SUMMARY

Aim. To study cognitive function at pre-school age in a cohort of children who were born preterm and required neonatal intensive care or care in neonatology departments in two Gdansk hospitals.

Participants and Methods. 99 preterm children, born from 2001 to 2003, and 115 full-term healthy children were enrolled in the study. The mean gestational age in the experimental group was 32 gestational weeks, the mean birth weight was 1760 grams, the mean Apgar score was 5.56, and the mean time spent in the NICU was 40 days. For purposes of analysis the experimental group was divided into three subgroups according to gestational age (I-III) and birth weight (IV-VI). Cognitive development was measured using the Columbia and Terman-Merrill scales, along with a battery of perceptual-motor tests.

Results. Preterm children showed lower scores than controls on all measured scales. Children from subgroups I and II showed lower scores on verbal and perceptual-motor scales than children from subgroup III. Children from subgroup IV had lower scores than children from subgroup VI. Preterm children with early brain impairments (IVH II, III, IV) had lower IQ scores than children from IVH I and preterms without brain damage. Hypoglycemic children had lower scores in verbal processing, perceptual-motor skills, and coordination, concentration and memory.

Conclusions. The results indicate that 0-3 services alone are not sufficient to prevent educational disadvantage in this population, and preterm children require intervention also in the kindergarten years.
INTRODUCTION

Premature infants, especially those born with very low birth weight, are at higher risk for morbidity and death, neurological impairments, cognitive delay, and behavior problems. Preterms are a fast growing population, not only in Poland, but also in other industrial countries. In 2005 in Poland there were 24,820 newborn children born before the 37th gestational week (GW), which accounts for 6.8% of all deliveries (Rocznik statystyczny, 2006). In the United States the percentage of preterm children in the population reaches 9.8%.

About 1.5% of all Polish children are born before the 32nd GW (Helwich, 2002). Two-thirds of these children have a birth weight lower than 1500 grams; 20% are born with a birth weight less than 1000 grams (Helwich, 2002a). Preterm infants born before the 28th GW, often with extremely low birth weight (<750 grams) represent 0.5-0.6% of all newborns (Helwich, 2002a). The development of neonatology and medical technology is responsible for a gradually increasing survival rate, especially among the most premature infants and those with a very low birth weight.

In Poland the actual survival rate for children born before the 28th GW is 63% (Prematuritas 2002, cited by Kułakowska, 2002). The increasing survival rate has motivated more and more research on the subsequent development of infants with low birth weight (LBW) and very low birth weight (VLBW); however, the primary focus of interest in these studies has been on neurological and cognitive deficits in infancy and early childhood.

The available research (e.g. Hoff, 2005; Schneider et al., 2004; Taylor et al., 2000; Chrzan, 2007) indicates that preterm birth and immaturity at the moment of birth strongly influence the child’s future cognitive, motor and psychosocial development. There are, however, some inconsistencies in the findings regarding the course of development of preterm children. The majority of longitudinal studies examining the functioning of VLBW children indicate continued problems in infancy and early childhood (Taylor et al., 2000; Wolke et al., 2001; Chrzan, 2007). On the other hand, preterm parturition is not necessarily associated with severe developmental problems: in the studies by Saigal (1990, 1995), more than half of the examined children born with extremely low birth weight (ELBW, <1000 grams) had normal intellectual development. Scherman and Sedin (2004) write about the well developed cognitive functions among 10-year-old; however, the children born between 23rd and 27th GW scored lower than controls in the achievement scale.

Hoff (2004) reported that the full scale intelligence quotient of 5-year-old preterm children born before the 28th GW was 12 points lower than in a control group. ELBW children show poorer school performance than their full term peers (Wolke et al., 1998; Schneider et al., 2004). In studies on cognitive function, some cognitive impairments or deficits may be present in the preterm population regardless of their average intellectual development: e.g. preterm VLBW kindergarten children scored lower on tests measuring lan-
guage achievement and pre-reading skills (Wolke et al., 1998; Schneider et al., 2004; Huber, Holditch-Davis, Brandon, 1993). ELBW children scored lower on tests measuring language achievement, such as spelling and phonemic hearing: 30% of ELBW children scored below the 5th percentile, as compared to only 4% of full term infants (Wolke et al., 2001).

These and similar results suggest that the cognitive problems range from global mental impairment to subtle weaknesses in specific neuropsychological domains, such as language, memory, executive function, and perceptual-motor co-ordination. Although there is some evidence that VLBW and ELBW children may have more marked impairments in the areas of visuo-spatial abilities and memory than in the language domain, the overall pattern is not yet clear. By contrast, studies of larger or low-risk preterm infants have not reported significant impairments or problems in their learning skills and school achievement (e.g., Schothorst, van Engeland, 1996, cited by Schneider et al., 2004) or only weak relationships between the language problems of at-risk children identified during the pre-school years and subsequent reading and spelling skills (Schneider et al., 2004). On the other hand, a recent longitudinal investigation reported alarming outcomes for mildly preterm children, presumed to be at lower risk for disability than children born at even lower birth weights and more prematurely. In this sample of children with a mean prematurity of 49 days and a mean birth weight of 2200 grams, 75% had been identified as having at least one of the following problems:

– learning disabilities;
– attention deficit disorder (ADD);
– language and articulation problems;
– mild neurological dysfunctions;

These symptoms can be understood as the sequelae of minimal brain damage (MBD). Behavioral disorders, specific learning problems, and perceptual–motor co-ordination are assumed to be the axial symptoms of MBD (Jaklewicz, 1992).

Some researchers have suggested that whereas biological and medical factors strongly influence psychomotor development in the first years of life, further functioning (e.g. in kindergarten years) is influenced by environmental factors (Aylward, 1989; Downig et al., 1991). Studies have shown that the effects of very premature birth are stronger than those of socio-economic differences, given that control children from families of low socio-economic status outperformed children at risk from families with high socio-economic status (Wolke et al., 1998). Very preterm children from a low socioeconomic background are thus at double risk for poor educational outcome. On the other hand, other research studies (Bennett & Scott, 1997) suggest that preterm children with average psychomotor development in early childhood can be diagnosed with mild neurological impairments or cognitive delays at
age 4 years. Cognitive deficits may manifest themselves along with the process of maturation and the necessity to acquire new cognitive skills. Aylward (1989) points out that developmental problems in the preterm population – in one in four cases – cannot be diagnosed sooner than between the 10th and 36th month of life. According to Huber, Holditch-Davis and Brandon (1993) only 8 of 19 children with developmental problems were diagnosed before age 3 years. Mild to moderate problems are revealed when children reach their kindergarten years, which is why at this age routine psychological testing seems advisable.

The pattern of findings suggests that school achievement is proportional to birth weight and gestational period, and that the deficits are long-lasting. ELBW and LBW children are – despite average intelligence level - at higher risk for specific learning and cognitive problems. Data suggest that perinatal events, particularly those that produce CNS insult, such as hypoxia, intraventricular hemorrhage and metabolic problems, lead to functional impairments or changes in brain structures, which may adversely influence further development.

The studies discussed to this point have been carried in Western European countries and the United States, where the organization and accessibility of early intervention programs differs from the situation in Poland, so that generalizing these results to a population of Polish preterm infants seems to involve some fairly dubious assumptions. The aims of the present study were:

– to evaluate the cognitive and psychomotor development of Polish kindergarten children who were born preterm;
– to investigate the magnitude of differences in cognitive development and achievement between very low birth weight and low birth weight children;
– to evaluate the psychomotor development of preterm children with early CNS insults, such as intraventricular hemorrhage and metabolic problems, including hypoglycemia.

MATERIAL AND METHODS

Participants

The total sample included 99 preterm children and 115 full-term children as a control group. The preterm cohort was recruited from a group of infants who had previously been treated in the Department of Obstetrics and Gynecology at the Medical Academy in Gdańsk, Poland, and in the NICU department at the St. Wojciech Hospital, also in Gdańsk, between January 1, 2001, and January 3, 2003. These children were born between the 24th and 37th GW (\(x = 32.36; \) SD = 3.48), with a birth weight ranging from 480 to 3350 g (\(x = 1775.91; \) SD = 734.80). The mean total days hospitalised in the preterm group was 40 days (range 3-108 days. Of these children, 29 had suf-
ferred an intraventricular hemorrhage, and 30 had been hypoglycemic after birth.

The control group included children born at term with no history of perinatal problems. All of these children were born between the 38th and 42nd GW and had a birth weight in the normal range. The differences between the groups in terms of age, sex, and socio-economic status at assessment were not significant; the mean age was 4.9 years. There was a significant difference (p<0.001) in the mothers’ educational level: 48 mothers in the preterm group, as compared to 6 in the control group, had no more than a vocational or primary education.

Methods

The psychological examination was based on the Columbia Mental Maturity Scale and the Terman-Merrill Scale. These two tests are widely used in Poland to assess the cognitive development of kindergarten children. The Walet interpretation system was used to interpret the Terman-Merrill results. The results of each subscale were analysed at the appropriate age level. Graphomotor efficiency (manual capacity and perceptual-motor coordination) was assessed on the basis of the revised Spionek test of copying geometrical figures and the Human Figure Drawing Test by F. L. Goodenough. Motor development was assessed on the basis of E. Schopler’s PEP-R Test.

The psychological examination was conducted in the Institute of Psychology at the University of Gdańsk, or in the Preterm Children’s Medical Center at the Gdańsk – Zaspa Hospital.

Data analysis

The data were analysed using the Statistical Package for the Social Sciences (SPSS 14 PL) for Windows. Group comparisons were made with parametric analysis of variance for $k$-independent samples, using the t-test to identify the differences between the two study groups.

RESULTS

The results achieved by both study groups in respect to intellectual and cognitive development are shown in Table 1. The comparison of the two groups shows that preterm delivery is associated with lower scores on all tests measuring intellectual and cognitive functions (p<0.001). Significant differences to the detriment of preterm infants were observed in the intelligence quotient (a difference of 18 points) and the particular tests of the Terman-Merrill Scale. The average level of achievement on the specific tests was at a level corresponding to less than 4 years of age, whereas the mean age in the preterm group was 4.9 years old. However, the variance in the preterm group was very high. Cognitive impairment was defined as standard score < 85, which was found in 31 children. Eighteen of these children had an IQ less than 69; the IQ...
of the remaining 13 ranged between 70 and 84 points. Fifty-three children in the preterm group had results within the age norms, ranging between 85 and 115, while 13 children scored higher than average. In the control group, only two children scored below average (<85 points), while 85 showed average intellectual development, and 27 were above average.

As Table 1 shows, the standard deviations in the preterm group are differentiated, as would have been expected, given the heterogeneous nature of the preterm group. The most consistent global predictor of poor outcome among preterm infants is the degree of maturity at birth, as indicated by birth weight and gestation week. An analysis of variance was carried out to study the relationship between these factors and psychomotor development. For the purpose of comparing the results to the control group, the preterm children’s results in the various scales were analysed according to gestational age:

- subgroup I: 24 – 28 GW (n=16);
- subgroup II: 29 – 32 GW (n=45);
- subgroup III: 32-36 GW (n=38).

The analysis of variance of inter-group differences in intellectual and cognitive development is presented in Figure 1.

Generally speaking, the preterm children scored lower than their control peers, but the inter-group differences were significant (p<0.000) only in the field of language abilities. The children in subgroup I scored lower (x = 36.1; SD = 45.06) than the children from subgroup II (x = 65.7; SD = 44.10) and subgroup III (x = 54.0; SD = 49.51). These results indicate that very preterm birth correlates negatively with verbal abilities, i.e. the capacity to understand the verbal environment, vocabulary, verbal fluency, and the ability to express oneself in words.

The preterm children’s achievement in particular scales was also analysed according to birth weight. Again, the children were divided into 3 groups:

- subgroup IV: <1500 grams (n=39);
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- subgroup V: 1501<2500 grams (n=46);
- subgroup VI: >2501 grams (n=14).

A comparative analysis of inter-group differences in intellectual and cognitive development is presented in Figure 2.

Fig. 1. Comparison of inter-group differences in the cognitive development of preterm and full-term children on the basis of the Columbia Mental Maturity Scale and the Terman-Merrill Scale (Walet interpretation) according to gestational weeks.

Fig. 2. Comparison of inter-group differences in the intellectual and cognitive development of preterm children, as evaluated by the Columbia Mental Maturity Scale and the Terman-Merrill Scale (Walet interpretation) according to birth weight.
Inter-group differences were significant in each scale except for arithmetic functions. The preterm children from group IV ($x = 35.0; \ SD = 18.49$) scored significantly lower on the word comprehension scale ($p<0.003$) than the children from group VI ($x = 40.9; \ SD = 13.39$). The preterm children from group IV ($x = 38.4; \ SD = 17.7$) exhibited a higher frequency of problems in perceptual-motor coordination than preterms with normal birth weight ($x = 44.4; \ SD = 9.22$). The mean score on the memory and concentration scale was also significantly lower ($p<0.006$) in group IV ($x = 35.5; \ SD = 20.87$) than in group VI ($x = 44.7; \ SD = 7.62$). The children from group IV also obtained significantly lower ($p<0.002$) scores in vocabulary and verbal fluency than their peers from group VI ($x = 48.80; \ SD = 6.68$). A similar effect was also observed in the comprehension scale.

Inter-group differences were also seen in IQ: the VLBW children ($x = 86.3; \ SD = 25.57$) and LBW children ($x = 92.0; \ SD = 22.26$) from group IV scored significantly lower ($p<0.001$) than preterms with birth weight in the normal range ($x = 106.6; \ SD = 13.51$).

A comparative analysis of group differences in perceptual–motor coordination and motor abilities is presented in Table 2. The control full term children had significantly higher results in all evaluated scales: graphomotor skills ($x = 12.5; \ SD = 3.14$), the revised Spionek test of copying geometrical figures ($x = 11.0, \ SD = 2.77$), the Human Figure Drawing Test by F.L. Goodenough ($x = 1.5; \ SD = 0.68$), and in motor development as measured by the PEP-R ($x = 33.8, \ SD = 0.62$). These results indicate that preterm children have greater problems with perceptual-motor coordination, which is a risk factor for specific learning problems in the future (Bogdanowicz, 1991, 2006).

The gestation age was significantly associated with lower scores obtained in perceptual–motor co-ordination tests: preterm children from I and II group, born before the 32nd week of gestation scored lower in tests evaluating their graphomotor skills, revised Spionek test of copying geometrical figures and the Human Figure Drawing Test by F.L. Goodenough.

Table 2. Comparison of the motor development of preterm and full term infants, as evaluated by the revised Spionek test of copying geometrical figures, the Human Figure Drawing Test by F.L. Goodenough, and PEP-R Schopler's Scale

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<th>Preterm Children</th>
<th>Full term children</th>
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<td></td>
<td>M</td>
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<tr>
<td>Human Figure Drawing Test (1)</td>
<td>1.03</td>
<td>0.866</td>
<td>1.47</td>
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<td>Revised Spionek test (2)</td>
<td>7.86</td>
<td>4.879</td>
<td>11.03</td>
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<tr>
<td>Graphomotor skills (1+2)*</td>
<td>6.89</td>
<td>5.541</td>
<td>12.51</td>
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<tr>
<td>Motor development (PEP-R)</td>
<td>30.55</td>
<td>7.443</td>
<td>33.82</td>
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Birth weight significantly differentiated preterm children. The VLBW and LBW children scored significantly lower in all evaluated scales: graphomotor skills (p<0.000), revised Spionek test of copying geometrical figures (p<0.001), the Human Figure Drawing Test by F.L. Goodenough (p<0.001), and motor development as measured by the PEP-R (p<0.001).

The analyses presented so far have pointed to a higher frequency of cognitive problems in children born before the 32nd GW and VLBW children. These children are also at greater risk for neonatal illnesses, which can additionally hinder their future development. The addition of medical and neurological morbidity has been found to have explanatory power and clinical significance for identifying categories of morbidity that are meaningful in children born at various degrees of medical risk.

Hypoglycemia, which can be associated with an episode of hypoxia and intraventricular hemorrhage, are common CNS insults that can take place in the first days of a premature infant’s life. Children born before the 24th and 29th GW are at higher risk of intraventricular hemorrhage (IVH; Helwich, 2002). Bleeding occurs in 40% of VLBW and 60% of ELBW children (Gomella, Cunningham, Eyal, 1993). The pathogenesis is related to fluctuating cerebral blood flow, e.g. a sudden excess of cerebral blood flow or cerebral venous pressure (Kułakowska, 2003). 60% of intraventricular hemorrhages occur in the first 24 hours after birth, 85% in the first 72 hours, 95% in the first week of life (Gomella, Cunningham, Eyal, 1993). The diagnosis of intraventricular hemorrhage used in the present study was based on the grading system of Papile (Gomella, Cunningham, Eyal, 1993):

- grade I – isolated subependymal germinal matrix hemorrhage;
- grade II – subependymal germinal matrix hemorrhage or choroid plexus hemorrhage with intraventricular hemorrhage and no ventricular dilation (10-50% of ventricular area on sagittal view);
- grade III – subependymal germinal matrix hemorrhage or choroid plexus hemorrhage with intraventricular hemorrhage and ventricular dilation (>50% of ventricular area or dilated ventricle);
- grade IV – subependymal germinal matrix hemorrhage or choroid plexus hemorrhage with intraventricular hemorrhage and ventricular dilation and intraparenchymal hemorrhage (Helwich, 2002; Gomella, Cunningham, Eyal, 1993, Szczapa, 2001).

In general, grade III to IV IVH is related to severe neurological and developmental deficits, whereas grade I or II is associated with milder neurodevelopmental problems (Kułakowska, 2003).

The purpose of our study was to assess the impact of the presence and severity of an IVH on further cognitive development. Table 3 presents a comparison of birth weight, gestational week and the age of children divided according to IVH grades.

Inter-group analysis showed no significant differences in the children’s age (p<0.92). The groups differed in birth weight (p<0.01) and gestational
The relationship between IVH grades and IQ was highly significant (p<0.007), which is shown in Fig. 3. Children with no IVH (n=70; x = 92.9; SD = 21.44) and children classified as having grade I (n = 12, x = 97.1; SD = 11.99) did not differ in their IQ. Children classified as having grade II scored lower (n = 8, x = 80.1; SD = 28.30) than children with grade I and those without IVH. Children who had grade III had a significantly lower IQ (n = 6, x = 68.0; SD = 14.14). Children classified as having grade IV had the lowest score (n = 3, x = 45.0; SD = 7.07).

Hypoglycemia also proved to have an adverse effect on the cognitive development of preterm children. Glucose is vital for normal cellular metabolism throughout the body, and is the main energy source for the brain. Hypoglycemia is one of the most common metabolic problems occurring in preterm newborn infants. Research studies (Kim, 2005) suggest that the developing brain is sensitive to the adverse effects of short-term hypoglycemia, especially when hypoglycemia is coupled with hypoxia. On the
basis of archival medical data obtained from the hospital, our subjects were divided in two groups on the basis of whether or not there had been a hypoglycemia episode. In our sample, hypoglycemia occurred in 30 preterm children. Significant inter-group differences were observed in the Terman-Merrill scale measuring perceptual-motor coordination, and a statistical tendency in the scale assessing word comprehension abilities and memory and concentration functions. The data are presented in Table 4.

The problems we observed may be associated with further learning difficulties, but other data from longitudinal study would be required to test this relationship.

**DISCUSSION**

The data we obtained confirm that there is a relationship between prematurity and a higher risk of cognitive problems: the control children outperformed the preterm children in all measured scales. These results are consistent with those of other studies (Taylor et al., 2000) indicating that children born prematurely and with a lower birth weight are at increased risk of developmental problems. In many studies, the majority of very preterm or very low birth weight children start school without major cognitive impairment, but are at a developmental disadvantage compared with healthy, full term children (Achenbach, 1990; Ornstein, 1991; Saigal et al., 1992; Schneider et al., 2004). The long-term effect of premature birth on cognitive function was more evident in extremely preterm children than in children born more mature. The observed deficits proved to be not only a function of low birth weight and early gestational age at birth, but also of the medical complications associated with preterm birth, such as hemorrhages, and metabolic and nutritional insults, which may cause cerebral abnormalities and impair normal brain development. Being born very preterm puts these children, as a group, at statistically and practically higher risk for these neonatal illnesses and in consequence,
higher risk of cognitive and intellectual impairment. On the other hand, one of the most important findings in our study was that the great majority (n = 66) of preterm children who needed intensive care neonatally had normal intellectual development at kindergarten age. In the present study, although VLBW and LBW scored some points below normal birth weight preterms and full term peers, they had a mean IQ in the average range (x = 86.26; SD = 25.57; x = 92.0; SD = 22.26). These scores may mask subtle deficits in: visual motor abilities, language functions, and memory abilities and attentional skills. Thus, in addition to IQ and achievement testing in follow-up, there should be an evaluation of executive functions and attention, language, sensorimotor functions, visuospatial processes, memory and learning processes.

The majority of VLBW children manifest some type of visual motor problem (e.g., Saigal et al., 1992; Vicari et al., 2004). These deficits include problems on neuropsychological tasks, such as those applied in our research: copying, as well as visual memory and visual-sequential memory. Moreover, these problems exist in children whose IQs are in the average range. Once again, the lower the birth weight, the greater the likelihood of these problems. Especially graphomotor skills and visual motor functions should be in the center of psychological assessment in the kindergarten years, considering their importance in preparing the child for school. Dysfunction in this sphere puts children at risk for future specific learning problems (Bogdanowicz, 1991, 2006). Our results indicate the necessity of an intervention program to stimulate the impaired functions (Bogdanowicz, 2006).

The results described here lead to a question about the nature and pathogenesis of cognitive impairments in preterm infants. The association between cerebral abnormalities and cognitive impairments usually observed in preterm children is not yet clearly defined (Curtis, Lindeke, Georgieff, & Nelson, 2002, 2001 cited by Vicari, Caravale, Carlesimo, Casadei, Allemand, 2004). Furthermore, some cognitive problems are diagnosed in children with normal ultrasound cranial assessment in the first year of life, and recent neuroimaging studies have reported specific brain abnormalities in children born preterm. Allin et al. (2001 cited by Vicari, Caravale, Carlesimo, Casadei, Allemand, 2004) documented reduced cerebellar volume in 67 adolescents who were preterm, compared with 50 age-matched, full-term control participants. On the other hand, cognitive development is not only a function of biological factors, but may be affected by the social, economical and educational backgrounds of the mothers, and this may also influence the prevalence of these disabilities (Chrzan, 2007; Schneider, 2004). Chrzan (2007) points that preterms with low medical risk (LBW) who grow up in multichildren families, with lower socioeconomic status, where parents have a vocational education or less, are at greater risk for slower intellectual development. The risk factors associated with the environment can undermine an earlier positive developmental prognosis.

Our results indicate that 0 to 3 services alone are not sufficient to prevent
educational disadvantage in this population, and preterm children require intervention also in the kindergarten years. The consequences of preterm birth do not fully compensate for motor development delays in the first years of life, but they may influence the child’s further functioning. The follow-up of preterm children should be carried at least to the moment of school entry, with the possibility of applying intervention programs in kindergarten years on the basis of e.g. the Good Start Method (Bogdanowicz, 2005) or the Sherborne Developmental Movement (Bogdanowicz, Kisiel, Przasnyska, 1992).

CONCLUSIONS

Our findings have important implications for diagnostic teams, specialists in early intervention, teachers, physicians, and parents, as follows:

Preterm birth is associated with cognitive problems in kindergarten children. Preterm children – in comparison to their full term peers – scored lower in IQ, verbal, memory and concentration and perceptual-motor coordination tests.

The long-term effect of prematurity birth on cognitive function was more evident in extremely preterm children (with very low birth weight and born extremely preterm, i.e. before the 32nd GW) than in children born more mature.

The consequences of the medical complications associated with preterm birth, such as hypoxia, intraventricular hemorrhages, and metabolic and nutritional insults may additionally cause cerebral abnormalities and impair normal brain development, which adversely affects the further development of the child’s cognitive skills.

While the major disabilities are usually identified during infancy, a high prevalence of dysfunctions of moderate and low severity becomes more obvious as the child grows older (i.e., kindergarten years) and needs to acquire new developmental skills. In order to identify the nature and prevalence of these problems, follow-up during the kindergarten years, school entry and beyond seems necessary.

It is essential to analyse the development of each child separately. The development of the children we examined is affected – apart from early medical conditions – by the level of environmental protection and the presence of risk factors, as well as by the individual history and the role in the family.

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