Maternal Supplementation With Very-Long-Chain n-3 Fatty Acids During Pregnancy and Lactation Augments Children's IQ at 4 Years of Age

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ABSTRACT. *Objectives.* **Docosahexaenoic acid (DHA; 22:6 n-3) and arachidonic acid (AA; 20:4 n-6) are important for development of the central nervous system in mammals. There is a growth spurt in the human brain during the last trimester of pregnancy and the first postnatal months, with a large increase in the cerebral content of AA and DHA. The fetus and the newborn infant depend on maternal supply of DHA and AA. Our hypothesis was that maternal intake of DHA during pregnancy and lactation is marginal and that high intake of this fatty acid would benefit the child. We examined the effect of supplementing pregnant and lactating women with very-long-chain n-3 polyunsaturated fatty acids (PUFAs; cod liver oil) on mental development of the children, compared with maternal supplementation with long-chain n-6 PUFAs (corn oil).**

Methods. **The study was randomized and double-blinded. Pregnant women were recruited in week 18 of pregnancy to take 10 mL of cod liver oil or corn oil until 3 months after delivery. The cod liver oil contained 1183 mg/10 mL DHA, 803 mg/10 mL eicosapentaenoic acid (20:5 n-3), and a total of 2494 mg/10 mL Σ n-3 PUFAs. The corn oil contained 4747 mg/10 mL linoleic acid (18:2 n-6) and 92 mg/10 mL α-linolenic acid (18:3 n-3). The amount of fat-soluble vitamins was identical in the 2 oils (117 μg/mL vitamin A, 1 μg/mL vitamin D, and 1.4 mg/mL dl-α-tocopherol). A total of 590 pregnant women were recruited to the study, and 341 mothers took part in the study until giving birth. All infants of these women were scheduled for assessment of cognitive function at 6 and 9 months of age, and 262 complied with the request. As part of the protocol, 135 subjects from this population were invited for intelligence testing with the Kaufman Assessment Battery for Children (K-ABC) at 4 years of age. Of the 135 invited children, 90 came for assessment. Six children did not complete the examination. The K-ABC is a measure of intelligence and achievement designed for children aged 2.5 years through 12.5 years. This multisubtest battery comprises 4 scales: Sequential Processing, Simultaneous Processing, Achievement (not used in the present study), and Nonverbal Abilities. The Sequential Processing and Simultaneous Processing scales are hypothesized to reflect the child's style of problem solving and information processing. Scores from these 2 scales are combined to form a Mental Processing Composite, which serves as the measure of intelligence in the K-ABC.**

Results. **We received dietary information from 76 infants (41 in the cod liver oil group and 35 in the corn oil group), documenting that all of them were breastfed at 3 months of age. Children who were born to mothers who had taken cod liver oil (n = 48) during pregnancy and lactation scored higher on the Mental Processing Composite of the K-ABC at 4 years of age as compared with children whose mothers had taken corn oil (n = 36; 106.4 [7.4] vs 102.3 [11.3]). The Mental Processing Composite score correlated significantly with head circumference at birth (r = 0.23), but no relation was found with birth weight or gestational length. The children's mental processing scores at 4 years of age correlated significantly with maternal intake of DHA and eicosapentaenoic acid during pregnancy. In a multiple regression model, maternal intake of DHA during pregnancy was the only variable of statistical significance for the children's mental processing scores at 4 years of age.**

Conclusion. **Maternal intake of very-long-chain n-3 PUFAs during pregnancy and lactation may be favorable for later mental development of children.** ***Pediatrics*** **2003;111:e39–e44. URL: http://www.pediatrics.org/cgi/content/full/111/1/e39;** ***dietary supplements, n-3 fatty acids, docosahexaenoic acid, arachidonic acid, pregnancy, breastfeeding, intelligence test, K-ABC.***

ABBREVIATIONS. DHA, docosahexaenoic acid; AA, arachidonic acid; PUFA, polyunsaturated fatty acid; K-ABC, Kaufman Assessment Battery for Children; EPA, eicosapentaenoic acid.

Docosahexaenoic acid (DHA; 22:6 n-3) and arachidonic acid (AA; 20:4 n-6) are important for development of the central nervous system in mammals.[1,2] There is a growth spurt in the human brain during the last trimester of pregnancy and the first postnatal months, with a large increase in the cerebral content of AA and DHA. The capacity for elongation and desaturation of α-linolenic acid (18:3 n-3) to DHA is inadequate in the fetus and the newborn.[3–6] Maternal very-long-chain polyunsaturated fatty acid (PUFA) status during pregnancy is critical for the very-long-chain PUFA status in the newborn,[7] and newborn infants depend on dietary supply of these fatty acids.[8,9] In contrast to most formulas, breast milk contains DHA and AA, but the concentrations of these very-long-chain PUFAs are variable, depending on the mother's diet.[10–12]

Several studies have shown a positive correlation between breastfeeding and cognitive development.[13–17] Lucas et al[13,15] indicated that breast milk

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includes biological factors that may be beneficial for mental development in preterm infants. This may be attributable to AA and DHA in the breast milk. However, studies on the effect of adding preformed very-long-chain n-3 and n-6 PUFAs to infant formulas have been inconclusive, because some studies of visual acuity, problem solving, and general neurologic development found enhanced performance,[6,18–22] whereas others showed no effect in term infants.[23–26] In 1 study, infants who received formula with DHA and without AA scored lower than infants in the breast milk or control formula groups on language assessments at 14 months of age.[27] Similar studies have been performed on infants who were born prematurely. Premature infants are probably more vulnerable to DHA deficiency than are term infants, because they do not receive the third-trimester intrauterine supply of DHA. They have small tissue stores, the metabolic transformation via elongation and desaturation of fatty acids is insufficient, and the intake of DHA from infant formulas is small.[4,5] Supplementation with DHA to premature infants may increase early maturation of visual function and information processing.[28–30]

In the present study, we tested the hypothesis that maternal intake of very-long-chain n-3 PUFAs is marginal and that the fetus and the newborn infant will benefit from increasing the mother's intake during pregnancy and lactation. Pregnant women were supplemented with very-long-chain n-3 PUFAs (cod liver oil) or n-6 long-chain PUFAs (corn oil) from 18 weeks of pregnancy, and the children were examined at 4 years of age with an intelligence test.

METHODS

Study Design

Pregnant women were enrolled between December 1994 and October 1996 at Rikshospitalet University Hospital and Baerum Central Hospital in the Oslo, Norway, area. Inclusion and exclusion criteria are listed in Table 1. The participating infants were followed up in the present study after examination of the effect of supplementing mothers with very-long-chain n-3 PUFAs on birth weight, gestational length, and infant development during first year of life.[31] A total of 341 mothers took part in the study until giving birth. All infants of these women were scheduled for assessment of cognitive function at 6 and 9 months of age, and 262 complied with the request. As part of the protocol, 135 subjects from this population were invited for intelligence testing with the Kaufman Assessment Battery for Children (K-ABC) at 4 years of age.[32] Of the 135 invited children, 90 came for assessment. Six children did not complete the examination.

The mothers randomly received either 10 mL/d cod liver oil or 10 mL/d corn oil from 18 weeks of pregnancy until 3 months after delivery. Peter Möller (Oslo, Norway) supplied both oils. The cod liver oil contained 1183 mg/10 mL DHA, 803 mg/10 mL eicosapentaenoic acid (EPA; 20:5 n-3), and a total of 2494 mg/10 mL Σ n-3 PUFAs. The corn oil contained 4747 mg/10 mL linoleic acid (18:2 n-6) and 92 mg/10 mL α-linolenic acid.[31] The amount of fat-soluble vitamins was identical in the 2 oils (117 μg/mL vitamin A, 1 μg/mL vitamin D, and 1.4 mg/mL dl-α-tocopherol). Norwegian guidelines for infant nutrition recommend that all infants receive 5 mL of cod liver oil daily from 4 weeks of age.

The study was double-blinded, and a computer program conducted the randomization. The participating women received written information and consented to enroll in the study, which was approved by the regional ethics committee. Information about the mothers was collected from pregnancy records and from food frequency questionnaires. Characteristics of the infants were collected from birth records and information given by the mothers via questionnaires.

TABLE 1. Inclusion and Exclusion Criteria

Inclusion criteria
Healthy women with single pregnancies between 19 and 35 years of age
Nulliparous or primiparous
Intention to breastfeed their infant
No supplement of long-chain n-3 PUFAs earlier during the pregnancy
Exclusion criteria
Premature births
Birth asphyxia
General infections
Anomalies in the infants that required special attention

Blood and Milk Samples

Blood samples were collected from the umbilical cords and from the infants by venipuncture at the age of 4 weeks and 3 months. Milk samples were collected at 4 weeks and 3 months after delivery. The samples were taken from a morning feed (never the first one), 3 to 5 minutes after the infant started suckling. The samples were collected the day before they were provided to the hospital and kept in a home refrigerator until the next day when they were frozen at −70°C under nitrogen. Before storage, the samples were sonicated, and ethylenediaminetetraacetic acid and butylated hydroxytoluene were added to a final concentration of 1.85 mg/mL and 75 μg/mL, respectively. The content of fatty acids in plasma and breast milk was determined by gas liquid chromatography.[12,33]

Dietary Evaluation

All participating mothers filled out a self-administered food frequency questionnaire when they entered the study (week 18) and at week 35 of pregnancy. The questionnaire has been validated repeatedly, demonstrating that the questionnaire may be used for estimation of dietary intake of very-long-chain n-3 fatty acids.[34–36] The mothers were asked to continue their habitual diet during the study period.

When the infants were 3 months old, the mothers answered a questionnaire covering the infants' usual diet. This included questions about breastfeeding and supplements with cod liver oil given to the infants.

Assessment of Intelligence

The K-ABC is a measure of intelligence and achievement designed for children aged 2.5 years through 12.5 years.[32] This multisubtest battery comprises 4 scales: Sequential Processing, Simultaneous Processing, Achievement (not used in the present study), and Nonverbal Abilities. The Sequential Processing and Simultaneous Processing scales are hypothesized to reflect the child's style of problem solving and information processing. Scores from these 2 scales are combined to form a Mental Processing Composite, which serves as the measure of intelligence in the K-ABC. The Nonverbal Scale is not an independent scale. It is composed of the subtests from the Sequential Processing and Simultaneous Processing scales that do not require words. The examiner may convey instructions through gestures, and the child may respond with movements. The Sequential Processing and Simultaneous Processing scales were designed to reduce the effects of verbal processing and of gender and ethnic bias. The Sequential Processing scale was designed to measure children's ability to solve problems that require the arrangement of stimuli in sequential or serial order, whereas the Simultaneous Processing scale was designed to measure children's ability to solve spatial, analogic, or organizational problems that require processing of many stimuli at once. Raw scores are transformed into standard scores with mean = 100 and standard deviation = 15. Internal consistency reliability for the Mental Processing Composite is, on the average, 0.91 for preschool children.[32] The Mental Processing Composite has an average standard error of measurement of 4.6 points for preschool children.[32] Because the K-ABC does not have a Norwegian standardization, the raw scores were converted to standard scores according to the US norms.

Statistics

Data are presented as means (standard deviations). Student t test was used to examine differences between different groups for continuous variables. For categorical values, the χ^2 test was used. Correlation coefficients were calculated using the Pearson test. Multiple regression analyses were also conducted. P values $\leq .05$ were considered significant. SPSS for Macintosh 6.1.1. (SPSS Inc, Chicago, IL) was used for calculations.

RESULTS

Study Population

Birth data of the study population and characteristics of their parents are described in Table 2. The study population did not differ from the population not tested with K-ABC on gestational length, birth weight, birth length, head circumference, placental weight, maternal age, maternal body mass index, maternal or paternal education, or parity.

We received dietary information from 76 infants (41 in the cod liver oil group and 35 in the corn oil group), documenting that all of them were breastfed at 3 months of age. The breast milk of mothers who received cod liver oil contained more DHA (approximately 270%) and less AA (88%) than breast milk of mothers who received corn oil (Table 3). At 3 months of age, 35 infants (19 in the cod liver oil group and 16 in the corn oil group) received cod liver oil.

Fatty Acid Patterns in Umbilical and Plasma Phospholipids

The concentrations of Σn-3, EPA, DHA, and the ratio Σn-3/Σn-6 in plasma phospholipids were significantly higher in the cod liver oil group as compared with the corn oil group, whereas the concentrations of AA and Osbond acid (22:5 n-6) were higher in the corn oil group (Table 4).

Maternal Dietary Intake

There were no differences between the cod liver oil group and the corn oil group in maternal nutrient intake at the start of the study (18 weeks of pregnancy; data not shown). After 35 weeks of pregnancy, there were significant differences between the 2 groups for intake of linoleic acid, AA, EPA, and DHA (Table 5), reflecting the intake of different supplements.

TABLE 2. Birth Data and Characteristics of the Parents of Children Assessed With K-ABC (Mean [SD])

	Cod Liver Oil (n = 48)	Corn Oil (n = 36)
Gestational length (d)	281.3 (9.6)	278.5 (11.2)
Weight (g)	3571 (485)	3471 (593)
Length (cm)	50.8 (2.2)	50.3 (2.5)
Head circumference (cm)	35.4 (1.4)	35.0 (1.8)
Placental weight (g)	662 (139)	625 (136)
Boys/girls	23/25	18/18
Maternal age (y)	28.5 (3.3)	28.0 (2.4)
BMI before pregnancy (kg/m^2)	22.7 (3.1)	22.3 (3.0)
Parity	0.3 (0.5)	0.3 (0.5)
Smoking (%)	11.4	18.2
Maternal education		
<10 y (%)	2 (4.2)	0 (0)
10–12 y (%)	10 (20.8)	11 (30.6)
>12 y (%)	36 (75.0)	25 (69.4)
Paternal education		
<10 y (%)	3 (6.3)	1 (2.8)
10–12 y (%)	12 (25.0)	8 (22.2)
>12 y (%)	33 (68.7)	27 (75.0)

SD indicates standard deviation; BMI, body mass index.

Cognitive Tests

Children in the cod liver oil group had significantly higher scores than the children in the corn oil group on the Mental Processing Composite of the K-ABC test at 4 years of age (106.4 [7.4] vs 102.3 [11.3]; $P = .049$; Fig 1). There was a clear tendency to higher scores for the Sequential Processing scale, Simultaneous Processing scale, and Nonverbal scale among children who were born to mothers who were given cod liver oil (Fig 1), but these differences were not statistically significant. No differences were observed between children who received cod liver oil or not (Table 6). The Mental Processing Composite score correlated significantly with head circumference at birth ($r = 0.23$; $P = .04$), but no relation was found with birth weight or gestational length.

No correlation was observed between very-long-chain n-3 PUFAs in umbilical plasma phospholipids and intelligence scores, but Mead acid (20:3 n-9) and Osbond acid correlated negatively with intelligence sores (Mead acid: Simultaneous Processing, $r = -0.24$, $P = .04$; Nonverbal Scale, $r = -0.25$, $P = .03$; Osbond acid: Mental Processing Composite, $r = -0.29$, $P = .01$; Sequential Processing, $r = -0.31$, $P = .008$, Nonverbal Scale, $r = -0.25$, $P = .03$). Moreover, intelligence scores at 4 years of age correlated with plasma phospholipid concentrations of docosapentaenoic acid n-3 (22:5 n-3; Mental Processing Composite, $r = 0.23$, $P = .03$) and DHA (Mental Processing Composite, $r = 0.28$, $P = .01$; Sequential Processing, $r = 0.22$, $P = .05$; Simultaneous Processing, $r = 0.25$, $P = .03$) at 4 weeks of age. Mental processing skills of the children correlated significantly with maternal intake of EPA (Mental Processing Composite, $r = 0.27$, $P = .02$; Simultaneous Processing, $r = 0.25$, $P = .04$) and DHA (Mental Processing Composite, $r = 0.26$, $P = .03$; Simultaneous Processing, $r = 0.24$, $P = .04$) during pregnancy.

In a regression model (backward stepwise) with Mental Processing Composite as dependent variable and maternal intake of DHA, gestational length, head circumference, maternal age, parity, parental education, maternal smoking, and cod liver oil intake of the infant as independent variables, maternal intake of DHA was the only variable with statistical significance ($r^2 = 0.07$; $P = .03$) unilaterally evaluated.

DISCUSSION

This is the first study to examine the long-term effects on children of maternal supplementation with very-long-chain n-3 PUFAs during pregnancy and lactation. Our present study shows that 4-year-old children have higher mental processing scores when the mothers are supplemented with very-long-chain n-3 PUFAs (from cod liver oil) during pregnancy and lactation, as compared with children of mothers who are supplemented with long-chain n-6 PUFAs (from corn oil).

TABLE 3. Fatty Acids in Breast Milk (wt%) 4 Weeks and 3 Months After Delivery (Mean [SD])

Fatty Acids	4 Weeks		3 Months	
	Cod Liver Oil (n = 46)	Corn Oil (n = 36)	Cod Liver Oil (n = 39)	Corn Oil (n = 34)
Saturates	42.39 (4.30)	42.12 (5.53)	43.82 (3.34)	42.20 (4.01)
Monoenes	39.07 (3.56)	39.07 (3.29)	38.24 (2.78)	39.45 (2.95)
Polyenes	15.71 (2.86)	16.10 (3.99)	15.02 (2.59)	15.56 (3.59)
Σn-6	12.36 (2.44)	14.42 (3.68)†	11.73 (2.01)	13.66 (3.24)†
18:2 n-6	11.31 (2.36)	13.24 (3.60)†	10.88 (1.92)	12.66 (3.15)†
20:3 n-6	0.33 (0.09)	0.39 (0.08)‡	0.26 (0.09)	0.32 (0.08)†
20:4 n-6	0.38 (0.08)	0.42 (0.07)*	0.33 (0.08)	0.38 (0.10)*
Σn-3	3.36 (1.14)	1.68 (0.43)‡	3.19 (0.97)	1.77 (0.63)‡
18:3 n-3	0.92 (0.28)	0.85 (0.29)	0.92 (0.21)	0.85 (0.27)
20:5 n-3	0.42 (0.18)	0.12 (0.05)‡	0.43 (0.18)	0.15 (0.09)‡
22:5 n-3	0.37 (0.16)	0.18 (0.05)‡	0.35 (0.14)	0.20 (0.09)‡
22:6 n-3	1.41 (0.63)	0.43 (0.16)‡	1.26 (0.49)	0.47 (0.27)‡
Σn-3/Σn-6	0.28 (0.10)	0.12 (0.02)‡	0.27 (0.07)	0.13 (0.04)‡
Total lipid§	3.85 (1.63)	4.30 (1.47)	3.94 (1.89)	3.77 (1.48)

* $P \leq .05$, † $P \leq .01$, ‡ $P \leq .001$ compared with mean values for the cod liver oil group.
§ The total lipid content is in mg/100 μL.

TABLE 4. Fatty Acids (μg/mL) in Umbilical Plasma Phospholipids and in Infant Plasma Phospholipids at 4 Weeks and 3 Months of Age (Mean [SD])

Fatty Acids	Birth		4 Weeks		3 Months	
	Cod Liver Oil (n = 43)	Corn Oil (n = 31)	Cod Liver Oil (n = 46)	Corn Oil (n = 36)	Cod Liver Oil (n = 41)	Corn Oil (n = 34)
20:3 n-9	2.0 (1.2)	2.3 (1.2)	1.0 (0.3)	1.4 (1.0)*	0.7 (0.3)	0.9 (0.5)*
Σn-6	162.4 (72.6)	166.4 (35.4)	318.8 (40.3)	367.8 (68.4)†	333.4 (66.6)	369.5 (55.6)*
20:4n-6	71.1 (16.9)	85.2 (19.0)†	92.2 (16.3)	115.1 (22.4)†	88.4 (17.6)	110.5 (19.7)†
22:5n-6	1.5 (0.7)	3.4 (1.5)†	1.1 (0.5)	3.1 (1.7)†	0.8 (0.4)	1.9 (0.9)†
Σn-3	83.8 (40.3)	48.9 (13.6)†	121.5 (27.0)	76.2 (17.0)†	145.1 (38.2)	97.6 (25.6)†
20:5n-3	12.4 (10.9)	2.7 (2.5)†	21.1 (9.7)	5.2 (2.5)†	28.6 (15.6)	10.2 (7.4)†
22:5n-3	5.8 (3.2)	2.7 (1.0)†	9.0 (2.2)	7.2 (1.8)†	10.9 (2.7)	9.8 (2.1)
22:6n-3	63.7 (26.8)	42.4 (11.6)†	87.3 (17.1)	60.3 (13.5)†	101.3 (24.7)	74.0 (18.9)†
Σn-3/Σn-6	0.5 (0.1)	0.3 (0.1)†	0.4 (0.1)	0.2 (0.0)†	0.4 (0.1)	0.3 (0.1)†

* $P \leq .05$, † $P \leq .001$ compared with mean values for the cod liver oil group.

The maternal intake of DHA during pregnancy seems to be important for mental development measured at 4 years of age. Higher maternal intake of DHA results in higher maternal plasma levels and thereby increased transfer of DHA to the fetus.[31,37] In an observational study, it was recently reported that stereoacuity at age 3.5 years was enhanced among full-term infants whose mothers had a DHA-rich diet during pregnancy.[38] Breastfeeding was also associated with enhanced stereopsis, compared with children who had not been breastfed.[38] In our study, at least 76 infants were breastfed at 3 months of age, thereby receiving AA as well as DHA via their mothers' milk. However, the infants of cod liver oil–supplemented mothers received approximately 2.7-fold more DHA than infants of corn oil–supplemented mothers postnatal. Approximately half of all of the infants in both groups received cod liver at 3 months of age. However, we did not observe any effect of cod liver oil supplementation to breastfed infants on later mental development.

The difference of 4.1 points in the scores on the Mental Processing Composite of the K-ABC between the 2 groups may have limited significance on individual basis but may be of epidemiologic importance. Didactic procedures increasing IQ with 4 points among school children, with no harmful side effects, would immediately be implemented in schools.

TABLE 5. Daily Intake of Energy and Nutrients as Evaluated by a Food Frequency Questionnaire in Week 35 of Pregnancy (Mean [SD])

	Cod Liver Oil (n = 39)	Corn Oil (n = 31)
Energy (MJ)	9.2 (2.7)	8.9 (2.1)
Protein (g)	79.7 (16.8)	79.8 (18.4)
Fat (g)	80.5 (27.1)	78.3 (28.0)
Carbohydrate-fiber (g)	287 (89)	270 (63)
Sugar (g)	70.2 (53.4)	60.3 (37.6)
Alcohol (g)	0.8 (1.5)	0.8 (2.3)
Fibers (g)	20.2 (5.6)	19.4 (6.1)
Cholesterol (mg)	292 (67)	258 (111)
Saturates (g)	31.0 (12.0)	29.1 (11.9)
Monoenes (g)	29.0 (9.1)	27.0 (9.9)
Polyenes (g)	14.3 (5.8)	16.2 (5.6)
18:2 n-6	9.3 (4.9)	13.8 (4.7)†
18:3 n-3	1.3 (0.7)	1.3 (0.7)
20:4 n-6	0.1 (0.04)	0.1 (0.04)*
20:5 n-3	0.9 (0.08)	0.1 (0.1)†
22:6 n-3	1.4 (0.1)	0.2 (0.1)†
Retinol (eq mg)	2.7 (1.2)	2.3 (0.6)
β-Carotene (mg)	3.6 (4.4)	3.0 (1.8)
Tocopherol (mg)	18.9 (1.5)	19.4 (1.9)
Vitamin D (μg)	13.4 (1.8)	13.5 (2.1)

* $P < .01$, † $P < .001$ compared with mean values for the cod liver oil group.

We also observed a significant correlation between

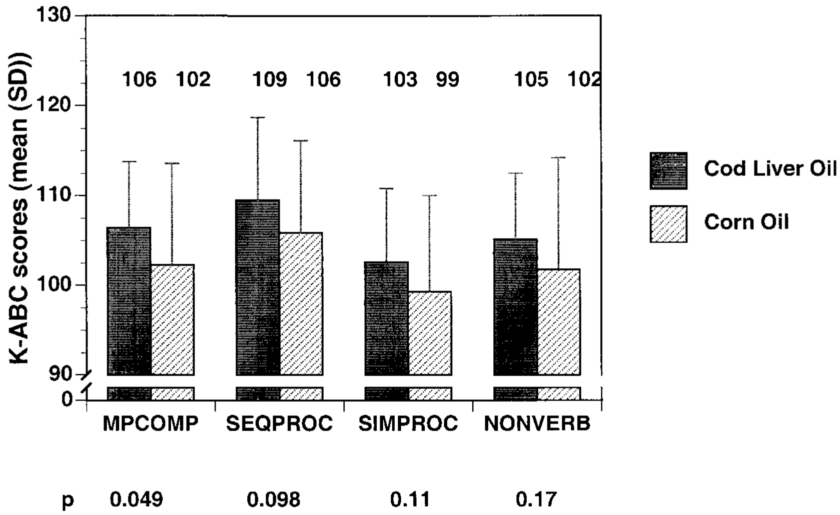

Fig 1. Scores on the K-ABC for children whose mothers had taken cod liver oil (n = 48) or corn oil (n = 36) during pregnancy and lactation. Values for the different subtests are shown. MPCOMP, Mental Processing Composite; SEQPROC, Sequential Processing; SIMPROC, Simultaneous Processing; NONVERB, Nonverbal Abilities.

TABLE 6. Mental Composite Scores for Infants Receiving Cod Liver Oil or Not When Mothers Received Supplements of Cod Liver Oil or Corn Oil (Mean [SD])

Maternal Supplementation	Infant Supplementation of Cod Liver Oil	MPCOMP
Cod liver oil		
n = 19	+	107.8 (7.6)
n = 22	−	106.1 (8.0)
Corn oil		
n = 16	+	101.7 (7.3)
n = 19	−	102.5 (14.1)

MPCOMP indicates Mental Composite Scores.

head circumference and mental processing skills. Severely reduced blood flow to the fetus associated with growth retardation may be followed by impairment of intellectual development and partial neurodevelopment delay.[39] Reduced supply of DHA and AA may explain some of the neurologic impairment. Children who are born small for gestational age have smaller head circumference than children who are born appropriate for gestational age, even at 13 months of age.[40] They also score lower on the Bayley Mental Scale of Infant Development. At school age, children who were born small for gestational age seem to show learning deficits.[41,42] Our study is the first to show such a correlation between head circumference at birth and mental processing skills in healthy term infants. Head circumference at 6 months of age has previously been shown to correlate with IQ at 3 years of age.[43]

We furthermore observed a relation between intelligence scores at 4 years of age and concentrations of docosapentaenoic acid n-3 and DHA in plasma phospholipids at 4 weeks of age but not at birth or at 3 months of age. It is possible that the small number of individuals in our groups makes it difficult to find significant correlations at different time points, but it is tempting to assume that DHA may be important for mental development at least during childhood. We will follow up our study population to the age of 7 years to evaluate whether cod liver oil supplementation to pregnant and lactating women will influence long-term mental skills among children.

At birth, Osbond and Mead acid correlated negatively with intelligence scores, and these fatty acids have been proposed to be markers of DHA depletion.[44] High levels of these fatty acids might also represent nonoptimal ligands for transcription factors, substrates for enzymatic activities, or structural components in the central nervous system.[45]

CONCLUSION

This study indicates that maternal supplementation with very-long-chain n-3 PUFAs during pregnancy and lactation improves the intelligence of children at 4 years of age. Perhaps adequate supply of very-long-chain PUFA during pregnancy is just as important as in the neonatal period.[46]

Whether supplementation during pregnancy or during lactation (or both) is of more importance remains to be elucidated. We still do not know whether cod liver oil supplements are important for formula-fed infants. Neither do we know whether length of the breastfeeding period beyond 3 months may be important.

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