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НЕДОНОШЕННОСТЬ КАК ФАКТОР РИСКА ОТКЛОНЕНИЙ В РАЗВИТИИ У ДЕТЕЙ РАННЕГО ВОЗРАСТА

PREMATURITY AS A RISK FACTOR FOR DEVELOPMENTAL DISORDERS IN
CHILDREN OF EARLY AGE

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Аннотация:

В статье раскрывается вклад недоношенности в формирование отклонений в развитии когнитивных функций у детей раннего возраста. Представлены результаты эмпирического исследования, посвященного анализу отношения шансов риска атипичного развития недоношенных детей в возрасте 3, 5, 10, 14 и 25 месяцев по скорректированному возрасту. В качестве диагностической методики была использована Bayley Scale of Infant Development, 3rd Edition (Bayley-III), с помощью которой были оценены: уровень когнитивного,

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Abstract:

Prematurity is a risk factor for delayed development of neurocognitive functions in children, which manifests from birth. Every year in the world many children are born preterm. Thus, the problem of formation of neurocognitive functions in such children is an important area of research.

The article presents the results of an empirical study devoted to the analysis of the odds ratio of risk of atypical development of premature infants aged 3, 5, 10, 14 and 25 months by corrected age. Bayley Scale of Infant

уровень коммуникативного и уровень моторного развития младенцев.

По результатам проведенного исследования сделан вывод, что недоношенность выступает фактором риска задержки в развитии и оказывает наибольшее влияние в возрасте до года. Кроме того, раннее рождение избирательно влияет на становление нейрокогнитивных функций в зависимости от возраста и сферы развития детей в возрасте 3, 5, 10, 14 и 25 месяцев.

Ключевые слова:

недоношенность, отношение шансов, нейрокогнитивное развитие, диагностика развития.

Development, 3d Edition (Bayley-III) was used as a diagnostic technique, with the help of which it is possible to assess the level of cognitive, communicative and motor development.

Based on the findings, it was concluded that prematurity as a risk factor in development has the greatest impact in the age of one year. In addition, early birth selectively affects the formation of neurocognitive functions depending on age and sphere of development.

Keywords:

prematurity, odds ratio, neurocognitive development, developmental diagnostics.

Relevance

Standardization of neonatal resuscitation methods, improvement of its efficiency, introduction of new criteria of live birth have led to an increase in the survival of infants born prematurely. Preterm infants have become a target group for the study of neurocognitive development of the immature brain, the interest in which is not weakened both in medical circles and among neuropsychologists.

Studies both in our country and abroad were conducted. It was proved that prematurity affects the level of development [1-3]. The complexity of the selection of adequate methods for assessing the formation of neurocognitive functions, as well as the process of diagnosis in infancy and early age, led to the fact that the main results were obtained and published mainly in children older than 2-3 years old.

At the same time, in recent studies, more attention is paid to extremely preterm children, who obviously have the worst prognosis and whose development cannot be affected by several pathological conditions associated with immaturity and brain damage [4-6]. It is believed that the development of neurocognitive functions in preterm infants, anamnesis of which is not complicated by critical somatic diseases or local brain lesions are interesting to neonatologists, neurologists, and neuropsychologists.

Materials and methods

The purpose of this empirical research was analysis of influence of the factor of premature birth on the development of neurocognitive functions in early age. It has

been hypothesized that prematurity increases the risk of atypical development in preterm infants between 3 and 25 months of corrected age.

A cross-sectional study was conducted from February 2016 to February 2018 based on the Laboratory of Brain and Neurocognitive development at the Ural Federal University named after the first President of Russia B.N. Yeltsin, Ekaterinburg, Russia. Two groups were formed according to the inclusion and exclusion criteria: the experimental group, which included preterm children, and the control group of full-term children.

Inclusion criteria: prematurity 28-36 weeks, birth weight not less than 1.0 kg, both sexes; absence of malformations of the brain, heart and other internal organs; absence of hemorrhages or hypoxic foci of any localization and degree according to the results of diagnostic sonography; absence of perinatal hyperbilirubinemia, absence of confirmed intrauterine infection.

Exclusion criteria: prematurity less than 28 weeks, very low birth weight-less than 1.0 kg, clinically confirmed malformations of the brain, heart and other internal organs, hemorrhages and ischemic foci of any localization and degree in the brain according to the results of diagnostic sonography; indication of perinatal hyperbilirubinemia in medical documents, confirmed intrauterine infection.

Children were examined at 3, 5, 10, 14 and 25 months.

Demographic characteristics and group size at each age in the experimental group are presented in Table 1.

Table 1.

Demographic characteristics of the experimental groups

Characteristics	Age				
	3 months n=17	5 months n=41	10 months n=41	14 months n=27	25 months n=20
Gestational age, mean (SD)	33,94 (1,68)	33,15 (2,20)	32,71 (2,31)	32,85 (2,48)	31,10 (2,31)
Chronological age, mean (SD)	4,23 (0,67)	6,26 (0,83)	11,43 (0,68)	15,67 (1,07)	25,84 (0,90)
Corrected age, mean (SD)	3,52 (0,54)	5,36 (0,79)	10,46 (0,71)	14,70 (0,86)	24,90 (0,90)
Sex (male), no. (%)	7 (41,18)	21 (51,22)	20 (48,78)	12 (44,44)	12 (60,00)

The control group included full-term children born on time (37-41 weeks), with a typical development and lack of follow-up in a pediatric neurologist for a history of Central nervous system disease.

Demographic characteristics and group size at each age in the control group are presented in Table 2.

Table 2.

Demographic characteristics of the control groups

Characteristics	Age				
	3 mounts n=18	5 mounts n=58	10 mounts n=65	14 mounts n=55	25 mounts n=33
Gestational age, mean (SD)	38,72 (1,60)	38,93 (1,42)	39,08 (1,47)	38,82 (1,39)	38,94 (1,43)
Chronological age, mean (SD)	3,58 (0,38)	5,80 (0,58)	10,68 (0,65)	14,85 (0,63)	25,12 (0,80)
Sex (male), no. (%)	9 (50,00)	38 (65,52)	38 (58,46)	32 (58,18)	22 (66,67)

To assess the level of neurocognitive development Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III) was used. The method consists of 5 scales and is designed to diagnose the level of cognitive development, receptive and expressive communication, as well as fine and gross motor skills in children aged 1-42 months [7].

Statistical processing was carried out using Microsoft Excel and SPSS Statistics 22 (SPSS Inc., Chicago, IL, USA). The odds ratio (OR), confidence interval (CI), Fisher's exact test and ϕ test was calculated.

Raw scores were used for data analysis. The scores obtained by the child for each of the five scales Bayley-III were compared with the average scores for age taken from the statistical tables of the Administrative manual [8]. If child showed scores equal or higher than the average for his age, this was interpreted as a positive outcome. If the child received values below average, it was interpreted as a negative outcome. Prematurity acted as a risk factor.

OR was defined as the ratio between the probability of an adverse outcome and the probability of a favorable outcome in the factor of prematurity, divided by the same ratio in the absence of prematurity. The interpretation of the results depended on the value of the OR relative to 1. If $OR=1$, the prematurity factor does not affect to development of functions; in $OR>1$, the prematurity factor increases the risk of an adverse outcome; in $OR<1$, it decreases accordingly. Statistical significance was due to the absence of 95% CI 1. Fisher's exact test was used for assessing the significance of differences between the values. To assess the relationship strength of the studied factors used ϕ test, the interpretation of the values presented in Table 3 [9]. OR was calculated for each of the scales Bayley-III at all 5 ages.

Table 3.

**Interpretation of ϕ and Cramer's V tests according to recommendations
by Rea & Parker**

Value of ϕ test	Relationship strength (interpretation)
<0,1	Negligible association
0,1 – <0,2	Weak association
0,2 – <0,4	Moderate association
0,4 – <0,6	Relatively strong association
0,6 – <0,8	Strong association
0,8 – 1,0	Very strong association

Results

The results of the statistical analysis of OR for each age of cross-sectional study are presented in Tables 4, 5, 6, 7, 8.

Table 4.

**The risk of developmental impairments by 5 scales Bayley depending on factor
of prematurity at the age of 3 months**

Scale	Odds ratio	95% confidence interval	Fisher's exact test (p)	Phi (ϕ)
Cognitive	5,60	1,93; 33,70	0,042*	0,436
Receptive communication	2,45	0,55; 11,01	0,143	0,428
Expressive communication	2,08	0,40; 10,88	0,215	0,426
Fine motor	3,33	0,53; 20,98	0,141	0,429
Gross motor	1,07	0,13; 8,93	0,397	0,424

* Significant differences marked in bold

According to Table 4, significant results at the age of 3 months between preterm and full-term infants were obtained only on the scale “Cognitive Development” (5,60 [1,93; 33,70]; $p=0,042$; $\phi=0,436$). The Value of Phi test indicates relatively strong association. Thus, preterm infants at 3 months have chance to have results on cognitive development lower than infants born in time in 5,60 times more.

Table 5.

The risk of developmental impairments by 5 scales Bayley depending on factor of prematurity at the age of 5 months

Scale	Odds ratio	95% confidence interval	Fisher's exact test (p)	Phi (ϕ)
Cognitive	1,35	0,48; 3,77	0,171	0,452
Receptive communication	1,26	0,55; 2,85	0,139	0,452
Expressive communication	1,33	0,11; 0,92	0,016*	0,490
Fine motor	2,22	1,87; 5,67	0,044	0,474
Gross motor	2,46	1,02; 5,92	0,021	0,485

* Significant differences marked in bold

According to Table 5, significant results at the age of 5 months between preterm and full-term infants were obtained on scales "Expressive communication" (1,33 [0,11; 0,92]; $p=0,016$; $\phi=0,490$), "Fine motor" (2,22 [1,87; 5,67]; $p=0,044$; $\phi=0,474$), "Gross motor" (2,46 [1,02; 5,92]; $p=0,021$; $\phi=0,484$). The Value of Phi test indicates relatively strong association on all 3 cases. So, we conclude that preterm infants at 5 months have chance to have results on expressive communication lower than infants born in time in 1,33 times; on fine motor – in 2,22 times; on gross motor – in 2,46 times more.

Table 6.

The risk of developmental impairments by 5 scales Bayley depending on factor of prematurity at the age of 10 months

Scale	Odds ratio	95% confidence interval	Fisher's exact test (p)	Phi (ϕ)
Cognitive	2,28	0,83; 6,24	0,052	0,487
Receptive communication	1,98	1,88; 4,45	0,039*	0,487
Expressive communication	1,35	0,57; 3,20	0,133	0,468
Fine motor	1,59	0,66; 3,81	0,100	0,473
Gross motor	3,98	1,52; 10,42	0,003	0,532

* Significant differences marked in bold

According to Table 6, significant results at the age of 10 months between preterm and full-term infants were obtained on scales "Receptive communication" (1,98 [1,88; 4,45]; $p=0,039$; $\phi=0,487$) and "Gross motor" (3,98 [1,52; 10,42]; $p=0,003$; $\phi=0,532$). The Value of Phi test indicates relatively strong association on all 2 cases. So, we conclude that preterm infants at 10 months have chance to have results on receptive communication lower than full-term infants in 1,98 times; on gross motor – in 3,98

times more.

Table 7.

The risk of developmental impairments by 5 scales Bayley depending on factor of prematurity at the age of 14 months

Scale	Odds ratio	95% confidence interval	Fisher's exact test (p)	Phi (φ)
Cognitive	1,25	0,27; 5,85	0,285	0,658
Receptive communication	1,13	0,38; 3,34	0,208	0,658
Expressive communication	0,90	0,35; 2,30	0,181	0,658
Fine motor	6,75	0,64; 71,56	0,092	0,675
Gross motor	1,74	0,41; 7,29	0,208	0,661

According to Table 7, significant results at the age of 14 months between preterm and full-term infants were not obtained.

Table 8.

The risk of developmental impairments by 5 scales Bayley depending on factor of prematurity at the age of 25 months

Scale	Odds ratio	95% confidence interval	Fisher's exact test (p)	Phi (φ)
Cognitive	1,50	0,38; 5,91	0,225	0,986
Receptive communication	0,98	0,31; 3,07	0,224	0,984
Expressive communication	0,89	0,21; 3,74	0,275	0,984
Fine motor	0,38	0,04; 3,85	0,285	0,987
Gross motor	1,17	0,36; 3,74	0,221	0,985

According to Table 8, significant results at the age of 25 months between preterm and full-term infants were not obtained.

Discussion and conclusions

In this study, not just the differences in the level of development of neurocognitive functions between preterm and full-term children were examined. Attention was focused on the risk of deviations in development, that is development is below average standards. Studies show that differences in neurocognitive development between full-term and preterm infants can be observed in different age and in different domains [10-13]. Thus, preterm infants and toddlers have a lower level of development of different functions compared to full-term children. At the same

time, according to the data, because of the study, it was found that premature children do not always show results below the average norm, which is the task of further research.

The development below the norm at the age of 3 months on a cognitive scale, at the age of 5 months – on the scales of receptive communication, fine and gross motor skills, at the age of 10 months – on an expressive scale and a scale of gross motor skills was revealed. At the same time, at the age of 14 and 25 months, the chances of having results below the norm in preterm children were not revealed.

This study exposed that prematurity has a greater negative impact on the first year of life, while this effect is selective. At the age of 14 to 25 months, this factor is leveled. At the same time, it cannot be argued that in later periods of ontogenesis prematurity will not have a negative impact. Probably, it is the age of 14 and 25 months are such periods when immature children are more consistent with the norms of development.

The data obtained are an important material that allows us to identify the periods in which the most noticeable changes in atypical development occur, when premature children not only show lower results compared to full-term, but also when they have a level of development below the average age. This information makes it possible to develop the most effective early intervention programs, which will be used in critical periods, when the atypical development is manifested. Early intervention aimed at a specific area is the most effective method that allows to neutralize or reduce the consequences of certain deviations in development.

There is no conflict of interests.

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