

Cognitive development in low risk preterms at three to four years of life

Barbara Caravale¹, Claudio Tozzi², Grazia Albino², Stefano Vicari¹

¹IRCCS, Ospedale Pediatrico Bambino Gesù, Santa Marinella, Roma, Italy

²Dipartimento di Ginecologia, Perinatologia e Puericultura, Università "La Sapienza", Roma, Italy

Corresponding author:

Barbara Caravale

U.O.S. di Neurologia e Riabilitazione

IRCCS, Ospedale Pediatrico Bambino Gesù

Lungomare Guglielmo Marconi 36, I-00058

Santa Marinella

Rome

Italy

Telephone.: 39.0766.5244258

Fax: 39.0766.5244244;

Email: bcaravale@libero.it;

Keywords: preterm, LBW, outcome, cognitive, neuropsychological assessment.

Abstract

Background: Significant neurological handicaps and neuropsychological disturbances are more frequent in ex-preterm children as compared to their counterparts born at term. The aim of this prospective study was to establish whether a characteristic neuropsychological profile exists in ex-preterm children who do not exhibit neurodevelopmental deficits on routine clinical examination.

Methods: Thirty intellectually normal children born preterm (30-34 weeks of gestation) without major neurological disabilities and a control group of term children matched for age, gender and parental educational and occupational status were assessed at three to four years of age to obtain a complete neuropsychological profile. Intellectual abilities, language comprehension and expression, perceptual and visual motor functions, working memory, attention and behavioral problems were investigated.

Results: We found that children born preterm, even in the absence of major neurological signs, achieved lower mean scores compared to controls on the Stanford-Binet Intelligence Scale (110.8 vs. 121.3, $p=0.002$), Visual Perception test (33.8 vs. 42.7, $p<0.001$) and Visual Motor Integration test (42.6 vs. 45.8, $p=0.05$), Memory for Location test (8.4 vs. 9.5, $p=0.003$), Sustained Attention test, (41.6 vs. 51.5, $p=0.009$), and the Picture Vocabulary test (33.2 vs. 44.7, $p=0.02$).

Conclusions: These findings suggest the possibility that neuropsychological abnormalities can be detected early in childhood in apparently normal ex-preterm children and are consistent with a growing body of evidence suggesting that prematurity may be associated with long term neuropsychological morbidity in childhood and adolescence.

Introduction

Preterm children may present, more frequently than children born at term, neurological problems that include severe neurological handicaps, such as cerebral palsy or severe mental retardation, or more subtle cognitive impairments.[1][2]

Recent studies on medium and long term outcomes have showed that very low birth weight infants (VLBW) or extremely low birth weight infants (ELBW), even in absence of major disabilities, may present learning difficulties, attention-deficit/hyperactivity disorder (ADHD), specific neuropsychological deficits and behavioral problems in 50% to 70% of cases.[3][4] Regarding neuropsychological specific deficits, it has been established that VLBW are more likely to develop visual perceptual and visual-motor impairments, delay in some language functions, working memory deficit [5][6] and, at school age, they may present learning problems and attention deficit. Much of this body of studies have included wide ranges of gestational age (GA), variable choice of cutting points on birth weight distributions, variable clinical inclusions criteria (groups including children with neurosensory impairments and children with normal development), making potential biases. Moreover, the majority of the investigations on this subject, are focused on VLBW or ELBW children or high risk preterm groups (neonatal intensive care populations) [7][8][9] and often consisted of data on motor development or cognitive level (or developmental quotient) in the first years of life and few specific abilities of the cognitive spectrum from 5 years of age to the whole school age. From many studies it is not clear whether an unfavorable outcome for preterm group, as a whole, is due to moderate to severe impairment in few infants or to slight impairment in the majority. Some researches have recently described by neuroimaging studies brain abnormalities in children and adolescents born preterm and their specific cognitive deficits: ventricular dilatation, atrophy of corpus callosum, reduced hippocampal volume have been described in these populations.[2] [10] It has also been showed that the cerebellum size is reduced in ex-preterm adolescents and significant correlations were found between cerebellar volume and IQ, digit span and reading age.[11] However the relationship between the lesions and the neurocognitive functions remain unclear in many studies.[12][13] Neuropsychological difficulties have been detected also in preterm children at school age or adolescence, who do not present neurological deficit or cerebral abnormalities.[14][15] Despite the documented relationship between prematurity and cognitive deficit and the absence of a clear relationship with cerebral alterations, few studies have addressed the question of which specific difficulties in cognitive measures may be present in preterm children with low risk of neurological deficit (like children with no history of perinatal complications or high risk factors or brain lesions). In fact, there are few studies on cognitive outcome exclusively in low risk population.[16][17][18] These reports, however, have suggested that even in low-risk infants there may be specific cognitive deficits as a function of preterm birth (visual-motor integration, explicit and auditory memory in combination with integrative functions). In a previous report from our group on part of the same sample of the present study, we reported that children without evident brain damage, evaluated at three to four years of age, may have difficulties in tasks that contemplate sustained attention, visuo-spatial processing and spatial working memory functions. [19]

The possibility of detecting specific cognitive deficit even in children with low risk of mental and neurological problems or in children with normal neuroimaging may have both a theoretical and a practical importance. It may add some information on the notability of the 'prematurity' *per se* on the cognitive deficit and may indicate the need of a detailed neuropsychological long term follow-up leading to specific rehabilitative strategies to prevent learning and/or behavioral problems.

The aim of this prospective study was to provide a comprehensive neuropsychological profile at three to four years of age in children born between 30 and 34 weeks of gestation with a reduced risk of developmental deficits. Children with major disabilities or developmental delay, as checked

during the two year long follow-up by a child neurologist, were excluded from the study. An age, gender, social class-matched control group of term children was compared.

Methods

Subjects

The cohort was selected from all preterm infants discharged from the Department of Gynecology, Perinatology and Child Health, Policlinico Umberto I, Rome, Italy, between January 1 and December 31, 1998, who were enrolled in the pediatric and neurological follow-up of the same Department. The inclusion criteria for this study were: (1) gestational age between 30-34 weeks and 6 days; (2) no congenital abnormalities; (3) enrolment in the program of pediatric and neurological follow-up for at least 2 years; (4) no major neurological signs. Forty six children fulfilled these criteria. Nine children were not enrolled in the study as parents had declined to participate and seven were no longer traceable. All thirty children of the final cohort had normal hearing and visual functions assessed in the first two years of life. Cranial ultrasounds were performed serially with an ATL Ultramark scanner using a 5 or 7.5 MHz transducer. At least two examinations were made on just 19 pre-term infants, one within the first 48 hours and one at the end of the first week of life. No abnormal cerebral ultrasound findings, including minimal changes during the neonatal period, were found in this group described in a previous study.[19]

The control group comprised thirty children born at term with no history of any perinatal problem matched for age, gender, parental education level and occupational status from four different schools of Rome. Information about parents socio-economic and educational status was obtained through a short questionnaire addressed to them in which they were asked background information about educational qualification and occupation of both mother and father, health problems and hospitalization of the child, child care settlements in the first two years of age (divided in first 6 months and following); child's age at school beginning. The same observers examined the study and the control groups.

Neuropsychological Evaluation

The following test battery was performed to the study and the control groups:

Intellectual development was assessed by the Italian version of the L-M form of the Stanford-Binet Intelligence Scale.[20]

Perceptual and motor abilities

Visual-Motor Integration Test (VMI). [21] This is a paper-pencil test in which the child has to copy a series of geometric shapes of increasing complexity one by one until he or she makes three consecutive wrong figures. The score indicates the accuracy of the copies and it ranges from 0 to 24. The lower the score, the less competent the performance. It is possible to convert the raw score in a mental age equivalent.

- Block construction. [22] Each child is presented with a set of eight wooden parallelepiped blocks measuring 7.5 x 5 x 2 cm. Using an identical set of blocks, the examiner constructs a model behind a screen, out of the sight of the child. After lifting the screen the examiner asks the subject to make a construction just as he had done. The child is asked to make six different block models and he can achieve a score of 0, 1 or 2 for each building. According to Stiles [22] the scoring system is divided into two sections: three models are designed as 'simple' constructions and three as 'complex'.

- TPV, perceptual tasks. [23] This is a perceptual test with four sections where the child is asked to observe a geometric shape and to recognize the same one or a similar one choosing from a group of others. In the first section he has to match the same figure within a group of figures that differ for spatial orientation; in the second he has to find the right shape in the context of overlapped images;

in the third section the child has to recognize the figure between images partially raised; in the fourth he must match the target with other figures that have the same shape but differ for dimension, color and/or spatial disposition. The standard score is obtained by the sum of the four sections and it ranges from zero to 70.

Language abilities

The language battery comprised two tests of language production and two of language comprehension

- Boston Naming Test (BNT). [24] This test measures lexical production elicited through pictures. The children is asked to name the objects shown in the pictures that are gradually less familiar. The score goes from zero to 60.

- Word and Phrase Retrieval Test (TRF). [25] It is a word and phrase repetition test designed to ascertain the children's ability to imitate verbal stimuli, particularly their morphological and syntactic aspects. The number of correctly pronounced sentences is scored. The score varies from zero to 56.

- Peabody Picture Vocabulary Test Revised (PPVT-R). [26] This is a widely used test, selected to provide a reliable measure of receptive vocabulary. From the raw scores and the chronological ages IQ levels may be obtained.

- Test of grammar comprehension (TCG). [27] It measures the ability of syntax comprehension. The child is asked to choose the correct picture (between four) after listening to a sentence. The number of correct answers is scored and it ranges from zero to 31.

Working Memory abilities

Memory for location . [28] It is a test of spatial short-term memory. The testing apparatus consisted of six identical plastic cups and two small toys. The child had to remember and find under which cup one or two toys are hidden after covering the cups with a screen for 1 second. In detail the test consists in two trial for each cups spatial arrangement (one toy under one of 4 and 6 cups arranged in straight lines, one toy under one of 6 cups on a diagonal disposition, one toy under one of 6 cups in an L shape configuration, two toys under two of 6 cups in a straight line). In each session the number of correct responses is scored and it ranges from zero to ten.

Attention Sustained test (Leiter International Performance Scale Revised, LIPS-R). [29] This test measures sustained attention for stimuli arranged in different spatial positions. It is a barrage task with a time limit (30 seconds). Each of the four sections of growing difficulty is composed of a sheet of paper on which are represented, the target picture (a puppet) on the top and a series of two different pictures (puppets and balls) below. The child is requested to select, by crossing them off, all the pictures identical to the target. The total number of correctly crossed out images is scored. The scoring ranges from zero to 64.

Each evaluation consisted in two or three sections of 25 to 50 minutes according to the availability of the child and of his/her family and was followed by a neurological examination focused on fine motors skills and coordination abilities.

Statistical analysis

Data was analyzed with the Statistical Package for Windows, Version 5.0 (StatSoft, Inc., Tulsa, OK, USA). [30] Single ANOVA and ANCOVA analyses were done to compare the results of each neuropsychological tests between the groups.

Ethics

The families of the study and the control groups provided informed consent according to the Hospital's institutional review board for studies on human subjects.

Results

We tested thirty LBW children born preterm at the Policlinico Umberto I, University of Rome Italy, between January 1 and December 31, 1998. The children selected were born between 30 and 34 weeks of gestation (mean 32) with a birth weight ranging between 910 and 2400 grams (mean 1755 grams). Twenty-five preterm children were AGA and 5 were SGA.

A gestational age and birth weight distribution of the two groups is showed in Figure 1.

Cognitive level

The intelligence quotient (IQ) scores of the preterms and the controls obtained with Stanford-Binet Intelligence Scale were in the normal range (94-130 and 100-143). However the mean IQ of the preterm group was significantly lower when compared with the control group, 110.8 (SD 10.4) vs. 121.3 (SD 10.6); $F(1,11)=15$; $p=0.002$ (see table 1).

To control for the effect of general intelligence on all the other performances, we covaried results obtained on the visual-perceptual and motor, language, attention and memory tests with IQ scoring.

Perceptual and motor abilities

In the VMI test, the preterm group performed less well when compared with term children (Mean=42.6 vs. 45.8). The significance was confirmed even when data were covaried with IQ levels $F(1,34)=4$; $p=0.5$.

On block construction tests the two groups differ significantly only in the simplified models task; the results were, anyhow, sensible to IQ levels (see table 2).

In the visual-perceptual test (TPV) the mean full-scale standard scores of the preterm children were significantly lower than those of the controls even when data were covaried with the IQ levels of the two groups (Means = 33.8 vs. 42.7; $F(1,47) = 24$; $p < 0.001$) (see table 2).

Attention

Preterm children achieved a lower scoring in the sustained attention task (Mean 41.6 vs. 51.5) and the differences between the groups were significant even when IQ levels were taken in account, $F(1,56) = 7.3$; $p = 0.009$ (see table 2).

Memory

The study group reached in the spatial working memory test a mean score which is lower than the control group (Mean 8.4 vs. 9.5) and the difference was statistically significant with the ANCOVA analysis too ($p = 0.003$) (see table 2).

Language skills

The language test results indicate a general difference between the preterm and the control group. In the lexical comprehension test (Peabody Picture Vocabulary Test Revised, PPVT-R), the difference between the two groups was significant even when ANCOVA analysis was applied, $F(1,56)=5.3$; $p = 0.021$, while the grammar comprehension test (test of grammar comprehension, TCG) approached significance, $F(1,57) = 7.3$; $p = 0.054$. The lexical and morphological production test (Boston Naming Test, BNT and Word and Phase retrieval test, TRF) did not reach the significance when data were covaried with the IQ levels (see table 3).

Table 1

Comparison of the performances obtained by the two groups on the cognitive level assessment.

TEST	Preterm (N=30)		Controls (N=30)		ANOVA
	Mean (SD)	range	Mean (SD)	range	P
<i>Stanford-Binet</i>					
<i>full scale IQ</i>	110,8 (10,41)	94-131	121 (10,63)	100-138	<0.001 *

Table 2

Neuropsychological test scores obtained by the two groups on the non-linguistic abilities.

TEST	Preterm (N=30)		Controls (N=30)		ANOVA	
	Mean (SD)	range	Mean (SD)	range	P	P cov/QI
<i>VMI</i>	42,56 (6,13)	35-57	47,36 (5,76)	38-64	0.0027	0.049*
<i>Block Constr simply</i>	2,33 (2,03)	0-6	3,03 (1,92)	0-6	0.17	0.51
<i>Block Constr complex</i>	4,76 (1,54)	0-6	5,6 (0,54)	4-6	0.0039	0.18
<i>TPV</i>	33,82 (8,39)	14-44	42,66 (4,74)	31-52	<0.001	<0.001*
<i>LIPS (Attention)</i>	41,62 (11,57)	13-60	51,5 (5,78)	42-63	<0.001	0.009*
<i>Memory Location</i>	8,37 (1,32)	6-10	9,53 (0,68)	8-10	<0.001	0.0073*

VMI indicates Visual-Motor Integration Test; *TPV*, perceptual tasks of Visual Perception Test; *LIPS*, Attention Sustained task of Leiter International Performance Scale.

Table 3

Neuropsychological test scores obtained by the two groups on the linguistic abilities.

TEST	Preterm (N=30)		Controls (N=30)		ANOVA	
	Mean (SD)	range	Mean (SD)	range	P	P cov/QI
<i>BNT</i>	14,86 (4,2)	6-22	18,13 (4,51)	8-29	0.0052	0.11
<i>TRF</i>	40,63 (7,17)	22-49	45,3 (4,83)	32-51	0.0045	0.084
<i>PPVT-R</i>	33,27 (13,35)	11-68	44,73 (11,6)	14-72	<0.001	0.021*
<i>TCG</i>	8,72 (5,38)	4-26	13,2 (7,43)	6-27	0.01	0.054

BNT indicates Boston Naming Test; *TRF*, Word and Phrase Retrieval Test; *PPTV-R*, Peabody Picture Vocabulary Test Revised; *TCG*, Test of Grammar Comprehension.

Discussion

This prospective, follow-up study with a matched control group showed that even preterm infants with a low risk of neurodevelopmental deficit may show many difficulties in specific cognitive areas at three to four years of life. In contrast with many earlier studies that included entire populations of preterm children, making no differentiation according to neurological status [5][6][31] we selected our study group using strict inclusion criteria to create a more possible homogeneous group without measurable neurological damage. Furthermore, very few studies focused on a comprehensive analysis of the neuropsychological outcome in premature children are available so far. It can be argued that the ultrasound technique is not 100% sensitive to accurately select subjects according to absence of brain lesion and that MRI may could give more exhaustive information on subtle brain lesions in these children.[2] This is certainly true, but the preterm children included in our study were very young and the MRI exam could only have been performed under general anesthesia. The absence of signs of neurological impairment did not justify the use of such an intrusive exam, and for ethical reasons it could not be performed only for research purposes.

The criteria used to match the preterms with controls took into account parental educational level and occupational status by a short questionnaire that considered also post-natal care arrangements in terms of hours per day the mother spent with the child in the first 6 months of life. More factors might influence the cognitive outcome in children but, according to literature we considered those to be the most important.[32]

The results strongly agree with earlier studies on cognitive outcome of LBW or VLBW children that described mean IQ levels 6-7 points or 0.5 SD less than control groups.[12][33] IQ levels appear to remain stable in VLBW subjects (high risk preterm), and it is still possible to appreciate significantly lower mean IQ scores than the controls even at 20 years of life.[34] However, moderately immature and low risk preterm children, in a long term prospective, appear to gradually attenuate the cognitive outcome differences with their counterparts born at term.[18]

There are few studies that account for general IQ level in the analysis of data on neuropsychological tests.[35] More often in studies that consider big sample of children researchers calculate the difference between preterms and term controls in the statistical analysis, first including all the group and then excluding children with cognitive or major neurological deficit.[36] We made the covariation analysis on all the neuropsychological measures accounting for the differences of IQ levels even if the preterm cognitive levels were in the normal range, in order to obtain more specific results of the real deficit.

In fact, some LBW children with apparently normal overall measures of motor and cognitive ability have specific deficits in certain areas of performance like attention, memory, language, visual-motor integration and visual-spatial skills.[1][17][31]

Considering the neuropsychological tests, there was a significant difference between the preterm and full-term groups for scores on the visual-perceptual and visual-motor integration tests in our study. No differences between groups are found in the block construction test. As far as we know is the first time that these abilities have been investigated at three years of age. Poor performance of LBW children in visual-motor abilities are well documented and have been described in several studies between 5 to 11 years of age.[31][37] Some previous studies found that preterm children may present disorders on visual and perceptual motor at school age when compared to children born at term or in a population based study.[38][39] These characteristics are described even in absence of neurological impairments.[14] Other studies have, in contrast, reported a small prevalence of

visual-perceptual dysfunction or the absence of any difference in visual processing in VLBW or ELBW children.[40]

Vocabulary delays were evident in our study group consistent with previous reports of language difficulties following premature birth [6][41]. In our study grammatical comprehension abilities were approaching significance. These data confirm a risk of language difficulties even in low risk preterm. Studies on language development have found that premature children are comparatively delayed in expressive and receptive language.[7][42] Some studies that compare preterm and full-term children suggested that early difference may disappear in the first years of life especially in some aspects. For example, Ment *et al.* described a group of VLBW infants included in a prospective long term follow-up study from 3 to 8 years old and demonstrated that preterm children may have difficulties in receptive verbal abilities but that this function can improve over time.[42] However, other more complex verbal processes, such as understanding of syntax, abstract verbal skills, verbal production and word fluency have been found to be deficient.[43]

Our results show that in the spatial working memory test the preterm group achieved a lower performance compared to controls. Selective memory deficit has been described in LBW children and preterms, relatively to controls, showed lower scores on spatial working-memory and planning tasks.[44] We described in a previous study the working memory deficit in a group of 19 preterm children who are part of the group we are describing here. Participants were selected for having at least two cranial ultrasound and normal findings. We found specific spatial working memory difficulties characterized by a progressive worsening considering the interval delay and the complexity of spatial configuration.[19]

Our data showed a significant difference between the study group and the controls on the sustained attention abilities. This task involves attention in terms of duration and direction and has been described to be correlated with problem-solving abilities and school performances. Similar findings compared with those of ours have been found earlier on VLBW without evident brain disorders. [14] In the majority of papers, attention difficulties in preterms are described in the context of the increased risk of attention deficit and hyperactivity disorder (ADHD).[45][46]

Our findings on neuropsychological outcome in children at low-risk of developmental disorder should clarify the necessity of specific cognitive assessments early in childhood even in populations of children than usually are followed-up for a short time.

Continued follow-up assessment is necessary to observe the behavior modifications over time and to determine whether the findings on neuropsychological outcome indicate a developmental lag in brain maturation that will change over time or whether other problems will become evident in these children as the demands become increasingly challenging (like at school).

Acknowledgements

The financial support of the Italian Ministry of Health Project 0AN/F "Hypoxic-ischemic brain damage in the newborn: epidemiological and experimental studies on diagnosis, therapy and rehabilitation" is gratefully acknowledged.

We thank Arianna Terrinoni and Cristina Vagnoni for their assistance in collecting data. We especially thank the children who participated in the study and their families.

Licence statement

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non-exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd and its Licensees to permit this article to be published in *Archives of Disease in Childhood* editions and any other BMJ PGL products to exploit all subsidiary rights, as set out in our licence (<http://adc.bmjournals.com/misc/ifora/licenceform.shtml>).

What is already known on this topic

There are lot of studies on medium and long term outcome on preterm children showing that very low birth weight infants (VLBW) and extremely low birth weight infants (ELBW) may have learning difficulties, attention-deficit/hyperactivity disorder (ADHD), specific neuropsychological deficits and behavioral problems in more than 50% of cases. The majority of the investigations on this subject are focused on VLBW or ELBW children or high risk preterm groups and often consisted of data on motor development or cognitive quotient in the first years of life and few specific abilities of the cognitive spectrum from 5 years of age to the whole school age.

What this study adds

This study is relevant for our understanding of the qualitative aspects of cognitive development in preterm children, also in those expected to have a normal outcome. We emphasized that neuropsychological abnormalities can be detected early in childhood in apparently normal preterm children but appropriate evaluations should be performed routinely to prevent later problems at school age. From a practical point of view, the finding of specific difficulties in sustained attention, visuo-spatial processing and spatial working memory and in some language aspects in LBW preterm children is worthy of consideration in the development of early educational and rehabilitative interventions to improve their cognitive and behavioral outcome.

References

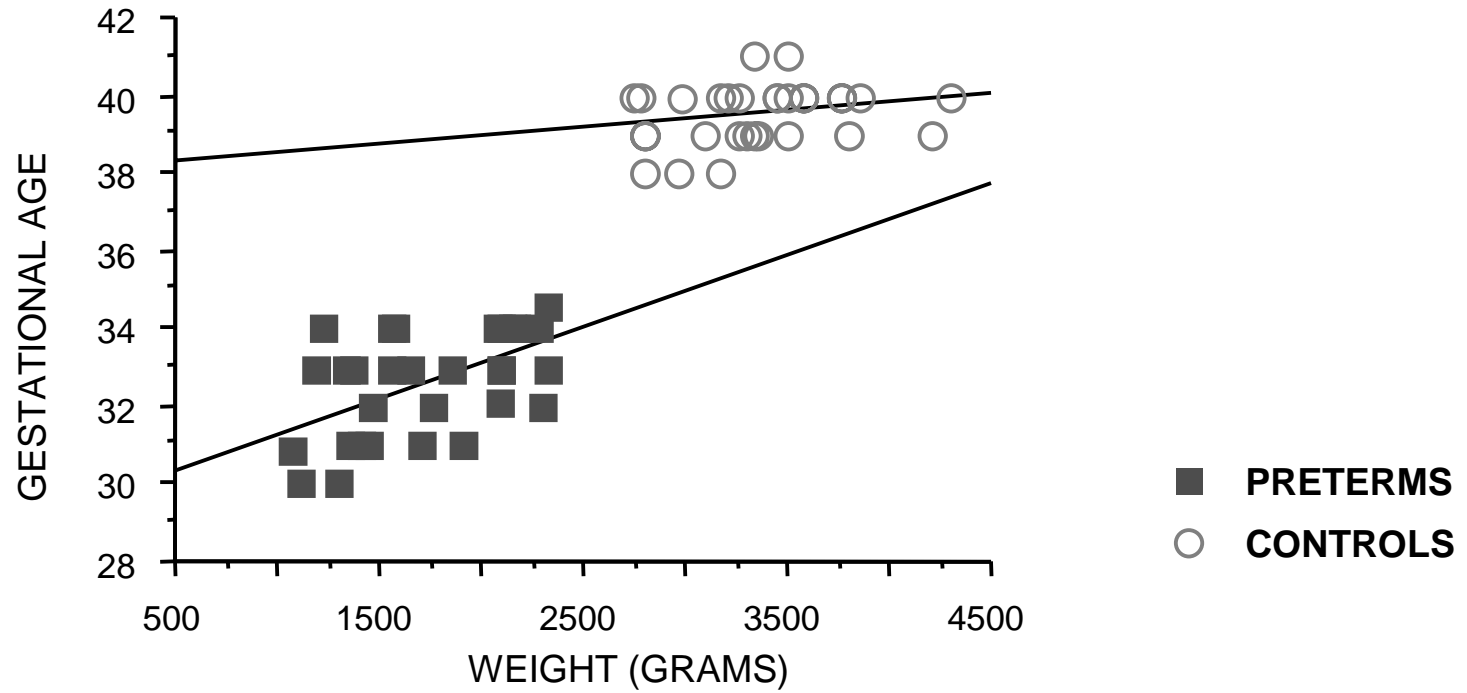
- 1 Mutch L, Leyland A, McGee A. Patterns of neuropsychological function in a low birth weight population. *Dev Med Child Neurol* 1993;**35**:943-56.
- 2 Stewart AL, Rifkin L, Amess PN, *et al.* Brain structure and neurocognitive and behavioural function in adolescents who were born very preterm. *Lancet* 1999;**35**:1653-7.
- 3 Msall ME, Buck GM, Rogers BT, *et al.* Risk factors for major neurodevelopmental impairments and need for special education resources in extremely premature infants. *J Pediatr* 1991;**119**:606-14.
- 4 Taylor HG, Klein N, Minich NM, *et al.* Middle school age outcome in children with very low birth weight. *Child Dev* 2000;**71**:1495-511.
- 5 Horwood LJ, Mogridge N, Darlow BA. Cognitive, educational, and behavioural outcomes at 7 to 8 years in a national very low birthweight cohort. *Arch Dis Child Fetal Neonatal Ed* 1998;**79**:2-20.
- 6 Jennische M, Sedin G. Linguistic skills at 6 1/2 years of age in children who required neonatal intensive care in 1986-1989. *Acta Paediatr* 2001;**90**:199-212.
- 7 Vohr BR, Garcia-Coll C, Oh W. Language and neurodevelopmental outcome of low-birthweight infants at three years. *Dev Med Child Neurol* 1989;**31**:582-90.
- 8 Saigal S, Robertson C, Sankaran K, *et al.* One-year outcome in 232 premature infants with birth weights of 750 to 1249 grams and respiratory distress syndrome randomized to rescue treatment with two doses of synthetic surfactant or air placebo. Canadian Exosurf Neonatal Study Group. *Pediatrics* 1995;**126**:61-7.
- 9 Wood NS, Marlow N, Costeloe K, *et al.* Neurologic and developmental disability after extremely preterm birth. EPICure Study Group. *N Engl J Med* 2000;**343**:378-84.
- 10 Isaacs EB, Edmonds CJ, Chong WK, *et al.* Cortical anomalies associated with visuospatial processing deficits. *Ann Neurol* 2003;**53**:768-73.
- 11 Allin M, Matsumoto H, Santhouse AM, *et al.* Cognitive and motor function and the size of the cerebellum in adolescents born very pre-term. *Brain* 2001;**124**:60-6.
- 12 Olsen P, Vainionpaa L, Pakko E, *et al.* Psychological findings in preterm children related to neurologic status and magnetic resonance imaging. *Pediatrics* 1998;**102**:329-336.
- 13 Rushe TM, Rifkin L, Stewart AL, *et al.* Neuropsychological outcome at adolescents of very preterm birth and its relation to brain structure. *Dev Med and Child Neurol* 2001;**43**:226-33.
- 14 Torrioli MG, Frisone MF, Bovini L, *et al.* Perceptual motor, visual and cognitive ability in VLBW children without ultrasound abnormalities. *Brain and Dev* 2000;**22**:163-8.
- 15 Curtis WJ, Lindeke LL, Georgieff MK, *et al.* Neurobehavioural functioning in neonatal intensive care unit graduates in late childhood and early adolescence. *Brain* 2002;**125**:1646-59.

- 16 Majnemer A, Brownstein A, Kadanoff R, *et al.* A comparison of neurobehavioral performances of healthy term and low-risk preterm infants at term. *Dev Med Child Neurol* 1992;**34**:417-24.
- 17 De Haan M, Bauer PJ, Georgieff MK, *et al.* Explicit memory in low-risk infant aged 19 months born between 27 and 42 week of gestation. *Dev Med Child Neur* 2000;**42**:304-12.
- 18 Tideman E. Longitudinal follow-up of children born preterm: cognitive development at age 19. *Early Hum Dev* 2000;**58**:81-90.
- 19 Vicari S, Caravale B, Carlesimo GA, *et al.* Spatial working memory deficits in children at ages 3-4 who were low birth weight, preterm infants. *Neuropsychology* 2004;**18**:673-8.
- 20 Terman LM, Merrill MA. *Stanford-Binet Intelligence Scale*. In Houghton ed. New York, 1964. Trad. italiana "Scala di Intelligenza Stanford-Binet". In Organizzazioni Speciali Firenze, 1993.
- 21 Beery K. *Developmental Tests of Visual-Motor Integration*. In Modern Curriculum Press ed. Parsippany, NJ, 1997.
- 22 Stiles J, Stern C, Trauner D, *et al.* The developmental change in spatial grouping activity among children with early focal brain injury: a modelling task. *Brain and Cognition* 1996;**31**:46-62.
- 23 Hammill D, Pearson N, Voress J. *TPV developmental test of visual perception*. In Pro-ed. Austin, Tex, 1993. Traduzione italiana. "TPV test di percezione visiva". In Erickson ed. Trento, 1994.
- 24 Goodglass H, Kaplan E. *The assessment of Aphasia and related disorders*. In Febbinger ed. Philadelphia, Pa, 1972.
- 25 Devescovi A, Caselli MC. Una prova di ripetizione di frasi per la valutazione del primo sviluppo grammaticale. *Psicologia dello sviluppo* 2001;**3**:341-64.
- 26 Dunn LM, Dunn L. *Peabody picture vocabulary test*. In Wilmington, Del, Guidance Associates 1981.
- 27 Rustioni D. *Prove di valutazione della comprensione linguistica*. In Organizzazioni Speciali Firenze, 1994.
- 28 Cossu MC, Antonucci G, Nava I. Memory for location 2, Revised. *I Quaderni, S.Lucia* 2000;**17**:1-46.
- 29 Roid GH, Miller LJ. *Leiter-R, International Performance Scale Revised*. In Organizzazioni Speciali Firenze, 1997.
- 30 StatSoft, Statistical Package for Windows (Versionon 5.0), Computer software. Tusla, OK.
- 31 Luoma L, Herrgard E, Marticainen A. Neuropsychological analysis of the visuo-motor problems in children born preterm at <32 weeks of gestation: a 5 years prospective follow-up. *Dev Med Child Neur* 1998;**40**:21-30.

- 32 Brooks-Gunn J, Han WJ, Waldfogel J. Maternal employment and child cognitive outcomes in the first three years of life: the NICHD Study of Early Child Care. National Institute of Child Health and Human Development. *Child Dev* 2002;**73**:1052-72.
- 33 Krageloh-Mann I. The cognitive outcome of very preterm children: how to interpret results. *Acta Paediatr* 2002;**91**:1285-7.
- 34 Hack M, Taylor HG. Perinatal brain injury in preterm infants and later neurobehavioral function. *JAMA* 2000;**284**:1973-4.
- 35 Isaacs EB, Lucas A, Chong WK, *et al*. Hippocampal volume and everyday memory in children of very low birth weight. *Pediatr Res* 2000;**47**:713-20.
- 36 Wolke D, Meyer R. Cognitive status, language attainment and pre-reading skills of 6 year old very preterm children and their peers: the Bavarian Longitudinal Study. *Dev Med Child Neurol* 1999;**41**:94-109.
- 37 Goyen TA, Lui K, Woods R. Visual motor, visual perceptual and fine motor outcomes in VLBW children at 5 years. *Dev Med Child Neurol* 1998;**40**:76-81.
- 38 Foreman N, Fielder A, Minshell C, *et al*. Visual search, perception and visual-motor skill in healthy children born 27-32 weeks' gestation. *J Exp Child Psychol* 1997;**64**:27-41.
- 39 Hard AL, Niklasson A, Svensson E, *et al*. Visual function in school-aged children born before 29 weeks of gestation: a population-based study. *Dev Med Child Neurol* 2000;**42**:100-105.
- 40 Teplin SW, Burchinal M, Johnson-Martin N, *et al*. Neurodevelopmental, health and growth status at 6 years of children with birth weights less than 1001 grams. *Journal of Pediatrics* 1991;**118**:768-77.
- 41 Luoma L, Herrgard E, Martikainen A, *et al*. Speech and language development of children born at ≤ 32 week's gestation: a 5 year prospective follow-up study. *Dev Med Child Neurol* 1998;**40**:380-7.
- 42 Ment LR, Vohr B, Allan W, *et al*. Change in cognitive function over time in very low-birth-weight infants. *JAMA* 2003;**289**:705-11.
- 43 Aylward GP. Cognitive and neuropsychological outcomes: more than IQ scores. *Ment Retard Dev Disabil Res Rev* 2002;**8**:234-40.
- 44 Luciana M, Lindeke L, Georgieff M, *et al*. Neurobehavioral evidence for working-memory deficits in school-aged children with histories of prematurity. *Dev Med Child Neurol* 1999;**41**:521-33.
- 45 Breslau N, Chilcoat HD. Psychiatric sequelae of low birth weight at 11 years of age. *Biol Psychiatry* 2000;**47**:1005-11.
- 46 Mick E, Biederman J, Prince J, *et al*. Impact of low birth weight on attention-deficit hyperactivity disorder. *J Dev Behav Pediatr* 2002;**23**:16-22.

Figure 1

Gestational Age by Weight Distribution of the Preterms and the Controls





Cognitive development in low risk preterms at three to four years of life

Barbara Caravale, Claudio Tozzi, Grazia Albino, et al.

Arch Dis Child Fetal Neonatal Ed published online June 14, 2005
doi: 10.1136/adc.2004.070284

Updated information and services can be found at:
<http://fn.bmj.com/content/early/2005/06/14/adc.2004.070284.citation>

	<i>These include:</i>
References	Article cited in: http://fn.bmj.com/content/early/2005/06/14/adc.2004.070284.citation#related-urls
P<P	Published online June 14, 2005 in advance of the print journal.
Email alerting service	Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

Advance online articles have been peer reviewed, accepted for publication, edited and typeset, but have not yet appeared in the paper journal. Advance online articles are citable and establish publication priority; they are indexed by PubMed from initial publication. Citations to Advance online articles must include the digital object identifier (DOIs) and date of initial publication.

To request permissions go to:
<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:
<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:
<http://group.bmj.com/subscribe/>