

Title page

*Title:* Promoting Factors of physical and mental development in early infancy: A comparison of preterm delivery/low birth weight infants and term infants

Kaori Hayashida<sup>a,b</sup>, Mikiya Nakatsuka<sup>a,\*</sup>

a Graduate School of Health Sciences, Okayama University 2-5-1 Shikata, Kita-ku, Okayama City, Okayama 700-8558, JAPAN

b Fukuyama Heisei University, 117-1 Kami-iwanari-shito, Miyuki-cho, Fukuyama City, Hiroshima 720-0001, JAPAN

### **Correspondence**

Mikiya Nakatsuka, M.D., Ph.D

Graduate School of Health Sciences, Okayama University

2-5-1 Shikata, Kita-ku, Okayama City, Okayama 700-8558, JAPAN

Phone & FAX #: +81-86-235-6895

E-mail: mikiya@cc.okayama-u.ac.jp

\*Address correspondence to Mikiya Nakatsuka, M.D., Ph.D

Graduate School of Health Sciences, Okayama University 2-5-1 Shikata, Kita-ku, Okayama City, Okayama 700-8558, JAPAN

Phone & FAX #: +81-86-235-6895 E-mail: mikiya@cc.okayama-u.ac.jp

*Keywords:* child-rearing anxiety, early infancy, infant development, low birth weight, preterm delivery

## **Abstract**

*Objective* We examined correlations between various factors and the physical and mental development of 4-month-old infants assessed using a multi-faceted evaluation.

*Methods* In Hiroshima prefecture, Japan, we distributed 1,402 self-administered questionnaires to consenting mothers of infants that underwent a 4-month health checkup. Questionnaires included the Japan Child and Family Research Institute (JCFRI) Child Rearing Support Questionnaire, and the KIDS type A. Data were examined from 318 of these mother-child pairs.

*Results* Comparison between infants in a preterm delivery or low birth weight (LBW) group (preterm and/or LBW group; n=31) and a term delivery appropriate for date (AFD) infant group (term AFD group; n=287) revealed that the preterm and/or LBW group had significantly higher mother child-rearing anxiety and difficult baby scores, along with significantly lower infant development and motor skill scores.

Within the term AFD group, infants of primipara mothers showed significantly higher scores for motor skill and sociability with adults than infants of multipara mothers. Language comprehension scores were significantly higher in infants that were exclusively breastfed than those formula-fed or combined breastfed and formula-fed. Verbalization scores were significantly higher in infants whose mothers worked than infants whose mothers did not work. Infants with siblings younger than 4 years old exhibited significantly lower scores for motor skill, verbalization, and sociability with adults than infants without siblings or with siblings at least five years old. In particular, we found a mother's child-rearing anxiety was related to many areas of infant development.

*Conclusions* Evaluating the absence or presence of such factors and conducting preventive treatment could promote healthy infant development.

## **Introduction**

There are various factors that influence the physical and mental development of children. It has been reported that psychological stress [1], depression[1,2], anxiety[1,2], and anger [2] experienced during pregnancy may affect child development. Exposure to environmental materials such as mercury [3] and cadmium [3], smoking [4], and alcohol consumption [5] during pregnancy are also known to affect development.

Malnutrition of infants is reported to affect their development in developing countries [6], while preterm delivery, low birth weight (LBW), maternal depression [7], and mother–infant interactions [8] such as inadequate parenting attitude and lack of affection for the infant are reported to affect development in developed countries. Furthermore, it was reported that child-rearing environmental factors such as family and overcrowding in day care centers affected development [9] .

Child development is evaluated by various indices. In most previous studies, however, it was evaluated by one aspect of observing points. The Denver Developmental Screening Test (DDST) [10] was devised to provide a simple method of screening for evidence of slow development in infants and preschool children. The Brazelton Neonatal Behavioral Assessment Scale (B-NBAS) [11] measures neonatal behavioral development while the Bayley Scales of Infant Development (BSID) [12] measures mental and motor development and tests the behavior of infants aged 1–42 months.

In the present study, we used the Kinder Infant Development Scale (KIDS) test, which includes the following six features: physical ability, verbal ability, cognitive abilities, social behavior for adults, social behavior for children, and manipulation [13]. This test was developed in Japan in 1989 and has been used for multifaceted assessment of infant development. It was standardized from the data of 6,000 infants, and its validity and

reliability has been proved in healthy infants and infants with special needs [14]. Furthermore, mothers without special knowledge can fill out a form of the test by observing her infant's behavior.

Previous research using KIDS has reported that supportive co-parenting and maternal cognitive stimulation greatly influence child development [15]. However, this research evaluated 9-month-old infants, which is a relatively late phase of development; therefore, it did not distinguish between term infants and preterm or low birth weight (LBW) infants. At 9 months, intervention for promoting development can be difficult because the mother-child relationship is established. Therefore, factors that impede infant development must be detected earlier. In addition, when compared with term infants, preterm infants are more likely to exhibit problems in language development [16] while LBW infants are more likely to exhibit delayed motor and social development [17]. Therefore, preterm and LBW infants should be examined separately from and term appropriate for date (AFD) infants.

In the present study, we conducted a multifaceted assessment of the development of 4-month-old infants using KIDS and compared the development of term infants with that of preterm and/or LBW infants. In addition, we investigated factors that may influence the development of healthy infants.

## **Materials and Methods**

Between July 2010 and August 2011, we distributed 1,402 self-administered questionnaires to consenting mothers living in Hiroshima prefecture, Japan, whose infants underwent the 4-month-old infant health checkup. Subjects completed the questionnaires at home and returned them by post. This study was conducted with the approval of the Ethics Committee of the Graduate School of Health Sciences, Okayama University.

The survey investigated the following: 1) mother's basic attributes (age, childbirth history, employment), 2) health during pregnancy and type of delivery, 3) maternal stress during pregnancy to the present, 4) infant's basic attributes (sex, age, and weight at birth and at the 1- and 4-month infant health checkups), 5) child-rearing state, 6) mother's child-rearing troubles and anxiety, 7) family function, and 8) household's economic state. Stress levels were self-assessed on a scale from 0, indicating "not stressed at all", to 10, indicating "very stressed".

Four of the six subscales of the Japan Child and Family Research Institute (JCFRI) Child Rearing Support Questionnaire, "mothers' feeling of child-rearing difficulty," "child-rearing anxiety," "family function state," and "difficult baby," excluding the two items of "husband poor mental and physical condition" and "child mental and physical state" were used to evaluate factors possibly related to the degree of the mother's child-rearing anxiety. KIDS type A, which can be used to evaluate healthy infants aged from 1 to 11 months, was used to assess infant development state.

### Statistical analysis

SPSS ver. 18.0 was used to perform statistical analyses. Student's *t*-test was used to compare continuous variables among groups, and the chi-squared test was used to compare categorical variables. The Mann–Whitney U test or the Kruskal–Wallis test was used to compare median values of non continuous variables in the KIDS and child-rearing support questionnaire scores. A p-value of  $<0.05$  was considered statistically significant.

### Results

We received questionnaires from 421 mother–child pairs (response rate: 30.0%). We excluded responses if an individual other than the mother completed the questionnaire or was the primary caregiver, if the infant was not 4 months old, if the infant was treated for an illness, or if the mother had multiple children. After exclusion, we analyzed data from 318 mother–child pairs. Data were assigned to one of two groups on the basis of the infant’s characteristics. One group included LBW (<2,500g) or preterm delivery (<37 gestational weeks) infants (preterm and/or LBW group), whereas the other included term delivery AFD infants (term AFD group).

### *1) Clinical features*

The rate of hospitalization during pregnancy and the rate of caesarean sections (CS) were significantly higher in the preterm and/or LBW group than in the term AFD group. Infant weight was significantly lower in the preterm and/or LBW group at both the 1- and 4-month checkups (Table 1). While no significant differences were observed between feeding methods, the answer “infant is feeding well” was significantly less common in the preterm and/or LBW group than in the term AFD group. When primipara and multipara mothers were compared in the term AFD group, the birth dates of infants born to primipara mothers were significantly later than those of infants born to multipara mothers.

### *2) Social characteristics*

Unwanted pregnancies were significantly more common in the preterm and/or LBW group (Table 2) than in the term AFD group. No significant differences were noted between the groups in terms of husband support during pregnancy, family composition, number of

children, employment status, and household annual income. Household income was significantly higher for multipara mothers than for primipara mothers.

### *3) Child-rearing anxiety, Psychological stress*

Scores for the mother's feeling of child-rearing difficulty and a difficult baby, as well as dysfunctional family scores, were significantly higher in the preterm and/or LBW group (Table 3) than in the term AFD group.

Items including "husband takes good care of our child and myself," "I am glad I married this person," and "my husband is happy" were reported with significantly lower frequency, while items such as "our household doesn't function well" and "my husband doesn't actively get involved in housework or child-rearing" were reported with significantly higher frequency, in the preterm and/or LBW group than in the term AFD group. Answers such as "I don't know what to do for my child" and "I don't quite understand the daily rhythm of my child" were also significantly more common in the preterm and/or LBW group than in the term AFD group.

In the term AFD group, primipara mothers had significantly higher scores for a difficult baby compared with multipara mothers. However, multipara mothers had significantly higher dysfunctional family scores. No significant difference was observed between primipara and multipara mothers in terms of the presence of someone to discuss childcare with and/or to help with child-rearing.

We also examined psychological stress and found that psychological stress was lower during hospitalization and higher during pregnancy and 2–3 days after discharge in both the preterm and/or LBW and term AFD groups. However, we observed no significant differences between groups for any of these periods.

Within the term AFD group, primipara mothers showed the highest psychological stress scores from discharge to the 1-month checkup. In contrast, multipara mothers showed the highest psychological stress scores during pregnancy. During hospitalization after delivery, during the 2–3 days after discharge, and from that time until the 1-month checkup, psychological stress scores were significantly higher in primipara mothers than in multipara mothers.

#### *4) Development (KIDS) of infants*

With regard to the KIDS scores, motor skills and language comprehension scores were significantly lower in the preterm and/or LBW group than in the term AFD group. No significant differences were observed for any other item (Table 4).

#### *Various factors associated with development (KIDS) in the term AFD group*

We investigated infant development and related factors within the term AFD group.

##### *1) Parity*

In the term AFD group, scores for motor skills and sociability with adults were significantly higher for infants born to primipara mothers than for those born to multipara mothers, while verbalization scores also tended to be higher (primipara:  $6.3 \pm 1.4$ , multipara:  $5.9 \pm 1.6$ , mean  $\pm$  SD). No significant differences were observed between groups in any of the other items (Table 4).

##### *2) Maternal age*

Infants born to mothers in their 40's had significantly higher verbalization scores compared with infants born to mothers in their 20's or 30's (Table 5). The proportion of primipara mothers in each age range was 66.0% (20's), 37.0% (30's), and 70.0% (40's). Therefore, no significant difference was observed between the proportion of primipara mothers in their 40's and 20's; however, the proportion of primipara mothers in their 30's was lower than that of primipara mothers in the other two age groups.

### *3) Type of delivery*

Infants born via CS had significantly lower diet scores compared with infants born normally (vaginal delivery:  $4.3 \pm 1.4$ , CS:  $3.8 \pm 1.3$ , mean  $\pm$  SD); motor skill scores also tended to be low in the former group (Table 6). No other significant relationships were observed between type of delivery and scores for any other items.

### *4) Fatigue at delivery*

No significant relationships were observed between fatigue at delivery and scores for other items (Table 6).

### *5) Sex of infant*

No significant relationships were observed between infant sex and scores for other items (Table 6).

### *6) Type of feeding*

Exclusively breastfed infants had significantly higher language comprehension scores compared with formula-fed or combined breastfed and formula-fed infants; motor skill scores also tended to be higher in the former than in the latter group (Table 7). No other significant relationships were observed between feeding method and scores for any other items.

### *7) Household lifestyle*

At 4 months after birth, infants born to working mothers had significantly higher verbalization scores compared with infants born to nonworking mothers (Table 8). No significant relationships were observed between household income or satisfaction with current lifestyle and scores for other items.

### *8) Family*

No significant differences were observed between those living with nuclear families and those living with extended families (Table 9). Compared with infants with no siblings or those with siblings aged  $\geq 5$  years, infants with siblings aged  $< 4$  years exhibited significantly lower motor skill scores, verbalization scores (no siblings:  $6.3 \pm 1.4$ , sibling aged  $< 4$  years:  $5.7 \pm 1.6$ , mean  $\pm$  SD), and scores for sociability with adults.

### *9) Analysis of factors that strongly influence 4-month-old infant development*

Multiple regression analysis was used to evaluate the influence of background factors on each development score. The results showed the following: [Motor score] =  $-0.068\chi^1$  [feeling of child-rearing difficulty scale] + 10.798; [Motor skill score] =  $0.807\chi^1$  [sibling age] -  $0.067\chi^2$  [feeling of child-rearing difficulty scale] +  $0.251\chi^3$  [gestational weeks at birth] +  $0.471\chi^4$  [feeding method] + 0.855; [Language comprehension score] =  $0.586\chi^1$  [feeding method] + 5.970; [Verbalization score] =  $0.585\chi^1$  [sibling is age] -  $0.052\chi^2$  [feeling of child-rearing difficulty scale] +  $0.969\chi^3$  [maternal age] + 6.562; [Sociability with adults score] =  $1.024\chi^1$  [sibling is age] -  $0.071\chi^2$  [feeling of child-rearing difficulty scale] + 13.363; [Diet score] =  $-0.059\chi^1$  [feeling of child-rearing difficulty scale] +  $0.159\chi^2$  [gestational weeks at birth] - 1.061.

## **Discussion**

In the present study, we examined six items that assessed the development of 4-month-old infants and revealed significant correlations for each item. Previous studies have revealed that postpartum depression can affect emotional development in 5-year-old children [18] and cognitive development in 3-year-old children [19]. In 4-year-old children, maternal antenatal anxiety affected the child's emotional development and was associated with behavioral issues such as inattention, hyperactivity, and conduct problems [20]. Furthermore, maternal smoking during pregnancy was related to impaired cognitive development [21]. In 2-year-old children, the parents' educational background and family's social class were related to the child's mental development [22].

Furthermore, developmental delays in 1-year-old children (12 to 18 months) were reportedly correlated with maternal depression during pregnancy [23]. In addition, it was reported that breastfeeding affected mental development in 12- and 14-month-old children [24,

25] and that mother and child interactions influenced the child's socio-emotional development [8]. It has also been reported that maternal anxiety and depression during the third trimester of pregnancy were related to delayed mental development in 8-month-old infants [26]. These studies indicate that maternal condition, both during pregnancy and after childbirth, along with the child's home environment, influence child development.

In the present study, we evaluated the development of 4-month-old infants. Early evaluation of development in infants and implementation of appropriate measures in case problems are detected can improve subsequent development. Currently in Japan, infants undergo a health checkup at 4 months. We believe that research on infants during this period can provide highly significant results that can influence government initiatives.

In a study of 4-month-old infants, it was reported that third trimester maternal anxiety and depressive state were related to the mother's reactions to infant behavior [27] and that the mother's expressions during mother–infant interactions influence subsequent emotional development [28]. Another study reported that in 3-month-old infants, prenatal stress was related to the infant's mental and psychomotor development as well as temperament [26]. However, these previous studies only investigated mental and developmental milestones in infants, whereas developmental delays were overlooked. Therefore, our study focused on developmental delays using the KIDS test and comprehensively evaluated scores for both behavioral and mental development.

#### *Preterm and/or LBW infants*

This study compared the development of 4-month-old infants (nonadjusted age) with LBW and/or preterm birth with that of term infants. We found that LBW and preterm birth infants showed lower scores for KIDS motor skills and language comprehension

development.

Previous studies also reported that developmental problems are common in LBW and/or preterm birth infants [16, 17]. This may be due to LBW or complications in neural development while in the womb or during delivery, there by influencing development [29] and leading to respiratory complications such as chronic respiratory tract disease or asthma [30] or cardiovascular disturbances [31] .

On the other hand, it was reported that greater maternal parenting stress leads to diminished communication skills in 3-month-old preterm infants [32]. Therefore, even when there is no problem in the preterm infant, mothers and/or the child-rearing environment may influence subsequent child development.

The results of the present study indicate that prenatal hospitalization and CS delivery were more common in mothers of LBW and/or preterm infants than in mothers of term AFD infants. It was reported that maternal prenatal hospitalization could cause post-traumatic stress symptoms in mothers, which can lower the quality of parent–infant interactions. The rate of postpartum depression is known to be higher in mothers who undergo CS than in mothers that undergo vaginal delivery [33], and this postpartum depression may lead to poor mother–child attachment. Furthermore, environmental factors during the infant’s hospitalization can also lead to poor mother–child attachment, which may exert adverse effects on the infant’s development.

In the present study, mothers of LBW and/or preterm infants had significantly higher scores for both the difficult baby and feeling of child-rearing difficulty subscales compared with mothers of term AFD infants. Past studies have also reported that mothers of preterm birth infants are susceptible to psychological stress for 2 years after delivery [20 , 28] . In addition, high maternal parenting stress can lead to confused mother–child interactions [34] and exert adverse effects on recognition development in 18-month-old infants [35] .

Other reports have confirmed a relationship between unwanted pregnancy and LBW infants [36]. In the present study, the rate of unwanted pregnancies was significantly higher among mothers of LBW and/or preterm infants than among mothers of term AFD infants. Furthermore, family dysfunction was more common among the former than among the latter, and marital relationships suffered when mothers felt dissatisfied with their husbands for not participating in housework or child-rearing. These environmental factors may also influence infant development.

It appears that the presence or absence of background factors such as unwanted pregnancy and family dysfunction should be confirmed in mothers of LBW and/or preterm infants. Moreover, a mother's feelings of child-rearing difficulty should be assessed early, and if a problem is detected, proactive intervention such as a health consultation with a public health nurse or midwife, health guidance, and child-rearing support should be provided.

#### *Developmental Risk Factors in Term Infants*

This study found several factors that influence the development of term AFD infants. These factors are discussed below.

##### *1) Parity*

Till date, no study has investigated relationships between maternal parity and the development of 3- to 4-month-old infants. Our study found that infants born to primipara mothers exhibited better development of motor skills, sociability with adults, and verbalization compared with infants born to multipara mothers.

We also found that primipara mothers more frequently experienced maternal

child-rearing anxiety and mental stress and felt that child-rearing was difficult; this could exert adverse effects on infant development. In particular, mental stress was common during hospitalization for delivery, during the 2–3 days following discharge, and from that time until the infant’s 1-month health checkup.

However, our investigation of family function found that multipara mothers more often answered “my husband is only involved in his work and hobbies” and were less likely to answer “my husband is happy”. Therefore, multipara mothers more often reported a poor relationship with their husband and showed higher family dysfunction scores compared with primipara mothers.

The poor marital relationships and family dysfunction commonly seen in multipara mothers may lead to decreased infant development scores. Therefore, we believe that support is not only necessary for mothers but also for couples and families as a whole. Moreover, multipara mothers also experience high levels of mental stress during their first experience with childbirth, subsequently adjusting to child-rearing. Therefore, proactive support for mothers that find child-rearing difficult may help in promoting the infant’s development.

## *2) Maternal age*

The infants of mothers in their 40’s had better verbalization scores compared with those of mothers in their 20’s and 30’s. Previous studies have also shown that increased maternal age at delivery contributed to higher naming vocabulary scores and lower strengths and difficulties scores (social and emotional difficulties) in 3-and 5-year-old children [37]. Furthermore, older mothers are better educated, have higher family incomes, are more often married, and have greater child well-being [37].

We also found that 100% teens, 65.0% subjects in their 20's, 36.4% subjects in their 30's, and 40.0% subjects in their 40's had an annual income of less than 4 million yen. Meanwhile, 0% teens, 96.2% subjects in their 20's, 99.4% subjects in their 30's, and 100% subjects in their 40's lived with a husband or partner. Therefore, there was a trend whereby increased age indicated a higher annual income and a greater likelihood of living with a husband or partner. These factors are likely to exert favorable effects on verbal development in infants.

### *3) Maternal Stress in late pregnancy*

Our study did not reveal any correlation between maternal mental stress and infant development scores. However, strong prenatal stress, as indicated by cortisol levels in late pregnancy [26], can delay both mental and motor development in 3- and 8-month-old infants. The present study asked mothers to self-evaluate their prenatal stress levels at 4 months postpartum, but this evaluation may not have been accurate. In the future, stress during late pregnancy should be prospectively evaluated using indicators such as biological markers in addition to self-evaluation.

### *4) Type of delivery*

We found that infants born via CS tended to exhibit delayed motor and diet development compared with infants born via vaginal delivery. Postpartum depression is more common with CS than with vaginal delivery [33], and CS delivery may influence mother-child attachment and infant development. Other studies indicate, however, that CS had no effect on intelligence or delayed motor development in 6- to 7-year-old children [38].

In the future, the subsequent development of infants with a tendency for delayed motor and diet development at 4 months should be monitored.

#### *5) Fatigue at delivery*

The present study found no correlation between the presence or absence of maternal fatigue at delivery and infant development scores. However, a study that examined mothers of 18-month-old children found a relationship between the mother's fatigue throughout the first 18 months after birth and infant development [39]. Therefore, long-term persistence of fatigue after birth may influence development throughout early childhood. Therefore, it may be necessary to evaluate fatigue at delivery and during the period following delivery and offer support to mothers with persistent fatigue to improve the child's development.

#### *6) Feeding*

Exclusively breastfed infants exhibited significantly higher scores for language comprehension compared with formula-fed or combined breastfed and formula-fed infants; they also tended to exhibit higher scores for motor skills. Past studies have shown that breastfed infants have significantly improved cognitive development compared with formula-fed infants, and these effects continue from 6 months to 15 years of age [40]. It was reported that long-chain polyunsaturated fatty acids (LCPUFAs), docosahexaenoic acid (DHA), and arachidonic acid (AA), all found in breast milk, support neuron development [40]. Moreover, increased maternal responsiveness promoted by the infant's suckling [41] also has a favorable effect on infant development, and mothers who engage in breastfeeding are generally more educated than formula-feeding mothers [22]. This also may have a favorable

effect on infant development.

### *7) Household lifestyle*

This study found that at 4 months after birth, the infants of working mothers had better verbalization development compared with infants of nonworking mothers. Working mothers in Japan are known to maintain child-rearing time by decreasing their workload and leisure time, even after returning to work after maternity leave [42]. Therefore, mother and infant contact time is maintained even if the mother is working. Furthermore, it is likely that working mothers regularly place infants in the care of a daycare center or their grandparents. Those environments may promote infant development. In support of this view, infants who spend long periods of time at daycare centers showed a favorable cognitive development [43]. This suggests that when mothers are not working, infants need to be introduced early to places such as playgroups, where they can be exposed early to relationships other than the mother–child relationship.

### *8) Family*

While no significant differences in infant development were observed between nuclear and extended families, poorer motor skills, verbalization, and sociability with adults were observed in infants with siblings aged <4 years compared with infants without siblings or siblings aged  $\geq 5$  years. Mothers with another child aged <4 years are likely to be heavily involved in that child's care, thus decreasing the amount of time they spend on the newborn infant. This may exert an adverse influence on the development of motor skills, sociability with adults, and verbalization.

A high proportion of multipara mothers in this study (74.7%) had another child aged <4 years. This could be why infants of multipara mothers exhibited significantly poorer development of motor skills, sociability with adults, and verbalization compared with primipara mothers. Furthermore, the proportion of mothers with another child aged <4 years was as follows: 32.1%, 20's; 43.9%, 30's; 10.0%, 40's. Therefore, a significantly higher proportion of mothers in their 20's and 30's had another child aged <4 years compared with mothers in their 40's. This could also be a factor behind poorer verbalization scores for infants born to mothers in their 20's and 30's than for infants born to mothers in their 40's.

#### *9) Analysis of factors that strongly influence 4-month-old infant development*

Multiple regression analysis in this study indicated that the feeling of child-rearing difficulty, sibling age, gestational age at birth, feeding method, and maternal age range were factors strongly related to 4-month-old infant development. In particular, the maternal feeling of child-rearing difficulty was related to infant development in many aspects. The maternal feeling of child-rearing difficulty needs to be objectively evaluated, and the scale for its evaluation needs to be optimized. Furthermore, taking early evaluation and intervention into consideration, prevention should begin prenatally with awareness campaigns and education at obstetrician clinics, and it is likely that assessment and support soon after childbirth could be effective.

This study revealed that various factors exert adverse effects on infant development. Future studies should examine whether preventive measures in support of pregnant women and mothers with infants in whom these factors are present has favorable effects on the child's subsequent development. Therefore, it is important that the 4-month-old infant checkup is used to assess overall infant development using the KIDS test and recorded by the mother.

In the present study, recovery rate of questionnaires was relatively low. To apply our tests to every single 4-month-old infant, carefully selected questionnaires and KIDS test should be sent in advance of the checkup.

In the future, further studies are required for the evaluation of infant development soon after birth, at the 1-month-old infant health checkup, to enable earlier intervention.

### **Acknowledgements**

This work was supported by Japan Society for the Promotion of Science (JSPS) KAKENHI Grant Number 24792603, Grant-in-Aid for Young Scientists (B).

### **Conflict of interest**

We do not have a financial relationship with any organization.

### **References**

1. Talge NM., Neal C. & Glover V. Antenatal maternal stress and long-term effects on child neurodevelopment: how and why? *Journal of Child Psychology and Psychiatry*. 2007;48: 245-261.
2. Field T, Diego M, Hernandez-Reif M, Schanberg S, Kuhn C, Yando R, et al. Pregnancy anxiety and comorbid depression and anger: effects on the fetus and neonate. *Depression and Anxiety*. 2003;17:140-151.
3. Windham GC, Zhang L, Gunier R, Croen LA, Grether, JK. Autism spectrum disorders in relation to distribution of hazardous air pollutants in the San Francisco Bay area. *Environmental Health Perspectives*, 2006;114:1438-44.

4. Braun JM, Froehlich TE, Daniels JL, Dietrich KN, Hornung R, Auinger P, Lanphear BP. Association of environmental toxicants and conduct disorder in U.S. children: NHANES 2001-2004. *Environmental Health Perspectives*. 2008;116:956-62.
5. Sood B, Delaney-Black V, Covington C, Nordstrom-Klee B, Ager J, Templin T, et.al. Prenatal alcohol exposure and childhood behavior at age 6 to 7 years: I. dose-response effect. *Pediatrics*, 2001;108: E34.
6. Walker SP, Wachs TD, Gardner JM., Lozoff B, Wasserman GA, Pollitt E, Carter JA. Child development: risk factors for adverse outcomes in developing countries. *Lancet*. 2007;369: 145-157.
7. Jacqueline M McGrath, Kathie Records, Michael Rice. Maternal depression and infant temperament characteristics. *Infant Behavior and Development*. 2008; 31:71-80.
8. Cerezo MA, Pons-Salvador G, Trenado RM. Mother-infant interaction and children's socio-emotional development with high- and low-risk mothers. *Infant Behavior and Development*. 2008; 31:578-89.
9. Evans GW. Child development and the physical environment. *Annual Review of Psychology*. 2006; 57: 423-451.
10. Frankenberg WK, Dodds J, Archer P, Shapiro H, Bresnick B. The Denver II: a major revision and restandardization of Denver developmental screening test. *Pediatrics*. 1992;89: 91-97.
11. Brazelton, TB, Nugent JK. *The Neonatal Behavioural Assessment Scale*. 3rd ed. *Clinics in Developmental Medicine* 137. London: MacKeith Press, CUP. 1995.
12. Bayley, N. *Bayley scales of infant development*. San Antonio, 2nd ed. The Psychological Corporation. Harcourt Brace & Company. 1993.
13. Miyake K, Ohmura M, Takashima M, Yamauchi S, Hashimoto K. *Kinder infant development scale Manual*: HattatsukagakuKenkyuKyoiku Center, Tokyo.1989. [Article

in Japanese]

14. Hashimoto K, Matsui N, Yakuwa H, Miyamura K. Evaluation of the family-rated kinder infant development scale (KIDS) for disabled children. *Jikeikai Medical Journal*. 2012; 59:5-10. [Article in Japanese]
15. Cheng S, Maeda T, Yamagata Z, Tomiwa K, Yamakawa N. Japan Children's Study Group. Comparison of factors contributing to developmental attainment of children between 9 and 18 months. *Journal Epidemiology*. 2010;20:S452-58.
16. Caravale B, Tozzi C, Albino G, Vicari S. Cognitive development in low risk preterm infants at 3-4 years of life. *Archives of Disease in Childhood. Fetal and Neonatal Edition*. 2005;90:F474-79.
17. Hediger ML, Overpeck MD, Ruan WJ, Troendle JF. Birth weight and gestational age effects on motor and social development. *Paediatric & Perinatal Epidemiology*. 2002;16; 33-46.
18. Murray L, Sinclair D, Cooper P, Ducournau P, Turner P, Stein A. The socio-emotional development of 5-year-old children of postnatally depressed mothers. *Journal of Child Psychology and Psychiatry*. 1999;40:1259-71.
19. Sharp D, Hay DF, Pawlby S, Schmücker G, Allen H, Kumar R. The impact of postnatal depression on boys' intellectual development. *Journal of Child Psychology and Psychiatry*. 1995;36:1315-36.
20. O'Connor TG, Heron J, Golding J, Beveridge M, Glover V. Maternal antenatal anxiety and children's behavioural/emotional problems at 4 years. Report from the Avon Longitudinal Study of Parents and Children. *The British Journal of Psychiatry*. 2002;180:502-8.
21. Julvez J, Ribas-Fitó N, Torrent M, Forns M, Garcia-Esteban R, Sunyer J. Maternal smoking habits and cognitive development of children at age 4 years in a population based birth cohort. *International Journal of Epidemiology*. 2007;36:825-32.

22. Gómez-Sanchiz M, Cañete R, Rodero I, Baeza JE, González JA. Influence of breast-feeding and parental intelligence on cognitive development in the 24-month-old child. *Clinical Pediatrics (Philadelphia)*. 2004;43:753-61.
23. Deave T, Heron J, Evans J, Emond A. The impact of maternal depression in pregnancy on early child development. *BJOG: An International Journal of Obstetrics and Gynaecology*. 2008;115:1043-51.
24. Guxens M, Mendez MA, Moltó-Puigmartí C, Julvez J, García-Esteban R, Forns J, et.al. Breastfeeding, long-chain polyunsaturated fatty acids in colostrum, and infant mental development. *Pediatrics*. 2011;128:e880-e889.
25. Eickmann SH, de Lira PI, Lima M de C, Coutinho SB, Teixeira M deL, Ashworth A. Breast feeding and mental and motor development at 12 months in a low-income population in northeast Brazil. *Paediatric & Perinatal Epidemiology*. 2007;21:129-37.
26. Buitelaar JK, Huizink AC, Mulder EJ, de Medina PG, Visser GH. Prenatal stress and cognitive development and temperament in infants. *Neurobiology of Aging*. 2003;24: Suppl, S53-60.
27. Davis EP, Snidman N, Wadhwa PD, Glynn LM, Schetter CD, Sandman CA. Prenatal maternal anxiety and depression predict negative behavioral reactivity in infancy. *Infancy*. 2004; 6:319-331.
28. Pauli-Pott U, Mertesacker B. Affect expression in mother-infant interaction and subsequent attachment development. *Infant Behavior and Development*. 2009;32: 208-215.
29. Candelaria M, O'Connell M, Teti DM, Cumulative psychosocial and medical risk as predictors of early infant development and parenting stress in an african-american preterm sample. *Journal of Applied Developmental Psychology*. 2006;27:588-597.
30. Duijts L. Fetal and infant origins of asthma. *European Journal of Epidemiology*. 2012;

27: 5-14.

31. Osmond C, Barker DJ. Fetal, infant, and childhood growth are predictors of coronary heart disease, diabetes, and hypertension in adult men and women. *Environmental Health Perspectives*. 2000;108:Suppl 3, 545-53.
32. Newnham CA, Milgrom J, Skouteris H. Effectiveness of a modified Mother-Infant Transaction Program on outcomes for preterm infants from 3 to 24 months of age. *Infant Behavior and Development*. 2009; 32: 17-26.
33. Petrosyan D, Armenian HK, Arzoumanian K. Interaction of maternal age and mode of delivery in the development of postpartum depression in Yerevan, Armenia. *Journal of Affective Disorders*. 2011;135:77-81.
34. Schatz D, Harder D, Schatz M, Harden K, Chilingar L, Fox D, Hoffman C. The relationship of maternal personality characteristics to birth outcomes and infant development. *Birth*. 2000;27:25-32.
35. Brummelte S, Grunau RE, Synnes AR, Whitfield MF, Petrie-Thomas J. Declining cognitive development from 8 to 18 months in preterm children predicts persisting higher parenting stress. *Early Human Development*. 2011;87:273-80.
36. Shah PS, Balkhair T, Ohlsson A., Beyene J, Scott F, Frick C, Intention to become pregnant and low birth weight and preterm birth: a systematic review. *Maternal and Child Health Journal*. 2011;15:205-216.
37. Sutcliffe AG, Barnes J, Belsky J, Gardiner J, Melhuish E. The health and development of children born to older mothers in the United Kingdom: observational study using longitudinal cohort data. *British Medical Journal*. 2012;345:18.
38. Khadem N, Khadivzadeh T. The intelligence quotient of school aged children delivered by cesarean section and vaginal delivery. *Iranian Journal of Nursing and Midwifery Research*. 2010;15:135-140.

39. Parks PL, Lenz ER, Milligan RA, Han HR. What happens when fatigue lingers for 18 months after delivery? *Journal of Obstetric, Gynecologic, & Neonatal Nursing*. 1999;28: 87-93.
40. Anderson JW, Johnstone, BM, Remley DT. Breastfeeding and cognitive development: a meta-analysis. *The American Journal of Clinical Nutrition*. 1999;70: 525-35.
41. Tharner A, Luijk MP, Raat H, Ijzendoorn MH, Bakermans-Kranenburg MJ, Moll HA, et al. Breastfeeding and its relation to maternal sensitivity and infant attachment. *Journal of Developmental & Behavioral Pediatrics*. 2012; 33: 396-404.
42. Hasegawa Y. Adjustment of time allocation and daily emotional experience during the transition to the role of a working mother. *ShinrigakuKenkyu*. 2010;81:123-31. [Article in Japanese]
43. Sylva K, Stein A, Leach P, Barnes J, Malmberg LE; FCCC-team. Effects of early child-care on cognition, language, and task-related behaviours at 18 months: an English study. *Br J Dev Psychol*. 2011;29:18-45.

Table 1. Medical background

	Preterm/low birth weight delivery (n=31)	Term AFD delivery (n=287)	p value	Term AFD delivery		p value
				Primipara (n=141)	Multipara (n=146)	
Maternal age	31.8±5.1 32.0 [19–38]	31.0±4.7 31.0 [17–43]	0.367	29.7±4.8 29.0 [17–43]	32.2±4.3 33.0 [21–42]	<0.001
Number of previous deliveries	1.7±7.6 2.0 [1–4]	1.6±7.4 2.0 [1–5]	0.993	1.0±0.0 1.0 [1–1]	2.3±0.5 2.0 [2–5]	<0.001
Prenatal hospitalization	12 (38.7%)	42 (14.7%)	0.002	17 (12.1%)	25 (17.2%)	0.245
CS	14 (45.2%)	39 (13.6%)	<0.001	21 (14.9%)	18 (12.3%)	0.606
Gestational age at birth	37.1±2.0 37.0 [34–41]	39.3±1.2 39.0 [37–42]	<0.001	39.5±1.1 40.0 [37–42]	39.0±1.2 39.0 [37–41]	0.001
Sex of Infant						
Male	15 (48.4%)	153 (53.7%)	0.577	70 (49.6%)	83 (57.6%)	0.192
Female	16 (51.6%)	132 (46.3%)		71 (50.4%)	61 (42.4%)	
Infant weight						
At birth	2,323.1±270.8	3,086.3±314.6	<0.001	3,079.2±319.0	3,093.3±311.6	0.705
1-month checkup	3,559.6±415.0	4,203.4±481.4	<0.001	4,184.9±439.5	4,221.1±519.6	0.540
4-month checkup	6,288.5±709.3	6,962.2±767.6	<0.001	6,960.8±808.3	6,963.5±730.5	0.716
Feeding method						
Breast milk	18 (58.1%)	183 (64.4%)	0.669	86 (61.4%)	97 (67.4%)	0.546
Formula	6 (19.4%)	40 (13.8%)		20 (14.3%)	19 (13.2%)	
Combined	7 (22.6%)	62 (21.4%)		34 (24.3%)	28 (19.4%)	
Feeds well	21 (70.0%)	261 (90.9%)	0.002	126 (89.4%)	135 (92.5%)	0.239

Table 2. Social background

	Preterm/low birth weight delivery (n=31)	Term AFD delivery (n=287)	P value	Term AFD delivery		P value
				Primipara (n=141)	Multipara (n=146)	
Unwanted pregnancy						
Yes	1 (3.2%)	8 (2.8%)	0.023	3 (2.1%)	5 (3.4%)	0.525
Not sure	10 (32.3%)	39 (13.6%)		22 (15.6%)	17 (11.7%)	
No	20 (64.5%)	239 (83.6%)		116 (82.3%)	123 (84.9%)	
Support from husband during pregnancy						
Yes	25 (80.6%)	246 (85.7%)	0.654	116 (82.2%)	130 (89.8%)	0.210
Not sure	4 (12.9%)	31 (10.8%)		18 (12.8%)	18 (12.4%)	
No	2 (6.5%)	10 (3.5%)		7 (5.0%)	7 (4.8%)	
Family composition						
Nuclear family	23 (74.2%)	247 (86.7%)	0.102	119 (84.4%)	128 (88.9%)	0.298
Extended family	8 (25.8%)	38 (13.3%)		22 (15.6%)	16 (11.1%)	
Number of children	1.6±0.7	1.6±0.7	0.881	1.0±1.9	2.2±0.5	< 0.001
	2.0 [1–4]	2.0 [1–4]		1.0 [1–3]	2.0 [1–4]	
Siblings						
Yes	16 (51.6%)	145 (50.7%)	1.000	2 (1.4%)	143 (98.6%)	< 0.001
No	15 (48.4%)	141 (49.3%)		139 (98.6%)	2 (1.4%)	
Employment status						
Homemaker	20 (64.5%)	167 (58.6%)	0.654	83 (58.9%)	84 (58.3%)	0.934
On maternity leave	9 (29.0%)	105 (36.8%)		51 (36.1%)	54 (37.5%)	
Working	2 (6.5%)	13 (4.6%)		7 (5.0%)	6 (4.2%)	
Annual income						
< 2 million yen	1 (3.8%)	12 (4.3%)	0.932	12 (8.6%)	0 (0.0%)	0.007
2 million yen ≤ 4 million yen	14 (53.9%)	123 (44.7%)		63 (45.0%)	60 (44.2%)	
4 million yen ≤ 6 million yen	9 (34.7%)	97 (35.2%)		44 (31.4%)	53 (39.0%)	
6 million yen ≤ 8 million yen	1 (3.8%)	26 (9.4%)		15 (10.7%)	11 (8.1%)	
8 million yen ≤ 10 million yen	1 (3.8%)	12 (4.3%)		5 (3.6%)	7 (5.1%)	
10 million yen ≤ 12 million yen	0 (0.0%)	4 (1.4%)		0 (0.0%)	4 (2.9%)	
12 million yen ≤ 14 million yen	0 (0.0%)	2 (0.7%)		1 (0.7%)	1 (0.7%)	

Table 3. Factors related to child-rearing anxiety and stress state

	Preterm/low birth	Term AFD	P	Term AFD delivery		P
	weight delivery	delivery		Primipara	Multipara	
	(n=31)	(n=287)		(n=140)	(n=146)	
	med range	med range	value	med range	med range	value
Factors related to child-rearing anxiety (JCFRI)						
Child-rearing anxiety	20.0 [13–37]	20.0 [11–42]	0.410	19.5 [11–42]	20.0 [11–38]	0.402
Feeling of child-rearing difficulty	18.5 [11–27]	17.0 [8–28]	0.018	16.5 [8–28]	17.0 [8–28]	0.321
Difficult baby	13.5 [8–35]	12.0 [8–28]	0.048	12.0 [8–28]	11.0 [8–24]	0.001
Family function	42.0 [26–78]	37.0 [25–80]	0.095	34.5 [25–78]	38.0 [25–80]	0.023
Stress						
During pregnancy	5.0 [0–10]	5.3 [0–10]	0.738	5.0 [0–10]	6.0 [0–10]	0.120
During hospitalization	3.0 [0–9]	3.0 [0–10]	0.510	4.0 [0–10]	3.0 [0–10]	0.010
2 to 3 days after discharge	5.0 [0–10]	5.0 [0–10]	0.198	5.3 [0–10]	4.0 [0–10]	0.025
Until 1-month checkup	4.0 [0–10]	5.0 [0–10]	0.214	6.0 [0–10]	5.0 [0–10]	0.022
At present	4.0 [0–9]	4.0 [0–10]	0.533	3.0 [0–10]	4.0 [0–10]	0.448

Table 4. Developmental state according to preterm or term delivery and primipara or multipara

	Preterm/low birth weight delivery		Term AFD delivery			Term AFD delivery				
	(n=31)		(n=286)		P	Primipara (n=140)		Multipara (n=146)		P
	med	range	med	range		med	range	med	range	
<b>Development (KIDS)</b>										
Motor score	10.0	[ 5–12]	10.0	[ 2–13]	0.240	10.0	[ 2–13]	10.0	[ 4–13]	0.326
Motor skills	9.0	[ 5–12]	11.0	[ 3–14]	0.001	11.0	[ 6–14]	10.0	[ 3–14]	0.001
Language comprehension	6.0	[ 1– 8]	7.0	[ 1– 8]	0.031	7.0	[ 1– 8]	7.0	[ 2– 8]	0.466
Verbalization	6.0	[ 3– 8]	6.0	[ 2– 8]	0.950	6.0	[ 3– 8]	6.0	[ 2– 8]	0.054
Sociability with adults	12.0	[ 4–16]	13.0	[ 6–19]	0.153	14.0	[ 6–19]	12.0	[ 6–19]	0.002
Diet	4.0	[ 1– 6]	4.0	[ 0– 7]	0.143	4.0	[ 0– 7]	4.0	[ 1– 7]	0.470

Table 5. Comparison of 4-month-old infant development according to maternal age group

	Maternal age				p value	Post hoc
	Teens(n=2) <sup>a</sup>	20's (n=106) <sup>b</sup>	30's (n=165) <sup>c</sup>	40's (n=10) <sup>d</sup>		
Motor score	11.0 [10–12]	10.0 [ 2–13]	10.0 [ 4–13]	10.5 [ 6–11]	0.752	
Motor skills	10.5 [ 9–12]	11.0 [ 6–14]	10.0 [ 5–14]	11.5 [ 9–14]	0.444	
Language comprehension	5.5 [ 5– 6]	7.0 [ 1– 8]	7.0 [ 2– 8]	7.0 [ 4– 8]	0.577	
Verbalization	7.5 [ 7– 8]	6.0 [ 3– 8]	6.0 [ 2– 8]	7.5 [ 5– 8 ]	0.037	b&d*, c&d*
Sociability with adults	9.0 [ 6–12]	13.0 [ 8–17]	13.0 [ 6–18]	13.5 [10–19]	0.217	
Diet	4.0 [ 4– 6]	4.0 [ 2– 7]	4.0 [ 0– 7]	4.0 [ 2– 7]	0.819	

\*p < 0.05

Table 6. Comparison of 4-month-old infant development according to delivery circumstances

	Type of delivery			Was it a difficult delivery?				Sex of Infant		
	Normal vaginal delivery (n=248)	CS (n=39)	P value	Yes (n=189)	Neither (n=45)	No (n=51)	P value	Male (n=153)	Female (n=132)	P value
Motor Score	10.0 [ 2–13]	10.0 [ 4–13]	0.451	10.0 [ 2–13]	10.0 [ 5–13]	10.0 [ 4–12]	0.478	10.0 [ 4–13]	10.0 [ 2–13]	0.533
Motor skills	11.0 [ 5–14]	10.0 [ 3–14]	0.076	11.0 [ 3–14]	11.0 [ 6–14]	10.0 [ 5–14]	0.571	11.0 [ 5–14]	11.0 [ 3–14]	0.251
Language comprehension	7.0 [ 2– 8]	6.0 [ 1– 8]	0.172	7.0 [ 1– 8]	7.0 [ 2– 8]	7.0 [ 2– 8]	0.32	7.0 [ 2– 8]	7.0 [ 1– 8]	0.236
Verbalization	6.0 [ 2– 9]	6.0 [ 3– 8]	0.718	6.0 [ 3– 8]	6.0 [ 3– 8]	6.0 [ 2– 9]	0.787	6.0 [ 2– 9]	6.0 [ 2– 8]	0.533
Sociability with adults	13.0 [ 6–19]	12.0 [ 6–18]	0.300	13.0 [ 6–18]	13.0 [ 6–17]	12.0 [ 8–19]	0.297	13.0 [ 6–19]	13.0 [ 6–19]	0.847
Diet	4.0 [ 0– 7]	4.0 [ 1– 7]	0.033	4.0 [ 0– 7]	4.0 [ 1– 7]	4.0 [ 1– 7]	0.758	4.0 [ 1– 7]	4.0 [ 0– 7]	0.895

Table 7. Comparison of 4-month-old infant development according to infant feeding state

	Feeding method			P value	Post hoc	Suckling		P value
	Breast milk (n=183) <sup>a</sup>	Formula (n=39) <sup>b</sup>	Combined (n=62) <sup>c</sup>			Good (n=261)	Irregular (n=26)	
Motor Score	10.0 [ 4–13]	9.0 [ 5–13]	10.0 [ 2–12]	0.132		10.0 [ 4–13]	9.5 [ 2–13]	0.365
Motor skills	11.0 [ 6–14]	10.0 [ 6–13]	10.5 [ 5–14]	0.058		11.0 [ 3–14]	10.0 [ 7–14]	0.579
Language comprehension	7.0 [ 2– 8]	6.0 [ 2– 8]	6.0 [ 1– 8]	0.005	a&b**, a&c*	7.0 [ 2– 8]	6.5 [ 1– 8]	0.381
Verbalization	6.0 [ 3– 8]	6.0 [ 3– 8]	6.5 [ 2– 8]	0.264		6.0 [ 3– 8]	6.0 [ 2– 8]	0.164
Sociability with adults	13.0 [ 6–19]	12.0 [ 7–18]	13.0 [ 6–19]	0.265		13.0 [ 6–19]	12.5 [ 8–17]	0.165
Diet	4.0 [ 0– 7]	4.0 [ 1– 7]	4.0 [ 2– 7]	0.639		4.0 [ 0– 7]	4.0 [ 1– 7]	0.675

\*p<0.05, \*\*p<0.01,

Table 8. Comparison of 4-month-old infant development according to household lifestyle

	Current employment status			Household income			P value	Satisfaction with current lifestyle			P value
	Not employed (homemakers and women on maternity leave) (n=272)	Employed (currently working) (n=13)	P value	Less than 2 million yen (n=12)	Over 2 million yen, less than 6 million yen (n=220)	6 million yen or more (n=44)		Satisfied (n=205)	Neither (n=54)	Dissatisfied (n=21)	
Motor score	10.0 [ 2-13]	10.0 [ 5-12]	0.989	10.5 [ 5-12]	10.0 [ 2-13]	10.0 [ 7-13]	0.488	10.0 [ 2-13]	9.0 [ 4-13]	10.0 [ 4-13]	0.145
Motor skills	11.0 [ 5-14]	11.0 [ 6-13]	0.402	10.0 [ 6-13]	11.0 [ 5-14]	11.0 [ 6-14]	0.851	11.0 [ 3-14]	11.0 [ 6-14]	10.0 [ 8-14]	0.862
Language comprehension	7.0 [ 1- 8]	6.0 [ 3- 8]	0.908	6.5 [ 3- 8]	7.0 [ 1- 8]	7.0 [ 3- 8]	0.119	7.0 [ 1- 8]	6.0 [ 3- 8]	6.0 [ 5- 8]	0.886
Verbalization	6.0 [ 2- 8]	7.0 [ 3- 8]	0.022	6.5 [ 3- 8]	6.0 [ 2- 8]	6.0 [ 3- 8]	0.808	6.0 [ 2- 8]	6.0 [ 3- 8]	6.0 [ 2- 8]	0.468
Sociability with adults	13.0 [ 6-19]	13.0 [ 6-19]	0.676	13.0 [ 6-15]	13.0 [ 6-19]	12.0 [6-19]	0.188	13.0 [ 6-19]	13.0 [ 8-18]	12.0 [ 8-18]	0.823
Diet	4.0 [ 0- 7]	4.0 [ 3- 7]	0.169	4.0 [ 2- 6]	4.0 [ 0- 7]	4.0 [ 2- 7]	0.745	4.0 [ 1- 7]	4.0 [ 1- 7]	4.0 [ 0- 7]	0.956

Table 9. Comparison of 4-month-old infant development according to family composition

	Family composition			Siblings			P value	Post hoc
	Nuclear family (n=247)	Extended family (n=38)	P value	None <sup>a</sup> (n=141)	<4 years <sup>b</sup> (n=108)	≥5 years <sup>c</sup> (n=35)		
Motor score	10.0 [ 2–13]	10.0 [ 4–13]	0.503	10.0 [ 2–13]	10.0 [ 4–13]	10.0 [ 6–13]	0.656	
Motor skills	11.0 [ 5–14]	10.0 [ 6–14]	0.898	11.0 [ 6–14]	10.0 [ 5–14]	11.0 [ 7–14]	0.001	a&b***, b&c*
Language comprehension	7.0 [ 1– 8]	6.0 [ 3– 8]	0.485	7.0 [ 1– 8]	7.0 [ 2– 8]	7.0 [ 3– 8]	0.187	
Verbalization	6.0 [ 2– 8]	7.0 [ 2– 8]	0.750	6.0 [ 3– 8]	6.0 [ 2– 8]	7.0 [ 4– 8]	0.001	a&b**, b&c**
Sociability with adults	13.0 [ 6–19]	13.0 [ 6–17]	0.341	13.0 [ 6–19]	12.0 [ 6–19]	13.0 [ 9–18]	0.002	a&b**, b&c**
Diet	4.0 [ 0– 7]	4.0 [ 2– 7]	0.145	4.0 [ 0– 7]	4.0 [ 1– 7]	4.0 [ 2– 7]	0.671	

\*p<0.05, \*\*p<0.01, \*\*\*p<0.001