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PREDICTORS FOR DEVELOPMENTAL DELAY IN CHILDREN WITH CEREBRAL PALSY AND AT-RISK CHILDREN

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SUMMARY

Background: The first three years of life (zero to three) are a period of great importance when discovering the congenital, as well as the acquired disorders and developmental delays. Recognizing milestones and manifestations of certain behaviors helps us identify developmental delays and disruptions. With this research we intended to determine the segments of developmental achievements and developmental discrepancies of psycho-motor development (general development achievements, motor functions, surrounding motor functions and communication) in infancy and early childhood (zero to three years old) in three groups of respondents.

Material/ Methods: The research sample included 104 respondents. Sixty-three of them had been diagnosed with cerebral palsy (thirty-three were without comorbidity convulsions, and thirty were with comorbidity convulsions-epilepsy), and forty-one respondents were born with a risk factor for a developmental delay. The research was conducted using the standardized developmental instrument Chuturic Developmental Scale for evaluation of the psycho-motor development, which encompasses oculomotorics, emotional development, speech, hearing-motor reactions, communication, socialization and verbalization, of infants and small children.

Results: The analysis of results concluded that there is a discrepancy in the developmental achievements of the three groups of respondents. Based on analysis of the values of the Global Development Coefficient (GDC), we have determined that the most affected group is the group of children with cerebral palsy and comorbidity convulsions where the average value of GDC is 47.77.

Conclusions: Early and precision diagnostics, as well as knowledge of the developmental characteristics of different categories of developmental delays will improve the prognosis and contribute to better utilization of the brain plasticity in children with cerebral damage and children born at risk. Early intervention and stimulation are more than necessary to maximize the child's full potential, reduce the primary effects of the damage or prevent secondary damages and difficulties.

Key words: psycho-motor development, cerebral palsy, comorbidity, risk factors, developmental delay

BACKGROUND

Infancy and predictors for possible developmental delay are significant both for children born at risk and children that have a medical diagnosis that limits normal psychophysical development. Cerebral Palsy (CP) is a motor disorder that results from injury to the developing brain (Swaiman, 1999; Pellegrino, 2001; Deluca&Ramey, 2002; Bax et all, 2005;). The definition of CP has become more precise in the last few years, describing the term CP as an umbrella that encompasses broad symptomatology and creates a simple system of classification. CP represents a group of non-progressive disorders of the movements and posture, caused by the damage or injury of the maturing brain which occurred during either the prenatal- or the perinatal- or during the early childhood period. It is a common cause of severe neuro-motor developmental disturbances in infants and early childhood, which is often accompanied by sensory integration problems, cognitive, communication, perception and behavior disorders. Pop-Jordanova (2011) points out that cerebral palsy is a non-progressive condition, but it is not necessarily a constant disorder of the movements and the posture; there are possible changes during the maturation of the nervous system. According current research, a great number of neuro-genetic syndromes, progressive disorders, inherited metabolic and heredodegenerative diseases, as well diseases of the spinal cord and muscle hypotonia are excluded from the cerebral palsy entity (Mejaski-Bosnjak, 2007). Striving to foster a unified classification of the cerebral palsy types and taking into consideration the variability of the symptoms, the European Union Project "Surveillance of Cerebral Palsy" (SCPE)[1] proposes a simplified classification based on the neurologic symptoms, and distinguishes three general types of cerebral palsy: spastic, dyskinetic and ataxic. Following modern trends and World Health Organization's guidelines, SCPE also proposes use of the Functional Abilities Assessment Methodology when trying to determinate appropriate habilitation and rehabilitation (Mejaski-Bosnjak, 2013).

According to SCPE, the prevalence of the cerebral palsy in Europe is 2-3 out of 1,000 live births. The significance of the influence and prevalence of the epilepsy in persons with cerebral palsy is questionable and controversial throughout the literature. Different studies report prevalence between 12% and 90%. Some authors argue that certain types of cerebral palsy are more susceptible to epilepsy. When considering the frequency of prevalence of the epilepsy as a comorbid condition of different types of cerebral palsy, studies have shown that the convulsions are most prevalent in cases with spastic diplegia (50-94%); there is a 30% prevalence rate in cases with spastic hemiplegia, and a 16-27% prevalence rate in cases with ataxia (Sankar, 2005).

[1] The Surveillance of Cerebral Palsy in Europe (SCPE) was established in 1998 as a collaboration of professionals and researchers working with cerebral palsy (CP) registries, bringing together pediatricians, pediatric neurologists, epidemiologists and therapists from across Europe. The aim is to disseminate knowledge about CP through epidemiological data, to develop best practice in monitoring trends in CP, to raise standards of care for individuals with CP, to inform for service planning, and to provide a framework for collaborative research.

Cerebral lesions associated with cerebral palsy imply biological constraints that affect typical developmental trajectories of certain cognitive functions of individuals with intellectual disability or specific cognitive impairments. Due to the nature of the basic lesions, it is expected for the children with cerebral palsy to develop a wide spectrum of cognitive impairments. Diffuse lesions of the white matter are a cause for low efficiency in data processing and affect more cognitive functions. Deficits in executive functions and attention are expected due to lesions in periventricular white matter. Damages in the region of basal ganglia and thalamic system affect focused attention and executive functions also, while visually-perceptive disorders are related to severe periventricular malacia (Bottcher, 2010).

The influence of many factors that have a negative effect on the fetal development can later be manifested during the child's development. Because of their biological background, children born under the influence of these factors enter the group of at-risk children. These children need special attention, continuous monitoring, early stimulation and early intervention services in order to use the brain plasticity (Matijevic, Mikelici et al, 2011). Risk factors are the ones that lead to different disorders and impairments in the newborn, but do not necessarily lead to such developmental disability or delay. A child at risk is not always a child with disability. Today, 10-15% of all live births are considered to belong to the at-risk group, and in 50% of them, mild, moderate or severe neurodevelopmental disorders will occur (Chichevska-Jovanova, Rashikj-Canevska, 2013).

Children's typical developmental progress can be monitored in five categories of skills: motor, cognitive, communication, social-emotional and adaptive skills. Some children may experience delays related to physical growth, while others take longer to interact either socially or emotionally. All children are unique, but it is expected that in children with CP, the digressions from the typical psychomotor development in some of the developmental segments, especially in terms of motor skills, may indicate presence of cerebral palsy. Early assessments and evaluations should be the standard of care because contemporary early interventions optimize neuroplasticity and functional outcomes (Damiano, 2006; Blauw-Hospers and Hadders-Algra, 2015; Novak et al., 2017). The systematic review of literature shows that diagnosis of cerebral palsy can be accurately made before 6 months' of age (Novak et al, 2017). In infants and young children, clinical signs and symptoms of cerebral palsy emerge and evolve before the age of 2; therefore, a combination of standardized tools in conjunction with clinical history should be used to predict risk. For at-risk or developmentally delayed children, the predictors for developmental delay and the developmental scales used to predict these delays are especially important.

Recognition of these early signs leads to an early diagnosis; however, most of the children are diagnosed around 18 months of age. Developmental signs that are indicators of cerebral palsy include: excessively rigid and stiff movements, problems in eye bulb movements, favoring unilateral movements, absence of laughter before three months of age, no independent holding of the head between age of 3 and 6 months, no hand-mouth coordination after the age of 3

months, inability to reach/ absence of reaching out for objects, lack of reaction to sound or light, inability to walk after being 18-months old, inability to recognize familiar people or objects, irregular muscle tone etc. The cases of mild, discrete cerebral palsy are usually misdiagnosed, as the symptoms are subtle and imperceptible, and these children are usually diagnosed in their pre-school or at-school age (Bochek, 2016). In that context, American Pediatric Academy recommends regular, repetitive developmental screenings at the age of 3, 6, 9, 18, 24 and 30 months.

In the last few decades efforts have been made and research studies have been conducted in the area of neurocognitive development that led to a new approach called constructivism-maturity model. The neuro-constructivist approach characterizes development as a trajectory that is shaped by multiple interacting biological and environmental constraints. The central aspect of understanding cognitive development in this framework is the explanation of how these constraints affect the development of the neural networks of the brain that give rise to progressively more complex mental representations. (Bottcher, 2010). Within the neuro-constructivist framework, developmental disorders can be understood through altered constraints that push the developmental trajectory off its normal track. Just like typical development, atypical development can be characterized as an adaptation to multiple interacting constraints, only with the exception that the constraints are different ones. These so called “atypical” constraints then lead to different i.e. sub-optimal outcomes possibly through a deflection in the process of representation construction.

Early intervention programs are designed to enhance the developmental competence of children and to prevent or minimize developmental delays. These programs are based on the sensitive periods in human life. Sensitive periods are extended periods of time where children are more receptive to environmental stimuli than they would be later in life (Cicchetti & Ruth, 2015; Meredith, 2015; Perlroth & Branco, 2017). Accordingly, there is every reason to assume that perceptual, motor and cognitive functions are more sensitive to environmental influences, such as training and other forms of stimulation, during childhood than later in life (Kral, 2013). The amazing developmental changes of the brain between pre-term age and the age of 1-year post-term offer opportunities for early intervention. Intervention has the highest impact when applied during the period when dendrites and synapses are produced at a high rate. The period during which the double cortical circuitry configuration wanes offers therefore large opportunities for early intervention (Van Der Bergh, Mulder, Mennes, Glover, 2004).

PURPOSE OF STUDY AND RESEARCH METHODS

This study was led by clinical experiences that provide early diagnostics and appropriate rehabilitation of children with cerebral palsy with or without comorbidity. Early stimulation of the affected segments of the psycho-motor develop-

ment may lead to significant results due to the use of the natural brain plasticity and transferring possibilities of the central nervous system – condition that occurs when healthy brain tissue takes over the functions of the damaged brain tissue (Jokovic-Turalija, 2002).

The goal of our study is to assess the developmental achievements and discrepancies in different aspects of the early development of three groups of children (children with cerebral palsy, children with cerebral palsy and epilepsy as comorbidity and children born at risk of zero-to-three-years age. The research outcomes will define predictors for developmental delay.

The research was conducted applying comparative and descriptive analysis, as well as analysis of documentation and testing.

Participants

The study included 104 participants at zero-to-three-years age. Sixty-three examinees were diagnosed with cerebral palsy, mainly at the Pediatric Clinic in Skopje and hospitalized for rehabilitation with the Bobath program in the St. Erazmo Specialized Hospital for Orthopedic and Traumatology in Ohrid. This group of examinees was divided in two sub-groups, one with 33 examines without comorbidity and the second one composed of 30 examinees with cerebral palsy and comorbidity, epilepsy. The other 41 participants were part of the control group, and these were infants born at risk and included in early stimulation program and continuous screening at the Maternity and Child Health Care Institute in Skopje.

Procedure

During the research participants were aware of and in agreement with the use of the information presented herein, and the parents of the children participants in our research signed the terms of free and informed permission and consent. Data was collected by testing and analysis of documentation. In the presence of one of their parents, children were tested individually using a standardized developmental instrument Chuturich Developmental Scale (CDS). Each parent provided information regarding the child's development, birth and pregnancy. Testing was done in a hospital specialized in orthopedics and traumatology. The test primarily aims to examine the psycho-motor development in infants, toddlers and pre-school children. Aside for being used for prevention, assessment and monitoring of progress of therapeutic interventions in children with disabilities, this instrument is also used for scientific research in the field of development of infants, toddlers and children of pre-school age (Cuturic, 1988). The test is composed of two parts – the first one examines the psycho-motor development of birth-to-2-year-old infants and toddlers, and the second one is used for assessment of children at the age between two and eight years. The first part of the test contains 15 subtests, and the second one contains 7 subtests used to examine the motor skills, eye motion coordination, emotional development, hearing-motor reactions and socialization.

Scoring and analysis

The data for each respondent was analyzed separately. The score for the given tasks was divided by the chronological age to obtain general coefficient of the psycho-motor development. Subsequently, special coefficients of different developmental aspects were calculated. With the maximum value of the Score Developmental Coefficient (GDC) being 100, a value over 80 GDC was considered as indicative of adequate-to-age psycho-motor development; a GDC of 60-79 would be indicative of a borderline development, and a value of GDC under 60 represents a developmental delay. Statistical measures such as distributive values and frequency, and T-test for determination of the differences between the groups of examinees were used.

RESULTS

The statistical analysis showed discrepancies in developmental achievements in various aspects of the psycho-motor development of the three assessed groups of children. Based on values of the Global Developmental Coefficient, it seems that the most affected is the group of children with cerebral palsy and epilepsy, with an average GDC of 47.77, which indicates a delayed developmental coefficient (see Tables 1 and 2). Children with cerebral palsy without epilepsy have a borderline GDC value – an average of 64.76. Children born with a risk for developmental delay have an average GDC value of 82.76.

The analysis of results concluded that there is a discrepancy in the developmental achievements of the three groups of respondents. Based on analysis of the values of the Global Development Coefficient (GDC), we have determined that the most affected group is the group of children with cerebral palsy and comorbidity convulsions where the average value of GDC is 47.77.

Table 1. Psychomotor developmental segments in children with cerebral palsy

Variable	**N**	**M**	**Mt**	**SD**	**Lowest achieved score**	**The highest achieved score**
Global development DQ	33	64,76	50	17,20	31	94
Motoric DQm	33	52,27	50	19,27	25	87
Eye motion skills DQo	33	68,57	50	22,70	18	99
Communication DQk	33	70,82	50	17,60	41	99

Table 2. Psychomotor developmental segments in children with cerebral palsy and epilepsy

Variable	**N**	**M**	**Mt**	**SD**	Lowest achieved score	The highest achieved score
Global development	30	47,77	50	17,91	23	91
DQ	30	46,13	50	18,07	21	94
Motoric	30	46,37	50	20,50	21	89
DQm	30	48,60	50	17,36	26	89

Data presented in table 1 show that beside the borderline value of the coefficient of global psycho-motor development, children with CP in the communication and eye-motion aspect of the psycho-motor development achieved the same results, which is not the case in terms of the achievements related to motor development. Motoric skills appear to be the most affected area of development, and the data indicated delayed development.

Within the group of children with CP and epilepsy, a significant discrepancy in the developmental achievements, which stems from the group's heterogeneity, was observed. Some of the children have normal development in all developmental aspects, other present completely disintegrated developmental abilities with clearly visible developmental regress. Similar to the previous group, they have the best achievements in communication, and the lowest in motoric skills. All development coefficients are below the theoretical arithmetic mean and there is a significant deviation from the expected achievements for a population without developmental delays.

Data analysis also showed a statistically significant difference in the results in terms of communication abilities of the members of the three examined groups. Developmental skills in the emotional, speech and socialization aspects of the communication are at most affected within the group of respondents with cerebral palsy and comorbidity. Children with CP without comorbidity have accomplished significantly higher results, more similar and closer to the scores adequate for the appropriate chronological age (Table 3 and 4).

The assessments of communication skills (emotional development, expressive and receptive speech, socialization and hearing-motor reactions) in children with cerebral palsy have given statistically significant higher results than assessments of motoric skills (muscle strength, mobility, movements of upper and lower limbs) in the same group (Table 5). The eye motion skills are also better developed than the basic motoric skills in children with cerebral palsy (Table 6). There

Table 3. Differences in global developmental coefficient between children with cerebral palsy and children born at risk

Variable	N	M	SD	Df	T	p
At risk children	41	82,76	10,52	72	5,54	.003
Cerebral palsy	33	64,76	17,20			

Table 4. Differences in global developmental coefficient between children with cerebral palsy and children with cerebral palsy and epilepsy

Variable	N	M	SD	df	t	p
Cerebral palsy	33	64,76	17,20	61	3,84	.00
Cerebral palsy and epilepsy	30	47,77	17,91			

Table 5. Differences in communication developmental coefficient between children with cerebral palsy and children with cerebral palsy and epilepsy

Variable	N	M	SD	df	T	p
Cerebral palsy	33	70,82	17,60	61	5,03	.006
Cerebral palsy and epilepsy	30	48,60	17,36			

Table 6. Differences in communication developmental coefficient between children with cerebral palsy and epilepsy and children born at risk

Variable	N	M	SD	df	T	p
Cerebral palsy and epilepsy	30	48,60	17,36	69	11,54**	.001
At risk children	41	86.71	10.35			

Table 7. Differences in the developmental areas “communication” and “motor skills” in children with cerebral palsy

Variable	N	M	SD	df	t	p
Communication	33	70,82	17,60	64	4,08	.00
Motoric	33	52,27	19,27			

Table 8. Differences in the developmental areas “eye motion skills” and “motor skills” in children with cerebral palsy

Variable	N	M	SD	df	t	p
Eye motion skills	33	68,57	22,70	64	3,14	.00
Motoric skills	33	52,27	19,27			

Table 9. Gender differences in achievements in the group of children with cerebral palsy and epilepsy

Variable	N		M1	M2	SD1	SD2	df	t	p
	M	**F**							
Developmental quotient	15	15	55,80	39,73	11,94	19,58	28	2,71	.00
Motoric	15	15	53,80	38,46	14,35	18,56	28	2,53	.00
Eye motion skills	15	15	55,67	37,07	14,38	21,88	28	2,75	.00
Communication	15	15	55,93	41,26	11,80	19,22	28	2,52	.00

is no significant difference among these developmental segments in the two other groups of children.

Regarding gender, results have shown that there is a significant discrepancy in the group of children with cerebral palsy and epilepsy as comorbidity only in instances where male examinees have achieved higher results in all evaluated developmental segments (Table 7).

DISCUSSION

This study supports and adds on to existing literature regarding of predictors for developmental delay in children with CP. We cross-referenced the data results obtained in similar studies in order to have scientific justification for the study. The results from this research align with the study results of Largo (1986) who assessed language development in 114 at-risk children aged 5 years and younger, of which 20 were with various levels of cerebral palsy. Children with cerebral palsy had shown significantly more expressive language developmental delays and articulation pathology compared to their peers born at-risk of cerebral palsy.

Our study also adds to the body of knowledge gained from a study by Dominik (1979) which examined the differences in the psycho-motor development and frequency of disorders in children with epileptic seizures as a result of an isolated

brain lesion, and children with epileptic seizures as a comorbidity of cerebral palsy. The evaluation of 46 children from 1-3 years of age had shown that there are more occurrences of delays in psycho-motor development among children with cerebral palsy and comorbidity. According to Chen et al. (2011), significant correlations between motor impairment severity and developmental functions have been revealed, and among developmental functions themselves. In our study, all development coefficients were below the theoretical arithmetic mean and significantly deviate from the expected achievements for a typical population.

Kakushadze (2005) analyzed the impact of the epilepsy onset on the developmental achievements in 121 children. Children were screened for 5 years and the results showed high correlation between the age of the onset and the level of developmental delays. Kakushadze's study showed that the earlier onset of the epileptic seizures leads toward poor developmental prognosis. The occurrence of epilepsy in children with cerebral palsy is associated with poor motor function. The occurrence of epilepsy in CP is associated with limitations in conscious motor functions (Bateman, 2008; Jekovec-Vrhovesk, 2012). Carlsson et al. (2003) concluded that there is a higher frequency of occurrence of epilepsy among children with cognitive impairment than among those without cognitive impairment. They also concluded that regardless of the prognosis of seizures, epilepsy was a major predictive factor of both the presence of intellectual disability and of the motor development of children with cerebral palsy. Our research results are in line with (support) this finding.

Botcher et al. (2010) measured the general cognitive functioning of 33 children using the Verbal Comprehension Index (VCI) of the WISC-III. Four subtests focusing on information, similarities, comprehension, and vocabulary are included in the index. The authors pointed that the mean score for the whole group was 92, which is a little below the population mean of 100, but still within the normal range. The difference between the study group and the norm population was not significant (p=0.10). The results of our study go hand in hand with Botcher's results; they also show better performance in terms of communication of children with cerebral palsy than in motoric abilities and borderline global developmental coefficient in average GDC 64.76, which means little below the children at risk of CP. The Botcher's finding of a slightly lower overall level of verbal cognitive functioning in children with spastic CP is in line with findings from other studies (such as Pirilia et al., 2004) where the neuropsychological assessment found that deficits in visuomotor and visuospatial processing were typical for the children with cerebral palsy and no association was found between the neonatal cranial findings and the IQ and neurocognitive scores. Sigurdardottir (2008) found that children with spastic diplegia and quadriplegia performed significantly less well on the performance tasks than on the verbal tasks. These differences in IQ subscales seemed to be more strongly related to the gestational age at birth than to motor impairment, and similar differences were not observed for children with hemiplegia or dyskinetic CP. These findings match the findings from our study.

The quantitative statistical analysis in our study based on the t-test pointed

out that developmental psycho-motor achievements in the area of communication are more affected in children with cerebral palsy and epilepsy, than in children with cerebral palsy without epilepsy or children born at risk. Critique values of t for df=61 are 1.67 at the level of significance 0.05 and 2.39 at level of significance 0.01 between the both groups with cerebral palsy and t values for df=69 are 1.67 at the level of significance 0.05 and 2.39 at level of significance 0.01 between the group of children with cerebral palsy and epilepsy and other group of children born at risk. A study by Romeo (2011) included 171 children with cerebral palsy older than 1 year, for examination of their motor and cognitive development, using Gross Motor Function Measure (GMFM), Gross Motor Function Classification System, and Bayley II and Wechsler Scale. The results have shown that female examinees younger than 4 years and with hemiplegia accomplished significantly better results in cognitive function compared to the gross motor functions. If we take into consideration that the developmental instrument used in our study suggests that the eye motion achievements are predictors of the cognitive abilities, then our findings correspond to those of Romeo, with the difference that in our study, the achievements are same for both male and female. In his study, Romeo determined that gender had various effects on the psychomotor development in different types of cerebral palsy. Our study points to the contrary.

Implications of this study for practice and future research

Every child has its own developmental pace. The trajectory of developmental delays can be easily altered in early childhood. Deficits in developmental milestones may indicate the presence of some neural or motor impairment. The need for an early recognition of cerebral palsy is emphasized, as treatment started later in life i.e. after the age of 1 or 2 years, when athetosis or spasticity are stronger and abnormal patterns of posture and movement established, can achieve only limited results (Novak, Morgan, Ade, 2017). Based on the best available evidence, there is also a growing consensus that early intervention can have substantial benefits to children developmentally at risk. Overall, interventions improve scores on developmental outcome measures, strengthen parent-child interactions, and provide a supportive environment for the family (Majnemer, 1998). Here, we refer to the achievements in the areas of psychical, emotional and cognitive development in order to emphasize the importance of early identification of the developmental delay predictors and implementation of the optimal early intervention program in order to exploit the plasticity of the developing brain and its remaining potentials. The achievements are of great significance for the developmental progress of each child. Knowledge of the basic characteristics and features of the psycho-motor development is necessary to provide appropriate early education and rehabilitation and maximum use of the physiological potential of the child. Further research in this area is needed in order to clearly define predictors for developmental delay in children with CP.

Limitations

One of the limitations is that this research was conducted on a small sample of children. To make the generalizations more feasible, a larger number of children should be included. Another limitation is that this was a transversal study. For definite results longitudinal studies should be conducted, starting from the age of 6 moths and then the cut offs should be made at the age of 1 year, 1.5 years and 3 years of age. Also, there is a lack of studies for comparison of results in regard to the time when the diagnosis was set. This research would add to the discussion of whether early diagnosis and early treatment lead to better developmental outcomes. The last limitation is in the sampling and equalization of the sample in regard to the type of CP. If such equality of samples is achieved that would lead to a greater generalization of the results for each group of children with CP.

CONCLUSION

Early detection of developmental delays can indirectly provide precise and timely diagnostics. If developmental delays are more expressed in some of the segments, especially in motoric skills they may indicate presence of cerebral palsy. The cases of mild, discrete cerebral palsy are usually identified and diagnosed in the late preschool years and a valuable period of the child's development is missed. The indicators provided within this research can lead to systematic developmental monitoring and contribute to an early diagnosis, which leads to a better prognosis and quality of life of the child.

In cerebral palsy, especially CP types associated with comorbidities such as epilepsy, a comprehensive developmental assessment of all developmental areas is needed because of the frequent deficits that the condition itself causes. Here, the motoric developmental skills are not exclusively affected. Other developmental segments can also be affected which was shown in this extensive research.

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