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Influence of Breastfeeding on Cognitive Outcomes at Age 6–8 Years: Follow-up of Very Low Birth Weight Infants

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The relation between breastfeeding and childhood cognitive development was examined in 1991–1993 among 439 school-age children weighing <1,500 g when born in the United States between 1991 and 1993. Measures of cognitive function included overall intellectual function, verbal ability, visual-spatial and visual-motor skill, and memory. Higher test scores for each domain of cognitive function except memory were observed among children who were breastfed directly. After covariate adjustment for home environment, maternal verbal ability, a composite measure of parental education and occupation, and length of hospitalization, the authors found that breastfed children evidenced an advantage only for measures specific to visual-motor integration (5.1 intelligence quotient (IQ) points, 95% confidence interval: 1.0, 9.2). Differences in test scores between breastfed children and those who did not receive any breast milk feedings were 3.6 IQ points (95% confidence interval: –0.3, 7.5) for overall intellectual functioning and 2.3 IQ points (95% confidence interval: –3.0, 7.6) for verbal ability. Indicators of social advantage confound the association between breastfeeding and cognitive function, but careful measurement can reduce residual confounding and may clarify causal relations.

breast feeding; child development; infant nutrition; infant, very low birth weight

Abbreviations: CI, confidence interval; DHA, docosahexaenoic acid; IQ, intelligence quotient; SES, socioeconomic status; VLBW, very low birth weight.

The majority of studies observe improved cognitive ability or academic performance among breastfed children, but it is not clear whether the modest advantage is due to beneficial properties of breast milk or results from residual confounding (1–3). Cognitive development is a complex process; a child's genetic potential is influenced by myriad environmental factors that may influence infant feeding decisions. Both initiation and duration of breastfeeding in industrialized countries are strongly associated with indicators of social advantage (4, 5–7), and the association between breastfeeding and estimates of cognitive ability is consistently attenuated by adjustment for socioeconomic status (SES) and environmental factors (1–3).

The construct and assessment of socioenvironmental factors are complex (8) and vary among studies examining the association between breastfeeding and cognitive ability. Combined measures of parental educational attainment and occupation, more than household income or occupation alone, influence perinatal outcomes (9, 10), and home cognitive enrichment explains significant variation in childhood intellectual development beyond SES and parental education (11). Parental intellect may influence childhood cognitive development through a genetic component as well as less tangible factors relating to parent-child interaction and cognitive stimulation (12, 13). However, few studies have included measures of maternal intellectual ability or home

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environment, and none involved very low birth weight (VLBW) infants (3, 12).

A stronger association between breastfeeding and cognitive outcomes has been observed in studies of low birth weight infants (3). Preterm delivery may be associated with increased vulnerability, but low birth weight infants are also at greater risk of neonatal complications that may affect infant feeding practices (4). Many components present in human milk may benefit neurodevelopment (14, 15), but attention has focused on docosahexaenoic acid (DHA). As DHA accumulates in the third trimester, preterm infants demonstrate low body stores at a time of high brain demand. Randomized clinical trials evaluating DHA and arachidonic acid-enriched formula observed improved visual acuity and motor development among preterm, but not term, infants at 12 months of age (16, 17).

It is not known whether breastfeeding influences the cognitive function of vulnerable subgroups of VLBW infants such as those experiencing cerebral injury or born extremely premature. Cerebral lesions detectable by neonatal ultrasonography, intraventricular hemorrhage, ventriculomegaly, echodensity, and echolucency occur more frequently in preterm infants (18). Myelination begins after the third trimester, and the time before onset of myelination is characterized by oligodendrocyte precursor cell migration and proliferation, processes that might be susceptible to injury or lack of necessary substrates (19). DHA has been shown to positively influence myelin formation in patients with generalized peroxisomal disorders (20), and provision of DHA through breast milk may be advantageous for infants born before 28 weeks of gestation or those who demonstrate neonatal cerebral lesions.

This study examined the association between infant feeding practices and cognitive function among VLBW infants after adjustment for maternal verbal ability, home environment, composite SES index, and neonatal morbidity. Multiple domains of cognitive function were assessed, including overall intellectual function, verbal ability, visual-spatial skill, visual-motor skill, visual-motor integration, and memory.

MATERIALS AND METHODS

Study design and measures

The sample for our study consisted of 439 children aged 6–8 years enrolled in follow-up studies of the Developmental Epidemiology Network cohort. This cohort, consisting of 1,665 infants weighing 1,500 g or less who were born in one of five hospitals in Massachusetts, New York, or New Jersey in 1991–1993, was assembled to investigate the epidemiology of brain injuries in VLBW infants and has been described previously (21, 22). Nearly all infants (n = 1,607) received serial ultrasonographic evaluation; 1,442 infants survived to hospital discharge. Maternal postpartum interviews were conducted, and data were abstracted from obstetric and neonatal charts.

Sampling for the Neuropsychological Outcomes Study was based on the presence of cerebral lesions, including echodensity, echolucency, and/or ventriculomegaly on any ultrasound scan. All surviving children with evidence of these ultrasound abnormalities (n = 119) were included, plus a random sample (1:4 ratio) of infants frequency matched for gestational age. All infants from twin and triplet births in New York and New Jersey medical centers were eligible for the Epidemiologic Study of Multiple Births. The analysis consisted of 439 children (57 percent of the target sample size) who had undergone the neuropsychological assessment and for whom parental questionnaires were complete by September 2002. Subject recruitment for other research objectives is ongoing, but this is the sole analysis examining the association between infant feeding and cognitive function in this VLBW cohort.

Approval was obtained from the institutional review boards at the Columbia Presbyterian Medical Center (New York) and Boston Children's Hospital (Massachusetts). Informed consent from the parent or guardian and verbal assent from the child were obtained.

The neuropsychological assessment included a neurological evaluation and a battery of standardized cognitive and behavioral tests. The Kaufman Assessment Battery for Children provided an estimate of overall intellectual function (23). Two assessments of verbal ability were obtained: the Peabody Picture Vocabulary Test–Third Edition evaluating single word comprehension (24) and the Clinical Evaluation of Language Fundamentals–Third Edition assessing comprehensive receptive and expressive language skills (25). Both English and Spanish versions of the Peabody Picture Vocabulary Test (24, 26) were administered to children from bilingual homes, and the Spanish version was used when a clear advantage was observed (>1 standard deviation of the English test score). Memory was evaluated by using the California Children's Verbal Learning Test (27). The Wide Range Assessment of Visual Motor Abilities provided measures of visual-spatial skill, including drawing, matching, and fine motor skill (28). The Kaufman Assessment Battery for Children, Peabody Picture Vocabulary Test, Clinical Evaluation of Language Fundamentals–Third Edition, and Wide Range Assessment of Visual Motor Abilities are standardized with a mean (100 points) and standard deviation (15 points). Two subtests from the Kaufman Assessment Battery for Children, triangle completion and gestalt closure, were examined separately. For children whose impairments prohibited completion of the Kaufman Assessment Battery for Children (n = 14), a value one point below the minimum test score was imputed.

Parents completed structured questionnaires so we could obtain demographic, behavioral, and developmental information. The Peabody Picture Vocabulary Test was administered to mothers in their language of preference (24, 26) as an estimate of verbal intelligence and is strongly correlated with more comprehensive measures of adult intelligence quotient (IQ) such as the Wechsler Adult Intelligence Scale (29). SES was assessed by using the Hollingshead Four Factor Index of Social Class that is based on occupation and educational attainment of both parents (30). Home cognitive enrichment was evaluated in a semistructured maternal interview, the elementary Home Observation for Measurement of the Environment Inventory (HOME)–short version, designed for children aged 6–10 years (31).

A mother reported whether her child ever received expressed milk feedings or direct breastfeedings. Infants were grouped into three categories: never received breast milk feedings, received expressed milk feedings without progression to direct breastfeedings, and received direct breastfeedings. Duration of human milk feedings was recorded in five categories: less than 1 week, 1–4 weeks, 1–3 months, 4–6 months, and more than 6 months.

Analysis

Chi-square tests and analysis of variance were used to determine significant differences in sociodemographic, maternal, and neonatal factors, as well as unadjusted test scores, among the infant feeding groups. The effect of potential confounding factors was assessed by multiple linear regression analysis, with feeding method as a categorical explanatory variable. Two dummy variables were coded for exposure to breast milk to accommodate the three infant feeding categories. Demographic and neonatal variables associated with breast milk feedings at a significance level of 0.15 or less were considered for inclusion in the regression model. A change of more than 10 percent in the regression coefficient for breastfeeding was used to determine whether the covariate was retained. The final model included maternal verbal ability, Hollingshead Index for SES, Home Observation for Measurement of the Environment Inventory score as a measure of home environment, and duration of hospitalization as an estimate of neonatal morbidity. A regression model with less precise, but more commonly available indicators of social advantage, for example, maternal educational attainment and annual household income, was also examined.

In this paper, associations are reported as mean differences in cognitive test scores between children who received direct breastfeedings and those who did not. The categories of expressed milk feedings and direct breastfeedings were combined to increase power for testing terms of interaction in the analysis of the association of breast milk feedings with measures of cognitive function for children demonstrating neonatal cerebral ultrasound abnormalities or birth before 28 weeks of gestation.

The potential for multicollinearity between covariates in the regression model was assessed. Pairwise correlations of the covariates in the final model were examined and ranged from 0.3 to 0.49. Generally, correlations greater than 0.7–0.8 suggest multicollinearity (32). Second, each covariate in the final model was regressed on all remaining independent variables to calculate the variance inflation factor, and multicollinearity between more than two variables was examined by using the eigenvalues of the correlation matrix. No evidence of harmful multicollinearity was observed.

Subjects who participated in follow-up studies were compared with those selected for inclusion in the follow-up studies. Compared with nonparticipating mothers, those who participated were older, were more educated, and were more likely to be married, be nonsmokers, and have private medical insurance. No differences were observed in parity, mode of delivery, or infant characteristics such as birth weight, gestational age, multiple birth status, or length of infant hospitalization.

RESULTS

A total of 153 infants (36 percent) received no human milk, 142 infants (32 percent) received expressed milk feedings without progressing to direct breastfeedings, and 125 infants (28 percent) received direct breastfeedings. The majority of directly breastfed infants first received expressed milk feedings; only three infants were fed directly from the breast at birth. Feeding status was unknown for 19 infants, and they were excluded from further analysis. Breast milk feedings of less than 1 week were uncommon (6.7 percent), but only 20 percent of infants received breast milk beyond 6 months of age. Median birth weight was 1,014 g (range, 500–1,500 g); median gestational age was 27.4 weeks (range, 23.3–35.1 weeks). Thirty-nine percent of infants were from multiple births. Evidence of at least one cerebral abnormality on neonatal ultrasound was demonstrated by 29 percent of infants.

Socioenvironmental and neonatal factors were strongly associated with type of infant feeding (table 1). Provision of breast milk feedings was positively associated with maternal verbal ability, educational attainment, SES, and home environment. Mothers who provided breast milk feedings tended to be older, married, and less likely to smoke cigarettes than mothers who did not initiate breast milk feedings. Gender, birth order, or inclusion in a multiple birth did not differ according to infant feeding group, but directly breastfed infants demonstrated higher birth weights and gestational ages. Longer hospital stays were observed for infants who received expressed milk feedings. As an indicator of the occurrence and severity of neonatal illness, prolonged hospitalization may decrease the likelihood of successful progression from expressed milk feedings to direct breastfeedings.

Test scores

Breast milk feedings were associated with higher unadjusted test scores for each domain of cognitive function except memory (table 2). The greatest advantages in cognitive performance were observed for children who received direct breastfeedings compared with those who did not receive any breast milk feedings. Expressed milk feedings were associated with higher test scores on the single domain of visual-motor integration. Children who were directly breastfed demonstrated a 10.7-point advantage in overall intellectual function and scored 10–14 points higher on measures of verbal ability compared with children who never received breast milk feedings.

The effect of covariate adjustment on the associations between breastfeeding and tests of cognitive ability is demonstrated in table 3. Adjustment for maternal verbal ability, home environment, and composite SES reduced the mean difference for individual test scores. In the regression model that included these indicators of social advantage and neonatal morbidity, the adjusted advantage in overall intellectual function associated with direct breastfeeding was reduced to 3.6 points (95 percent confidence interval (CI):

TABLE 1. Maternal, sociodemographic, and neonatal characteristics† associated with infant feeding history‡ for 439 very low birth weight infants recruited from five hospitals in New York, New Jersey, and Massachusetts in 1991–1993

Characteristic	No breast milk feedings (n = 153)	Expressed milk feedings (n = 142)	Direct breastfeedings (n = 125)
Maternal age (years)	35.6 (6.6)	36.8 (5.2)	40.0 (4.5)***
Maternal verbal ability§	94.0 (13.2)	97.0 (15.4)	102.2 (16.2)***
Maternal education			
High school diploma or less	24.3	14.8	3.6***
Some college	55.6	50.4	38.9
Bachelor of science degree or greater	20.1	34.8	57.5
Cigarette smoking (% smokers)	27.3	22.7	10.6**
Marital status (% married)	58.6	64.3	84.4***
HOME¶ score	12.4 (3.4)	13.5 (3.2)	15.3 (2.7)***
SES#	39.4 (14.0)	44.0 (14.6)	51.2 (12.6)***
Annual household income			
<$39,999	39.7	26.2	15.7***
$40,000–99,999	37.6	33.3	29.8
>$100,000	22.7	40.5	54.5
Gender (% male)	48.0	46.3	54.8
Multiple birth	38.5	38.2	41.7
Parity (% firstborn)	31.0	27.4	26.3
Birth weight (g)	1,012 (261)	988 (266)	1,091 (234)**
Gestational age (weeks)	27.8 (2.5)	27.7 (2.4)	28.7 (2.4)*
Length of hospital stay (days)	57.7 (29.5)	67.6 (36.9)	51.2 (24.7)***

* $p < 0.01$; ** $p < 0.001$; *** $p < 0.0001$.

† For continuous variables, values are given as mean (standard deviation); for categorical variables, the values are percentages.

‡ Feeding status was unknown for 19 infants.

§ Peabody Picture Vocabulary Test (24).

¶ HOME, Home Observation for Measurement of the Environment Inventory-short version (31); range, 6–19; higher scores indicate a more enriched home environment.

Socioeconomic status (SES) was assessed by using the Hollingshead Four Factor Index of Social Class (30); range, 10–66; higher scores indicate a more prominent social standing.

–0.3, 7.5). Adjusted differences for test scores of verbal ability, fine motor skill, and visual-spatial skill were also substantially reduced, but a beneficial effect of breast milk feedings remained for the domain of visual-motor integration. Directly breastfed children performed better on both the Wide Range Assessment of Visual Motor Abilities drawing test (5.1 points, 95 percent CI: 1.0, 9.2) and a subtest of the Kaufman Assessment Battery for Children test, triangle completion (0.8 points, 95 percent CI: 0.1, 1.7), than children who received no breast milk feedings. Significantly higher adjusted test scores were also observed among breastfed children on a third assessment of visual-motor integration administered to a subset of the cohort (n = 279), the WISC Object Test (33). Furthermore, expressed milk feedings were associated with higher adjusted test scores on the Wide Range Assessment of Visual Motor Abilities drawing test (5.0 points, 95 percent CI: 1.1, 9.5).

Another set of multiple regression analyses were conducted with less precise, but more common indicators of social advantage. The regression model including maternal educational attainment and annual household income attenuated the observed associations between breastfeeding and cognitive outcomes to a lesser extent than the model adjusting for maternal verbal ability, home environment, and composite SES (table 3). The association between duration of breast milk exposure and cognitive performance was also examined. No significant differences were observed between adjusted test scores for children with the greatest exposure to breast milk (those breastfed for ≥4 months) and children who did not receive breast milk feedings (data not shown). However, the magnitude of the effect associated with breastfeeding duration on the domain of visual-motor integration (Wide Range Assessment of Visual Motor Abilities drawing test: 4.1 points, 95 percent CI: –0.8, 9.0; triangle

TABLE 2. Unadjusted cognitive test scores (mean (standard deviation)) at age 6–8 years according to infant feeding history† for 439 children recruited at birth from five hospitals in New York, New Jersey, and Massachusetts in 1991–1993

Domain of cognitive function	Assessment of cognitive ability‡	Test scores		
		No breast milk feedings (*n* = 153)	Expressed milk feedings (*n* = 142)	Direct breastfeedings (*n* = 125)
Overall intellectual function	K-ABC mental processing score	92.3 (15.3)	94.2 (17.3)	102.8 (15.2)***
Verbal ability	PPVT-III	92.6 (17.2)	94.1 (18.6)	102.7 (16.5)***
	CELF-3	88.5 (21.6)	89.5 (22.9)	102.4 (19.4)***
Memory	CVLT short-term recall	43.8 (11.2)	44.5 (12.0)	46.4 (11.6)
	CVLT delayed recall	5.9 (3.7)	6.2 (3.2)	6.4 (3.0)
Visual-spatial skill	WRAVMA matching	89.8 (15.5)	91.6 (17.0)	98.1 (17.2)***
	K-ABC gestalt closure	9.7 (3.0)	9.7 (3.0)	9.9 (3.0)
Visual-motor skill	WRAVMA drawing	90.6 (13.5)	94.5 (16.7)	97.7 (14.6)**
	K-ABC triangle completion	9.1 (2.5)	9.9 (3.0)	10.6 (3.0)**
Fine motor skill	WRAVMA pegboard	91.1 (20.2)	89. (20.4)	97.6 (17.1)*

* $p < 0.01$; ** $p < 0.001$; *** $p < 0.0001$.

† Feeding status was unknown for 19 infants.

‡ Tests of cognitive ability included the following: Kaufman Assessment Battery for Children (K-ABC) (23), Peabody Picture Vocabulary Test (PPVT-III) (24), Clinical Evaluation of Language Fundamentals–Third Edition (CELF-3) (25), California Children's Verbal Learning Test (CVLT) (27), and Wide Range Assessment of Visual Motor Abilities (WRAVMA) (28).

completion test: 0.7 points, 95 percent CI: –0.2, 1.6) was similar to that observed for direct breastfeedings.

Subgroup analyses

The association between breast milk feedings and cognitive development was examined among children with special vulnerabilities, including cerebral ultrasound abnormalities and young gestational age. Evidence of cerebral ultrasound abnormalities during the neonatal period was observed in 119 children, and 225 children were born before 28 weeks of gestation. Lower unadjusted test scores on all domains of cognitive function were observed for children with neonatal ventriculomegaly and echodensity, and children with

TABLE 3. Effect of covariate adjustment on the differences in cognitive test scores among children aged 6–8 years who received direct breastfeedings and those who received no breast milk feedings* recruited as very low birth weight infants from five hospitals in New York, New Jersey, and Massachusetts in 1991–1993

Domain of cognitive function	Assessment of cognitive ability†	Unadjusted model		+ Maternal verbal ability‡		+ Home environment§		+ Composite measure of SES¶		Final model#		Less precise covariate model**	
		RC††	95% CI††	RC	95% CI	RC	95% CI	RC	95% CI	RC	95% CI	RC	95% CI
Overall intellectual function	K-ABC mental processing score	10.7	7.0, 14.4	8.8	5.0, 13.1	6.5	2.6, 10.4	7.5	3.8, 11.2	3.6	–0.3, 7.5	5.5	1.6, 9.4
Verbal ability	PPVT-III	10.0	6.2, 13.7	7.0	3.1, 10.9	3.8	–0.3, 7.7	6.3	2.0, 10.6	2.3	–3.0, 7.6	4.3	0.4, 8.2
	CELF-3	14.1	8.8, 19.2	10.4	5.3, 15.5	5.5	0.6, 10.4	6.3	1.2, 11.4	1.3	–3.8, 6.4	4.9	0.4, 9.4
Fine motor skill	WRAVMA pegboard	6.5	1.5, 10.9	5.7	1.0, 10.4	4.3	–0.6, 9.2	4.8	–0.1, 9.7	2.7	–2.5, 7.6	3.6	–1.5, 8.7
Visual-spatial skill	WRAVMA matching	8.4	4.5, 12.3	6.9	3.0, 10.8	5.0	1.1, 8.9	6.5	2.4, 10.6	3.4	–0.9, 7.7	5.0	0.9, 9.1
Visual-motor skill	WRAVMA drawing	6.5	3.0, 10.0	6.4	2.7, 10.3	5.4	1.7, 9.1	5.7	2.2, 9.8	5.1	1.0, 9.2	5.5	1.6, 9.4
	K-ABC triangle completion	1.5	0.7, 2.1	1.2	0.5, 1.9	1.2	0.5, 1.9	1.1	0.4, 1.8	0.8	0.1, 1.7	1.0	0.2, 1.8

* Feeding status was unknown for 19 infants.

† Tests of cognitive ability included the following: Kaufman Assessment Battery for Children (K-ABC) (23), Peabody Picture Vocabulary Test (PPVT-III) (24), Clinical Evaluation of Language Fundamentals–Third Edition (CELF-3) (25), and Wide Range Assessment of Visual Motor Abilities (WRAVMA) (28).

‡ Maternal Peabody Picture Vocabulary Test (24).

§ Home Observation for Measurement of the Environment Inventory-short form (31).

¶ Socioeconomic status (SES) was assessed by using the Hollingshead Four Factor Index of Social Class (30).

\# The final model contained maternal verbal ability, home environment, composite SES, and length of hospital stay.

** Contains annual household income, maternal education, and length of hospital stay.

†† RC, regression coefficient; CI, confidence interval.

TABLE 4. Association between breast milk feedings* and cognitive test scores among children demonstrating neonatal cerebral ultrasound abnormalities or a gestational age of <28 weeks recruited as very low birth weight infants from five hospitals in New York, New Jersey, and Massachusetts in 1991–1993

Domain of cognitive function	Assessment of cognitive ability†	Adjusted interaction terms‡							
		Cerebral ultrasound abnormalities§				Gestational age (weeks)			
		Yes (*n* = 119)		No (*n* = 320)		<28 (*n* = 225)		≥28 (*n* = 214)	
		RC¶	95% CI¶	RC	95% CI	RC	95% CI	RC	95% CI
Overall intellectual function	K-ABC mental processing score	2.0	–2.5, 8.5	1.7	–5.1, 7.9	0.6	–2.9, 4.1	–1.5	–7.3, 4.5
Verbal ability	PPVT-III	0.3	–7.2, 7.7	0.5	–6.5, 7.5	1.3	–3.2, 5.8	–4.0	–13.8, 5.8
	CELF-3	1.6	–7.0, 10.2	–0.2	–8.2, 7.9	2.1	–3.0, 6.5	1.7	–4.5, 7.2
Fine motor skill	WRAVMA pegboard	4.8	–5.2, 15.6	5.4	–2.4, 9.4	1.4	–3.6, 6.4	3.9	–5.9, 13.7
Visual-spatial skill	WRAVMA matching	0.3	–6.9, 7.6	0.4	–6.8, 7.7	–0.6	–4.9, 3.7	3.4	–4.4, 11.2
Visual-motor skill	WRAVMA drawing	3.2	–3.7, 10.1	2.6	–4.3, 9.5	3.1	–1.0, 7.2	2.8	–5.0, 10.6
	K-ABC triangle completion	0.05	–2.1, 2.2	–0.2	–8.0, 7.6	–0.08	–0.8, 0.7	0.3	–5.6, 6.2

* Feeding status was unknown for 19 infants.

† Tests of cognitive ability included the following: Kaufman Assessment Battery for Children (K-ABC) (23), Peabody Picture Vocabulary Test (PPVT-III) (24), Clinical Evaluation of Language Fundamentals–Third Edition (CELF-3) (25), and Wide Range Assessment of Visual Motor Abilities (WRAVMA) (28).

‡ Adjusted for maternal verbal ability, home environment, composite socioeconomic status, and length of hospital stay.

§ At least one of the following neonatal ultrasound abnormalities: intraventricular hemorrhage, ventriculomegaly, echolucency, echodensity.

¶ RC, regression coefficient; CI, confidence interval.

neonatal intraventricular hemorrhage scored lower on tests of each domain except memory. We found no evidence of an increased influence of breast milk feedings on cognitive test scores among any subgroups of VLBW infants (table 4).

DISCUSSION

Consistent with previous research, directly breastfed children scored higher on unadjusted measures of overall intellectual function and visual ability as well as on tests of visual-spatial and visual-motor ability. However, substantial confounding by socioenvironmental factors was observed. Adjustment for the most precise measures of social advantage available in this study, maternal verbal ability, home environment, and composite SES, markedly reduced the magnitude of the overall intellectual advantage observed among breastfed children from 10.7 IQ points (95 percent CI: 7.0, 14.4) to 3.6 IQ points (95 percent CI: –0.3, 7.5). Adjustment for less comprehensive indicators of social advantage, maternal education and household income, resulted in an apparent benefit (5.5 IQ points, 95 percent CI: 1.6, 9.4) among breastfed children. Given the substantial reduction observed for control of socioenvironmental factors, the lack of statistical significance, and the well-established difficulties in measuring the construct of social advantage, these results suggest that part of the enhanced cognitive performance attributed to breastfeeding may be due to residual confounding. Similar results have been reported for full-term infants. Jacobsen et al. (12) also observed that the cognitive advantage associated with breastfeeding was no longer statistically significant after maternal verbal ability and home environment were added to the regression model containing social class and maternal education.

A greater effect of breast milk feedings on measures of cognitive development among low birth weight infants compared with full-term infants has been described (3, 34, 35), but previous studies may not have adequately adjusted for socioenvironmental confounders. The composite advantage observed in a meta-analysis of studies including low birth weight infants (5.16 IQ points, 95 percent CI: 3.59, 6.77) was based on studies that did not include measures of maternal verbal ability or home environment (3). The stronger association between breastfeeding and cognitive function observed in previous studies of low birth weight infants may reflect residual confounding rather than biologic susceptibility (3, 36, 37). The majority of studies examining the association between breastfeeding and cognitive development have assessed breastfeeding as a dichotomous variable. Studies of VLBW infants may distinguish between expressed milk feedings and direct breastfeedings, and this comparison has been used to differentiate the biologic effect of exposure to breast milk from the intangible effects of maternal bonding associated with direct breastfeedings. Lucas et al. (35) observed higher intellectual performance (7.5 IQ points) among low birth weight infants receiving only expressed milk feedings, an advantage similar to that observed for infants who progressed to direct breastfeedings (8.3 IQ points). However, our results and those of Doyle et al. (38) suggest a minimal effect of expressed milk feedings on measures of cognitive function except for the domain of visual-motor integration. The observation of cognitive advantage associated with increasing duration of breastfeeding has been considered evidence of a dose-response relation (3, 36, 39). Indicators of social advantage also positively correlate with breastfeeding duration (5, 37). After covariate adjustment, we did not observe an association between breastfeeding and overall intellectual functioning, verbal ability, or visual-spatial skill even among children who were breastfed for 4 or more months.

Although more precise covariate adjustment attenuated most cognitive advantages, both expressed milk feedings and direct breastfeedings were associated with improved visual-motor function in this cohort of VLBW infants. Triangle construction and drawing both assess the underlying construct of visual-motor integration—the ability to look at spatial information, process it, and then use motor skills to reproduce it through drawing or assembling a puzzle. Visual-spatial reasoning involves perspective, orientation, rotation, and size discrimination but does not require organization of the motor system to coordinate gross and fine motor movements. Few studies have examined the association between breastfeeding and measures of visual-motor integration. Advantages in tests of visual-motor integration were observed for breastfed children in some (40, 41) but not all (6) studies. VLBW infants are at greater risk of visual-motor impairment (42), and improved scores were observed on all three tests of this domain. Furthermore, the association between breastfeeding and visual-motor skill was observed when breast milk exposure was assessed as expressed milk feedings, direct breastfeedings, and duration of breastfeeding.

To our knowledge, this is the first examination of the association between breastfeeding and cognitive development among children with evidence of neonatal cerebral injuries. Although cognitive impairment was more common in these children, we found no indication that breast milk feedings ameliorated the deficits.

Several limitations of this analysis must be considered. Information regarding infant feeding practices was collected retrospectively. Previous research has observed that recall of breastfeeding initiation agreed with written records for 85 percent of mothers interviewed after 14–15 years (43) but that recall of breastfeeding duration was less precise, with 37–79 percent of mothers reporting accurately within 1 month (44, 45).

Quantification of the amount of breast milk consumed was not available, and the majority of VLBW infants did not receive long-term breast milk feedings. It is possible that increased breast milk exposure, through either exclusive breastfeeding or a longer duration, is associated with larger cognitive advantages.

Many domains of cognitive development were assessed, and multiple comparisons could increase the possibility of observing a statistically significant finding by chance. However, the combination of more precisely measured covariates and assessment of multiple domains of cognitive function helped to clarify the role of residual confounding and to identify a specific domain of cognitive function that might be influenced by breast milk consumption.

Finally, observational epidemiologic studies may be limited in their ability to evaluate the causal association between breastfeeding and cognitive development. Even the most precise measures of social advantage available in this study may not have adequately controlled for confounding. This study used the short version of the Home Observation for Measurement of the Environment Inventory questionnaire that omitted home visitation, maternal intellectual function was assessed by a verbal estimate rather than a full-scale measure, only single assessments of socioenvironmental indicators were available, and complete control of SES is unachievable. On the other hand, adequate covariate adjustment is more complex than identifying, conceptualizing, and measuring potential confounding factors. Because breastfeeding intent is strongly associated with social advantage, attributing all outcome variance shared by breastfeeding and SES indicators to the construct of social advantage may exaggerate the impact of socioenvironmental variables and underestimate the observed association between breastfeeding and cognitive ability. Despite these methodological constraints, the specificity of the effect of breast milk feedings to a single domain of cognitive function highlights the importance of socioenvironmental factors in studies of breastfeeding and cognition and supports the possibility that the observed advantage in visual-motor integration did not result from residual confounding.

The public health significance of the modest effect of breastfeeding on cognitive performance may be debated. Although the magnitude of the effect of breastfeeding on measures of cognition is less than that observed for iron deficiency anemia (46), infant feeding recommendations affect the entire population instead of a small subset of children. Even a slight shift in the mean IQ of the population would result in fewer children being categorized as low functioning, which might be especially important for VLBW infants at increased risk of cognitive deficits. The advantage in visual-motor integration associated with breastfeeding may translate functionally into improved skills such as writing and other physical tasks that involve eye-hand coordination.

In this follow-up study of VLBW infants, adjustment for socioenvironmental factors substantially reduced the cognitive advantages observed for children who received direct breastfeedings. Regression models including more precise socioenvironmental indicators such as maternal verbal ability, composite SES index, and home environment reduced confounding compared with models that included maternal educational attainment and annual household income only. Breast milk feedings were associated solely with improved visual-motor performance after adjustment for these precise indicators. The possibility that breast milk enhances the development of visual-motor integration warrants further research. Careful measurement of socioenvironmental indicators is critical to advancing our understanding of the potential influence of breastfeeding on cognitive development.

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