ORIGINAL ARTICLE

Cognitive Development at Age 8 Years in Very Low Birth Weight Children in Taiwan

Shu-Chi Mu,[1] Kuo-Su Tsou,[2] Chyong-Hsin Hsu,[3] Li-Jung Fang,[4] Suh-Fang Jeng,[5] Chia-Han Chang,[6] Kuo-Inn Tsou[7]*

Background/Purpose: All children should have some developmental screening periodically throughout childhood, especially those who were born prematurely. There is limited information about the development of children with very low birth weight (VLBW; birth weight < 1500 g) beyond the preschool age in Taiwan. We evaluated intelligence quotient (IQ) and cognitive ability of prematurely born school-aged children in Taiwan.

Methods: This was a multicenter study of VLBW and full-term children born between 1995 and 1997 at four hospitals in northern Taiwan. We used the Wechsler Intelligence Scale for Children, 3rd Edition (WISC-III), to assess these children. Demographic data were recorded including maternal and paternal age, education, birth weight, gestational age, and gender.

Results: A total of 189 children (130 with VLBW born prematurely and 59 born at full term) were recruited. There were significant differences in performance IQ (PIQ; 90.16 ± 17.05 *vs.* 108.51 ± 15.65, $p < 0.001$), verbal IQ (VIQ; 97.43 ± 15.62 *vs.* 111.78 ± 13.65, $p < 0.001$), full-scale IQ (FSIQ; 93.14 ± 16.33 *vs.* 111.05 ± 14.81, $p < 0.001$), verbal comprehension index score (VCIS; 98.06 ± 15.53 *vs.* 112.47 ± 13.74, $p < 0.001$), perceptional organization index score (POIS; 92.39 ± 17.13 *vs.* 109.42 ± 14.87, $p < 0.001$) and freedom from distractibility index score (FDIS; 98.34 ± 17.71 *vs.* 110.53 ± 10.94, $p = 0.008$). There was no correlation between perinatal outcomes and FSIQ.

Conclusion: Our results suggest that VLBW children have significantly lower PIQ, VIQ, FSIQ, VCIS, POIS and FDIS at primary school compared with full-term children. [*J Formos Med Assoc* 2008;107(12):915–920]

Key Words: freedom from distractibility index score, full-scale intelligence quotient, intelligence quotient, perceptional organization index score, performance intelligence quotient, verbal comprehension index score, verbal intelligence quotient, very low birth weight

The increasing survival of very low birth weight (VLBW; birth weight < 1500 g) infants has led to increased prevalence of adverse neurodevelopmental outcomes.[1–4] About 10–15% of children born with VLBW have major physical impairments that usually require special educational provision, but the majority do enter mainstream schools.[5] Studies of these children have shown that as many as 40% may have learning difficulties, often associated with problems of visuospatial

[1]Department of Pediatrics, Shin-Kong Wu Ho-Su Memorial Hospital, Institute of Clinical Medicine, National Yang-Ming University, and College of Medicine, Fu Jen Catholic University; [2]Taipei Child Development Assessment Center, Taipei City Hospital; [3]Department of Pediatrics, Mackay Memorial Hospital; [4]Department of Neonatology, Branch for Women and Children, Taipei City Hospital; [5]School and Graduate Institute of Physical Therapy, College of Medicine, National Taiwan University, and Department of Rehabilitation and Physical Medicine, National Taiwan University Hospital, Taipei; [6]Department of Pediatrics, Shin-Kong Wu Ho-Su Memorial Hospital; [7]College of Medicine, Fu Jen Catholic University and Department of Pediatrics, Catholic Tien Hospital, Taipei, Taiwan.

Received: December 13, 2007
Revised: April 16, 2008
Accepted: June 6, 2008

***Correspondence to:** Dr Kuo-Inn Tsou, College of Medicine, Fu Jen Catholic University, 510 Zhongzheng Road, Xinzhuang City, Taipei 242, Taiwan.
E-mail: 049687@mail.fju.edu.tw

perception, minor motor impairments, and behavioral difficulties.[6,7]

Most children born with VLBW seem to experience difficulties in academic achievement, attention, and fine motor functioning.[8] School difficulties appear to be the main sequelae in children with extremely low birth weight.[9–11] School-aged children with VLBW, when compared with their peers with normal birth weight, have significantly higher rates of educational assistance, grade failure, and placement in special classes.[12–14] They score significantly lower on standardized tests of mathematics, reading and spelling, with arithmetic standing out as a common problem area.[13,14] Even neurologically intact children born prematurely who have average intelligence demonstrate poorer academic achievement than their full-term peers with normal birth weight.[9,12]

VLBW children who experience difficulties at birth that increase their risk of developmental difficulties need to participate in a high-risk follow-up program.[15] All children should have some developmental screening periodically throughout childhood, especially in those born prematurely. We do not have sufficient data to understand the progressive development of children with VLBW beyond the school age of 8 years in Taiwan.[16]

We designed a follow-up program of screening and evaluation tests to identify delays across major areas of development. We aimed to obtain basic data to assess cognitive ability in prematurely born school-aged children in Taiwan.

Subjects and Methods

Participants

The professional team included: (1) pediatricians to evaluate the physical status and neurologic development of the children, and to direct the main caregivers as to how to take care of their children; and (2) psychologists to evaluate development, intelligence, attention and hyperactivity, assist in finishing questionnaires and data collection, and provide help for parents to know their child.

Procedures

This was a multicenter study of a group of VLBW neonates who weighed < 1500 g who were delivered at National Taiwan University Hospital, Mackay Memorial Hospital, Branch for Women and Children of Taipei City Hospital, and Shin-Kong Wu Ho-Su Memorial Hospital. Samples were collected from the premature neonates as the study group, and full-term neonates as the control group, born in the same period from 1995 to 1997. The premature neonates had a gestational age of < 36 weeks and a birth weight of < 1500 g. Full-term neonates had a gestational age of ≥ 37 weeks. We lost some premature neonates because of poor coordination or inconvenience of parents. In the study group, the rate of follow-up was 24–45% and there were 43, 54, 17, and 16 premature neonates in National Taiwan University Hospital, Mackay Memorial Hospital, Branch for Women and Children of Taipei City Hospital, and Shin-Kong Wu Ho-Su Memorial Hospital, respectively. In the control group, the rate of follow-up was 11–52% and there were 23, 20, 4, and 12 full-term infants in the National Taiwan University Hospital, Mackay Memorial Hospital, Branch for Women and Children of Taipei City Hospital, and Shin-Kong Wu Ho-Su Memorial Hospital, respectively. The full-term infants were delivered in the same period from 1995 to 1997 and were enrolled by random number sampling as our control group. There was one pediatrician from each of the four hospitals, and two psychologists (one for Shin-Kong Wu Ho-Su Memorial Hospital and one for the other three hospitals). All infants were free of known major congenital anomalies. Demographic data were recorded, including maternal and paternal age, education, birth weight, gestational age and gender. Gestational age was determined by menstrual history, antenatal ultrasound, and Ballard assessment.[17] The premature and full-term neonates were both of school age and had just reached 8 years old. The study was supported by the premature foundation and approved by the institutional review board of Shin-Kong Wu Ho-Su Memorial Hospital; parental consent was obtained.

The Wechsler Intelligence Scale for Children, 3rd Edition (WISC-III), is used for the psychological assessment of children aged > 6 years to teenagers aged < 17 years. The validity, reliability and standards were derived from the manual of WISC-III Taiwan Edition.[18] The subtests of WISC-III include the following: (1) six verbal subtests: information, arithmetic, similarities, vocabulary, comprehension, and digit span; (2) seven performance subtests: picture completion, coding, picture arrangement, block design, object assembly, symbol search, and maze. These subtests evaluate the verbal and nonverbal abilities of subjects. From their scores, we derived three major scales: verbal intelligence quotient (VIQ), performance intelligence quotient (PIQ), and full-scale intelligence quotient (FSIQ); and composite subscales: verbal comprehension index score (VCIS), perceptional organization index score (POIS), and freedom from distractibility index score (FDIS). VCIS contained four subtests: information, similarities, vocabulary and comprehension. POIS included four subtests: picture completion, picture arrangement, block design and object assembly. FDIS was composed of arithmetic and digit span.

Statistical analysis

Values were expressed as mean ± standard deviation (SD). Independent *t* test and Pearson's χ^2 test were used for statistical analysis. Linear regression was applied to calculate the risk. All β and *p* values were adjusted for sex, paternal and maternal education, and paternal and maternal age. The statistical models fitted the data remarkably well. A value of $p < 0.05$ was considered significant. Analyses were performed using SPSS version 13 (SPSS Inc., Chicago, IL, USA).

Results

A total of 189 children (130 with VLBW born prematurely and 59 born at full term) were identified as having been born in the area and period specified. There were 86 boys (45.5%). We excluded subjects with intrauterine growth restriction (IUGR). There were differences in gestational age (29.44 ± 2.84 *vs.* 39.29 ± 1.08 weeks, $p < 0.001$) and birth weight (1168.63 ± 239.14 *vs.* 3312.29 ± 379.56 g, $p < 0.001$). The Figure shows the distribution of gestational age according to the weight of the preterm and full-term infants. Gender and paternal and maternal age were similar in the two groups (Table 1). Maternal and paternal education of > 9 years (higher than senior high school) was more common in the control group. There was no significant difference in rearing environment between VLBW and control groups (marriage 93.1 *vs.* 96.6%, divorce 5.4 *vs.* 3.4%, unmarried 1.5 *vs.* 0%, $p = 0.522$).

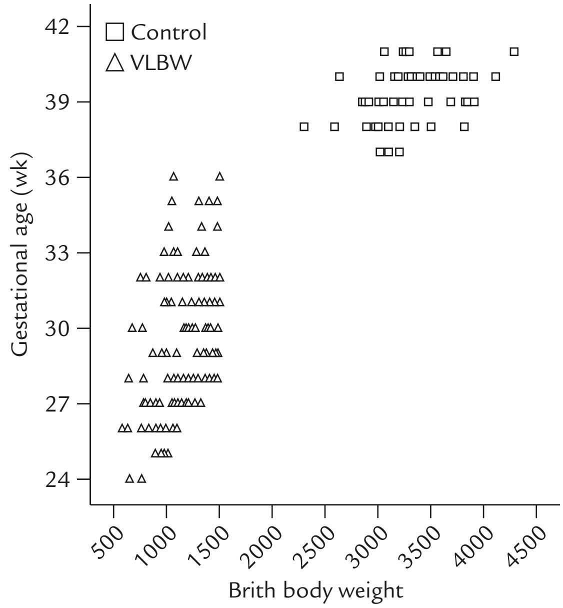

Figure. Gestational age and birth body weight of the very low birth weight (VLBW) and control groups.

The WISC-III test in the VLBW and control groups showed that there were significant differences in PIQ ($p < 0.001$), VIQ ($p < 0.001$), FSIQ ($p < 0.001$), VCIS ($p < 0.001$), POIS ($p < 0.001$), and FDIS ($p = 0.008$) (Table 2).

There was a significantly inferior tendency of PIQ, VIQ, FSIQ, VCIS, POIS and FDIS adjusted for sex, paternal and maternal education, and paternal and maternal age in the VLBW group compared with the control group (Table 3).

There were no correlations between FSIQ and perinatal outcomes for Apgar score, intraventricular hemorrhage, intermittent positive pressure

Table 1. Demographic characteristics*

	VLBW ($n = 130$)	Control ($n = 59$)	p
Maternal age (yr)	38.67 ± 5.02	39.34 ± 3.64	0.323
Paternal age (yr)	41.77 ± 4.75	41.71 ± 3.95	0.932
Paternal education > 9 yr	101 (77.7)	56 (94.9)	0.003†
Maternal education > 9 yr	107 (86.3)	57 (96.6)	0.038†
Birth weight (g)	1165.04 ± 238.90	3312.29 ± 379.56	< 0.001†
Gestational age (wk)	29.54 ± 2.72	39.29 ± 1.08	< 0.001†
Male	58 (44.6)	28 (47.5)	0.754

Data presented as mean ± standard deviation or n (%); †statistical significance defined as $p < 0.05$. VLBW = very low birth weight.

Table 2. IQ measured using the Wechsler Intelligence Scale for Children, 3rd Edition (WISC-III)*

	VLBW ($n = 130$)	Control ($n = 59$)	p
WISC-III			
PIQ	90.16 ± 17.05	108.51 ± 15.65	< 0.001†
VIQ	97.43 ± 15.62	111.78 ± 13.65	< 0.001†
FSIQ	93.14 ± 16.33	111.05 ± 14.81	< 0.001†
VCIS	98.06 ± 15.53	112.47 ± 13.74	< 0.001†
POIS	92.39 ± 17.13	109.42 ± 14.87	< 0.001†
FDIS	98.34 ± 17.71	110.53 ± 10.94	< 0.001†

Data presented as mean ± standard deviation; †statistical significance defined as $p < 0.05$. VLBW = very low birth weight; PIQ = performance IQ; VIQ = verbal IQ; FSIQ = full-scale IQ; VCIS = verbal comprehension index score; POIS = perceptional organization index score; FDIS = freedom from distractibility index score.

Table 3. Linear regression of IQ in the very low birth weight (VLBW) and control groups*

	β	95% CI	p
WISC III			
PIQ	−13.66	−18.80, −8.55	< 0.001†
VIQ	−10.64	−15.46, −5.82	< 0.001†
FSIQ	−13.37	−18.29, −8.44	< 0.001†
VCIS	−10.43	−15.23, −5.62	< 0.001†
POIS	−12.37	−17.39, −7.36	< 0.001†
FDIS	−9.64	−14.75, −4.53	< 0.001†

Adjusted for sex, paternal and maternal education, and paternal and maternal age; †statistical significance defined as $p < 0.05$. WISC-III = Wechsler Intelligence Scale for Children, 3rd Edition; PIQ = performance IQ; VIQ = verbal IQ; FSIQ = full-scale IQ; VCIS = verbal comprehension index score; POIS = perceptional organization index score; FDIS = freedom from distractibility index score.

ventilation, days of oxygen use, and length of hospital stay (Table 4).

Discussion

The present prospective and follow-up study showed that VLBW preterm infants had a risk of cognitive dysfunction. Some previous studies included entire populations of preterm children and made no differentiation according to neurologic status.[19–21] However, evaluations of neuropsychologic outcome in premature children has been scarce.

We enrolled the premature cases according to birth weight. Use of birth weight as the inclusion criterion has both advantages and disadvantages. Cohorts were based on birth weight because weight seems more reliable than gestational age

Table 4. Correlation of perinatal outcomes and full-scale IQ

	r	*p*
Apgar score at 1 min	–0.014	0.949
Apgar score at 5 min	0.004	0.984
IVH (No)	0.069	0.754
IVH grade ≥ III	0.016	0.942
IPPV (No)	0.024	0.915
Days of oxygen use	–0.153	0.486
Hospital days	0.215	0.324

IVH = intraventricular hemorrhage; IPPV = intermittent positive pressure ventilation.

estimations. A disadvantage of using birth weight as an inclusion criterion is the increasing frequency of growth-retarded infants at higher gestational ages. IUGR may have been associated with infants' underlying disease, thus explaining the high rate of comorbidity and syndromes that affect outcome. In our study, 9/139 subjects (6.5%) had IUGR. We did not analyze this group and they should be considered in a future study.

The role of paternal factors in determining the risk of adverse pregnancy outcome has received less attention than maternal factors. Similarly, the interaction between the effects of socioeconomic status and pregnancy outcomes is not well known. Our interest was to assess the relative importance of paternal *vs.* maternal education in relation to risk of VLBW and cognitive function. We chose 9 years of parental education as the cut-off point because there are 9 years of compulsory education in Taiwan. There was a difference and significant impact of paternal and maternal education on performance of IQ tests between VLBW and control groups.

IQ tests are generally designed and used because they are found to be predictive of later intellectual achievement, such as educational achievement. In our study, there were significant differences between the VLBW and control groups in PIQ, VIQ, FSIQ, VCIS, POIS and FDIS. Individual subtest scores tend to correlate with one another, even when seemingly disparate in content. This kind of factor analysis has led to the theory that a single factor underlies these disparate cognitive tasks, termed the general intelligence factor, which corresponds with the common-sense concept of intelligence. In our study, the VLBW children did have significantly lower scores for all IQ test items. Several factors can lead to significant cognitive impairment, particularly if they occur during pregnancy and childhood when the brain is growing and the blood-brain barrier is less effective. Such impairment may sometimes be permanent, and sometimes it may be partially or wholly compensated for by later growth. We do not support the suggestion that perinatal outcomes positively influence cognitive development. However, several factors in children born with VLBW may combine and cause some impairment. We need to extend the analysis for perinatal outcomes.

In conclusion, VLBW preterm children had reduced overall PIQ, VIQ, FSIQ, VCIS, POIS and FDIS. Parental education did have some impact on the cognitive development of VLBW children. We cannot speculate whether perinatal outcomes influence cognitive development in VLBW children at preschool age.

Acknowledgments

This work was supervised by the Ethics Committee and Institutional Review Board of Shin-Kong Medical Center. We thank Ms Huang Sue-Hui for evaluation of IQ tests, Ms Li Yu-Ling for technical assistance, manuscript preparation and computational analyses, and Dr Bai Chyi-Huey for statistical analysis. This project was supported by a grant from Shin-Kong Wu Ho-Su Memorial Hospital (SKH-FJU-94-23).

References

1. Tin W, Wariyar U, Hey E. Changing prognosis for babies of less than 28 weeks' gestation in the north of England between 1983 and 1994. *Br Med J* 1997;314:107–11.
2. Darlow BA, Cust AE, Donoghue DA. Improved outcomes for very low birthweight infants: evidence from New Zealand national population based data. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F23–8.

3. Meadow W, Lee G, Lin K, et al. Changes in mortality for extremely low birth weight infants in the 1990s: implications for treatment decisions and resource use. *Pediatrics* 2004;113:1223–9.
4. Hack M, Fanaroff AA. Outcomes of children of extremely low birthweight and gestational age in the 1990s. *Semin Neonatol* 2000;5:89–106.
5. Cooke RW. Annual audit of 3-year outcome in very low birth weight infants. *Arch Dis Child* 1993;69:295–8.
6. Botting N, Powls A, Cooke RW, et al. Cognitive and educational outcome of very low birth weight children in early adolescence. *Dev Med Child Neurol* 1998;40:661–6.
7. Botting N, Powls A, Cooke RW, et al. Attention deficit hyperactivity disorders and other psychiatric outcomes in very low birth weight children at 12 years. *J Child Psychol Psychiatry* 1997;38:931–41.
8. Hack M, Klein NK, Taylor HG. Long-term developmental outcomes of low birthweight infants. *Future Child* 1995;5: 176–94.
9. Leonard CH, Piecuch RE. School age outcome in low birthweight preterm infants. *Semin Perinatol* 1997;3:240–53.
10. Saigal S, Szatmari P, Rosenbaum P, et al. Cognitive abilities and school performance of extremely low birthweight children and matched term control children at age 8 years: a regional study. *J Pediatr* 1991;188:751–60.
11. Teplin SW, Burchinal M, Johnson-Martin N, et al. Neurodevelopmental, health, and growth status at age 6 years of children with birthweights less than 1001 grams. *J Pediatr* 1991;188:768–77.
12. Halsey CL, Collin MF, Anderson CL. Extremely low-birthweight children and their peers: a comparison of school-age outcomes. *Arch Pediatr Adolesc Med* 1996;150:790–4.
13. Klebanov PK, Brooks-Gunn J, McCormick MC. School achievement and failure in very low birthweight children. *J Dev Behav Pediatr* 1994;15:248–56.
14. Resnick MB, Gomatam SV, Carter RL, et al. Educational disabilities of neonatal intensive care graduates. *Pediatrics* 1998;192:308–14.
15. Powls A, Botting N, Cooke RW, Pilling D, Marlow N. Growth impairment in very low birthweight children at 12 years: correlation with perinatal and outcome variables. *Arch Dis Child Fetal Neonatal Ed* 1996;75:F152–7.
16. Wang LW, Huang CC, Wang ST. Validity of the Clinical Adaptive Test (CAT)/Clinical Linguistic and Auditory Milestone Scale (CLAMS) as a screening instrument for very low birth weight infants in Taiwan. *J Dev Behav Pediatr* 2005;26:412–8.
17. Ballard JL, Khoury JC, Wedig K, et al. New Ballard score, expanded to include extremely premature infants. *J Pediatr* 1991;119:417–23.
18. Chen YH. *The Wechsler Intelligence Scale for Children,* 3rd edition, Taiwan edition. Taiwan: Chinese Behavior Science Corporation, 1997:42–277.
19. 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.
20. Jennische M, Sedin G. Linguistic skills at 6½ years of age in children who required neonatal intensive care in 1986–1989. *Acta Paediatr* 2001;90:199–212.
21. Luoma L, Herrgard E, Marticainen A. Neuropsychological analysis of the visuo-motor problems in children born preterm at < 32 weeks of gestation: a 5 year prospective follow-up. *Dev Med Child Neurol* 1998;40:21–30.