Maternal fatty acid intake and fetal growth: evidence for an association in overweight women. The 'EDEN mother-child' cohort (study of pre- and early postnatal determinants of the child's development and health).

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Abstract

Background

Recent studies suggest a benefit of seafood and n-3 Fatty Acids (FA) intake on fetal growth and infant development.

Objectives

To study the association between FA intake and fetal growth in French pregnant women.

Design

Pregnant women included in the EDEN mother-child cohort study answered food frequency questionnaires on their usual diet 1) in the year prior to pregnancy and 2) during the last three months of pregnancy (n=1439). Conversion into nutrient intakes was performed using data on portion size and a French food composition table. Associations between maternal FA intakes and several neonatal anthropometric measurements were studied using linear regressions adjusted for center, mother's age, smoking habits, height, parity, gestational age and newborn's sex. Due to significant interaction, analyses were stratified according to maternal pre-pregnancy overweight status.

Results

Neither total lipid nor saturated, monounsaturated or polyunsaturated (PUFA) fat intake were significantly associated with newborn size. In overweight women only (n=366), a high pre-pregnancy n-3FA intake (% n-3FA/PUFA) was positively associated with newborn 's birthweight (p=0.01), head, arm and wrist circumferences and sum of skinfolds (p<0.04). A substitution of one percent of n-3FA per day before pregnancy by other PUFA was related to an average decrease in birthweight of 60 g (p=0.01). Relationships with n-3FA intake at the end of pregnancy were weaker and not significant.

Conclusions

A high pre-pregnancy ratio n-3FA/PUFA may sustain fetal growth in overweight women. Follow-up of the children may help determine whether this has beneficial consequences for the child's health and development.

MESH Keywords Adolescent ; Adult ; Birth Weight ; Body Height ; Diet ; Fatty Acids ; administration & dosage ; Fatty Acids, Omega-3 ; administration & dosage ; Fatty Acids, Unsaturated ; administration & dosage ; Female ; Fetal Development ; physiology ; France ; Humans ; Infant, Newborn ; Maternal Nutritional Physiological Phenomena ; Middle Aged ; Overweight ; metabolism ; Pregnancy ; Pregnancy Complications ; metabolism ; Prenatal Exposure Delayed Effects ; Prospective Studies ; Regression Analysis ; Seafood ; Social Class

Author Keywords Epidemiology ; Pregnancy ; n-3 Fatty Acids ; Birthweight ; Overweight

INTRODUCTION

An adequate amount of dietary fat is essential for health, particularly for pregnancy and lactation. Essential fatty acids (EFA) play a major role during pregnancy. They provide the precursors for prostaglandins and leucotrienes and are present mainly in highly specialized membranes (retina and synapses). The consumption of EFA is deemed important for normal growth and development in infants. The interest in EFA in relation to pregnancy stemmed from both epidemiological observations1 –7 and intervention studies8 , 9 . They showed

longer gestation, larger babies and in some cases, reduced numbers of pregnancy complications such as intrauterine growth retardation, pregnancy-induced hypertension, pre-delivery, in association with higher marine FA (long-chain polyunsaturated fatty acid (LC-PUFA) or n-3 FA), fish or fish oil intake.

Several mechanisms have been suggested for explaining these associations. The first one is a delayed spontaneous delivery, resulting from altered balance between the prostaglandins involved in the initiation of the labour10 , 11 . The second one is an increased fetal growth rate, resulting from improved placental blood flow due to lowered thromboxane/prostacyclin ratio12 and blood viscosity4 . Moreover, marine fat could reduce the risk of pre-term delivery13 , 14 and of intrauterine growth retardation15 .

However results in the literature are not consistent. Indeed, in one study, Olsen et al.16 could not detect any association between on the one hand the length of gestation, birthweight and length and on the other hand the intake of n-3 FA in the second trimester of pregnancy, whether intake was quantified by a validated questionnaire or biochemical measurements. More importantly, an other randomised control trial in pregnant women failed to detect effects of n-3 and n-6FA supplementation on gestational length, birthweight and length, head circumference or placental weight17 . Nevertheless, several studies in both animals and humans have shown that deficiency of dietary n-3 PUFA are associated with biochemical changes in the brain and with disturbances in vision and other neurological parameters18 . The most vulnerable period of neural development is during embryonic and fetal growth. EFAs, especially docosahexaenoic acid (DHA), are required for fetal brain, nervous system and retinal growth in late pregnancy. The maternal plasma concentration of individual FA, and hence the composition of the maternal diet, may have large effects on LC-PUFA delivery to the foetus.

In the “EDEN mother-child” cohort study, we previously reported that a difference in pre-pregnancy fish and shells consumption from less than five to more than nine times per month was associated with a difference in birthweight of 5.0% (from 3,248 g to 3,412 g; p= 0.0006), in overweight women only19 . The mother's fat store is relevant to the maternal hormonal responses and to the nourishment of the embryo and fetus during pregnancy, and provides the basis for subsequent fat storage and utilization during pregnancy20 , 21 . We hypothesised that the association between fish intake and fetal growth may be related to differences in the fatty acid contents of fat stored and was enhanced in overweight women because of a greater availability from fat stored.

Objectives

The aim of the present analysis was, therefore, to study the relationship between FA intake before and during pregnancy and fetal growth in the same French population and to evaluate whether it is a possible mediator of the observed association with fish intake in overweight women19 .

MATERIAL AND METHODS

Population and study design

Pregnant women seen for a prenatal visit at the departments of Obstetrics and Gynaecology of the University Hospitals of Nancy and Poitiers before 24 weeks of amenorrhea (WA) were invited to participate. Enrolment started in February 2003 in Poitiers and September 2003 in Nancy, it lasted 27 months in each center and ended up with the inclusion of 2,002 women. Exclusion criteria were twin pregnancies, known diabetes before pregnancy, not being able to speak and read French, planned moving away from the region. Among women who fulfilled these inclusion criteria, 55 % agreed to participate. The study was approved by the Ethic Committee of the Bicêtre Hospital. Written consents were obtained from the mother for herself at inclusion and for her newborn child after delivery.

At a visit performed between 24–28 WA by midwives research assistants, maternal height was measured with a wall Seca 206 stadiometer (Hamburg, Germany) to the nearest 0.2 cm and maternal weight was measured using electronic Terraillon SL 351 scales (Hanson Ltd, UK) to the nearest 0.1 kg. Skinfolds were measured using a commercial Harpenden caliper (Chasmor Ltd, London, UK) three times in the following order: tricipital (posterior aspect of the arm, at midpoint between the acromion and the olecranon), bicipital (anterior aspect of the arm, at midpoint between the acromion and the olecranon), subscapular (1 cm below the lower angle at the scapula) and supra-iliac (1 cm over the iliac crest, at the midaxillary line). After a five minute rest, three measures of systolic and diastolic blood pressures were performed at two-minute intervals with an Omron M4I device (Omron Healthcare Europe, Hoofddorp, The Netherlands). Women came to the examination in a fasting state and received a 50 g glucose oral load. Glucose concentrations were measured on fasting and one hour after the glucose challenge. Weight before pregnancy, educational level and smoking habits during pregnancy were obtained by interview. Prepregnancy body mass index (pBMI) was computed as reported weight (kg)/measured height squared (m^2). According to references of the International Obesity Task Force, overweight was defined as a BMI of 25 kg/m^2 or more and obesity as a BMI of 30 kg/m^2 and above. Average number of cigarettes consumed per day during pregnancy was computed.

A second visit was performed for newborns by the same research assistants on average 1.8 days after delivery. Mother's weight and skinfolds were obtained with the same protocol as above. Several anthropometric measurements were performed on the newborn. Circumferences were measured to the nearest 0.1 cm using a tape in duplicate: left arm circumference, measured at midpoint between the acromion and the olecranon; left wrist circumference, measured at the level of the styloid processes of the radius and ulna; head

circumference, measured at the largest occipitofrontal circumference. Skinfolds were measured in triplicate using a commercial Holtain caliper (Chasmor Ltd, London, UK)) in the following order: tricipital skinfold, measured at the same level as the midarm circumference; subscapular skinfold, measured at the lower angle of the scapula.

Gestational age at delivery (determined from the date of the last menstrual period and early ultrasound assessment), newborn admission to a reanimation or neonatal unit, birth weight and length, placental weight (in Poitiers only) were extracted from clinical records. In the two obstetric departments, electronic Seca scales (Hamburg, Germany: Seca 737 in Nancy and Seca 335 in Poitiers) were used to measure infant weight and wooden somatometer (Testut, Béthune, France) to measure infant length.

Dietary assessment

Mothers completed two food frequency questionnaires (FFQs) similar to the questionnaire developed for the French population in the Fleurbaix-Laventie Ville Santé Study (FLVS)22 . This food frequency questionnaire has been validated against a series of 24 hour recalls 23 . The questionnaire used in the EDEN study is very close to that of the FLVS study with the addition of some questions for a more specific assessment of the intake of foods rich in folates, n-3 FA and vitamin A and of fish and trophallergic foods. It inquires about the intake of 137 different foods or food groups with a 7-item scale ranking from never to more than once a day.

The first-trimester FFQ (completed at recruitment, on average 15 WG) concerned the usual diet during the year prior to pregnancy; the second FFQ (completed in the first few days following delivery) was related to food intake during the last three months of pregnancy. To compute energy and nutrient intakes, we multiplied, for each food, the intake frequency by the nutrient composition for a portion size. Portion size were determined using pictures for 12 food types (meats, French fries, pastas, vegetables, cakes, cheese…) on a three level scale or were standard portions for the French adult population24 . We then summed contributions across all foods to obtain average daily total intake of energy and intake of various macro-and micronutrients. Food composition was obtained from the SU.VI.MAX. nutrient composition database25 , which is based on a French nutrient composition database26 and US department of Agriculture publications and is continually incremented by other published sources and personal communications from laboratories and manufacturers27 –29 . Energy and nutrient intake was not estimated when more than 3 items of the FFQ were missing. Moreover, women with estimated total energy intake under 4,186.8 kJ/day (1,000 kcal/day) or over 20,934 kJ/day (5,000 kcal/day) were not included in the analyses. N-3 FA included linolenic acid, docohexaenoic acid (DHA), docosapentaenoic acid and eicosapentaenoic acid (EPA). The FFQ gave also information on type of oil used for cooking or seasoning.

Variable description and statistical analyses

Mean consumptions of total lipid and different FAs (saturated (SFA), mono-unsaturated (MUFA) and poly-unsaturated (PUFA), as well as n-3 and n-6 FA), in grams per day were compared between centers by Student's t test. Relationships with the socio-demographic characteristics of women were studied by multiple linear regressions adjusted for center and mother's age (in years).

We studied relationships between lipid consumption and fetal growth using the nutrient density method, i.e. we used the relative percentage of contribution of lipid intake to total energy intake, the relative percentage of contribution of SFA, MUFA or PUFA to total lipid intake or the relative percentage of contribution of n-3FA to total PUFA intake. Multiple linear regressions adjusted for different set of confounding variables (centre, mother's age and height, smoking habits, parity, gestational age, newborn's sex, BMI, and delay between birth and anthropometric measures) were performed to study these relationships.

As we had additional information on the type of fat used for cooking or seasoning, we used it to study whether this source of FA was associated with our outcome variables. We defined a four level variable from the answers to three questions asking for the type of oil used for cooking or seasoning. The first level corresponds to women who used with no preference any type of fat, the second level corresponds to women who used more often saturated fat (butter, hard margarine), the third level corresponds to women who used more often fat rich in n-6 FA (sunflower oil, corn oil) and the last level corresponds to women who used more often fat rich in n-9 FA (olive oil, groundnut oil). Only 3 women consumed preferentially fat rich in n-3 FA (colza oil), so they were classified in the 4 others groups according to the other type of fat they used. We tested whether the “type of fat used for cooking or seasoning” variable modified the relationships between FA intakes and fetal growth.

Separate analyses were performed for intake prior to and during the last three months of pregnancy. Interaction terms between FA consumption and center, gestational length, BMI (continuous then categorical variable), average cigarettes per day smoked during pregnancy and educational level were tested. Significant interaction was found for BMI ($p<0.05$), therefore analyses were stratified according to overweight status (BMI<25 vs. ≥25 kg/m^2). Several additional adjustments for educational level and maternal health variables (systolic or diastolic arterial pressure, fasting plasma glucose) were also made.

All analyses were performed with SAS version 9.1 (Cary, N.C., USA).

RESULTS

Subjects characteristics

Analyses included the 1,446 women who completed the two FFQs and for whom nutrients intake could be evaluated (67 were not included because of at least one missing FFQ and 374 because nutrient intake could not be estimated: 285 because more than three items of the FFQ were missing, 50 because total energy intake was under 4,186.8 kJ/day and 39 over 20,934 kJ/day. Also, newborns for whom delay between birth and anthropometric measures spaced from more than seven days were not included (n=9). The main characteristics of included women (and their newborn), compared to the 450 excluded women, are shown in Table 1 . Excluded women had less often reached a university level and were more often single than included women. The percentage of newborn transfer to reanimation or a neonatal unit was higher for excluded women. Mean birthweight was significantly lower for offspring of excluded women compared to the others (3,224 vs. 3,295 g). Mean maternal age was 29 years in both groups (range 17–45). For included women, mean pBMI was 23 kg/m^2 , 9.5 % of women had a pBMI < 18.5 kg/m^2 , 17.5 % were overweight and 7.7 % were obese. Overweight women had less often reached a university level and were less often single than non-overweight women (Table 2). Mean birth weight and length were significantly lower for offspring of non-overweight women compared to the others (3,269 vs. 3,362 g and 49.4 vs 50.0 cm respectively).

The average intake of energy, proteins, carbohydrates, lipids and different families of FA (SFA, MUFA and PUFA) prior to and in the last three months of pregnancy are given in Table 3 . Intakes were normally distributed except alcohol consumption. Significantly higher total energy intake and percent of fat in total energy intake (with and without taking into account alcohol in total energy intake) were observed at the end of pregnancy compared to before pregnancy (9,948 vs. 9,596 kJ/day, 39 vs. 38% and 39.2 vs. 38.7% respectively, $p<0.001$). Nevertheless, the part of PUFA in total lipid intake increased by 0.4% during pregnancy ($p<0.0001$); as well as the part of n-3 FA in total PUFA intake which decreased by 0.1% ($p=0.08$). Same trends were observed in non-overweight or overweight women, except for the part of n-3 FA in total PUFA which decreased in overweight women. There was no significant difference in estimated total fat and FA intake according to maternal overweight status.

Relationships between maternal fat and FA intakes prior to pregnancy and socio-demographics characteristics of women

Differences in consumptions were observed between centers for MUFA, PUFA and n-3FA, as well as the part of PUFA in total lipid intake with higher intakes in Nancy, but there was no difference for the part of n-3FA in total PUFA intake. Total fat and FA intake (SFA, MUFA, PUFA) did not change significantly with age but n-3FA consumption increased by 0.1 g (1%) per decade ($p=0.0002$). Women with university level ate less fat than the others (95.1 vs. 99.8 g/day; $p=0.03$), in particular MUFA (34.8 vs. 37.1 g/day; $p=0.004$) and SFA (42.6 vs. 44.5 g/day; $p=0.06$). There were no significant difference for PUFA (11.5 vs. 11.8 g/day; $p=0.32$). No significant difference in intake of total lipid and the different types of FA was observed according to income level, marital status or smoking status during pregnancy. The same relationships were observed for intake during the last three months of pregnancy.

Fatty acid intakes and fetal growth

There was no relationship between the part of lipid in total energy intake before pregnancy and newborn anthropometric measures in the whole sample of women (Table 4). The same results were found for the part of SFA, MUFA and PUFA in total lipid intake, as well as the part of n-3 or n-6 FA in total PUFA intake before and in the last three months of pregnancy. However, maternal overweight before pregnancy modified the relationship between FA intake and most outcome parameters (for instance $p<0.04$ for birthweight). Interaction were also significant for BMI as a categorical variable, so we decided to conduct the analyses separately for women < and ≥ 25 kg/m^2 , which separate overweight and obese women from the others.

In overweight women (n=366), no association was found between the part of lipid in total energy intake and fetal growth when adjusted for centre, mother's age and height, smoking habits, parity, gestational age, newborn's sex and delay between birth and anthropometric measures (Table 5). A substitution of pre-pregnancy lipid intake of 6.2% (1 SD) to other macronutrients was associated with a 25g lighter birthweight ($p=0.27$) and 7 mm smaller head circumference ($p=0.25$). In models also adjusted for total energy intake, results were unchanged (Data not shown). Same results were found for lipid intake during the last trimester of pregnancy. No significant association was observed with the different FA families even when models were adjusted for total lipid intake (see for PUFA/lipid in table 5). Results were unchanged when adjusted for educational level.

To study the relationships between n-3FA consumption and fetal growth, we first used a regression model adjusted for center, mother's age and height, smoking habits, parity, gestational age, newborn's sex and delay between birth and anthropometric measures (Table 6). A substitution of 0.3% (1 SD) of the part of n-3FA in total lipid intake to other macronutrients before pregnancy was related to an average increase in birthweight of 87g ($p=0.002$), length of 28mm ($p=0.02$), head circumference of 18mm ($p=0.02$), arm and wrist circumferences of 16 and 13mm respectively ($p<0.007$) and sum of skinfolds of 0.3mm ($p=0.01$) (Model 1). Further adjustment on total lipid intake shows that fetal growth was strongly associated with a greater contribution of n-3FA to total lipid intake (Model 2).

Similar results were found for the part of n-3FA in total PUFA intake. A substitution of 2.4% (1 SD) of this intake to other type of PUFA before pregnancy was related to an average increase in birthweight of 60g ($p=0.01$), head circumference of 13mm ($p=0.04$), arm and

wrist circumferences of 14 and 9mm respectively ($p<0.006$) and sum of skinfolds of 0.2 mm ($p=0.03$). Further adjustment on total PUFA intake shows that fetal growth was more strongly associated with a higher contribution of n-3FA to total PUFA intake (Model 4). Results were unchanged when adjusted for educational level (Model 5). Relationships with n-3FA intake during the last trimester of pregnancy were weaker and not significant (Table 6).

After further adjustment for systolic or diastolic arterial pressure, fasting glucose and triglycerides (at 6th month of pregnancy) these associations remained unchanged. Before pregnancy, a substitution of 2.4% of n-3FA to other PUFA was related to an increase in birthweight of 41g to 51g, depending on the adjustments ($0.03\leq p\leq 0.09$). For n-3FA intake during pregnancy, the range of variation was 26g to 36g and was not significant (data not shown).

The type of fat used for cooking or seasoning was not associated with newborn anthropometric measures (Data not shown). Moreover, previous associations found between total n-3FA intake estimated by the FFQ and the newborn anthropometric measures were unchanged when we took into account the type of fat used for cooking or seasoning (data not shown).

Correlation coefficients between number of fish and shells consumptions per week and PUFA intake (% PUFA/energy intake) was 0.12 for intake before pregnancy and 0.06 for intake in the last three months of pregnancy ($p<0.04$). Correlation was very strong for n-3FA/PUFA ($r=0.38$ and $r=0.35$ for intakes prior to and during pregnancy respectively, $p<0.0001$). Moreover, fish and shells consumption explained more than 32% of the variability in n-3FA intake. When average monthly fish and shells consumption before pregnancy was added to the model, the relationship with n-3FA in total PUFA intake was reduced to no significant level. Relationship with fish and shells consumption remained significantly associated with fetal growth.

There were too few obese women to be studied separately, but excluding obese women from the analyses did not change the associations found in women with a BMI $\geq$ 25 kg/m^2 .

No statistically significant associations were found with placental weight and length of gestation.

No statistically significant associations were found in non overweight women, as shown in Figure 1 for the association between birthweight and the part of n-3FA in total PUFA intake divided into tertiles.

DISCUSSION

In this French cohort, increased proportion of n-3FA in total PUFA intake before pregnancy, and to a lesser extent of intake during the last three months of pregnancy, was not associated with fetal growth in the total sample of women. However, in overweight women, it was associated with increased fetal growth, appreciated by birthweight, head, arm and wrist circumferences and skinfolds. Several epidemiologic studies conducted in Northern countries with usual high mean fish and shells intake as well as marine n-3FA by pregnant women found an association with an increased birthweight either due to an increase in length of gestation or an increase in fetal growth rate but without considering the maternal BMI status5 , 30 –32 .

Although pBMI may be affected by recall bias, we did not consider BMI estimated using measured weight during pregnancy as an accurate measure of maternal nutritional status. It is affected by plasma volume expansion related to pregnancy and fetal and placental weight. However for 1042 women who had a first visit before 15 WA, we found similar results when using measured BMI, i.e. significant interaction with maternal overweight and positive association with maternal n-3/PUFA intake and fetal growth.

In our study, the women excluded from the dietary analysis were different from included women for some characteristics such as educational level. It may be related to a greater ability of educated women to average intake frequency and to concentrate on a long series of questions. Nevertheless, adjustment for educational level had no effect on our results. Even if it is not possible to exclude possible recall bias in the report of consumptions before pregnancy, FFQ appears to be the only way to evaluate nutrient intakes before pregnancy in our study.

The percentage of overweight and obese could appear low but was similar to the general population of French women. In France, albeit the prevalence is notably lower than in the USA, the frequency of obesity has nearly doubled between 1997 and 2006. In women 20–39 years old, it increased from 5.2% to 11% during this period33 .

Furthermore, evaluation of nutrient intakes with a food frequency questionnaire has some limits. This may have altered our observed differences in food intake and therefore our ability to detect differences between groups. For example, the estimation of PUFA intake with the FFQ did not included the type of fat and oils used for cooking or seasoning. In order to take into account differences in type of fat used for cooking or seasoning, we studied whether using predominantly (or not) SFA or fat rich in n-6 or n-9FA, was associated with fetal growth and found no specific association.

Several previously published studies have demonstrated a heavier placenta and a longer gestation among women who consumed more n-3 FA34 but we did not observed these associations in our study. Because of the imprecision in the gestational age assessment, however, the effect of FA consumption on the prolongation of the intrauterine growth period may be difficult to detect. Another explanation would be that this effect requires higher n-3 FA intake than that observed in our study. In an intervention study by Olsen et al.4 , 13 , the level of n-3 FA intake was higher than in our study (6.1g/day for the intervention group vs. 2.7 g/day in the control group, whereas in our study the estimated mean intake was 1.2g/day).

There was no significant association between birth anthropometry and FA intakes in non-overweight women. Associations found in subgroups need to be considered with caution because of likely more false positive results. However there may be some rationale for such a selective effect in overweight women.

Overweight women have a higher fat mass. Differences in FA intake are associated with variations in the composition of FA stored in the adipose tissue. In fact, several studies showed that FA composition of the diet could influence FA composition of the adipose tissue. Arterburn et al. 35 showed that tissue contents in EPA and DHA increase in response to supplementation with theses FA, which means n-3FA in tissue increase with their presence in diet. Katan et al. 36 estimated that EPA levels in adipose tissue reflected intake over a period of months and even years for DHA. Correlations between % n-3 FA in total fat intake estimated by FFQ and % n-3 FA in total fat measured in adipose tissue ranked from 0.38 to 0.42 in another study37 . Therefore, overweight women may have an enhanced ability to release FA from adipose tissue to sustain fetal growth. We previously suggested that the specific relationship between fish and shells or n-3 FA intake and fetal growth in overweight women illustrates a special role of stored FA in the adipose tissue. This is reinforced by the fact that fish and shells as well as n-3FA consumption before pregnancy is more strongly associated with fetal growth than consumption during the last three months of pregnancy, as also observed by Olsen et al.16 . The storage of LC-PUFA and the balance of the n-3 and n-6 families in maternal adipose tissue are of great importance since they represent a pool of FA, which can be used via placenta's transfer to supply the developing foetus38 , 39 . There is evidence that the placenta itself may play a role in initiating the mobilisation of fatty acid from the maternal adipose tissue in response to fetal needs40 .

In our study, significant relationships were observed between n-3FA intake and fetal growth when adjusted for PUFA intake. This result shows the importance of the balance n-3/n-6 which seems more essential than the absolute intake of n-3FA. There is a competition between the two FA families for entry and release from cellular phospholipids, as well as for the enzymes that catalyse their conversion to produce, for instance, arachidonic acid-derived eicosanoïdes, such as the prostaglandins ($PGF_{2\alpha}$ and PGE_2)10 , 41 . The balance plays a major role in the availability of n-3 FA for the developing foetus. The concomitant intake of n-6 FA may explain part of the discrepancies in the literature about fish or n-3 FA consumption and fetal growth. All of the n-6 and n-3 FA accumulated by the foetus are derived by transfer across the placenta, which is provided with a specific system to ensure this function. The substrate of the placenta is provided by the maternal diet and the high rate of mobilization from maternal adipose stores and the mother adapts her metabolism to support the continuous draining of substrates by the fetus42 –44 .

Fish and shells intake removed the association between the contributions of n-3FA/PUFA on fetal growth in our study whereas the type of fat used for cooking or seasoning which is another major source of PUFA was not associated with fetal growth and did not removed this association. Fish and shells is indeed the main source of the variation of n-3FA/PUFA in our sample of French women19 . These results consolidate the hypothesis of an effect of the n-3FA from fish and shells, in particular EPA and DHA, which are mainly present in fish and shells.

In conclusion, our study finds a relationship between the ratio of maternal n-3FA/PUFA intake and fetal growth in the French population, which is specific to overweight women. We suggest that the enrichment in long chain n-3 FA in the maternal adipose tissue stored before conception is a possible mediator of this relationship. The fact that the ratio n-3/n-6 appears more strongly related to fetal growth than the absolute intake of n-3FA may explain some of the discrepancies in the literature concerning the association of fish and shells intake and fetal growth. However, because our results stem from a subgroup analysis, replication is needed before firm conclusion can be made.

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Footnotes:

Conflicts of interest and contribution of each author to the manuscript

There is no conflict of interest. Peggy Drouillet performed the study's analysis and wrote the paper. Anne Forhan was in charge of the coordination of the data file and analysis. Blandine De Lauzon-Guillain participated in the setting of the dietary data files. Marie-Aline Charles coordinates the EDEN study, supervised the analysis and participated in the design of the EDEN study, as well as Monique Kaminski, Pierre Ducimetière, Michel Schweitzer and Guillaume Magnin. Valérie Goua and Olivier Thiébaugeorges coordinate the EDEN study in Poitiers and Nancy. All co-authors reviewed the paper.

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Figure 1

Adjusted mean birthweight† and % of n-3 fatty acid intake in total polyunsaturated fatty acid intake (% n-3 FA/PUFA) before * Tertiles 1: [5.58 – 9.65[/2 : [9.65 – 11.38[/3 : [11.38 – 24.97] % † Means (SE) adjusted for centre, mother's age and height, smoking habits, Parity, gestational age, newborn's sex and delay between birth and anthropometric measures

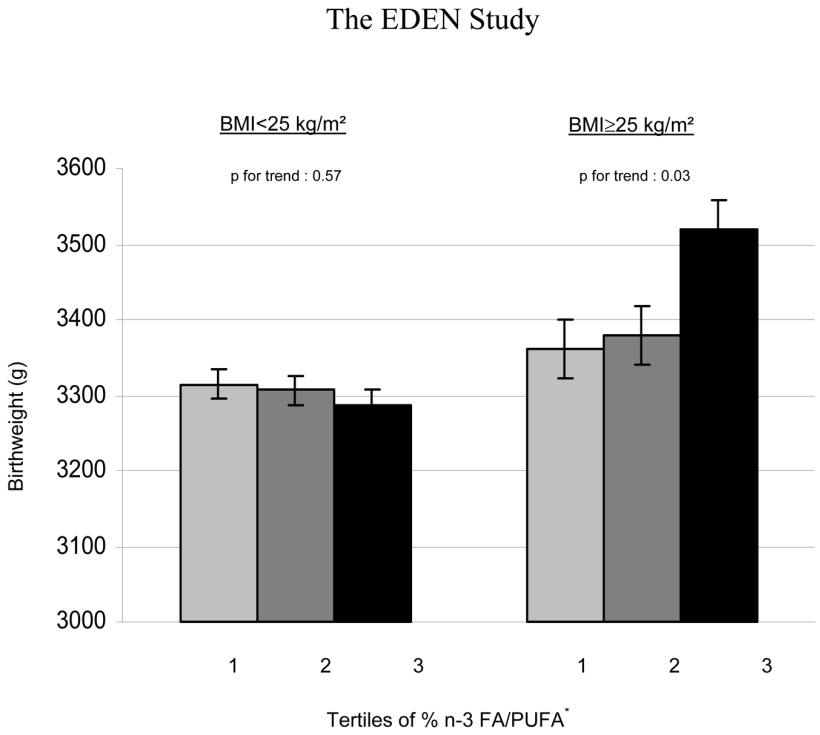

Table 1

Maternal and neonatal characteristics of the cohort (n=1896)

	Mean (standard deviation) or %	
	Included (n=1446)	**Non included (n=450)**
Age (years)	29.2 (4.8)	28.7 (5.2)
Height (m)*	1.64 (0.06)	1.63 (0.07)
Prepregnant BMI (kg/m^2)	23.1 (4.4)	23.5 (5.0)
University Level*	57%	40%
Parous	54%	57%
Unmarried*	7%	0%
Smoke during pregnancy	25%	28%
Gestational length (weeks)	39.3 (1.7)	39.1 (2.0)
Birth weight (g)*	3,295 (493)	3,224 (569)
Birth length (cm)	49.6 (2.3)	49.4 (2.4)
Ponderal Index (kg/m3)	27.0 (2.8)	27.0 (3.0)
Transfer$^{\Delta}$*	6%	11%

* p<0.05

$^{\Delta}$ % of transfer in reanimation or neonatal unit

Table 2

Maternal and neonatal characteristics of included women according to their BMI

	Mean (standard deviation) or %	
	BMI<25kg/m^2 (n=1055)	**BMI≥25kg/m^2 (n=364)**
Age (years)	29.1 (4.8)	29.5 (5.0)
Height (m)*	1.64 (0.06)	1.63 (0.07)
Prepregnant BMI (kg/m^2)*	21.1 (2.0)	29.1 (4.2)
University Level*	60%	47%
Parous*	52%	61%
Unmarried	8%	5%
Smoke during pregnancy	26%	23%
Gestational length (weeks)	39.3 (1.6)	39.3 (1.8)
Birth weight (g)*	3,269 (479)	3,362 (528)
Birth length (cm)*	49.4 (2.3)	50.0 (2.5)
Ponderal Index (kg/m3)*	27.1 (2.8)	26.8 (3.0)
Transfer$^{\Delta}$	5.4%	8.2%

* p<0.05

Δ % of transfer in reanimation or neonatal unit

Table 3

Maternal lipid and fatty acids intakes prior to and in the last three months of pregnancy

	Mean (Std)		
	Before pregnancy	**In the last three months of pregnancy**	**P**
All women (n=1446)			
Total Energy (kJ/day)	9,596 (3,144)	9,948 (3,186)	<0.0001
Protein (% energy intake)	17.2 (3.1)	17.2 (3.2)	0.40
Carbohydrate (% energy intake)	42.6 (7.3)	43.4 (7.3)	0.0003
Lipid (% energy intake)	37.8 (6.4)	39.1 (6.2)	<0.0001
Alcohol (% energy intake)	2.3 (4.1)	0.4 (1.3)	<0.0001
SFA (% lipid intake)	43.4 (18.7)	47.8 (19.8)	<0.0001
MUFA (% lipid intake)	35.8 (14.5)	37.6 (14.7)	<0.0001
PUFA (% lipid intake)	11.6 (4.8)	12.0 (5.0)	<0.0001
n-3 FA (% PUFA intake)	10.8 (2.4)	10.7 (2.6)	0.08
n-6 FA (% PUFA intake)	84.4 (3.1)	84.4 (3.5)	0.98
BMI<25kg/m^2 (n=1055)			
Total Energy (kJ/day)	9,584 (3,073)	10,044 (3,165)	0.73
Protein (% energy intake)	17.1 (3.0)	17.0 (3.1)	0.02
Carbohydrate (% energy intake)	42.9 (7.2)	43.5 (7.3)	<0.0001
Lipid (% energy intake)	37.7 (6.4)	39.1 (6.2)	<0.0001
Alcohol (% energy intake)	2.4 (4.1)	0.4 (1.3)	<0.0001
SFA (% lipid intake)	44.4 (4.2)	45.7 (4.4)	<0.0001
MUFA (% lipid intake)	36.8 (2.2)	36.2 (2.3)	<0.0001
PUFA (% lipid intake)	12.2 (2.4)	11.7 (2.5)	<0.0001
n-3 FA (% PUFA intake)	10.8 (2.4)	10.6 (2.6)	0.01
n-6 FA (% PUFA intake)	84.4 (3.2)	84.5 (3.5)	0.37
BMI≥25kg/m^2 (n=364)			
Total Energy (kJ/day)	9,609 (3,316)	9,651 (3,266)	0.81
Protein (% energy intake)	17.8 (3.2)	17.6 (3.5)	0.21
Carbohydrate (% energy intake)	41.7 (7.5)	43.0 (7.4)	0.002
Lipid (% energy intake)	38.2 (6.2)	39.0 (6.2)	0.01
Alcohol (% energy intake)	2.3 (4.0)	0.4 (1.1)	<0.0001
SFA (% lipid intake)	44.4 (4.3)	45.8 (4.3)	<0.0001
MUFA (% lipid intake)	37.0 (2.3)	36.2 (2.4)	<0.0001
PUFA (% lipid intake)	12.0 (2.4)	11.5 (2.4)	0.0002
n-3 FA (% PUFA intake)	10.7 (2.4)	10.9 (2.7)	0.28
n-6 FA (% PUFA intake)	84.4 (3.1)	84.1 (3.6)	0.08

Table 4

Associations of lipid and FA intake before pregnancy with newborn anthropometric measures in the EDEN mother-child cohort, in separate regression models*

	Lipid (% energy intake)		PUFA (% lipid intake)		n-3FA (% PUFA intake)	
	β^Δ	p	β^Δ	p	β^Δ	p
Birthweight (g)	−5.20	0.62	−0.23	0.98	6.40	0.54
Birth length (cm)	0.03	0.58	0.02	0.75	−0.00	0.70
Head circumference (cm)	−0.02	0.53	−0.02	0.41	0.02	0.41
Arm circumference (cm)	0.02	0.41	−0.01	0.79	0.01	0.56
Wrist circumference (cm)	0.00	0.93	0.01	0.47	0.01	0.40
Sum of skinfolds (mm)	−0.05	0.25	−0.00	0.96	0.00	0.97

Δ Regression coefficient: consumption considered as a continuous variable. β corresponds to the increase of the variable for an increase of 1 SD of the intake consumed per day (1 SD = 6.4%, 2.4% and 2.4% for lipid, PUFA and n-3FA respectively)

* Models adjusted for centre, mother's age and height, smoking habits, parity, gestational age, newborn's sex, delay between birth and anthropometric measures, and BMI

Table 5

Associations of % of energy from lipid intakes and % of PUFA in total lipid intake with newborn anthropometric measures in overweight women in the EDEN mother-child cohort, in separate regression models*

	Lipid (% energy intake)				PUFA (% lipid intake)			
	Before pregnancy		Last three months of pregnancy		Before pregnancy		Last three months of pregnancy	
	β^Δ	p	β^Δ	p	β^Δ	p	β^Δ	p
Birthweight (g)	−25.22	0.27	−30.74	0.19	4.48	0.85	−6.00	0.79
Birth length (cm)	−0.08	0.42	−0.04	0.74	0.11	0.30	−0.02	0.87
Head circumference (cm)	−0.07	0.25	−0.03	0.71	−0.01	0.87	−0.05	0.42
Arm circumference (cm)	−0.02	0.64	−0.06	0.21	−0.02	0.71	−0.01	0.88
Wrist circumference (cm)	−0.02	0.42	−0.04	0.23	0.01	0.65	0.08	0.79
Sum of skinfolds (mm)	−0.06	0.53	−0.03	0.77	0.01	0.93	−0.00	0.98

Δ Regression coefficient: consumption considered as a continuous variable. β corresponds to the increase of the variable for an increase of 1 SD of the intake consumed per day (1 SD = 6.2%, 6.2% for Lipid and 2.4%, 2.4% for PUFA, before and during pregnancy respectively)

* Models adjusted for centre, mother's age and height, smoking habits, parity, gestational age, newborn's sex and delay between birth and anthropometric measures

Table 6

Associations of % n-3 FA in total lipid or PUFA intakes, before and during the last three months of pregnancy, with newborn anthropometric measures in overweight women in the EDEN mother-child cohort, in separate regression models*

	Model 1*		Model 2*		Model 3*		Model 4*		Model 5*	
	β^Δ	p	β^Δ	p	β^Δ	p	β^Δ	p	β^Δ	p
BEFORE PREGNANCY										
Birthweight (g)	86.82	0.002	97.44	0.0008	60.44	0.01	76.24	0.003	59.01	0.01
Birth length (cm)	0.28	0.02	0.29	0.02	0.11	0.34	0.16	0.23	0.01	0.41
Head circumference (cm)	0.18	0.02	0.20	0.01	0.13	0.04	0.17	0.02	0.14	0.03
Arm circumference (cm)	0.16	0.007	0.18	0.004	0.14	0.006	0.17	0.003	0.14	0.008
Wrist circumference (cm)	0.13	0.0002	0.15	<0.0001	0.09	0.003	0.12	0.005	0.09	0.005
Sum of skinfolds (mm)	0.30	0.01	0.35	0.003	0.23	0.03	0.30	0.007	0.22	0.03
LAST THREE MONTHS OF PREGNANCY										
Birthweight (g)	6.28	0.80	7.42	0.78	36.17	0.11	38.87	0.11	38.36	0.10
Birth length (cm)	0.21	0.06	0.20	0.08	0.15	0.14	0.19	0.08	0.15	0.15
Head circumference (cm)	−0.02	0.74	−0.01	0.84	0.13	0.03	0.13	0.04	0.14	0.02
Arm circumference (cm)	−0.00	0.97	0.00	0.95	0.05	0.32	0.05	0.36	0.05	0.32
Wrist circumference (cm)	0.01	0.73	0.01	0.78	0.04	0.16	0.05	0.12	0.04	0.18
Sum of skinfolds (mm)	0.09	0.41	0.06	0.60	0.10	0.28	0.15	0.15	0.11	0.26

Δ Regression coefficient: n-3 FA (% total lipid or PUFA consumed daily) considered as a continuous variable. β corresponds to the increase of the variable for an increase of 1 SD of the %. (1SD = 0.3 and 0.6 for n-3FA (% lipid intake); 2.4 and 2.7 for n-3FA (% PUFA intake), before and during pregnancy respectively)

* Model 1: n-3FA (% lipid intake), adjusted for centre, mother's age and height, smoking habits, Parity, gestational age, newborn's sex and delay between birth and anthropometric measures
Model 2 = Model 1 + adjusted for total lipid intake
Model 3: n-3FA (% PUFA intake), adjusted for centre, mother's age and height, smoking habits, Parity, gestational age, newborn's sex and delay between birth and anthropometric measures
Model 4 = Model 3 + adjusted for total PUFA intake
Model 5 = Model 4 + adjusted for educational level