Breastfeeding, Long-Chain Polyunsaturated Fatty Acids in Colostrum, and Infant Mental Development

WHAT'S KNOWN ON THIS SUBJECT: Several studies have reported positive associations between breastfeeding and children's cognition. Parental factors are thought to explain a large part of this association. However, the potential role of long-chain polyunsaturated fatty acid (LC-PUFA) content in breast milk remains uncertain.

WHAT THIS STUDY ADDS: This study is the first to assess the association between LC-PUFA levels in colostrum and children's mental development in a large population-based study. LC-PUFA levels seem to play a beneficial role, particularly in children who are breastfed for longer durations.

abstract

BACKGROUND: Breastfeeding has been associated with improved neurodevelopment in children. However, it remains unknown to what extent nutritional advantages of breast milk may explain this relationship.

OBJECTIVE: We assessed the role of parental psychosocial factors and colostrum long-chain polyunsaturated fatty acid (LC-PUFA) levels in the relationship between breastfeeding and children's neurodevelopment.

METHODS: A population-based birth cohort was established in the city of Sabadell (Catalonia, Spain) as part of the INMA-INfancia y Medio Ambiente Project. A total of 657 women were recruited during the first trimester of pregnancy. Information about parental characteristics and breastfeeding was obtained by using a questionnaire, and trained psychologists assessed mental and psychomotor development by using the Bayley Scales of Infant Development in 504 children at 14 months of age.

RESULTS: A high percentage of breastfeeds among all milk feeds accumulated during the first 14 months was positively related with child mental development (0.37 points per month of full breastfeeding [95% confidence interval: 0.06–0.67]). Maternal education, social class, and intelligence quotient only partly explained this association. Children with a longer duration of breastfeeding also exposed to higher ratios between *n*-3 and *n*-6 PUFAs in colostrum had significantly higher mental scores than children with low breastfeeding duration exposed to low levels.

CONCLUSIONS: Greater levels of accumulated breastfeeding during the first year of life were related to higher mental development at 14 months, largely independently from a wide range of parental psychosocial factors. LC-PUFA levels seem to play a beneficial role in children's mental development when breastfeeding levels are high. *Pediatrics* 2011;128:e880–e889

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KEY WORDS

child development, cognition, breastfeeding, fatty acids, unsaturated, intelligence

ABBREVIATIONS

LC-PUFA—long-chain polyunsaturated fatty acid
IQ—intelligence quotient
ALA—α-linolenic acid
EPA—ecosapentaenoic acid
DPA—docosapentaenoic acid
DHA—docosahexaenoic acid
LA—linoleic acid
GLA—γ-linolenic acid
DGLA—dihomo-γ-linolenic acid
AA—arachidonic acid
ADA—adrenic acid
OA—osbond acid
CI—confidence interval

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Although several observational studies have reported positive associations between breastfeeding and children's cognitive development,[1–13] randomized trials with infant formulas supplemented with long-chain polyunsaturated fatty acids (LC-PUFAs) have generally not found any clear effects.[14,15] Factors related to parental characteristics such as intelligence quotient (IQ), education, or social class,[1,2,6,8,16] as well as factors associated with the feeding environment, including physical and psychological contact between parents and children,[10,17–20] have been postulated to explain associations between child cognition and breastfeeding. Despite the inconclusive results of trials, the nutritional advantages of breast milk, in particular its greater content of LC-PUFAs than infant formulae, could also partly explain these associations.[21] Conversely, breastfeeding is a potential source of exposure to synthetic persistent lipophilic compounds, such as organochlorine compounds, which could potentially undermine the beneficial effects of this natural practice.[22]

Given the public health impact of breastfeeding, identifying biological and social factors that explain its effects on child health, including cognition, will enable the development of appropriate and effective recommendations as well as interventions to improve breastfeeding practices. We aim to assess the role of 3 sets of potential explanatory factors in the link between duration of breastfeeding and children's neurodevelopment at 14 months: parental factors such as IQ, education, and social class; psychological influences on the feeding environment, as reflected in parent-child attachment and parental mental health; and colostrum LC-PUFA levels.

METHODS

Design and Study Participants

A population-based birth cohort was established in the city of Sabadell (Catalonia, Spain) as part of the INMA (Infancia y Medio Ambiente [Environment and Childhood]) Project.[23] Between July 2004 and July 2006, pregnant women who visited the public health center of Sabadell for an ultrasound in the first trimester were recruited, providing they fulfilled the inclusion criteria (age older than 16 years, intention to deliver at the reference hospital, no problems of communication, singleton pregnancy, and no assisted conception); 99.5% of Spaniards have public health insurance, and an estimated 70% to 90% of women use public health services during pregnancy.[24] The participation rate was 60%. They were followed up during pregnancy, and their children enrolled at birth and followed up through 14 months. Colostrum samples were collected at delivery in a random subsample. Informed consent was obtained from all participants, and the study was approved by the Clinical Research Ethical Committee of the Municipal Institute of Health Care (Barcelona, Spain).

Child Neurodevelopment Test

Mental and psychomotor development of the children was assessed at ~14 months of age (range: 12–17 months) using the Bayley Scales of Infant Development.[25] The mental scale consists of 163 items that assess age-appropriate mental development, including performance abilities, memory, and early language skills. The psychomotor scale consists of 81 items assessing fine and gross motor development. All testing was done in the health care center in the presence of the mother, by 2 specially trained psychologists. Psychologists were not aware of any exposure information. Bayley tests were performed on 568 children. Nine tests were excluded because of specific pathologies. Psychologists also flagged children difficult to evaluate because of less than optimal cooperation ($n = 24$) who were classified as having neurodevelopment tests of uncertain quality. Raw scores were standardized to a mean of 100 and an SD of 15. We applied a strict protocol, including interobserver trainings and 3 sets of quality controls. The interrater reliability was estimated by intraclass correlation with 0.90 for mental scale and 0.96 for psychomotor scale. To determine the internal consistency, Cronbach's α coefficient was calculated as 0.78 for mental scale and 0.73 for psychomotor scale.

Breastfeeding Definition

Detailed information about child feeding was completed by interviewer-administered questionnaires with mothers at 6 and 14 months (Supplemental Fig 3).

Cumulative Intensity of Breastfeeding

Breastfeeding intensity was defined as the percentage of breast milk feeds among all formula or milk-based feeds.[26,27] Monthly breastfeeding intensity was calculated for each of the first 14 months of life. Cumulative intensity of breastfeeding was the sum of the monthly intensities of breastfeeding over this 14-month period. A 1-unit increase in this variable represents the equivalent of 1 month of full breastfeeding, whether accumulated in a single month or over several months of partial breastfeeding.

Exclusive Breastfeeding Duration

Exclusive breastfeeding was defined as receiving breast milk only but allowing supplementation of nonmilk liquids (eg, water or water-based drinks such as sweetened and flavored water, teas, infusions), fruit juice, oral rehydration salts solution, drops, and syrup forms of vitamins, minerals, and medicines.[28] Duration of exclusive breastfeeding was categorized into 4 groups: children who were breastfed but never exclusively (reference group), short-term (≤4 months, according to the Spanish law that provides for maternity leave of up to 16 weeks), long-term (4–6 months, according to the World Health Organization recommendations), and very long-term (>6 months).

Women who chose not to breastfeed were excluded (n = 41 [7.5%]) because the focus of this study was on the duration of breastfeeding.

LC-PUFA in Colostrum

Colostrum was collected the first 48 to 96 hours' postpartum at the hospital by an experienced nurse. The sample was collected in the morning and at the end of the feeding, in sterile polypropylene tubes, by mechanical expression of 1 breast using a breast pump. Milk was transported to the laboratory in ice boxes <2 hours after collection, where samples were stored at −80°C until analysis. Fatty acid methyl esters were prepared with sodium methylate and methanolic boron trifluoride and extracted into hexane following the method developed and validated by Moltó-Puigmartí et al.[29] Fatty acids were then separated and quantified by using fast-gas chromatography with flame ionization detection. During the method validation, between-day precision values for the different PUFA (relative SD of the percentages obtained analyzing the same sample in consecutive days) ranged between 0.37% and 6.51% for PUFA, showing a low assay variation.

Thirty-eight fatty acids were identified and quantified, including the fatty acids of interest for the present study: α-linolenic acid (ALA; C18:3n-3), eicosapentaenoic acid (EPA, C20:5n-3), docosapentaenoic acid (DPA, C22:5n-2), docosahexaenoic acid (DHA, C22:6n-3), linoleic acid (LA, C18:2n-6), γ-linolenic acid (GLA, C18:3n-6), dihomo-γ-linolenic acid (DGLA, C20:3n-6), arachidonic acid (AA, C20:4n-6), adrenic acid (ADA, C22:4n-6), and osbond acid (OA, C22:5n-6).

Other Parental and Child Variables

Information on parental education (in years), social class (using the UK Registrar General's 1990 classification according to parental occupation by ISCO88 code), country of birth, age, maternal height and prepregnancy weight, parity, diet, and marital status were obtained through questionnaires during the first trimester of pregnancy. Maternal social class was coded from the longest-held job during the pregnancy or, if the mother did not work during pregnancy, the last job before the pregnancy. When social class could not be derived, the last job of the father was used (n = 49). Information regarding maternal tobacco and alcohol use, secondhand smoke at home or in the workplace, and use of a gas stove at home during pregnancy were collected through questionnaires during the third trimester of pregnancy. Information related to the child's gestational age, gender, anthropometric measures, and Apgar score at birth was obtained from clinical records. In a subsequent interview at 14 months, data on main caregiver, nursery attendance, child secondhand smoke exposure, and infections during the first year was collected. All questionnaires were administered face-to-face by trained interviewers. When children were 14 months of age, parental IQ were assessed by using scales 2 and 3 of Factor "G" of the Cattell and Cattell test, which seeks to measure nonverbal IQ.[30] Parental mental health assessments used the 12-item General Health Questionnaire, recommended as an easily administered and accurate screening tool for common mental disorders.[31] Parental-child attachment was assessed through the self-administered Condon questionnaire, which scores parent's emotional response to his or her infant.[32,33] Levels of organochlorine compounds (hexachlorobenzene, β-hexachlorocyclohexane, dichlorodiphenyl dichloroethylene, and polychlorinated biphenyls) were analyzed in maternal serum extracted in the first trimester of pregnancy, using methods described elsewhere.[34,35] Total mercury levels were analyzed in cord blood, using thermal decomposition, amalgation, and atomic absorption spectrometry.

Statistical Analysis

Only subjects with complete neurodevelopment and breastfeeding data were included. Among these subjects, multiple imputation of missing values for the remaining variables was performed using chained equations in which 100 completed data sets were generated and analyzed by using the standard combination rules for multiple imputation (Supplemental Table 8, Supplemental Table 9, Supplemental Table 10, and Supplemental Table 11).[36,37]

Generalized additive models were used to assess the linearity of the relationship between breastfeeding definitions and infant mental development by graphical examination and likelihood ratio test. Multivariable linear regression models were performed to examine the relationship between both cumulative intensity of breastfeeding and exclusive breastfeeding duration and children's mental development at 14 months of age as a continuous normal variable. Models always included exact age of the child (in days), psychologist, and quality of the neuropsychological test. Cumulative intensity of breastfeeding was also adjusted for age of solid food introduction. To assess the influence of each maternal and paternal psychosocial factor (social class, education, IQ, attachment to the child, and mental health), a series of models were run adding these variables 1 by 1. Moreover, a model adding persistent toxic compounds measured in mother and cord blood was performed to explore if the breastfeeding coefficient was modified. Finally, a multivariable-adjusted model was performed including all parental psychosocial variables plus additional confounders identified as specified in the following description.

Second, to assess the relation between PUFAs (high versus low levels dichotomized at the median) and mental development, multivariable linear regression models were performed using PUFA levels in colostrum as the exposure variable. Also, to assess the hypothesis that increases in infant mental scores were associated with higher PUFA concentrations in breast milk as well as with total breast milk intake, a variable combining PUFA levels (high versus low) with tertiles of cumulative intensity of breastfeeding were created. The reference group was subjects within the lowest tertile of cumulative breastfeeding who also had low PUFA levels. Interaction terms between cumulative breastfeeding duration and colostrum PUFA concentrations were also tested.

To assess the effect of potential explanatory factors on coefficients for associations with each exposure variable—cumulative intensity of breastfeeding, exclusive breastfeeding duration, and PUFA levels in colostrum—a series of models were run for each exposure to assess the effect of additionally adjusting 1 by 1 for the characteristics of interest, after adjusting for several core confounders included a priori. Core confounders included key predictors of test scores (children's exact age at testing, psychologist administering the test, and quality of neuropsychological testing), as well as parental education, social class, attachment to the child, IQ, and mental health. These core variables were included in all models because a primary objective was to assess whether associations with breastfeeding variables remained significant independent of these key characteristics. Additional variables included in the final multivariable-adjusted models were those related to mental scores ($P < .20$) that also modified the coefficients of 1 of the exposure variables by >15%. These additional confounders were maternal age, maternal alcohol use during pregnancy, and use of gas cooking at home during pregnancy.

In supplementary analyses, we confirmed that excluding infants not born at term (<37 and >42 weeks) (n = 18) did not meaningfully change results (data not shown). Statistical significance was set at $\alpha < 0.05$ (2-tailed). Statistical analyses were conducted by using Stata 10.1 (Stata Corp, College Station, TX).

RESULTS

A total of 657 pregnant women were recruited at the first trimester of pregnancy and then followed up during pregnancy (Fig 1). A total of 622 (94.7%) children were enrolled at birth, and 582 (88.6%) were followed up through 14 months. A total of 504 subjects with complete neurodevelopment and breastfeeding data were included. Between the 504 children included and the original 622, no differences in characteristics—including age, maternal alcohol and fish consumption during pregnancy, paternal education, parental country of birth, gestational age, or child's gender—were found ($P > .05$). However, children not included had lower parental social class, lower maternal education, higher maternal smoking use, and lower mean birth weight. Children missing colostrum PUFA levels had a higher maternal social class, higher paternal education, low birth weight, and fewer siblings ($P < .05$). No differences in mental and psychomotor development, breastfeeding, parental IQ, mental health, attachment to their child, and the rest of variables were found.

Child, maternal, and paternal characteristics of the study population are shown in Tables 1, 2, and 3, Supplemental Table 12, and Supplemental Table 13. Mean mental development scores increased among tertiles of cumulative and groups of exclusive breastfeeding, whereas no association was found with psychomotor development scores (Table 4). Cumulative intensity of breastfeeding was linearly and positively associated with mental development scores (increase of 0.37 points [95% confidence interval (CI): 0.06–0.67]) on mental developmental score per each accumulated month of breastfeeding, whether accrued in a single month, or over several months of partial breastfeeding) (gain of linearity, $P = .45$) (Supplemental Figure 4). Duration of exclusive breastfeeding was also linearly and positively associated with infant mental development (increase of 0.37 points [95% CI: 0.14–0.88]) on mental development score per month of exclusive breastfeeding) (gain of linearity, $P = .47$) (Supplemental Figure 4).

Adjusting individually for maternal education, social class, and IQ only slightly attenuated the association between cumulative intensity of breastfeeding and mental development (Table 5). Paternal social class and educational level had a weaker attenuating effect, whereas paternal IQ, both parent's attachment to the child, and parental mental health had no meaningful effect on this relationship. Moreover, after adjusting for maternal levels of organochlorine compounds at the first trimester of pregnancy and mercury levels in cord blood, results remained almost identical. Children exclusively breastfed for >6 months had on average an increase of 5.48 points (95% CI: 0.96–10.00) in mental

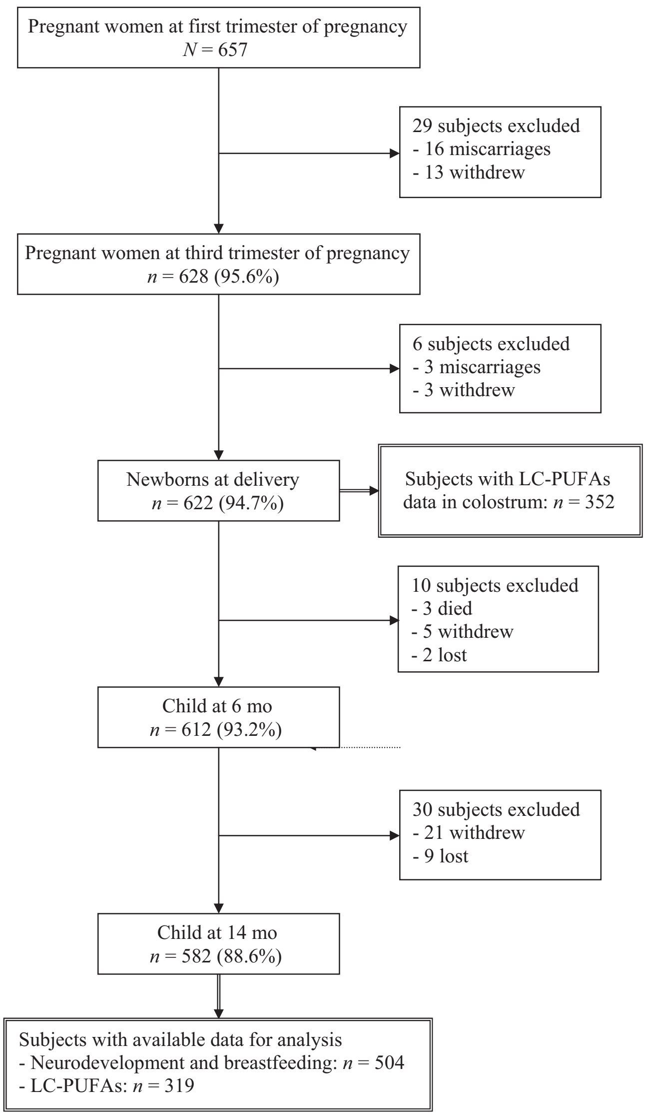

FIGURE 1
Main phases of the study.

TABLE 1 Child Characteristics of the Study Population ($N = 504$)

Characteristic	*n*	Distribution[a]	No. of Missings
Gender			0
Male	257	51.0	
Female	247	49.0	
Gestational age, wk	504	39.7 (1.4)	0
Birth weight	503	3257.6 (416.6)	1
No. of siblings at child's birth			2
0	300	59.8	
≥1	202	40.2	
Main caregiver at 14 mo			17
Mother	229	47.0	
Both parents with/without grandparents	148	30.4	
Other combinations	110	22.6	
Nursery attendance at 14 mo			12
Yes	340	69.1	
No	152	30.9	

[a] Values are percentages for categorical variables and mean (SD) for continuous variables.

development score (Table 5), whereas no significant association was shown at smaller durations of exclusive breastfeeding (increase of 2.23 points [95% CI: −1.26 to 5.72] for exclusively breastfeeding <4 months and 1.76 points [95% CI: −1.62 to 5.14] for exclusively breastfeeding between 4 and 6 months). Similar results for exclusive breastfeeding were obtained after adjusting for each of the parental characteristics examined, with the exception of paternal IQ, which had a somewhat stronger attenuating effect than those revealed on cumulative intensity of breastfeeding variable.

Except for DHA/OA ratio, all *n*-3/*n*-6 PUFA ratios were <1, signaling a higher content of *n*-6 PUFAs in colostrum (Table 6). In general, higher levels of *n*-3 PUFAs and higher ratios between *n*-3/*n*-6 PUFAs were positively associated with infant mental scores, whereas most associations with *n*-6 PUFAs were negative, although none of these associations reached statistical significance). When PUFA levels were combined with tertiles of cumulative intensity of breastfeeding (Fig 2 and Table 7), we observed a stronger positive gradient between tertiles of cumulative breastfeeding and infant mental development scores in the group with high versus low *n*-3 PUFA levels. Moreover, subjects with high levels of total *n*-3 PUFAs and *n*-3/*n*-6 PUFA ratios in colostrum who also had a longer duration of breastfeeding had significantly higher mental scores than did subjects with low levels of these PUFAs and short breastfeeding duration (Fig 2 and Table 7). Among children with longer breastfeeding duration, associations with mental scores were stronger when breast milk had a higher content of *n*-3 PUFAs. However, perhaps due in part to the modest sample size, interactions between breastfeeding duration and the PUFA concentrations

TABLE 2 Maternal Characteristics of the Study Population ($N = 504$)

Characteristic	n	Distribution[a]	No. of Missings
Education level			3
Primary or less	123	24.6	
Secondary	215	42.9	
University degree	163	32.5	
Social class			0
I/II managers/technicians	122	24.2	
III/IV skilled manual/nonmanual	245	48.6	
V/VI semiskilled/unskilled	137	17.2	
Age at child's birth, y	503	31.6 (4.2)	1
Country of birth			6
Spain	447	89.8	
Foreign	51	10.2	
Family status			1
Biparental	495	98.4	
Monoparental	8	1.6	
Smoking at third trimester			2
Yes	433	86.3	
No	69	13.7	
Use of gas stove during pregnancy			1
Yes	308	61.2	
No	195	38.8	
Prepregnancy BMI			0
Underweight	17	3.4	
Normal weight	350	69.5	
Overweight	98	19.4	
Obese	39	7.7	
Maternal IQ	478	100.3 (14.7)	26
Mother-to-child attachment	475	58.3 (5.2)	29
Maternal mental health	474	10.2 (4.3)	30

[a] Values are percentages for categorical variables and mean (SD) for continuous variables.

TABLE 3 Paternal Characteristics of the Study Population ($N = 504$)

Characteristic	n	Distribution[a]	No. of Missings
Education level			5
Primary or less	171	34.3	
Secondary	214	42.9	
University degree	114	22.8	
Social class			0
I/II managers/technicians	129	25.6	
III skilled manual/nonmanual	214	42.5	
IV/V semiskilled/unskilled	161	31.9	
Age at child's birth, y	502	33.4 (4.8)	2
Country of birth			3
Spain	441	88.0	
Foreign	60	12.0	
Paternal IQ	102	99.5 (15.0)	402
Father-to-child attachment	456	49.5 (4.0)	48
Paternal mental health	453	9.3 (3.7)	51

[a] Values are percentages for categorical variables and mean (SD) for continuous variables.

did not reach statistical significance ($P > .05$ for all interaction terms).

DISCUSSION

The present study is, to our knowledge, the first to assess the association between LC-PUFA levels in colostrum and children's mental development in a large population-based study. Higher cumulative breastfeeding during the first 14 months of life was related with an increase in mental development scores at 14 months. Moreover, higher levels of various *n*-3 PUFAs in colostrum and high ratios between *n*-3 and *n*-6 PUFAs had a beneficial effect on mental development especially when children received high levels of breastfeeding. In this analysis, maternal education, social class, and IQ did not fully explain the association between breastfeeding and mental development. Adjusting for paternal education, social class, and IQ had little effect. Parental attachment to the child and mental health had no confounding effect. Xenobiotic levels in maternal serum did not change these findings. No relation was found between breastfeeding and psychomotor score at 14 months.

Several systematic reviews have summarized the literature on the effect of breastfeeding on cognitive development using different approaches.[1–12] The great majority of published articles have important methodologic issues and, as some reviewers note, it is not yet possible to fully understand this relationship. The main limitations of previous studies are poor design and data quality (as a consequence of retrospective data collection), small sample sizes, and insufficient adjustment for critical potential confounders such as maternal IQ and parenting skills. Perhaps most importantly, the majority of studies also suffer from poor treatment of the breastfeeding variable, as most have examined effects of any versus no breastfeeding, without taking into account both duration and intensity, which are essential for estimating children's cumulative exposure to breastfeeding. Our results are from a population-based birth cohort study with prospective data collection. We incorporated multivariable adjustment for a large array of key factors including parental IQ, education, and social class, parental attachment to their child, parental mental health, and infections during the first year of life, organochlorine and mercury levels during pregnancy, and PUFA levels

TABLE 4 Mental and Psychomotor Development Scores According to Breastfeeding Status

Variable	*n* (%)	Mental Score[a]		Psychomotor Score[a]	
		Mean	95% CI	Mean	95% CI
Cumulative intensity of breastfeeding					
First tertile	168 (33.3)	100.0	97.9–102.1	100.5	98.2–102.8
Second tertile	167 (33.3)	101.0	98.9–103.1	100.4	98.2–102.7
Third tertile	169 (33.3)	103.4	101.3–105.5	99.3	97.0–101.5
Exclusive breastfeeding					
Never	82 (16.3)	99.4	96.5–102.4	101.2	98.1–104.3
≤4 mo	162 (32.1)	101.7	99.5–103.8	100.6	98.4–102.9
4–6 mo	206 (40.9)	101.2	99.3–103.1	99.4	97.5–101.4
>6 mo	54 (10.7)	104.9	101.4–108.5	99.0	95.2–102.7

[a] Adjusted for psychologist, child's age in days, and quality of the neuropsychological test. Cumulative intensity of breastfeeding was also adjusted for age of food introduction.

TABLE 5 Association Between Breastfeeding and Infant Mental Development at 14 Months ($n = 504$)

	Cumulative Intensity of Breastfeeding[a]	Exclusive Breastfeeding (>6 mo vs Never)
Model 1[b]	0.37 (0.06 to 0.67)	5.48 (0.96 to 10.00)
Model 1[b] + maternal social class	0.30 (0.05 to 0.61)	4.58 (0.05 to 9.12)
Model 1[b] + maternal education	0.30 (−0.01 to 0.61)	4.80 (0.29 to 9.31)
Model 1[b] + maternal IQ	0.34 (0.03 to 0.64)	4.89 (0.36 to 9.41)
Model 1[b] + mother-to-child attachment	0.37 (0.06 to 0.67)	5.52 (0.96 to 10.04)
Model 1[b] + maternal mental health	0.38 (0.07 to 0.68)	5.63 (1.10 to 10.15)
Model 1[b] + paternal social class	0.35 (0.04 to 0.65)	5.20 (0.67 to 9.72)
Model 1[b] + paternal education	0.35 (0.04 to 0.66)	5.21 (0.66 to 9.76)
Model 1[b] + paternal IQ	0.36 (0.06 to 0.66)	4.31 (−0.23 to 8.85)
Model 1[b] + father-to-child attachment	0.36 (0.06 to 0.67)	5.53 (1.01 to 10.05)
Model 1[b] + paternal mental health	0.36 (0.06 to 0.67)	5.47 (0.94 to 9.99)
Model 1[b] + persistent toxic compounds[c]	0.37 (0.07 to 0.68)	5.22 (0.69 to 9.75)
Adjusted model[d]	0.34 (0.04 to 0.65)	3.45 (−1.08 to 7.99)

Values given as β coefficient and 95% CI.

[a] A 1-unit increase represents the equivalent of 1 month of full breastfeeding, whether accumulated in a single month or over several months of partial breastfeeding.

[b] Adjusted for psychologist, child's age in days, and quality of the neuropsychological test. Cumulative intensity of breastfeeding was also adjusted for age of food introduction.

[c] Organochlorine compounds in maternal serum at first trimester of pregnancy and mercury in cord blood.

[d] Adjusted for variables in model 1 plus maternal and paternal education, maternal and paternal social class, maternal and paternal attachment to the child, maternal and paternal IQ, maternal and paternal mental health, maternal age, maternal alcohol use during pregnancy, and use of a gas stove at home during pregnancy.

in colostrum. We also obtained accurate information on child feeding during the first year of life and examined breastfeeding patterns, taking into account both duration and intensity.

Although colostrum PUFAs were used as a proxy of breast milk fatty acid profiles during lactation, fatty acid percentages in breast milk have been reported to vary during the course of lactation.[38,39] Despite typical decreases in LC-PUFA percentages over the first month of lactation, the increase in milk total fat content[38,39] permits LC-PUFA concentration to remain fairly constant.[38]

Another weak point is that we did not have PUFA concentrations in colostrum for all mother-child pairs. Nevertheless, multiple imputation of missing values allows taking into account the entire sample in the analyses and provides similar results that complete the case analyses (Supplemental Table 9, Supplemental Table 10, and Supplemental Table 11). A second limitation was that we did not have information among partial breastfeeders on the amount or types of PUFAs provided by infant formulae, which may have highly variable composition. However, because there is still not enough evidence that LC-PUFA fortification of infant formula is beneficial for neurodevelopment,[12,14,15,40] adjusting for LC-PUFA content in formula is unlikely to meaningfully change our results. In addition, an important limitation of the exclusive breastfeeding definition was that all partial breastfeeders were classified together as nonexclusive, regardless of whether their level of breastfeeding intensity was relatively high.

Breast milk has a high content of LC-PUFAs, critical nutrients for brain development. Human and animal studies indicate that dietary insufficiency of LC-PUFAs is associated with impaired learning and neurodevelopment.[12] Some studies have reported an association between higher levels of maternal fish consumption or *n*-3 LC-PUFAs supplementation during pregnancy and cognitive development.[41–43] However, results of studies on maternal supplementation during lactation have been inconsistent.[44] Meta-analyses of randomized clinical trials of formula supplemented with LC-PUFAs reported that there is not enough evidence to conclude definitively that LC-PUFAs supplementation is beneficial for neurodevelopment.[12,14,15,40]

In our study, higher levels of various *n*-3 PUFAs and high ratios between *n*-3 and *n*-6 PUFAs were positively associated with infant mental development, especially among children with high levels of cumulative breastfeeding. We found positive associations with several LC-PUFAs hypothesized a priori to play a beneficial role in mental development, including the *n*-3 fatty acid DHA, the ALA/LA ratio, and the DHA/AA ratio. Gustafsson et al[45] reported finding colostrum LC-PUFA levels to be significantly associated with cognitive development at 6.5 years of age, specifically reporting beneficial effects of DHA and the DHA/AA ratio, and a negative relationship with AA, albeit in a

TABLE 6 Descriptive PUFA Levels and Association Between Infant Mental Development Score at 14 Months and PUFA Levels

	PUFA Levels in Colostrum (Weight %) ($N = 504$)	PUFA Levels in Colostrum (High vs Low) ($N = 504$)[a]	
	Mean (SD)	β	95% CI
n-3 PUFAs			
ALA (C18:3*n*-3)	0.35 (0.09)	1.25	−1.43 to 3.93
EPA (C20:5*n*-3)	0.06 (0.02)	0.63	−2.18 to 3.44
DPA (C22:5*n*-3)	0.40 (0.13)	1.35	−1.39 to 4.08
DHA (C22:6*n*-3)	0.64 (0.27)	0.58	−2.08 to 3.23
Total *n*-3 PUFAs	1.45 (0.41)	1.76	−0.88 to 4.40
n-6 PUFAs			
LA (C18:2*n*-6)	12.62 (2.57)	−0.44	−3.23 to 2.35
GLA (C18:3*n*-6)	0.04 (0.02)	0.18	−2.56 to 2.93
DGLA (C20:3*n*-6)	0.85 (0.26)	0.64	−1.87 to 3.15
AA (C20:4*n*-6)	1.08 (0.29)	0.70	−1.94 to 3.34
ADA (C22:4*n*-6)	0.64 (0.22)	−1.03	−3.67 to 1.61
OA (C22:5*n*-6)	0.16 (0.05)	−0.48	−3.09 to 2.13
Total *n*-6 PUFAs	15.38 (2.74)	−0.39	−3.17 to 2.38
n-3/*n*-6 PUFA ratios			
ALA/LA ratio	0.03 (0.01)	1.72	−0.94 to 4.39
EPA/AA ratio	0.05 (0.02)	1.21	−1.48 to 3.89
DPA/ADA ratio	0.65 (0.16)	1.60	−1.05 to 4.25
DHA/OA ratio	4.20 (1.52)	1.04	−1.63 to 3.71
DHA/AA ratio	0.59 (0.18)	1.26	−1.47 to 3.98
Total *n*-3/*n*-6 PUFAs ratio	0.10 (0.03)	2.00	−0.78 to 4.78

Values are given as β coefficient and 95% CI.

[a] All models were adjusted for psychologist, child's age in days, quality of the neuropsychological test, maternal and paternal education, maternal and paternal social class, maternal and paternal attachment to the child, maternal and paternal IQ, maternal and paternal mental health, maternal age, maternal alcohol use during pregnancy, use of a gas stove at home during pregnancy, and child's age of food introduction.

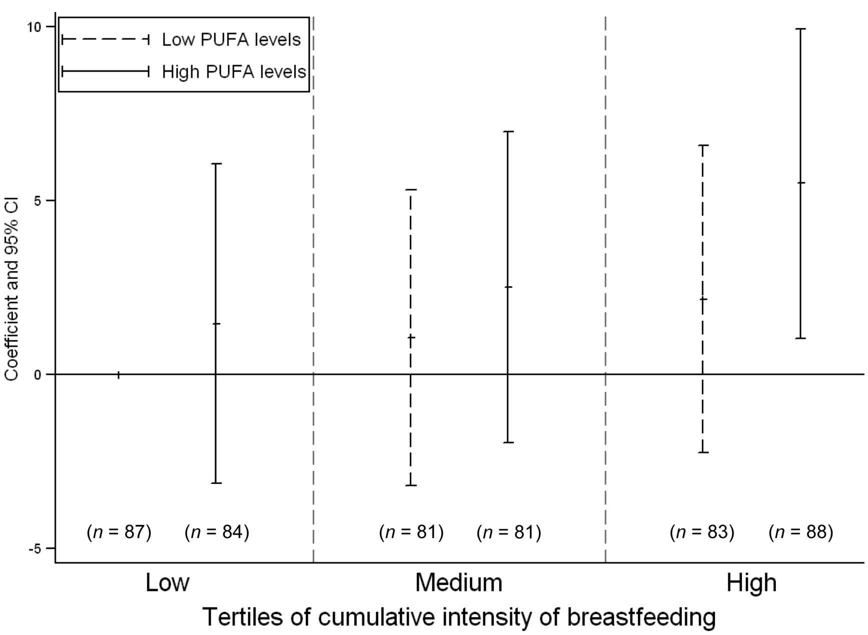

FIGURE 2

Association between PUFA levels (total *n*-3/*n*-6 PUFAs ratio), tertiles of cumulative intensity of breastfeeding, and infant mental development score.[1] The reference group was subjects with low tertile of cumulative breastfeeding and low PUFA levels. β coefficients were adjusted for psychologist, child's age in days, quality of the neuropsychological test, parental education, social class, attachment to the child, IQ, and mental health, maternal age, maternal alcohol use during pregnancy, use of a gas stove at home during pregnancy, and child's age of food introduction.

very small sample ($n = 28$). The study of individual fatty acids is complex because many of these compounds form part of the same metabolic chains. Moreover, infant levels of various *n*-3 and *n*-6 fatty acids depend not only on maternal levels but also on metabolizing enzyme activity as well as levels of preceding fatty acids in the same chain. Genetic polymorphisms influencing maternal and child activity of enzymes involved in PUFA metabolism, such as the genes *FADS1* and *FADS2*,[46] play an important role in determining PUFA levels in breast milk[47,48] or in infants' ability to convert precursor fatty acids into their long-chain derivatives. Caspi et al[49] found that the association between breastfeeding and IQ was modified by a genetic variant in *FADS,* which supports the effect of fatty acids on neurodevelopment. Future studies examining breast milk fatty acids in relation to child development should take into account mother and child genetic variation in LC-PUFA–metabolizing enzymes.

CONCLUSIONS

Higher levels of accumulated breastfeeding during the first year of life were associated with an increase in infant mental development scores at 14 months. LC-PUFA levels in colostrum, specifically high *n*-3 versus *n*-6 fatty acids, seem to play a beneficial role in child neurodevelopment when infants receive large amounts of breast milk during the first year of life; parental psychosocial factors explained only a small part of this association. The follow-up of our birth cohort will allow us to explore if this effect on cognitive development seem stronger at older ages. Overall, our results suggest that the effect of breastfeeding in child neurodevelopment seems to be driven in part by breast milk's LC-PUFA content.

TABLE 7 Association Between Infant Mental Development Score at 14 Months and PUFA Levels in Colostrum According to Tertile of Cumulative Intensity of Breastfeeding

	Low PUFA levels					High PUFA levels					
	Low Tertile of Breastfeeding	Medium Tertile of Breastfeeding		High Tertile of Breastfeeding		Low Tertile of Breastfeeding		Medium Tertile of Breastfeeding		High Tertile of Breastfeeding	
		β	95% CI	β	95% CI	β	95% CI	β	95% CI	β	95% CI
n-3 PUFAs											
ALA (C18:3*n*-3)	Ref	0.70	−3.84 to 5.24	2.22	−2.17 to 6.62	0.62	−3.83 to 5.08	1.80	−2.59 to 6.18	4.59	−0.01 to 9.20
EPA (C20:5*n*-3)	Ref	0.56	−4.62 to 5.75	1.39	−3.75 to 6.53	−0.39	−5.08 to 4.30	0.82	−3.70 to 5.34	3.58	−1.01 to 8.17
DPA (C22:5*n*-3)	Ref	−0.07	−4.45 to 4.32	2.05	−2.34 to 6.44	0.04	−4.46 to 4.54	2.02	−2.38 to 6.43	4.01	−0.35 to 8.37
DHA (C22:6*n*-3)	Ref	0.04	−4.49 to 4.56	2.19	−1.97 to 6.35	−0.53	−4.92 to 3.85	1.26	−2.88 to 5.40	3.44	−0.90 to 7.78
Total *n*-3 PUFAs	Ref	0.47	−4.03 to 4.98	2.56	−1.72 to 6.84	1.22	−3.23 to 5.67	2.56	−1.73 to 6.85	4.85	0.48 to 9.23
n-6 PUFAs											
LA (C18:2*n*-6)	Ref	0.82	−3.68 to 5.31	2.99	−1.22 to 7.20	−0.50	−5.04 to 4.05	0.63	−3.71 to 4.96	2.53	−2.04 to 7.10
GLA (C18:3*n*-6)	Ref	0.50	−5.12 to 6.13	2.03	−3.45 to 7.51	−0.39	−5.44 to 4.67	0.79	−4.14 to 5.72	3.18	−1.88 to 8.25
DGLA (C20:3*n*-6)	Ref	−1.24	−5.73 to 3.26	1.95	−2.52 to 6.43	−1.21	−5.65 to 3.22	1.72	−2.72 to 6.16	2.67	−1.79 to 7.13
AA (C20:4*n*-6)	Ref	−0.02	−4.43 to 4.39	1.45	−2.87 to 5.77	−0.87	−5.40 to 3.67	1.02	−3.35 to 5.39	3.97	−0.58 to 8.52
ADA (C22:4*n*-6)	Ref	0.60	−3.86 to 5.06	3.37	−1.01 to 7.74	−0.93	−5.46 to 3.61	0.31	−3.99 to 4.61	1.66	−2.79 to 6.11
OA (C22:5*n*-6)	Ref	1.52	−3.27 to 6.30	3.81	−0.66 to 8.28	0.59	−3.96 to 5.13	1.10	−3.23 to 5.44	2.81	−1.79 to 7.40
Total *n*-6 PUFAs	Ref	−0.60	−5.23 to 4.02	1.26	−3.03 to 5.56	−2.27	−7.00 to 2.45	−0.05	−4.59 to 4.49	2.46	−2.30 to 7.23
n-3/*n*-6 PUFA ratios											
ALA/LA ratio	Ref	2.86	−1.47 to 7.19	2.99	−1.38 to 7.36	2.90	−1.61 to 7.41	2.07	−2.38 to 6.52	6.12	1.63 to 10.62
EPA/AA ratio	Ref	1.63	−2.74 to 6.00	3.36	−0.90 to 7.62	1.95	−2.63 to 6.53	2.13	−2.06 to 6.33	4.51	0.12 to 8.89
DPA/ADA ratio	Ref	0.60	−3.73 to 4.94	3.04	−1.25 to 7.34	1.42	−3.12 to 5.96	2.52	−1.67 to 6.71	4.30	0.00 to 8.60
DHA/OA ratio	Ref	0.49	−3.83 to 4.80	2.59	−1.64 to 6.83	0.43	−4.12 to 4.98	1.76	−2.40 to 5.91	3.84	−0.47 to 8.15
DHA/AA ratio	Ref	0.72	−3.53 to 4.98	2.16	−2.02 to 6.34	0.50	−4.05 to 5.05	1.60	−2.45 to 5.64	4.30	0.03 to 8.57
Total *n*-3/*n*-6 PUFAs ratio	Ref	1.06	−3.19 to 5.31	2.17	−2.24 to 6.58	1.47	−3.12 to 6.05	2.52	−1.95 to 6.99	5.50	1.05 to 9.94

Values are given as β coefficient and 95% CI. All models were adjusted for psychologist, child's age in days, quality of the neuropsychological test, maternal and paternal education, maternal and paternal social class, maternal and paternal attachment to the child, maternal and paternal IQ, maternal and paternal mental health, maternal age, maternal alcohol use during pregnancy, use of a gas stove at home during pregnancy, and child's age of food introduction. Ref indicates reference.

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REFERENCES

1. Anderson JW, Johnstone BM, Remley DT. Breast-feeding and cognitive development: a meta-analysis. *Am J Clin Nutr*. 1999;70(4):525–535
2. Der G, Batty GD, Deary IJ. Effect of breast feeding on intelligence in children: prospective study, sibling pairs analysis, and meta-analysis. *BMJ*. 2006;333(7575):945
3. Drane DL, Logemann JA. A critical evaluation of the evidence on the association between type of infant feeding and cognitive development. *Paediatr Perinat Epidemiol*. 2000;14(4):349–356
4. Gordon AG. Breast-feeding, breast-milk feeding, and intelligence quotient. *Am J Clin Nutr*. 2000;72:1063–1064
5. Ip S, Chung M, Raman G, et al. Breastfeeding and maternal and infant health outcomes in developed countries. *Evid Rep Technol Assess (Full Rep)*. 2007;(153):1–186
6. Jacobson SW, Jacobson JL. Breastfeeding and IQ: evaluation of the socio-environmental confounders. *Acta Paediatr*. 2002;91(3):258–260
7. Jacobson SW, Jacobson JL. Breast feeding and intelligence in children. *BMJ*. 2006;333(7575):929–930
8. Jain A, Concato J, Leventhal JM. How good is the evidence linking breastfeeding and intelligence? *Pediatrics*. 2002;109(6):1044–1053
9. Kramer MS, Aboud F, Mironova E, et al; Promotion of Breastfeeding Intervention Trial (PROBIT) Study Group. Breastfeeding and child cognitive development: new evidence from a large randomized trial. *Arch Gen Psychiatry*. 2008;65(5):578–584
10. Michaelsen KF, Lauritzen L, Mortensen EL. Effects of breast-feeding on cognitive function. *Adv Exp Med Biol*. 2009;639:199–215
11. Rey J. Breastfeeding and cognitive development. *Acta Paediatr Suppl*. 2003;92(442):11–18
12. McCann JC, Ames BN. Is docosahexaenoic acid, an *n*-3 long-chain polyunsaturated fatty acid, required for development of normal brain function? An overview of evidence from cognitive and behavioral tests in humans and animals. *Am J Clin Nutr*. 2005;82(2):281–295
13. Simmer K. An intervention promoting exclusive and prolonged breast feeding improved verbal intelligence scores in children at 6.5 years. *Evid Based Med*. 2008;13(6):181
14. Simmer K, Patole SK, Rao SC. Longchain polyunsaturated fatty acid supplementation in infants born at term. *Cochrane Database Syst Rev*. 2008;(1):CD000376

15. Smithers LG, Gibson RA, McPhee A, Makrides M. Effect of long-chain polyunsaturated fatty acid supplementation of preterm infants on disease risk and neurodevelopment: a systematic review of randomized controlled trials. *Am J Clin Nutr*. 2008;87(4):912–920
16. Jacobson SW, Chiodo LM, Jacobson JL. Breastfeeding effects on intelligence quotient in 4- and 11-year-old children. *Pediatrics*. 1999;103(5). Available at: www.pediatrics.org/cgi/content/full/103/5/e71
17. Feldman R, Eidelman AI. Direct and indirect effects of breast milk on the neurobehavioral and cognitive development of premature infants. *Dev Psychobiol*. 2003;43(2):109–119
18. Poobalan AS, Aucott LS, Ross L, et al. Effects of treating postnatal depression on mother-infant interaction and child development: systematic review. *Br J Psychiatry*. 2007;191:378–386
19. Surkan PJ, Schnaas L, Wright RJ, et al. Maternal self-esteem, exposure to lead, and child neurodevelopment. *Neurotoxicology*. 2008;29(2):278–285
20. Treyvaud K, Anderson VA, Howard K, et al. Parenting behavior is associated with the early neurobehavioral development of very preterm children. *Pediatrics*. 2009;123(2):555–561
21. Koletzko B, Lien E, Agostoni C, et al; World Association of Perinatal Medicine Dietary Guidelines Working Group. The roles of long-chain polyunsaturated fatty acids in pregnancy, lactation and infancy: review of current knowledge and consensus recommendations. *J Perinat Med*. 2008;36(1):5–14
22. Mead MN. Contaminants in human milk: weighing the risks against the benefits of breastfeeding. *Environ Health Perspect*. 2008;116(10):A427–A434
23. Guxens M, Ballester F, Espada M, et al. The INMA—INfancia y Medio Ambiente—(Environment and Childhood) Project. *Int J Epidemiol*. 2011; doi:10.1093/ije/dyr054
24. Regidor E, Martinez D, Calle ME, Astasio P, Ortega P, Domínguez V. Socioeconomic patterns in the use of public and private health services and equity in health care. *BMC Health Serv Res*. 2008;8:183
25. Bayley N. *Escalas Bayley de Desarrollo Infantil*. Madrid, Spain: TEA Ediciones; 1977
26. Li R, Fein SB, Grummer-Strawn LM. Association of breastfeeding intensity and bottle-emptying behaviors at early infancy with infants' risk for excess weight at late infancy. *Pediatrics*. 2008;122(suppl 2):S77–S84
27. Piper S, Parks PL. Use of an intensity ratio to describe breastfeeding exclusivity in a national sample. *J Hum Lact*. 2001;17(3):227–232
28. World Health Organization. Indicators for Assessing Breastfeeding Practices. Geneva, Switzerland: World Health Organization, 1991. Available at: www.emro.who.int/cah/pdf/bf_indicators.pdf. Accessed [January 6, 2011]
29. Moltó-Puigmartí C, Castellote AI, López-Sabater MC. Conjugated linoleic acid determination in human milk by fast-gas chromatography. *Anal Chim Acta*. 2007;602(1):122–130
30. Cattell RB, Cattell AKS. *Manual de Factor "g." Escalas 2 y 3*. Madrid, Spain: TEA Ediciones; 1977
31. Goldberg DP, Gater R, Sartorius N, et al. The validity of two versions of the GHQ in the WHO study of mental illness in general health care. *Psychol Med*. 1997;27(1):191–197
32. Condon JT, Corkindale CJ. The assessment of parent-to-infant attachment: development of a self-report questionnaire instrument. *J Reprod Infant Psychol*. 1998;16:57–76
33. Condon JT, Corkindale CJ, Boyce P. The assessment of paternal-infant attachment: development of a questionnaire instrument. *J Reprod Infant Psychol*. 2008;26(3):195–210
34. Goñi F, López R, Etxeandia A, Millán E, Amiano P. High throughput method for the determination of organochlorine pesticides and polychlorinated biphenyls in human serum. *J Chromatogr B Analyt Technol Biomed Life Sci*. 2007;852(1–2):15–21
35. Alvarez-Pedrerol M, Guxens M, Ibarluzea J, et al. Organochlorine compounds, iodine intake, and thyroid hormone levels during pregnancy. *Environ Sci Technol*. 2009;43(20):7909–7915
36. Spratt M, Carpenter J, Sterne JA, et al. Strategies for multiple imputation in longitudinal studies. *Am J Epidemiol*. 2010;172(4):478–487
37. Sterne JA, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ*. 2009;338:b2393
38. Marangoni F, Agostoni C, Lammardo AM, Giovannini M, Galli C, Riva E. Polyunsaturated fatty acid concentrations in human hindmilk are stable throughout 12-months of lactation and provide a sustained intake to the infant during exclusive breastfeeding: an Italian study. *Br J Nutr*. 2000;84(1):103–109
39. Molto-Puigmarti C, Castellote AI, Carbonell-Estrany X, Lopez-Sabater MC. Differences in fat content and fatty acid proportions among colostrum, transitional, and mature milk from women delivering very preterm, preterm, and term infants. *Clin Nutr*. 2010;30(1):116–123
40. Simmer K, Schulzke SM, Patole S. Longchain polyunsaturated fatty acid supplementation in preterm infants. *Cochrane Database Syst Rev*. 2008;(1):CD000375
41. Mendez MA, Torrent M, Julvez J, Ribas-Fitó N, Kogevinas M, Sunyer J. Maternal fish and other seafood intakes during pregnancy and child neurodevelopment at age 4 years. *Public Health Nutr*. 2009;12(10):1702–1710
42. Hibbeln JR, Davis JM, Steer C, et al. Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): an observational cohort study. *Lancet*. 2007;369(9561):578–585
43. Helland IB, Smith L, Saarem K, Saugstad OD, Drevon CA. Maternal supplementation with very-long-chain *n*-3 fatty acids during pregnancy and lactation augments children's IQ at 4 years of age. *Pediatrics*. 2003;111(1). Available at: www.pediatrics.org/cgi/content/full/111/1/e39
44. Jensen CL, Lapillonne A. Docosahexaenoic acid and lactation. *Prostaglandins Leukot Essent Fatty Acids*. 2009;81(2–3):175–178
45. Gustafsson PA, Duchén K, Birberg U, Karlsson T. Breastfeeding, very long polyunsaturated fatty acids (PUFA) and IQ at 6 1/2 years of age. *Acta Paediatr*. 2004;93(10):1280–1287
46. Glaser C, Heinrich J, Koletzko B. Role of FADS1 and FADS2 polymorphisms in polyunsaturated fatty acid metabolism. *Metabolism*. 2010;59(7):993–999
47. Moltó-Puigmartí C, Plat J, Mensink RP, et al. FADS1 FADS2 gene variants modify the association between fish intake and the docosahexaenoic acid proportions in human milk. *Am J Clin Nutr*. 2010;91(5):1368–1376
48. Xie L, Innis SM. Genetic variants of the FADS1 FADS2 gene cluster are associated with altered (*n*-6) and (*n*-3) essential fatty acids in plasma and erythrocyte phospholipids in women during pregnancy and in breast milk during lactation. *J Nutr*. 2008;138(11):2222–2228
49. Caspi A, Williams B, Kim-Cohen J, et al. Moderation of breastfeeding effects on the IQ by genetic variation in fatty acid metabolism. *Proc Natl Acad Sci U S A*. 2007;104(47):18860–18865

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