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CLINICAL RESEARCH

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| S Da Statist Data In Manuscript Liter | s' Contribution: itudy Design A ta Collection B ical Analysis C terpretation D : Preparation E ature Search F ds Collection G | ABDG 1 BCDE 1 BF 1 E 1 E 1 E 1 AG 2 CD 3,4 | Lucie Švandová D Radek Ptáček Martina Vňuková Hana Ptáčková Martin Anders Petr Bob Simon Weissenberger D Daniela Marková Ivan Sebalo D Jiří Raboch | Department of Psychiatry, First Faculty of Medicine Charles University and General University Hospital in Prague, Prague, Czech Republic Department of Pediatrics and Inherited Metabolic Disorders, First Faculty of Medicine at Charles University and General University Hospital in Prague, Prague, Czech Republic University of Central Lancashire, School of Psychology and Computer Science, Preston, United Kingdom Mersey Care National Health Service Trust, Ashworth High Secure Hospital, North Maghul, United Kingdom National Institute of Mental Health, Klecany, Czech Republic |
| | | ABDE 5 | | |
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| | Back Material/M | ground: Nethods: | and extremely low birth weight (ELBW opare the cognitive and socioemotional d with children born with normal birth we The clinical group consisted of 118 VLI with NBW at ages 5 to 9 years. The rest Development Scales (IDS), A Development the Behavior Rating Inventory of Execution | d socioemotional dysfunction in very low birth weight (VLBW <1500 g) 1000 g) children. This study from the Czech Republic aimed to com- evelopment at 5 and 9 years of age of children born with VLBW/ELBW ight (NBW ≥2500 g). 3W/ELBW children and the control group consisted of 101 children earch battery included selected subscales from the Intelligence and ntal Neuropsychological Assessment – second edition (NEPSY-II), and ve Function (BRIEF). Data were analyzed using STATA IC v. 15 software sis of variance (ANOVA), correlations, multivariate analysis of variance |
| | | Results: | We found a statistically significant differ with VLBW/ELBW and those with NBW 96.38, while that of NBW children was 1 all subtests of the IDS (<i>P</i> <0.001) as well a | ence in cognitive and socioemotional development between children The average intelligence quotient (IQ) of VLBW/ELBW children was 2.98 points higher (P <0.001). NBW children achieved better results on s in affect recognition (P <0.001). All results for both groups were with- children did not recognize impaired executive functioning (P =0.494). |
| | Conc | lusions: | This study has shown significant cognit when evaluated at 5 and 9 years of age. | ve and socioemotional deficit in children born with VLBW and ELBW |
| | Key | ywords: | Child Development • Cognitive Dysfur Infant, Very Low Birth Weight | ction • Infant, Extremely Low Birth Weight • |
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Cognitive and Socioemotional Development



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Background

All citizens, residents, and employees in the Czech Republic have access to healthcare via compulsory general healthcare insurance [1]. However, current medical and psychological care provided for premature children and their families remains inadequate, as it is largely unsystematic and is directly dependent on the varying capacities of the local perinatal centers [2]. Furthermore, continuous monitoring of mental development is mandated only from infancy through 2 years of age [2]. This is not sufficient for the care of low-birth-weight children and children, as it is often impossible to generate an accurate prognosis of their developmental trajectory at this young age [2,3]. Birth weight is the first weight of the fetus or neonate obtained after birth. According to the World Health Organization (WHO), birth weight is divided into low birth weight (LBW <2500 g), very low birth weight (VLBW <1500 g), and extremely low birth weight (ELBW <1000 g) [4]. Premature birth before the 37th week of pregnancy and/or growth faltering in the womb increase the risk of low birth weight [5]. The number of LBW children born in the Czech Republic has been increasing in recent years. In 2018, 6.9% of all live children born in the Czech Republic were identified as LBW [6]. Along with efforts to reduce child mortality, experts have also focused on treatment options that might be used to reduce morbidity both in the neonatal period and later on in life [2]. Children with ELBW are the group that is most at risk for these complications [7-9].

There is strong evidence indicating that children born with VLBW and ELBW have a greater predisposition to develop cognitive deficits and/or delayed cognitive development [11,13-18]. Impaired attention, memory, perceptual-motor skills, and visual-motor skills are among the deficits that are most frequently reported in studies of cognitive development of VLBW/ELBW children [9,11,18-20]. Speech and language disabilities or delays (both receptive and expressive) have also been reported [12,21-25]. Impairment has also been reported in the areas that include executive functions [7,26-28]. The aforementioned deficits are detected most often at school age, when children are facing increasing demands, notably in mathematics, reading, and spelling [25,29-34]. Although studies that address measurements of intelligence quotient (IQ) in VLBW and ELBW children show great variability [35-37], it is clear that VLBW/ELBW children may have a limited capacity for intellectual and overall cognitive development compared to children born at term at the normal birth weight (NBW ≥2500 g) [37,38]. Some of the deficits observed among VLBW/ELBW children relate to the development of socioemotional competencies [7,8,39-42]. Johnson and Marlow described the "preterm behavioral phenotype", which is characterized by an increased risk of developing symptoms and disorders associated with inattention/hyperactivity, emotional, and social difficulties. Individuals with this phenotype are also at an increased risk for internalizing

rather than externalizing problems [43]. Children born with VLBW or ELBW are also more vulnerable to attention deficit hyperactivity disorder (ADHD) and impulsivity, with symptoms more likely to persist into adulthood [39,44,45]. Other studies report an increased risk of pervasive developmental disorders; the incidence of autism spectrum disorders (ASDs) has been reported to range from 3.65% to 8% among VLBW/ELBW children [44,46]. These children also experience a higher incidence of depressive symptoms, low self-esteem, and anxiety disorders [8,47]. However, a whole population longitudinal study from birth to adulthood found that VLBW children were not at persistently increased risk for anxiety and mood disorders [48]. Other studies have reported difficulties in affect recognition among VLBW/ELBW children at preschool age [42,49]; some of these deficits may persist into middle childhood, notably with those involving the recognition of anger [50,51]. Problems with affect recognition and facial expressions result in an overall impairment in social skills and social adaptation [50], and can also lead to problems with the regulation of emotions [52,53], with a significant impact on relationships with peers, parents, and teachers [54,55]. Difficulties with social adaptation tend to appear early and persist into adolescence [56]. Although a number of the above studies demonstrate that these impairments can have a major long-term impact on children and their families and require long-term support and interventions, in the Czech Republic these children are not given the long-term attention they need [2].

To the best of our knowledge, there are no published studies that explore the relationship between birth weight and cognitive and socioemotional development at 5 and 9 years of age of children residing in the Czech Republic. The development of these children has not yet been mapped. In 2015/2016, we conducted a research project entitled "New Methods in the Follow-Up Care for Children with Perinatal Stress" at the Center for Follow-up Care of Ex-preterm Babies within the Department of Pediatrics and Inherited Metabolic Disorders, First Faculty of Medicine, Charles University and General University Hospital in Prague. Most often, babies born in one of Prague's maternity hospitals with a perinatal burden come under the care of the center. This was a large-scale project focused on the development of multidisciplinary care for children with specific perinatal burdens. Over the course of a given day, each child underwent a comprehensive evaluation that included pneumatological, routine pediatric, rehabilitative, psychological, and psychiatric assessments. One goal of the study was to evaluate the mental development of VLBW/ELBW children who were then between 5 and 9 years of age. Socioemotional and cognitive development was measured by subtests selected from the Intelligence and Development Scales (IDS) [57] and Developmental Neuropsychological Assessment, second version (NEPSY-II) [58,59]. Executive functions were examined using the Behavior Rating Inventory of Executive Function (BRIEF) [60]. This project was followed by the present study, which aimed to compare the cognitive and socioemotional development at 5 and 9 years of age of 118 children born with VLBW/ELBW with 101 children born with NBW. Based on our review of the literature, we proposed 4 hypotheses. H1 0: There is no statistically significant difference between the cognitive development of children with VLBW/ELBW and children with normal birth weight. H1: Children with normal birth weight have statistically significantly better cognitive development than children with VLBW/ELBW. H2 0: There is no statistically significant difference in socioemotional development between children with VLBW/ELBW and children with normal birth weight. H2: Children with normal birth weight have statistically significantly better socioemotional development than children with VLBW/ELBW.

Material and Methods

Ethics Statement

The research project has been carefully considered in all aspects of its research and ethical content by the institutional review board for "Medical Psychology and Psychopathology" at the First Faculty of Medicine, Charles University. The parents of the children in both groups were informed of the goals and the procedures involved in this research project, and all signed a written informed consent form. An emphasis was placed on the current well-being of the child throughout the evaluation period.

Procedure and Participants

One hundred and eighteen children aged 5 to 9 years were selected for participation in this study. Inclusion criteria were: age 5 to 9 years who were VLBW or ELBW. All children were monitored and treated at the Center for Follow-up Care of Expreterm Babies. This was a non-probability sampling method as the children and parents were selected from among those who were already receiving care in this center. Children with severe sensory impairments, mutism, and severe ASD were excluded from the study. The research studies took place primarily during the morning hours at the Center for Follow-up Care of Ex-preterm Babies within the Department of Pediatrics and Inherited Metabolic Disorders, First Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic. The duration of the assessment of the child was about 1 hour, plus an interview with the parent for about 15 minutes.

A control group recruited in 2017-2019, included NBW children who were 5 to 9 years of age who were not receiving mental health care. The participants were selected from a voluntary response sample from Prague and its close surroundings. The control group included 101 children who underwent the psychological examination only. The examination took place at the Institute of Psychology, Prague, Czech Republic.

Children came for the assessment with their parent (mostly with their mother). Subsequently, the child and the parents were told what the assessment entailed. The child underwent the assessment without the presence of the parent. During testing, an emphasis was placed on the current well-being of the child. If the test situation was too stressful for the child or caused any distress or anxiety, the child was given some time to familiarize him/herself with the situation, take a break from the test, or go back to the parent. An alternative testing date could have been arranged, but in neither case was it necessary.

Measures

IDS is appropriate for children at 5-10 years of age. The administration of the entire battery of tests typically requires 1.5-2 hours. For this reason, we administered selected subtests only, including those focused on visual perception, selective attention, phonological memory, visual-spatial memory, auditory memory, visual-motor skills, and receptive and expressive language, using validated Czech language standards [57].

NEPSY-II is a comprehensive battery of neuropsychological tests designed to evaluate neurocognitive development in preschoolers, children, and adolescents (ie, 3-16 years of age) [58,59]. We used only the subtest designed to evaluate affect recognition.

BRIEF is a questionnaire for parents or teachers that allows them to assess executive function in children aged 5 to 18 years. The BRIEF has 3 main indices: (1) Metacognition Index (MI) assesses the ability to initiate, organize, plan, and remember the steps needed to achieve a specific goal; (2) Behavior Regulation Index (BRI) evaluates the ability to manage and control behavior and emotional responses; and (3) Global Executive Composite (GEC – a composite of the 2 aforementioned indices) [60].

Statistical Analysis

Data were analyzed using STATA IC v. 15 software. Post hoc statistical power was calculated in G*Power. Birth weight was coded as a discrete dichotomous variable (0 – control, 1 – VLBW/ ELBW) and was used as the predictor (independent) variable in all of our analyses. IQ, IDS subscales, as well as the NEPSY-II and BRIEF subscales were linear continuous variables that were included as outcome (dependent) variables.

The overall IQ score as determined by the IDS was used as the single-outcome variable, and analysis of variance (ANOVA)

was performed with the control group was used as a reference. ANOVA is a statistical method used to compare means of multiple groups to find out if the differences between them are statistically significant.

However, because the total IQ score is calculated from IDS subscales, our second analysis included the simultaneous use of visual perception, selective attention, phonological memory, visual-spatial memory, auditory memory, visual-motor skills, and receptive and expressive language as dependent variables and birth weight as the independent variable. A multivariate analysis of variance (MANOVA) was performed to accommodate the co-existence of multiple outcome variables. MANOVA is similar to ANOVA in that it is a mean comparison test with multiple dependent variables. Correlations were performed in conjunction with this process because the dependent variables evaluated in the MANOVA should be correlated with one another.

Socioemotional development was also evaluated using ANOVA. In this case, the birth weight group was the independent variable, and the results of the affect recognition subtest of NEPSY-II were the dependent variables.

Responses from parents were evaluated in a separate MANOVA in which the BRIEF BRI and MI subscales were included as the dependent variables and birth weight as the independent variable.

The effect size was calculated using the ² value obtained from the ANOVAs together with a post hoc power analysis.

Results

Descriptive Statistics

One hundred and eighteen LBW children were enrolled in our study, including 59 boys (50%) and 59 girls (50%). Forty-one (34.8%) of the participants were VLBW children and 77 (65.3%) were ELBW (65.3%) children. The mean age was 76.5 months (range, 60-115 months). The average birth weight was 918.07 g (range 405-1470 g). The control group of 101 children included 53 boys (52.5%) and 48 girls (47.5%) girls. The mean age was 81.2 months (range 60-107 months). The average birth weight was 3363.55 g (range 2600-4800 g). Quantitative analysis revealed no correlation between gender or age (preschool or young school-age) and the overall IQ. Likewise, our analysis revealed no significant differences between the groups of VLBW and ELBW children (t [71]=0.37, P=0.71). Therefore, we divided the participants into 2 groups according to birth weight (ie, NBW and VLBW/ELBW cohorts) for all subsequent statistical analyses.

Analyses of IDS

ANOVA revealed significant differences in cognitive development (F [1.217]=41.49, P<0.001). Overall, birth weight explained only ~16% of the variance in IQ. The average IQ of VLBW/ ELBW children was 96.38, while the average IQ of NBW children was 12.98 points higher (Table 1). The individual scores are presented in Figure 1. A post hoc power analysis of the IQ data revealed a statistical power of 0.99 (Table 2). Before computing the MANOVA for cognitive development, we evaluated the results from the IDS subscales in a correlation matrix (Table 3). The results revealed a moderate correlation between the results from the IDS subscales (Table 4). The Wilks' lambda value was significant (F [8.210]=7.73, P<0.001) as were all the IDS subscales. Furthermore, our findings revealed that NBW children as a group performed better than VLBW/ELBW children on all subscales evaluated. The strongest associations (as per the R² value) were observed for subscales of visual perception, phonological memory, and selective attention. The partial η^2 (=0.22) was used to calculate the effect size, ie, $f^2(V)=0.22/(1-0.22)=0.29$. A post hoc power analysis of overall cognitive development revealed a high statistical power (0.99; Table 5). Collectively, our findings revealed that NBW children performed better than VLBW/ELBW children on all cognitive domains measured by the IDS scale when evaluated at 5-9 years of age.

Analysis of NEPSY-II

ANOVA revealed significant differences in socioemotional development (F [1.217]=11.79, P < 0.001). Birth weight explained ~4.7% of the total variance in affect recognition (**Table 6**). VLBW/ELBW children achieved an average score of 9 on this evaluation, while NBW children achieved significantly higher scores. The individual scores on this subtest are shown in **Figure 2**. A post hoc power analysis revealed a high statistical power for this evaluation (**Table 7**). Collectively, our results revealed that NBW children (5-9 years of age) performed significantly better on subtests of affect recognition than children born with VLBW/ELBW.

Analysis of BRIEF

Finally, results from the BRI and MI BRIEF subscales were evaluated by MANOVA. The results from tests using these subscales were based on responses to questionnaires completed by the parents of the study participants. The differences observed in this case did not reach statistical significance (F [2.216]=0.71, P=0.494). Table 1. Analysis of Variance (ANOVA) comparison of intelligence quotient (IQ) and birth weight. The mean (M) IQ score was 100 with a standard deviation (SD) of 15. ANOVA revealed significant differences (F [1.217]=41.49, P<0.001). Overall, birth weight explained only ~16% of the variance in IQ. The average IQ of children with very low birth weight (VLBW <1500 g) or extremely low birth weight (ELBW <1000 g) was 96.38, while the average IQ of children with normal birth weight (NBW ≥2500 g) was 12.98 points higher.</p>

| Means for each group | | | | | | | |
|--------------------------|------------|-----|-----------|--------|-------|--|--|
| Mean IQ | | | SD | | N | | |
| VLBW/ELBW | 96.38 | | 15.95 | | 118 | | |
| NBW | 109.36 | 5 | 13.49 | | 101 | | |
| Total | 102.36 | 5 | 16.193 | | 219 | | |
| ANOVA | | | | | | | |
| | SS df MS F | | | | | | |
| Between groups | 9175.75 | 1 | 9175.75 | 41.49 | 0.000 | | |
| Within groups | 47987.28 | 217 | 221.13 | | | | |
| Total | 57163.04 | 218 | 262.21 | | | | |
| Post-Hoc Bonferroni test | | | | | | | |
| | | | VLBW/ELBW | | | | |
| | NBW | | | 12.98* | | | |

* p<0.001.

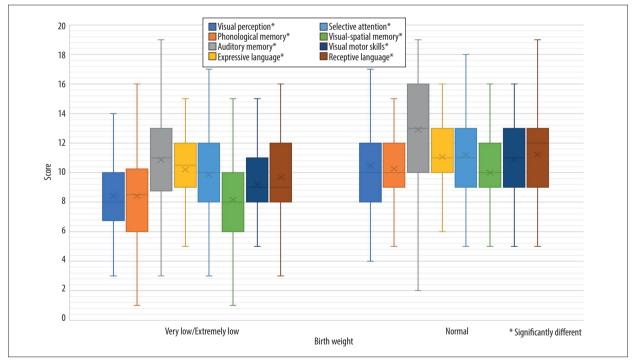


Figure 1. Scores on subscales of Intelligence and Development Scales (IDS). IDS subscale scores have a mean (M) of 10 with a standard deviation (SD) of 3. The test scores of children with very low birth weight (VLBW <1500 g) or extremely low birth weight (ELBW <1000 g) and with normal birth weight (NBW ≥2500 g) were not below the standardized average. NBW children performed significantly better than their VLBW/ELBW counterparts on all IDS subtests evaluated. The figure was prepared in Microsoft Excel, version 2112, Microsoft 365.

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Table 2. Post hoc power analysis of intelligence quotient (IQ). A post-hoc power analysis revealed a statistical power of 0.99.

| Input: Effect size f2(V) | 0.44 | Output: Noncentrality parameter $\boldsymbol{\lambda}$ | 42.39 |
|--------------------------|------|--|-------|
| α err prob | 0.05 | Critical F | 3.88 |
| Total sample size | 219 | Numerator df | 1 |
| Number of groups | 2 | Denominator df | 217 |
| | | Power (1-β err prob) | 0.99 |

Table 3. Correlation matrix of subscales of Intelligence and Development Scales (IDS). The results revealed a moderate correlation between the results from the IDS subscales.

| | Visual perception | Selective attention | Phonological memory | Visual-spatial memory | Auditory memory | Visual-motor skills | Expressive language | Receptive language |
|--------------------------|-------------------|---------------------|---------------------|--------------------------|--------------------|------------------------|------------------------|-----------------------|
| Visual perception | 1 | | | | | | | |
| Selective attention | 0.34 | 1 | | | | | | |
| Phonological memory | 0.24 | 0.28 | 1 | | | | | |
| Visual-spatial memory | 0.28 | 0.30 | 0.22 | 1 | | | | |
| Auditory memory | 0.24 | 0.33 | 0.32 | 0.38 | 1 | | | |
| Visual-motor skills | 0.37 | 0.32 | 0.25 | 0.35 | 0.28 | 1 | | |
| Expressive language | 0.38 | 0.21 | 0.26 | 0.33 | 0.41 | 0.33 | 1 | |
| Receptive language | 0.40 | 0.22 | 0.33 | 0.33 | 0.31 | 0.24 | 0.40 | 1 |

Table 4. Multivariate analysis of variance (MANOVA) for subscales of Intelligence and Development Scales (IDS) and birth weight. Number of observations (N)=219. The Wilks' lambda value was significant (F [8.210]=7.73, P<0.001) as were all the IDS subscales. The strongest associations (as per the R² value) were observed for subscales of visual perception, phonological memory, and selective attention. Children with normal birth weight (NBW ≥2500 g) as a group perform better than children with very low birth weight (VLBW <1500 g) or extremely low birth weight (ELBW <1000 g) on all subscales evaluated.</p>

| Source | Statistic | | df | F(df1) | F(df2) | F | Prob >F | |
|--------------|-----------|------|-----|--------|--------|------|---------|---|
| Birth weight | W | 0.77 | 1 | 8.0 | 210.0 | 7.73 | 0.000 | e |
| | Р | 0.22 | | 8.0 | 210.0 | 7.73 | 0.000 | e |
| | L | 0.29 | | 8.0 | 210.0 | 7.73 | 0.000 | e |
| | R | 0.29 | | 8.0 | 210.0 | 7.73 | 0.000 | e |
| | Residual | | 217 | | | | | |
| | Total | | 218 | | | | | |

W – Wilks' lambda; P – Pillai's trace; L – Lawley-Hotelling trace; R – Roy's largest root; e – exact bound on F.

Table 4 continued. Multivariate analysis of variance (MANOVA) for subscales of Intelligence and Development Scales (IDS) and birth
weight. Number of observations (N)=219. The Wilks' lambda value was significant (F [8.210]=7.73, P<0.001) as
were all the IDS subscales. The strongest associations (as per the R² value) were observed for subscales of visual
perception, phonological memory, and selective attention. Children with normal birth weight (NBW \geq 2500 g) as
a group perform better than children with very low birth weight (VLBW <1500 g) or extremely low birth weight
(ELBW <1000 g) on all subscales evaluated.</th>

| Equation | Observations | Parameters | RMS | E | R ² | | F | р |
|-----------------------|--------------|------------|------|----|----------------|---|--------|----------------------------------|
| Visual perception | 219 | 2 | 2.73 | | 0.12 | | 30.56 | <0.001 |
| Selective attention | 219 | 2 | 2.77 | | 0.10 | | 24.19 | <0.001 |
| Phonological memory | 219 | 2 | 3.69 | | 0.07 | | 16.50 | <0.001 |
| Visual-spatial memory | 219 | 2 | 2.66 | | 0.02 | | 5.39 | 0.021 |
| Auditory memory | 219 | 2 | 2.92 | | 0.05 | | 11.82 | <0.001 |
| Visual motor skills | 219 | 2 | 2.61 | | 0.11 | | 26.94 | <0.001 |
| Expressive language | 219 | 2 | 2.94 | | 0.07 | | 17.78 | <0.001 |
| Receptive language | 219 | 2 | 2.86 | · | 0.06 | | 16.13 | <0.001 |
| | Coefficie | ent SE | м | 1 | t | | P>t | 95% Confidence interval [CI]) |
| Visual perception | | | | | | | | |
| Birth weight | 2.04 | 0. | 37 | 5 | .53 | | <0.001 | 1.31-2.77 |
| Constant | 8.39 | 0. | 25 | 33 | .40 | • | <0.001 | 7.90-8.89 |
| Selective attention | | | | | | | | |
| Birth weight | 1.85 | 0. | 37 | 4 | .92 | | <0.001 | 1.10-2.59 |
| Constant | 8.40 | 0. | 25 | 32 | .90 | | <0.001 | 7.90-8.91 |
| Phonological memory | | | | | | | | |
| Birth weight | 2.03 | 0. | 50 | 4 | .06 | | <0.001 | 1.04-3.02 |
| Constant | 10.86 | 0. | 34 | 31 | .92 | | <0.001 | 10.19-11.53 |
| Visual-spatial memory | | | | | | | | |
| Birth weight | 0.83 | 0. | 36 | 2 | .32 | | 0.021 | 0.12-1.54 |
| Constant | 10.21 | 0. | 24 | 41 | .69 | | <0.001 | 9.72-10.69 |
| Auditory memory | | | | | | | | |
| Birth weight | 1.36 | 0. | 39 | 3 | .44 | | <0.001 | 0.58-2.14 |
| Constant | 9.85 | 0. | 26 | 36 | .65 | | <0.001 | 9.32-10.38 |
| Visual-motor skills | | | | | | | | |
| Birth weight | 1.83 | 0. | 35 | 5 | .19 | | <0.001 | 1.14-2.53 |
| Constant | 8.16 | 0. | 24 | 33 | .92 | | <0.001 | 7.68-8.63 |
| Expressive language | | | | | | | | |
| Birth weight | 1.68 | 0. | 39 | 4 | .22 | | <0.001 | 0.89-2.47 |
| Constant | 9.18 | 0. | 27 | 33 | .86 | | <0.001 | 8.65-9.72 |
| Receptive language | | | | | | | | |
| Birth weight | 1.55 | 0. | 38 | 4 | .02 | | <0.001 | 0.79-2.32 |
| Constant | 9.67 | 0. | 26 | 36 | .71 | | <0.001 | 9.15-10.19 |

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 Table 5. Post hoc power analysis of subscales of Intelligence and Development Scales (IDS). A post-hoc power analysis of overall cognitive development revealed a high statistical power (0.99).

| Input: Effect size f ² (V) | 0.29 | Output: Noncentrality parameter $\boldsymbol{\lambda}$ | 64.16 |
|---------------------------------------|------|--|-------|
| α err prob | 0.01 | Critical F | 2.59 |
| Total sample size | 219 | Numerator df | 8 |
| Number of groups | 2 | Denominator df | 210 |
| Response variables | 8 | Power (1-β err prob) | 0.99 |
| | | Pillai V | 0.05 |

 η^2 ((8×7.73)/(8×7.73+210)=0.22)) was used to calculate the effect size, i.e., f^2 (V)=0.22/(1-0.22)=0.29.

Table 6. Analysis of variance (ANOVA) for Affect recognition subtest of Developmental Neuropsychological Assessment,

second version (NEPSY-II) and birth weight. The ANOVA revealed significant differences in socioemotional development (F [1.217]=11.79, P<0.001). Birth weight explained ~4.7% of the total variance in affect recognition.

| | | Means for each | group | | | | |
|--------------------------|---------|----------------|-------|-----------|---------|--|--|
| | Mean I | Q | SD | | N | | |
| VLBW/ELBW | 9 | | 2.89 | | 118 | | |
| NBW | 10.30 | | 2.70 | | 101 | | |
| Total | 9.60 | | 2.87 | | 219 | | |
| ΑΝΟΥΑ | | | | | | | |
| | SS | df | MS | F | Prob >F | | |
| Between groups | 92.95 | 1 | 92.95 | 11.79 | 0.000 | | |
| Within groups | 1711.48 | 217 | 7.88 | | | | |
| Total | 1804.43 | 218 | 8.27 | | | | |
| Post-Hoc Bonferroni test | | | | | | | |
| | | | | VLBW/ELBW | | | |
| | NBW | | | 1.30* | | | |

* p<0.001.

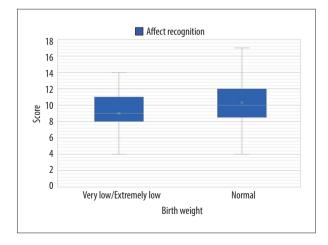


Figure 2. Scores on the affect recognition subtest of Developmental Neuropsychological Assessment, second version (NEPSY-II). Age-adjusted scaled scores include mean (M) 10 with a standard deviation (SD) 3. Children with very low birth weight (VLBW <1500 g) or extremely low birth weight (ELBW <1000 g) achieved an average score of 9 on this evaluation, while children with normal birth weight (NBW ≥2500 g) achieved

Microsoft Excel, version 2112, Microsoft 365.

significantly higher scores. The figure was prepared in

| Input: Effect size f ² (V) | 0.22 | Output: Noncentrality parameter $\boldsymbol{\lambda}$ | 10.59 |
|---------------------------------------|------|--|-------|
| α err prob | 0.05 | Critical F | 3.88 |
| Total sample size | 219 | Numerator df | 1 |
| Number of groups | 2 | Denominator df | 217 |
| | | Power (1-β err prob) | 0.89 |

 Table 7. Post hoc power analysis of Affect recognition subtest of Developmental Neuropsychological Assessment, second version (NEPSY-II). A post hoc power analysis revealed a high statistical power for this evaluation (0.89).

Discussion

The results of this study revealed that VLBW/ELBW children have diminished levels of cognitive and socioemotional development compared to their NBW peers at 5-9 years of age. The average intelligence quotient (IQ) of children with NBW was higher. NBW children achieved better results on all subtests of the IDS as well as in affect recognition. All the results for both groups were within normal range. Parents of VLBW/ ELBW children or children with NBW did not recognize impaired executive functioning.

While the average IQ of NBW children in our study was 109.36, ELBW/VLBW children had an average score of 96.38, representing a 12.98-point difference. These findings are consistent with the results of a meta-analysis published by Gu et al that reported lower (albeit normal) IQs among VLBW/ELBW children compared to those born at NBW [37]. Recently published systematic reviews document individuals with LBW to have around 5-12 points lower IQ scores [10,37,61]. These authors also reported a gradient relationship between different levels of LBW and IQ score [37]; interestingly, our results did not confirm this finding. However, we recognize that only 5 of 7 subscales used to determine IQ were performed in the study. The scores of the omitted subtests were included as weighted averages. Therefore, these results should be interpreted with caution. Our results revealed that NBW children performed significantly better than their VLBW/ELBW counterparts on all IDS subtests evaluated. These findings are consistent with those previously reported in the medical literature and include differences in selective attention, perceptual-motor skills, visual motor skills [9,11,19,20], memory (phonology, auditory, visualspatial) [21,45], and language development [12,21,22,24]. We also found that NBW children performed significantly better than VLBW/ELBW children on subtests of affect recognition. These results are also in agreement with those reported in previously published studies [42,49-51]. Interestingly, parents did not report impaired executive function on the BRIEF questionnaire. This implies that the parents believe that their children are all able to manage and control behavior and emotional responses and also can initiate, organize, plan, and remember the steps needed to achieve a specific goal. We recognize that this is a fully subjective evaluation. We cannot rule out the possibility of a bias based on social desirability. Several studies reported that VLBW/ELBW children have impairments in executive functions, predominantly those involving planning and organization, cognitive flexibility, working memory, attention, inhibition processes, verbal fluency, and behavioral and emotional control [7,26-28]. Overall, our results are in general agreement with findings reported in the literature [7,8,40,44]. Our quantitative analysis revealed significant differences in cognitive and socioemotional development when comparing the VLBW/ELBW group to the NBW controls. However, it is important to recognize that the results of all the psychological evaluations of children (including those in the VLBW/ELBW group) were within the normal range. In other words, while the test scores of the VLBW/ELBW children were statistically different from those of NBW children, the results as a whole were not below the standardized average.

The comparatively strong results achieved by the children in our VLBW/ELBW cohort may relate directly to the individualized, long-term, and comprehensive care provided by a multidisciplinary team at our hospital. We recognize that this level of comprehensive care does not reach all VLBW/ELBW children in the Czech Republic. The review by Spittle et al (2015) suggests that early developmental interventions improve cognitive outcomes up to preschool age. Little evidence was found of an effect on long-term cognitive outcomes (up to school age). Were included 25 randomized or quasi-randomized controlled trials of early developmental interventions for preterm children. Variability among these early developmental intervention programs limits the conclusions that can be drawn about their effectiveness [62].

Going forward, it is important to focus on several steps. In the Czech Republic there are currently significant shortcomings in follow-up psychological care both for the premature baby and the parents and family. The availability of high-quality psychological services might be expanded together with efforts to provide standardized methods for screening, assessing, and increasing the awareness of the need to monitor the behavior of these children and their families [2]. Further insight into the potential mechanisms associated with the socioemotional and cognitive development of LBW/preterm children could be provided by neuroscience, such as further study of changes in the structural and functional architecture of brain networks involved in emotion regulation and other parts of the brain. To better understand the whole issue, it is desirable to perform further research, not only in young children, but also in adolescents and adults born with low birth weight. The consequences of low birth weight are not yet sufficiently mapped for these periods.

This study had several limitations. As noted above, all VLBW/ELBW children enrolled in this study have undergone extensive long-term monitoring at the Center for Follow-up Care of Ex-preterm Babies. This level of care far exceeds the current standards in the Czech Republic. Also, we recognize that all our participants were active volunteers. Thus, the participants may have included only children with particularly motivated parents who also provided their children with superior attention and care. We also recognize that our study lacked socio-economic demographic data. Parental education, employment, and income, as well as the number of siblings in the family, have all been identified as predictors of cognitive development [63-66].

As noted above, there is no standard Czech language version of the NEPSY-II. We had only limited decision-making capacity in this regard, as the instruments to be used for this study were selected by an outside expert commission. Furthermore, the omission of the structural and conceptual thinking subscales of the IDS limited our overall analysis of cognition. Other limitations relate to the testing conditions. During the course of one day, the children underwent a comprehensive

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psychological and physical examination. Although we all agreed that the psychological examination would be performed first to avoid possible bias caused by fatigue, this plan was not followed in all cases.

Conclusions

This study has shown significant cognitive and socioemotional deficits in children born with VLBW and ELBW when evaluated at 5 and 9 years of age. Although the study had several limitations, our results confirm that LBW remains a major risk factor for delayed mental development. We hope that the results of the study will raise awareness of the effects of perinatal stress and its impact on mental development. Our results highlight the need to improve the availability of systematic follow-up focused on both medical and psychological care of VLBW/ELBW children even after their discharge from perinatal centers.

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Declaration of Figures' authenticity

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have been previously published in whole or in part.

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