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Pre-school cognitive development of very low birth weight preterm children

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Abstract

Objective: To examine the cognitive development of school-aged children born preterm and with very low birthweight.

Methods: A cohort of premature infants born between January, 1991, and September, 1993 was examined at pre-school age. All fo them were born in a public Neonatal Intensive Care Unit, with birth weight less than 1,500g. The WPPSI-R Test was used for cognitive evaluation and applied by psychologists. Babies with malformations, genetic syndromes, congenital infections, transferred from other institutions or born at home, and those with conditions which precluded the application of the test, were excluded. A group of pre-school children in the same city, born at term, were tested for comparison.

Results: 79 children were studied, with mean birthweight 1,219.6 g (±168.9); of these, 44 (72.1%) attended school. No significant statistical difference was found between the groups (study and loss). The WPPSI-R Test mean scores were: 75.6±11.9 (total); 77±12.9 (performance) and 78.6±11.1 (verbal) for the study group, and 85.1±13.2 (total); 85.3±13.8 (performance) and 87.7±13.9 (verbal) for the comparison group. This difference was significant for total ($p < 0.0001$), verbal ($p < 0.0001$) and performance scores ($p = 0.002$), as well as for the subtests of the WPPSI-R Test.

Conclusions: Children who entered this study showed to have a borderline intellectual functioning at the moment of the evaluation. Results indicate they may face learning difficulties at school, thus requiring adequate stimuli that should be provided by the family and the school.

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Introduction

The higher survival rate in the neonatal period as a result of improved neonatal intensive care may influence the neuropsychomotor development of low-birthweight infants. Only the prevalence of severe sequelae, such as cerebral palsy, severe visual and hearing impairment, is not enough to assess the quality of survival in this age group. Studies have shown various disorders in motor, cognitive and behavioral areas, which may compromise the social life of these children.[1,2]

Preterm birth may pose risks to learning through cognitive and behavioral disorders, especially due to perception, attention and hyperactivity disorders.[3-6] Bhutta et al. demonstrated that preterm infants have lower cognitive scores than full-term controls, which are correlated with

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birthweight and gestational age.[2] According to Silbertin et al.,[7] cognitive disorders in general are observed at a later stage and are grouped into developmental disabilities and disorganization disorders that affect mainly cognitive functions, such as memory and/or language, and that may be associated with psychomotor instability.

The aim of the present study was to assess cognitive development in the preschool period of very-low-birthweight infants, born in a public hospital in Rio de Janeiro, and to determine the cognitive development areas that were mostly affected. Part of the results has been previously published.[8-11]

Methods

This research is part of a cohort study conducted to investigate prognostic factors for abnormal cognitive development in very-low-birthweight preterm infants, born between January 1991 and September 1993.[8] Preterm infants with birthweight less than or equal to 1,500 g, discharged from the neonatal intensive care unit (NICU) of a public hospital of the city of Rio de Janeiro, were assessed between November 1996 and March 1998. Infants with congenital malformations, genetic syndromes, congenital infection, transferred from another hospital after the seventh day of life or who were born at home were excluded from the study. Exclusion criteria also included the presence of disorders that hindered the application of the chosen test: significant emotional disorder, autism, deafness, severe mental retardation, spastic quadriplegia and blindness. The study protocol was approved by the local Research and Ethics Committee.

Newborn infants were classified according to their birthweight and gestational age, assessed by the Capurro method, used at the NICU at the time these infants were born, as appropriate for gestational age (AGA), small for gestational age (SGA) and large for gestational age (LGA), based on the intrauterine growth curve developed by Battaglia & Lubchenco.[9]

To assess cognitive development, we used the Wechsler Preschool and Primary Scale of Intelligence – Revised (WPPSI-R).[10] This test was applied by four psychologists who were blinded to the patients' medical chart information. While the test was being applied to the infants, their mothers were interviewed by another psychologist in a different room, after the infant allowed his/her mother to leave the room.

The WPPSI-R is a psychometric test that assesses intellectual functioning by measuring individual skills through different tasks, applied to children aged between three years and 11 months and seven years and three months. The child's performance is scored based on two subtest groups, the verbal scale and the performance scale. The verbal scale measures verbal memory and the ability to retain immediate and long-term verbal information, verbal comprehension, conceptual skills, ability to establish a relationship between numeric concepts and arithmetic operations, associative and rational thinking, ability to summarize. The performance scale measures perceptual skills, analysis and synthesis, organization, visual motor coordination, spatial orientation and prediction, graphic visual-motor organization and planning. In the verbal scale, the assessed functions are influenced by the family's cultural environment, school education received and by the child's capacity to concentrate and pay attention. In the performance scale, the tested functions are influenced by the child's attention, concentration, motor functioning, vision, and perceptual skills. Scores between 85 and 115 are considered normal and values between 8 and 12 are considered as appropriate for different subtests. Concomitantly, a group of children in the same age group was assessed in a slum in the same city. This school was chosen for its similarity between the place of residence of families in both groups, which presupposes equivalent socioeconomic and cultural level of the two populations. After consent from the school, mothers were contacted and they answered a questionnaire about their children's birth status. Only those children whose mothers informed they were born at full term and had not been admitted to an NICU were included in the study. Written consent was obtained from parents or primary caregivers.

The interrater reliability between the psychologists who applied the test revealed the following intraclass correlation coefficients (ICC): 0.82 (95%CI 0.56 – 1.00) for the total score, 0.89 (95%CI 0.71 – 1.00) for the verbal score and 0.91 (95%CI 0.24 – 1.00) for the performance score.[11]

The means and proportion of demographic, social and family characteristics and of the hospitalization diagnoses of this population were calculated. When losses were analyzed, the frequencies of prognostic factors and population characteristics were compared. The chi-square test and two-tailed Fisher's exact test were used in situations in which the values of cells were lower than 5, and Student's *t* test was used for equality of the means of two independent samples for continuous variables. Epi-Info, version 6.0, and SPSS, version 6.1, were used for the statistical analysis.

Results

Between January 1991 and September 1993, 277 newborns weighing 1,500 g or less were admitted to the NICU of the referred hospital; among whom 94 died in the neonatal period and four died after hospital discharge, 13 were transferred to another hospital and 37 were excluded (25 in the neonatal period and 12 at preschool age). A total of 129 children were included in the study, 79 of whom were assessed at preschool age (61.3%). The study and excluded groups are similar. Of the 21 perinatal factors tested, there was statistical significance ($p < 0.05$) only for higher frequency of pneumonia in the excluded group, and for maternal hypertension in the study group. Eleven continuous variables were compared, and neither of them was statistically significant, except for the Apgar score at five minutes ($p < 0.05$). Tables 1 and 2 show the clinical complications and characteristics of the patients, as well as

the results of the comparison between the study and excluded groups.

Table 3 shows the characteristics of the study population. Predominance of females and SGA infants was observed. The mean birthweight was 1,219.6 g (±168.9) with gestational age between 28 weeks and 36 weeks and three days. Mean maternal age at delivery was 27.4 years (±6.9), ranging from 11 to 42 years; 17.6% of the mothers (n = 13) were 20 years old or younger and 18.9% (n = 14) were 35 years old or older. None of the interviewed mothers was illiterate; most of them (56.1%) had not completed high school, and a large percentage of them (37.9%) had completed high school.

Most mothers (54.5%) did not have a job. There was predominance of married mothers (63.2%); 30.9% were separated and 5.9% were widowed. Income ranged from one to seven minimum wages (approximately US$ 87 to US$ 605) in 57.4% of the families; 38.2% had an income greater than eight minimum wages (around US$ 693) and only 4.4% of the families earned less than one minimum wage.

In the study group, 11 children presented mild neurological disorders: behavioral disorder (three), neuromotor dysfunction (four), diplegia (two), hemiplegia (three). No children presented with hearing impairment, one child had visual impairment and five had convergent strabismus. Thirty children received motor stimuli in the first years of life. Children were assessed at the average age of 55.4 months (±6.5), range of 48 to 71 months.

Information about school education was obtained for 61 children at the time of examination, 53 out of 61 children (86.8%) were attending school. In this group, 10 children had attended a day care center before entering school and eight were not in school yet. The mean age of entry to day care center was 28 months (SD 13.5, range of 6 to 48 months), with a higher frequency at 24 months. As for entry to school, mean age was 43.3 months (SD 8.1, range of 24 to 60 months), with a higher frequency at 48 months. At the time of evaluation, eight of 61 children were not attending school, 46 were in preschool, six were learning how to write and only one was attending the first grade.

Table 1 - Results of the comparison between the excluded and study groups regarding sex, birth place, pregnancy, type of delivery and prognostic factors present in the perinatal period

Variable	n of exclusions	n of children studied	χ^2 Yates	p
Type of pregnancy	Single 40/51 Twin 11/51	Single 64/78 Twin 14/78	0.08	0.778
Frequency of AGA/SGA	AGA 24/51 SGA 27/51	AGA 34/77 SGA 43/77	0.02	0.887
Sex	Male 20/51 Female 31/51	Male 27/78 Female 51/78	0.12	0.731
Type of delivery	Cesarean 29/51 Vaginal 22/51	Cesarean 52/78 Vaginal 26/78	0.88	0.347
Birth at Instituto Fernandes Figueira	44/51	71/78	0.31	0.576
Maternal hypertension	17/51	42/78	4.43	0.035
Fetal suffering	13/49	31/77	1.92	0.166
Resuscitation at the delivrey room	5/50	11/78	0.17	0.681
Asphyxia	8/50	19/78	0.83	0.363
Cerebral hemorrhage	5/50	9/78	0.00	0.985
Neonatal seizure*	2/51	4/78		1.000
Sepsis	23/51	31/78	0.18	0.674
Apnea	27/51	37/78	0.19	0.666
Hyaline membrane	21/51	27/78	0.32	0.570
Pneumonia	18/51	14/78	4.09	0.043
Arterial channel persistence	11/51	12/78	0.44	0.508
Cardiorespiratory arrest*	1/51	5/78		0.401
Bronchopulmonary dysplasia	5/51	8/78	0.05	0.829
CPAP	18/51	31/78	0.10	0.746
Mechanical ventilation	19/51	25/78	0.18	0.674
Abnormal transfontanellar ultrasound	4/50	15/78	2.22	0.136

* Fischer's exact test. AGA = adequate for gestational age; SGA = small for gestational age; CPAP = continuous positive airway pressure.

Table 2 - Results of the comparison between the mean birth weight, gestational age, length of hospital stay, weight loss during hospital stay and time for the recovery of birth weight, duration of mechanical ventilation and 1st and 5th min Apgar in the excluded and studied groups

Variable	n of excluded/ studied infants	Mean (SD) excluded infants	Mean (SD) studied infants	T	p
Gestational age (days)	51/77	225.7 (13.5)	224.3 (11.4)	0.639	0.524
Birth weight (g)	51/78	1,243.9 (183.4)	1,219.6 (168.9)	0.772	0.441
Length of hospital stay (days)	51/78	48.6 (19.8)	45.7 (17.3)	0.877	0.382
Minimum weight (g)	50/77	1,090.2 (174.4)	1,067.2 (171.8)	0.732	0.465
Age of minimum weight	50/77	7.2 (3.4)	6.9 (2.9)	0.540	0.590
Percentage of birth weight loss	50/77	12.7 (5.5)	12.8 (5.2)	-0.177	0.860
Recovery of birth weight (days)	51/77	20 (7.3)	18.6 (6.6)	1.217	0.226
Weight at hospital discharge (g)	51/78	1,956.7 (275.6)	1,942.7 (267.8)	0.286	0.775
Ventilation (hours)	19/25	140.6 (120.1)	172.9 (38.3)	-0.749	0.458
1st min Apgar	50/76	6.1 (2.3)	5.7 (2.4)	0.982	0.328
5th min Apgar	49/78	8.4 (1.1)	7.9 (1.5)	1.945	0.054

t test for comparison of mean of both independent samples. SD = standard deviation.

As for the comparison group, since children were selected at school at preschool age, we do not have accurate information on neonatal characteristics, such as weight and neonatal age. However, we only selected children who were born at full term and who had stayed in a rooming-in facility. Schoolchildren were assessed at the time of the test application and considered able to take the test if they did not suffer from major disorders (encephalopathy, severe hearing or visual impairment). At the time of evaluation, the children's mean age was 62.7 months (±10.5), range of 48 to 81 months, and 22 (53.7%) were male and 19 (46.3%) female.

Table 3 - Characteristics of the study population regarding the neonatal factors

Characteristics	n (%)
Birth at our service	72 (91.1)
Single pregnancy	65 (82.3)
Twin pregnancy	14 (17.7)
Cesarean delivery	53 (67.1)
Vaginal delivery	26 (32.9)
Male	28 (35.4)
Female	51 (64.6)
AGA	35 (44.3)
SGA	43 (54.4)
	Mean±SD
Birth weight	1,219.6±168.9
Gestational age (days)	224.3±11.4
1st min Apgar	5.7±2.4
5th min Apgar	7.9±1.5
Length of hospital stay (days)	45.7±17.3
Percentage of birth weight loss (%)	12.8±5.2
Recovery of birth weight (days)	18.6±6.6
Minimum weight	1,067.2±171.8
Age of minimum weight during hospital stay (days)	6.9±2.9
Weight at hospital discharge	1,942.2±267.8
Time of mechanical ventilation in hours	172.9±38.3

Total number of children studied = 79. AGA = adequate for gestational age;
SGA = small for gestational age.

The mean total score of the WPPSI-R was 75.6±11.9. The mean performance score was 77±12.9 and that of the verbal score was 78.6±11.1. The results obtained from schoolchildren were 85.1±13.2 for the total score, 85.3±13.8 for the performance score, and 87.7±13.9 for the verbal score. There was a significant difference between the means (Table 4).

By comparing the mean results of the subtests of both groups, the major differences were related to subtests Mazes and Vocabulary, followed by Comprehension, Arithmetic, Puzzle, Information, Picture Completion and Geometric Design. Subtests Block Design and Similarities did not show any significant differences (Table 5).

Discussion

In this population, the mean intelligence quotient (total score of the WPPSI-R test) was below normal due to the high incidence of children with involvement of specific cognitive areas. These results are worse than those reported in the literature, which show lower mean IQ values in the group of very-low-birthweight preterm infants, but within normal limits.[2,12-15] In our group, the mean results ranged from 65 to 89 points in the different scores proposed by the test (total, verbal and performance). This means that these children's intellectual functioning was close to being deficient, at the time of evaluation. Bhutta et al., in a meta-analysis, reported a difference of 10.2 points in the mean score, between the control and preterm groups, which is significantly correlated to gestational age and birthweight.[2] In our study, very-low-birthweight preterm infants had lower scores, which are consistent with the literature.

Specific cognitive disorders have been described in very-low-birthweight infants, such as those that affect visual motor coordination and memory,[16] spatial and visual perceptual skill,[17] visual motor and perceptual motor coordination[18] and visual motor and visual perceptual coordination.[19] In the study group, the mean performance score was slightly lower than the verbal score. As for the subtests, only the mean obtained by the study group in subtest Picture Completion was as expected for this age group, albeit significantly different from that of schoolchildren. In the other subtests, the results were at least two points below expected. The compromised areas corresponded to the following functions: planning, visual motor functioning, conceptual formation, verbal and numeric skills, rational and associative thinking, capacity to summarize, perceptual organization, spatial orientation, remote memory. These results are in accordance with those reported in recent studies on preterm infants, where involvement of visual motor coordination, memory, arithmetic, associative processes, graphic and language capacity (both comprehensive and expressive) has been observed.[21,22]

The tests assess the aspects related to systematic learning influenced by family and social environments. In the study population, approximately one third of the children were not attending school, without receiving proper systematic and pedagogical stimuli, which might contribute to unfavorable results in comparison to those described in the literature.[2,4,13-15] The fact that the children were attending different grades in school, due to their ages, does not affect the test results, since the test is age-matched. The individual observation of the best results showed children with access to different schools, who belong to a socially and culturally privileged group in the population seen in our service. On the other hand, those children whose family had a low income belonged to the low birthweight group.

Wolke & Meyer showed that preterm infants had multiple cognitive deficits, involving especially simultaneous processing function and problems with processing complex

Table 4 - Mean total scores, performance and verbal scores of studied and control children and the difference between the means with the results of the *t* test for the difference between the means

Scores	Mean±SD	Difference between the means	*t* test	p	95% CI
Total					
Preterm (n = 75)	75.61±11.91	-9.48	-3.938	0.000	-14.26 to -4.71
School (n = 41)	85.10±13.25				
Performance					
Preterm (n = 75)	77.04±12.88	-8.25	-3.213	0.002	-13.34 to -3.17
School (n = 41)	85.29±13.83				
Verbal					
Preterm (n = 75)	78.59±11.10	-9.17	-3.882	0.000	-13.85 to -4.49
School (n = 41)	87.76±13.92				

Table 5 - Means of the results of each subtest of preterm and school children and the differences between the means with the results of *t* test for the differences of the means

Subtest	Mean±SD	Difference between the means	*t* test	p	95% CI
Blocks					
Preterm (n = 75)	6.75±2.53	-0.67	-1.271	0.206	-1.71 to 0.37
School (n = 41)	7.41±3.01				
Geometric design					
Preterm (n = 74)	6.23±2.73	-1.01	-2.068	0.041 *	-1.99 to -0.0043
School (n = 41)	7.24±2.07				
Picture completion					
Preterm (n = 73)	8.34±3.15	-1.48	-2.280	0.024 *	-2.77 to -0.19
School (n = 41)	9.82±3.57				
Maze					
Preterm (n = 73)	5.33±3.09	-2.41	-4.188	0.000 †	-3.56 to -1.27
School (n = 39)	7.74±2.53				
Puzzle					
Preterm (n = 73)	5.22±3.22	-1.73	-2.686	0.008 *	-3.01 to -0.45
School (n = 41)	6.95±3.45				
Arithmetic					
Preterm (n = 75)	6.11±2.72	-1.48	-2.793	0.006 *	-2.53 to -0.43
School (n = 41)	7.59±2.74				
Comprehension					
Preterm (n = 75)	6.47±2.58	-1.80	-3.345	0.001 †	-2.87 to -0.73
School (n = 41)	8.27±3.1				
Information					
Preterm (n = 75)	6.04±2.23	-1.25	-2.560	0.012 *	-2.22 to -0.28
School (n = 41)	7.29±2.98				
Similarities					
Preterm (n = 75)	6.85±2.42	-0.57	-1.163	0.247	-1.53 to 0.40
School (n = 38)	7.42±2.51				
Vocabulary					
Preterm (n = 74)	6.85±2.75	-2.95	-5.20	0.000 †	-4.08 to -1.83
School (n = 41)	9.8±3.2				

Items of the performance score: Blocks, Geometric design, Picture completion, Maze and Puzzle. Items of the verbal score: Arithmetic, Comprehension, Information, Similarities, and Vocabulary.
* $p < 0.05$ † $p < 0.005$

information that demand logical thinking and spatial orientation skills.[21] Abnormalities persisted even when social class differences were controlled, with preterm infants showing the worst results in all classes. Ment et al. found an increase in cognitive scores between the ages of 36 and 96 months for the assessed preterm infants, except for those who had cerebral hemorrhage in the neonatal period and severe CNS injury, whose scores decreased.[23] The factors associated with the best results at 96 months of life were maternal level of education and the fact that the children belonged to well-structured families, with father and mother living in the same household. The study conducted by Ment et al. highlights the importance of continuing cognitive stimulation in children who are discharged from NICUs, especially preterm infants. Our results suggest that, although the sample is reasonably homogenous from a clinical viewpoint, individual results varied, probably due to the clinical histories of each child, his/her capacities to respond to injuries and also the environmental and family's capacity to facilitate his/her development, which is in agreement with Ment et al.

Gregory[24] recalls that there are biological tools as far as intelligence is concerned. The processes used to take good advantage and to make use of these tools produces intelligent behavior - cognition. These processes or skills depend on the individual's biological, social and emotional

history, which may favor or hinder the proper utilization of these resources, and consequently, favor or hinder a healthier cognitive development. Preterm infants have skills that are characteristic of their developmental stage, but their exposure to neonatal intensive care and to early interaction, requires the participation of yet absent competencies, overloading their overall developmental process. Thus, health professionals in charge of caring for these infants after their hospital discharge should be attentive to detect problems and intervene whenever necessary, and the assessment of intellectual functioning is an important component of this follow-up.

According to Silbertin et al.,[7] the problems often arise at the entry to nursery school, and worsen during graphic tasks and while learning to read and to make calculations, which may produce coercive attitudes towards learning by the family, which in some cases may become permanent. In other words, these disorders, when not properly detected, may cause poor school achievement even in those children with a good intellectual performance. Understanding this is important so that these children and their families can receive adequate support.

Sample size was one of the limitations of our study. However, the major problem was the high loss rate. No statistically significant differences were noted between the two groups. Losses therefore occurred at random, not contributing to the selection bias, despite the high percentage observed. It should be underscored that children with severe disorders were not tested and were excluded from the study, not interfering with the mean scores. Moreover, in order to minimize the possibility of classification bias, interrater reliability was analyzed, showing excellent concordance between the psychologists.

As for the comparison group, children in the same age group were evaluated, despite the difference in gender distribution within the group. These children attended a school in the slums, but their families had a socioeconomic level that was similar to that of children in the study group. Since no entrance exams were required by this school, it was not possible to have a systematic biased selection of children with better intellectual potential.

Studies with cohort of preterm infants show some peculiarities in this population. However, these peculiarities should be carefully analyzed in order to avoid "labeling" these patients; thus preterm birth should not be understood as the only risk for these babies, at the cognitive and relational level. Several factors contribute to the future performance of these children, which requires the observation of their skills through a dynamic approach, where different situations may interfere in specific stages of their development, compromising future learning.

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