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The Comprehensive Assessment of the Trajectory of Neurocognitive Skills Development in Premature Infants in Longitude

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Abstract

Introduction. This paper aims to give a comprehensive account of differences in the development of cognitive and sensorimotor functions in premature and full-term infants. Prematurity is an important risk factor for neurological and psychomotor disorders, as well as for impaired cognitive development. This study represents a first attempt to conduct a comprehensive assessment using modern instrumental and behavioral methods in a longitudinal perspective.

Methods. The experimental sample was comprised of 42 premature infants (32.4 ± 2.1 weeks of gestation). The control group consisted of 60 full-term infants with typical development and absence of diseases of the central nervous system. The longitudinal study was conducted at 5, 10, 14, and 24 months of age. The participants' eye movements were recorded with the SMI RED 500 eye-tracking system. The Bayley Scales of Infant Development, Third Edition (BSID III) were used to assess cognitive development, receptive and expressive communication skills, as well as gross and fine motor skills.

Results. Compared to the control group premature infants showed significantly lower results by the Bayley cognitive and communicative sub-scales at 5 and 10 months of age, as well as a lag in motor development at 14 and 24 months of age. In addition, the experimental group demonstrated a decrease in the stability and speed of visual attention switching and a lower result in visual search of a simple non-social stimulus at 14 months of age. No significant intergroup differences were found in the perception of social stimuli and the development of joint attention.

Discussion. Prematurity selectively influences the development of neurocognitive functions. The outcomes of prematurity partially disappear by the end of the second year of life.

Keywords

cognitive development, attention, motor development, communicative development, visual perception, prematurity, infancy, early childhood, Bailey Scales, eye tracking

Highlights

► Premature infants demonstrate a developmental lag in cognitive and speech functions during in infancy and a developmental lag in motor skills in the second year of life.

► The level of development of involuntary attention decreases significantly in premature infants at 14 months of age.

► Premature and full-term infants do not differ in their abilities for perceiving social information.

► The outcomes of prematurity partially disappear by the end of the second year of life.

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Introduction

The periods of infancy and early childhood are characterized by the most intensive development of the organism and its adaptation to the environment. In early childhood children are characterized by a number of significant new formations in cognitive and sensorimotor spheres, which include the main components of thinking, motor functioning, sensory perception, speech, and socio-emotional skills (Baranov, Maslova, & Namazova-Baranova, 2012). At the same time, the pace and characteristics of the development of children in these ontogenetic periods depends entirely upon biological risk factors and environmental impacts (Belousova, Prusakov, & Utkuzova, 2009; Weijer-Bergsma, Wijnroks, & Jongmans, 2008). Prematurity is one of such risk factors (Safina, Volyanyuk, Potapova, & Fisheleva, 2018).

Today, there is a significant increase in the number of children born prematurely, which is associated with the development of intensive care technologies for newborns and a significant increase in the survival rate for children with low and extremely low birth weight. According to the most recent statistics, the rate of preterm birth varies from 5 to 18% of the total number of newborns in 184 countries. According to Russian official data, the survival rate for children weighing less than 1000 g at birth is about 85% (Safina et al., 2018). Moreover, this category of patients is the main risk group for neurological and psychomotor abnormalities, including those leading to disability (Safina et al., 2018; Filkina, Dolotova, Andreiuk, & Vorobeva, 2010; Barkun, Lysenko, Zhuravleva, Kosenkova, & Buchkina, 2013; Dolinina, Gromova, & Kopylova, 2014). In numerous clinical studies, prematurity is considered to be a factor in the formation of cerebral palsy (Namazova-Baranova et al., 2016), autism (Hofheimer, Sheinkopf, & Eyler, 2014; Elsabbagh et al., 2009) and attention-deficit/hyperactivity disorder (Franz et al., 2018).

However, atypical development in cognitive and psychomotor spheres is often observed even in somatically healthy infants with mild and moderate degree of prematurity (gestational age < 28 weeks, body weight at birth < 1500 g) (Emberson, Boldin, Riccio, Guillet, & Aslin, 2017; Blencowe et al., 2012). A large amount of data indicates various disorders in the development of cognitive functions in premature infants, including an increased risk of attention and memory deficits, as well as deficits in information processing speed and executive functions (Emberson et al., 2017; Ross-Sheehy, Perone, Macek, & Eschman, 2017; Ionio et al., 2016; Oudgenoeg-Paz, Mulder, Jongmans, van der Ham, & Van der Stigchel, 2017; Yaari et al., 2018; Zmij, Witt, Weitkämper, Neumann, & Lücke, 2017; Williamson & Jakobson, 2014). Many researchers also note that compared to children with normative development, those born prematurely are at increased risk of motor impairments (Oudgenoeg-Paz et al., 2017; Yaari et al., 2018; Geldof et al., 2016; Zuccarini et al., 2018; You, Shamsi, Hao, Cao, & Yang, 2019; Kaul et al., 2019; Peyton, Schreiber, & Msall, 2018).

The issue of the development of visual functions and the perception of visual information in premature children remains much less studied. Meanwhile, this aspect seems to be important for studying, as the pace and characteristics of the development of visual perception in infancy are undoubtedly associated with the subsequent neurocognitive development of children.

It is known that since the first months of life children have a general tendency to focus on faces and stimuli similar to faces (Konishi Yukihiko et al., 2012; Beier, & Spelke, 2012). The preference for social stimuli in infancy is considered by researchers as an indicator of the further development of social skills (e. i. following another person's gaze of another person and joint attention) (Imafuku et al., 2017). In turn, many researchers recognized that the development of joint attention by the second year of life is as a reliable predictor for speech development in younger and older preschool children (De Schuymer, Groote, Desoete, & Roeyers, 2012; Frischen, Bayliss, & Tipper, 2007; Tomasello, Carpenter, & Lizkowski, 2007). It was found that the frequency of initiating joint attention in infants is associated with speech acquisition, information processing, as well as with individual differences in intelligence and social competencies (Van Hecke et al., 2007).

Eye-tracking is the method for recording and analyzing eye movements that is used for the assessment of visual perception. This method is one of the most widespread for the study of cognitive processes in infants, as it does not require a verbal response from respondents and has high reliability in repeated testing in this age group (Navab, Gillespie-Lynch, Johnson, Sigman, & Hutman, 2012).

Infants start to demonstrate cortical control when switching attention from one visual object to another since 4 months of age. Thus, the characteristics of the subjects' fixation on stimuli may be considered as effective early indicator of attention disorders and impairments of cortical structures associated with atypical development resulting from prematurity (Atkinson & Braddick, 2012). As previous studies have suggested, premature infants or those with low birth weight are at increased risk of impaired perception and recognition of faces (De Schuymer et al., 2012; Telford et al., 2016; Perez-Roche et al., 2017). In the work of E. J. Telford et al. the authors report that compared to infants from a normative group the premature ones spent significantly more time examining the social content of stimuli (Telford et al., 2016). The findings of L. De Schuymer et al. demonstrate that compared to full-term infants their premature peers more often and for a longer time break eye contact with their parents by gaze aversion (De Schuymer et al., 2012).

However, despite numerous studies on deviations associated with premature birth, the results on the outcomes of neurocognitive development in such children are heterogeneous. The literature describes that early exposure to the external environment can both cause harm and become an advantage for the development of the nervous system (Ionio et al., 2016; Peña, Arias, & Dehaene-Lambertz, 2014; Vandormael, Schoenhals, Hüppi, Filippa, & Tolsa, 2019).

Thus, identifying the characteristics of cognitive and socio-communicative development of premature infants in infancy and early childhood is an important issue. An early assessment of oculomotor activity and various components of visual attention seems promising for predicting rates of maturation of mental functions in normative and deviant child development.

In this paper, we have turned our attention to studying the differences in the level of development of cognitive and sensorimotor functions in premature and full-term infants.

This study represents a first attempt to conduct comprehensive longitudinal study using modern instrumental and behavioral methods in the Russian sample of premature and normally developing infants and children. For the first time, the Bayley Scales of Infant Development, Third Edition (BSID III) was tested in a sample of Russian-speaking children. We compared the results obtained in our study with those of previously published data.

Methods

Sample characteristics

The study was conducted in the Laboratory for Brain and Neurocognitive Development, Ural Federal University named after first President of Russia B.N. Yeltsin.

The experimental sample was comprised of 42 premature infants, 22 of whom were boys (32.4 ± 2.1 weeks of gestation, 1614 ± 406 g average birth weight).

The subjects were recruited from the City Perinatal Center in Yekaterinburg.

The experimental sample was comprised of 42 premature infants (22 boys and 20 girls, 32.4 ± 2.1 weeks of gestation, 1614 ± 406 g average birth weight).

Criteria for inclusion in the experimental group: prematurity at 28–36 weeks of age, body weight of at least 1.0 kg, absence of malformations of the brain, heart, and other organs, absence of cerebral haemorrhages or hypoxic foci of any localization and degree according to the results of neurosonography, absence of neonatal hyperbilirubinemia, and absence of confirmed intrauterine infection.

The control group consisted of 60 full-term infants (40 boys and 20 girls) with typical development and absence of diseases of the central nervous system.

We obtained signed informed consent for examination and personal data processing from parents of each child involved in our study. The study design was approved by the Local Ethics Committee of the Ministry of Health of Russia (protocol no. 1, February 20, 2015).

The longitudinal study was conducted at 5, 10, 14 and 24 months of age (± 2 weeks in each longitudinal test).

According to the literature, in most cases the development of 2-year-old prematurely born infants meets the developmental criteria for their corrected age (Lebedeva, Nevryuzina, & Frolova, 2011; Harel-Gadassi et al., 2018). Thus, the subjects were unified by their corrected age (the difference between the actual age and the weeks of prematurity).

Some of the subjects were withdrawn from the study after the request of their parents or by other circumstances. The criteria for inclusion of subjects in the statistical analysis were the presence of eye-movement recordings in each longitudinal test and the sufficient quality of the obtained data. Table 1demonstrates the total of subjects and age characteristics of the groups.

Table 1

Age characteristics of the groups

Longitudinal test	Subjects (n)	Mean chronological age (months), m ± SD	Mean corrected age (months), m ± SD
Control group			
5 months	17 (м = 9)	5,89 ± 0,78	–
10 months	29 (м = 16)	10,50 ± 0,22	–
14 months	36 (м = 20)	14,89 ± 1,05	–
24 months	19 (м = 12)	24,68 ± 0,62	–
Experimental group			
5 months	9 (м = 5)	6,23 ± 0,82	5,85 ± 0,77
10 months	18 (м = 10)	11,92 ± 0,63	10,34 ± 0,52
14 months	22 (м = 13)	15,20 ± 1,22	14,48 ± 0,93
24 months	11 (м = 6)	25,19 ± 1,23	24,68 ± 0,84

Note: m – number of boys

The Bayley Scales of Infant Development, Third Edition (BSID III)

The Beyley Scales of Infant Development is the most widely used technique for assessing the early development of neurocognitive functions in early childhood. In 1969 this technique was developed by Nancy Bailey together with her colleagues at the University of Berkeley; it was intended for diagnosing children aged 1 to 42 months (Bayley, 2006). In this work, we used its third edition, revised and approved in 2008, which includes three subscales of the mental scale(cognitive subscale, expressive subscale, and receptive communication)and two subscales of the psychomotor scale (gross and fine motor skills).

Each subscale had a fixed number of tasks and items used to assess each particular skill. The experimenter can independently choose the order of the tests, depending on children's' temperament, his/her interest in performing certain tasks, as well as on the degree of contact. The variability of the order of the tests allowed us to obtain an adequate idea of different aspects of the development of the child.

Eye-Movement Recording Method

In this work, we used the SMI RED 500 eye-tracking system representing a non-contact, remotely controlled infrared camera that automatically tracks eye movements. During the experiment, the infant sat on the parent's lap or alone in the car seat. The location of the eye-tracker system was corrected so that the middle of the monitor was at the same height with the child's eyes at a distance of 60–70 cm.

Stimulus materials were provided by a research group from the Center for Brain and Cognitive Development (Birkbeck, University of London, UK), where experimental procedures for the development of infants were developed and tested as a part of the European project for the study of risk factors for autism spectrum disorders (ASD) and attention deficit/hyperactivity disorder (ADHD).

The stimulus materials included the following three blocks:

1) 8 pictures with five different objects, one of which represented the image of a person's face (a social stimulus). The other four objects were distractors and represented non-social stimuli: a bird, a car, a phone, and a blurred face image. Similar tests were used in the work of Telford et al. (2016).

2) 16 pictures including seven identical stimuli and a differing one. The identical (irrelevant) stimuli represented a diagonal cross; the differing (relevant) stimuli represented a circle in simple tests and a vertical cross in complex ones.

3) 6 videos representing three objects: a model (woman) and two toys. The model sits with her head down, then raises her head and attracts the attention of the child, looking straight ahead and raising her eyebrows; then she looks at one of the toys, which is a relevant stimulus in this case. Similar trials were used by Senju & Csibra (2008).

To calculate the number of trials performed by each subject we used certain criteria. In the first block, the test was considered performed if the first fixation of the child's gaze was in the face area. In the second block, to perform the test it was necessary to find a different object. In other words, we assessed the presence of fixations in the area of a relevant stimulus. In the third block, the child was considered to look away from the relevant stimulus.

Statistical processing

To assess the differences between the groups of subjects we used the Mann-Whitney test. The analysis was carried out according to the following variables:

1) "raw" scores for 5 Bayley-III subscales: cognitive communication (CogRaw), receptive communication (RecRaw), expressive communication (ExpRaw), gross (GmRaw) motor skills, and fine motor skills (FmRaw).

2) Block 1: the number of valid (VT) and performed tests (CompT), the duration of fixations (ms) on the images of a face (faceFD), a blurred face image (noiseFD), a bird (birdFD), a car (carFD), and a phone (phoneFD).

3) Block 2: the number of valid test (VT); performed 'simple' (CompO) and 'complex' (CompPl) tests; time of reaction (ms) to distractors (DisRT), a circle (ORT), and a vertical cross (PlRT).

4) Block 3: the number of valid tests (VT), the number of tests with the first gaze at relevant (Rel) and irrelevant (Unrl) stimuli, the duration of gazing (ms) relevant (RelFD) and irrelevant (UnrlFD) stimuli.

The calculations were performed using the IBM SPSS Statistics 22 software for Windows.

Results

Table 2 presents the results of statistical analysis to assess differences in the development of neurocognitive functions in a sample of full-term and premature infants.

There are intergroup trend differences in the first longitudinal trial by two subscales: cognitive development and receptive communication. At the age of 5 months, neurologically healthy infants had higher scores in comparison with premature infants both in the cognitive subscale (29.12 ± 3.53 vs 25.80 ± 2.16) and in recessive communication (9.71 ± 1.40 vs 8.00 ± 0.70).

In the second longitudinal trial we observed significant differences in three subscales: cognitive development (39.41 ± 4.06 vs 36.40 ± 4.06), receptive communication (13.71 ± 2.05 vs 11.60 ± 1.89), and gross motor skills (39.88 ± 3.30 vs 35.33 ± 3.96).

Table 2
U-test for Bayley Scales

Longitudinal tests	Means, significance level (U-test)				
	CogRaw	RecRaw	ExpRaw	FmRaw	GmRaw
5 months	**18.5;0.06***	**10.5;0.01****	26.0;0.18	22.5;0.11	26.5;0.21
10 months	**160.5;0.04****	**119.5;0.003****	**176.5;0.08***	190.5;0.16	**98.5;0.001****
14 months	276.0;0.56	253.0;0.31	237.0;0.17	**208.5;0.06***	**191.0;0.03****
24 months	39.0;0,11	41.5;0,15	45.0; 0,20	58.0;0.62	**32.0;0.04****

Note: ** – significant differences *($p < 0.05$)*,* – trend differences *($p < 0.1$)*

At the age of 14 months, the subjects demonstrated pronounced differences only in the field of motor development. According to the subscale of fine motor skills, healthy subjects scored higher than premature infants (33.56 ± 2.95 vs 31.83 ± 2.72). Similar results were obtained when evaluating gross motor skills (49.14 ± 2.90 vs 46.78 ± 4.32).

Finally, at the last longitudinal trial the only differences we observed were those in large motor skills. The actual level of motor skills in the control group was significantly higher than that observed in the experimental one (59.74 ± 4.01 vs 56.42 ± 2.37).

Table 3 presents intergroup differences in the trials of the first block of the experiment measured by eye-tracking.

We observed significant differences in the number of valid trials among subjects aged 14 months. Thus, in the first block normative children had statistically more valid trials compared with premature infants (6.33 ± 1.51 vs 5.50 ± 1.82).

In addition, significant intergroup differences were found in the duration of gazing the images of birds in subjects aged 10 months (690.97 ± 289.06 ms in full-term infants, 281.85 ± 129.99 ms in premature infants), as well as in the duration of gazing the telephone images in subjects aged 14 months (630.46 ± 377.86 ms vs 330.59 ± 149.58 ms, full-term and premature subjects, respectively).

Table 3
U-test for the first block of stimuli for eye-tracker

Longi-tudinal tests	Means, significance level (U-test)						
	VT	CompT	faceFD	noiseFD	birdFD	carDF	phoneFD
5 months	39.0; 0.78	39.0;0.78	37.0;0.67	33.0;0.45	37.5; 0.69	30.0; 0.33	32.0; 0.41
10 months	248.5; 0.62	199.5; 0.13	245.0; 0.57	242.0; 0.53	**126.0; 0.002****	215.0; 0.24	246.0; 0.58
14 months	**207.0; 0.04****	277,0; 0,48	306.0; 0.87	**218.0; 0.07***	308.0; 0.90	260.0; 0.32	**182.5; 0.014****
24 months	68.0; 0.65	62.0; 0.45	60.0; 0.396	74.0; 0.91	69.0; 0.71	65.0; 0.56	56.0; 0,28

Note: ** – significant differences *(p < 0.05)*,* – trend differences *(p < 0.1)*

Table 4 presents intergroup differences in the trials of the second block for eye-tracker.

Table 4
U-test for the second block of stimuli for eye-tracker

Longi-tudinal tests	Means, significance level (U-test)					
	VT	CompO	CompPI	DisRT	ORT	PIRT
5 months	26.5; 0,373	34.0; 0.84	31.0; 0.63	29.0; 0.51	25.0; 0.30	30.0; 0.76
10 months	156.5; 0.19	213.5; 0.78	221.0; 0.92	183.0; 0.31	151.0; 0.38	91.0; 0.55
14 months	245.5; 0.48	**190.5; 0.057***	244.0; 0.45	**157.0; 0.011****	202.0; 0.18	219.00; 0.90
24 months	67.0; 0.81	58.0; 0.43	50.5; 0.22	72.0; 1.00	66.0; 0.91	27.00; 0.46

Note: ** – significant differences *(p < 0.05)*,* – trend differences *(p < 0.1)*

We obtained significant differences in the response time to distractors in subjects at 14 months (658.25 ± 118.37 ms versus 772.61 ± 165.46 ms, normative and premature infants, respectively). In this case the reaction time is the period from the beginning of the presentation of the trial or the change in the stimulus to the end of a saccade towards the target or distractor (measured in milliseconds). Compared to prematurely born children, normatively developing ones reacted more quickly to the presentation and switching of stimuli at the age of 14 months.

Moreover, there were trend differences in the number of "simple" trials between groups. In most cases, normative children found a differing stimulus of round form compared to premature infants (6.85 ± 1.26 versus 4.43 ± 0.81).

Table 5 demonstrates differences in the performance of trials from the third block for eye-tracker.

Table 5
U-test for the third block of stimuli for eye-tracker

Longitudinal tests	Means, significance level (U-test)				
	VT	Rel	Unrl	RelFD	UnrlFD
10 months	45.0; 0.22	55.5; 0.65	60.0; 0.85	61.0; 0.907	61.0; 0.907
14 months	137.5; 0,65	142.5; 0.84	119.5; 0.32	108.0; 0.19	**75.0; 0.018****
24 months	84.0; 0.13	92.5; 0.35	116.0; 0.97	101.0; 0.55	96.0; 0.42

Note: ** – significant differences *($p < 0.05$)*,* – trend differences *($p < 0.1$)*

According to this block, significant intergroup differences in the duration of gazing an irrelevant object were observed at the age of 14 months. Compared to the experimental group, the children from the control group fixed their gaze at incongruent stimuli for a longer time (1112.26 ± 429.01 ms vs 750.83 ± 328.02 ms full-term and premature infants, respectively).

Discussion

Statistical processing of the data obtained using the Bayley Scales of Infant Development, Third Edition (BSID III) clearly shows the dynamics of the development of various neurocognitive functions in premature infants compared to the normative sample. There is a lag in mental and socio-communicative development during the first year of the postnatal period of ontogenesis in children born prematurely. However, by the end of the second year of life, the intergroup differences in the level of formation of cognitive and communicative skills disappear.

The data obtained are consistent with previous studies suggesting that premature infants have an increased risk of speech disorders, in particular, speech perception, which may be associated with delayed maturation of neural pathways and morphofunctional immaturity of certain structures of the cerebral cortex (Adams-Chapman, Bann, & Vaucher, 2013; Torras-Mañá, Guillamón-Valenzuela, Ramírez-Mallafré, Brun-Gasca, & Fornieles-Deu, 2014; Velikos et al., 2015).

The absence of significant differences in the groups in the subscales of gross and fine motor skills in the first year of life and also differences in these parameters in the next two longitudinal tests do not find unambiguous literary confirmation, which may be presumably explained by the characteristics of the sample and the characteristic of the research technique.

In this study the analysis of visual search was carried out in the context of the pop-out paradigm (Gliga, Elsabbagh, Andravizou, & Johnson, 2009). According to this research paradigm, the time spent by the target stimulus does not depend on the number of distracting objects (distractors), because it differs significantly from distractors due to the presence of a unique perceptual trait, such as color, shape, or spatial arrangement. In this case, the detection of a visual stimulus is determined by the mechanisms of involuntary attention and information processing by the primary regions of the visual cortex.

Differences in the number of valid trials in the first block show that at 14 months of age children from the control group demonstrated higher stability in the duration of gazing the images. Meanwhile premature subjects demonstrated higher exhaustion of attention. We also observe no significant differences in this parameter in other longitudinal tests, which demonstrates a kind of "failure" in the development of involuntary visual attention in children born prematurely. This may be explained by the myelination of neural pathways in the frontal visual region that controls oculomotor behavior in children with this perinatal pathology (Atkinson & Braddick, 2012). The characteristics of the development of attention span in preterm infants are confirmed by the data obtained from the second visual search test for eye-tracker.

As mentioned above, the ability to visually perceive social information during infancy plays an important role in the further development of a child's communicative and speech skills.

Conclusions

1. At 5 months, premature infants showed a lower level of development of cognitive skills and receptive communication compared with their healthy peers.
2. At 10 months years of age, premature infants showed lower results by the subscales of cognitive development, receptive and expressive communication, as well as in gross motor skills.
3. At 14 months years of age, premature infants showed lower developmental rates in fine and gross motor skills, a decrease in the stability and speed of switching of visual attention, as well as lower results in the visual search for a simple non-social stimulus.
4. At 2 years of age, children with prematurity demonstrated a lower level of development of gross motor skills compared with normatively developing children.

Thus, it is obvious that the influence of prematurity on the rate of formation of visual attention and also cognitive and communicative skills partially disappear by the end of the second year of life.

Nevertheless, from the first days of their life children born prematurely require extraordinary attention, as well as clinical and psycho-preventive measures, aimed at maintaining their somatic and neuropsychiatric well-being.

Aknowlegments

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