Catch-Up Growth and Neurobehavioral Development among Full-Term, Small-for-Gestational-Age Children: A Nationwide Japanese Population-Based Study

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Objective To examine the relationship between catch-up growth of full-term, small for gestational age (SGA) children and their neurobehavioral development.

Study design Data were obtained from a population-based nationwide Japanese longitudinal survey that started in 2001. Study participants were full-term children with information on height at 2 years of age (n = 32 533). Catch-up growth for SGA infants was defined as achieving a height at 2 years of age of more than -2.0 standard deviations for chronological age. Logistic regression analyses were used to estimate ORs and 95% CIs for the associations of SGA and catch-up growth status with neurobehavioral development at 2.5 and 8 years of age, adjusting for potential infant- and parent-related confounding factors.

Results Fifteen percent of term SGA infants failed to catch up in height. At 2.5 years of age, SGA children without catch-up growth were more likely to be unable to climb stairs (OR, 10.42; 95% CI, 5.55-19.56) and unable to compose a 2-word sentence (OR, 3.58; 95% CI, 1.81-7.08) compared with children with normal growth at birth. Furthermore, SGA children without catch-up growth were at increased risk for aggressive behaviors (OR, 3.85; 95% CI, 1.19-12.47) at 8 years of age.

Conclusions Continuous follow-up for full-term SGA infants with failure of catch-up growth or poor postnatal growth may be beneficial for early detection and intervention for behavioral problems. *(J Pediatr 2017;■■:■■-■■).*

Full-term, small for gestational age (SGA) infants are at increased risk for neurologic problems, such as cerebral palsy and cognitive delay,[1-3] as well as neurobehavioral difficulties through 8 years of age.[4,5] However, term SGA infants are an inhomogeneous group with diverse risk factors, and there is limited evidence to aid in the identification of particularly vulnerable subgroups. This information would be beneficial in assisting pediatricians in providing appropriate long-term developmental follow-up.

Evaluation of catch-up growth or postnatal growth may be useful in stratifying risk for developmental outcomes. A previous study showed that term SGA infants, (defined as a birth weight 2 or SDs below the mean), who caught up to a weight of more than -2 SDs at 1 year of age had favorable cognitive outcomes at 4 years of age compared with those who did not catch up.[6] However, previous studies examining the relationship between catch-up growth and neurologic development were conducted among mostly preterm children.[7-9] Only 2 studies included term SGA children, but they focused only on cognitive function, including the above-mentioned studies.[6-8,10]

The purpose of this study was to examine the relationship between catch-up growth at 2 years of age and neurobehavioral development at 2.5 and 8 years of age among term SGA children using data from a nationwide population-based survey conducted in Japan.

Methods

The Japanese Ministry of Health, Labour and Welfare has been conducting an annual survey of newborn infants and their parents, the Longitudinal Survey of Babies in the 21st Century, since 2001.[11,12] Briefly, baseline questionnaires were distributed to all families throughout the country with 6-month-old infants born between January 10 and 17 or between July 10 and 17, 2001. Of 53 575 mailed

AGA	Appropriate for gestational age
GA	Gestational age
SGA	Small for gestational age

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questionnaires, 47 015 were completed and returned (88% response rate). Birth records were also linked to each child included in this survey.

Children were excluded if they did not have information on birth weight and birth length (n = 152) or gestational age (GA; n = 6). In the present study, we focused on full-term infants and excluded children born before 37 weeks of gestation (n = 2320) and after 42 weeks of gestation (n = 413), leaving 44 124 children for analysis (**Figure**; available at www.jpeds.com).

SGA and Catch-Up Growth Status

The Japanese guidelines for growth hormone replacement therapy for SGA-related short stature[13,14] define SGA as (1) a birth weight below the 10th percentile for GA and birth length below -2.0 SDs for GA, or (2) birth weight below -2.0 SDs for GA and birth length below the 10th percentile for GA. SGA infants were classified based on this definition using the Japanese reference value for birth size according to GA in days from the Committee for Newborns of the Japanese Pediatric Society.[15,16] Infants who were not SGA at birth were classified as appropriate for GA (AGA).

The Japanese guidelines for growth hormone replacement therapy for SGA-related short stature[13,14] also were used to define catch-up growth. The guidelines are consistent with the general definition of catch-up growth for SGA infants[17] and define catch-up growth as a height at 2 years of age above -2.0 SDs for age. The report on growth development for children in fiscal 2000[18] was used to calculate SDs for each month at 2 years of age. Finally, SGA children were classified as having catch-up growth or no catch-up growth at 2 years of age. Because height at 2 years of age was queried in the third survey, children were excluded if there was no height information available in the third survey owing to loss to follow-up (n = 11 444) or if this information was not provided (n = 147), leaving 32 533 children eligible for the final analysis (**Figure**).

Age-appropriate neurobehavioral outcomes were queried by survey questions at 2.5 (ie, in the third survey) and 8 (ie, in the eighth survey) years of age.[11,12] The questions at 2.5 years of age were: (1) Can your child walk? (2) Can your child run? (3) Can your child climb stairs? (4) Can your child say words with meaning? (5) Can your child compose 2-word sentences? and (6) Can your child use a spoon to eat? These 6 items were consistent with Denver II.[19] The survey questions at 2.5 years of age were divided into 3 categories dealing with gross motor development, language development, and personal–social development.[19] Most children have these abilities by 2.5 years of age[19]; thus, we defined the inability to perform each behavior at 2.5 years of age as developmental delay.

The 7 questions posed at 8 years of age were consistent with the Child Behavior Checklist/4-18 Japanese Edition, designed for children aged 4-18 years.[20] Three questions were related to attention problems[5,21,22]: (1) Does your child interrupt people? (2) Can your child wait his/her turn during play? And (3) Can your child pay attention to surrounding areas when crossing the street? The remaining 4 questions were related to aggressive behaviors[5,21,22]: 4) Does your child tell lies? (5) Does your child destroy toys and/or books? (6) Does your child hurt other people? and (7) Does your child cause disturbances in public? We also defined an outcome of "all attention problems" as the existence of all 3 attention problems, and an outcome of "all aggressive behaviors" as the existence of all 4 aggressive behaviors, according to previous studies.[5,21,22]

Statistical Analyses

Logistic regression models and estimated ORs and 95% CIs were used to evaluate each outcome with AGA children as the reference category. Associations between the SGA and catch-up growth status and behavioral outcomes were evaluated at 2.5 and 8 years of age. Controlling for potential child- and parent-related confounding factors was based on previous studies[4,5,11,12] and clinical relevance. Child factors included sex, singleton or not, gestational week, and parity. Parental factors included maternal age at delivery, maternal smoking habits, maternal educational attainment, and paternal educational attainment. The child's sex, singleton or not, gestational week, parity, and maternal age at delivery were listed in the birth record. Maternal smoking status was ascertained at the first survey (at 6 months of age). Maternal and paternal educational attainment was obtained from the second survey (at 18 months of age) and classified into 3 categories: high school or less, junior college (2 years) or vocational school, and university (4 years) or higher. We excluded missing and incomplete cases.

In the sensitivity analyses, we excluded children who had visited clinics or hospitals for congenital diseases between 7 and 18 months of age to remove possible selection bias, because children with disabilities might have been born SGA. We had no information on visits made before 6 months of age.

All CIs were calculated at the 95% level. Analyses were performed using Stata statistical software (Stata SE version 14, Stata Corp, College Station, Texas). This study was approved by the Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences Institutional Review Board (No. 1506-073).

Results

Table I shows the baseline characteristics of the participants according to SGA and catch-up growth status. Overall, the mean ± SD birth weight and birth height among the eligible participants were 3074 ± 379 g and 49.1 ± 2.0 cm, respectively. Of the 581 SGA infants, 15% (n = 86) did not catch up at 2 years of age. Height was assessed at 30.0 ± 1.0 months. SGA children without catch-up growth (SGA and no catch-up group) were more likely to have more siblings and parents with lower education compared with the other 2 categories (AGA and SGA and catch-up growth, **Table I**). SGA children with catch-up growth (SGA and catch-up group) were more likely to be girls and to have smoking mothers compared with the other 2 categories (AGA and SGA and no catch-up, **Table I**). Among the eligible participants (**Figure**), children without information on behavioral outcomes at 8 years of age were more

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