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Original article

A longer body length and larger head circumference at term significantly influences a better subsequent psychomotor development in very-low-birth-weight infants

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Abstract

Aim: To clarify the influence of intra- and extra-uterine growth on subsequent psychomotor development in very-low-birth-weight (VLBW) infants.

Methods: Two hundred and eighty VLBW infants (28.4 ± 2.6 weeks, 1000 ± 294 g) were enrolled. Psychomotor development was determined at 37.1 ± 2.1 months after birth using the Kyoto Scale of Psychological Development (KSPD), which includes Postural-Motor (P-M), Cognitive-Adaptive (C-A) and Language-Social (L-S) subscales. Subjects were divided into two groups based on whether each developmental quotient (DQ) was ≥85, and the perinatal variables that contributed to a DQ of ≥85 (for each DQ) were determined. The twelve variables that were evaluated included the z scores for body weight (zBW), body length (zBL), head circumference (zHC), which were obtained at birth and at term.

Results: The median P-M, C-A, L-S values and total DQ were 92, 83, 81 and 83, respectively, and the percentage of patients with a DQ of ≥85 were 53%, 44%, 35% and 39%, respectively. A multivariate analysis revealed significant associations between the following variables and the DQs: P-M ≥ 85, GA [odds ratio; OR = 1.11] and zBL at term [OR = 1.26]; C-A ≥ 85, male gender [OR = 0.30], GA [OR = 1.14] and zHC at term [OR = 1.84]; L-S ≥ 85, male gender [OR = 0.55], GA [OR = 1.20] and zHC at term [OR = 1.45]; total DQ ≥ 85, male gender [OR = 0.39], GA [OR = 1.19] and zBL at term [OR = 1.69].

Conclusion: In addition to less prematurity and female gender, a longer body length and larger head circumference at term were important indicators that influenced better psychomotor development in VLBW infants at three years of chronological age.

Keywords: Very-low-birth-weight (VLBW); z score of body weight; z score of body length; z score of head circumference; Psychomotor development at three years of age; Kyoto Scale of Psychological Development (KSPD)

1. Introduction

Most very-low-birth-weight (VLBW) infants are discharged from the neonatal intensive care unit (NICU) without any severe acute complications. However, they are often experience subsequent developmental problems [1,2]. Several factors, including gender

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differences [3], the degree of prematurity [4,5], and medical complications including bronchopulmonary dysplasia [6,7], severe retinopathy of prematurity [8], might be involved with this morbidity even if a radiological evaluation shows no evidence of intracranial damage. In addition, growth restriction during NICU admission is likely to be a significant problem [9,10]. Growth restriction is classified into two categories: intra-uterine growth restriction (IUGR) which is synonymous with small for gestational age (SGA) and another is extra uterine growth restriction (EUGR) which indicates growth restriction observed at the term period regardless of the presence of IUGR. Evaluating the involvement of each to subsequent psychomotor development is likely to be important for clinical practice.

Recently, we obtained three anthropometric z-scores, z score of body weight, z score of body length and z score of head circumference, around the expected date of confinement (EDC) using the Japanese neonatal anthropometric charts [11].

In the present study, we divided VLBW infants into two groups according to their developmental quotients (DQs) and compared perinatal variables between the two groups. In addition, we evaluated the association between each variable on the total and subscale DQs ≥ 85 to determine which factors contribute most to a better subsequent psychomotor development.

2. Subjects and methods

Since April 2008, we have recommended that VLBW infants receive a medical checkup including a physical examination and psychomotor developmental function tests with the Kyoto Scaled Psychomotor Development (KSPD) at three years of chronological age [12]. The KSPD is a standardized and validated developmental test for Japanese children, and the developmental characteristics on the KSPD are well-correlated with those on the Bayley III [13]. A follow-up study of the Neonatal Research Network, Japan, recommended this method be used to evaluate the psychomotor development during the infantile period and the infants' psychomotor development be judged as follows: DQ ≥ 85 as normal, DQ 70 to <85 as border, DQ < 70 as delayed. Informed consent was obtained from parents of each subject according to the registration manual of Neonatal Research Network, Japan.

From 2005 to 2014, 507 VLBW infants were discharged alive from the neonatal nursery in the National Hospital Organization, Saga Hospital. Among them, 6 subjects died after discharge, and 25 had severe neurological complications, including congenital malformation or severe cerebral palsy due to bilateral periventricular leukomalacia or severe intracranial hemorrhage, leaving them unable to sit on their own; therefore, the outcome in 31 subjects was severe. Thirty-five subjects relocated to another prefecture during early infancy, and 90 subjects were lost to follow-up. The remaining 355 subjects received the medical checkup, but 65 failed to complete this examination because of a lack of cooperation. Another 10 were omitted from enrollment because of uncertain anthropometric records during NICU admission. Ultimately, 280 subjects were enrolled in this retrospective cohort study, and the entry rate for those without a severe outcome was 280/476 (59%).

None were observed to have any severe intracranial complications, such as IVH grade ≥ 3, post hemorrhagic hydrocephalus or bilateral cystic PVL, on a serial study of intracranial ultrasound during their stay in the NICU or on magnetic resonance imaging (MRI) before discharge. None were complicated with cerebral palsy of more than level 2 according to the Gross Motor Function Classification System-Expanded and Revised [14] at this evaluation. Head circumference was measured at the occipitofrontal line using a soft measuring tape. The gestational age was determined by the mothers' menstrual history and the findings of antenatal ultrasound in the obstetric chart. We also obtained the three anthropometric z-scores at the expected date of confinement (EDC) using the Japanese neonatal anthropometric charts. Because this anthropometric chart indicates the corresponding z-score from 22 to 41 weeks' gestation, we were able to obtain the z-value at any postconceptional age if the baby was discharged before EDC [15]. However, few effects of early discharge were noted, since no VLBW infants were discharged from our nursery before 38 weeks' gestation.

The KSPD was administered and interpreted by two clinical psychologists (M.H. and T.S) without any association with the acute management in the NICU. They evaluated the psychomotor development of VLBW infants between 30 and 47 months of chronological age (median age 37.0 months). The KSPD consisted of three subscales: Postural-Motor (P-M), Cognitive-Adaptive (C-A) and Language-Social (L-S). The DQs of the three subscales were obtained in each subject.

The subjects were divided into two groups based on each DQ value (<85 or ≥ 85), and 12 perinatal variables, including the presence of multiple birth, maternal height, history of antenatal corticosteroid, gestational age, gender, the incidence of small for gestational age (SGA), z-score of body weight (BW) at birth and EDC, z-score of body length (BL) at birth and EDC, z score of head circumference (HC) at birth and EDC, were compared to clarify which ones were significantly associated with a DQ of ≥ 85 (in total and for each subscale). SGA was defined as when the BL and BW values at birth were less than ten %tile.

This study was approved by the institutional ethics committee (H29-13). Student's unpaired *t*-test, the

Table 1
Profile of study subjects during admission in the neonatal nursery.

Number (male)	280 (135)
Multiple birth (%)	52 (18.6%)
Antenatal corticosteroid (%)*	195 (70.1%)
Maternal height (cm)**	157.2 ± 5.5
Gestational age (weeks)	28.6 ± 3.0
SGA (%)	94 (33.6%)
BW at birth (g)	1000 ± 294
z score of BW at birth	−1.11 ± 1.33
BL at birth (cm)	35.0 ± 3.8
z score of BL at birth	−0.82 ± 1.34
HC at birth (cm)	25.2 ± 2.5
z score of HC at birth	−0.41 ± 0.88
BW at term (g)	2517 ± 280
z score of BW at term	−1.59 ± 1.43
BL at term (cm)	45.7 ± 2.8
z score of BL at term	−1.88 ± 1.45
HC at term (cm)	33.9 ± 1.7
z score of HC at term	0.42 ± 1.30

BW: body weight, BL: body length, HC: head circumference.
All data except the incidence of multiple birth and antenatal corticosteroid were expressed as the mean ± standard deviation.
* Data could not be obtained in two cases.
** Data could not be obtained in seven cases.

Mann-Whitney *U* test and the chi-squared test were used to compare between two groups, and a logistic regression analysis was used to detect the significant variables. The statistical analysis was performed using the software program IBM SPSS Statistics Desktop for Japan, Ver. 19.0 (Tokyo Japan), and a p value <0.05 was defined as significant.

3. Results

The mean gestational age and anthropometric value at birth were 28.4 ± 2.6 weeks, 1000 ± 294 g for BW, 35.0 ± 3.8 cm for BL and 25.2 ± 2.5 cm for HC. The anthropometric z-score at birth was −1.11 ± 1.33 for BW, −0.82 ± 1.33 for BL and −0.42 ± 0.88 for HC, and the incidence of SGA was 94/280 (33.6%). The anthropometric value at term was 2517 ± 280 g for BW, 45.7 ± 2.8 cm for BL and 33.9 ± 1.7 cm for HC. The anthropometric z-score at term was −1.59 ± 1.43 for BW, −1.88 ± 1.45 for BL and 0.42 ± 1.30 for HC (Table 1). A histogram of each subscale and the total DQ in the KSPD test for all study subjects is shown in

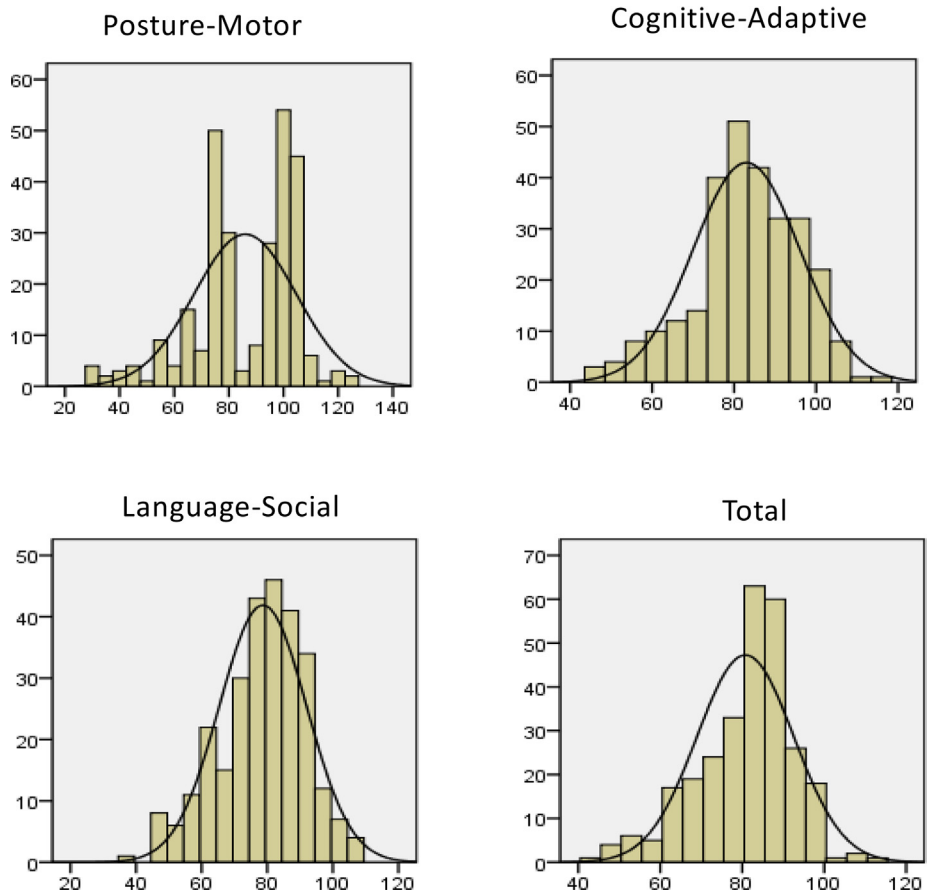

Fig. 1. A histogram of the total developmental quotient (DQ) and the DQs of the three subscales of Postural-Motor (P-M), Cognitive-Adaptive (C-A) and Language-Social (L-S) according to the Kyoto Scale of Psychological Development (KSPD). The median (mean ± SD) DQ of P-M, C-A, L-S was 92 (86.0 ± 18.7), 83 (83.0 ± 13.0) and 81 (78.7 ± 13.4), respectively, and the median (mean ± SD) total DQ was 83 (80.8 ± 11.8). These four histograms did not have a Gaussian distribution according to a Kolmogorov-Smirnov test.

Table 2
Score of each developmental quotient for the KSPD.

Age, months (mean ± SD)	37.1 ± 2.1
Range (median)	30–47 (37)
Total DQs (mean ± SD)	80.7 ± 11.8
Range (median)	43–111 (83)
P-M DQs (mean ± SD)	86.0 ± 18.7
Range (median)	30–124 (92)
C-A DQs (mean ± SD)	83.0 ± 13.0
Range (median)	46–117 (83)
L-S DQs (mean ± SD)	78.7 ± 13.4
Range (median)	37–108 (81)

KSPD: Kyoto Scaled Psychomotor Development, DQ: developmental quotient, P-M: Posture-Motor, C-A: Cognitive Adaptive, L-S: Language-Social, SD; standard deviation.

Fig. 1. The median (mean ± standard deviation) DQ was 92 (86.0 ± 18.7) for P-M, 83 (83.0 ± 13.0) for C-A and 81 (78.7 ± 13.4) for L-S, and the overall DQ was 83 (80.8 ± 11.8) (Table 2). The number (%) of subjects with a DQ ≥ 85 was 148 (53%) in P-M, 122 (44%) in C-A, 97 (35%) in L-S and 108 (39%) in total. The values of the eleven perinatal variables are compared between the DQ ≥ 85 and DQ < 85 groups in Table 3. There were no significant differences in the incidence of multiple birth or the history of receiving antenatal corticosteroids, maternal height or the z-score of BW, BL or HC at birth in total or in any of the three subscale DQs. However, significant differences were observed for every anthropometric z-score at term, gestational age and gender.

A multivariate analysis was performed to clarify the variables significant associated with a score of ≥85 for the total and each subscale DQ. Only the independent variables with a p-value <0.20 in the univariate analysis were adopted for subsequent analyses. A logistic regression analysis revealed that male gender with a p value of 0.001 (odds ratio [OR] = 0.39, 95% confidence interval [CI] = −0.23 to 0.67), gestational age with a p value of <0.001 (OR = 1.19, 95% CI = 1.09–1.31) and zBL at term with a p value of <0.001 (OR = 1.69, 95% CI = 1.37–2.08) were significant variables for a total DQ ≥ 85. Furthermore, gestational age with a p value of 0.017 (OR = 1.11, 95% CI = 1.02–1.20) and zBL at term with a p value of 0.008 (OR = 1.26, 95% CI = 1.06–1.43) were significant variables for a P-M DQ ≥ 85; male gender with a p value of <0.001 (OR = 0.30, 95% CI = 0.18–0.52), gestational age with a p value of 0.005 (OR = 1.14, 95% CI = 1.04–1.25) and zHC at term with a p value of <0.001 (OR = 1.84, 95% CI = 1.45–2.34) were significant variables for a C-A DQ ≥ 85; and male gender with a p value of 0.029 (OR = 0.55, 95% CI = 0.33–0.94), gestational age with a p value of <0.001 (OR = 1.20, 95% CI = 1.09–1.31) and zHC at term with a p value of 0.001 (OR = 1.45, 95% CI = 1.16–1.81) were significant variables for a L-S DQ ≥ 85 (Table 4).

4. Discussion

Growth trajectories of anthropometric z-scores for VLBW infants during NICU admission have demonstrated that each z-score continues to decline from birth to 30–32 weeks after gestation, followed by a flat or modest rising trend until the late preterm period [16,17]. Thereafter, notable catch-up growth of HC is observed, regardless of the length of the gestation period [16,17]. Consequently, most VLBW infants obtain catch-up growth for HC until term (*i.e.,* zHC at term > zHC at birth) [18]. In contrast, such abrupt catch-up growth after the late preterm period is not observed for the zBW or zBL [16,17]; thus, fewer VLBW infants obtain catch-up growth until term [18]. Although the mechanism of the different growth patterns among the zHC, zBW, and zBL until term is unclear, it may be important to explore the critical period and the anthropometric markers that predict subsequent psychomotor development.

In the present study, the z scores of each anthropometric value at birth decreased in order of BW, BL and HC but changed to BL, BW and HC at term. Among the perinatal six anthropometric indices, three anthropometric z scores of DQ ≥ 85 group were almost equivalent with those of DQ < 85 group at birth, but significant difference were observed between two groups for every three z scores at term. In addition, a larger HC and longer BL at term might be important marker to indicate subsequent better psychomotor development at three years of age.

Previous studies have shown that insufficient head growth (z-score < −2.0; microcephalus) is a significant predictor of a poor neurodevelopmental outcome [19–21], especially when evaluated in the later infantile period. In addition, a significant relationship between postnatal head growth and the neurodevelopmental outcome has been observed in VLBW infants [22,23]; all of these findings were in line with the results of the present study. Now, it is an important problem whether the HC accurately reflects the brain volume. In our nursery, we routinely examine the brain MRI findings for VLBW infants before their discharge and conduct a qualitative assessment, including assessing the presence of abnormal signals in the white matter and ventricular wall irregularities. Unfortunately, we have no established procedure for analyzing the brain volume of each component quantitatively, which is a major limitation associated with this study. However, a few reports have described the relationship between the HC and brain volume using MRI. Cheong et al. showed that the quantitative evaluation of the brain volume at term was strongly correlated with the HC at the same period [24], which may suggest that the HC measured at term may reflect the total brain volume.

Table 3
A comparison of the perinatal information between DQ ≥ 85 and DQ < 85 determined by the KSPD.

	P-M DQ ≥ 85	P-M DQ < 85	*p*-value
Number (male)	148 (72)	132 (63)	0.904
Multiple birth (%)	31 (20.9%)	21 (15.9%)	0.356
Antenatal corticosteroid (%)	118 (74.1%)	86 (65.6%)	0.149
Maternal height	157.2 ± 5.6	157.1 ± 5.4	0.810
GA	29.1 ± 2.9	28.1 ± 3.0	0.007
SGA (%)	53 (35.8%)	41 (31.0%)	0.449
zBW at birth	−1.10 ± 1.24	−1.10 ± 1.43	0.997
zBL at birth	−0.83 ± 1.34	−0.81 ± 1.34	0.919
zHC at birth	−0.41 ± 0.86	−0.42 ± 0.92	0.928
zBW at term	−1.43 ± 1.28	−1.78 ± 1.56	0.037
zBL at term	−1.67 ± 1.33	−2.15 ± 1.54	0.004
zHC at term	0.62 ± 1.19	0.19 ± 1.39	0.007
	C-A DQ ≥ 85	C-A DQ < 85	*p*-value
Number (male)	122 (43)	158 (92)	<0.001
Multiple birth (%)	22 (18.0%)	30 (19.0%)	0.878
Antenatal corticosteroid (%)	84 (70.0%)	111 (70.3%)	1.00
Maternal height (cm)	157.3 ± 5.2	157.0 ± 5.8	0.709
GA	29.3 ± 2.7	28.1 ± 3.1	0.001
SGA (%)	47 (38.5%)	47 (29.7%)	0.128
zBW at birth	−1.07 ± 1.28	−1.14 ± 1.37	0.687
zBL at birth	−0.85 ± 1.40	−0.79 ± 1.28	0.699
zHC at birth	−0.41 ± 0.89	−0.42 ± 0.88	0.883
zBW at term	−1.21 ± 1.22	−1.89 ± 1.51	<0.001
zBL at term	−1.40 ± 1.29	−2.26 ± 1.46	<0.001
zHC at term	0.85 ± 1.07	0.08 ± 1.36	<0.001
	L-S DQ ≥ 85	L-S DQ < 85	*p*-value
Number (male)	97 (39)	183 (96)	<0.001
Multiple birth (%)	15 (15.5%)	37 (20.2%)	0.420
Antenatal corticosteroid (%)	65 (67.7%)	130 (71.4%)	0.582
Maternal height (cm)	157.7 ± 5.1	156.9 ± 5.7	0.223
GA	29.6 ± 2.8	28.1 ± 3.0	<0.001
SGA (%)	35 (36.1%)	59 (32.2%)	0.595
zBW at birth	−1.20 ± 1.24	−1.06 ± 1.37	0.419
zBL at birth	−0.85 ± 1.34	−0.80 ± 1.33	0.794
zHC at birth	−0.44 ± 0.83	−0.40 ± 0.91	0.697
zBW at term	−1.30 ± 1.39	−1.75 ± 1.42	0.011
zBL at term	−1.53 ± 1.43	−2.07 ± 1.43	0.003
zHC at term	0.76 ± 1.19	0.24 ± 1.32	0.001
	Total DQ ≥ 85	Total DQ < 85	*p*-value
Number (male)	108 (39)	172 (96)	0.001
Multiple birth (%)	20 (18.5%)	32 (18.6%)	1.000
Antenatal corticosteroid (%)	71 (67.0%)	124 (72.1%)	0.419
Maternal height (cm)	157.5 ± 5.2	157.0 ± 5.7	0.434
GA	29.6 ± 2.8	28.1 ± 3.0	<0.001
SGA (%)	38 (35.2%)	56 (32.6%)	0.697
zBW at birth	−1.10 ± 1.18	−1.11 ± 1.41	0.959
zBL at birth	−0.78 ± 1.35	−0.85 ± 1.33	0.668
zHC at birth	−0.44 ± 0.86	−0.40 ± 0.90	0.709
zBW at term	−1.15 ± 1.25	−1.88 ± 1.46	<0.001
zBL at term	−1.32 ± 1.28	−2.24 ± 1.44	<0.001
zHC at term	0.85 ± 1.13	0.15 ± 1.33	<0.001

KSPD: Kyoto Scale of Psychomotor Development, DQ: developmental quotient, P-M: Postural-Motor, C-A: Cognitive-Adaptive, L-S: Language-Social, GA: gestational age, zBW: z-score of body weight, zBL: z-score of body length, zHC: z-score of head circumference.
All data except the incidence of male gender, multiple birth and antenatal corticosteroid were expressed as the mean ± standard deviation.

In the current study, not the BW but the BL at term was a significant indicator predicting the subsequent psychomotor development. We usually focus on the daily variation in the BW during NICU admission, and a larger increment in the BW until term seems to be a useful marker for predicting a good outcome [25].

Table 4
Logistic regression analyses to predict each DQ ≥ 85 in VLBW infants at 3 years of age.

P-M DQ ≥ 85	B	Wald	P value	Exp(B)	95% CI
GA	0.100	5.73	0.017	1.105	1.018 1.200
zBL at term	0.229	6.94	0.008	1.258	1.060 1.432
C-A DQ ≥ 85	B	Wald	P value	Exp(B)	95% CI
Male	−1.194	18.62	P < 0.001	0.303	0.176 0.521
GA	0.131	8.04	0.005	1.141	1.041 1.249
zHC at term	0.612	24.89	P < 0.001	1.843	1.450 2.344
L-S DQ ≥ 85	B	Wald	P value	Exp(B)	95% CI
Male	−0.591	4.766	0.029	0.554	0.326 0.941
GA	0.180	14.57	P < 0.001	1.197	1.091 1.312
zHC at term	0.370	10.38	0.001	1.448	1.156 1.814
Total DQ ≥ 85	B	Wald	P value	Exp(B)	95% CI
Male	−0.942	11.64	0.001	0.388	0.225 0.668
GA	0.175	13.47	<0.001	1.191	1.085 1.308
zBL at term	0.522	24.03	<0.001	1.685	1.368 2.075

Only independent variables whose p-value was <0.05 are shown.
DQ: developmental quotient, P-M: Postural-Motor, C-A: Cognitive-Adaptive, L-S: Language-Social, zBL: z score of body length, zBW: z score of body weight, CI: confidence interval.

However, unexpected weight gain was sometimes observed without any increase in the energy intake and therefore the total BW may not accurately reflect the lean body mass. We pay less attention to weekly variations in the BL than to those variations in the HC, but the trajectory of BL until term should be monitored. Watanabe et al. found that the z scores of the BL and HC at term were significant determinants of the white matter volume obtained by MRI, while the z score of the BW at term was not [26].

Several other limitations associated with the present study in addition to the lack of quantitative evaluation of the brain volume by brain MRI warrant mention. First, we were unable to take the social status of the subjects into consideration because it was difficult to obtain information on the economic situation of the subjects' families. Second, the check-rate of the KSPD among the total subject population, except for those exhibiting severe outcomes, was 59%, which might be lower than in other follow-up studies. The strengths of this study were that it was a retrospective cohort study conducted at a single facility and that all of the data were treated in a structured and uniform manner.

5. Conclusion

In addition to less prematurity and a female gender, a longer BL and a larger HC at term may be significant markers influencing a better psychomotor development in early childhood. However, it is not clear whether or not similar effects will continue at later periods. Therefore, further follow-up is necessary to clarify this relationship.

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