

OBSTETRICS

Large for gestational age and long-term cognitive function

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OBJECTIVE: As we have previously published, small-for-gestational-age (<3% birthweight [BW]) newborns exhibit catch-up cognitive functioning by age 2 years. Our objective was to compare cognitive functioning in children born with $\geq 90\%$ vs 5-89% BW for gestational age (WGA) between 9 months and kindergarten.

STUDY DESIGN: Nonanomalous singletons from Early Childhood Longitudinal Study-Birth Cohort with BW $\geq 90\%$ vs 5-89% were compared. Cognitive and academic functioning was measured at 4 time points: 9 months, and 2, 3.5, and 5.5 years. Associations between WGA and cognitive functioning at each time point was

examined using confounder-adjusted general linear model-based methods.

RESULTS: Of 2930 cases, 271 (9.2%) were $\geq 90\%$ WGA. In terms of cognitive performance, children $\geq 90\%$ WGA were not statistically different ($P = .068$) from normal WGA at any time point, nor did they change at different rates across early childhood.

CONCLUSION: There is no difference in cognitive function in children with BW 5-89% vs $\geq 90\%$ for GA.

Key words: cognitive functioning, large-for-gestational-age infants

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There has been considerable evidence over recent decades linking aberrant fetal growth, both small-for-gestational-age (SGA) and large-for-gestational-age (LGA) infants, with long-term metabolic derangements, including obesity, type 2 diabetes, cardiovascular disease, and metabolic syndrome.¹⁻⁷

There are limited data, however, regarding the relationship between aberrant fetal growth and neurodevelopmental outcomes. The American Congress of Obstetricians and Gynecologists practice bulletin on intrauterine growth restriction, with the use of studies with varying standards, noted that SGA

increases the risk of major neurologic sequelae 2-fold.⁸ Previously we reported that while delay in cognitive function does exist in those infants with birthweight (BW) <3%, catch-up occurs by kindergarten,⁹ but the impact of LGA, defined as BW >90% for gestational age (GA), on cognitive function has not been ascertained.

Our objective in this study is to use the same database, the Early Childhood Longitudinal Study-Birth Cohort (ECLS-B), to determine if LGA infants, compared to newborns at 5-89%, have any delay in cognitive function during 4 time points measured through early childhood.

MATERIALS AND METHODS

We used data from the large nationally representative ECLS-B, which was developed and conducted through the US Department of Education to assess early development and academic performance. It uses a prospective design, following children, born in 2001, from birth through the first year of kindergarten. Four waves of data included measures of cognitive and academic functioning and were taken at ages: 9 months, 2 years, 3.5 years, and 5 years. At 9 months and at 2 years, child cognitive functioning was measured with the Mental Developmental Subscale of the Bayley Scales of Infant Development, short form (BSID). The BSID produces 2

subscale scores that broadly characterize a child's motor (Motor Developmental Subscale) and cognitive (Mental Developmental Subscale) development, with the Mental Developmental Subscale showing moderate correlations with IQ at later ages. At ages 4 years and 5 years, participants were administered direct cognitive tests that tapped early reading and math abilities. These cognitive assessments were developed for the ECLS-B using Item-Response Theory and adaptive testing to allow for accurate measurement of children with widely varying abilities. The reading portion of this assessment taps basic skills, vocabulary, global understanding of context, interpretation of stories, and overall comprehension. The math portion of the assessment taps sense of numbers, measurement, spatial sense, understanding of probability, and identification of patterns. As the ECLS-B team developed these tests, several rounds of testing and refinement were used to generate tests that ultimately showed good internal consistency (reading reliability coefficient, 0.84-0.93; math, 0.89-0.92).¹⁰ Because of the high correlation between these 2 metrics and the strong association between reading abilities and general intelligence, data on reading ability were used for all models. To allow for comparison across BSID and reading assessments, all scores were standardized

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by conversion to percentiles prior to analysis.

The ECLS-B used a nationwide cluster sampling strategy to select a representative sample of live births in 2001. The inclusion criteria were singletons, no major anomalies noted, complete assessment of cognitive function at all 4 time points, present data for maternal prepregnancy weight and weight gain during pregnancy, and sufficient information to calculate the weight for GA (WGA) percentile. Using the normative BW conversion tables published by Oken et al,¹¹ BW for GA was calculated as a percentile for each case. Newborns were categorized as <5%, ≥90%, and normal for GA (cases with intermediate values). Because of previously identified differences among children who are <5% WGA, these cases were excluded from analysis. The association among maternal prepregnancy weight, weight gain during pregnancy, and child LGA status was assessed with complex samples confounder-adjusted logistic regression models. The association between WGA and child cognitive functioning at each time point was examined using a general linear model that was adjusted for all 4 confounders detailed below. Final statistical models were adjusted to control for child race (categorized as white, African American, Latino, and other), child gender, maternal education (years of school), and maternal socioeconomic status (a composite index of occupational status, income, and education). All statistical models were adjusted for clustering and weighting in the complex sampling design of the ECLS-B to produce robust variance estimates. Because the ECLS-B data set used in this study contains no information that can be used to identify subjects, the institutional review board at Eastern Virginia Medical School reviewed this study and determined that it does not fall under human subjects research regulatory requirements.

RESULTS

The ECLS-B initially sampled 13,921 live births, and among them 10,688 entered the study. Because of a planned sample reduction through the kindergarten

Characteristic	BW ≥90% for GA (N = 271)	BW 5-89% for GA (N = 2659)	P value
Maternal age, y	30.42 (29.7–31.1)	28.76 (28.5–29.0)	
19-34	76.7% (202) ^b	79.2% (2068)	.082
≥35	23.3% (67)	18.5% (504)	
Race/ethnicity			.002
African American	7.8% (22)	13.9% (422)	
White	77.1% (154)	61.4% (1169)	
Hispanic	10.0% (28)	16.1% (347)	
Asian	0.9% (22)	3.4% (355)	
Other	4.1% (45)	5.2% (357)	
GA, wk	39.87 (39.8–40.0)	39.04 (38.94–39.14)	.065
Maternal education			.200
<High school	6.5% (18)	10.1% (262)	
High school diploma	22.4% (63)	23.9% (517)	
AA or some college	34.4% (85)	31.1% (656)	
College degree	17.9% (50)	22.1% (471)	
Advanced degree	18.7% (41)	12.8% (338)	
Socioeconomic quintile ^a			.244
Lowest	4.6% (21)	9.8% (267)	
Second	13.3% (39)	16.4% (368)	
Third	19.6% (52)	20.4% (444)	
Fourth	29.3% (62)	25.7% (506)	
Highest	33.3% (84)	27.7% (660)	
Route of delivery			.013
Vaginal	68.3% (190)	77.6% (1939)	
Cesarean	31.7% (79)	22.4% (708)	

Data presented as % (N) or means and 95% confidence intervals (for maternal age and for GA).

AA, associate's degree; BW, birthweight; GA, gestational age.

^a At age 9 mo; ^b Actual cell counts reported—percentages and χ^2 reflect weighted rates and are expected to vary somewhat from raw rates.

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wave, only 5830 completed the study as of this time point. Within the ECLS-B follow-up scheme, this ultimate sample represents retention of 74% of the sample. We additionally excluded 1643 twins, 29 anomalous newborns, 516 who were missing some of the 4 cognitive assessments, and 712 with incomplete birth certificate information. Compared to included cases, excluded cases were more often characterized by: significantly lower maternal education

and socioeconomic status, Latino race, and birth that occurred 0.4 weeks earlier on average. For analyses that involved maternal prepregnancy weight and weight gain during pregnancy, an additional 892 cases were excluded because of incomplete maternal data.

Our sample of 2930 was 51% male with a racial distribution of: 45% white, 15% African American, 13% Latino/Hispanic, 13% Asian, and 14% others (Table 1). Preterm (<37 weeks) births comprised

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