0021-7557/11/87-04/281
Jornal de Pediatria

Developmental outcomes and quality of life in children born preterm at preschool- and school-age

Martina Estevam Brom Vieira,[1] Maria Beatriz Martins Linhares[2]

Abstract

Objective: To review literature published in the last 5 years on the effects of premature birth on the development and quality of life of preschool- and school-age children.

Sources: Systematic review of empirical studies published in the last 5 years and indexed on PubMed, MEDLINE, LILACS, SciELO and PsycINFO. Keywords were chosen that relate prematurity to developmental and quality of life outcomes.

Summary of the findings: In the studies chosen, four global indicators of development were identified (neurological, neurodevelopment, executive functions and quality of life), in addition to seven specific indicators of development (cognition, motor function, behavior, language, academic performance, attention and memory). The most prevalent indicators were cognition and motor function. Premature children had worse performance in all developmental indicators than children born full term. Additionally, the younger the gestational age, the worse the performance in developmental indicator assessments. The studies identified both risk factors (lower birth weight, intraventricular hemorrhage and low maternal educational level) and protective factors (larger head circumference, breastfeeding and higher family income) for development of children born preterm.

Conclusion: Children born extremely premature (≤ 30 weeks' gestational age) are vulnerable to developmental and quality of life problems.

J Pediatr (Rio J). 2011;87(4):281-291: Child development, quality of life, premature.

Introduction

A child's gestational age and weight at birth are important indicators of biological risk of developmental problems.[1-3] Infants born preterm (at gestational ages less than 37 weeks) and with low birth weight (LBW, weight below 2,500 g) are a high-risk group in view of the increased likelihood of them suffering morbidity and mortality.[4-6]

Prematurity can be classified as follows: borderline preterm (BPT, 35 to 36 weeks' gestational age), moderate preterm (MPT, 31 to 34 weeks' gestational age) and extreme preterm (EPT, gestational age ≤ 30 weeks).[7] Newborn infants with LBW can be further classified as very LBW (VLBW, less than 1,500 g) or extreme LBW (ELBW, less than 1,000 g).[7]

Children born prematurely are biologically immature and, consequently, there is a greater probability that they will suffer health and development problems, when compared with children born at full term (FT).[1,8,9] This difference can already be observed when the development of preschool

1. Professora especialista, Curso de Fisioterapia, Universidade Estadual de Goiás (UEG), Goiânia, GO, Brazil. Mestranda, Departamento de Neurociências e Ciências do Comportamento, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo (USP), Ribeirão Preto, SP, Brazil.
2. Professora associada livre-docente, Departamento de Neurociências e Ciências do Comportamento, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo (USP), Ribeirão Preto, SP, Brazil.

No conflicts of interest declared concerning the publication of this article.

Financial support: Conselho Nacional de Pesquisa e Desenvolvimento Científico (CNPq), Brazil.

Suggested citation: Vieira ME, Linhares MB. Developmental outcomes and quality of life in children born preterm at preschool- and school-age. J Pediatr (Rio J). 2011;87(4):281-91.

Manuscript submitted Feb 03 2011, accepted for publication Mar 14 2011.

doi:10.2223/JPED.2096

children born full term and preterm is compared.[10] Preterms' biological vulnerability may be compounded by psychosocial environmental risk factors.[11-13] In such cases, the child is exposed to multiple risks, with a negative impact on development.

Development is a continuous process of changes through which functional performance in many different developmental indicators improves.[14,15] These improvements include acquisition and development of abilities in a range of areas (cognition, language, motor function, behavior and others).[14] One important indicator of development is quality of life, which is a combination of objective and subjective aspects of wellbeing, happiness and satisfaction.[16]

In view of the relevance of monitoring the developmental progress of these more vulnerable children, the objective of the present study was to review indexed literature published in the last 5 years on the effects of premature birth on the development and quality of life of children at preschool and school ages. The questions that guide this review article are as follows:

- What developmental indicators are assessed in samples of children born preterm when they are in the age range of 3 to 12 years?
- How are developmental indicators and quality of life measures assessed?
- What are the major findings of assessments of developmental indicators and quality of life measures reported in the literature?

Methods

A systematic review was undertaken of literature indexed in the databases PubMed, MEDLINE, LILACS, SciELO and PsycINFO using the following combination of keywords: *Infant, Premature OR Premature Birth AND Child Development OR Developmental Disabilities OR Outcome Assessment (Healthcare) OR Developmental Outcomes OR Neurodevelopmental Outcomes OR Quality of Life*. These keywords were chosen after searching for terms on Mesh (PubMed), Decs (MEDLINE, LILACS and SciELO), Index Terms (PsycINFO) and by testing different searches.

The criteria for including articles in the review were as follows: empirical studies that assessed the developmental and quality-of-life outcomes of premature subjects aged 3 to 5 years (preschool) and 6 to 12 years (school age), according to the age classification proposed by Papalia & Olds[17]; studies published in the last 5 years (January 2005 to June 2010) in English, Portuguese or Spanish.

The initial searches identified 587 articles in the databases using the keywords above. Thirty-four repeated references for articles that were indexed in more than one database were excluded. The abstracts of the remaining 553 articles were then read. After analysis of the abstracts, a further 515 articles that did not meet the inclusion criteria were excluded. This review therefore covers 38 articles.

Results and discussion

Characteristics of the studies reviewed

Thirty-five of the 38 articles were published in English[18-52] and three were published in Portuguese.[53-55] Twenty-one studies investigated preterm children at preschool age,[18-21,26-29,31-33,36,41,42,44-46,48,51,55] and 17 articles described school-age children.[23-25,30,34,35,37-40,43,47,49,50,52-54]

Twenty-eight articles had prospective longitudinal designs,[19-27,31,33-43,46-52] with samples recruited in the neonatal period. Six articles were about cross-sectional studies,[28-30,45,53,54] and four had retrospective longitudinal study designs.[18,32,44,55] With regard to the types of analysis applied to the developmental indicators, it was found that 32 studies[18-21,23-31,33-38,40,41,43-45,47-49,51-55] compared subsets differentiated by gestational age, birth weight, biological risk classification, sex or developmental assessment scores. Predictive analyses were conducted in 19 studies[20,22-25,27,32,33,35,38,39,41,42,45-48,50,53] with the objective of determining variables that predict developmental risk or protection.

For the purposes of this review, the developmental indicators investigated by the studies were classified as global or specific. Global indicators are assessments of more than one developmental area in conjunction, providing a wider-ranging overview of the child's development. Specific indicators, in turn, are assessments of a single developmental area.

It will be observed from Table 1 that the most prevalent indicator in the whole 38-study sample was cognition,[18-22,27,30,33-39,43,46,47,49,51-53] followed by motor development[19,20,22-24,25-28,31-33,35,37,39,40,42,45,54] and then neurosensory development.[20,23,24,27,28,31,32,46,47,51,52,55] Motor development was the most prevalent developmental indicator among the studies of preschool children,[19,20,22,25-28,31-33,42,45] whereas for schoolchildren the equivalent was cognition.[30,34,35,37-39,43,47,49,52,53]

Table 2 lists the many different instruments and measures employed, totaling 59 different instruments and measures for assessing children's development.

It is notable that the Wechsler Preschool and Primary Intelligence Scale for assessing cognition was used in more than 30% of the studies,[20,21,27,30,34,35,37,39,49,51,52,55] and standard neurological examination, which is clinical assessment, was used in around 20% of the studies.[23,24,31,32,35,46,47,51,55]

Global developmental indicators

Sensorineural or neurological development

Sensorineural or neurological development was assessed in 13 articles and consisted either of a neurological

Table 1 - Prevalence of developmental indicators assessed in the studies reviewed

	Age group					
	Preschool (n = 21)		School age (n = 17)		Total (n = 38)	
Developmental indicators	f	%	f	%	f	%
Global indicators						
Sensorineural/neurological	9	43	4	23	13	34
Neurodevelopment	6	28	0	0	6	16
Executive functions	2	9	1	6	3	8
Quality of life	2	9	1	6	3	8
Specific indicators						
Cognition	10	48	11	65	21	55
Motor function	11	52	7	41	18	47
Behavior/emotional	7	33	4	23	11	29
Language	8	38	2	12	10	26
Learning/ academic performance	4	19	4	23	8	21
Attention	3	14	3	18	6	16
Memory	3	14	1	6	4	10

f = frequency.

examination in the form of clinical observation by specialist professionals[23,24,31,32,36,46,47,51,55] or by administering a standardized instrument.[20,28,32,33] The neurological development indicator was the result of assessing the status of mental function, motor function, sensitivity, coordination, walking and balance.[20,21,24,28,31,32,33,36,46,47,51]

Nine studies analyzed neurological development during the preschool phase.[20,27,28,31,32,36,46,51,55] Moderate or severe neurological dysfunction was defined as compromised motor function in upper and lower limbs, inability to walk independently, significant functional compromise and auditory and/or visual deficiency.[28,33] Among EPT children of preschool age, this type of dysfunction was observed in 17 to 23% of samples[31,36]; whereas in a sample of MPT children, the frequency of moderate or severe neurological dysfunction was just 12%.[36]

From 11 to 25% of EPT children of preschool age had a diagnosis of cerebral palsy in five studies.[20,31,32,36,51] The frequency of cerebral palsy in MPT samples was 6 to 15%.[36,51] Considering gestational age and birth weight in combination, it was observed that just 8% of children born premature and small for gestational age (SGA) had cerebral palsy, whereas, in the same study, 20% of preterm children with birth weight appropriate for their gestational age (AGA) had cerebral palsy.[27] This difference can be explained by the distinct biological characteristics of the two groups, since the AGA group had lower mean gestational age and contained a larger proportion of children with abnormal transfontanellar ultrasound findings.

The majority of risk factors for neurological dysfunction at preschool age in EPT and VLBW children were related to the neonatal period (from birth to 28 days' postnatal age) and were as follows: prolonged duration of mechanical ventilation,[46] intraventricular hemorrhage grades III and IV,[32,46] retinopathy,[46] low Apgar score[32] and perinatal convulsions.[32] Additionally, low maternal educational level was an important psychosocial risk factor for neurological dysfunction.[46] In contrast, greater gestational age[36] and gain in body weight and increase in head circumference between birth and hospital discharge[46] were identified as protective factors for the neurological development of EPT and VLBW children.

Only four studies assessed neurological development in school-age children.[23,24,47,52] Moderate or severe neurological dysfunction was identified in around 20% of EPT[47,52] and 16% of MPT children.[24] Risk factors for EPT children having neurological dysfunctions at school age were as follows: prolonged duration of mechanical ventilation in the neonatal period, intraventricular hemorrhage grades III and IV, periventricular leukomalacia and maternal age close to 40 years at the time of birth.[47]

Studies that assessed subsets differentiated by gestational age identified greater compromise to neurological development among children born preterm, both at preschool age and at school age. When compared with either the MPT group or the FT group, the EPT children had more neurological dysfunctions, cerebral palsy and visual deficiencies.[23,28,36,51]

Table 2 - Instruments and measures used to assess development in the studies reviewed

Developmental indicators	Instruments and measures
Global indicators	
Sensorineural/Neurological	Modified Partial Touwen Test[20,32,33]
	Health Status Classification System Preschool Version[28]
	Standardized Neurological/Sensory Examination[23,24,31,32,35,46,47,51,55]
Neurodevelopment	Gesell Developmental Diagnosis[21]
	Denver II Test[18,55]
	Bayley Scales of Infant Development[18,31]
Executive functions	Developmental Neuropsychological Assessment[20,27,48]
	Cambridge Neuropsychological Test Assessment Battery[30]
Quality of life	Infant and Toddler Quality of Life Questionnaire[28]
	Quality of Life Questionnaire (17D)[45]
	Revised Children Quality of Life - Questionnaire[47]
Specific indicators	
Cognition	Stanford-Binet Intelligence Scale[19,22]
	Wechsler Preschool and Primary Intelligence Scale[20,21,27,30,34,35,37,39,49,51,52,55]
	Revised Amsterdam Children's Intelligence Test[29]
	Kaufman Assessment Battery for Children[32,36,38,43,48,47]
	Raven's Colored Progressive Matrices – Special Scale[53]
Motor	Visual-Motor Integration Test[19,37]
	Block Construction[19]
	Visual-Perceptual Task[19]
	Pediatric Extended Examination at Three[22]
	Developmental Scale, Motor-Perceptual Development[25]
	Developmental Neuropsychological Assessment[29]
	Movement Assessment Battery for Children[23,29,39,52,54]
	Bayley Scales of Infant Development - Psychomotor Development Index[31]
	Gross Motor Function Classification Scale[45,47]
	Zurich Neuromotor Assessment[24]
	Visuo-Manual Pointing Task[36,40]
Behavioral/emotional	Child Behavior Checklist[22,23,28,29,32,48,50]
	Strengths and Difficulties Questionnaire (Parent Form)[33,47,51]
	Conflict Subscale (9-item) from the Family Environment Scale[50]
	Goodenough Draw-a-Person Test[53]
	Rutter Child Behavior Scale[53]
	Conners' Parent Rating Scale Revised[55]
Language	Boston Naming Test[19]
	Word and Phrase Retrieval Test[19]
	Peabody Picture Vocabulary Test[19,37,41]
	Test of Grammar Comprehension[19]
	Developmental Neuropsychological Assessment[20,27]
	Pediatric Extended Examination at Three[22]
	Dutch Language Screening Test[29]
	Preschool Language Scale-3 (UK)[38]
	Age-Appropriate Modification of the ETS Test of Verbal Fluency[41]
	Preschool Version of the Clinical Evaluation of Language Fundamentals Test[51]
	Nicolosi Sequence of Language Development[18]
Learning/academic performance	Questionnaire About School Performance[29,33]
	Records in the Public School Student Database[44]
	Phonological Abilities Test[38]
	Academic Achievement Score[38]
	Wide Range Achievement Test[39,49]
	Wechsler Individual Achievement Test[43]
Attention	Attention Sustained Test[19]
	Developmental Neuropsychological Assessment[20,25,27]
	Attention Questionnaire[22]
	Parent's Version Conners' Rating Scale Revised-Long Form[25]
	Digit Span Forwards Test[25]
	Spatial Span Forwards Test[25]
	Trail Making Test-Test B[25]
	Test of Everyday Attention in Children[30]
Memory	Memory for Location[19]
	Developmental Neuropsychological Assessment[20,27]
	Cambridge Neuropsychological Test Assessment Battery[30]

Neurodevelopment

Six studies[18,21,29,31,44,55] assessed neurodevelopment, all at preschool age. Neurodevelopment assessment involved investigation of the following areas of development: personal and social behavior, cognition, language and fine and gross motor functions.[18]

The studies employed one of three different approaches to assessing neurodevelopment: using a single standardized instrument,[18,21,31,55] a combination of different instruments (each one accessing a different area)[29] and analysis of data from health service records.[44]

In a sample of 3-year-old children, it was observed that around 70% of EPT with gestational ages of less than 27 weeks had neurodevelopmental problems,[31] in contrast with just 3% of preterms with gestational ages greater than 33 weeks.[21] The extreme difference between these results may derive from the samples' different biological characteristics and the different assessment instruments used in each study. De Groote et al.[31] studied children who, in addition to younger gestational age, also had lower birth weight, and used the Bayley Scales of Infant Development for assessment, whereas Peng et al.[21] used the Gesell Developmental Diagnosis.

The importance of gestational age was also evident in studies that compared different groups, where BPT children proved to be at greater risk of neurodevelopmental delays and/or disorders when compared with FT children at 3 years of age.[44]

Birth weight was also relevant in studies that investigated neurodevelopment, since it was observed that preterm children with LBW scored lower on neurodevelopment tests at 3 years when compared with FT children born at normal weight.[21] There was not, however, any difference in neurodevelopment at age 3 when a group of children born premature and LBW were compared with a group born full term, but SGA.[21]

Neurodevelopment had significant associations with other developmental indicators, such as performance at school, since EPT children with educational problems at age 5 had more neurodevelopmental disorders than EPT children without educational problems.[29] The association between neurodevelopment and language in children born preterm indicated that those with abnormal language acquisition at 3 also had more neurodevelopmental problems at the same age.[18] Furthermore, behavioral problems at 12 and 24 months had a strong association with neurodevelopmental problems at 3 years of age.[55]

Executive functions

Neuropsychological assessments of the executive functions included the following domains: memory, self control, attention, language, sensory-motor and visuospatial development.[20,30,48] Just three studies assessed these functions, two studies of preschool children[20,48] and one study of school-age children.[30]

Feldman[48] followed premature babies up to 5 years of age, focusing on regulatory processes, and found that poor cardiac vagal tone during the neonatal period, greater disorganization of the sleep-wake cycle, also during the neonatal period, reduced emotional regulation at 12 months and reduced attention regulation at 2 years were risk factors for executive function disorders at 5 years.

Extreme prematurity was one biological factor that impacted on executive function assessments, since EPT children performed badly on these tests when compared with a sample of FT at 5[20] and 9 years of age.[30]

The importance of stratifying risk within a single gestational age category is illustrated by the observation that infants born preterm and classified as at high neonatal risk according to the Clinical Risk Index for Babies (CRIB) exhibited greater compromise of executive functions at 5 years than those classified as having low neonatal critical risk.[48] The CRIB provides a score that estimates the neonatal risk of morbidity and mortality, obtained by summing points scored for the presence of its component indicators.[48] It is administered during the first 12 hours of life and the higher the score the greater the biological risk.[48] The variables assessed are birth weight, gestational age, congenital malformations, elevated pH (in blood gas analysis) and minimum and maximum oxygenation.[48]

Quality of life

Quality of life was only covered by two of the preschool studies[28,45] and one of the studies of school-age children.[47] Although it involves subjective aspects, quality of life can be measured using scales specifically for this purpose, by administering instruments such as the Infant and Toddler Quality of Life Questionnaire,[28] the Quality of Life Questionnaire[45] and the Revised Children's Quality of Life Questionnaire.[47]

When groups of children born preterm were compared with groups of FT children, it was found that they had worse quality of life scores, both at preschool[28,45] and at school age.[47] Furthermore, when different subsets of premature children were compared with each other (EPT vs. MPT)[28]; SGA vs. AGA[45]) there was no difference between them; all of the premature children studied exhibited compromise to some aspects of quality of life.

Just one study investigated predicting the quality of life at five years of babies born preterm and VLBW on the basis of prenatal and neonatal factors. The presence of congenital malformations was the only risk factor identified in connection with lower quality of life scores.[45] On the other hand, older gestational age, higher birth weight and multiple pregnancies were shown to be protective factors for the future quality of life of these children.[45]

Specific developmental indicators

Cognition

Cognition is an important higher cortical function and was assessed in 21 of the studies. The measures used to verify the cognitive function of children were the intelligence quotient (IQ)[19-22,27,30,34,35,37,39,49,51-55] and the Mental Processing Composite (MPC),[33,36,38,43,46,47] which is basically an equivalent measure to IQ.

Ten studies analyzed the children's cognition at preschool age.[19-22,27,33,36,46,51,55] Cognitive function was classified as below normal if the IQ or NPC school was below 85 or less than -1 standard deviation (SD). The percentage of EPT children classified as having below normal cognition at preschool age varied from 33 to 36%[36,51] and from 29 to 36% for MPT children.[36,51] Mental deficiency was defined as an IQ or MPC score of less than 70 or less than -2 SD. According to these criteria, 9% of the EPT children with ELBW[20] and 10% of the EPT with VLBW[22] were diagnosed with mental deficiency at preschool age.

Five studies assessed predictive factors for cognition at preschool age of children born preterm.[20,22,27,33,46] These studies observed that the risk factors for cognitive compromise at five years in EPT children were related to the following prenatal and neonatal variables: male sex,[20] not taking steroids during the prenatal period,[20] multiple pregnancy,[20] vaginal delivery,[20] low birth weight,[46] prolonged duration of mechanical ventilation[46] and intraventricular hemorrhage grades III or IV.[20,46]

Of note was the fact that motor development delays or disorders at 5 years in MPT children proved to be a factor predicting risk of cognitive compromise at the same age.[33] Furthermore, neurodevelopmental delay during early infancy and an abnormal neurological test result at 5 years had an association with low IQ at the same age.[55]

On the other hand, greater gestational age,[36] heavier birth weight,[20] body weight gain between birth and hospital discharge,[46] increase in head circumference between hospital discharge and 5 years,[46] larger head circumference at 5 years[27] and greater family spending power[20] were all identified as factors of protection for the cognitive development of EPT children at preschool age. In addition to these factors, sleeping patterns during the neonatal period also had a protective effect on the cognitive function of preschool age preterms, since newborn infants who slept with more rapid eye movement (REM) and long pauses in breathing had higher IQ scores at 3 years.[22]

Cognition at school age was investigated in 11 studies.[30,34,35,37-39,43,47,49,52,53] Cognitive function was classified as below normal in around 40 to 68% of the samples of EPT children.[38,43,47,52] Risk factors for cognitive compromise in EPT children at school age were as follows: male sex,[38] intraventricular hemorrhage grades III or IV or periventricular leukomalacia during the neonatal period[47] and prolonged duration of mechanical ventilation while in hospital.[47] Larger head circumference at 2 and 8 years was a protective factor for cognitive function at 8 years.[39]

The majority of studies that compared subsets differentiated by gestational age observed similar results, both at preschool age and school age, since several samples of children born preterm had greater cognitive compromise than FT children.[19-21,30,34-38,43,49,51-53] However, one study that compared the cognitive development of subsets of the preterms who passed through a neonatal intensive care unit found that the subset of EPT children had a lower prevalence of below normal IQ scores at 4 years than the MPT subset.[51] The article does not, however, discuss these results and does not mention what statistical tests were used nor the level of significance adopted.

Motor development

Motor development was investigated in 18 articles.[19,20,22-24,26-28,31-33,35,37,39,40,42,46,54] Motor development assessments basically covered the following areas: gross motor function (stability and locomotion) and fine motor function (activities involving fine coordination and manipulation).[24] Motor development was the most prevalent indicator among the studies of preschool age children and was studied in 11 articles.[19,20,22,26-28,31-33,42,46] It was observed that the percentage of EPT children with motor development delays or disorders at preschool age varied from 29 to 42%,[20,31-33,42] whereas they were present in 39% of a sample of MPT children.[33]

Studies that analyzed predictive factors for the motor development of EPT children at preschool age identified prenatal and neonatal biological variables, developmental variables from early infancy and social variables. The biological variables identified as risk factors were as follows: male sex,[20,42] younger gestational age,[42] intraventricular hemorrhage grades III or IV,[42,46] prolonged duration of mechanical ventilation[46] and retinopathy of prematurity.[46]

Motor and mental development delays identified using the Bayley Scales of Infant Development at 2 years proved to be a developmental variable that predicted risk of motor compromise detected by the Movement ABC at 5 years.[41] Furthermore, a study by Franz et al.[46] showed that low maternal educational level is a social variable that predicts risk of motor development. In counterpoint, the only protective factors for motor development of EPT children were being born in a more complex hospital[17] and increase in head circumference between birth and hospital discharge.[46]

The prenatal and neonatal risk factors for motor development delays or disorders in MPT children at preschool age were as follows: acute fetal suffering,[33] abnormalities in central nervous system white matter,[33] intraventricular hemorrhage grades III or IV[33] and postnatal corticoid therapy.[33] Breastfeeding,[33] multiple pregnancy[33] and sleeping with more REM and long pauses in breathing during the neonatal period were identified as protective factors for the motor development of preschool age MPT children.[22]

Six studies[19,20,26-28,33] of preschool age children analyzed subsets of children differentiated by gestational age and all reported similar results, since motor development deficits were greater among those subsets with younger gestational age, i.e. among EPT children when compared with FT or MPT,[20,26-28,33] and among MPT children when compared with FT children.[19,26,28] However, when preterms were compared according to adequacy of birth weight for gestational age, it was found that there was no difference between SGA and AGA subsets in motor development assessed at 5 years.[20,27]

Seven studies assessed the motor development of school-age children[23,24,35,37,39,40,54] and 57% of MPT children with VLBW had motor development delays or disorders,[54] whereas in a sample of LBW preterms the figure was 35%.[23]

Prenatal and neonatal biological risk factors related to motor development delays or disorders in school-age preterms were multiple pregnancy,[24] respiratory problems[23] and higher grade of periventricular leukomalacia or intraventricular hemorrhage.[24]

Abnormal sensorineural development at 6 years,[24] inability to grasp an object successfully at 4 years,[23] low quality movement when trying to grasp an object at 6 months[23] and immobile postural behavior at 4 and 6 months[23] were risk factors for motor development delays or disorders in preterm children at 6 years of age. Indeed, just two variables that protect motor development were identified in the studies of school-age children: heavier body weight at discharge[39] and larger head circumference at 2 and 8 years of age.[39]

It should be pointed out that the motor assessments conducted at preschool age included both the gross motor function and fine motor function areas, whereas in school-age studies, fine motor development was assessed in the form of specific abilities, such as a test of hand-eye coordination when pointing.[35,37,40] Comparison of fine motor performance of different subsets differentiated by gestational age showed that premature children suffered greater compromise in this areas than subsets of FT children[35,37,40] and that an EPT subset had greater fine motor compromise than a sample of MPT children.[40]

Stratification of biological risk is also important when assessing motor development, since premature newborn infants considered at high biological risk (5-minute Apgar less than 3, respiratory problems or patent ductus arteriosus) suffered from a higher frequency of motor development problems at 6 years than children at low biological risk.[23]

Behavior and emotional control

Eleven articles assessed the behavior and emotional control of children born preterm.[22,23,28,32,33,47,48,50,51,53,55] This is an important indicator for development of the processes of socialization and self-control of behavior.[48]

The preschool-age behavior of children born preterm was investigated in seven studies.[22,28,32,33,48,51,55] Behavioral problems were either of the "internalizing" type, characterized by anxiety and withdrawal, or "externalizing," characterized by impulsivity and antisocial behaviors. These problems were observed in 22 to 37% of samples of preschool EPT children,[31,51] in 13% of preschool MPT children[51] and 60% of preschool-age preterm LBW.[55]

Studies that analyzed predictive factors for behavior of preschool-age children born preterm found that items tested at different stages of child development were linked with behavior at 5 years. Poor neonatal cardiac vagal tone,[48] reduced emotional regulation at 12 months,[48] reduced regulation of attention at 2 years[48] and motor development delay at 5 years[33] were risk factors for behavioral problems in 5-year-old children. In addition to these, psychosomatic behavior detected by Conners' Parent Rating Scales Revised at 5 years was also significantly associated with an abnormal neurological examination at the same age.[55]

Four studies dealt with behavior at school age.[23,47,50,53] Behavioral problems were detected in 28% of a sample of 8-year-old EPT children[47] and the risk factors for this negative outcome were reduced cognitive function (IQ less than 70) at 8 years and low maternal educational level.[47] Reduced cognitive function was also a risk factor for behavioral problems in a sample of 9-year-old MPT children with VLBW.[53]

Among LBW preterm children, a difficult temperament at 12 months[50] and a high level of family conflict at 7 years[50] were predictive variables for risk of behavioral problems at 8 years. It should be pointed out that, in a study conducted by Fallang et al.[23] into children born preterm and LBW, immobile postural behavior at 6 months was a risk factor for behavioral problems at 6 years and these children also suffered more internalizing behavioral problems (anxiety and depression) than a group of FT children. The authors therefore suggested that the origin of these behavioral problems could lie in unfitness and weakness of motor abilities, associated with dysfunctions in the children's monoaminergic systems.[23]

Other studies that made comparisons between subsets differentiated by gestational age found similar results, since the groups with younger gestational age were at a disadvantage having more behavioral problems than the control group, both at preschool age and school age.[23,47,53] The only exception is a study by Schiariti et al.[28] in which no difference was observed between EPT children and MPT or between MPT and FT children in terms of behavior assessed with the Child Behavior Checklist at 3 years of age. Notwithstanding, the authors stated that further studies were needed in order to elucidate this question of the prevalence of behavioral problems in samples of premature children who have spent time in intensive care units. A study by Woodward et al.[51] compared EPT and MPT children from a neonatal intensive care unit using the Strengths and Difficulties Questionnaire and found that the EPT group had more behavioral problems than the MPT group at 4 years of age.

Language

The specific developmental indicator language was investigated in 10 articles, eight in preschool children[18-20,22,27,28,41,51] and just two in school-age children.[37,38] Delays or disorders in language development in preschool EPT children varied from 32 to 48%[28,51]; and 30 to 35% of MPT had language problems[28,51]; although more than 50% of one sample of children born preterm LBW were affected.[18] Language problems may affect expression, related to speech, or reception, related to understanding.[18,41,51]

In a study by Rose et al.,[41] it was observed that good performance in language, memory, attention, central processing velocity and representational competence at 12 months are related to adequate language development at 3 years for children born preterm and VLBW and are therefore protective factors. Similarly, larger head circumference at 5 years[27] and sleep with more REM and long pauses in breathing during the neonatal period[22] were identified as protective factors for the language development of preschool-age premature and LBW children. It should be pointed out that the only risk factor identified in these studies was male sex,[38] which is a predictive variable for risk of language delay in school-age EPT children.

The majority of studies that have compared subsets differentiated by gestational age found that samples of children born preterm (EPT or MPT) had worse performance on language assessment tests than FT children, both in studies of preschool[19,20,27,28,51] and school-age children[38]. However, when compared with an FT group at 3 years, the VLBW preterms were only worse with receptive language skills and there was no difference between the subsets in terms of expressive language abilities.[41] No difference was detected between EPT and FT language assessments at 12 years in a study by Constable et al.[37]

Learning or academic performance

Eight studies assessed the learning or academic performance of children born preterm.[29,32,33,38,39,43,44,49] This specific indicator was assessed in three ways: using a standardized instrument,[39,49] using instruments created by the study authors[29,33] or using data from school databases.[44]

Four studies assessed the academic performance of preschool children.[29,32,33,44] Kleine et al.[32] reported that around 9% of their sample of 339 EPT and VLBW children needed special needs education by 5 years of age. The percentage of preschool children with learning delays or difficulties was 37% of EPT and VLBW children.[29] It is of note that among MPT children, motor problems at 5 years are a risk factor for problems with academic performance at the same age.[33]

Comparison of public education system data on preschool age BPT and FT children showed that the premature group had increased risk of suspension and retention in kindergarten and increased probability of being referred for special needs education at 5 years.[39]

Learning and academic performance were investigated in greater detail in four studies of school-age children.[38,39,43,49] Difficulties at school were reported by the teachers of 50% of 6-year-old EPT children[38] and 13% of EPT children attended schools offering special needs education by 11 years of age.[43] Furthermore, more than half the EPT sample had problems with reading, and 70% had significant problems with mathematics at 11 years.[43]

A study by Kan et al.[39] identified certain factors protective of academic performance of EPT children at 8 years of age in three basic abilities: reading, spelling and mathematics. It was found that heavier birth weight, heavier body weight at 2 years and larger head circumference at 2 and 8 years were protective factors for reading ability. Protective factors for spelling were heavier body weight at 2 years and larger head circumference at 2 and 8 years. Only larger head circumference at 2 years was a protective factor for performance in mathematics.

Studies that compared academic performance between groups of school-age EPT or BPT children and FT children found that children born preterm had more general problems at school[38] than FT children and more specific problems with reading,[38,43,49] spelling[49] and mathematics.[43,49]

Attention

Attention was investigated in three studies undertaken with preschool children[19,20,27] and three with school-age children.[23,25,30] Attention is one of the executive functions and is defined as the construct by which the minds focuses on and selects stimuli, establishing relationships between them.[25] Therefore, this indicator is analyzed on the basis of a neuropsychological assessment.[20,25,27]

The attention of school-age children born preterm was related to their motor development in early infancy. Greater velocity of movement when grasping an object (fine motor ability) at 4 months was a risk factor for attention problems in premature LBW children at 6 years.[23] Similarly, motor delays or disorders at 2 years were a predictive factor for risk of attention problems in EPT ELBW children at 8 years.[25]

Studies of preschool[19,20] and school-age children[30] that have compared attention in children born preterm (EPT or MPT) with attention in FT children found that they suffered greater compromise than the FT children. However, Schiariti et al.[28] compared EPT with MPT and did not detect a difference between them since both subsets' attention was equally compromised.

Studies that compared subsets differentiated by appropriateness of weight to gestational age between preterm SGA and AGA also failed to detect a difference in attention assessments at 5 years of age.[20,27]

Memory

Memory is another developmental indicator that is one of the executive functions. It is the intellect's capacity to retain, retrieve, store and evoke information. This indicator was investigated by three studies at preschool age[22,23,27] and one at school age.[30]

All of the studies that assessed memory only performed analyses of comparison between groups. Those that compared groups categorized by gestational age found that FT children performed better in memory tests than children born preterm, irrespective of level of prematurity (EPT or MPT).[19,20,27,30]

However, studies that compared groups divided by appropriateness of weight to gestational age reported contrasting results, since, in one of them children born preterm classified as SGA had more memory problems at 5 years (lower scores on the Developmental Neuropsychological Assessment) than children born preterm and AGA[27]; whereas this difference was not observed in the other study,[20] and yet both administered the same instrument to children of the same age, i.e. 5 years. These conflicting findings may be related to the characteristics of the samples, since in the study that did detect a difference between groups,[27] the SGA children had more neonatal complications, such as intraventricular hemorrhage and respiratory problems, than the AGA group.

Conclusions

With regard to the developmental indicators assessed in samples of preterm children at ages from 3 to 12 years, studies were identified assessing both global and specific indicators of development. The most prevalent global development indicator across all studies was neurological assessment, and the most prevalent specific indicator was cognition. Considering the two age ranges, preschool and school age, it was observed that motor development was the most often assessed among preschool children, while for school-age children the most prevalent indicator was cognition. Cognitive function assessment gained a prominent place in this review, both because of the prevalence of its use and because of the associations with other developmental indicators. The relevance of assessing cognitive function is based on its characteristics, including different higher cortical functions and processes. It was apparent that future studies should invest in assessing executive functions, quality of life, and processes of attention and memory in children born preterm at both preschool and school age, since these factors have been little studied up to the time of writing.

With regard to the procedures used for assessment of developmental and quality of life indicators, it was found that a wide variety of instruments and measures were used. Systematic assessments with standardized instruments, assessments with instruments developed by the authors themselves, non-systematic observational measures and analyses of records in health system databases. All quality of life assessments and some behavior and academic performance assessments were based on parent and/or teacher reports, even though school-age children are already capable of responding to questionnaires that assess quality of life. The large number of available instruments emphasizes the care researchers must take when choosing the correct instrument or measure to suit the objective, research question, age of sample and area of development to be investigated; bearing in mind that this review should help in making this choice.

With regard to the principal results of developmental and quality of life assessments found in the literature, it was observed that studies that made comparisons between groups of children born preterm and groups of children born full term found evidence that the preterms performed worse in all of the developmental indicators investigated. This review supports the tendency for researchers to stratify their analyses of prematurity into BPT, MPT and EPT. In analyses that did use prematurity levels, children classified as extremely premature were the most vulnerable in all comparisons, with the exception of quality of life, behavior and language, in which all the different subsets of preterms were similarly compromised.

The main biological risk factors for developmental problems from 3 to 12 years of age in children born preterm were as follows: prolonged duration of mechanical ventilation during the neonatal period, intraventricular hemorrhage or periventricular leukomalacia, male sex and lower birth weight. The main psychosocial risk factors were low maternal educational level and high level of family conflict. In compensation, the main protective factors for the development of children born preterm were as follows: older gestational age, higher birth weight, larger head circumference, better quality of sleep during the neonatal period, breastfeeding and higher family income.

With regard to the implications for clinical practice, this review article underscores the importance of health professionals making the investment to undertake longitudinal follow-up of the different areas of a preterm child's development, particularly for those born at 30 weeks' gestational age or less. This monitoring should include investigation of potential risk factors for developmental problems with the objective of facilitating identification of the most vulnerable children and initiating preventative action including stimulating and activating those factors that protect development.

Acknowledgements

The authors are grateful to the Conselho Nacional de Pesquisa e Desenvolvimento Científico (CNPq) for financial support: CNPq grant 131100/2010-6 and CNPq grant 302893/2007-5 awarded to the authors.

References

1. Bühler KE, Flabiano FC, Mendes AE, Limongi SC. Construção da permanência do objeto em crianças nascidas pré-termo muito baixo peso. Revista CEFAC. 2007;9:300-7.
2. Santos DC, Campos D, Gonçalves VM, Mello BB, Campos TM, Gagliardo HG. Influência do baixo peso ao nascer sobre o desempenho motor de lactentes a termo no primeiro semestre de vida. Rev Bras Fisioter. 2004;8:261-6.
3. Da Silva ES, Nunes ML. The influence of gestational age and birth weight in the clinical assesment of the muscle tone of healthy term and preterm newborns. Arq Neuropsiquiatr. 2005;63:956-62.
4. Fundo das Nações Unidas para a Infância. Situação mundial da infância 2008: sobrevivência infantil. Brasília: UNICEF; 2008.
5. Silveira MF, Santos I, Barros AJ, Matijasevich A, Barros FC, Victora CG. Increase in preterm births in Brazil: review of population-based studies. Rev Saude Publica. 2008;42:957-64.
6. Rugolo LM. Crescimento e desenvolvimento a longo prazo do prematuro extremo. J Pediatr. 2005;81: S101-10.
7. Leone CR, Ramos JL, Vaz FA. O Recém Nascido Pré-termo. In: Marcondes E, Vaz FA, Ramos JL, Okay Y. Pediatria básica. Vol I. 9. ed. São Paulo: Savier; 2002. p. 348-52.
8. Mewes AU, Hüppi PS, Als H, Rybicki FJ, Inder TE, McAnulty GB, et al. Regional brain development in serial magnetic resonance imaging of low-risk preterm infants. Pediatrics. 2006;118:23-33.
9. Pereira MR, Funayama CA. Avaliação de alguns aspectos da aquisição e desenvolvimento da linguagem de crianças nascidas pré-termo. Arq Neuropsiquiatr. 2004;62:641-8.
10. Meio MD, Lopes CS, Morsch DS, Monteiro AP, Rocha SB, Borges RA, et al. Desenvolvimento cognitivo de crianças prematuras de muito baixo peso na idade pré-escolar. J Pediatr (Rio J). 2004;80:495-502.
11. Kiechl-Kohlendorfer U, Ralser E, Pupp Peglow U, Reiter G, Trawoger R. Adverse neurodevelopmental outcome in preterm infants: risk factor profiles for different gestational ages. Acta Paediatr. 2009;98:792-6.
12. Resegue R, Puccini RF, Silva EM. Fatores de risco associados a alterações no desenvolvimento da criança. Pediatria (Sao Paulo). 2007;29:117-28.
13. Spinillo A, Montanari L, Gardella B, Roccio M, Stronati M, Fazzi E. Infant sex, obstetric risk factors, and 2-year neurodevelopmental outcome among preterm infants. Dev Med Child Neurol. 2009;51:518-25.
14. Flehmig I. Texto e atlas do desenvolvimento normal e seus desvios no lactente. Rio de Janeiro: Atheneu; 2002.
15. Biscegli TS, Polis LB, Santos LM, Vicentin M. Avaliação do estado nutricional e do desenvolvimento neuropsicomotor em crianças freqüentadoras de creche. Rev Paul Pediatr. 2007;25:337-42.
16. Colver A. Quality of life and participation. Dev Med Child Neurol. 2009;51:656-9.
17. Papalia DE, Olds SW. Desenvolvimento humano. 7. ed. São Paulo: Artmed; 2000.
18. Schirmer CR, Portuguez MW, Nunes ML. Clinical assessment of language development in children at age 3 years that were born preterm. Arq Neuropsiquiatr. 2006;64:926-31.
19. Caravale B, Tozzi C, Albino G, Vicari S. Cognitive development in low risk preterm infants at 3-4 years of life. Arch Dis Child Fetal Neonatal Ed. 2005;90:F474-9.
20. Mikkola K, Ritari N, Tommiska V, Salokorpi T, Lehtonen L, Tammela O, et al. Neurodevelopmental outcome at 5 years of age of a national cohort of extremely low birth weight infants who were born in 1996-1997. Pediatrics. 2005;116:1391-400.
21. Peng Y, Huang B, Biro F, Feng L, Guo Z, Slap G. Outcome of low birthweight in China: a 16-year longitudinal study. Acta Paediatr. 2005;94:843-9.
22. Holditch-Davis D, Belyea M, Edwards LJ. Prediction of 3-year developmental outcomes from sleep development over the preterm period. Infant Behav Dev. 2005;28:118-31.
23. Fallang B, Oien I, Hellem E, Saugstad Od, Hadders-Algra M. Quality of reaching and postural control in young preterm infants is related to neuromotor outcome at 6 years. Pediatr Res. 2005;58:347-53.
24. Schmidhauser J, Caflisch J, Rousson V, Bucher HU, Largo RH, Latal B. Impaired motor performance and movement quality in very-low-birthweight children at 6 years of age. Dev Med Child Neurol. 2006;48:718-22.
25. Jeyaseelan D, O'Callaghan M, Neulinger K, Shum D, Burns Y. The association between early minor motor difficulties in extreme low birth weight infants and school age attentional difficulties. Early Hum Dev. 2006;82:249-55.
26. Hemgren E, Persson K. Associations of motor co-ordination and attention with motor-perceptual development in 3-year-old preterm and full-term children who needed neonatal intensive care. Child Care Health Dev. 2007;33:11-21.
27. Mikkola K, Kushnerenko E, Partanen E, Serenius-Sirve S, Leipälä J, Huotilainen M, et al. Auditory event-related potentials and cognitive function of preterm children at five years of age. Clin Neurophysiol. 2007;118:1494-502.
28. Schiariti V, Hoube JS, Lisonkova S, Klassen AF, Lee SK. Caregiver-reported health outcomes of preschool children born at 28 to 32 weeks' gestation. J Dev Behav Pediatr. 2007;28:9-15.
29. van Kessel-Feddema B, Sondaar M, de Kleine M, Verhaak C, van Baar A. Concordance between school outcomes and developmental follow-up results of very preterm and/or low birth weight children at the age of 5 years. Eur J Pediatr. 2007;166:693-9.
30. Bayless S, Stevenson J. Executive functions in school-age children born very prematurely. Early Hum Dev. 2007;83:247-54.
31. De Groote I, Vanhaesebrouck P, Bruneel E, Dom L, Durein I, Hasaerts D, et al. Outcome at 3 years of age in a population-based cohort of extremely preterm infants. Obstet Gynecol. 2007;110:855-64.
32. de Kleine MJ, den Ouden AL, Kollée LA, van Baar A, Nijhuis-van der Sanden MW, Ilsen A, et al. Outcome of perinatal care for very preterm infants at 5 years of age: a comparison between 1983 and 1993. Paediatr Perinat Epidemiol. 2007;21:26-33.
33. Arnaud C, Daubisse-Marliac L, White-Koning M, Pierrat V, Larroque B, Grandjean H, et al. Prevalence and associated factors of minor neuromotor dysfunctions at age 5 years in prematurely born children: the EPIPAGE Study. Arch Pediatr Adolesc Med. 2007;161:1053-61.

34. Mu SC, Tsou KS, Hsu CH, Fang LJ, Jeng SF, Chang CH, et al. Cognitive development at age 8 years in very low birth weight children in Taiwan. J Formos Med Assoc. 2008;107:915-20.

35. Van Braeckel K, Butcher PR, Geuze RH, van Duijn MA, Bos AF, Bouma A. Less efficient elementary visuomotor processes in 7- to 10-year-old preterm-born children without cerebral palsy: an indication of impaired dorsal stream processes. Neuropsychology. 2008;22:755-64.

36. Larroque B, Ancel PY, Marret S, Marchand L, André M, Arnaud C, et al. Neurodevelopmental disabilities and special care of 5-year-old children born before 33 weeks of gestation (the EPIPAGE study): a longitudinal cohort study. Lancet. 2008;371:813-20.

37. Constable RT, Ment LR, Vohr BR, Kesler SR, Fulbright RK, Lacadie C, et al. Prematurely born children demonstrate white matter microstructural differences at 12 years of age, relative to term control subjects: an investigation of group and gender effects. Pediatrics. 2008;121:306-16.

38. Wolke D, Samara M, Bracewell M, Marlow N; EPICure Study Group. Specific language difficulties and school achievement in children born at 25 weeks of gestation or less. J Pediatr. 2008;152:256-62.

39. Kan E, Roberts G, Anderson PJ, Doyle LW; Victorian Infant Collaborative Study Group. The association of growth impairment with neurodevelopmental outcome at eight years of age in very preterm children. Early Hum Dev. 2008;84:409-16.

40. Schneider C, Nadeau L, Bard C, Lambert J, Majnemer A, Malouin F, et al. Visuo-motor coordination in 8-year-old children born pre-term before and after 28 weeks of gestation. Dev Neurorehabil. 2008;11:215-24.

41. Rose SA, Feldman JF, Jankowski JJ. A cognitive approach to the development of early language. Child Dev. 2009;80:134-50.

42. Janssen AJ, Nijhuis-van der Sanden MW, Akkermans RP, Tissingh J, Oostendorp RA, Kollée LA. A model to predict motor performance in preterm infants at 5 years. Early Hum Dev. 2009;85:599-604.

43. Johnson S, Hennessy E, Smith R, Trikic R, Wolke D, Marlow N. Academic attainment and special educational needs in extremely preterm children at 11 years of age: the EPICure study. Arch Dis Child Fetal Neonatal Ed. 2009;94:F283-9.

44. Morse SB, Zheng H, Tang Y, Roth J. Early school-age outcomes of late preterm infants. Pediatrics. 2009;123:e622-9.

45. Rautava L, Häkkinen U, Korvenranta E, Andersson S, Gissler M, Hallman M, et al. Health-related quality of life in 5-year-old very low birth weight infants. J Pediatr. 2009;155:338-43.

46. Franz AR, Pohlandt F, Bode H, Mihatsch WA, Sander S, Kron M, et al. Intrauterine, early neonatal, and postdischarge growth and neurodevelopmental outcome at 5.4 years in extremely preterm infants after intensive neonatal nutritional support. Pediatrics. 2009;123:e101-9.

47. Stahlmann N, Rapp M, Herting E, Thyen U. Outcome of extremely premature infants at early school age: health-related quality of life and neurosensory, cognitive, and behavioral outcomes in a population-based sample in northern Germany. Neuropediatrics. 2009;40:112-9.

48. Feldman R. The development of regulatory functions from birth to 5 years: insights from premature infants. Child Dev. 2009;80:544-61.

49. Nomura Y, Halperin JM, Newcorn JH, Davey C, Fifer WP, Savitz DA, et al. The risk for impaired learning-related abilities in childhood and educational attainment among adults born near-term. J Pediatr Psychol. 2009;34:406-18.

50. Whiteside-Mansell L, Bradley RH, Casey PH, Fussell JJ, Conners-Burrow NA. Triple risk: do difficult temperament and family conflict increase the likelihood of behavioral maladjustment in children born low birth weight and preterm? J Pediatr Psychol. 2009;34:396-405.

51. Woodward LJ, Moor S, Hood KM, Champion PR, Foster-Cohen S, Inder TE, et al. Very preterm children show impairments across multiple neurodevelopmental domains by age 4 years. Arch Dis Child Fetal Neonatal Ed. 2009;94:F339-44.

52. Roberts G, Anderson PJ, De Luca C, Doyle LW; Victorian Infant Collaborative Study Group. Changes in neurodevelopmental outcome at age eight in geographic cohorts of children born at 22-27 weeks' gestational age during the 1990s. Arch Dis Child Fetal Neonatal Ed. 2010;95:F90-4.

53. Linhares MB, Chimello JT, Bordin MB, Vita AE, Martinez CF. Desenvolvimento psicológico na fase escolar de crianças nascidas pré-termo em comparação com crianças nascidas a termo. Psicol Refl Crit. 2005;18:109-17.

54. Magalhães LC, Rezende FC, Magalhães CM, Albuquerque PD. Análise comparativa da coordenação motora de crianças nascidas a termo e pré-termo, aos 7 anos de idade. Rev Bras Saúde Mater Infant. 2009;9:293-300.

55. Espírito Santo JL, Portuguez MW, Nunes ML. Cognitive and behavioral status of low birth weight preterm children raised in a developing country at preschool age. J Pediatr. 2009;85:35-41.

Correspondence:
Maria Beatriz Martins Linhares
FMRP, Campus Monte Alegre, USP
Avenida Tenente Catão Roxo, 2650, salas 52/53
CEP 14051-140 – Ribeirão Preto, SP – Brazil
Tel.: +55 (16) 3602.4610
Fax: +55 (16) 3602.4504
E-mail: linhares@fmrp.usp.br