Breast-Feeding Influences Cognitive Development in Filipino Children

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ABSTRACT The importance of breast-feeding (BF) for cognitive development has been researched widely over the past several decades. Although scholars agree that children who breast-feed are generally more intelligent, it is uncertain whether this advantage is due to BF effects or to other accompanying healthy characteristics of women who breast-feed. This is a problem in nearly every study, and even in studies controlling for known confounding variables, residual confounding remains a concern. This study tried a new approach, evaluating the relation between BF and cognitive development or ability in a population in which BF was inversely correlated with socioeconomic advantages and other healthy maternal behaviors. Normal birthweight (NBW, n = 1790) and low birthweight (LBW, n = 189) (<2500 g) infants born in 1983–84 in Metropolitan Cebu, Philippines were followed from birth through middle childhood. Cognitive ability was assessed at ages 8.5 and 11.5 y with the Philippines Nonverbal Intelligence Test. Multivariable linear regressions were created to estimate crude and adjusted relations of various BF measures and later cognitive ability. After controlling for confounding variables, scores at 8.5 y were higher for infants breast-fed longer (1.6 points and 1.8 points higher among NBW and LBW infants, respectively, breast-fed for 12 to <18 mo vs. <6 mo). BF coefficients in both NBW and LBW 11.5-y models were attenuated but remained positive. This analysis highlights the importance of long-term BF after initial introduction of complementary foods, particularly in LBW infants born close to term... J. Nutr. 135: 2580–2595, 2005.

KEY WORDS: breast-feed * intelligence * cognitive development * infant * nutrition

Since initial research in 1929 (1), the majority of published studies have concluded that breast-feeding (BF) has a beneficial effect on cognitive development (2,3). Possible mechanisms relate either to milk composition, or to the physical act of breast-feeding. Breast milk contains a complex array of nutrients, trophic factors, and other bioactive ingredients (4–6). Docosahexaenoic acid is abundant in human milk and rapidly incorporated into the central nervous system during the first 3 mo of life (7). Milk levels of choline (8) and possibly taurine (9) may have an effect, as may numerous other peptides and oligosaccharide components. The act of BF may also favor infant intellectual development through increased mother-infant positive interaction resulting in better long-term relationships. BF is also thought to elicit beneficial hormonal responses in mothers, reducing stress and depression and resulting in improved care quality (7,10). These pathways operate simultaneously when BF occurs, but their effects are difficult to separate, and most studies have measured combined pathways.

Despite many potential pathways that could explain benefits for intelligence, the topic continues to be debated. Because randomly assigning women to breast or formula feed is inappropriate, observational studies must be used. Nearly all studies to date have been conducted in developed countries in which women who breast-feed also exhibit other positive health-related characteristics that may facilitate cognitive development [e.g., better socioeconomic status (SES), education, intelligence, responsiveness, or home environment]. Disentangling the positive effects of these other characteristics from those of BF has been a tremendous challenge. Investigating the effects of BF in a wide variety of settings was proposed as the only way to verify an effect (11).

Imperfect measurement of BF has also caused uncertainty in the current literature. Jain et al. (3) recently specified 4 criteria for quality feeding data, i.e., a definition of BF specifying the extent of exclusivity, collection of BF data within a specific part of life, use of mother or health records as the data source, and a measurement of duration of at least 1 mo; however, found only 9 of 40 studies met these criteria.

This study took 2 unique approaches to investigating the relation between BF and childhood cognitive development. First, data were from the Philippines—a context in which confounders are distributed differently from those in developed countries. In this cohort, women who breast-fed the longest were from the poorest environments, had the least education, and were least able to afford quality breast milk alternatives. Under these circumstances, confounders tended to obscure
The study design. The Cebu Longitudinal Health and Nutrition Survey collected data on all pregnant women in 33 randomly selected barangays (administrative units) of Metropolitan Cebu, who gave birth between May 1, 1983, and April 30, 1984 (12). Families surveyed lived in a variety of circumstances, including densely populated urban areas, urban squatter settlements, periurban neighborhoods, rural areas stretching into the mountains, and some small surrounding islands. The survey was designed to assess infant feeding patterns, including the sequencing of feeding events, factors affecting feeding decisions, and the implications of these feeding decisions for health and nutrition as well as demographic and economic outcomes. Further details are discussed elsewhere (13). The data included a wide range of measurements related to infants and children, and information on a large array of potential confounding variables. The original survey included 3080 singleton live births. After loss to death (n = 167) or loss to follow-up (n = 649), 2264 children remained in 1991. Of these, 2209 had cognitive development test scores and adequate BF measurements. Preterm status was the most frequently missing variable (absent for 3.4%) and 1984 children had full data for the present analysis. Children excluded from this analysis were those at extremes of SES, i.e., either those from poorer backgrounds who died early, or those from relatively affluent households who moved outside of the study area. Characteristics of these children were similar to those of children included in the study, i.e., there were no differences in household income, age, marital status, place of birth, or place of death (13). In 3% of them observed in urban areas (P = 0.05). We assumed these differences to be negligible. The survey protocol and current analysis were approved by the School of Public Health Institutional Review Board at the University of North Carolina at Chapel Hill.

BF data. Trained study personnel collected BF data at birth and at each follow-up visit. Mothers recalled all foods and liquids fed in the past 24 h. If women fed infants other foods or stopped BF since the previous survey, they were asked when this occurred. BF outcomes were censored at 24 mo. Nutrition other than colostrum given in the first 2 d of life was ignored because cultural norms discouraged feeding colostrum to newborns, and behavior during this period did not reflect a woman's later BF behavior (14).

The BF experience, for most infants, consists of a combination of early predominant BF followed by a long period of BF complemented with other foods. However, there are many ways to represent BF, and the ideal method depends on the hypothesis in question. For purely nutritional effects, total dose (volume) of breast milk over time may be most relevant; for behavioral effects, duration of suckling or contact/interaction with the mother may be the more appropriate measure (e.g., h/kg × total weeks). The effects of BF on cognitive development are most likely to be both biological and behavioral. Given the difficulty in measuring BF with this amount of precision, we felt that the best possible compromise involved measuring duration in days of exclusive, predominant, and total BF. We created alternate definitions of BF to test whether cognitive benefits were due to the total duration of any BF, the durations of exclusive or predominant BF, or a combination of both. Our definitions followed those set forth by the WHO for exclusive BF (no food or drink other than breast milk, and drops or syrups containing vitamins or medication), predominant BF (allow small amounts of liquid such as tea, oral rehydration solution, and juice), and partial BF (BF mixed with other feeding) (15). Our definitions differed only in that we allowed nonnutritive liquids (water and tea) to be consumed in our exclusive category, and up to 20 kcal/d (93.8 kJ/d) from nutritive liquids or foods in our predominant BF category. Women in this population commonly used nonnutritive liquids in infant feeding (16), and these more lenient definitions reduced misclassification of women who were still predominantly BF. Duration of exclusive BF was a continuous outcome obtained from questions about when foods other than breast milk were first introduced. Predominant BF was based on calculations of nutrients from 24-h recalls and was available only at mo 2, 4, and 6. Predominant BF after 6 mo was rare. Any BF was a continuous measure defined as the age when the infant stopped breast-feeding, or (when breast-feeding > 24 mo) was last known to breast-feed.

Test of cognitive ability. Cognitive ability was measured using the Philippines nonverbal intelligence test of fluid abilities (i.e., analytic and reasoning skills) developed by Guthrie et al. (17). The test was administered when children were 8.5 and 11.5 y old by individuals unaware of their BF status. The test questions are similar to those in the Columbia Mental Maturity Scale (18) and require children to discriminate differences among 3 pictures on each of 100 cards. Children must make abstract categorizations that will classify 4 of the pictures as similar and one as different; for example, "four of the five are birds." The basis for classification shifts with every item. Before use in this population, the test was standardized by the developers in Manila, using data from 100 children in each grade. However, the test is neither culturally transferable nor standardized to the same scale as other intelligence tests, and therefore intended only for within-sample comparison (17). The instrument was previously shown to correlate with performance on reading comprehension and mathematics achievement tests administered at 11.5 y in this cohort (19) and correlations resembled those between BF and IQ reported elsewhere (20,21). Further evaluation of this instrument included test-retest reliability and validity assessment. Validity was assessed by comparing test scores with known correlates of cognitive development, including positive correlates (family SES, attendance at school, and home environment indicators) and negative correlates (i.e., indicators of biomedical risk including delivery complications, preterm status, and vaccination status) were considered.

Potential confounding variables. We considered multiple potential confounding variables including: child characteristics (gender, birthweight, gestational age); SES variables (household income, non-income-producing assets, index of urbanicity); maternal characteristics (parity, education, order, parity, place of birth, smoking habit); paternal characteristics (education, presence in home); measures of child care (delivery complications, vaccination status, number of baths per week, dietary variety at 2 y, home environment measures (the presence of books in the home, whether the mother reads, the presence of household servants, hygiene of the home environment, electricity in the home). The current literature was our basis for evaluating many of these variables (2,2,23,24). Other variables (e.g., smoking, electricity) were chosen theoretically based on their potential for confounding in a developing country context.

Potential confounding variables were evaluated for significant bivariate associations with cognitive development test scores and at least one BF outcome. Variables not associated with both test scores and BF were excluded from further analysis. Associated variables were included in multivariate models. Height, smoking habit, and environmental hygiene were used to identify and remove variables not confounding BF coefficients by ≥10%. Confounding variables meeting all criteria included: child gender; SES variables (household income (peso/wk), non-income-producing assets (monetary value)); maternal characteristics (education (y), parity (number of previous births), height), paternal characteristics (education (y), presence in home (baseline)); child care (dietary variety at 2 y, baths, books, and home environment measures (electricity, books in the home, mother reads (yes/no), and environmental hygiene). Environmental hygiene was measured via a summary index (scored 0–5) indicating the presence of a flush/water-sealed toilet, a lack of fecal material around the house or yard, regular municipal garbage collection, a clean food area, and a piped water source. Reports of children's usual daily intake were used to calculate dietary variety on a scale of 0–8, with 1 point awarded for intake of ≥1 food

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in each of the following categories: fish, animal source foods, staple cereals, other starches, vegetables, fruits, beans and nuts, and dairy.

Variables representing maternal age, alcohol use in pregnancy, and preterm status did not meet confounding criteria but were included in final models for comparability with the literature. Children were classified as preterm if gestational age was <37 wk. Gestational age was based on the date of the mother's last menstrual period, unless pregnancy complications occurred or if the infant was low birthweight (born weighing <2500 g). In those cases, Ballard clinical assessments by trained nurses were used to estimate gestational age (24); 71 children weighing >3000 g, whose gestational age was not available, were also classified as term.

**Statistical analysis.** Retest reliability and validity of the intelligence test were evaluated using Pearson's correlations and t tests. Linear models of test scores were predicted using several versions (e.g., continuous, quadratic, and categorical) of each defined BF measure. This allowed us to avoid assuming a linear relation between BF and test scores, and helped determine which BF representation was most useful for predicting test scores. Because feeding transitions (movement from exclusive or predominant BF to partial BF to no BF) are timed differently for each woman and may affect a child's cognitive development, we also visualized different feeding scenarios by cross-classifying selected BF variables and calculating mean cognitive test scores for resulting categories. Linear regressions were used to test for statistical interactions of gender and birthweight with BF in predicting test scores; P values < 0.20 were considered significant interactions. Bivariate relations of potential confounding variables with test scores and BF were assessed via independent samples t tests, ANOVA with Bonferroni tests, Kruskal-Wallis test (for nonparametric comparisons), and Pearson's correlation coefficients.

Crude and adjusted cognitive development scores at ages 8.5 and 11.5 y were predicted from individual BF variables using linear regressions. We also tested models containing multiple representations of BF. For instance, we tested whether predominant BF could explain additional variance in cognitive development scores if it was included with any BF in adjusted models. Combined models also included an indicator variable representing absolute exposure (ever breast-fed) to facilitate interpretation as recommended by McKnight (25) in models containing multiple characteristics of an exposure. For combined models, cognitive ability was predicted at 8.5 and 11.5 y for normal birthweight (NBW) children and the full sample. Low birthweight (LBW) combined models were not created because cross-tabulating LBW children by both BF variables resulted in small cell sizes.

Collinearity checks for multivariable models were conducted using variance inflation factors and condition indices. Outliers were identified with residual analysis and tested for influence on models. R² statistics among models with and without BF were considered to minimize the predictive power of BF. Post hoc simulations of predicted test scores were computed from linear models. Differences of P values < 0.05 were considered to be significant. Stata 8 was used for all analyses (26).

**RESULTS**

Any BF explained the most variance in test scores when categorized into 6-mo increments. The predominant and exclusive BF variables gave similar results; however, the predominant BF measure had the greatest precision because it was a better measure of total BF dose in the first 6–8 mo of life. Therefore, only results for the any BF and predominant BF variables are presented.

**Validation of the test of cognitive ability.** Test scores at ages 8.5 and 11.5 y were significantly correlated (r = 0.606, P < 0.0001), thus supporting reliability. The mean score increased over time (51.4 at 8.5 y, and 69.3 at 11.5 y), reflecting increases in cognitive ability with maturation. Test scores at 8.5 y were positively correlated with baseline measures of maternal and paternal education (r = 0.37, P < 0.0001; r = 0.38, P < 0.0001), and family SES as measured by household income (r = 0.18, P < 0.0001) and non-income-producing assets (r = 0.20, P < 0.0001). Relations were similar for scores at 11.5 y of age. Home environment indicators (a symbol of whether a book was in the house, electricity, and environmental hygiene) were positively related to improved cognitive ability. Test scores at 8.5 y were 5.7 points higher if mothers read, 5.6 points higher if books were in the home, and 5.9 points higher if electricity was present (P < 0.0001 for all). Correlation between environmental hygiene and cognitive ability was 0.30, P < 0.0001). Scores at 11.5 y followed similar patterns.

Indicators of biomedical risk were not all negatively correlated with test scores as we expected. Preterm status did not significantly relate to cognitive ability; this is likely because only preterm infants born close to term survived to 8.5 y in this context (98.3% of sample reached 35–wk gestation). Children who were vaccinated (at least 1 measles or 2 DPT vaccinations by age 1 y) had significantly higher test scores at 8.5 y (8.5 y difference = 4.0 points, P = <0.0001; 11.5 y difference = 3.8 points, P = <0.0001). In contrast, children with delivery complications had higher test scores than those without (8.5 y difference = 1.7 points, P = 0.02; 11.5 y difference = 1.9 points, P = 0.01). However, mothers reporting delivery complications had higher incomes and higher levels of education; thus the trend may actually reflect increased awareness of birth details, increased communication with birthing attendants among better educated mothers, or increased mortality among infants with birthing complications born to less educated mothers.

**Descriptive statistics.** Demographic characteristics of children by BF duration differed markedly. Because both BF variables showed similar trends with background characteristics, only any BF is depicted (Table 1). Women who breast-fed longer had lower education and household incomes, were less likely to reside in an urban area, have access to flush/water sealed toilets or have electricity, and were less likely to report reading. Trends in education for fathers (not shown) were similar to those for mothers. Environmental hygiene scores (not shown) also declined consistently with increasing durations of any BF.

The quality of transitional foods among cohort infants was highly variable. The number of infants in the cohort receiving any breast milk was high at 2 mo (81%), declining to 56% at 12 mo. Mothers replaced breast milk strictly with formula in only a few instances; other common early foods included other breast milk substitutes (condensed milk, whole cow's milk), juices, rice or corn gruels, and semisolid foods such as well-cooked starches and vegetables (27).

Crude cross-classifications of BF variables (Table 2) revealed that women who predominately breast-fed longer also had the longest durations of any BF. Among children predominantly breast-fed for <2 mo, any BF was most often terminated before 6 mo. Among children predominantly breast-fed for 2 to <6 mo, any BF most often lasted 12–24 mo. Crude test scores were higher among children with any BF for 6 mo <12 mo compared with other categories. Crude test scores generally declined with increasing duration of predominant BF.

**Model specification.** Previous studies indicated that BF effects on neurodevelopment differ among infants of different birthweight (2), and gender (28). We found no interactions with gender. Birthweight did not interact significantly with predominant BF, but did interact with any BF in prediction of test scores. Analyses of any BF and cognitive ability were stratified accordingly by birthweight (<2500 g = low; ≥2500 g = high).

In outlier analysis, 7 individuals with Studentized residuals exceeding 3 SD from the mean were identified. These indivi-
TABLE 1
Baseline sociodemographic characteristics of Filipino children by duration of any BF

<table>
<thead>
<tr>
<th>Any BF, mo</th>
<th>0 to &lt;6</th>
<th>6 to &lt;12</th>
<th>12 to &lt;18</th>
<th>18 to &lt;24</th>
<th>24+</th>
<th>P-value*2</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>459</td>
<td>274</td>
<td>573</td>
<td>408</td>
<td>270</td>
<td></td>
</tr>
<tr>
<td>Mother's education, y</td>
<td>9.2 ± 3.4</td>
<td>7.5 ± 3.1</td>
<td>8.5 ± 2.6</td>
<td>6.0 ± 2.5</td>
<td>5.7 ± 2.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Household income, pesos/wk</td>
<td>415.2 ± 694.9</td>
<td>288.6 ± 305.6</td>
<td>248.4 ± 395.6</td>
<td>242.4 ± 354.3</td>
<td>199.0 ± 258.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>P-value*3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

Urban residence: 90.4 80.3 71.4 68.6 63.3 <0.001
Toilet in home: 21.6 14.6 8.7 7.6 7.0 <0.001
Electricity in home: 71.7 58.4 42.0 36.5 35.6 <0.001
Mother reads: 75.8 70.7 51.3 48.0 45.9 <0.001

*1 Values are means ± SD or %; total n = 1984.
*2 Values of P correspond to Kruskal-Wallis test statistics for nonparametric comparisons.
*3 Values of P based on Pearson's x² test.
*4 Flush or water-sealed toilet.

Models stratified by birthweight were also generated (not shown) to determine whether effects differed for NBW and LBW infants. In crude NBW models, all coefficients showed significantly reduced cognitive ability scores (ranging from -3.4 to -7.2 points) with increased BF. Coefficients from crude LBW models were all nonsignificant. After adjusting for confounding variables, all NBW coefficients became nonsignificant. LBW coefficients remained nonsignificant, except predominant BF 4 to <6 mo, which resulted in a developmental benefit of nearly 6 test points (5.94; 95% CI 1.29-10.59).

A small subgroup of children (n = 48) (data not shown) were exclusively breast-fed beyond 6 mo of age, and having substantially lower cognitive ability than other children predominantly breast-fed for 6+ months even after controlling for confounding variables. Inclusion of these children lowered BF coefficients in the 6+ mo category [without these children the 8.5 y coefficient = 0.14 (95% CI 1.71, 1.98)] and may reflect the nutritional inadequacy of exclusive BF after 6 mo, or may be a result of residual unmeasured confounders operating in cases in which extreme poverty stimulates protracted exclusive BF.

Combined BF models. If BF affects cognitive development, it is important to understand whether duration of predominant BF or duration of any BF is more influential. We evaluated this with adjusted full sample models containing

TABLE 2
Cognitive ability test scores of children at 8.5 y of age by months of predominant and any BF

<table>
<thead>
<tr>
<th>Predominant BF*3</th>
<th>Any BF*2, mo</th>
<th>0 to &lt;6</th>
<th>6 to &lt;12</th>
<th>12 to &lt;18</th>
<th>18 to &lt;24</th>
<th>24+</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 mo</td>
<td>53.88 ± 13.32 (414)</td>
<td>56.68 ± 12.00 (80)</td>
<td>53.83 ± 11.32 (72)</td>
<td>51.72 ± 10.06 (46)</td>
<td>52.39 ± 10.77 (33)</td>
<td>53.99 ± 12.64 (645)</td>
<td>53.99 ± 12.64 (645)</td>
</tr>
<tr>
<td>2 to &lt;4 mo</td>
<td>53.26 ± 14.63 (34)</td>
<td>53.36 ± 14.24 (69)</td>
<td>51.70 ± 11.12 (135)</td>
<td>48.50 ± 12.97 (96)</td>
<td>47.95 ± 10.49 (60)</td>
<td>50.78 ± 12.52 (389)</td>
<td>50.78 ± 12.52 (389)</td>
</tr>
<tr>
<td>4 to &lt;6 mo</td>
<td>49.64 ± 13.11 (11)</td>
<td>51.20 ± 12.90 (101)</td>
<td>51.25 ± 10.96 (277)</td>
<td>50.11 ± 11.76 (180)</td>
<td>51.84 ± 12.02 (108)</td>
<td>50.99 ± 11.67 (687)</td>
<td>50.99 ± 11.67 (687)</td>
</tr>
<tr>
<td>6+ mo</td>
<td>49.71 ± 13.06 (24)</td>
<td>49.40 ± 12.96 (80)</td>
<td>49.40 ± 12.96 (80)</td>
<td>49.40 ± 12.96 (80)</td>
<td>49.40 ± 12.96 (80)</td>
<td>49.40 ± 12.96 (80)</td>
<td>49.40 ± 12.96 (80)</td>
</tr>
<tr>
<td>Total</td>
<td>53.73 ± 13.40 (459)</td>
<td>53.13 ± 12.91 (274)</td>
<td>51.40 ± 11.40 (573)</td>
<td>49.17 ± 12.17 (408)</td>
<td>49.36 ± 11.78 (270)</td>
<td>51.44 ± 12.43 (1804)</td>
<td>51.44 ± 12.43 (1804)</td>
</tr>
</tbody>
</table>

*1 Values are means ± SD (n).
*2 Duration of any BF in months.
*3 Duration of predominant BF in months defined as feeding <20 kcal (<83.3 kJ) from non-breast milk in a single day.
TABLE 3
Results from linear models of the relation between amount and type of BF and cognitive ability scores

<table>
<thead>
<tr>
<th></th>
<th>8.5 y score (crude)</th>
<th>8.5 y score (adjusted)</th>
<th>11.5 y score (crude)</th>
<th>11.5 y score (adjusted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any BF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NBW children</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>1789</td>
<td>1717</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 to 6 mo</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>6 to 12 mo</td>
<td>-1.74 (95% CI 0.25, 3.10)</td>
<td>-2.15 (95% CI 0.69, 4.10)</td>
<td>0.36 (95% CI -1.38, 2.10)</td>
<td>1.41 (95% CI 0.00, 2.80)</td>
</tr>
<tr>
<td>12 to 18 mo</td>
<td>-3.33 (95% CI 0.90, 4.70)</td>
<td>-2.04 (95% CI 0.45, 3.56)</td>
<td>-5.57 (95% CI -7.79, -3.36)</td>
<td>-0.69 (95% CI -2.32, 0.94)</td>
</tr>
<tr>
<td>18 to 24 mo</td>
<td>-5.53 (95% CI 0.23, 2.88)</td>
<td>0.10 (95% CI 0.66, 1.77)</td>
<td>-0.66 (95% CI -1.24, 2.54)</td>
<td>-0.81 (95% CI -1.04, 2.64)</td>
</tr>
<tr>
<td>24+ mo</td>
<td>-4.79 (95% CI 0.67, 2.67)</td>
<td>-3.97 (95% CI -5.80, -2.14)</td>
<td>-0.81 (95% CI -1.04, 2.64)</td>
<td></td>
</tr>
<tr>
<td>LBW children</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>188</td>
<td>181</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 to 6 mo</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>6 to 12 mo</td>
<td>7.96 (95% CI 13.83, 3.08)</td>
<td>8.42 (95% CI 13.98, 2.86)</td>
<td>0.34 (95% CI -5.24, 5.91)</td>
<td>1.32 (95% CI -4.23, 6.88)</td>
</tr>
<tr>
<td>12 to 18 mo</td>
<td>3.66 (95% CI 8.48, 1.15)</td>
<td>9.83 (95% CI 14.49, 4.76)</td>
<td>-1.22 (95% CI -5.63, 3.38)</td>
<td>3.89 (95% CI -1.27, 8.09)</td>
</tr>
<tr>
<td>18 to 24 mo</td>
<td>2.19 (95% CI 7.87, 3.46)</td>
<td>6.63 (95% CI 12.12, 1.14)</td>
<td>-1.06 (95% CI -6.38, 4.27)</td>
<td>2.64 (95% CI -2.77, 8.06)</td>
</tr>
<tr>
<td>24+ mo</td>
<td>-3.93 (95% CI 2.01, -8.88)</td>
<td>7.12 (95% CI 3.63, 1.60)</td>
<td>-4.70 (95% CI -10.27, 0.87)</td>
<td>2.51 (95% CI -4.02, 9.10)</td>
</tr>
<tr>
<td>Predominant BF</td>
<td>(All children)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>1977</td>
<td>188</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 to 6 mo</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>6 to 12 mo</td>
<td>-3.31 (95% CI -1.07, -1.79)</td>
<td>0.20 (95% CI 1.65, -2.26)</td>
<td>-3.38 (95% CI -4.84, -1.92)</td>
<td>-0.18 (95% CI -1.60, 1.24)</td>
</tr>
<tr>
<td>12 to 18 mo</td>
<td>-3.07 (95% CI -1.78, -4.38)</td>
<td>1.39 (95% CI 2.69, 0.08)</td>
<td>-3.23 (95% CI -4.47, -1.98)</td>
<td>0.65 (95% CI -0.62, 1.92)</td>
</tr>
<tr>
<td>18 to 24 mo</td>
<td>-6.99 (95% CI -5.24, 8.74)</td>
<td>-0.67 (95% CI 1.08, -2.40)</td>
<td>-5.40 (95% CI -7.06, -3.73)</td>
<td>-0.02 (95% CI -1.71, 1.66)</td>
</tr>
</tbody>
</table>

Models were adjusted for parental education, paternal presence in home, maternal age, parity, alcohol during pregnancy, preterm status of child, mother's smoking habit, child's gender, births (n/wk), dietary variety at 2 y, household income, non-income-producing assets, electricity in home, and environmental hygiene score.

NBW defined as 3.250 kg.

Duration of predominant breast-feeding in months defined as feeding <20 kcal (83.6 kcal) from breast milk in a single day.

In both BF variables, children with any BF < 6 mo and predominant BF < 2 mo were our comparison group. Holding predominant BF constant at < 6 mo, there were significant increases in cognitive development with any BF for 6 to 12 mo (1.97; 95% CI 0.03, 3.91), and 12 to 18 mo (2.64; 95% CI 0.79, 4.49) at 8.5 y. Holding any BF constant at < 6 mo, test scores did not differ significantly with increases in predominant BF. Test scores of never breast fed children also did not differ from the comparison group. In NBW models trends were similar but of a smaller magnitude and all nonsignificant for any BF 6 to 12 mo (0.96; P = 0.352) and any BF 12 to 18 mo (1.63; P = 0.096).

Adjusted full-sample models at 11.5 y with a similar comparison group (6 mo any, < 6 mo predominant BF) found significant improvements only among children with any BF 12 to 18 mo (1.87; 95% CI 0.07, 3.67). Test scores did not differ significantly with increasing duration of predominant BF or with never breast-fed status. NBW model coefficients were again nonsignificant.

Further analyses. We investigated how much of the variance in cognitive ability at 8.5 and 11.5 y was explainable by BF vs. other predictors by contrasting R² values from adjusted models with and without BF variables. Changes in overall model R² values remained similar (within a range of ±0.005) except in the LBW models; duration of any BF explained 5% of the variance in test scores at 8.5 y, with adjusted R² dropping from 0.216 to 0.1563 when BF variables were removed. In the 11.5 y LBW model, any BF was no longer beneficial in explaining test score variation.

DISCUSSION
In this analysis, poor education and suboptimal living conditions among BF mothers were strong negative confounders, causing inverse crude associations between BF and cognitive ability in NBW children, a situation opposite to that in the current literature. In spite of this, increased duration of any BF was of significant benefit for cognitive development at both 8.5 and 11.5 y in NBW infants, although the effects were small. The analysis depended heavily on statistical adjustment for confounding variables to detect these benefits, and some may regard the associations skeptically. However, the selected confounding variables represent major and relevant factors associated with both cognitive development and BF, and their inclusion in the models is unmasking a real effect.

More striking than the effects in NBW infants, however, were the increases and adjusted associations found among LBW infants. In crude models of cognitive ability at 8.5 y, children with 0 to 6 mo any BF scored 8.0 points lower than those breast-fed 6 to 12 mo. After adjusting for confounding children 0 to 6 mo any BF were 6.6 to 9.8 points lower than infants in every other category, and all associations were significant. Also when predominant BF models were stratified, only LBW children benefited significantly from longer duration of predominant BF. We evaluated whether other factors influencing cognitive development could explain these marked differences between NBW and LBW children by stratifying on sociodemographic statistics (parental education, household income, urbanicity, and environmental hygiene) by birthweight. Trends were less pronounced in LBW children, but still indicated somewhat poorer conditions among children breast-fed longer. We also evaluated whether there were differences in the weaning diet of the 2 groups by comparing mean dietary variety scores. At 24 mo, there was no difference in the number of food groups eaten daily by LBW and NBW infants. Adair and Popkin (25) previously also reported no differences in diet of NBW and LBW infants after 6 mo of age in this cohort.

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Two other observational studies considered the effects of BF on mental development in term, small for gestational age (SGA) infants. Both found strong effects. Morley et al. (30) measured Bayley Mental Development Index (MDI) scores in a cohort of infants and found that at 18 mo, breast-fed infants had MDI scores 11.7 points higher. After adjusting for 2 sets of potential confounding variables, the association was ~5 points higher among breastfed infants. However, the authors did not find a clear dose-response relation with either partial or exclusive BF. Rao et al. (31) found that infants who were exclusively breast-fed >12 wk had mean performance IQs 5 points higher at 5 y of age than children exclusively breast-fed <12 wk. Their model predicted that exclusively BF for 24 wk would give SGA children an advantage of 11 IQ points over those breast-fed for ≤12 wk (31). Our study found a strong relation between BF and cognitive ability in LBW infants born near term, and is particularly provocative because it is the longest reported follow-up of such a cohort to investigate this relation, and the only one in a context in which BF is not positively correlated with other advantages.

WHO and UNICEF currently recommend exclusive BF until 6 mo and then introduction of complementary foods with continued BF until the child reaches 2 y of age or beyond (32). We found cognitive ability at 8.5 y was improved in LBW infants predominantly breast-fed for 4 to <6 mo after adjusting for confounding. We also found that any BF persisting 12 to <18 mo resulted in higher adjusted cognitive ability at 8.5 y for NBW and LBW infants. The any BF association was particularly strong in LBW infants, and persisted after adjusting for duration of predominant BF in the model including both NBW and LBW infants. BF 18 to ≤24 mo appeared slightly less beneficial than 12 to <18 mo, but was still significantly better than <6 mo BF for LBW infants. The decrease in effect after 18 mo may be attributable to residual confounding; therefore further research is needed. These results indicate the importance of both predominant and long-term partial BF in the care of LBW infants.

The decline in associations of both predominant and any BF with cognitive ability at 11.5 y is perplexing and difficult to explain. The test may be less adequate to measure cognitive ability at 11.5 y, although the moderately strong correlation between test scores at different ages indicates reliability. BF may have less influence on cognitive ability as children age, or other factors may become relatively more influential with increased age.

The current study has a number of limitations. As in all observational studies, the likelihood of confounding was high. Despite careful consideration, unmeasured variables may have affected results. A strong SES gradient existed across BF levels and it is unlikely that the confounding analysis captured all important differences. No measures of parenting styles (e.g., maternal training, authoritative ideology) or childhood experiences existed for this cohort. We also lacked measures of parental intelligence, although we did assess presence of books in the home and the mothers' reading behavior.

Measures of caregiver stimulation were not available for this sample, which may have affected our estimates. The most common concern in the literature is that increased parental responsiveness may accompany BF and produce cognitive benefits mistakenly attributed to BF. To the extent that stimulation is correlated with our socioeconomic status variables, confounding by stimulation was removed. We found that measures most logically related to stimulation (the presence of books in the home and whether the mother reads) were strongly related to SES measures (weekly income and parental education), which supports the idea that controls for SES can also be valuable for measuring differences in stimulation in certain contexts. It is also important to note that in this sample, residual confounding by stimulation was most likely to attenuate BF effect estimates because mothers who breast-fed less (our comparison group) were from the better environments (e.g., better educated, more hygienic environments). Therefore, these estimates are conservative. Stimulation may also be an indirect positive effect of BF (e.g., if BF results in reduced maternal depression and/or increased parent-child interaction), but we do not consider this a source of bias.

A further limitation is the wide variety of foods and liquids other than breast milk that infants in this cohort received. Low-quality weaning foods and breast milk substitutes would be expected to increase developmental differences between BF and non-BF infants, and inflate effect estimates. However, because large differences in the non-breast milk diet between LBW and NBW infants were not present, this limitation cannot negate the large benefits of BF on cognitive development we found in LBW infants. In addition, the socioeconomic factors that correlated negatively with BF would correlate positively with quality of non-breast milk foods consumed. Controlling for these confounding variables would therefore have accounted for at least some of these dietary differences that were not otherwise captured.

In spite of limitations, the analysis provides valuable evidence that BF improves cognitive development because of its unique setting and its detailed BF data. The study has several other strengths as well. The sample size was large, allowing comparison of BF effects in NBW and LBW infants. LBW infants were not numerous, but numbers were adequate for this analysis and provide incentive for further research in similar contexts. Dietary variety at 2 y was taken into account; previous studies have not considered the potential effect of the weaning diet. The study is also one of the first to consider the effects of BF on cognitive development in children who were born predominantly full term but SGA rather than children who are very low birthweight due to extremely preterm delivery.

Much research remains to be done to elucidate the mechanisms through which breast milk affects neurodevelopment. However, given the known health benefits and the obvious economic savings accompanying BF, this lack of understanding should not dampen BF promotion. Currently, there is no evidence to indicate that alternatives to BF improve intelligence above the level attainable through BF. However, there is much to suggest that feeding alternatives may put infants at a disadvantage. The current study, in spite of strong contrary confounding, found results supporting beneficial effects of BF on cognitive development. Although BF remains strongly connected to higher SES in developed countries, other populations and contexts can provide more optimal settings for exploration. We encourage further research in developing countries with the hope that it may provide additional evidence on this important topic.

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LITERATURE CITED


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