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Visual functioning and cerebral visual impairment in children with infantile spasms – West syndrome

Визуелно функционисање и церебрално оштећење вида код деце са инфантилним спазмима – Вестовим синдромом

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SUMMARY

Cerebral visual impairment (CVI) is the most common cause of visual impairment in children in both developed and developing countries, making it a relevant research topic on the functional status of neuro-risk children in recent decades. The multifactorial nature of West syndrome and the variability in visual functions and visual functioning hinder the timely diagnosis of this type of visual impairment. The atypical way of following stimuli, establishing and maintaining visual contact, and sustaining visual attention are the first indicators of deviations in visual behavior that may suggest neuro-risk. Changes in visual behavior may manifest as alterations in the quality or absence of visual responsiveness, deficits in various visual functions, and oculomotor skills, often associated with atypical findings in visual evoked potentials. Cortically mediated visual functions, such as visual acuity, visual field, contrast sensitivity, and oculomotor skills, are also at risk in children with infantile spasms and West syndrome. In addition to basic visual functions, visuo-perceptual and visuo-motor skills are significantly affected, which is manifested in everyday behavior and motivation to observe. The degree and manifestations of CVI in children with infantile spasms depend on numerous factors. Multidisciplinary diagnostic procedures that determine whether cerebral visual impairment results from genetic factors, West syndrome, or other neurological conditions are crucial for creating treatment plans and predicting outcomes.

Keywords: visual impairment; epilepsy; functional vision

Сажетак

Церебрално оштећење вида (ЦВИ) је најчешћи узрок оштећења вида код деце у развијеним и земљама у развоју што га последњих неколико деценија чини актуелном истраживачком темом у оквиру дисциплина које се баве функционалним статусом неуроризичне деце. Мултифакторска условљеност Вестовог синдрома и варијабилност стања визуелних функција и визуелног функционисања отежавају благовремену дијагностику ове врсте оштећења вида. Атипичан начин праћења стимулуса, успостављања и одржавања визуелног контакта, задржавање визуелне пажње, су први показатељи одступања у домену визуелног понашања, који могу да укажу на постојање неуроризика. Промене у визуелном понашању могу да се манифестују кроз промену квалитета или изостанак визуелне респонзивности, дефиците у различитим видним функцијама и окуломоторици што се повезује са измењеним налазом визуелних евоцираних потенцијала. Кортикално посредоване видне функције – оштрина вида, видно поље, осетљивост на контраст, и окуломоторика код деце са инфантилним спазмима и Вест синдромом су такође у ризику. Осим базичних видних функција, значајно су угрожене визуо-перцептивне и визуо-моторичке способности што се манфестује у свакодневном понашању и утиче на мотивацију за гледање. Степен и манифестације ЦВИ код деце са инфантилним спазмима зависе од бројних фактора. Мултидисциплинарни дијагностички поступци којима може да се установи да ли је церебрално оштећење вида последица генетских фактора, Вест синдрома или других неуролошких стања, су од великог значаја за креирање плана и предвиђање исхода третмана.

Кључне речи: оштећење вида; епилепсија; функционални вид

INTRODUCTION

West syndrome is a severe form of childhood epilepsy characterized by specific type of seizures (infantile spasms), an electroencephalogram finding showing hypsarrhythmia, and, depending on the age, developmental regression or delay [1, 2, 3, 4, 5]. Infantile spasms occur at an early age, between four and seven months. They are most often the result of hypoxic-ischemic

encephalopathy, cortical dysplasia, or genetic anomalies [6]. The onset of this type of seizure can be very subtle, making it difficult to recognize milder forms when the first symptoms appear [7]. These seizures are most commonly manifested by flexions and extensions of individual muscle groups, usually after waking up or before sleep. Myoclonus can last from five to 30 minutes and consist of 5-100 spasms [8]. If medication therapy is ineffective, the seizures negatively affect the condition of the immature brain, leading to delays or regression in the child's development [9, 10].

West syndrome is a cause of generalized epilepsy. However, it can be associated with localized cerebral damage, primarily in the temporal-occipital regions. Infantile spasms can pathologically affect the optic radiation and/or visual cortical areas, leading to cerebral visual impairment (CVI). Timely recognition of this association is a significant challenge for pediatric ophthal-mologists and neuro-ophthalmologists [11, 12]. The multifactorial nature of West syndrome and the variability in visual functions and visual functioning hinder timely diagnosis. Some studies have confirmed that visual functioning deteriorates with the onset of the first spasms caused by West syndrome, leading to impairments in visual functions controlled by the cerebral cortex, such as visual acuity, visual field, and visual attention [13]. Deficits in visual functioning, primarily related to damage to the visual pathways after the chiasm and cerebral structures are commonly referred to as cerebral visual impairment [11, 14]. Cerebral visual impairment is the most common cause of pediatric visual impairment [15], i.e., disturbances in visual functioning and visual perception in children in both developed and developing countries [15, 16, 17]. In recent decades, cerebral visual impairment has been a highly relevant research topic on the functional status of neuro-risk children [18, 19].

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS OF CVI

The extensive literature on this impairment uses three terms: cortical visual impairment, cerebral visual impairment, and cognitive visual impairment, all abbreviated as CVI [20]. The need to determine the appropriate term arises from the fact that limitations in visual functioning cannot be attributed to ocular damage. The term "cortical" explains bilateral vision loss due to damage to the visual areas of the cerebral cortex [21], with normal pupil response and clinical examination [18]. The term "cerebral" encompasses a broader range of lesions within the central nervous system, with visual impairments not only related to the cortex but also to subcortical structures [22]. One of the recent papers by Kosta [20] emphasizes the importance of terminological alignment. This author believes that terminology should serve to integrate anatomical

and physiological characteristics and that central visual impairment (CVI) should be the umbrella term encompassing both cortical visual impairment (CoVI) and cerebral visual impairment (CeVI).

Cerebral visual impairment is associated with various neurological conditions, such as hypoxic-ischemic encephalopathy, periventricular leukomalacia, intraventricular hemorrhages, syndromes, etc. [15]. These conditions often cause co-occurring disorders and impairments, such as cerebral palsy, hemiparesis, microcephaly, hydrocephalus, epilepsy, hearing problems, developmental delays, etc. Therefore, differential diagnosis is essential for treatment purposes [12, 23, 24]. Researchers state that it is challenging to isolate cases in which CVI is genetically determined or congenital from those resulting from West syndrome or other neurological conditions. Lack of interest in the environment, which is typical of autism or intellectual disability, inability to perform saccades (rapid eye movements) in a child with motor apraxia, or delays in visual maturation can mimic CVI. In these cases, the diagnosis may be rushed, incorrect, and not reflect the child's actual condition [11]. Symptoms of cerebral visual impairment include the absence of social communication and smooth eye movements, difficulties in fixation, visual scanning, and searching the materials and the environment, as well as the presence of nystagmus [12]. However, without a detailed analysis of all parameters and transdisciplinary collaboration, a diagnosis cannot be made, and treatment cannot be proposed [14].

CVI – SPECIFIC FEATURES IN WEST SYNDROME

The relation between infantile spasms – West syndrome and cerebral visual impairment derives from the fact that they have the same causes [25]. Infantile spasms coincide with the most intensive visual development, which explains the difficulties in visual functioning [5]. These difficulties may be a signal for detecting neurological changes, particularly when the seizures are subtle and cannot be timely identified by parents or professionals [1, 7].

CVI is a complex condition, most commonly caused by damage to cerebral structures and/or visual pathways. Authors increasingly report that ocular problems, such as anomalies of the fundus or optic papilla and damage to other structures of the peripheral visual system, are also observed alongside cerebral structural damage [26]. Conditions such as strabismus, refractive errors, nystagmus, etc., frequently co-occur with CVI, negatively impacting visual functioning [27]. In acquired CVI, the most common ocular changes include strabismus, visual field deficits or alterations, and a pale optic papilla [14]. The range of these changes indicates that difficulties

in visual functioning can vary from delayed to complete absence of visual responsiveness [14, 28]. These changes may manifest as alterations in the quality or absence of visual responsiveness, deficits in various visual functions, and oculomotor skills [13], often associated with altered findings in visual evoked potentials. The first deviations in visual behavior observed by parents involve the way a child tracks stimuli, maintains visual attention, and establishes and sustains eye contact [29]. Loss of social contact and visuo-social responsiveness may signal the presence of West syndrome [4]. Furthermore, studies have shown that the loss of visual responsiveness coincides with the onset of seizures [30]. Numerous researchers identify unstable visual attention and fixation disorders as primary symptoms of cerebral visual impairment [31]. Cortically mediated visual functions—visual acuity, visual field, contrast sensitivity and oculomotor skills are at risk in children with infantile spasms and West syndrome [5, 32]. Oculomotor disturbances are common, with upward gaze deviation and nystagmus being the most frequently observed [13, 30]. According to some authors, these disturbances result from pathological changes in brain activity [33]. Delayed fixation shifts and brief visual attention are already noticeable at the age of three months and may be associated with sleep difficulties and damage to ascending tracts [13, 30]. In West syndrome, the visual tracking skill is often absent or inconsistent and fragmented [33]. Visual behavior in children with CVI and West syndrome is characterized by frequent blinking, eye squinting, and latency in detecting stimuli during visual scanning [14, 30, 32]. In addition to basic visual functions, visuo-perceptual and visuomotor abilities, particularly hand-eye coordination are significantly impaired in children with CVI and West syndrome [13]. Difficulties in visuospatial abilities, caused by reduced blood flow in the parieto-occipital region, are manifested during orientation and mobility, as well as while determining spatial relations [34]. Regression in cognitive functioning affects the motivation for observing and maintaining visual attention, making visual scanning and searching the materials and the environment challenging for these children [30, 35].

INFANTILE SPASMS – WEST SYNDROME THERAPY AND VISUAL FUNCTIONING

Determining therapy with favorable long-term effects is closely related to the timing of seizure detection and identifying the cause, i.e., the etiology of infantile spasms (IS), which often requires genetic testing [6]. In 70% of cases, typically in symptomatic IS, the etiology of seizures can be identified, while the remaining cases are of unknown origin [6]. Changes in visual functioning, as well as other developmental domains, are closely related to seizure control and the

use of medication therapy. If the therapy does not have the expected effect, it is necessary to make adjustments, monitor the child's development, and conduct assessments every six months [2]. In children with infantile spasms leading to cerebral visual impairment, the results are noticeable after a few months of therapy unless severe visual system damage previously occurred [11, 31]. The negative impact of infantile spasms on all domains of development and functioning, along with pronounced resistance to numerous antiepileptics, sometimes requires the implementation of more aggressive therapy. Therapy for infantile spasms is based on the use of valproate (valproic acid) or adrenocorticotropic hormone (ACTH) [2, 8]. Medications used in treating infantile spasms, such as vigabatrin or corticosteroids, often have sedative effects and can influence visual attention and visual functioning, manifested through prolonged visual latency. However, it is sometimes difficult to determine whether this behavior is a result of the medication or the persistence of seizures [1, 30].

Vigabatrin is the medication of choice for treating infantile spasms. However, its toxic effects on the retina are often emphasized, as evidenced by findings obtained through electroretinography and optical coherence tomography [10]. Long-term vigabatrin therapy can lead to permanent concentric narrowing of the visual field. On the other hand, exposure to this medication for less than nine months is not a significant risk factor for visual impairment, especially in children who started therapy after their first year of life [36, 37]. In some children, difficulties in visual functioning are not related to the use of vigabatrin, as they were present before the medication was administered [10]. Most researchers agree that the results depend on the medication dosage, the therapy duration, and the presence of additional ophthalmological conditions [36, 37]. Unlike valproate, adrenocorticotropic hormone and prednisone do not have a negative impact on visual functions [2]. Alternative forms of therapy include medications such as topiramate, zonisamide, and clonazepam, as well as the implementation of a ketogenic diet under strict professional supervision. Studies have shown that these medications successfully control seizures in individual cases. However, there is no evidence that they are more effective than primary therapy, making them only a potential supplementary option [2].

IMPLICATIONS FOR EARLY INTERVENTION

When considering the role of vision in brain development, particularly the importance of early visual experience, the right of children with West syndrome to be included in early intervention programs focused on vision and visual functioning is indisputable. In children with infantile spasms, assessing visual functioning alongside an ophthalmological examination is essential to

form a comprehensive visual profile and select a treatment to improve functional vision [18]. Direct functioning assessment in children with CVI and multiple disabilities is very challenging since there is often no appropriate way for the examiner to cooperate with them. Therefore, researchers worldwide have developed various assessment methods, including both quantitative and qualitative measures [38]. The principle that various child characteristics require multiple methods, i.e., thorough assessment, plays a key role in the comprehensive diagnosis and selection of rehabilitation programs for children with CVI [39]. We can gain insight into the child's functional vision and visual functioning by observing the child in various situations, collecting data from family members about the specifics of visual behavior, and directly assessing visual abilities [11]. This is particularly significant at an early age, especially in the presence of risk factors that may lead to difficulties in visual attention, processing, and understanding what is observed. The assessment of unique behavioral characteristics in children with CVI, timely inclusion in vision (re)habilitation, and monitoring the impact of epilepsy and medication therapy on visual functioning, using different protocols, allows for the observation of the child's progress over time [40]. According to data from 2020, 1.4 million people in Serbia had some form of visual impairment, of which 116,000 face serious consequences in visual functioning [41]. Given that there is no official registry for CVI and that priority in treatment is given to the primary condition, it can be assumed that the number of people who need support in the area of visual functioning is significantly higher. Although consensus on terminology, diagnostic methods, monitoring, and rehabilitation has not yet been reached, when CVI is confirmed through multiple assessment methods, various types of adaptations in everyday conditions and visual training can improve the child's visual functioning [38]. The relation between visual functioning and cognitive abilities strongly indicates the importance of vision rehabilitation [13], and the unique characteristics allow for creating individualized intervention guidelines, which include environment modifications and counseling for parents. Along with vision rehabilitation based on the assessment of vision and visual functioning, an individualized approach can contribute to creating conditions for achieving optimal development levels in children with West syndrome [4]. Considering that there is often a white matter reduction in these children, the consequences on cognitive functioning can be diametrically different [6, 9], leading to a significant number of uncertainties related to the planning, course, and outcomes of treatment.

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CONCLUSION

The diversity of factors that influence the functioning characteristics of individuals with West

syndrome (epidemiology, location of damage, frequency of infantile spasms, age of onset, etc.)

makes this population highly heterogeneous, presenting specialists with complex tasks related

to the assessment of functioning, treatment planning, and predicting treatment outcomes. The

pathological impact of this type of epilepsy on the optic radiation and/or visual cortex areas,

visual functions, and visual functioning clearly emphasizes the importance of controlling the

spasms. Timely detection of sometimes subtle behavioral changes in a child and inclusion in

diagnostic procedures to detect central nervous system damage, specifically West syndrome,

can mitigate its impact on visual functions and visual functioning. If CVI is identified in chil-

dren with West syndrome, environmental adaptation should be implemented in accordance with

the degree of visual difficulties. The results of intervention-oriented transdisciplinary assess-

ment form the basis for creating a treatment plan. Future research should aim to develop stand-

ardized assessment protocols for CVI specifically adapted to the needs of children with infantile

spasms.

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