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POSSIBLE PATHOGENETIC MECHANISMS OF PROGRESSION AND THE OCCURRENCE OF INTELLECTUAL AND COGNITIVE IMPAIRMENT IN PATIENTS WITH DOWN SYNDROME

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Down Syndrome (DS), trisomy - 21, - is one of the most common chromosomal diseases. As a result, three copies of the 21st chromosome disrupt the functioning of the genes responsible for the formation and functioning of the brain, and therefore their carriers lag behind their peers in mental development from the very first days of life [3,6,12]. DS does not have any temporary, ethnic, or geographical differences between parents of the same age. In recent decades, there has been a significant increase in the occurrence of DS, an average of one case per 700 births [2,9]. The severity of neurological disorders in these children is not the same. Despite the widespread occurrence of this genetic abnormality, an insufficient number of works is devoted to the analysis of changes in the neurological status of such children; the mechanisms leading to cognitive deficit are not fully understood [1,5]. According to literature data, in DS there is a decrease in the density of nerve tissue, insufficient myelination, a decrease in the volume of cerebellar structures, immaturity and pathological activity of cortical neurons, impaired synthesis and functions of neurotransmitters [7, 10,11]. Hand-eye centers (parietal lobes) are better developed; therefore, training based on hand-eye perception (hand-eye) is the most successful in these children [2].

Mental development problems in children with DS are associated with the OLIG1 and OLIG2 genes, which are located on chromosome 21. They are responsible for the formation of GABA (Gamma Amino Butyric Acid) neurons, the main "brakes" of the nervous system, the first part of DNA inhibiting their formation, and the second accelerating this process [13,14].

Congenital heart defects (CHD) are one of the clinical symptoms of numerous syndromes associated with known chromosomal abnormalities. A striking example is DS - a frequent form of dementia, combined with characteristic somatic symptoms. 40% of children with DS are born with congenital heart disease, which can potentially disrupt cerebral circulation [1,3].

Compared with normally developing children, children with DS have a greater number of behavioral problems, difficulties in attracting and concentrating attention, concomitant disorders (10% have autism spectrum disorders, about 8% have a diagnosis of Attention deficit hyperactivity disorder) [5,8,12].

Often, children with Down syndrome and concomitant disorders have a lower level of IQ, severe forms of stereotyped behavior [6].

Studies have been shown that children with DS have a type of cognitive development unique to them, which fundamentally distinguishes them from other children with genetic abnormalities [4,8,15]. The cognitive sphere suffers significantly and the diagnosis of DS primarily means a certain degree of cognitive deficiency. Diagnosis of DS can be made due to the characteristic features of the phenotype: slanting eyes, skin folds on the neck, flat nape, small arched palate, macroglossia, wide nasal bridge, low-lying ears, brachycephaly, transverse fold in the palm of hand [10,15]. Based on these findings, we determined the need for an in-depth study of intellectual and cognitive impairment in children with DS.

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The aim of our study was to assess changes in the neurological status of patients with Down syndrome, to search for possible pathogenetic mechanisms of progression and the occurrence of intellectual and cognitive impairment in such children.

Materials and methods: we have examined 36 children with a diagnosis of Down syndrome aged 3 to 8 years (16 girls, 20 boys). All cases of the disease were confirmed genetically; all had complete trisomy on 21 chromosomes. Patients were examined by a neurologist, pediatrician, audiologist, dentist, cardiologist and neuropsychologist. According to many authors, to study the intellectual development of children aged 3 to 5 years, the Stanford Binet scale is most applicable, and examination of children from 4 years of age and older is recommended using WPPSI (Wechsler Preschool and Primary Scale of Intelligence) test. Considering that the children with DS examined by us had signs of a lag in intellectual development, we used the Stanford Binet scale for a more objective assessment. The scale is designed to measure IQ from 3 to 5 years, which consisted of six questions for each age level [6].

Instrumental studies were performed - EEG, ECG, Echocardiography and MRI.

Result of our study, data were obtained indicating that in children with trisomy 21 chromosomes in neurological status, in almost all cases (94%) were noted muscle hypotension, decreased tendon reflexes, coordinating, articulatory disorders of various severity. All children had a cognitive deficit in the form of impaired speech and mental development. There was motor awkwardness, lack of formation of subtle differentiated motor acts. All proband parents denied the presence of genetic abnormalities (carriage), occupational hazards and degree of kinship.

In children with Down syndrome, due to structural features of the articulatory apparatus, muscle hypotension, low memory, hearing loss, undeveloped higher cortical functions, and structural features of the brain, speech disturbances of varying severity were noted. The main speech impairment syndromes were dysarthria, which was detected in 24 patients (66.7 %), speech development delay in 8 children (22.2%), sensory and motor alalia in 4 children (11.1%). In all the children examined, the function of voluntary attention suffered. The examined 18 (50%) children did not control the function of the pelvic organs.

The results of the assessment of mental development in children with DS syndrome using the Stanford Binet diagnostic scale are presented in table 1.

Table 1

The distribution of children with Down syndrome by the level of intellectual development based on the results of the Stanford Binet scale

№	Degrees of mental retardation (according to ICD 10)	Intellectual development coefficient in points (Stanford Binet scale)	Number of children with Down syndrome
1	50-69 point mild mental retardation	53-60	8
2	35-49 points moderate mental retardation	39-45	26
3	20-34 points severe mental retardation	32	2

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4	less than 20 points deep mental retardation	-	-
5	Total:		36

According to the table, it can be seen that all children with Down syndrome have a lag in mental development. According to our research, moderate mental retardation was found in 26 (72.2%) children, and mild mental retardation in 8 children (22.2%). So, in 2 children (5.6%), the coefficient of intellectual development is lower than 34, as a result of which severe mental retardation is detected.

Deep mental retardation was not detected in any children from this contingent of patients. All this indicates a lag in the intellectual development of children with Down syndrome. During testing, the children quickly got tired, could not concentrate. Analyzing the results of testing the examined children, it was found that the development of a child with Down syndrome is subject to the general laws of development, but it differs significantly and does not coincide in pace, quality and the ratio of different mental functions with respect to a specific age.

Examination of all children (100%) faced dental problems, such as abnormal tooth growth, prognathism (jaw protruding forward), periodontitis.

When conducting EEG, a single focus of epic activity in the occipital region was noted, a low-amplitude type of EEG was recorded in 8 children, high-amplitude, slowly wave tetta activity was observed in 4 children. Decreased bioelectric activity of the brain, pronounced cerebral changes were observed in 4 patients. Slowing of the back dominant rhythm, dysfunction in the middle structures of the brain were recorded in 3 children. Acute slow-wave pathological activity in the subcortical structures of the brain was recorded in 3 patients. All children had interhemispheric asymmetry of the brain.

In order to study the state of the cardiovascular system in all children, a research method was performed - echocardiography. Congenital heart diseases were diagnosed in 21 children, which amounted to 58.3%. In the structure of these abnormalities in children with Down syndrome, an atrial septal defect (ASD) was more often noted, which amounted to 38% (8/21) cases. Patent Foramen Ovale (PFO) was 28.6% (6/21), and Patent Ductus Arteriosus (PDA) was 23.8% (5/21). Other malformations, such as tetralogy of Fallot, the full form of the open atrioventricular canal amounted to 9.5% (2/21).

As a result of an audiological study, a conductive type of hearing impairment was detected in 12 children (33.3%), which is due to the anatomical structure of the craniofacial skeleton. In 3 children (8.3%) have found sensor neural hearing impairment.

MRI scan of the brain was performed in 13 children with Down syndrome. Cerebellar hypoplasia was revealed in 8 children, which complicates the formation of equilibrium reactions and the implementation of activities that require coordination, hypotension, impaired functioning of articulatory muscles, as well as smoothness of speech. Hippocampal sclerosis was recorded in 5 children. The hippocampus is one of the key areas of the brain responsible for perception and memory, and has extensive neural connections with many brain structures.

In the children we have observed with Down syndrome, the intellectual sphere suffers greatly, there is constant distraction from objects and fatigue, dysarthria, delayed speech development and alalia, dental problems, and hearing impairment. More than half of children with Down syndrome (58.3%) had pathology of the cardiovascular system.

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Thus, the results of our studies confirm that with Down syndrome, an intellectual defect is combined with damage to a number of systems such as cardiovascular, auditory, speech, etc.

Conclusions: A comprehensive study of the internal regular relationships between the etiology, pathogenesis, and pathophysiological mechanisms of trisomy-21 creates the basis for a systematic analysis of the defect structure, because polymorphism of clinical signs confirm that this group of children especially needs specially organized medical and social assistance with a multidisciplinary approach.

Literature:

1. Bysterveldt A. K. van, Gillon G., Foster-Cohen S. Integrated speech and phonological awareness intervention for pre-school children with Down syndrome // International Journal of Language and Communication Disorders. 2010. Vol. 45, Iss. 3. P. 320—335.
2. Davidson, M.A. Primary care for children and adolescents with Down syndrome Text. / M.A. Davidson // Pediatr Clin North Am. — 2008. — Vol. 55(5). — P. 1099-111.
3. Easter M. L. Improving the Speech Intelligibility of Adults with Down Syndrome (DS) using the Core Vocabulary Approach. 2016. URL: https://repositories.lib.utexas.edu/handle/2152/39416.
4. Fenoll R., Pujol J., Esteba-Castillo S., de Sola S., Ribas-Vidal N., García-Alba J., Sánchez-Benavides G., Martínez-Vilavella G., Deus J., Dierssen M., Novell-Alsina R., de la Torre R. Anomalous White Matter Structure and the Effect of Age in Down Syndrome Patients. // J. Alzheimers Dis. 2017;57(1):61-70. doi: 10.3233/JAD-161112.
5. Handen B.L., Cohen A.D.,Channamalappa U., Bulova P., Cannon S.A., Cohen W.I., Mathis C.A., Price J.C., Klunk W.E. Imaging brain amyloid in nondemented young adults with Down syndrome using Pittsburgh compound B. // Alzheimers Dement. 2012; Nov; 8(6):496-501. doi: 10.1016/j.jalz.2011.09.229.
6. Ilyina M.N. Psychological assessment of intelligence in children // Textbook. 2006
7. Kolcheva Yu.A. / Pathogenetic basis of neurological disorders in Down syndrome. BISSA 2017 Vol. 6 No. 4. 19-21p.
8. Korbel JO, Tirosh-Wagner T, Urban AE, et al.: The genetic architecture of Down syndrome phenotypes revealed by high-resolution analysis of human segmental trisomies. Proc Natl AcadSci U S A. 2009; 106(29):12031–12036. 10.1073/pnas.0813248106.
9. Morris JK, Alberman E, Mutton D, et al.: Cytogenetic and epidemiological findings in Down syndrome: England and Wales 1989–2009. Am J Med Genet A. 2012; 158A(5):1151–1157.
10. Rafii M.S., Lukic A.S., Andrews R.D., Brewer J., Rissman R.A., Strother S.C., Wernick M.N., Pennington C.,Mobley W.C. Ness S., Matthews D.C. PET Imaging of Tau Pathology and Relationship to Amyloid, Longitudinal MRI, and Cognitive Change in Down Syndrome: Results from the Down Syndrome Biomarker Initiative (DSBI) // J. Alzheimers Dis. 2017; 60(2):439-450. doi: 10.3233/JAD-170390.
11. Raitano Lee N, Pennington BF, Keenan JM: Verbal short-term memory deficits in Down syndrome: phonological, semantic, or both? J.NeurodevDisord. 2010; 2(1):9–25. 10.
12. Salehi A, Delcroix JD, Belichenko PV, Zhan K, Wu C, Valletta JS, Takimoto-Kimura R, Kleschevnikov AM, Sambamurti K, Chung PP, Xia W, Villar A, Campbell WA, Kulnane LS, Nixon RA, Lamb BT, Epstein CJ, Stokin GB, Goldstein LS, Mobley WC. Increased App expression in a mouse model of Down's syndrome disrupts NGF transport and causes

AMERICAN ACADEMIC PUBLISHER
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cholinergic neuron degeneration. Neuron. 2006; 51:29–42. doi: 10.1016/j.neuron.2006.05.022.
13. Vazquez-Antona C.A., Lomeli C., Buendia A., Vargas-Barron J. Pulmonary hypertension in children with Down's syndrome and congenital heart disease. Is it really more severe? // Arch. Cardiol. Mex. – 2006. – Vol. 76, № 1. – P. 16-27.
14. Vida V.L., Barnoya J., Larrazabal L. A. et al. Congenital cardiac disease in children with Down's syndrome in Guatemala // Cardiol. Young. – 2005. – Vol. 15. – № 3. – P. 286-290.
15. Zhao W, Chen F, Wu M, et al.: Postnatal Identification of Trisomy 21: An Overview of 7,133 Postnatal Trisomy 21 Cases Identified in a Diagnostic Reference Laboratory in China. PLo S One. 2015; 10(7):e0133151. 10.1371/journal.pone.0133151.