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(Head of Doctoral School: Dr. habil Zsolt Demetrovics)

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(Head of Programme: Dr. Judit Balázs, PhD)

ANETT NAGY

INTELLIGENCE AND EXECUTIVE FUNCTIONS IN 9-10 YEAR-OLD PRETERM CHILDREN IN FUNCTION OF BIRTH WEIGHT AND PERINATAL COMPLICATION

Summary of doctoral dissertation

Supervisor: Dr. Magda Kalmár, emeritus professor

Introduction

According to an international consensus neonates born before the 37. week of gestation are considered preterms. Prematurity is the most common perinatal risk: the average rate of preterm births is between 9% and 12% of all live births in the higher- and lower-income countries, respectively (WHO, 2018). In Hungary 8,1% of the newborn babies were preterms in 2017 (KSH, 2018).

The degree of risk for the development of the individual involved in premature birth depends on a range of factors. The population of premature babies is very heterogeneous. The earlier the baby is born and the less the birthweight the risk is greater. Birth weight serves as a basis for a classification of preterm neonates most frequently used in medical praxis according to the recommendation by the BNO 10. The categories are the following: extremely low birth weight (< 1000 grams, ELBW); very low birth weight (1000–1499 grams, VLBW); low birth weight (1500–2499 grams, LBW) (Behrman & Butler, 2007).

Perinatal complications may further increase the risk. The immature organism is more vulnerable to diseases affecting the respiratory organs (respiratory distress-syndrome, RDS), the central nervous system, and the sensory systems. The prevalence of the intraventricular haemorrhage (IVH) among the ELBW infants is 50% (Balla & Szabó, 2013) and the more immature the baby the IVH tends to be more severe (stades III and IV). Periventricular leukomalacy (PVL) is a typical white-matter injury in preterm infants which, along with the more severe degrees of IVH, may cause cerebral paresis and the loss of oligodendroglial cells (Mulder, Pitchford, Hagger, & Marlow, 2009). A chronic lung disease, bronchopulmonal dysplasia (BPD) is also a common concomitant of premature birth, occurring in more than 40% of ELBW preterms (Glass et al., 2015). Ventilatory therapy (mostly by hyperoxia) may cause an abnormal vascular proliferation of the immature retina, leading to an ocular disease called rethinopathy of prematurity (ROP) (Behrman & Butler, 2007).

The development of the central nervous system in preterm infants deviates from that in their full-term counterparts. Anomalies are often found in the structure of both the white and the gray matter. The entorhinal cortex and the corpus callosum can be thinner (Feldman, Lee, Yeatman, & Yeom, 2012) and the volume of the hippocampus as well as that of the cerebellum can be smaller than in term newborns (de Kieviet, van Elburg, Lafeber, & Oosterlaan, 2012). The effects of prematurity on the CNS development seem to differ across the brain regions. One region may be affected severely while others may remain intact. In low-risk preterm infants

there were no significant differences in the volume of the dorsal prefrontal and the orbitofrontal lobe which are related to the executive function (Peterson et al., 2000).

It is apparent that the neurodevelopmental consequences of premature birth affect the development of cognitive functions and academic abilities, although the bulk of research evidence is not consistent. The IQs of the VLBW/ELBW preterm children as a group were found to fall into the average (Grunewaldt, Løhaugen, Austeng, Brubakk, & Skranes, 2013) or low-average zone (Stålnacke, Lundequist, Böhm, Forssberg, & Smedler, 2019). However, according to a recent meta-analysis reviewing 71 studies comparing the IQ-s of very preterm children to those of term comparison groups the preterms significantly lagged behind (Twilhaar et al., 2018). The authors of the meta-analysis also noted the heterogeneity of results across studies. In the studies by Grunewaldt et al. (2014), e.g., the preterms had deficits only on a single cognitive measure out of several ones.

Research interest in executive functions (EFs) – which is an umbrella term encompassing the conscious, goal-directed problem-solving thinking and the higher-order control processes (Lee, Bull, & Ho, 2013; Zelazo, Carlson, & Kesek, 2008) – is relatively recent. A universally accepted theoretical model of EF is not yet available, but cognitive flexibility (shifting), updating/working memory, and inhibition have been generally regarded as its core components (Diamond, 2016; Józsa & Józsa, 2018; Miyake et al., 2000; Miyake & Friedman, 2012). The higher-order executive functions (thinking, problem-solving, and planning) are built out of these core components (Diamond, 2016). Similarly to the prefrontal lobe the maturation of the EFs is a long process, lasting until adolescence (Csépe, 2005). The various components mature in different rates, then in time they start to decline (Diamond, 2016).

Premature birth involves a risk for executive deficits. Four year-old preterm children performed more poorly than the term comparison group on direct measures of EF, and their teachers reported that they had more difficulties with inhibition, working memory, planning/organisational skills, and self-control (O'Meagher, Kemp, Norris, Anderson, & Skilbeck, 2017). School-age ELBW/VLBW preterms scored poorer as compared to their non-risk counterparts in tasks requiring inhibition, working memory, and shifting (i.e., cognitive flexibility) (Aarnoudse-Moens, Duivenvoorden, Weisglas-Kuperus, Van Goudoever, & Oosterlaan, 2012; Ford et al., 2011; Stålnacke et al., 2019). In the study of Ritter, Nelle, Perrig, Steinlin & Everts (2013) 8-10 year-old VLBW children performed significantly poorer than the controls in inhibition, working memory, and shifting, whereas the 10-13 year old VLBW children reached the same level as the controls in all three EFs. The authors concluded that the poor performances of the younger VLBW children might reflect a delay rather than a deficit.

The catch-up tendency presumably stems from the plasticity of function and organisation of the human brain (Ford et al., 2011). In addition, Ritter and colleagues (2013) argued for the potential remedial effects of environmental factors. The study by Costa et al. (2017) calls attention to the variety of developmental trends of executive functions in ELBW children. In the majority of their subjects the EFs remained stable between 8 and 18 years of age, with more than half of them scoring in the typical range and 15% performing persistently low. However, the EF performances of about ¹/₄ of the subjects changed markedly, with late-onset difficulties and remitting trends occurring in equal proportions.

The substantial inter-individual variations within the preterm children underline the issue of prediction of the development of EFs. O'Meagher et al. (2017) found that social risks, particularly low maternal education were the strongest associates of impaired EF outcomes while the perinatal variables had no predictive power. In contrast, a study by Ford et al. (2011) provided evidence on the impact of neurobiological risks on EF performances and revealed interactions between neurobiological risk factors and maternal education in ELBW children. It suggests that the adverse effects of neurobiological risks can be attenuated by favourable social backgrounds. A recent 18-year long longitudinal study by Stålnacke and colleagues (2018) revealed a complex mechanism underlying the development of EFs, using a serial multiple mediator model. The results showed a remarkable stability of both working memory and cognitive flexibility from 5 $\frac{1}{2}$ to 18 years of age. Parental education had direct effect on both 5 $\frac{1}{2}$ -year EF measures, while perinatal medical complications and intrauterine growth had direct effects on cognitive flexibility at 18 years. In addition, mental development at 10 months of age mediated the influences of perinatal variables and gender by having direct relation to the 5 $\frac{1}{2}$ -year EF measures.

Aim of the study

The aim of our research was to evaluate the school-age outcomes of Hungarian VLBW/ELBW preterm children in basic cognitive abilities and executive function as compared to typically developing, full-term children. Following recommendations in the literature (Ford et al., 2011; Ritter, Nelle, Perrig, Steinlin, & Everts, 2013) we chose a short age range. We considered the age of 9-10 years interesting. In typical development the IQ can be expected to stabilize around 5 -7 years, i.e., from then it can predict the later IQ rather reliably. Kalmár (2007) in a follow-up of preterm children found that the perinatal risks delayed the stabilization, and around 7 years major shifts occurred. The IQs measured at 9-10 years were powerful

predictors of the IQ in late adolescence. At the same time in certain aspects of the cognitive development important changes take place around this age (Duan, Wei, Wang, & Shi, 2010; Lee et al., 2013).

The research into the EF in terms of the theoretical foundations and the terminology has not yet settled. In our work we have adopted the terminology of Miyake et al (2000), focusing on the three core components of EF: updating/working memory, inhibition, and cognitive flexibility (shifting). We were attempting to tap the background of individual differences in the outcomes by analysing the effects of perinatal and social-economic factors.

Hypotheses

1. The IQs of both the ELBW and the VLBW preterm children will be lower than the IQs of the term comparison children (Aarnoudse-Moens, Weisglas-Kuperus, Duivenvoorden, van Goudoever, & Oosterlaan, 2013; Balla & Szabó, 2013; Behrman & Butler, 2007; Iwata et al., 2012; Kalmár, 2007; Twilhaar et al., 2018), and the IQs of the ELBW preterms will lag behind even their VLBW counterparts (Gu et al., 2017).

2. In the tasks measuring the inhibition, cognitive flexibility (shifting), and updating/working memory the performance of the preterm children will be lower than that of the term comparison children, but the preterm groups will not differ from each other (Arhan et al., 2017; Ford et al., 2011; Iwata et al., 2012; Mulder et al., 2009).

3. The individual differences among the preterm children as far as the perinatal states and complications are concerned will influence their performances in the IQ test as well as the tasks measuring the EF at 9-10 years of age (Mulder et al., 2009; O'Meagher et al., 2017; Stålnacke et al., 2019).

4. Maternal education will have stronger effects than the perinatal state and complications on the performances of the preterm children at 9-10 years of age (Ford et al., 2011; Stålnacke et al., 2019).

5. Preterm girls will outperform the preterm boys both in the IQ test and the tasks measuring the EF (Aarnoudse-Moens et al., 2013; Baron, Ahronovich, Erickson, Gidley Larson, & Litman, 2009; O'Meagher et al., 2017).

6. The infant development can predict the 9-10-year performances in the IQ test and the tasks measuring the EF to some extent; the predictive power of the 2-year scores will be stronger than that of the 1-year scores (Breeman, Jaekel, Baumann, Bartmann, & Wolke, 2015; Doyle et al., 2015; Ribiczey & Kalmár, 2009).

7. In the individual performances in the various components of the intelligence and EF meaningful patterns can be identified. The subgroups of subjects displaying each of the patterns will differ in the backgroung factors influencing the performances.

8. By means of a factor analyis the relationships between the performance measures and the latent variables underlying the performance measures can be identified and interpreted.

The study was approved by the Scientific and Research Ethics Committee of the Health Science Council (13425-2/2016/EKU)

Method

Subjects:

The subjects were 105 children, aged 9–10 years (mean = 113,7 months; SD = 3,51; range 108-119). 72 children were born preterm. The majority of the preterm sample were participants of the follow-up program of the Semmelweis University, Budapest. Further subjects were recruited via the internet. 32 of the preterm children were born with birthweights <1000 grams (ELBW) and 40 with birthweights between 1000–1490 grams (VLBW). The non-risk comparison group (control) was recruited from schools. The criteria of inclusion were full-term birth, birth weight > 2500 grams, lack of perinatal complications, and a typical developmental course. The 33 full-term comparison children (FT) were born at 38–41 weeks gestation, with birthweights > 2500 grams. The three groups (ELBW, VLBW, FT) were matched on age, gender, and maternal education.

All of the children attended mainstream general schools and none of them was diagnosed with ADHD or learning disability, or had any developmental disorder endangering the understanding of instructions.

Instruments, measures, and procedure:

Intelligence:

The Wechsler Intelligence Scales for Children (WISC-IV) (Wechsler, 2008, Hungarian adaptation: Nagyné Réz et al, 2009); measures: Full Scale IQ (IQ), Verbal Comprehension Index (VCI), Perceptual Reasoning Index (PeRI), Working Memory Index (WMI), Processing Speed Index (PrSI).

Executive function:

The tests of executive functions were administered in digital versions (PEBL version 0.13 test package (Mueller & Piper, 2014) using a personal computer.

Memory:

Corsi Block Tapping Task (Corsi, 1973; Milner, 1971); the number of correct trials - forward (for spatial-visual short-term memory) and the number of correct trials - backward (for updating/working memory).

Cognitive flexibility (shifting):

Wisconsin Card Sorting Test (WCST), (Grant & Berg, 1948; Heaton, Chelune, Talley, Kay, & Curtiss, 1993); number of completed categories, numbers of perseverational and non-perseverational errors.

Inhibition:

Stroop Color and Word Test (SCWT), (Stroop, 1935); numbers of errors (color reading, color naming, stroop effect), time (color reading, color naming, stroop effect), interference error and time.

Tower of Hanoi Task (ToH), (Humes, Welsh, Retzlaff, & Cookson, 1997): number of extra steps, percentage of patterns completed using the minimum number of steps, time of completing the task.

Background variables:

For the total sample gender and maternal education.

For the preterm children, in addition: perinatal characteristics and complications (birth weight, gestational age, bronchopulmonal dysplasia, intraventricular haemorrhage, rethinopathy of prematurity).

Potential predictors (for the preterm children only):

Brunet-Lèzine Developmental Scale performances (Developmental Quotient and the component quotients: Postural Coordination, Language, Social) at 1 and 2 years of age.

Statistical analysis

The data analysis was performed using the SPSS 22 (IBM, Armonk, NY, USA). The results were considered significant if p < 0.05 (two-sided). The Kolmogorov-Smirnov test was used to check the normality of the data distribution. The three groups were compared using a one-way MANOVA with Bonferroni correction, or, in case the data distribution did not fulfil the criteria of normality, using the Kruskall-Wallis test. Two-group comparisons were computed using the two-sample t test or the Mann-Whitney U test with Bonferroni correction. To test the relationships between the variables correlation analysis (Pearson or Spearman) or Chi-square test were used. In order to test the contribution of the background variables to the results General Linear Models were computed. The first models covered the total sample with gender and maternal education as independent variables. Further models applied only to the preterm subjects aiming to check the role of perinatal variability. In this model maternal education, birth weight, gestational age, and the perinatal complications were included in the analysis. The dependent variables were the WISC-IV IQ, the WISC-IV indices, and the executive function measures. The groups of individuals showing similar performance patterns were identified by a hierarchical cluster analysis with Ward's method. Logistic regression was computed to tap into the background factors explaining the cluster memberships. The latent variables behind the performances were revealed using a principal component analysis.

Results

The performances of each group are shown in the following tables:

Measure		Group	Mean	SD	Range	Statistical results MANOVA, post-hoc Bonferroni,
						Pairwise group
						comparisons
						Kruskal-Wallis, Mann-
						Whitney
		ELBW	102.7	14.04	78-126	F(2, 101) = 10.32;
WISC-IV	FsIQ	VLBW	109	10.56	83-126	p < 0.0001;
		Control	116.6	12.03	94-132	$\eta^2 = 0.17$
						ELBW < Control
						p < 0.001
						VLBW < Control
						p = 0.028
		ELBW	108	11.49	85-125	F(2, 101) = 5.48;
	VCI	VLBW	112.6	9.39	89-127	p = 0.006;
		Control	117	11.68	93-138	$\eta^2 = 0.098$

Table 1. The significant performances of the three groups

$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							ELBW < Control
$ \left \begin{array}{c c c c c c c c c c c c c c c c c c c $							p = 0.004
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			ELBW	ELBW	100.7	13.36	F(2, 101) = 9.89;
$ \begin{tabular}{ c c c c c c c c c c c c c c c c c c c$		PeRI	VLBW	VLBW	106.1	9.93	p < 0.001;
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			Control	Kontroll	113.5	11.5	$\eta^2 = 0.164$
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							ELBW < Control
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							<i>p</i> < 0.001
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							VLBW < Control
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							p = 0.024
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			ELBW	99.3	12.94	71-120	F(2, 101) = 5.9;
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		WMI	VLBW	105.9	11.36	77-129	p = 0.004;
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			Control	110	13.6	80-134	$\eta^2 = 0.105$
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							ELBW < Control
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							p = 0.003
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			ELBW	97.3	14.13	65-126	F(2, 101) = 7.12;
$ \left \begin{array}{c c c c c c c c c c c c c c c c c c c $		PrSI	VLBW	107.1	14.42	74-133	p = 0.001;
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			Control	109.2	11.9	89-137	$\eta^2 = 0.124$
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							ELBW < Control
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							p = 0.002
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							ELBW < VLBW
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							p = 0.009
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		Correct trials	ELBW	5.4	1.76	2-8	$\chi^2(2, N=105) = 9.48;$
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Corsi	(number)	VLBW	6.2	1.7	3-11	p = 0.009
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	Block	forward	Control	6.8	1.99	2-11	ELBW < Control
Task Correct trials (number) ELBW VLBW 5.8 1.99 6.8 2-10 1.99 χ^2 (2, N=105) = 18.05; p < 0.001 backward Control 8 1.73 5-12 <i>ELBW</i> < Control	Tapping						U = 306; Z = -2.96;
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	Task				1.00	2.10	p = 0.003; r = 0.37
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		Correct trials	ELBW	5.8	1.99	2-10	χ^2 (2, N=105) = 18.05;
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		(number)	VLBW	6.8	1.69	1-10	p < 0.001
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		backward	Control	8	1./3	5-12	ELBW < Control
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							U = 220.5; Z = -4.11;
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							p < 0.001, 1 = 0.51
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							VLBW < Collifor U = 430.5; 7 = 2.50;
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $							n = 0.01; $r = 0.30$
Stroop task error VLBW 1.0 1.69 0.8 $p = 0.049$ Kask Control 0.6 1.09 0.4 ELBW < Control		С	FLBW	2.1	4 31	0-24	$y^2 (2 \text{ N}=105) = 6.048$
Instruct Instruct	Stroop	error	VLBW	1.0	1 69	0-8	n = 0.049
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	task	CITO	Control	0.6	1.09	0-4	FLBW < Control
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	usk		Control	0.0	1.09		U = 356; Z = -2.476;
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							p = 0.013; $r = 0.307$
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		CW	ELBW	8.7	9.76	0-38	χ^2 (2, N=105) = 10.765;
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		error	VLBW	4.0	4.18	0-18	p = 0.005
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			Control	2.9	4.48	0-22	Control < ELBW
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							p = 0.609
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							ELBW < Control
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$							U = 295; Z = -3.094;
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$							p = 0.002; r = 0.384
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		С	ELBW	139.7	36.74	90.2-273.7	χ^2 (2, N=105) = 9.61;
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		time (sec)	VLBW	122.7	19.38	86.1-168.2	p = 0.008
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			Control	115.7	20.78	79.6-162.2	Control < ELBW
CW time (sec)ELBW VLBW Control 227.7 $193.656.5840.04143.4-420117.9-357.5p = 0.003; r = 0.374p = 0.021Control Interference(error)ELBWVLBWControl46.95193.6117.9-357.540.04p = 0.021130.5-285.8Interference(error)ELBWVLBWControl4.53.11.774.412.69-1-12-2.5-8.8p = 0.027Control Interference(error)ELBWVLBWControl3.11.773.192.69-2.5-8.8-2.5-8.8Control < ELBWU = 286; Z = -2.422;$							U = 298; Z = -3.018;
$\begin{array}{ c c c c c c c c c c c c c c c c c c c$		CTT I		207.7		140.4.400	p = 0.003; r = 0.374
time (sec)VLBW Control204.3 193.646.95 40.04117.9-357.5 130.5-285.8 $p = 0.021$ Control < ELBW $U = 322; Z = -2.703;$ $p = 0.007; r = 0.335$ Interference (error)ELBW VLBW Control4.5 3.1 1.774.41 3.19 2.69-1-12 -1-14.5 -2.5-8.8 χ^2 (2, N=99) = 7.222; p = 0.027 Control < ELBW U = 286; Z = -2.422;		CW	ELBW	227.7	56.58	143.4-420	$\chi^2(2,N=105) = 7.709;$
Interference (error) ELBW 4.5 4.41 -1-12 $\chi 2$ (2, N=99) = 7.222; p = 0.027 VLBW 3.1 3.19 -1-14.5 p = 0.027 Control 1.77 2.69 -2.5-8.8 Control < ELBW		time (sec)	VLBW Control	204.3	46.95	11/.9-35/.5	p = 0.021
Interference (error) ELBW 4.5 4.41 -1-12 $\chi 2 (2, N=99) = 7.222;$ VLBW 3.1 3.19 -1-14.5 $p = 0.027$ Control 1.77 2.69 -2.5-8.8 Control < ELBW			Control	193.0	40.04	130.3-285.8	Control < ELBW
Interference (error)ELBW VLBW4.5 3.1 1.774.41 3.19 2.69-1-12 -1-14.5 -2.5-8.8 $\chi 2 (2, N=99) = 7.222;$ $p = 0.027$ 							U = 522; L = -2.703; p = 0.007; r = 0.225
InterferenceDLD w4.54.41 $-1-12$ $\chi 2 (2, 1N-99) = 7.222;$ (error)VLBW 3.1 3.19 $-1-14.5$ $p = 0.027$ Control 1.77 2.69 $-2.5-8.8$ Control < ELBW		Interformen	EI DW/	15	<u> </u>	1 10	p = 0.007, 1 = 0.000
Control 1.77 2.69 $-2.5-8.8$ $Control < ELBW$ $U = 286; Z = -2.422;$		(error)	VI RW	4.5	3 10	-1-12 _1_14 5	$h^2(2, 1) = 99) = 7.222;$ n = 0.027
U = 286; Z = -2.422;		(01101)	Control	1 77	2.69	-2 5-8 8	P = 0.027 Control < FLRW
			Control	1.,,,	2.07	2.0 0.0	U = 286; Z = -2.422:

						p = 0.015;
Tower of	Time (sec)	ELBW	1107.4	311.74	502.8-1812.5	χ^2 (2, N=105) = 10.447;
Hanoi		VLBW	961.7	359.14	570.7-2170	p = 0.005
		Control	876.2	254.88	522-1513	Control < ELBW
						U = 297; Z = -3.031;
						p = 0.002; r = 0.376
						VLBW < ELBW
						U = 419; Z = -2.504;
						p = 0.012; r = 0.353

Note: Stroop Task: W: the patricipants are reguired to read names of colors; C: to name different color patches; CW: stroop effect

In searching for the background of the performances and the explanation of the massive within-group scatters of scores General Linear Models were computed. The significant results are shown on the following tables.

		Independent variables			Partial eta
	Measure		F(df)	р	
	FsIQ	Maternal education	31.738(1)	< 0.001	0.237
WISC-IV	VCI	Maternal education	37.482(1)	< 0.001	0.27
	PeRI	Maternal education	20.911(1)	< 0.001	0.17
	WMI	Maternal education	8.366(1)	0.005	0.076
	PrSI	Maternal education	9.384(1)	0.003	0.084
	Correct items	Maternal education	7.177(1)	0.009	0.066
Corsi	(number) forward				
Block	Correct items	Maternal education	11.54(1)	0.001	0.102
Tapping	(number)				
Task	backward				
	Completed	Gender	4.231(1)	0.042	0.04
WCST	categories				
	(number)				
	Number of	Gender	4.479(1)	0.037	0.042
	perseverational				
	errors				
Stroop	W	Gender	4.105(1)	0.046	0.042
task	error				
	CW error	Maternal education	4.456(1)	0.037	0.044
	W	Maternal education	4.4(1)	0.039	0.044
	time (sec)				
	Interference	Maternal education	4.072(1)	0.046	0.041
	error				
Tower of	number of	Gender	8.058(1)	0.005	0.073
Hanoi	"extra"steps				
	percent of trials in	Gender	4.876(1)	0.029	0.046
	which the shortest				
	path was found				

Table 2. General Linear Models: Total sample

Table 3. General Linear Models: Preterm s

Independ		Independent variables			Partial eta
Measure			F(df)	р	
	FsIQ	Maternal education	17.049(1)	< 0.001	0.218
WISC-IV		Gender	4.602(1)	0.036	0.07

	VCI	Maternal education	21.571(1)	< 0.001	0.261
		Gender	5.821(1)	0.019	0.087
			~ /		
	PeRI	Maternal education	7.546(1)	0.008	0.11
	WMI	Maternal education	5.41(1)	0.023	0.081
	PrSI	Maternal education	5.994(1)	0.017	0.089
		Gender	4.094(1)	0.047	0.063
	Correct items	Maternal education	5.149(1)	0.027	0.078
Corsi	(number)				
Block	backward				
Tapping					
Task					
	Number of	BPD	8.442(1)	0.005	0.122
WCST	perseverational				
	errors				
Stroop	С	BPD	5.121(1)	0.028	0.084
task	error				
	CW error	Birth weight	4.052(1)	0.049	0.067
		SGA	5.722(1)	0.02	0.093
	W	Gestational Age	5.755(1)	0.02	0.093
	time (sec)	Maternal education	4.24	0.044	0.07
		Gender	9.735(1)	0.003	0.148
	С	SGA	10.779(1)	0.002	0.161
	time (sec)	Gender	18.935(1)	< 0.001	0.235
	CW	SGA	4.288(1)	0.043	0.071
	time (sec)	BPD	6.781(1)	0.012	0.108
		Gender	11.957(1)	0.001	0.176
	Interference	BPD	7.384(1)	0.009	0.117
	time (sec)	Gender	5.024(1)	0.029	0.082
	Interference	SGA	6.758(1)	0.012	0.108
	error				
Tower of	percent of trials in	Gender	8.867(1)	0.003	0.139
Hanoi	which the shortest				
	path was found				

The results of the cluster analysis are shown on the following table:

Table 3. Significant performances of the three clusters – total sample

	Dependent	Cluster 1	Cluster 2	Cluster 3	MANOVA post hoc
	variable	N = 15	N = 38	N = 52	Bonferroni
		mean	mean	mean	Kruskal-Wallis Test, Mann-
		SD	SD	SD	Whitney Test
		range	range	range	
WISC-IV	VCI	98.47	120.92	110.97	F(2. 102) = 38.85; p<0.001;
		8.21	8.40	8.87	$\eta^2 = 0.43$
		89-115	104-138	85-129.5	1 < 2
					p < 0.001
					1 < 3
					p < 0.001
					3 < 2
					p < 0.001
	PeRI	91.33	115.58	104.63	F(2. 102) = 36.28; p<0.001;
		11.41	8.71	9.78	$\eta^2 = 0.42$
		70-120	98-138	86-130	1 < 2
					p < 0.001
					1 < 3
					p < 0.001
					3 < 2

					<i>p</i> < 0.001
	WMI	90.87	115.45	102.27	F(2. 102) = 35.69; p<0.001;
		12.42	8.99	10.46	$\eta^2 = 0.41$
		71-106	94-134	77-125.2	1 < 2
					p < 0.001
					1 < 3
					p < 0.001
					n < 0.001
	PrSI	84.27	114.54	103.42	F(2, 102) = 44.73: p<0.001:
	1101	8.56	9.91	11.53	$n^2 = 0.47$
		65-97	91-137	86-133	1 < 2
					p < 0.001
					1 < 3
					p < 0.001
					3<2
Care: Dia ala		4.22	7.24	5.0	p < 0.001
Corsi Block	(number)	4.33	1.24	5.9	χ^2 (2. N=105) = 25.79;
Tapping Task	(number)	2-8	5-11	2-9	p < 0.001 1 < 2
	101 ward	2.0	5 11	2)	U = 51: $Z = -4.70$: p
					<0.001;
					$1 < 3^{'}$
					U = 196.5; Z = -2.96;
					p = 0.003;
					3 < 2
					U = 599.5; Z = -3.27; p =
	Compat trials	4.4	0	6 70	0.001
	(number)	2.03	0 1 74	1 39	χ^2 (2. N=103) = 31.20, n <0.001
	backward	1-8	3-12	3-10	1 < 2
					U = 51; Z = -4.69; p
					<0.001;
					l < 3
					U = 137; Z = -3.884;
					3 < 2
					U = 559.5; $Z = -3.58$; p
					<0.001;
WCST	Completed	3	6.55	4.71	χ^2 (2. N=105) = 26.28;
	categories	1.73	2.06	2.2	p <0.001
	(number)	0-6	2-9	1-9	1 < 2
					U = 58; Z = -4.52; p
					< 0.001;
					I < 3 I = 2215; Z = -257;
					p=0.011:
					3 < 2
					U = 537.5; Z = -3.71; p
					<0.001;
	Number of	31	17.87	23.02	χ^2 (2. N=105) = 16.86;
	perseverational	17.56	10.50	8.23	p < 0.001
	enors	0-00	10-30	/ -44	$U = 1185 \cdot 7 = -329$
					p=0.001:
					2 < 3
					U = 580.5; Z = -3.33;
					p=0.001
	Number of	20.36	11.66	17.36	χ2 (2. N=105) = 12.94;
		11.44	6.67	8.97	p=0.002

	non- perseverational errors	2-35	2-29	1-41	2 < I U = 145; Z = -2.503; p=0.012;
					2 < 3 U = 584; Z = -3.3; p =0.001;
Stroop Task	W error	1.47 1.73 0-5	0.5 1.16 0-5	0.17 0.51 0-3	$\chi 2 (2. N=105) = 15.83;$ p<0.001 2 < 1 U = 174.5; Z = -2.59; p=0.01; 3 < 1 U = 102 5; Z = -2.09;
	C	2 47	0.66	0.81	U = 192.3; Z = -3.98; p < 0.001; 22.(2, N = 105) = 12.51;
	error	2.33 0-8	1.02 0-4	1.23 0-4	p=0.002 $2 < I$ $U = 131; Z = -3.26; p=0.001$ $3 < I$ $U = 195.5; Z = -3.19;$ $p=0.001;$
	CW error	13.93 8.99 3-30	2.45 3.08 0-13	4.5 6.2 0-38	$\chi 2 (2. N=105) = 27.14;$ p<0.001 2 < 1 U = 35; Z = -5.01; p<0.001; 3 < 1 U = 113.5; Z = -4.18; p<0.001;
	C time (sec)	151.72 40.65 111.08-273.73	114 23.73 79.56-189.45	126.72 20.15 83.16-168.15	$\chi 2 (2. N=105) = 21.42;$ p<0.001 2 < 1 U = 81; Z = -4.03; p<0.001; 2 < 3 U = 575; Z = -3.37; p =0.001;
	CW time (sec)	246.26 67.16 168.41-420	181.81 33.19 117.95-298.67	216.23 44.45 127.5-357.49	$\chi^2 (2. \text{ N=105}) = 22.62;$ p<0.001 2 < 1 U = 78; Z = -4.09; p<0.001; 2 < 3 U = 513; Z = -3.88; p <0.001;
	Interference time (sec)	115.86 52.67 26.14-243.43	79.97 23.34 31.71-148.95	104.03 36.06 50.44-227.04	$\chi 2 (2. N=105) = 15.78;$ p<0.001 2 < 1 U = 111; Z = -3.44; p=0.001; 2 < 3 U = 591; Z = -3.24; p =0.001;
	Interference error	7.27 3.70 1-11	1.87 2.6 -1.5-10	3.09 5.55 -2.5-14.5	$\begin{array}{c} \chi 2 \ (2. \ N=99) = 15.251; \\ p<0.001 \\ 2 < 1 \\ U = 46.5; \ Z = -3.918; \\ p<0.001; \\ 3 < 1 \\ U = 108; \ Z = -3.143; \\ p=0.002; \end{array}$

Tower of	Number of	122.07	102.24	179.02	χ^2 (2. N=105) = 30.17;
Hanoi	"extra"steps	75.05	45.32	67.08	p<0.001
	_	3-238	4-188	77-409	2 < 3
					U = 315; Z = -5.5;
					p <0.001;
	Percent of trials in	36.27	47.03	30.73	χ^2 (2. N=105) = 33.21;
	which the shortest	15.83	13.93	7.77	p<0.001
	path was found	11-75	25-85	13-47	1 < 2
	_				U = 156; Z = -2.55; p=0.011
					3 < 2
					U = 278; Z = -5.8;
					p <0.001;
	Time (sec)	1115.41	803.98	1068.02	χ^2 (2. N=105) = 19.76;
		355.39	223.07	335.46	p<0.001
		571.45-	502.81-	591.21-	2 < 1
		1812.48	1425.92	2167.97	U = 121; Z = -3.24;
					p=0.001;
					2 < 3
					U = 491; Z = -4.06; p
					< 0.001;

Logistic regression was computed to tap into the background factors explaining the cluster memberships. The results are shown in the table 4.

Compared clusters	Omnibus teszt	Odds ratio	Significant	Effect
			predictor variable	
1-2	$\chi^2(2) = 20.369;$	47.1-63.1%	Gestational age	W(1) = 5.97
	p < 0.001			p = 0.015
				Exp(B) = 2.074
1-3	$\chi^2(2) = 19.698;$	30.5-44.8%	Gestational age	W(1) = 9.975
	p < 0.001			p = 0.002
			Maternal	Exp(B) = 1.857
			education	W(1) = 5.854
				p = 0.016
				Exp(B) = 2.946

 Table 4. Logistic regression – preterm sample

The latent variables behind the performances were revealed using a principal component analysis. Three factors were detected. The correlations between the three new variables (factors) and the measured of the IQ test varied across birthweight groups, which was the most salient in factor 2 (planning).

Discussion

Our results are in line with published previous research which found that at group levels even moderate risk preterm children performed lower than their full-term counterparts in measures of intelligence (Arhan et al., 2017; O'Meagher et al., 2017), but within the average range (Kalmár, 2007; Nagy, Beke, Cserjési, Gráf, & Kalmár, 2018; Ribiczey & Kalmár, 2009).

The literature predicted an increased disadvantage of the preterms born with birthweigths < 1000 grams, however, it was not confirmed by our data. In the publications usually only the IQs are compared. In our study was complemented by the comparisons of the IQ test indices which pointed to the domain most sensitive to the heightened risks, the processing speed.

In the executive functions the disadvantage of the preterms is not that clear-cut. Both preterm groups performed significantly lower than the control group in the updating/working memory (Corsi Block Tapping Task, the number of correct trials – backward). In the inhibition only the ELBW group lagged behind the control, mainly in the response inhibition (the error measures of the Stroop task). In cognitive flexibility the groups did not differ. The short-term memory was weaker only in the ELBW preterms as compared to the control, and there was no difference between the two preterm groups. The group differences may be explained by the uneven rates of the development in each of the EF core components. The development of the cognitive flexibility lasts longer than that of the others; it becomes distinct only as late as after 11 years of age (Best & Miller, 2010; Lee et al., 2013). Underlying the lack of difference between the groups in this component may be the age-based immaturity of cognitive flexibility – which therefore affected all three groups alike.

Some authors claim that the core components of the EF are related with each other (Miyake et al., 2000; Miyake & Friedman, 2012). Our data, however, failed to support it, with the exception of the ELBW preterms between the updating/working memory and the cognitive flexibility.

The results of the preterms (mainly those of the ELBW group) supported the distinction of the EF core components (Duan et al., 2010; Miyake et al., 2000; Stålnacke et al., 2019).

The General Linear Model which tested contribution of the background variables to the performances in the total sample showed the exclusive effect of maternal education in the measures of the IQ test: higher maternal education was related to higher scores. As far as the EFs are concerned maternal education explained the memory performances (Corsi Block Tapping Task, the number of correct trials – forward and backward) and the inhibition (measures of the Stroop task), while gender had an effect on cognitive flexibility (measures of the WCST) and on inhibition (measures of the Hanoi Tower).

The General Linear Model for the preterm children included gender and maternal education, and, in addition, perinatal variables like gestational age, birth weight, BPD, and intra-uterine retardation (SGA) as independent variables. The intelligence in the preterms was explained by both maternal education and gender. Underlying the gender effect (the boys scored lower than the girls) multiple causality can be guessed (O'Driscoll, McGovern, Greene, &

Molloy, 2018). The boys are biologically more vulnerable, and less efficient in correcting the early insults to the CNS (Reis, de Mello, Morsch, Meio, & da Silva, 2012). The preterm children of more educated mothers, just like in the total sample, were likely to score higher. Maternal education is certainly not a direct cause. It is a distant and static measure but easily available and at the same time related to a number of factors relevant to the development of the child (Kalmár, 2007). The more educated mothers are more likely to pay attention to the needs of their children which results in better health conditions in them, and to create learning-fostering conditions (van Houdt, van Wassenaer-Leemhuis, Oosterlaan, van Kaam, & Aarnoudse-Moens, 2019).

In the executive functions maternal education was less influential than the perinatal characteristics and complications (BPD and SGA) and the gender. It supports the results of the meta-analysis by Twilhaar et al. (2018) according to which BPD is a strong predictor of the cognitive outcome rather than gestational age, birth weight, mild IVH, or periventricular leucomalacy. The untoward effects of the BPD on the development of the CNS were corroborated by other authors too (Behrman & Butler, 2007; Sriram et al., 2018).

Our results suggest that in the preterm children the executive function is more sensitive to the biological risk than the elementary cognitive abilities assessed by the IQ test. The correlations between the measures of the IQ test and the measures of the tasks of executive function differ across the birthweight groups. In the full-term comparison group the only significant correlate of the IQ was the updating/working memory (Corsi Block Tapping Task, the number of correct trials – backward) which is in line with the findings of Friedman et al. (2006) on typically developing adults and Duan et al. (2010) on typically developing children. In the preterm groups there were several significant correlates of IQ: In the ELBW children the updating/working memory (Corsi Block Tapping Task, the number of correct trials – backward) and cognitive flexibility (WCST, perseverational errors); in the VLBW children the same, and, in addition, the response inhibition (Stroop task, interference errors). The correlations of the indices of the IQ test with the core components of the EF also differ across birthweight groups.

The distinct correlations between the components of IQ test and the components of executive function across groups underline the distinct developmental pathways in each of the groups. Diamond et al. (2013) reported a strong correlation between the processing speed and the updating/working memory and interpreted it as the crucial role of processing speed in the executive function. Lee et al. (2013) also emphasized the importance of processing speed, claiming that the development of response inhibition and working memory was mediated by the development of processing speed. In our study the link between the processing speed and

the updating/working memory is supported only in the case of the VLBW preterms. In the ELBW preterms the measures of the IQ test (IQ, working memory, processing speed) were related to the cognitive flexibility, hence corroborating the claim by Rose et al. (2011) that there is a direct link between the birth status and the cognitive flexibility. In this study the effect of processing speed was significant for all three core components of executive function, but preterm birth had an independent impact on the cognitive flexibility. The authors failed to explain it, but assumed that perseveration might be independent of processing speed.

The results of the cluster analysis suggested that the impacts of the assets and disadvantages stemming from the maternal education and in the preterms also from the perinatal state (and from further factors which were not available for us) were not specific but rather general in the various components of intelligence as well as the executive function.

To reveal the latent variables underlying the performance measures a principal component analysis was computed. The correlations between the three new variables (factors) and the measured of the IQ test varied across birthweight groups, which was the most salient in factor 2 (planning). This is a further manifestation of the distinct developmental pathways in the preterm children.

The main results of our study fit well in the picture drawn by the literature of the development of the preterm children in that prematurity is a risk influencing the development well into school-age. Our preterms as groups had deficits as compared to their full-term, non-risk counterparts. Among the preterms those born with extremely low birthweights are more disadvantaged than those born with very low birthweights. The birth weight, however, is not a variable with real explanatory power. As it was revealed by more refined analyses the sources of the development hampering effects are more often other perinatal factors – immaturity or complications which are associated with the extremely low birthweight. Nevertheless we would argue for the use of the categorization of preterms based on birth weight, primarily in the practical field. Birth weight is a measure easily available, and at group level the lower the birth weight the higher the developmental risk.

The marked scatter behind the group means is important because it shows that preterm children, even those born with extremely low birth weights, may have chances for developmental outcomes comparable to the well achieving on risk, full-term children. Clearly the outcome depend on various further risk and protective factors. Our results suggest that some of the powerful protective factors are associated with maternal education.

The conclusion of our study is that the long-term follow-up of the preterm children is essential.

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¹ADATLAP

a doktori értekezés nyilvánosságra hozatalához

I.A doktori értekezés adatai A szerző neve: Nagy Anett MTMT-azonosító: 10032866

 II. A doktori értekezés címe és alcíme: A koraszülöttek végrehajtó működésének vizsgálata 9-10 éves korban, a születési súly és a perinatális szövődmények tükrében.

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A doktori iskola neve: ELTE PPK Pszichológiai Doktori Iskola

A doktori iskolán belüli doktori program neve: Fejlődés – és Klinikai Gyermekpszichológia program

A témavezető neve és tudományos fokozata: Dr. Kalmár Magda professor emeritus

A témavezető munkahelye: ELTE PPK Fejlődés – és Klinikai Gyermekpszichológia Tanszék

II. Nyilatkozatok

1. A doktori értekezés szerzőjeként³

a) hozzájárulok, hogy a doktori fokozat megszerzését követően a doktori értekezésem és a tézisek nyilvánosságra kerüljenek az ELTE Digitális Intézményi Tudástárban. Felhatalmazom a Pszichológiai .Doktori Iskola hivatalának ügyintézőjét Kulcsár Dánielt, hogy az értekezést és a téziseket feltöltse az ELTE Digitális Intézményi Tudástárba, és ennek során kitöltse a feltöltéshez szükséges nyilatkozatokat.
b) kérem, hogy a mellékelt kérelemben részletezett szabadalmi, illetőleg oltalmi bejelentés közzétételéig a doktori értekezést ne bocsássák nyilvánosságra az Egyetemi Könyvtárban és az ELTE Digitális Intézményi Tudástárban;⁴

c) kérem, hogy a nemzetbiztonsági okból minősített adatot tartalmazó doktori értekezést a minősítés (dátum)-ig tartó időtartama alatt ne bocsássák nyilvánosságra az Egyetemi Könyvtárban és az ELTE Digitális Intézményi Tudástárban;⁵

d) kérem, hogy a mű kiadására vonatkozó mellékelt kiadó szerződésre tekintettel a doktori értekezést a könyv megjelenéséig ne bocsássák nyilvánosságra az Egyetemi Könyvtárban, és az ELTE Digitális Intézményi Tudástárban csak a könyv bibliográfiai adatait tegyék közzé. Ha a könyv a fokozatszerzést követőn egy évig nem jelenik meg, hozzájárulok, hogy a doktori értekezésem és a tézisek nyilvánosságra kerüljenek az Egyetemi Könyvtárban és az ELTE Digitális Intézményi Tudástárban.⁶

2. A doktori értekezés szerzőjeként kijelentem, hogy

a) az ELTE Digitális Intézményi Tudástárba feltöltendő doktori értekezés és a tézisek saját eredeti, önálló szellemi munkám és legjobb tudomásom szerint nem sértem vele senki szerzői jogait;

b) a doktori értekezés és a tézisek nyomtatott változatai és az elektronikus adathordozón benyújtott tartalmak (szöveg és ábrák) mindenben megegyeznek.

3. A doktori értekezés szerzőjeként hozzájárulok a doktori értekezés és a tézisek szövegének plágiumkereső adatbázisba helyezéséhez és plágiumellenőrző vizsgálatok lefuttatásához.

Kelt: Budapest, 2019. július 8.

a doktori értekezés szerzőjének aláírása

¹ Beiktatta az Egyetemi Doktori Szabályzat módosításáról szóló CXXXIX/2014. (VI. 30.) Szen. sz. határozat. Hatályos: 2014. VII.1. napjától.
² A kari hivatal ügyintézője tölti ki.

³ A megfelelő szöveg aláhúzandó.

⁴ A doktori értekezés benyújtásával egyidejűleg be kell adni a tudományági doktori tanácshoz a szabadalmi, illetőleg oltalmi bejelentést tanúsító okiratot és a nyilvánosságra hozatal elhalasztása iránti kérelmet.

⁵ A doktori értekezés benyújtásával egyidejűleg be kell nyújtani a minősített adatra vonatkozó közokiratot.

⁶ A doktori értekezés benyújtásával egyidejűleg be kell nyújtani a mű kiadásáról szóló kiadói szerződést.