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Maternal fat intake during pregnancy and behavioral problems in 5-y-old Japanese children

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ABSTRACT

Objective: The aim of this cohort study was to investigate the relationship between maternal fat consumption during pregnancy and behavioral problems in 1199 Japanese children at age 5 y.
Methods: Dietary intake of mothers during pregnancy was assessed using a diet history questionnaire. Emotional, conduct, hyperactivity, and peer problems in children were assessed using the Strengths and Difficulties Questionnaire; the four scale scores were dichotomized, comparing children with borderline and abnormal scores to children with normal scores. Logistic regression analysis was applied to estimate adjusted odds ratios and 95% confidence intervals for each behavioral problem according to the quartile of dietary factors under study, adjusting for potential confounding factors.
Results: Higher maternal intake of monounsaturated fatty acids, α-linolenic acid, ω-6 polyunsaturated fatty acids, and linoleic acid during pregnancy was independently associated with an increased risk for childhood emotional problems. The adjusted odds ratios between extreme quartiles (95% confidence intervals, P_{trend}) were 1.85 (1.11 – 3.17, 0.04), 1.60 (0.99 – 2.60, 0.03), 2.06 (1.24 – 3.46, 0.002), and 2.09 (1.26 – 3.51, 0.002), respectively. No such positive associations were observed for the other outcomes. No relationships were found between maternal intake of total fat, saturated fatty acids, ω-3 polyunsaturated fatty acids, eicosapentaenoic acid, docosahexaenoic acid, arachidonic acid, or cholesterol, or the ratio of ω-3 to ω-6 polyunsaturated fatty acid intake during pregnancy and any of the outcomes.
Conclusions: Maternal consumption of monounsaturated fatty acids, α-linolenic acid, ω-6 polyunsaturated fatty acids, and linoleic acid during pregnancy may increase the risk for childhood emotional problems.

Introduction

Lipids are of particular interest due to their high concentration in the central nervous system, constituting ~50% to 60% of dry weight of the mature human brain [1]. Of these, 35% is comprised of polyunsaturated fatty acids (PUFAs), especially arachidonic acid (AA) and docosahexaenoic acid (DHA) [1,2]. Fatty acids have been shown to enhance gene expression and neuronal activity, promote neurogenesis and synaptogenesis, and inhibit both neuroinflammation and apoptosis [3]. In contrast to the generally proinflammatory eicosanoids derived from the ω-6 PUFA family, the eicosanoids and docosanoids derived from the ω-3

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PUFA family are less proinflammatory or have antiinflammatory effects, as do ω-6–derived lipoxins [2]. Usually, an overabundance of saturated fatty acids (SFAs) generates harmful outcomes, whereas monounsaturated fatty acids (MUFAs) yield quite beneficial results [3].

The mother's diet is the only source of nutrition for fetal growth, and therefore could have an effect on fetal neurodevelopment [4]. Epidemiologic evidence on the association between PUFAs and childhood behavioral problems is sparse and the results have been inconsistent [5–10]. Only one study investigated the relationship between maternal PUFA intake during pregnancy and childhood behavioral problems; in ALSPAC (Avon Longitudinal Study of Parents and Children), maternal ω-3 PUFA intake during pregnancy was not related to the risk for oppositional development disorder/conduct disorder or attention-deficit/hyperactivity disorder (ADHD) in children age 7.9 y [8]. With regard to fat intake other than PUFAs, intake levels of total energy, total fat, and saturated fat were higher in 11 adolescents with ADHD than in 8 control adolescents [6].

In view of the lack of epidemiologic information regarding the relationship between maternal consumption of specific types of fatty acids during pregnancy and the risk for childhood behavioral problems in non-Western populations, the present prebirth cohort study investigated this issue among 5-y-old Japanese children using data from KOMCHS (Kyushu Okinawa Maternal and Child Health Study).

Methods

Study population

The KOMCHS, a prospective prebirth cohort study, was conducted to examine risk and preventive factors for maternal and child health problems. The baseline survey of the KOMCHS has been described in detail elsewhere [11]. The baseline survey was performed between April 2007 and March 2008. At 423 obstetric hospitals in seven prefectures on Kyushu Island in southern Japan, with a total population of ~13.26 million, and in Okinawa Prefecture, an island chain in the southwest of Japan, with a total population of nearly 1.37 million, a set of leaflets explaining the KOMCHS, an application form to participate in the KOMCHS, and a self-addressed and stamped return envelope were provided to as many pregnant women as possible. Pregnant women who intended to participate in the KOMCHS mailed the application form along with a written description of their personal information to the data management center. After assessing eligibility based on this personal information, research technicians explained the KOMCHS in detail to each eligible pregnant woman by telephone and got permission to send them a self-administered questionnaire. In all, 1757 pregnant women between weeks 5 and 39 of pregnancy gave their written informed consent to take part in the KOMCHS and answered a self-administered questionnaire. Of the 1757 pregnant women, 1590, 1527, 1430, 1362, 1305, 1264, and 1201 mother–child pairs participated in all surveys from the baseline survey to the second (after delivery), third (~4 mo postpartum), fourth (~12 mo postpartum), fifth (~24 mo postpartum), sixth (~36 mo postpartum), seventh (~48 mo postpartum), and eighth (~60 mo postpartum) surveys, respectively. Two pairs with missing data on household income were excluded, leaving data on 1199 pairs available for analysis. The KOMCHS was approved by the ethics committees of the Faculty of Medicine, Fukuoka University and Ehime University Graduate School of Medicine.

Measurements

A self-administered questionnaire was used in each survey. At the time of each survey, participants filled out questionnaires and mailed them to the study's data management center. Research technicians completed missing or illogical data by telephone interview.

In the baseline survey, the first part of the questionnaire elicited information on maternal age, gestation, region of residence, number of children, maternal and paternal education, and household income. A Japanese version [12] of the Center for Epidemiologic Studies Depression Scale (CES-D) [13] also was included in the first part of the questionnaire. The CES-D is a 20-item, self-reported scale designed to assess the frequency of a variety of depressive symptoms within the previous week. Each item is rated on a scale ranging from 0 (*rarely*) to 3 (*most or all of the time*), and the CES-D generates a total score with a range between 0 and 60. Consistent with the validation studies [12,13], a cutoff of ≥16 was used to classify pregnant women with depressive symptoms.

As the second part of the first questionnaire, a semiquantitative, comprehensive diet history questionnaire (DHQ) was used to assess dietary habits during the preceding month [14–20]. Values for daily intake of foods (including 150 foods), energy, and selected nutrients were estimated using an ad hoc computer algorithm for the DHQ based on the Standard Tables of Food Composition in Japan [21]. Information on dietary supplements was not used in the calculation of dietary intake. In a validation study of 92 Japanese women ages 31 to 69 y, the Pearson correlation coefficient between the DHQ and 16-d semiweighted dietary records was 0.62 for total fat, 0.75 for SFAs, 0.57 for MUFAs, 0.36 for ω-3 PUFAs, 0.27 for α-linolenic acid (ALA), 0.58 for eicosapentaenoic acid [EPA], 0.53 for DHA, 0.50 for ω-6 PUFAs, 0.39 for cholesterol, and 0.87 for alcohol [16]. All dietary variables were adjusted for total energy intake using the residual method [22].

The questionnaire in the second survey ascertained the baby's sex, birthweight, date of birth, and maternal smoking during pregnancy. We collected information on household smoking and breastfeeding duration from the questionnaires in the third and fourth surveys. To assess children's behavioral problems at age 5, the questionnaire in the eighth survey included the Japanese parent-report version of the Strengths and Difficulties Questionnaire (SDQ), which was designed to assess the behavior and emotions of 3- to 16-y-old children [23]. The SDQ consists of five scales—emotional problems, conduct problems, hyperactivity, peer problems, and prosocial scales—which are scored according to five items each, resulting in 25 items. Each item was rated on a 3-point scale: 0 (*not true*), 1 (*somewhat true*), and 2 (*certainly true*). Positively worded items were reverse-scored. The items on each scale were summed to generate a score from 0 to 10. Scale scores were categorized as normal, borderline, or abnormal according to cutoff points that had previously been reported in a sample of Japanese children [24].

Statistical analysis

Intake of each of the dietary factors under study was categorized at quartile points on the basis of its distribution among 1199 mothers. The first four scale scores were dichotomized, comparing children with borderline and abnormal scores with children with normal scores; we defined emotional, conduct, hyperactivity, or peer problems as present when a child had a borderline or abnormal score in the respective scale. For the prosocial scale, higher scores indicated better social functioning; thus, the present study was restricted to the four difficulty scores. Maternal age, gestation at baseline, region of residence at baseline, number of children at baseline, maternal and paternal education, household income, maternal depressive symptoms during pregnancy, maternal alcohol intake during pregnancy, maternal smoking during pregnancy, child's birthweight, child's sex, breastfeeding duration, and smoking in the household during the first year of life were selected a priori as potential confounding factors. Age, gestation, and birth weight were used as continuous variables.

Logistic regression analysis was applied to estimate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for each behavioral problem according to the quartile of dietary factors under study, with the lowest quartile as the reference. Trend of association was assessed by a logistic regression model assigning consecutive integers (1–4) to the quartiles of the exposure variables. All statistical analyses were performed using the SAS software package version 9.4 (SAS Institute, Inc., Cary, NC, USA).

Results

The prevalence values of emotional, conduct, hyperactivity, and peer problems were 12.9%, 19.4%, 13.1%, and 8.6%, respectively, among the 1199 children ages 59 to 71 mo. The mean maternal age and gestation at baseline were 31.6 y and 18.1 wk, respectively, and about 18% of mothers had depressive symptoms during pregnancy (Table 1). Median daily total energy consumption and median daily energy-adjusted intake of SFAs, MUFAs, ω-3 PUFAs, and ω-6 PUFAs during pregnancy were 7126.7 kJ, 16.4 g, 19.9 g, 2.2 g, and 10.9 g, respectively.

Table 2 provides adjusted ORs and their 95% CIs for childhood behavioral problems by quartiles of maternal consumption of specific fats during pregnancy. As for maternal intake of MUFAs during pregnancy, compared with the first quartile, intake in the second and fourth quartiles, but not the third, was independently associated with an increased risk for childhood emotional problems, showing a significant positive linear trend. The adjusted OR between extreme quartiles was 1.85 (95% CI, 1.11 – 3.17,

Table 1
Distribution of selected characteristics of 1199 parent–child pairs

Variable	n (%)
Baseline characteristics	
Maternal age, y, mean ± SD	31.6 ± 4
Gestation, wk, mean ± SD	18.1 ± 5.3
Region of residence	
Fukuoka Prefecture	693 (57.8)
Prefecture on Kyushu Island other than Fukuoka	393 (32.8)
Okinawa Prefecture	113 (9.4)
Number of living children already born to same mother	
0	484 (40.4)
1	480 (40)
≥2	235 (19.6)
Maternal education, y	
<13	250 (20.9)
13 – 14	399 (33.3)
≥15	550 (45.9)
Paternal education, y	
<13	343 (28.6)
13 – 14	173 (14.4)
≥15	683 (57)
Household income, Japanese yen/y	
<4 000 000	386 (32.2)
4 000 000–5 999 999	449 (37.5)
≥6 000 000	364 (30.4)
Maternal depressive symptoms during pregnancy	218 (18.2)
Maternal alcohol intake during pregnancy	158 (13.2)
Maternal daily intake*, median (IQR)	
Total energy, kJ	7126.7 (6117.4 – 8465.3)
Total fat, g	57.3 (51.8 – 63.5)
Saturated fatty acids, g	16.4 (14.2 – 18.8)
Monounsaturated fatty acids, g	19.9 (17.5 – 22.4)
ω-3 Polyunsaturated fatty acids, g	2.2 (1.9 – 2.6)
α-Linolenic acid, g	1.7 (1.4 – 1.9)
Eicosapentaenoic acid, g	0.15 (0.10 – 0.21)
Docosahexaenoic acid, g	0.26 (0.19 – 0.35)
ω-6 Polyunsaturated fatty acids, g	10.9 (9.5 – 12.2)
Linoleic acid, g	10.6 (9.3 – 11.9)
Arachidonic acid, g	0.13 (0.10 – 0.16)
Cholesterol, mg	272.4 (215.7 – 353.8)
Characteristics at the postnatal assessment	
Maternal smoking during pregnancy	87 (7.3)
Birth weight, g, mean ± SD	3005.5 ± 397.6
Male sex	568 (47.4)
Breastfeeding duration, mo	
<6	130 (10.8)
≥6	1069 (89.2)
Smoking in the household during the first year of life	329 (27.4)

IQR, interquartile range; SD, standard deviation.
* Nutrient intake was adjusted for total energy intake using the residual method.

$P_{trend} = 0.04$). A significant positive exposure–response relationship was found between maternal ALA intake during pregnancy and the risk for childhood emotional problems, although the adjusted OR between extreme quartiles was just short of significance level. The adjusted OR between extreme quartiles was 1.60 (95% CI, 0.99 – 2.60, $P_{trend} = 0.03$). Higher maternal consumption of ω-6 PUFAs, especially linoleic acid (LA), during pregnancy was independently associated with an increased risk for emotional problems in children. The adjusted OR between extreme quartiles was 2.06 (95% CI, 1.24 – 3.46, $P_{trend} = 0.002$) for ω-6 PUFAs and 2.09 (95% CI, 1.26 – 3.51, $P_{trend} = 0.002$) for LA. Maternal intake of total fat, SFAs, ω-3 PUFAs, EPA, DHA, AA, and cholesterol and the ratio of ω-3 to ω-6 PUFA intake during pregnancy were not significantly related to childhood emotional problems. No significant associations were observed between maternal intake of total fat, SFAs, MUFAs, ω-3 polyunsaturated fatty acids, ALA, EPA, DHA, ω-6 PUFAs, LA, AA, or cholesterol or the ratio of ω-3 to ω-6 PUFA intake during pregnancy and the risk for conduct, hyperactivity, or peer problems in children.

Discussion

To our knowledge, this is the first prebirth cohort study to show that higher maternal consumption of MUFAs, ALA, ω-6 PUFAs, and LA during pregnancy is independently associated with an increased risk for emotional problems in their children. LA is the main dietary ω-6 PUFA, and is likely the main driver of the observed association between ω-6 PUFAs and emotional problems. No such positive associations were observed for childhood conduct, hyperactivity, or peer problems. There were no significant relationships between maternal intake of total fat, SFAs, ω-3 PUFAs, EPA, DHA, AA, or cholesterol or the ratio of ω-3 to ω-6 PUFA intake during pregnancy and any of the outcomes under study.

A previously cited study in the ALSPAC showed no relationship between maternal ω-3 PUFA intake (estimated based on answers to three questions on seafood consumption) during pregnancy and the risk for oppositional development disorder/conduct disorder or ADHD in children age 7.9 y [8]. A cross-sectional study of 584 European children at 7.5 or 8 y of age found no associations between intake of EPA or DHA and behavioral problems based on the Child Behavior Checklist [10]. A study in Australia showed that 79 children ages 6 to 13 y with ADHD had higher intake of ALA and ω-3 PUFAs and lower intake of AA than the general population of the same age; however, there were no differences in intake of EPA or DHA between the two groups [7]. In a cohort study in Germany, higher concentrations of DHA in cord blood serum reduced hyperactivity scores, whereas higher concentrations of AA reduced emotional problems scores [9]. Additionally, higher concentrations of EPA were related to higher scores for conduct problems [9]. A study in Taiwan found that 58 children with ADHD showed a higher content of oleic acid and lower contents of LA, AA, and DHA in the phospholipids isolated from red blood cell membranes compared with those of 52 control children, whereas there were no differences in content of ALA or EPA between the groups [5]. An intervention study found no significant differences in an emotional problems scale, a conduct problems scale, a hyperactivity scale, a peer problems scale, and a prosocial scale between children ages 7 y whose mothers received fish oil supplementation (1.5 g/d ω-3 long-chain PUFAs) or olive oil during lactation [25]. With regard to a lack of association with dietary intake of EPA or DHA, these findings are in partial agreement with the present results [7–10,25]. The inconsistency of our results with those of previous studies, which examined fatty acids other than EPA or DHA, may be at least partly explained by differences in the dietary habits of the populations examined, the evaluation method of fatty acids, definitions of behavioral problems, confounding factors used, and statistical power [5,7,9].

We cannot presently explain why we found positive associations between maternal intake of MUFAs, ALA, ω-6 PUFAs, and LA during pregnancy and childhood emotional problems. Eicosanoids derived from the ω-6 PUFA family are generally proinflammatory [2]. An animal study demonstrated that maternal exposure to a diet high in ω-6 PUFAs during pregnancy increases aggressiveness and locomotor activity and shortens immobility in the swim test in male and female mouse offspring; also, maternal exposure to a diet high in ω-6 PUFAs increases offspring's protein kinase C activity in the hypothalamus [26]. Results

Table 2
ORs and 95% CIs for behavioral problems assessed by the Strength and Difficulties Questionnaire in 1199 children age 5 y by Qs of maternal consumption of specific fats during pregnancy

Variable*	Emotional problems		Conduct problems		Hyperactivity problems		Peer problems	
	Risk (%)	Adjusted OR (95% CI)†	Risk (%)	Adjusted OR (95% CI)†	Risk (%)	Adjusted OR (95% CI)†	Risk (%)	Adjusted OR (95% CI)†
Total fat								
Q1 (46.8)	10.4	1.00	19.7	1.00	14.4	1.00	8	1.00
Q2 (54.6)	13.7	1.31 (0.79 – 2.21)	20.3	1.04 (0.69 – 1.57)	14.3	0.95 (0.59 – 1.53)	9	1.05 (0.58 – 1.91)
Q3 (60.0)	13.3	1.29 (0.77 – 2.17)	19.0	0.93 (0.61 – 1.41)	11.7	0.74 (0.45 – 1.21)	8.3	0.99 (0.55 – 1.82)
Q4 (68.7)	14.3	1.28 (0.77 – 2.15)	18.7	0.84 (0.55 – 1.28)	12.0	0.77 (0.47 – 1.26)	9	0.98 (0.54 – 1.78)
P_{trend}		0.41		0.35		0.19		0.90
Saturated fatty acids								
Q1 (12.6)	14.1	1.00	19.4	1.00	14.4	1.00	9	1.00
Q2 (15.4)	12.3	0.85 (0.52 – 1.39)	20.3	1.03 (0.68 – 1.56)	10.7	0.68 (0.41 – 1.11)	6.7	0.69 (0.37 – 1.28)
Q3 (17.5)	12.7	0.86 (0.52 – 1.42)	16.7	0.78 (0.50 – 1.19)	16.0	1.07 (0.67 – 1.71)	8.3	0.89 (0.49 – 1.60)
Q4 (20.7)	12.7	0.72 (0.44 – 1.18)	21.3	1.06 (0.70 – 1.60)	11.3	0.67 (0.40 – 1.10)	10.3	0.97 (0.56 – 1.72)
P_{trend}		0.22		0.88		0.35		0.86
Monounsaturated fatty acids								
Q1 (15.5)	8.7	1.00	19.4	1.00	14.1	1.00	8.4	1.00
Q2 (18.8)	14.0	1.74 (1.03 – 3.00)	19.7	1.05 (0.69 – 1.60)	13.0	0.86 (0.53 – 1.40)	9.7	1.18 (0.67 – 2.11)
Q3 (20.9)	12.7	1.56 (0.91 – 2.71)	19.3	1.01 (0.66 – 1.53)	13.7	0.96 (0.60 – 1.55)	7	0.84 (0.45 – 1.55)
Q4 (24.7)	16.3	1.85 (1.11 – 3.17)	19.3	0.91 (0.59 – 1.38)	11.7	0.78 (0.47 – 1.28)	9.3	1.01 (0.56 – 1.82)
P for trend		0.04		0.63		0.43		0.75
ω-3 Polyunsaturated fatty acids								
Q1 (1.6)	14.1	1.00	21.1	1.00	15.7	1.00	8.4	1.00
Q2 (2.1)	10.0	0.73 (0.43 – 1.21)	17.3	0.83 (0.55 – 1.27)	13.0	0.82 (0.51 – 1.31)	9.3	1.16 (0.65 – 2.07)
Q3 (2.4)	12.0	0.93 (0.57 – 1.53)	22.0	1.15 (0.77 – 1.73)	11.3	0.75 (0.46 – 1.22)	7.3	0.93 (0.50 – 1.71)
Q4 (2.9)	15.7	1.22 (0.76 – 1.96)	17.3	0.79 (0.52 – 1.20)	12.3	0.80 (0.49 – 1.29)	9.3	1.12 (0.63 – 2.01)
P for trend		0.29		0.58		0.31		0.89
α-Linolenic acid								
Q1 (1.2)	11.7	1.00	19.7	1.00	15.1	1.00	8.4	1.00
Q2 (1.5)	9.7	0.82 (0.48 – 1.40)	18.3	0.91 (0.60 – 1.38)	14.7	0.93 (0.59 – 1.49)	8.7	1.07 (0.59 – 1.93)
Q3 (1.8)	12.7	1.11 (0.67 – 1.85)	21.3	1.20 (0.80 – 1.82)	11.0	0.73 (0.44 – 1.20)	7.3	0.92 (0.49 – 1.69)
Q4 (2.1)	17.7	1.60 (0.99 – 2.60)	18.3	0.82 (0.54 – 1.26)	11.7	0.72 (0.44 – 1.18)	10.0	1.13 (0.64 – 2.02)
P_{trend}		0.03		0.65		0.13		0.79
Eicosapentaenoic acid								
Q1 (0.07)	14.4	1.00	21.4	1.00	14.7	1.00	7.7	1.00
Q2 (0.12)	13.3	0.96 (0.59 – 1.56)	20.7	1.08 (0.72 – 1.62)	12.7	0.90 (0.55 – 1.46)	10.7	1.51 (0.85 – 2.72)
Q3 (0.17)	13.3	1.07 (0.65 – 1.75)	18.7	0.91 (0.60 – 1.39)	12.7	0.92 (0.56 – 1.49)	8	1.15 (0.62 – 2.14)
Q4 (0.28)	10.7	0.88 (0.52 – 1.47)	17.0	0.88 (0.57 – 1.36)	12.3	0.97 (0.59 – 1.59)	8	1.23 (0.66 – 2.30)
P_{trend}		0.75		0.45		0.91		0.75
Docosahexaenoic acid								
Q1 (0.15)	14.7	1.00	20.7	1.00	14.4	1.00	8.7	1.00
Q2 (0.23)	12.3	0.88 (0.53 – 1.44)	20.0	1.00 (0.66 – 1.51)	11.7	0.85 (0.52 – 1.39)	9.7	1.21 (0.68 – 2.16)
Q3 (0.30)	12.7	1.01 (0.62 – 1.65)	19.3	0.99 (0.65 – 1.50)	13.0	1.01 (0.62 – 1.65)	7	0.85 (0.46 – 1.57)
Q4 (0.45)	12.0	0.97 (0.59 – 1.59)	17.7	0.92 (0.60 – 1.40)	13.3	1.07 (0.66 – 1.73)	9	1.22 (0.68 – 2.19)
P_{trend}		0.97		0.69		0.66		0.80
n-6 Polyunsaturated fatty acids								
Q1 (8.4)	9.4	1.00	21.4	1.00	14.4	1.00	9.0	1.00
Q2 (10.2)	10.7	1.10 (0.64 – 1.92)	18.3	0.87 (0.58 – 1.32)	15.3	1.05 (0.66 – 1.68)	7.7	0.87 (0.48 – 1.58)
Q3 (11.5)	14.3	1.63 (0.97 – 2.77)	18.0	0.86 (0.56 – 1.30)	11.0	0.75 (0.45 – 1.23)	8.7	0.94 (0.53 – 1.68)
Q4 (13.3)	17.3	2.06 (1.24 – 3.46)	20.0	0.89 (0.59 – 1.34)	11.7	0.81 (0.49 – 1.33)	9.0	0.96 (0.54 – 1.71)
P_{trend}		0.002		0.57		0.22		0.95
Linoleic acid								
Q1 (8.2)	9.4	1.00	21.7	1.00	14.7	1.00	9.0	1.00
Q2 (9.9)	11.0	1.15 (0.66 – 2.00)	18.7	0.88 (0.58 – 1.33)	15.3	1.03 (0.65 – 1.64)	7.7	0.87 (0.48 – 1.58)
Q3 (11.2)	13.7	1.52 (0.90 – 2.59)	17.3	0.80 (0.53 – 1.22)	10.3	0.67 (0.40 – 1.11)	8.7	0.93 (0.52 – 1.65)
Q4 (13.0)	17.7	2.09 (1.26 – 3.51)	20.0	0.87 (0.58 – 1.31)	12.0	0.81 (0.49 – 1.32)	9.0	0.95 (0.53 – 1.70)
P_{trend}		0.002		0.44		0.18		0.92
Arachidonic acid								
Q1 (0.09)	12.7	1.00	17.1	1.00	13.7	1.00	9.4	1.00
Q2 (0.12)	12.0	1.01 (0.61 – 1.68)	21.0	1.42 (0.93 – 2.18)	12.3	0.92 (0.56 – 1.51)	7.3	0.83 (0.45 – 1.50)
Q3 (0.14)	13.3	1.06 (0.65 – 1.74)	19.7	1.26 (0.82 – 1.93)	14.7	1.10 (0.69 – 1.77)	9.0	0.93 (0.53 – 1.65)
Q4 (0.18)	13.7	1.19 (0.73 – 1.96)	20.0	1.35 (0.88 – 2.07)	11.7	0.91 (0.55 – 1.50)	8.7	1.01 (0.57 – 1.79)
P_{trend}		0.47		0.27		0.92		0.90
ω-3/ω-6 Polyunsaturated fatty acid ratio								
Q1 (0.17)	13.7	1.00	19.7	1.00	12.4	1.00	8.7	1.00
Q2 (0.19)	13.7	1.03 (0.64 – 1.68)	21.3	1.18 (0.78 – 1.79)	15.0	1.34 (0.83 – 2.18)	9.7	1.12 (0.63 – 1.98)
Q3 (0.21)	12.7	1.04 (0.63 – 1.71)	18.0	0.93 (0.61 – 1.43)	13.7	1.24 (0.75 – 2.04)	7.7	0.93 (0.51 – 1.71)
Q4 (0.25)	11.7	0.95 (0.57 – 1.58)	18.7	0.99 (0.64 – 1.51)	11.3	0.97 (0.58 – 1.63)	8.3	1.04 (0.57 – 1.89)
P_{trend}		0.86		0.69		0.84		0.96

(*continued on next page*)

Table 2 (*continued*)

Variable*	Emotional problems		Conduct problems		Hyperactivity problems		Peer problems	
	Risk (%)	Adjusted OR (95% CI)†	Risk (%)	Adjusted OR (95% CI)†	Risk (%)	Adjusted OR (95% CI)†	Risk (%)	Adjusted OR (95% CI)†
Cholesterol								
Q1 (184.0)	10.4	1.00	18.7	1.00	13.0	1.00	9.7	1.00
Q2 (244.7)	14.3	1.51 (0.91 – 2.53)	18.0	1.06 (0.69 – 1.62)	12.3	1.00 (0.61 – 1.64)	8.3	0.89 (0.50 – 1.58)
Q3 (310.4)	13.3	1.36 (0.81 – 2.30)	19.0	1.06 (0.69 – 1.61)	14.7	1.14 (0.70 – 1.84)	7.3	0.69 (0.38 – 1.25)
Q4 (401.7)	13.7	1.45 (0.87 – 2.45)	22.0	1.36 (0.90 – 2.05)	12.3	1.01 (0.61 – 1.66)	9.0	0.97 (0.55 – 1.71)
P_{trend}		0.24		0.17		0.84		0.71

CI, confidence interval; OR, odds ratio; Q, quartile.

* Quartile medians in g/d (except for cholesterol, mg/d) adjusted for energy intake using the residual method are given in parentheses, except for the ratio of ω-3 to ω-6 polyunsaturated fatty acids, which was based on crude intake in g/d.

† Adjustment for maternal age, gestation at baseline, region of residence at baseline, number of children at baseline, maternal and paternal education, household income, maternal depressive symptoms during pregnancy, maternal alcohol intake during pregnancy, maternal smoking during pregnancy, child's birthweight, child's sex, breastfeeding duration, and smoking in the household during the first year of life.

from the present study regarding MUFAs, ALA, EPA, and DHA are incompatible with the hypothesis that high intake of these fatty acids is beneficial for mental health as has been suggested [2,27]. The lack of associations with maternal EPA or DHA intake might be ascribed to the fact that Japanese people consume large amounts of fish. A protective association between maternal EPA or DHA intake and childhood behavioral problems may exist in populations with lower fish consumption. Alternatively, unrecognized active agents in fish such as methylmercury might have counteracted the advantage of higher maternal intake of EPA and DHA during pregnancy in protecting against childhood behavioral problems.

The present study had methodological strengths. The data were obtained in a prebirth cohort study with a relatively large sample size and a relatively long duration of follow-up. The prospective design was likely to reduce the possibility of recall bias. Several potentially important confounders were controlled for.

There were limitations in the present study that deserve recognition. With regard to exposures, the validity of the DHQ regarding dietary fatty acids under study seems reasonable as described here. Nevertheless, the DHQ could only approximate consumption and was designed to assess dietary intake for 1 mo before completing the DHQ. Moreover, study participants answered the DHQ anywhere between weeks 5 and 39 of pregnancy. The consequence of nondifferential exposure misclassification would have introduced a bias toward an underestimation of the true exposure effect.

The children's parents answered the SDQ, which could be a source of bias. The possibility of nondifferential outcome misclassification might have led to an underestimation of values in our results. Moreover, it is uncertain whether the cutoff points of dichotomization of the outcomes under investigation based on a report conducted in Japan [24] were reasonable. The distribution of scale scores may differ from one country to another; thus, the present study was based on the Japanese report.

Of the 1757 participants at baseline, 556 mother–child pairs did not take part in the eighth survey. There were no material differences between the 556 nonparticipants and the 1201 participants in the eighth survey with regard to distribution of number of children, depressive symptoms during pregnancy, and alcohol intake during pregnancy. Compared with nonparticipants in the eighth survey, participants were more likely to be older, to have participated in the baseline survey earlier in their gestation, to live in Fukuoka Prefecture, and to report high maternal and paternal educational levels and high household income. Moreover, at baseline, we could not estimate the participation rate because we do not have exact figures for the number of pregnant women who were provided with a set of leaflets explaining the KOMCHS, an application form, and a self-addressed and stamped return envelope by the 423 collaborating obstetric hospitals. Of the 1757 participants at baseline, 978 participants lived in Fukuoka Prefecture. According to the government of Fukuoka Prefecture, the number of childbirths was 46 393 in 2007 and 46 695 in 2008; thus, the participation rate must have been low. Participants in the present study were probably not representative of Japanese women in the general population. For example, a population census conducted in 2000 in Fukuoka Prefecture found that the percentages of women ages 30 to 34 y with <13, 13 – 14, ≥15, and an unknown number of years of education were 52%, 31.5%, 11.8%, and 4.8%, respectively [28]. The corresponding figures for this study were 20.9%, 33.3%, 45.9%, and 0%, respectively. Thus, participants in the present study were more educated and probably more aware of health issues than are women in the general population.

Although adjustment was made for several confounding factors, residual confounding effects could not be ruled out. Data on paternal history of depressive symptoms and parental behavioral problems and substance use were not available in the present study.

The current prebirth cohort study in Japan suggests that maternal consumption of MUFAs, ALA, ω-6 PUFAs, and LA during pregnancy may increase the risk for emotional problems in children at the age of 5 y. Further epidemiologic investigation of the effects of maternal dietary fat intake in pregnancy on childhood behavioral problems is required.

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