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Feeding Infants at the Breast or Feeding Expressed Human Milk: Long-term Cognitive, Executive Function, and Eating Behavior Outcomes at Age 6 Years

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Abstract

Objective—To examine how expressed milk feeding diverges from feeding at the breast in its association with neurodevelopment and behavior. We hypothesized that longer and exclusive feeding at the breast only (ie, no formula, no feeding expressed milk) would be associated with the optimal cognitive developmental, executive function and eating behaviors, and expressed milk feeding would be associated with less optimal outcomes.

Study design—The Moms2Moms cohort (Ohio, USA) reported infant feeding practices at 12 months postpartum and children's global cognitive ability, executive function, and eating behaviors at 6 years. Linear and log-binomial regression models estimated associations with durations of feeding at the breast, expressed milk, human milk (modes combined), and formula.

Results—Among 285 participants, each month of exclusive feeding at the breast only was associated with a decreased risk of clinically-meaningful executive function (working memory) deficit (adjusted RR=0.78, 95% confidence interval (CI): 0.63, 0.96), but was unassociated with inhibition (adjusted RR=0.92, 95% CI: 0.85, 1.01). Feeding expressed milk was not clearly related

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to executive function outcomes. No associations with global cognitive ability were observed. Weak associations were observed with eating behaviors for some feeding practices.

Conclusions—Feeding at the breast may offer advantages to some aspects of executive function that expressed milk may not. Large, prospective studies exploring mechanisms could further distinguish the effect of feeding mode from that of nutrients.

Keywords

Breastfeeding; eating behavior; pumping; human milk expression; executive function

With the accessibility of breast pumps and increasing interest in providing human milk while working outside the home, milk expression (pumping) has become popular in the US more than 85% of infants fed human milk are fed expressed milk at least sometimes.¹

Compared with formula feeding, a longer duration of breastfeeding and breastfeeding exclusivity are associated with enhanced cognitive development in childhood, although residual confounding by socioeconomic status and maternal cognitive ability remains a concern for observational studies.^{2–6} Several studies have reported benefits to behavioral outcomes like attention and hyperactivity^{7,8} and associations with food-related behaviors (e.g., less food fussiness, greater satiety responsiveness).^{9,10} Although some studies have examined associations between breastfeeding and higher-level cognitive abilities that are predictive of school success, often considered under the umbrella term “executive function,”¹¹ almost no studies have examined the mode of feeding human milk (breast vs bottle) and such outcomes.^{12,13} Expressed milk feeding diverges from feeding at the breast and instead parallels formula feeding in several ways that could affect neurodevelopment and behavior. Failure to distinguish between modes of feeding human milk could introduce exposure misclassification if infants fed human milk from a bottle are errantly classified as formula fed, thereby introducing bias that would underestimate any beneficial effect of breastfeeding on outcomes.

Several studies examined the mode of human milk feeding in relation to long-term developmental or behavioral outcomes, and these focused only on the first 3–6 months of infant feeding.^{14–16} The present study was designed to examine human milk infant feeding practices, including distinguishing expressed milk feeding versus feeding at the breast. We examine important long-term outcomes including executive function (working memory, inhibition), global cognitive development, and eating behaviors, in a longitudinal study of US mothers and children to age 6 years. We hypothesized that longer and more exclusive feeding at the breast only (i.e., no formula, no feeding expressed milk) would be associated with the most optimal global cognitive development, executive function and eating behaviors, with expressed milk feeding associated with somewhat less optimal outcomes.

Methods

In 2012, 1,244 adult (>18 years), English-speaking women who delivered a live-born singleton infant (>24 weeks' gestation) at The Ohio State University Wexner Medical Center (Columbus, OH, USA) over a period of 5 months in 2011 were potentially eligible for the

Moms2Moms (M2M) study. The original objective of the M2M study was to study peer to peer human milk sharing. Women were not recruited if they lacked valid contact information (n=111), were prisoners (n=11), or had infants who did not survive delivery or the hospital stay (n=6).¹⁷ Because the “bottle feed” designation on this labor and delivery unit was for women who intended to exclusively formula feed their infant, women whose medical record indicated their intention to “bottle feed” were also not recruited (n=303).

Eligible women (n=813) were mailed a survey at 12 months’ postpartum to assess lactation and infant feeding behaviors from delivery to the time of the survey, and sociodemographic information (maternal education, marital status, maternal race/ethnicity, household income, enrollment in the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC), maternal employment/school attendance, child care participation, smoking, child’s sex). Five hundred and one women participated. Additional maternal and child characteristics were abstracted from the obstetric record (maternal age, health insurance status, parity, mode of delivery, and child gestational age, birthweight, and sex). Participants received a \$10 incentive. This original study was approved by the Institutional Review Board at The Ohio State University, and further details have been reported previously.¹⁷

6-year follow up

Mothers were re-contacted in 2017 for the current follow-up study to assess child neurodevelopmental and behavioral outcomes at age 6 years and lactation and infant feeding beyond 12 months. Of 501 original M2M participants, 10 had a change in legal guardianship, had missing or incomplete data from the original survey, or had significant difficulty understanding the prior survey in English, leaving 491 for whom re-contact was attempted. Participants were invited to complete a 10-minute phone survey that included questions about lactation and infant feeding practices again, and a 30-minute, electronic survey via REDCap that included questions about child global cognitive ability, executive function, eating behaviors, and overall health.¹⁸ If participants needed assistance or could not complete the REDCap survey, the survey was administered via phone or postal paper survey. Participants received a \$15 incentive. If all required study activities were completed, the mother was entered into a drawing to win a FitBit activity tracker. This 6-year follow up was approved by the Institutional Review Board at Nationwide Children’s Hospital.

Infant feeding measures and variables

The instrument used to assess lactation and infant feeding at both time points asked about the child’s age when they started and stopped each feeding practice (i.e., feeding at the breast, feeding expressed milk, and feeding formula). The values recorded on the survey at 12 months were used for the present analysis unless the respondent reported they were still engaging in a particular feeding practice at that time. In those instances, values reported on the 6-year survey were used. Four binary variables were created for whether the dyad ever fed at the breast, ever fed expressed milk, ever fed human milk (i.e., ever fed at the breast or expressed milk), and ever fed formula. Continuous variables were created for the duration of each feeding practice by subtracting the starting age from the stopping age, in days, and then converting to months for ease of interpretation. A second set of continuous variables was created for the duration the dyad exclusively fed using each feeding practice. We defined

“exclusive” as no feeding by the other human milk or formula feeding methods, but the child may have been fed other liquids or solid foods (e.g., exclusive expressed milk feeding was defined as being fed expressed milk during that time period without feeding at the breast and without feeding formula, but other liquids or foods were possible).

Child neurodevelopmental outcome measures and variables

The Developmental Profile 3 (DP-3, up to 38-item cognitive function sub-test) is a parent-completed questionnaire appropriate for children from birth to age 12 years used to identify a child’s cognitive strengths and weaknesses.¹⁹ An example question included, “*Could the child take out 12 objects from a group of 20 objects when asked?*” Parents indicated “Yes” if their child had demonstrated the ability and, “No” if they had not. “Yes” responses were summed, and norms were referenced to generate standardized cognitive scores with a mean of 100 and standard deviation of 15. Scores < 85 were considered below average or delayed. The Childhood Executive Functioning Inventory (CHEXI) is a 24-item caregiver-completed assessment of child executive function for children ages 4–11 years.²⁰ Example items included, “*Has difficulty with tasks or activities that involve several steps.*” and “*Has difficulty holding back his/her activity despite being told to do so.*” Items are rated on a 5-point scale, from “Definitely Not True” to “Definitely True.” Two subscales are validated for the age group in this study: working memory (sum of working memory and planning items) and inhibition (sum of inhibition and regulation items), with higher continuous scores indicating greater difficulties in the given domain.^{21,22} Binary variables were also created based on a cutoff of 35 for working memory and 32 for inhibition which have been shown to have excellent sensitivity and specificity for identifying children with Attention Deficit-Hyperactivity Disorder (ADHD).²²

Child eating behavior measures and variables

The Children’s Eating Behaviour Questionnaire (CEBQ) is a caregiver-reported measure to assess children’s eating styles.^{23,24} It includes 35 items rated on a 5-point scale of “Never” to “Always,” and consists of eight scales: food responsiveness, enjoyment of food, emotional over-eating, desire to drink, satiety responsiveness, slowness in eating, emotional under-eating, and food fussiness. Mean scores for each sub-scale were used for analysis, with higher scores on the food responsiveness and enjoyment of food scales indicating greater food enjoyment, and higher scores on the remaining subscales indicating a higher observed frequency of the specific behavior.

Data analysis

Descriptive statistics characterized the sample, and chi-square and t-tests compared those who participated in the current follow up study with those who did not participate. This comparison was done to assess the potential selection bias from all the reasons an individual might not be in the follow-up sample: non-response, change in legal guardianship, having missing or incomplete data. Associations between the duration of each human milk feeding practice (continuous variables in units of months) and the continuous, standardized cognitive, working memory, inhibition and eating behavior outcome variables were examined using linear regression. Adjusted models controlled for potential confounders selected *a priori* based on prior literature (maternal age, education, marital status, race,

ethnicity, household income, WIC enrollment, insurance status, maternal employment postpartum, child care participation, maternal smoking, parity, mode of delivery, and child sex and gestational age). Analyses were repeated using log-binomial regression for the dichotomized outcome variables to examine the risk of scoring in the delayed or below average range for cognitive ability, or above clinical cutoffs for working memory and inhibition.

Results

Sample characteristics

Of 491 respondents for whom re-contact was attempted, 305 participated, and 285 had data for at least one outcome measure and were included in the present analysis (Table 1). Mothers were an average of 31 years old at delivery, most identified as white (84%) and non-Hispanic (95%), and most had at least a Bachelor's degree (76%). Household income varied, with over one third of mothers reporting \$55,000 or less (37%). The majority worked or attended school greater than 20 hours per week at some time during the first year postpartum (68%). Both feeding at the breast and feeding expressed milk were common in this cohort (92% and 91% ever did, respectively) (Table 2). Durations varied widely, but mothers fed at the breast for a median of 7.9 months (IQR=1.4–12.0), fed expressed milk for a median of 4.8 months (IQR=1.6–9.0), and fed formula for a median of 10.8 months (IQR=2.0–12.0). Those who participated in the follow-up study differed on some maternal and child characteristics as compared with those who did not participate in the follow-up study (i.e., education, race, income, WIC participation, health insurance status, parity, birthweight, and gestational age), but not on other characteristics (i.e., maternal age, marital status, ethnicity, maternal employment, child care, smoking, mode of delivery, and child sex). At the time of the follow-up study, children were a mean of 69 months old (SD=2, IQR=68–70).

Descriptive statistics for outcome measures

The sample scored slightly above norms on the DP-3 (mean=109, SD=15). Fourteen children (5%) scored in the delayed or below average range. The median working memory score was 26 (IQR=21–31), and the median inhibition score was 27 (IQR=23–31). Approximately 11% of children (31) scored above the clinical cutoff for working memory, and 21% (59) of children scored above the clinical cutoff for inhibition, indicating symptoms congruent with an ADHD diagnosis. Mean CEBQ scores and standard deviations for the sample were: food responsiveness (2.3, 0.7), enjoyment of food (3.6, 0.8), emotional over-eating (1.7, 0.6), desire to drink (2.6, 1.0), satiety responsiveness (3.0, 0.5), slowness in eating (2.7, 0.5), emotional under-eating (2.6, 0.8), and food fussiness (2.7, 0.3).

Associations between feeding practices and outcomes

None of the feeding practice duration variables were associated with global cognitive ability (e.g., adj β for exclusive human milk feeding=0.08, 95% CI: -0.16, 0.32, Table 3). Each additional month of exclusive feeding at the breast only was associated with slightly lower (better) working memory scores (adj β =-0.20, 95% CI: -0.38, -0.01). Similar associations with working memory were observed for the duration of feeding human milk (at the breast

or expressed) and the duration of exclusively feeding human milk only (adj β ranged -0.18 to -0.16). Associations for exclusively feeding expressed milk only were similar in magnitude but less precise, and the confidence interval included the null. The results for inhibition were in the same direction but effect estimates were closer to the null, and only the estimate for the duration of feeding human milk had a confidence interval that excluded the null (adj $\beta = -0.12$, 95% CI: -0.25 , -0.00).

Longer duration of feeding at the breast was associated with an 11% reduced risk of having a working memory score above the clinical cutoff (adj RR=0.89, 95% CI: 0.81, 0.99, Table 4). Duration of exclusive feeding at the breast only was even more strongly associated with a working memory score above the cutoff (adj RR=0.78, 95% CI: 0.63, 0.96). Duration of feeding expressed milk was not associated with the risk of having an elevated (above the clinical cutoff) working memory score. The effect estimate for exclusive expressed milk feeding only duration was well below the null but very imprecise (RR=0.67, 95% CI: 0.22, 2.04). When the duration of feeding at the breast and feeding expressed milk were combined, the associations were similar to those observed for feeding at the breast (adj RR ranged 0.84–0.87). None of the feeding practices were associated with the risk of inhibition scores above the clinical cutoff.

Longer exclusive feeding at the breast only was associated with a small increase in emotional overeating (adj $\beta = 0.02$; 95% CI: 0.00, 0.03) and food fussiness (adj $\beta = 0.01$, 95% CI: 0.00, 0.02) (Table 5; available at www.jpeds.com). The duration of feeding human milk was associated with slightly greater enjoyment of food and also food fussiness in adjusted models (e.g., exclusive feeding human milk only and enjoyment of food: $\beta = 0.01$; 95% CI: 0.00, 0.03). Results from unadjusted models were similar and are not shown.

For all outcomes, the results for formula feeding were approximately the inverse of those for feeding human milk because those practices were mutually exclusive.

Discussion

In the present study, feeding at the breast for longer periods of time was associated with clinically-meaningful advantages in working memory ability at 6 years of age after controlling for confounders in our model where working memory was a binary outcome, for each additional month of exclusive feeding at the breast only, the risk of a working memory score compatible with an ADHD diagnosis decreased by 22%. When feeding at the breast and feeding expressed milk were combined, this association persisted. However, the association was not clearly present for expressed milk feeding by itself. Results for inhibition did not display a similar pattern in the models with binary outcomes, and results for the models where the outcome was continuous were not as clear. Human milk feeding practices were not associated with global cognitive ability based on the DP-3. Additionally, feeding human milk and exclusively feeding human milk only were associated with increased food enjoyment, and exclusively feeding at the breast only was associated with increased emotional overeating at age 6. Feeding human milk and feeding at the breast (and exclusivity of each) were associated with increased food fussiness at age 6. All of the associations with eating behaviors were of small magnitude, however.

Our results for working memory suggest that the mode of feeding human milk may be important to the development of executive function. Core executive functions see particularly rapid development by the preschool years.²⁵ Although the hippocampus is involved in all executive functions and is particularly important for working memory,²⁶ these functions are subserved by the frontal cortex,²⁷ which develops across the lifespan and is sensitive to nutritional alterations.^{28–30} Optimal development of these brain areas requires appropriate nutrition, such as high levels of iron,³¹ fatty acids,³² iodine, and choline,³³ nutrients which are enriched in human milk.^{2,3,7} Additionally, the early development of working memory is highly sensitive to parenting and the home environment.^{34–38} Feeding at the breast may offer infants greater opportunities for bonding that lead to a more stimulating parent-child relationship supportive of early executive function compared with feeding expressed milk. In contrast, with expressed milk feeding,¹⁵ the physical contact between mother and infant during feeding is reduced or eliminated, which may impede the development of maternal sensitivity to infant cues and maternal-infant bonding.³⁹ These features may undermine the benefits typically attributed to “breastfeeding.” On the other hand, residual confounding or reverse causality may explain the association between feeding at the breast and working memory. For instance, executive function is somewhat heritable, and maternal executive function deficits may also lead to less feeding at the breast with more feeding of expressed milk and a less stimulating home environment.^{40–42} Finally, children with poor executive function at age 6 may have been particularly difficult to feed at the breast as infants, a form of reverse causation. However, the fact that we did not observe a similar pattern of results for the inhibition outcome suggests against these alternative explanations. Working memory and inhibitory control are related but distinct facets of executive function. Why feeding at the breast may benefit working memory but not inhibitory control merits further study with more in-depth outcome assessment through studies that include complementary, multimodal measures of child cognition (parent report, teacher report, and objective laboratory assessments) to explore the nuance of this finding.

A prior study examined the mode of feeding human milk in relation to cognitive development is the GUSTO study.¹⁶ GUSTO investigators reported advantages to some aspects of memory across early childhood among the children fed exclusively at the breast compared with those fed exclusively human milk (but not exclusively at the breast). They also reported no association with executive function outcomes including planning, inhibitory control, and attention and also global cognitive ability at 24 and 54 months (although they reported much worse performance at 48 months among the exclusive at-the-breast group). The findings of the present study are consistent with GUSTO in reporting no advantage in global cognitive ability and inhibition for feeding at the breast. GUSTO did not directly assess working memory to enable comparison with the present study on that outcome, as it focused on feeding practices at 3 months of age only. Because GUSTO focused on children of Chinese, Malay, or Indian ethnicities, whether the results apply to a broad sample of US children is unknown.

Two prior studies examined the mode of feeding human milk in relation to later child eating behaviors. DiSantis et al reported reduced satiety responsiveness among children fed human milk from a bottle for the first 3 months of life rather than at the breast, but no association with food responsiveness or enjoyment of food.¹⁴ However, this study measured feeding

practices retrospectively (3–6 years in the past) and only for the first 3 months of life. Meanwhile, the US Infant Feeding Practices Study II (IFPS II) reported no association between bottle-feeding intensity and satiety responsiveness or food responsiveness¹⁵. However, neither study used all of the CEBQ sub-scales to enable direct comparison with the present study, and the DiSantis et al study did not include data on feeding practices beyond 3 months.^{14,43} Given the results of these prior studies and the small associations reported in the present study, it may be that the mode of feeding human milk is not very important for later eating behavior outcomes, but the nutrients in human milk may be, given the prior literature highlighting differences between breast and formula fed groups.⁹ It is also possible that the CEBQ is not sensitive enough to detect differences or is subject to maternal reporting biases that are differential by feeding mode.

One limitation of the present study included the lack of direct assessment of executive function by objective assessors. For instance, if women who tended to feed at the breast also tended to over-report working memory abilities in their children, this may have biased our effect estimates away from the null. Although some studies have reported positive correlations between parent reports of child cognitive abilities and laboratory-based assessments and the CHEXI has specifically been validated against laboratory Go/No-Go and word span tasks administered by trained researchers, it is ideal to capture both parent reports and direct assessments.^{20,44,45} For some outcomes, parent reports can be especially important for day-to-day behaviors that may not be readily observed in a laboratory setting (e.g., typical eating behaviors). Another limitation was the potential for recall bias during survey collection of infant feeding practices which may have introduced measurement error, although the recall was limited to the infancy period rather than many years. Another source of possible measurement error was that we did not collect information about temporary changes in feeding practices (e.g., if a participant stopped pumping for some time and then re-started) or the proportions of feeds that were one mode versus another in time periods when multiple modes were used. Our limited sample size may have precluded observing more robust associations for feeding expressed milk, particularly for exclusive feeding of expressed milk only, which was practiced for relatively short time periods compared with exclusive feeding at the breast only. Loss to follow up may have induced selection bias. We did observe some socio-demographic differences between those who participated in the follow-up survey versus the original cohort. For example, the follow-up sample was somewhat better educated and more likely to identify as white than the original cohort. If loss was differential by both exposure and outcome, our results could be biased, particularly attenuated toward the null if those who tended to formula feed more and had children with poorer executive function were more likely to be lost. However, it is not possible to know if loss to follow-up was differential by exposure and outcome jointly or by outcome alone. Our results may not be generalizable to the entire population of women and children given our sample characteristics differ from the U.S. as a whole. Finally, residual confounding is always a possibility in observational research, including by unmeasured factors like maternal cognitive ability. Whether children had started kindergarten could be a mediator of our associations, but we were unable to examine this because we did not have data on school participation. These limitations are balanced by key strengths of the study, including its prospective cohort design, use of established, validated outcome measures targeting key

aspects of child development, and detailed lactation and infant feeding measures that separated feeding at the breast from feeding expressed milk and included all of infancy and beyond.

Feeding at the breast may offer advantages to executive functions like working memory that feeding expressed milk may not offer. Future prospective research with large samples, careful control of confounding, multi-modal assessment of outcomes, and examination of potential mechanisms is needed to clarify and distinguish the effect of the mode of infant feeding from that of the content of human milk.

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Abbreviations/Acronyms:

ADHD	Attention Deficit-Hyperactivity Disorder
CHEXI	Childhood Executive Functioning Inventory
CEBQ	Children's Eating Behaviour Questionnaire
DP-3	Developmental Profile-3
M2M	Moms2Moms Study

References

1. Labiner-Wolfe J, Fein SB, Shealy KR, Wang C. Prevalence of Breast Milk Expression and Associated Factors. *Pediatrics*. 2008;122(Supplement 2):S63–S68. [PubMed: 18829833]
2. Anderson JW, Johnstone BM, Remley DT. Breast-feeding and cognitive development: a meta-analysis. *Am J Clin Nutr*. 1999;70(4):525–535. [PubMed: 10500022]
3. Kramer MS, Aboud F, Mironova E, et al. Breastfeeding and child cognitive development: new evidence from a large randomized trial. *Arch Gen Psychiatry*. 2008;65(5):578–584. [PubMed: 18458209]
4. Belfort MB, Rifas-Shiman SL, Kleinman KP, et al. Infant Feeding and Childhood Cognition at Ages 3 and 7 Years: Effects of Breastfeeding Duration and Exclusivity. *JAMA Pediatr*. 2013.
5. Bernard JY, De Agostini M, Forhan A, et al. Breastfeeding duration and cognitive development at 2 and 3 years of age in the EDEN mother-child Cohort. *The Journal of pediatrics*. 2013;163(1):36–42. e31. [PubMed: 23312681]
6. Victora CG, Horta BL, de Mola CL, et al. Association between breastfeeding and intelligence, educational attainment, and income at 30 years of age: a prospective birth cohort study from Brazil. *The Lancet Global Health*. 2015;3(4):e199–e205. [PubMed: 25794674]
7. Groen-Blokhuis MM, Frani S, van Beijsterveldt CE, et al. A prospective study of the effects of breastfeeding and FADS2 polymorphisms on cognition and hyperactivity/attention problems. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*. 2013;162(5):457–465.

8. Hayatbakhsh MR, O'Callaghan MJ, Bor W, Williams GM, Najman JM. Association of breastfeeding and adolescents' psychopathology: a large prospective study. *Breastfeed Med.* 2012;7(6):480–486. [PubMed: 22612623]
9. Boswell N, Byrne R, Davies PS. Eating behavior traits associated with demographic variables and implications for obesity outcomes in early childhood. *Appetite.* 2018;120:482–490. [PubMed: 29024677]
10. Brown A, Lee M. Breastfeeding during the first year promotes satiety responsiveness in children aged 18–24 months. *Pediatr Obes.* 2012;7(5):382–390. [PubMed: 22911888]
11. Goldstein S, Naglieri JA. *Handbook of Executive Functioning.* New York: Springer; 2013.
12. Tumwine J, Nankabirwa V, Abdoulaye Diallo H, et al. Exclusive Breastfeeding Promotion and Neuropsychological Outcomes in 5–8 Year Old Children from Uganda and Burkina Faso: Results from the PROMISE EBF Cluster Randomized Trial. *PLoS One.* 2018;13(2):1–17.
13. Julvez J, Ribas Fito N, Forns M, Garcia-Esteban R, Torrent M, Sunyer J. Attention behavior and hyperactivity at age 4 and duration of breast-feeding. *Acta Paediatr.* 2007;96:842–847. [PubMed: 17537012]
14. DiSantis K, Collins B, Fisher J, Davey A. Do infants fed directly from the breast have improved appetite regulation and slower growth during early childhood compared with infants fed from a bottle? *International Journal of Behavioral Nutrition and Physical Activity.* 2011;8(89):1–11.
15. Li R, Fein SB, Grummer-Strawn LM. Do infants fed from bottles lack self-regulation of milk intake compared with directly breastfed infants? *Pediatrics.* 2010;125(6):e1386–1393. [PubMed: 20457676]
16. Pang WW, Tan PT, Cai S, et al. Nutrients or nursing? Understanding how breast milk feeding affects child cognition. *Eur J Nutr.* 2019.
17. Boone K, Geraghty S, Keim S. Feeding at the Breast and Expressed Milk Feeding: Associations with Otitis Media and Diarrhea in Infants. *J Pediatr.* 2016;174:118–125. [PubMed: 27174145]
18. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) - A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform.* 2009;42(2):377–381. [PubMed: 18929686]
19. Alpern GD. *Developmental Profile 3, DP-3: Manual.* Los Angeles, CA: Western Psychological Services; 2007.
20. Thorell LB, Nyberg L. The Childhood Executive Functioning Inventory (CHEXI): A new rating instrument for parents and teachers. *Dev Neuropsychol.* 2008;33(4):536–552. [PubMed: 18568903]
21. Thorell LB, Eninger L, Brocki KC, Bohlin G. Childhood Executive Function Inventory (CHEXI): A promising measure for identifying young children with ADHD? *J Clin Exp Neuropsychol.* 2010;32(1):38–43. [PubMed: 19381995]
22. Catala C, Meulemans T, Thorell LB. The Childhood Executive Function Inventory: Confirmatory Factor Analyses and Cross-Cultural Clinical Validity in a Sample of 8-to 11-Year-Old Children. *Journal of Attention Disorders.* 2015;19(6):489–495. [PubMed: 23355496]
23. Wardle JGC, Sanderson S, Rapoport L. Development of the Children's Eating Behavior Questionnaire. *Journal of Child Psychology and Psychiatry.* 2001;42(7):963–970. [PubMed: 11693591]
24. Sleddens EF, Kremers SP, Thijs C. The Children's Eating Behaviour Questionnaire: factorial validity and association with Body Mass Index in Dutch children aged 6–7. *International Journal of Behavioral Nutrition and Physical Activity.* 2008;5(1):49.
25. Bull R, Espy KA, Wiebe SA. Short-term memory, working memory, and executive functioning in preschoolers: Longitudinal predictors of mathematical achievement at age 7 years. *Dev Neuropsychol.* 2008;33(3):205–228. [PubMed: 18473197]
26. Squire LR. Memory and the hippocampus: a synthesis from findings with rats, monkeys, and humans. *Psychol Rev.* 1992;99(2):195. [PubMed: 1594723]
27. Collette F, Hogge M, Salmon E, Van der Linden M. Exploration of the neural substrates of executive functioning by functional neuroimaging. *Neuroscience.* 2006;139(1):209–221. [PubMed: 16324796]

28. Aid S, Vancassel S, Poumes-Ballihaut C, Chalon S, Guesnet P, Lavielle M. Effect of a diet-induced n-3 PUFA depletion on cholinergic parameters in the rat hippocampus. *J Lipid Res.* 2003;44(8):1545–1551. [PubMed: 12754277]
29. Rubia K, Smith AB, Woolley J, et al. Progressive increase of frontostriatal brain activation from childhood to adulthood during event-related tasks of cognitive control. *Hum Brain Mapp.* 2006;27(12):973–993. [PubMed: 16683265]
30. Yuan P, Raz N. Prefrontal cortex and executive functions in healthy adults: a meta-analysis of structural neuroimaging studies. *Neurosci Biobehav Rev.* 2014;42:180–192. [PubMed: 24568942]
31. Doom JR, Georgieff MK. Striking while the iron is hot: understanding the biological and neurodevelopmental effects of iron deficiency to optimize intervention in early childhood. *Current pediatrics reports.* 2014;2(4):291–298. [PubMed: 25512881]
32. Miller J, Beharie MC, Taylor AM, Simmenes EB, Way S. Parent Reports of Exclusive Breastfeeding After Attending a Combined Midwifery and Chiropractic Feeding Clinic in the United Kingdom: A Cross-Sectional Service Evaluation. *J Evid Based Complementary Altern Med.* 2016;21(2):85–91. [PubMed: 26763046]
33. Mehedint MG, Craciunescu CN, Zeisel SH. Maternal dietary choline deficiency alters angiogenesis in fetal mouse hippocampus. *Proceedings of the National Academy of Sciences.* 2010;107(29):12834–12839.
34. Farah MJ, Betancourt L, Shera DM, et al. Environmental stimulation, parental nurturance and cognitive development in humans. *Developmental science.* 2008;11(5):793–801. [PubMed: 18810850]
35. Byford M, Kuh D, Richards M. Parenting practices and intergenerational associations in cognitive ability. *Int J Epidemiol.* 2011;41(1):263–272. [PubMed: 22422461]
36. Nakao T, Matsumoto T, Morita M, et al. The degree of early life stress predicts decreased medial prefrontal activations and the shift from internally to externally guided decision making: an exploratory NIRS study during resting state and self-oriented task. *Front Hum Neurosci.* 2013;7:339. [PubMed: 23840186]
37. Davis EP, Hankin BL, Glynn LM, Head K, Kim DJ, Sandman CA. Prenatal Maternal Stress, Child Cortical Thickness, and Adolescent Depressive Symptoms. *Child Dev.* 2019.
38. Kopala-Sibley DC, Cyr M, Finsaas MC, et al. Early childhood parenting predicts late childhood brain functional connectivity during emotion perception and reward processing. *Child Dev.* 2020;91(1):110–128. [PubMed: 30102429]
39. Britton JR, Britton HL, Gronwaldt V. Breastfeeding, sensitivity, and attachment. *Pediatrics.* 2006;118(5):e1436–1443. [PubMed: 17079544]
40. Kuntsi J, Rogers H, Swinard G, et al. Reaction time, inhibition, working memory and ‘delay aversion’ performance: genetic influences and their interpretation. *Psychol Med.* 2006;36(11):1613–1624. [PubMed: 16882357]
41. Miyake A, Friedman NP. The nature and organization of individual differences in executive functions: Four general conclusions. *Curr Dir Psychol Sci.* 2012;21(1):8–14. [PubMed: 22773897]
42. Cuevas K, Deater-Deckard K, Kim-Spoon J, Wang Z, Morasch KC, Bell MA. A longitudinal intergenerational analysis of executive functions during early childhood. *Br J Dev Psychol.* 2014;32(1):50–64. [PubMed: 25284715]
43. Li RSK, May A, Rose C, Birch L. Bottle-Feeding Practices During Early Infancy and Eating Behaviors at 6 Years of Age. *Pediatrics.* 2014;134(Suppl 1):S70–S77. [PubMed: 25183759]
44. Bortolus R, Parazzini F, Trevisanuto D, Cipriani S, Ferrarese P, Zanardo V. Developmental assessment of preterm and term children at 18 months: reproducibility and validity of a postal questionnaire to parents. *Acta Paediatr.* 2002;91(10):1101–1107. [PubMed: 12434897]
45. Perra O, McGowan JE, Grunau RE, et al. Parent ratings of child cognition and language compared with Bayley-III in preterm 3-year-olds. *Early Hum Dev.* 2015;91(3):211–216. [PubMed: 25703315]

Table 1.

Participant Characteristics (n=285, 2017–18, Ohio, USA)

Maternal or child characteristic	Original Cohort (n=499)	Followed Up (n=285)	Not Followed Up (n=214)
	Mean, SD or n, %		
Maternal age at delivery	30 (5)	30 (4)	30 (5)
Maternal education		-	
Less than high school diploma	11 (2)	4 (1) *	7 (3)
High school graduate or GED or equivalent	57 (11)	27 (9)	30 (14)
Some college or Associate degree	92 (18)	38 (13)	54 (25)
Bachelor's degree	176 (35)	113 (40)	63 (29)
Graduate or professional degree	159 (32)	103 (36)	56 (26)
Missing	4 (1)	0 (0)	4 (2)
Marital status		-	
Married or living with partner	439 (88)	259 (91)	180 (84)
Separated, divorced, widowed or never married	56 (11)	26 (9)	30 (14)
Missing	4 (1)	0 (0)	4 (2)
Maternal race		-	
White	391 (78)	239 (84) *	152 (71)
Black or African-American	55 (11)	23 (8)	32 (15)
Other	50 (10)	23 (8)	27 (13)
Missing	3 (1)	0 (0)	3 (1)
Maternal ethnicity		-	
Hispanic	24 (5)	14 (5)	10 (5)
Non-Hispanic	473 (95)	271 (95)	202 (94)
Missing	2 (0)	0 (0)	2 (0)
Household income		-	
<\$15,000	68 (14)	27 (9) *	41 (19)
\$15,000–<\$35,000	85 (17)	45 (16)	40 (19)
\$35,000–<\$55,000	61 (12)	33 (12)	28 (13)
\$55,000–<\$75,000	68 (14)	47 (16)	21 (10)
\$75,000	212 (42)	132 (46)	80 (37)
Missing	5 (1)	1 (0)	4 (2)
Enrolled in Special Supplemental Nutrition Program for Women, Infants, and Children in pregnancy or infancy		-	
Yes	139 (28)	65 (23) *	74 (35)
No	355 (71)	219 (77)	136 (64)
Missing	5 (1)	1 (0)	4 (2)
Mother had public health insurance at time of delivery		-	
Yes	108 (22)	40 (14) *	68 (32)

Maternal or child characteristic	Original Cohort (n=499)	Followed Up (n=285)	Not Followed Up (n=214)
	Mean, SD or n, %		
No	388 (78)	245 (86)	143 (67)
Missing	3 (1)	0 (0)	3 (1)
Went to work or school 20 hours per week during first year postpartum		-	
Yes	340 (68)	193 (68)	147 (69)
No	156 (31)	92 (32)	64 (30)
Missing	3 (1)	0 (0)	3 (1)
Child ever attended day care during infancy		-	
Yes	243 (49)	144 (51)	99 (46)
No	252 (51)	140 (49)	112 (52)
Missing	4 (1)	1 (0)	3 (1)
Mother smoked during pregnancy or first year postpartum		-	
Yes	39 (8)	17 (6)	22 (10)
No	456 (91)	268 (94)	188 (88)
Missing	4 (1)	0 (0)	4 (2)
Parity		-	
0	248 (50)	156 (55) *	92 (43)
1	155 (31)	78 (27)	77 (36)
2	94 (19)	51 (18)	43 (20)
Missing	2 (0)	0 (0)	2 (1)
Mode of delivery		-	
Cesarean section	186 (37)	105 (37)	81 (38)
Vaginal	282 (57)	166 (58)	116 (54)
Missing	31 (6)	14 (5)	17 (8)
Child sex		-	
Female	242 (49)	137 (48)	105 (49)
Male	255 (51)	148 (52)	107 (50)
Missing	2 (0)	0 (0)	2 (1)
Child birthweight (grams)**	3273 (656)	3339 (627) *	3185 (685)
Gestational age at birth	38 (2)	39 (2) *	38 (3)

* Chi-square or t-test comparing the follow-up cohort to the portion of the original cohort not followed up p<0.05

** for the follow-up cohort: median=3430, IQR=680, range=680–5642; for the portion of the original cohort not followed: median=3360, IQR=680, range=567–5642

Table 2.

Human Milk Feeding Practices (n=285, 2017–18, Ohio, USA)

Feeding Practice	Prevalence for ever adopting the feeding practice for 1 day or more(n, %)	Duration in months (median, IQR)
Feeding at the breast - any	262, 92%	7.9, 1.4–12.0
Feeding at the breast only - exclusive	184, 65%	0.1, 0.0–2.0
Feeding expressed milk - any	259, 91%	4.8, 1.6–9.0
Feeding expressed milk only - exclusive	28, 10%	0, 0 [*]
Feeding human milk - any	279, 98%	7.9, 3.0–12.9
Feeding human milk only - exclusive	212, 74%	1.8, 0–11.0
Feeding formula- any	251, 88%	10.8, 2.0–12.0
Feeding formula only - exclusive	192, 67%	4.0, 0–9.2

* mean duration was 0.3 months, standard deviation=1.5

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Table 3. Associations between human milk feeding practices (duration, months) and working memory (CHEXI), inhibition (CHEXI), and global cognitive ability (DP-3) scores (n=285, 2017–18, Ohio, USA)

	Cognitive ability (DP-3) (n=285) (β, 95% CI)		Working memory (CHEXI) (n=282) (β, 95% CI)		Inhibition (CHEXI) (n=282) (β, 95% CI)	
	Unadjusted	Adjusted*	Unadjusted	Adjusted*	Unadjusted	Adjusted*
Feeding at the breast - any	0.09 (-0.14, 0.33)	0.07 (-0.21, 0.36)	-0.12 (-0.24, 0.01)	-0.15 (-0.31, 0.01)	-0.06 (-0.17, 0.05)	-0.10 (-0.23, 0.03)
Feeding at the breast only - exclusive	0.11 (-0.20, 0.43)	0.16 (-0.18, 0.49)	-0.11 (-0.28, 0.06)	-0.20 (-0.38, -0.01)**	-0.06 (-0.21, 0.08)	-0.14 (-0.29, 0.02)
Feeding expressed milk - any	0.16 (-0.22, 0.53)	-0.07 (-0.51, 0.38)	-0.32 (-0.95, 0.32)	-0.08 (-0.33, 0.17)	-0.09 (-0.26, 0.08)	-0.01 (-0.22, 0.20)
Feeding expressed milk only - exclusive	-0.07 (-1.25, 1.11)	0.02 (-1.10, 1.13)	-0.32 (-0.95, 0.32)	-0.35 (-0.95, 0.25)	-0.18 (-0.72, 0.36)	-0.19 (-0.71, 0.32)
Feeding human milk - any	0.12 (-0.13, 0.36)	0.08 (-0.19, 0.34)	-0.14 (-0.27, -0.01)**	-0.18 (-0.32, -0.04)**	-0.07 (-0.19, 0.04)	-0.12 (-0.25, -0.00)**
Feeding human milk only - exclusive	0.09 (-0.14, 0.31)	0.08 (-0.16, 0.32)	-0.11 (-0.24, 0.01)	-0.16 (-0.29, -0.03)**	-0.05 (-0.15, 0.06)	-0.08 (-0.20, 0.03)
Feeding formula - any	0.01 (-0.35, 0.37)	0.04 (-0.33, 0.42)	0.11 (-0.08, 0.31)	0.14 (-0.07, 0.34)	0.03 (-0.13, 0.20)	0.07 (-0.11, 0.24)
Feeding formula only - exclusive	-0.01 (-0.41, 0.39)	0.11 (-0.32, 0.53)	0.15 (-0.07, 0.36)	0.15 (-0.08, 0.38)	0.08 (-0.10, 0.27)	0.14 (-0.06, 0.33)

* For adjusted models where feeding at the breast was the feeding practice of interest, adjusted models included a variable for the duration of expressed milk feeding. For models where feeding expressed milk was the feeding practice of interest, adjusted models included a variable for the duration of feeding at the breast. All adjusted models also included maternal age, education, marital status, race, ethnicity, household income, WIC enrollment, insurance type, maternal employment postpartum, child day care attendance, maternal smoking, parity, mode of delivery, child gestational age, and child sex. CHEXI = Childhood Executive Functioning Inventory; DP-3 = Developmental Profile 3. Lower scores on CHEXI variables indicate better abilities.

** p<.05

Table 4.

Associations between feeding practices (duration, months) and the risk of delayed or below average cognitive ability (DP-3) or working memory (CHEXI) and inhibition (CHEXI) scores above clinical cutoffs (n=285, 2017–18, Ohio, USA)

	Cognitive ability (DP-3; Delayed or Below Average) (n=285) RR (95% CI)		Working memory (CHEXI score >35) (95% CI)		Inhibition (CHEXI score >32) (n=282) RR (95% CI)	
	Unadjusted	Adjusted*	Unadjusted	Adjusted*	Unadjusted	Adjusted*
Feeding at the breast - any	1.00 (0.93, 1.07)	1.02 (0.92, 1.14)	0.93 (0.87, 0.99)**	0.89 (0.81, 0.99)**	0.98 (0.95, 1.02)	0.95 (0.89, 1.01)
Feeding at the breast only - exclusive	0.98 (0.87, 1.10)	0.97 (0.82, 1.14)	0.87 (0.74, 1.02)	0.78 (0.63, 0.96)**	0.98 (0.93, 1.04)	0.92 (0.85, 1.01)
Feeding expressed milk - any	0.98 (0.87, 1.10)	1.00 (0.84, 1.20)	0.92 (0.83, 1.01)	1.00 (0.87, 1.15)	0.99 (0.93, 1.05)	1.05 (0.96, 1.14)
Feeding expressed milk only - exclusive	0.90 (0.51, 1.61)	0.70 (0.18, 2.68)	0.80 (0.42, 1.53)	0.67 (0.22, 2.04)	0.99 (0.82, 1.20)	0.96 (0.78, 1.18)
Feeding human milk - any	0.99 (0.92, 1.07)	1.00 (0.90, 1.12)	0.92 (0.86, 0.99)**	0.87 (0.79, 0.97)**	0.98 (0.94, 1.02)	0.95 (0.90, 1.01)
Feeding human milk only - exclusive	0.95 (0.87, 1.04)	0.91 (0.78, 1.06)	0.92 (0.85, 0.99)**	0.84 (0.74, 0.95)**	1.00 (0.96, 1.04)	0.97 (0.92, 1.02)
Feeding formula - any	1.06 (0.94, 1.20)	1.14 (0.94, 1.38)	1.07 (0.98, 1.16)	1.13 (1.00, 1.27)**	0.98 (0.92, 1.03)	1.00 (0.93, 1.08)
Feeding formula only - exclusive	0.97 (0.86, 1.10)	0.92 (0.77, 1.11)	1.07 (0.98, 1.16)	1.09 (0.97, 1.22)	1.01 (0.94, 1.07)	1.04 (0.96, 1.13)

* For adjusted models where feeding at the breast was the feeding practice of interest, adjusted models included a variable for the duration of expressed milk feeding. For models where feeding expressed milk was the feeding practice of interest, adjusted models included a variable for the duration of feeding at the breast. All adjusted models also included maternal age, education, marital status, race, ethnicity, household income, WIC enrollment, insurance type, maternal employment postpartum, child day care attendance, maternal smoking, parity, mode of delivery, child gestational age, and child sex. CHEXI = Childhood Executive Functioning Inventory; DP-3 = Developmental Profile 3

** p<.05

Table 5 (Online Only).

Associations between human milk feeding practices (duration, months) and children’s eating behavior outcomes at age 6 years (n=281, 2017–18, Ohio, USA)

	Adjusted (β , 95% CI)*									
	Food responsiveness	Enjoyment of food	Emotional overeating	Desire to drink	Satiety responsiveness	Slowness in eating	Emotional undereating	Food fussiness		
Feeding at the breast - any	0.01 (-0.01, 0.02)	0.01 (-0.00, 0.03)	0.01 (-0.00, 0.02)	0.00 (-0.02, 0.02)	0.01 (-0.00, 0.01)	-0.00 (-0.01, 0.01)	-0.00 (-0.02, 0.01)	0.01 (0.00, 0.01)		
Feeding at the breast only - exclusive	0.00 (-0.01, 0.02)	0.02 (-0.00, 0.03)	0.02 (0.00, 0.03)**	0.00 (-0.02, 0.03)	0.00 (-0.01, 0.02)	-0.01 (-0.02, 0.01)	-0.01 (-0.02, 0.01)	0.01 (0.00, 0.02)**		
Feeding expressed milk - any	0.00 (-0.02, 0.02)	0.01 (-0.01, 0.03)	-0.02 (-0.03, 0.00)	-0.02 (-0.04, 0.01)	-0.01 (-0.02, 0.01)	0.02 (0.00, 0.03)	0.01 (-0.02, 0.03)	-0.00 (-0.01, 0.01)		
Feeding expressed milk only - exclusive	-0.00 (-0.05, 0.05)	-0.00 (-0.06, 0.06)	-0.01 (-0.05, 0.04)	-0.05 (-0.12, 0.03)	-0.01 (-0.05, 0.03)	0.03 (-0.01, 0.07)	0.01 (-0.05, 0.07)	0.00 (-0.02, 0.03)		
Feeding human milk - any	0.01 (-0.01, 0.02)	0.02 (0.01, 0.03)**	0.01 (-0.00, 0.02)	-0.01 (-0.02, 0.01)	0.00 (-0.01, 0.01)	0.00 (-0.00, 0.01)	0.00 (-0.01, 0.02)	0.01 (0.00, 0.01)**		
Feeding human milk only - exclusive	0.01 (-0.01, 0.02)	0.01 (0.00, 0.03)	0.01 (-0.00, 0.02)	-0.00 (-0.02, 0.01)	0.00 (-0.01, 0.01)	0.00 (-0.01, 0.01)	0.00 (-0.01, 0.02)	0.01 (0.00, 0.01)		
Feeding formula - any	-0.01 (-0.03, 0.01)	-0.01 (-0.03, 0.01)	-0.01 (-0.03, 0.00)	0.00 (-0.02, 0.03)	0.00 (-0.01, 0.02)	0.00 (-0.01, 0.01)	-0.01 (-0.03, 0.02)	-0.00 (-0.01, 0.01)		
Feeding formula only - exclusive	-0.01 (-0.03, 0.01)	-0.03 (-0.05, -0.01)	-0.00 (-0.02, 0.01)	0.01 (-0.02, 0.04)	-0.00 (-0.02, 0.01)	-0.01 (-0.02, 0.01)	-0.00 (-0.02, 0.02)	-0.00 (-0.01, 0.01)		

* For models where feeding at the breast was the feeding practice of interest, adjusted models included a variable for the duration of expressed milk feeding. For models where feeding expressed milk was the feeding practice of interest, adjusted models included a variable for the duration of feeding at the breast. All adjusted models also included maternal age, education, marital status, race, ethnicity, household income, WIC enrollment, insurance type, maternal employment postpartum, child day care attendance, maternal smoking, parity, mode of delivery, child gestational age, and child sex.

** p<.05