN PRESCHOOL CHILDREN AND THE DEVELOPMENT OF A TRIPLEX ULTRASOUND EXAMINATION**

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The purpose of the study was to elucidate the profile of non-strabismic binocular vision dysfunction and its relationship with intraorbital hemodynamic features in preschool children. The prospective study conducted on 1000 patients diagnosed with transient ischemic attack in the neonatal period of life, according to the clinical characteristics of the transition from infancy to the preschool stage of life. These patients were examined dynamically (3 months–3 years, and then from 3 to 6 years): determinations of eye refraction, dynamic refraction, the state of the inner membranes of the eyes, the level of constant potentials of the cerebral cortex of brain. The ophthalmic artery blood flow, the vasomotor supply of the eyes, optical-vestibular sensitivity and neuroplasticity variants are assessed. The most common non-strabismic disorders of binocular vision were accommodation spasm (39.0 %), convergence insufficiency (13.6 %), convergence excess (9.1 %), accommodation insufficiency (15.9 %), basic exophoria (3.5 %), basic esophoria (6.1 %), and inferior oblique muscle hyperfunction (6.4 %).

**Key words:** binocular vision, non-strabismic disorders, accommodation, transient ischemic attack, children.

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### **ЗМІНИ ОРГАНА ЗОРУ, НЕ ПОВ'ЯЗАНІ ЗІ СТРАБІЗМОМ, У ДІТЕЙ ДОШКІЛЬНОГО ВІКУ ТА РОЗРОБКА ТРИПЛЕКСНОЇ МЕТОДИКИ УЛЬТРАЗВУКОВОЇ ДІАГНОСТИКИ**

Метою дослідження було з'ясування профілю нестрабізмичної дисфункції біокулярного зору та її зв'язку з особливостями інтраорбітальної гемодинаміки у дітей дошкільного віку. Проспективне дослідження проведено на 1000 пацієнтах із діагнозом минулі гострі порушення мозкового кровообігу в неонатальному періоді життя за клінічними ознаками в період переходу від дитячого до дошкільного етапу життя. У цих пацієнтів проводилося динамічне обстеження (з 3 місяців до 3 років, а потім з 3 до 6 років): визначення рефракції ока, динамічної рефракції, стану внутрішніх оболонок очей, рівня постійних потенціалів кори великих півкуль головного мозку. Оцінювали кровотік очноямкової артерії, вазомоторне постачання очей, оптико-вестибулярну чутливість і варіанти нейропластичності. Найпоширенішими нестрабізмичними порушеннями біокулярного зору були спазм акомодатії (39,0 %), недостатність конвергенції (13,6 %), надлишок конвергенції (9,1 %), недостатність акомодатії (15,9 %), базова екзофорія (3,5 %), базова езофорія (6,1 %) і гіперфункція нижнього косого м'яза (6,4 %).

**Ключові слова:** біокулярний зір, нестрабізмичні порушення, акомодатія, транзиторна ішемічна атака, діти.

Formation of the visual organ, development and improvement of visual functions, age-related increase in visual acuity and the ability to perceive the depth and life of a child and continues until 16–18 years. The main point of such development is the formation of the optical system of the eye, visual acuity and binocular perception functions. Detailed knowledge of age-related features is necessary for early detection of pathology, since they require immediate treatment and, in case of untimely diagnosis, lead to irreversible disorders [14]. Accommodation and binocular vision disorders are the second most common visual impairments in the clinical pediatric population after refractive errors [10]. These dysfunctions are collectively termed Non-Strabismic Binocular Vision Abnormalities (NSBVA). NSBVA mainly affects

binocularity, clarity, and impairs comfort, visual performance, and efficiency of patients, especially those with near vision difficulties [13]. Early detection of NSBVA is important because these abnormalities may decompensate without treatment and become strabismus, leading to loss of stereopsis and suppression development. Early detection and treatment provide the best opportunity for academic success in school-age groups. A major part of a child's education is learning through reading. Reading involves both accommodative and vergence mechanisms, and an imbalance between the sensorimotor integrative functions results in non-strabismic accommodative and/or binocular visual anomalies. Thus, any abnormality in the visual system will affect the cognitive development and academic performance of children. NSBVA mainly affects school-aged children who have an increased need to use the accommodative and vergence systems. The symptoms of eye strain, eye pain, fatigue and discomfort are further aggravated by prolonged near tasks, thereby affecting the overall quality of life [1, 10].

With the increasing use of computers and mobile phones, the number of near and intermediate tasks has increased dramatically and therefore a large percentage of people are found to have binocular vision problems and ocular discomfort [10, 13]. Undiagnosed binocular vision disorders and oculomotor dysfunctions can manifest as discomfort, leading to adverse consequences for both clinical training and academic performance [2, 12]. Non-strabismic anomalies related to binocular vision are particularly common among school-aged children [7, 10]. The most common problem is convergence insufficiency, followed by accommodation impairment. An imbalance between sensorimotor integrative functions causes non-strabismic accommodative and/or binocular visual anomalies. Thus, any abnormality in the visual system will impact cognitive growth and performance [2, 12].

The International Classification of Headache Disorders, 3rd edition (2018) defined ocular causes of headache, which include headaches associated with refractive errors (HARE), convergence insufficiency (CI), and accommodative spasm (AS). HARE is more severe in patients with a high degree of refractive error. Patients with CI or AS may have diplopia and strabismus [8].

HARE include asthenopia, which is a term used to describe headache associated with eye strain. Asthenopia is caused by ametropia, extraocular muscle imbalance, abnormal reading or working habits, and the environment. It includes a variety of complaints such as lacrimation, irritation, redness, eye pain, orbital pain, headache (especially frontal), visual fluctuation, blurred vision, or discomfort when reading [8]. HARE is considered to be the result of multiple risk factors. Most studies have recognized that moderate anisometropia and astigmatism are the most involved; probably due to the visual blurriness they cause.

**The purpose** of the study was to elucidate the profile of non-strabismic binocular vision dysfunction and its relationship with intraorbital hemodynamic features in preschool children.

**Materials and methods.** Over the past 15 years, out of 3,500 children examined by us aged from 3 months to 3 years, and subsequently in dynamics from 3 to 6 years, with the assistance and cooperation of the Children's Neurological Hospital, the Department of I and II Neurology and Medical Genetics of the AMU, the Republican Perinatal Center and the Research Institute of Pediatrics, 1,500 children were diagnosed with acute cerebrovascular accident in the neonatal period of life.

This is a prospective study conducted on 1,000 patients out of 1,500 children who were diagnosed with transient ischemic attack (TIA) in the neonatal period of life, according to the clinical characteristics of the transition from infancy to the preschool stage of life, 75 % had a remitting course, and 10 % had a progressive course. These patients were examined dynamically at the stages of development at the age from 3 months to 3 years, and then dynamically from 3 to 6 years.

Based on the methodology of our scientific study of the management of these patients, a positive decision was received from the Eurasian Patent Organization to issue a Eurasian patent for application No. 202391111/invention No. 046458, priority dated March 15, 2024 [11].

The objective of the invention is to simplify and reduce the labor intensity of the study of eye parameters, and also creates the ability to freely determine the necessary parameters of the studied eyes and brain in children under three years of age. "The method for diagnosing neuro-ophthalmological pathology in children under three years of age" includes determinations of eye refraction, dynamic refraction, the state of the inner membranes of the eyes, the level of constant potentials (LCP) of the cerebral cortex of brain. The ophthalmic artery blood flow is determined, the vasomotor supply of the eyes (VMOS), optical-vestibular sensitivity (OVS) and neuroplasticity variants are assessed. The final new feature of the proposed invention is that neuroplasticity variants are assessed, allowing the proposed solution to demonstrate a new property, which consists in identifying variants of excessive and aberrant brain plasticity in children, leading to an increase in the conditions for the further development of ophthalmological pathologies in a child after three years of age with an increase in visual load [11].

The study in the dynamics of these children from 3 to 6 years of age was carried out in two aspects: according to optometric and hemodynamic indicators.

All participants underwent an optometric examination in the following sequence. Visometry for distance was performed using the Tomey projector (Japan) at a distance of 3 m, also using the Preschool LED Insta-Line Quantum, and for near vision using a special LEA SYMBOLS® line test table on one side and the LEA NUMBERS® line test on the other side of the NEAR VISION CARD to assess near visual acuity (at the patient's functional distance). With rare exceptions, visual acuity was determined using the Single Symbol Book table, which does not require a verbal response from the child. When conducting this test, the child is shown a table with certain pictures (a house, a circle, a square, and an apple) of different sizes, corresponding to a certain visual acuity. If the interocular difference in visual acuity is insignificant, the doctor takes this factor into account.

Next, using the Plusoptix A16 Binocular Autorefractor (pediatric autorefractometer), we determine the refraction of each eye (static and dynamic). With a noticeable interocular difference in dynamic refraction, this factor is noted as a deviation from the normal refractogenesis of the eyes and is taken into account by the doctor when diagnosing the possible development of pathology. Next, using a manual retinoscope (for example, KEELER) and skiascopic rulers, we determine the dynamic and static refraction of each eye. After that, we compare the results of the above definitions, which allow us to identify the accommodative response of each eye.

The analysis used the Duane classification, according to which accommodative dysfunctions are divided into: 1) accommodative insufficiency; 2) instability of accommodation; 3) accommodative rigidity; 4) spasm of accommodation.

When analyzing vergence dysfunctions, a modified Duane classification was used, according to which vergence dysfunctions are divided into: 1) convergence insufficiency; 2) excess of divergence; 3) basic exophoria; 4) excess of convergence; 5) basic esophoria; 6) impaired fusional vergence; 7) vertical phoria.

The diagnostic methods used in studies of vergence anomalies, although varied, we use in children – the test with covering the eye (“carpet test”), the von Grefe (VG) method of measuring heterophoria and the push-up-to-break technique (PUB) for measuring the nearest point of convergence (NPC). Fusion vergents could not be assessed in children. The diagnostic criteria of NPC included the following signs: exophoria near is greater than far, distant nearest point of convergence.

Binocular vision, examined using the four-point Worth color test for distance and near, could not be determined in this age group of patients. The eye cover test (“carpet test”) and the alternate eye cover test (“alternate carpet test”) were performed for distance at 6 m, for near – at 40 cm. The nearest point of convergence was estimated by a vertical target strip on the RAF (Royal Air Force) ruler. The test was repeated 10 times. The objective (divergence of one eye after suppression) results were recorded. Monocular Method of Estimating Skiascopy (MMES) used to estimate the volume of accommodation depending on the stimulus. The object for MMES was selected depending on age. The patient was asked to name the optotypes for distance and the results of the skiascopy were recorded. Dopplerographic studies were performed mainly on the color and gray-screen triplex ultrasound system NEMIO XG SSA-580 A by TOSHIBA based on the special technique by Kasimov EM, Salmanova SZ and Hajiyeva SA for children aged 3 to 6 years at an ultrasound signal depth of  $20.05 \pm 0.7$  mm. Visualization was performed in the ophthalmic artery basin with a study of the maximum systolic linear blood flow velocity along the vessel ( $V_{max}$ ), minimum linear diastolic blood flow velocity along the vessel ( $V_{min}$ ) and the resistance index (RI). It should be noted that the study of the state of the vessels of the eyeball and, first of all, the ophthalmic artery (OA) is carried out using the B-mode, color Doppler mapping (CDM), power Doppler mapping (PDM) and power Doppler research (PD) methods using an ultrasound sensor with a frequency of 7.5 MHz.

Statistical processing was performed by calculation of the mean value (M), standard error of mean (m) and interval (min–max). Absolute numbers and their proportion (%) of occurrence of qualitative features were also calculated. Statistical processing of the research results was carried out using the statistical computer program Statistica 12.0 by StatSoft (USA).

**Results of the study and their discussion.** A preliminary analysis of the material showed the feasibility of tracking the dynamics of cerebral visual impairment (CVI) and optical-kinetic maladaptation (OKD) from TIA beginning of the early neonatal period and mandatory consideration of neuro-sonography, CT and MRI data of the brain. We have found that 85 % of children with TIA in the early neonatal period have catecholamine excitation-dumping syndrome, which is characterized by a “flood” of blood with adrenergic mediators and, at the same time, a depression of their desynchronizing effect on the EEG.

The indicators of vestibular support had a direct linear correlation with the severity of clinical manifestations in children with TIA. Follow-up and study of the state of adrenal-cholinergic relationships in dynamics showed that by the age of 1 year reflex mechanisms are gradually restored in almost half of children suffering from catecholamine excitation-dumping (CA excitation-dumping) syndrome. However, in more than one third of these children, by the age of one year, a tendency to increased dysregulation of the mechanisms of vascular supply of the visual analyzer appeared, associated with cholinergic irritation, and it negatively affected the effectiveness of pleoptic therapy. We have established that this mechanism acquires a threatening character for the vision of children with exacerbation of cholinergic irritation associated with the layering of craniocerebral trauma or viral infections.

According to the clinical characteristics of the transition from infancy to the preschool stage of life with compensated recovery was 15 %, with a remitting course – 75 %, with a progressive course – 10 % of children. Then, in the 3- to 6-year age category, out of 1,000 patients, 574 were diagnosed with non-strabismic binocular vision disorders. The average age of patients was  $3.6 \pm 0.08$  years. Of the 574 patients, 295 were emmetropic and 279 were ametropic. Of these, 166 were girls and 308 were boys. Of the 574 patients who had non-strabismic binocular vision disorders, the prevalence of each feature is shown in Fig. 1.

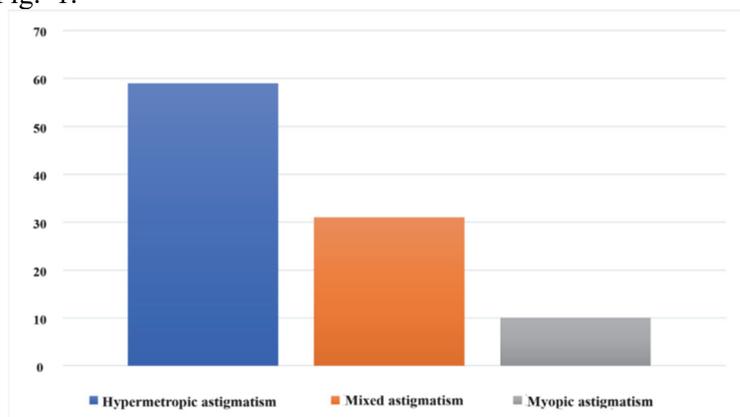


Fig. 1. Distribution of children by refractive disorders (with hypermetropic astigmatism 59 %, with mixed astigmatism 31 %, with myopic astigmatism 10 %).

The results of this study show that the most common non-strabismic disorders of binocular vision and accommodation in the study population are accommodation spasm (39.0 %), convergence insufficiency (13.6 %), convergence excess (9.1 %), accommodation insufficiency (15.9 %), basic exophoria (3.5 %), basic esophoria (6.1 %), and inferior oblique muscle hyperfunction (6.4 %).

In the study highly informative Triplex method according to our developed methodology of non-strabismic pathology and at the age of 3–6 years, a slight decrease in linear blood flow velocities is observed and, accordingly, the resistance index increases.

The literature data indicate that despite the absence of a linear relationship between the early manifestations of intrauterine or perinatal damage to the central nervous system, and therefore the central nervous system, most researchers are inclined to believe that the occurrence and nature of the consequences of pre- and perinatal encephalopathy, especially TIA, are largely determined by the degree of dysfunction of the medio-basal parts of the brain in the initial and early periods of the disease [6]. The theoretical basis for this statement is mainly the results of studies devoted to the study of the so-called structures of the brain, which revealed certain functional relationships of the most important integrative parts of the brain and open up new opportunities for a more adequate study of the systemic organization of the activity of a growing organism, naturally the brain [9]. Probably, it cannot be considered a coincidence that in recent years the number of clinical and experimental studies devoted to the study of the pathogenetic significance of the state of fine regulatory mechanisms of central hemodynamics, general and local cerebral blood flow, including orbital and intraorbital hemodynamics in various diseases of the central nervous system, visual analyzer and, in particular, in children with pre-, perinatal pathology has increased [7]. The same pathomorphological changes in the consequences of pre-, perinatal encephalopathy (PPE) can manifest themselves in various clinical syndromes, therefore their objective assessment can be carried out not only on the basis of the presence and severity of individual symptoms and syndromes, but also with the obligatory consideration of the entire dynamic picture of the disease. From this position, we try to interpret any visual damage in children in the light of age-related features of the entire anamnesis of life (anamnesis vitae), as well as all stages of the dynamics and mechanisms of possible transformations of the supposed nosological unit (anamnesis morbi). However, the literature data indicate that despite the lack of a linear relationship between early manifestations of intrauterine or perinatal (birth) damage to the central nervous system, and therefore the central nervous system, most researchers are inclined to believe that the occurrence and nature of the consequences of pre-, perinatal encephalopathy, especially TIA, are largely

determined by the degree of dysfunction of the medio-basal parts of the brain in the initial and early periods of the disease [6].

Renowned scientists prove that color duplex scanning has significant diagnostic potential in assessing the hemodynamic parameters of the vessels of the eyeball and orbit. This method allows obtaining reliable information on the linear blood flow velocity and the state of vasoresistance in different parts of the vascular system of the eye and establishing a relationship between changes in hemodynamic parameters and the severity of vascular lesions. Many authors show that there are still no uniform standards for blood flow parameters in the vessels of the eye, since a number of factors affect the results of the CDC. Its disadvantages are: operator-dependence of the method (equipment, sensors and qualifications of the doctor), dependence of hemodynamic parameters on physiological parameters (blood pressure level, heart rate, stenosis and deformation of the main arteries of the head, etc.). A number of studies have shown daily variability of blood flow parameters in vessels, as well as their unstable nature over the course of a week and one month [3]. It has been proven that the decisive mechanisms of recovery options depend on the orientation of the hypothalamic-pituitary relationships and the nature of homeostatic aberrations. The vast majority of these children over these many years experienced catecholamine excitation-dumping syndrome, had a clinical picture of both cerebral pathology and cerebral visual impairment.

Using histograms, it was possible to establish that the influence of cholinergic mechanisms on general hemodynamics was less pronounced than on intraorbital blood circulation. In other words, the assessment of hemodynamic reactivity to the stimulus revealed a more significant fluctuation in the indices of intracranial than general hemodynamics. Dispersion analysis of the results made it possible to prove that the stability of the average dynamic blood pressure is one of the leading mechanisms for stabilizing the adaptive homeostatic neuroplasticity of the central nervous system and the visual analyzer. And autoregulation disorders in the ophthalmic artery basin at a certain depth play a key role in cerebral visual impairment. The impact of accommodative (non-strabismic binocular vision disorders) on the academic performance and quality of life of the patient is well documented in both foreign and domestic ophthalmological literature [2, 12, 13]. Epidemiological studies such as this one, are needed to raise awareness and educate ophthalmologists about the frequency and prevalence of these disorders and what to expect in their daily practice. In Australia, Canada, England, South Korea, Spain and the United States, epidemiological studies on the prevalence of accommodative and non-strabismic binocular vision disorders in school-age populations have been completed, as well as the correlation with learning disabilities. Other studies have also correlated accommodative and non-strabismic binocular vision disorders with learning disabilities [4, 13]. All of these studies provide practicing ophthalmologists in these countries with basic information on the frequency of these disorders to better assess their patients and implement the most appropriate treatment strategies and manage these strategies when needed. The studies reviewed above are unable to provide clear information on the prevalence of accommodative and non-strabismic binocular vision disorders in patients with symptoms of asthenopia in the general population. There is no consensus among authors due to different populations and diagnostic criteria used by each author. There are several studies reporting the frequency of these visual conditions, but there is no correlation of symptoms [4, 5]. It should be noted that we have conducted a number of studies where we confirmed the highly informative and multifunctional triplex method in children with cerebral disorders and revealed a direct correlation between general, cerebral and intraorbital hemodynamics in children with cerebral visual disorders at the stages of recovery from pre-, perinatal encephalopathy [7].

## **Conclusions**

1. The most common non-strabismic disorders of binocular vision and accommodation in the study population are accommodation spasm (39.0 %), convergence insufficiency (13.6 %), convergence excess (9.1 %), accommodation insufficiency (15.9 %), basic exophoria (3.5 %), basic esophoria (6.1 %), and inferior oblique muscle hyperfunction (6.4 %).

2. In order to improve the clinical examination of children suffering from the consequences of perinatal TIA, their transition from infancy to the preschool stage of life (at the age of 3) in their medical records should be clearly distinguished by one of 3 course options - with compensated recovery – 15 %, with remitting recovery – 75 %, with a progressive course – 10 %.

Thus, it is recommended to follow the sequence of studies: studying the characteristics of the mother's pregnancy period, the course of labor itself, the ophthalmological and neurological status of newborns, and subsequently – dynamic monitoring of the course and transformation of syndromes (in infancy, early childhood, preschool and during primary school) at the stages of syndrome transformation.

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