

SHORT THESIS FOR THE DEGREE OF DOCTOR OF
PHILOSOPHY (PHD)

Longitudinal examination of early cognitive
development and psychological characteristics
among preterm and low birthweight (LBW)
children

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INTRODUCTION

One of the most significant sensitive periods of child development is early childhood (0-6 years) when the impact of developmental factors can be particularly crucial. Experiences from the environment, as well as the child's emotional well-being and social competence provide the basis for cognitive development and altogether they contribute and promote later adaptive behaviour and social integration (Danis et al., 2011).

Preterm birth and the resulting low birthweight are the most common risk factors of early development (8-11% in Hungary; WHO, 2015). In the last decades, the advances in the fields of perinatal and neonatal care resulted in higher survival rates of preterm children (Martin et al., 2011). Parallel with this tendency among low birthweight (LBW) children, the issue of long-term neurological development and developmental morbidity became a pragmatic and imperative matter in the field of developmental psychology.

The children's later development, quality of life and mental well-being are not only dependent on the socio-economic status of their families but chronic neonatal morbidities as well, such as retinopathy of prematurity (ROP), bronchopulmonary dysplasia (BPD) or intraventricular haemorrhage (IVH) (Balla & Szabó, 2013).

The last decades saw an increase of research activity in developmental aspects of preterm children, however, there are still controversial or yet unknown areas left.

AIMS

1. Developmental and psychological characteristics of low birthweight (LBW) children at 2 years

The aim of our research was to examine the cognitive, language and motor skills, as well as the social-emotional and adaptive behaviour skills of the 3 groups of low birthweight children (ELBW: <1000g; VLBW: 1000-1500g; LBW: 1500-2500g) at 2 years, moreover, to identify distinct developmental profiles. We also aimed to identify any mild or severe delay in cognitive, language and motor development and to assess the risk of developmental delay among extremely low birthweight (ELBW) children at 2 years.

In addition to the developmental characteristics, we also explored the health-related quality of life (HrQoL) and the occurrence of any internalizing (emotional symptoms, peer problems) and externalizing (behavioural problems, hyperactivity and attention problems) behaviours in relation to parental mental health factors such as perceived stress, symptoms of anxiety and depression, and satisfaction with life. Furthermore, we examined the associations between perinatal and demographic factors and the psychological aspects of the children and their parents.

2. Cognitive development and psychological characteristics of low birthweight (LBW) children at 4 years

The aim of our research was to examine the cognitive skill development and IQ of 4-year-old LBW children in domains such as verbal comprehension, visual-spatial ability, fluid reasoning, working memory and processing speed in relation to several demographic and perinatal factors.

In addition to cognitive development, we also assessed the health-related quality of life and internalizing and externalizing behaviours of 4-year-old LBW children in relation to parental mental health factors.

3. Associations of developmental and psychological characteristics of low birthweight (LBW) children at 2 and 4 years

The aim of our research was to examine the associations and predictive value of the Bayley-III scales (cognitive, language, motor) assessed at the age of 2 in relation to the 4-year-old IQ and cognitive skills development measured by the Wechsler Preschool Primary Scales of Intelligence test. Furthermore, regarding the predictive values of Bayley-III indexes at 2 years, we also compared the Cohen's Kappa scores for both chronological and adjusted age in order to measure their predictive efficacy of later cognitive delay.

Moreover, we also assessed the changes in quality of life and the parent-reported internalizing and externalizing behaviours of LBW children after the 2-year follow-up period.

METHODS

Procedure

We conducted a 2-year longitudinal cohort study in our thesis work.

In the first phase of the research, we examined the age-adjusted development (BSID-III) of the children in the domains of cognitive, language, motor, social-emotional and adaptive behaviour skills. In this phase, we administered self-designed anamnestic and demographic questionnaires and retrospective analysis of neonatal final reports for each child was also carried out.

In the second phase of the research, the participants were called back at the age of 4 for intelligence assessment (WPPSI-IV). In each case, the psychodiagnostic assessments (BSID-III and WPPSI-IV) were followed by a parent consultation about the results in each case.

In both phases (at the ages of 2 and 4), a battery of psychological questionnaires and checklists was also completed by the mothers. The examinations were conducted at the Clinical Child Psychology and Psychosomatics Unit of the Pediatric Clinic, at the Clinical Center of the University of Debrecen as part of the

clinical care. An examination required approximately 70-120 minutes in each cases. The mothers/primary caretakers were present during the assessment, therefore the diagnostic examination and questionnaire completion took place simultaneously.

Sample

First phase

In the first phase of the study, we assessed 24 months old (adjusted age) preterm children, who were born between 2014 and 2016 at the Obstetrics and Gynaecology Clinics of the University of Debrecen. As part of clinical care, every child born below 1500 grams - VLBW (very low birthweight) and ELBW - at the aforementioned clinic was asked to participate in the developmental examination at 2 years. In the first examination period, 207 out of 294 children were present at the examination. We also selected 152 LBW (1500-2500g birthweight) children from the MedSolution Neonatal Database with proper adjustments for age and sex. 98 out of 152 LBW children participated in the examination. Therefore, in the first phase of the study (September 2016 - September 2018), the overall sample included 305 low birthweight preterm children and their parents.

Second phase

The second phase of our research was carried out between September 2018 and January 2020. By the time of the follow-up study, 158 out of the 305 preterm children turned 4 years old, therefore they were asked to participate. 114 of them were present at the time of the examination, therefore our overall sample includes 114 children after the follow-up.

Measures

First phase

Bayley Scales of Infant and Toddler Development, 3rd Edition (BSID-III, Bayley, 2006; Hungarian adaptation: Kő et al., 2017) psychodiagnostic tool was used to assess the neurodevelopment of preterm children at 2 years. The measurement provides objective and differentiated information about cognitive, expressive and receptive language, fine- and gross motor skills development, moreover it contains 2 questionnaires for primary caregivers assessing social-emotional and adaptive functioning.

Self-designed demographic and anamnestic questionnaires were also administered, which assessed the socio-economic status of the families and several pre-, peri- and postnatal factors. In each case, retrospective analysis of neonatal final reports was used to collect data about chronic neonatal morbidities in the postnatal period.

The battery of questionnaires for mothers/primary caregivers included the following:

- Pediatric Quality of Life Inventory 4.0; PedsQL™ (Mapi Research Institute) – to assess the quality of life of children
- Strengths and Difficulties Questionnaire; SDQ (Goodman et al., 1998) – to assess the mental health of children
- Perceived Stress Scale (PSS, Cohen et al., 1983) – to assess maternal perceived stress
- Beck Anxiety Inventory; BAI (Beck et al., 1988) – to assess maternal anxiety
- Beck Depression Inventory; BDI (Beck & Steer, 1993) – to assess maternal depression
- Satisfaction with Life Scale; SWLS (Diener et al., 1985) – to assess maternal satisfaction with life
- Ways Of Coping Questionnaire; WOC (Lazarus & Folkman, 1984) – to assess maternal coping with stress

Second phase

Wechsler Preschool Primary Scales of Intelligence, 4th Edition (WPPSI-IV, Wechsler, 2012; Hungarian adaptation: Kó et al., 2014) psychodiagnostic tool was used to assess the cognitive skill development and intelligence of LBW children at 4 years. The measurement provides objective and differentiated information about verbal comprehension, visual-spatial ability, fluid reasoning, working memory and processing speed.

The battery of questionnaires for mothers/primary caregivers included the following:

- Pediatric Quality of Life Inventory 4.0; PedsQL™ (Mapi Research Institute) – to assess the quality of life of children
- Pediatric Quality of Life Inventory 4.0 Family Impact Modul; PedsQL™ FIM (Mapi Research Institute) – to assess the impact of pediatric chronic health conditions on parents and the family
- Strengths and Difficulties Questionnaire; SDQ (Goodman et al., 1998) – to assess the mental health of children
- Perceived Stress Scale (PSS, Cohen et al., 1983) – to assess maternal perceived stress

Statistical analysis

IBM SPSS Statistics v22 (IBM SPSS Statistics, IBM Corporation, Armonk, NY) was used for statistical analysis. Descriptive statistics were used in the analysis of demographic, perinatal and neonatal variables, the mental health factors of the children and their parents, as well as the BSID-III and WPPSI-IV scores. Kruskal-Wallis test and Mann-Whitney U-test were used for the analysis regarding birthweight groups, since the majority of the variables showed paranormal distribution (Kolmogorov-Smirnov test and Chi-square test; $p < 0,05$ significance level). Pearson correlation and Spearman rank correlation tests were used to assess the associations between the continuous variables, BSID-III and WPPSI-IV subscales.

We examined the risks of developmental delay at 2 years by calculating odds ratios (OR) using 95% confidence interval (CI). Hierarchical cluster analysis of cases and Ward's method were performed to determine whether there were distinguishable developmental profiles of children within the sample, based on Bayley scores. For the model-development, we used principal component analysis (PCA) for dimensionality reduction to explore the structure of the independent variables of psychological characteristics in children and their parents. We used paired T-tests to analyse the individual differences between the diagnostic tools (BSID-III, WPPSI-IV), then we calculated the predictive values of the BSID-III indexes and the stability of cognitive categorization by using Cohen's Kappa (κ). The values of Cohen's Kappa are the following: 0.0-0.4 - slight to fair agreement; 0.4-0.6 – moderate; 0.6-1.0 - substantial to perfect agreement (Landis & Koch, 1997). For the comparison of the two tests during statistical analysis, we also calculated the mean scores ($\sum C-L-M$) of the BSID-III indexes (cognitive, language, motor), which is not part of the BSID-III test.

RESULTS

Characteristics of the sample

First phase

Regarding the territorial distribution, our sample (N=305) provides data from 3 Hungarian regions: North Great Plain region, North Hungary region, Southern Great Plain region. Using the recommended birthweight classification of WHO (1961), the children were distributed into birthweight groups approximately evenly: LBW: 2500–1500g (N=98); VLBW: 1500–1000g (N=96); ELBW: <1000g (N=111).

The 305 children had a mean birthweight of 1367.46 ± 575.7 g (min.: 330 g; max.: 2490 g) and gestational age of 30.48 ± 3.81 weeks (min.: 22; max.: 36). 76% of the children was born with section caesarea. Gemini (27.5%) and trigemini (9.1%) pregnancies also occurred. Regarding chronic neonatal morbidities, 14.6% of the children received BPD, 13% ROP, 11% IVH and 2.5% necrotizing enterocolitis (NEC) diagnosis in the postnatal period. 50% of the sample (N=155) was male.

Second phase

114 children and their parents participated in the 2-year follow-up study. The mean birthweight and gestational age were similar to the sample in the first phase (M =1310.08g; 30.0 weeks). 80.7% of the children was born with section caesarea. Gemini (21.9%) and trigemini (19.2%) pregnancies also

occurred. Regarding chronic neonatal morbidities, 15.7% of the children received ROP, 14.9% BPD and 13% IVH diagnosis. Only 2 children developed NEC in the postnatal period. Using the recommended birthweight classification of WHO (1961), the children were distributed into birthweight groups approximately evenly: LBW: N=32; VLBW: N=38; ELBW: N=44. 43% of the sample (N=50) was male.

1. Developmental and psychological characteristics of low birthweight (LBW) children at 2 years

Performance on each BSID-III scales was within the Average range. Children performed the highest scores on the Cognitive scale (M=89.51; SD=15.46), which was followed by the Motor (M=87.85; SD=15.34) and Language (M=87.79; SD=15.40) scales. Expressive communication (M=7.35; SD=2.85) and Gross motor skills (M=7.69; SD=2.52) were found to be the least developed among LBW children at 2 years. After age adjustment, 31.1% of the children showed mild or severe cognitive delay, 33.7% of them language delay and 28.5% of them showed delay in motor skills.

Regarding the developmental profiles of 2-year-old LBW children, we identified 3 consistent profiles (High, Mildly Delayed and Severely Delayed) and 3 inconsistent, average profiles with high variability in (mainly expressive) language skills.

Birthweight was found to be an important factor of developmental delay by calculating OR indicators: among ELBW children, the risk of severe developmental delay in motor skills was 12 times (OR=12.73; 95% CI=2.81-57.55), in cognitive skills was 9 times (OR=9.81; 95% CI=3.24-29.66) and in language skills was 4 times (OR=3.91; 95% CI=1.61-9.47) greater compared to children in the other two birthweight groups.

Regarding adaptive behaviour, parents reported significantly poorer performance on the Social ($\chi^2=11.08$; $p=0.004$) and Practical ($\chi^2=6.10$; $p=0.047$) adaptive domains among ELBW children at 2 years. On the other hand, we found no significant differences regarding the Conceptual ($\chi^2=2.88$; $p=0.236$) composite scores. Self-care skills seem to be the least developed regardless of birthweight in all birthweight categories.

Regarding the quality of life at the age of 2, parents evaluated the lowest quality of life in emotional functioning, whereas they reported more behavioural and hyperactivity/inattention deficit problems.

We found the following risk factors for mental health problems: birthweight below 1000 g ($\chi^2=21.47$; $p<0.001$); diagnoses of neonatal ROP ($\chi^2=8.204$; $p=0.017$), BPD ($U=11.05$; $p=0.001$) and IVH ($\chi^2=6.844$; $p=0.033$).

Protective factors were the duration of breast feeding ($r=0.365$; $p<0.001$), higher maternal education ($\chi^2=17.01$; $p<0.001$),

higher socioeconomic status of the family ($\chi^2=16.73$; $p<0.001$) and non-ethnic identity ($U=274.50$; $p=0.001$).

Regarding the mental health problems of the preterm children, parental mental health characteristics (perceived stress, anxiety, depression and satisfaction with life) showed an explanatory power of 26.15%. It was followed by the variables indicating biological vulnerability, such as birthweight and neonatal chronic morbidities with an explanatory power of 21.78%. Lastly, the third component we found contained the variables of demographic risk factors with an explanatory power of 20.04%.

Regarding the parental ways of coping with stress, we found more frequent use of coping strategies, especially Positive Reappraisal ($U=2368.0$; $p=0.004$) and Distancing ($U=2628.5$; $p=0.05$).

2. Cognitive development and psychological characteristics of low birthweight (LBW) children at 4 years

The cognitive performance of the preterm children ($N=114$) fell into the average range regarding the scales of the WPPSI-IV test. The lowest performance was found in Fluid Reasoning skills at 4 years. Examining the performance individually, 42.1% of the children performed in the Average range, 24.5% in the ranges above average and 33.3% in the ranges of below average.

We found that perinatal and neonatal risk factors for lower cognitive functioning are birthweight ($r=0.383$; $p<0.001$),

neonatal retinopathy (U=342.50; p=0.003), intraventricular haemorrhage (U=437.0; p=0.023) and bronchopulmonary dysplasia (U=309.50; p=0.001).

The sociodemographic characteristics of the families were found to be also crucial in the cognitive development at the age of 4. Primary maternal education (U=239.50; p<0.001), lower socioeconomic status (U=17.50; p<0.001) and Roma ethnicity (U=283.0; p=0.001) were identified as risk factors.

Regarding the quality of life (PedsQL) at 4 years old, the parents reported the most difficulties in emotional functioning. They also reported more emotional and hyperactivity/inattention deficit problems (SDQ). 24.5% of the 4-year-old children fell into a problematic range regarding difficulties in activity and attention. Using the birthweight categorization, we found significant differences in the case of both the PedsQL ($\chi^2=18.11$; p<0.001) and SDQ ($\chi^2=21.59$; p<0.001) total scores.

Significant associations were found between IQ and both the quality of life and mental health of the children. We found positive correlation between IQ and HrQoL (r=0.354; p<0.001), whereas negative correlation was found with mental health problems (r=-0.324; p=0.001). 37 children, who performed in the below average range (IQ<90), were reported to show significantly more internalizing (U=966.5; p=0.011) and externalizing (U=957.0; p=0.010) behaviours, as well as lower

total HrQoL scores ($U=1009.0$; $p=0.015$) compared to their average or above average peers.

Regarding parental quality of life, parents expressed more difficulties with worrying, which was mostly associated with birthweight ($<1000\text{g}$) ($r=0.347$; $p<0.001$) and the diagnoses of IVH and ROP. Parental quality of life showed a moderate positive correlation with parent-reported quality of life of the children ($r=0.557$; $p<0.001$), whereas strong negative correlation with the parent-reported SDQ problem scores ($r=-0.556$; $p<0.001$).

3. Associations of developmental and psychological characteristics of low birthweight (LBW) children at 2 and 4 years

BSID-III total scores showed the strongest correlation with WPPSI-IV IQ, moreover, this correlation coefficient was found to be the strongest between the 2 tests ($r=0.683$). Regarding cognitive performance at 2 (BSID-III) and 4 (WPPSI-IV) years, we found a mean difference of $+6.5$ (95% CI: $22.115 - -35.115$). Only 58.7% of the children performed in the same range at 4 years old as did two years before. 8 children performed in a lower range compared to their 2-year-old performance, whereas 39 could reach a higher range.

Regarding the prediction of mild and severe delay, the specificity of BSID-III proved to be higher in every cases than the sensitivity of the test. Therefore, it showed greater

predictive value for normal development, compared to mild or severe delay.

Regarding age adjustment, we found higher Kappa values in case of chronological age, which indicates stronger predictive value for later moderate and severe cognitive delay diagnoses. Overall, the concordance between the two tests is moderate ($\kappa=0.459$) regardless the severity of delay, whereas in case of severe delay, the concordance is higher ($\kappa=0.682$), which indicates considerable concord.

We also found significant differences between the psychological characteristics (PedsQL and SDQ) of the children at the ages of 2 and 4. Parents reported significantly lower quality of life for their 4-year-old children in emotional functioning ($t=3.126$; $p=0.002$) and social functioning ($t=2.044$; $p=0.043$) compared to 2 years before. On the other hand, significantly fewer difficulties were found regarding SDQ: parents reported significantly fewer internalizing ($t=2.587$; $p=0.011$) and externalizing ($t=5.679$; $p<0.001$) behaviour problems than 2 years ago. The reported difficulties in activity and attention were also present in 52% of the children at 4 years old.

Examining the individual differences, approximately 60% of the children were reported no changes regarding their mental health. 10% were reported having more problems, whereas 30% of them were reported showing less internalizing and externalizing behavioural problems.

DISCUSSION

1. Developmental and psychological characteristics of low birthweight (LBW) children at 2 years

Our results support the findings of other studies that ELBW is associated with increased risk of developmental delays compared to not only their full-term peers (Barre et al., 2011), but to the VLBW and LBW populations as well. We found the most severe delay in language skills: the expressive-receptive language delay may manifest in poorer active and passive vocabulary, as well as in verbal comprehension and expression skills (Bayley, 2006), which may bring about specific developmental disorders of speech and language and/or language-based learning disabilities (Barre et al., 2011). In this regard, we identified high risk children, who showed average skill structure yet severely delayed language skills. Their expressive-receptive language delay might be an important symptom, which may indicate the risk of later speech developmental disorder.

Our results indicate, that cluster analysis might be a new and useful statistical method to identify the developmental profiles of preterm children, which might result in a more complex understanding of cognitive and psychomotor development in early childhood (Ross et al., 2016). Using developmental profiles has several merits: at the individual level, it may help in the follow-up of the children's development, whereas in

research framework, it may provide new insights in longitudinal and case-control studies as well.

Our results also support the previous findings, that ELBW children show lower functioning in social-emotional skills, even at the age of 2 (Cheong et al., 2017). This developmental domain reflects on functional emotional skills, such as self-regulation (arousal, motor and especially affection and behaviour) in particular skill areas like communicating their needs or the purposeful and interactive use of emotions.

Behavioural problems and difficulties in activity and attention were the leading cause of problems at 2 years old in families of LBW children. Previous studies found higher risk of ADHD diagnosis among school-aged children compared to the control group (OR = 2.64: (Bhutta et al., 2002); OR = 3.04; (Franz et al., 2018)). Based on our research, difficulties in development are detectable after the age of 2. Therefore, we emphasize the importance and need of early neonatal, pediatric and psychological prevention and intervention, in order to prevent the exacerbation of symptoms and minimize the burden of ADHD later in this population.

We confirmed the findings, that parents of ELBW children experience higher levels of stress and more symptoms of anxiety and depression compared to parents of full-term children (Spear et al., 2002; Kaaresen et al., 2006), which is still detectable after 2 years of birth. The identified psychological

burden led the parents to use significantly more coping strategies.

The emotional support of mothers and fathers after premature birth should be an important intervention during the early years, not only for their mental health and quality of life but their children's as well. We recommend utilizing the help of mental health professionals, clinical and health psychologists in paediatric clinics and obstetric and new-born care units in order to provide support for parents of premature children.

2. Cognitive development and psychological characteristics of low birthweight (LBW) children at 4 years

Based on our results we can conclude that preterm children – especially ELBW are at risk of cognitive delay. We also found that neonatal chronic morbidities, such as ROP, IVH or BPD are risk factors for the cognitive development (Chiriboga et al., 2003; Patra et al., 2006; Mattes, 2017).

Several studies found positive associations between parental education and intellectual performance of children (Benavente-Fernández et al, 2019), which our results corroborate. we must emphasize, that early intervention programs for cognitive development should consider implementing the education of the parents and the promotion of competent parenthood to broaden their and their children's perspectives in life. Another crucial task is monitoring the development of preterm children with neonatal chronic morbidities and providing them with the

earliest interventions to nurture cognitive skill development, and attention and executive functioning which may promote the optimal development of academic skills and prevent delays or school-drop out.

Similarly to previous research, we also found significantly more internalizing and externalizing behaviour problems among lower birthweight children at 4 years old (Bhutta et al., 2002; Bora et al., 2014), regarding mainly emotional problems and difficulties in activity and attention.

In accordance with the EPIPAGE study (Delobel-Ayoub et al., 2009), parents reported significantly more internalizing and externalizing behaviour problems and lower quality of life among children who fell into the below average IQ range (<90).

3. Associations of developmental and psychological characteristics of low birthweight (LBW) children at 2 and 4 years

As far as we are concerned, the present research is the second longitudinal cohort study that examined the associations between cognitive performances measured by BSID-III and later WPPSI and the first that used the latest (IV.) edition of WPPSI. Our research shows similar, yet promising results to studies, which found adequate predictive validity of Bayley Scales of Infant Development 1st and 2nd Editions (BSID-I; BSID-II) on later functioning (Munck et al., 2012; Potharst et al., 2012) – based on our results, the total scores of BSID-III at

2 years showed strong predictive value regarding severe delays in cognitive functioning at 4 years.

In every cases, the specificity of BSID-III proved to be higher than the sensitivity of the test, which finding corresponds with meta-analysis of 24 studies (Wong et al., 2016). At the individual level, the low sensitivity indicators manifested in an average 6.5-point increase in performance after the follow-up. These results can be explained by the high heterogeneity of the sample, as well as by the complex interaction of factors, such as children's unceasing developmental potential, resiliency and environmental factors (e.g. beneficial early interventions).

Regarding age adjustment, age-adjusted BSID indexes were closer to 4-year-old WPPSI-IV indexes. In terms of predictive value, on the other hand, chronological BSID indexes proved to be more reliable predictors of later cognitive performance in almost every case.

The psychological characteristics of the children changed significantly over the years: parents reported lower emotional and social functioning and less internalizing and externalizing behaviour problems. In accordance with the EPIPAGE study (Delobel-Ayoub et al., 2009), more than half of the children was reported similar emotional and behavioural problems after 2 years at 4 years old.

Regarding the high stability of early mental health problems, our research calls attention to the importance of early screening

(questionnaires, checklists) in the health care system at the age of 2, thus identifying symptoms which could predict later mental disorders.

CONCLUSION

The identified severe language delay in our sample indicates the necessity and importance of early language intervention programs, of which primary goal is the shaping of the children's home environment through the parents' knowledge, attitude and behavior, as well as the material environment. Institutional education also plays a vital role in language development and training. Based on the national pedagogical practice, children, who are presenting language delay at 2 years, receive home-training, in which a speech therapist educates the parents how to train the language skills of their children at home.

Among preterm children - especially below 1000 g birthweight – it may also be crucial to promote self-regulation skills in order to prevent later mental health problems. Self-regulation training programs are usually conducted in groups in institutional education settings. However, it is proven, that parents play a vital role in the development of early self-regulation, therefore the interventions should be planned accordingly: in addition to promoting the development of the children's self-regulation skills, it should also promote parental self-regulation and parent-child relationship.

Among preterm children (especially the at-risk group based on the SDQ screening questionnaire), early intervention for attention skill development must be prioritized, since it may have a beneficial impact on executive functioning (Cuevas et al., 2018). Several practical training and computer-based games are available for attention skill development, which can also affect other domains of cognitive processing (Rueda et al., 2011). Regarding hyperactivity and attention problems it must be emphasize, that these early regulation difficulties (such as inadequate impulse-control) are not directly linked to be the precursors of the onset of later ADHD due to the lack of evidence-based research. On the other hand, early screening may play a vital role in secondary prevention of later mental health problems.

Regarding the mental well-being of preterm children, our results draw attention to the necessity of relationship-based early intervention programs, which promote the active inclusion and support of parents (e.g. through their own development in self-regulation skills), while providing extra focus on supporting underprivileged families (thus underprivileged children) by direct interventions. In addition to increasing the parental educational levels, the promotion of competent parenthood is also a universal need in today's society to foster the mental health and optimal cognitive development of the next generation.

SUMMARY

In the field of psychology, early screening and diagnostics gains more ground in the 21st century Hungary. However, the number of the Hungarian studies are limited, therefore we found it important to conduct a complex, longitudinal cohort study that identifies the problematic aspects of development, mental health and quality of life of Hungarian preterm children, as well as examines their connections with perinatal, demographic and parental factors.

Our initial sample includes 305 low birthweight (LBW) two-year-old children and their parents and 114 of them participated in a follow-up study at 4 years old.

Comparisons of the birthweight categories (VLBW, LBW, ELBW) and the odd ratios indicate, that extremely low birthweight children, who therefore are at higher biological risk, had considerably lower performance in all developmental domains. Based on the results we can conclude that the use of cluster analysis can be an effective way to identify the developmental profiles of preterm (or other at risk) children, therefore to achieve a more complex understanding of development regarding the early cognitive, language and motor skills. During the analysis of the predictive value of BSID-III at 2 years, we found that the indexes – calculated by chronological age – proved to be strong and valid predictors of later cognitive delay at 4 years old.

In our research we also found LBW children are at higher risk of behavioural and emotional difficulties at 2 years, which persisted until the age of 4 in half of the cases. Further risks are the presence of neonatal chronic morbidities the lower socio-economic status of the family, such as primary education and lower than average financial income). We found breastfeeding (skin-to-skin contact, increased feeling of bonding and balanced emotional state) to be a protective factor for both the children's and the mother's mental health. We also found maternal mental health to be crucial for their children's mental health and quality of life.

Based on our result, we find the comprehensive screening of low birthweight (especially the ELBW) population to be essential at 2 years old in favour of relationship-focused early interventions to prevent later cognitive, language and motor deficits, internalizing and externalizing problems and the consequent mental health problems and school drop-out.

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DOI: <http://dx.doi.org/10.1080/17518423.2020.1764651>
IF: 1.707 (2019)
3. **Kenyhercz, F.**, Nagy, B. E.: A new perspective: establishing developmental profiles of premature infants based on Bayley-III scores at age 2.
Appl. Neuropsychol.-Child. [Epub ahead of print], 1-8, 2020.
DOI: <http://dx.doi.org/10.1080/21622965.2020.1771338>
IF: 1.293 (2019)
4. **Kenyhercz, F.**, Nagy, B. E.: Emotional and behavioural difficulties and quality of life of preterm children at 2 years regarding parental mental health.
Early Child Dev. Care. [Epub ahead of print], 1-15, 2020.
DOI: <http://dx.doi.org/10.1080/03004430.2020.1755667>
IF: 0.968 (2019)





List of other publications

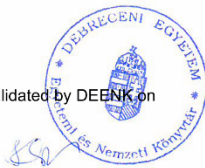
5. **Kenyhercz, F.**, Sveda, B., Nagy, B. E.: Koraszülöttek kétéves kori pszichomotoros fejlődése a leggyakoribb krónikus utóbetegségek vonatkozásában.
Orv. hetil. 161 (5), 183-192, 2020.
DOI: <http://dx.doi.org/10.1556/650.2020.31630>
IF: 0.497 (2019)
6. **Kenyhercz, F.**, Kató, S., Nagy, B. E.: Health-related quality of life of premature infants at 2 years in relation to breastfeeding and maternal emotional state: a retrospective cohort study.
Early Child Dev Care. [Epub ahead of print], 1-12, 2019.
DOI: <http://dx.doi.org/10.1080/03004430.2019.1676241>
IF: 0.968
7. Nagy, B. E., Szele, A. S., **Kenyhercz, F.**: The features of children's drawing.
In: *Gyermekvilágok II..* Ed.: Mária Bujdosó, Didakt Kft., Debrecen, 2018, 2018.
8. **Kenyhercz, F.**, Nagy, B. E.: Koraszülöttek kétéves kori életminősége a szoptatás és az anyai érzelmi állapot függvényében.
In: *Professzorok az Európai Magyarorszáért Egyesület - PhD Konferencia, 2017 / Professzorok az Európai Magyarorszáért Egyesület, Professzorok az Európai Magyarorszáért Egyesület, Budapest, 19-27, 2017.*
9. **Kenyhercz, F.**, Nagy, B. E.: Koraszülött gyermekek kétéves kori pszichomotoros fejlődése társas-környezeti tényezők függvényében.
Orvosi Hetilap. 158 (1), 31-38, 2017.
DOI: <http://dx.doi.org/10.1556/650.2017.30628>
IF: 0.322

Total IF of journals (all publications): 6,723

Total IF of journals (publications related to the dissertation): 4,936

The Candidate's publication data submitted to the iDEa Tudóstér have been validated by DEENK on the basis of the Journal Citation Report (Impact Factor) database.

04 May, 2021



National and international conference presentations and posters in relation to the thesis work

Kenyhercz F. Koraszülött gyermekek pszichomotoros fejlődésének vizsgálata rizikótényezőkkel összefüggésben, kétéves korban. In: Orvos- és egészségtudományi TDK Konferencia: Absztraktkötet. Konferencia helye, ideje: Debrecen, 2016. február 23-26. pp. 400.
(Orvos és egészségtudományi szekció 2. helyezés)

Kenyhercz F., Nagy B. Koraszülött gyermekek pszichomotoros fejlődésének vizsgálata, kétéves korban. (poszter) In: Múlt és jelen összeér, A Magyar Pszichológiai Társaság XXV. Jubileumi Országos Tudományos Nagygyűlése: Kivonatkötet. Konferencia helye, ideje: Budapest, 2016. június 2-4. pp. 303-304.

Nagy B., **Kenyhercz F.** Környezeti tényezők szerepének vizsgálata a koraszülött gyermekek pszichomotoros fejlődésében, egészségpszichológiai szempontból. In: Múlt és jelen összeér, A Magyar Pszichológiai Társaság XXV. Jubileumi Országos Tudományos Nagygyűlése: Kivonatkötet. Konferencia helye, ideje: Budapest, 2016. június 2-4. pp. 106-107.

Nagy B., **Kenyhercz F.** Pszichomotoros fejlődés vizsgálata koraszülötteknél. In: Magyar Pszichoszomatikus Szülészeti és Nőgyógyászati Társaság IX. Kongresszusa: Program. Kongresszus helye, ideje: Szeged, 2016. október 28-29. pp. 20.

Kenyhercz F. Koraszülött gyermekek pszichomotoros fejlődésének vizsgálata rizikótényezőkkel összefüggésben, kétéves korban. Orvosképzés, 2017, XCII., 2., 311. (Országos Tudományos Diákköri Konferencia, Orvos- és Egészségtudományi Szekció, Pécsi Tudományegyetem, 2017. április 18-21.)
(Orvos és egészségtudományi szekció 1. helyezés)

Kenyhercz F. Nagy B. E., Koraszülöttek kétéves kori pszichomotoros fejlődése krónikus utóbetegségek tükrében. (poszter) In.: Személyes tér közös világ, A Magyar Pszichológiai Társaság XXVI. Országos Tudományos Nagygyűlése: Kivonatkiötet. Konferencia helye, ideje: Szeged, 2017. június 1-3. pp. 295-296.

Nagy B. E., **Kenyhercz F.** A retinopathia és az intraventricularis haemorrhagia hatása a későbbi pszichomotoros fejlődésre koraszülötteknél. (poszter) In.: Magyar Pszichoszomatikus Szülészeti- és Nőgyógyászati Társaság 25 éves Jubileumi Kongresszusa, Múlt-jelen-jövő: Programfüzet. Konferencia helye, ideje: Székesfehérvár, 2017. szeptember 22-23. pp. 12.

Kenyhercz F., Nagy B. E., Koraszülött gyermekek életminősége csecsemőkori jellemzőkkel összefüggésben. In.: Magyar Pszichoszomatikus Szülészeti- és Nőgyógyászati Társaság 25 éves Jubileumi Kongresszusa, Múlt-jelen-jövő: Programfüzet. Konferencia helye, ideje: Székesfehérvár, 2017. szeptember 22-23. pp. 59-60.

Kenyhercz F., Nagy B. E., Koraszülöttek kétéves kori életminősége a szoptatás és az anyai érzelmi állapot függvényében. (poszter) In.: Professzorok az Európai Magyarorszáért Egyesület XV. PhD – Konferencia, 2017. Konferencia helye, ideje: Budapest, 2017. november 8.

Szóllós A., **Kenyhercz F.,** Balázs G., Elek N., Fehér Cs., Horváth Zs., Katona N., Kovács J., Kovács-Pászthy B., Kovács T., Kotormán T., Nagy K., Polonkai E., Riszter M., Nagy B. E., Balla Gy.: A koponya ultrahang vizsgálat jelentősége a neurológiai kimenetel előrejelzésében. In.: FINETA 3.0 Fialat Neonatológusok III. Találkozója Programfüzet, 2018. Konferencia helye, ideje: Kecskemét, 2018. május 31 – június 2, pp. 49-50.

Kenyhercz F., Nagy B. E., A szoptatás és az életminőség összefüggései koraszülötteknél. In.: *Gyermekgyógyászat*, 2018; 69. évf., 5. szám. Konferencia helye, ideje: Magyar Gyermekorvosok Társasága 2018. évi Nagygyűlése. Debrecen, 2018. szeptember 20-22, pp. 321.

Kenyhercz F., Nagy B. E.: Képességprofilok azonosítása a kétéves kori kognitív és pszichomotoros készségek mentén, koraszülöttek körében. (poszter) In: Összetart a sokszínűség: A Magyar Pszichológiai Társaság XXVIII. Országos Tudományos Nagygyűlése. Konferencia helye, ideje: Debrecen, 2019. május 30 - június 1. Programfüzet, pp. 50.

(Poszterszekció I. helyezés)

Nagy B. E., **Kenyhercz F.,** Szele A. Sz., Szabó É.: Az intraventricularis haemorrhagia (IVH) és a kora gyermekkori pszichomotoros teljesítmény közötti összefüggés koraszülött gyermekeknél. In.: *Rehabilitáció*, 2019, 29. évf., 2-3. szám. Konferencia helye, ideje: Magyar Rehabilitációs Társaság XXXVIII. Vándorgyűlése. Debrecen, 2019. október 3-5, pp 87.

Kenyhercz F., Nagy B. E. Koragyermekkori internalizáló, externalizáló viselkedés és az életminőség alakulása koraszülötteknél a szülők mentális egészségének tükrében. (poszter) In: Magyar Pszichiátriai Társaság XXIII. Jubileumi Vándorgyűlése. Konferencia helye, ideje: Budapest, 2020. január 22-25.

(Poszterszekció I. helyezés)

Kenyhercz F.: A koragyermekkori életminőség és mentális egészség viszonya koraszülötteknél a szülők pszichés dimenzióinak tükrében. Konferencia helye, ideje: Debreceni Egyetem ÚNKP Konferencia. Debrecen, 2020. január 27.

