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Polyunsaturated fatty acid levels at birth and child-to-adult growth: Results from the MEFAB cohort


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ABSTRACT

Background: Prenatal exposure to polyunsaturated fatty acids (PUFAs) may influence childhood growth. However, available evidence mostly derived from short-term studies is inconsistent.

Objective: To assess whether fetal PUFA exposure is associated with height and body mass index (BMI), a common measure of adiposity, from 6 months to 23 years of age.

Methods: In the MEFAB cohort, we assessed cord blood phospholipid n-3 and n-6 PUFA levels, reflecting fetal exposure in late pregnancy. For 250 (45.2% females) participants, we collected a total of 1770 (n = 802 for females) repeated growth measurements from infancy to young adulthood. We examined sex-specific associations of PUFAs with height and BMI at different developmental ages (infant: 6 months; toddler: 2 years; preschooler: 4 years; school-aged child: 7 years; adolescent: 12 years; and young adult: 23 years) using fractional polynomial mixed models adjusted for important covariates.

Results: Higher n-3 PUFA levels were associated with higher infant length in males (β = 0.44 cm [95% CI: 0.07, 0.82] per SD increase), whereas, for females, higher n-6 PUFA concentrations were associated with lower length in infancy (β = −0.69 cm [95% CI: −1.08, −0.30] per SD increase). A higher ratio of n-3 to n-6 PUFAs was associated with higher infant length in both sexes (β = 0.40 cm [95% CI: 0.01, 0.78] and 0.42 cm [95% CI: 0.05, 0.79] per unit increase for males and females, respectively). These associations were not detectable later in childhood and young adulthood. No associations with BMI were found at any time point examined.

Conclusions: Our findings suggest a small sex-specific influence of PUFA status at birth on length in infancy, but this does not persist in later life up to young adulthood. PUFA status at birth does not seem to affect BMI from infancy till young adulthood.

1. Introduction

Height and body mass index (BMI), a measure of body weight relative to height, are recognized as important markers of health. Accumulating evidence suggests that lower stature and higher BMI in both children and adults are associated with higher risk of later cardiovascular disease [1–3]. Therefore, gaining knowledge about modifiable factors that may influence growth is highly relevant for the prevention of future disease risk.

Fetal life is a critical period of susceptibility during which a nutritional stressor can permanently alter body physiology and metabolism, the consequences of which are often observed much later in life [4].
this context, there has been an increasing interest in the potential programming effect of prenatal exposure to polyunsaturated fatty acids (PUFAs).

Animal and in vitro studies have suggested that n-3 PUFAs can inhibit inflammation, promote osteoblastogenesis, and decrease adipose tissue deposition, while those of the n-6 family seem to exhibit opposite effects [5–7]. Human studies assessing childhood height in relation to prenatal PUFA exposure have mostly focused on n-3 long-chain PUFA supplementation, and have not shown a clear and consistent effect [8–11]. Cohort studies have also provided little evidence to confirm an association of prenatal PUFA status with later BMI [12–14]. Likewise, evidence from trials assessing childhood BMI does not support or refute an effect of maternal fish oil supplementation [15].

Limitations of prior studies not allowing conclusions to be drawn include the relatively short duration of follow-up and inconsistencies in timing and definition of exposure. Moreover, the effects of prenatal PUFA exposures have been traditionally examined at one time point in childhood, which may only partially capture their impact on growth. It is well established that individuals experience different rates of growth over time. Examining the long-term effects of early-life exposures at different ages, preferably on the child to adult transition, is important for more accurate identification of modifiable risk factors and for understanding when these factors exhibit their maximum influence. Hence, we used long-term longitudinal data from the Maastricht Essential Fatty Acid Birth (MEFAB) cohort to investigate the associations of cord blood phospholipid PUFA levels, reflecting fetal exposure in late pregnancy, with height and BMI at different developmental ages: infant, 6 months; toddler, 2 years; pre-schooler, 4 years; school-aged child, 7 years; adolescent, 12 years; and young adult, 23 years.

2. Materials and methods

2.1. Study population

The MEFAB (Maastricht Essential Fatty Acid Birth, www.mefab.org) study prospectively examines a population-based sample of pregnant women and their children in the province of Limburg, the Netherlands. Pregnant women attending three maternity clinics for their first antenatal visit between 1989 and 1995 were invited to participate in the study. To be included in the study, women had to have a gestational age of less than 16 weeks, diastolic blood pressure of less than 90 mmHg, and no cardiovascular, neurological, renal, or metabolic disorders. A total of 1203 singletons were followed up until delivery. Face-to-face structured questionnaires along with self-administered questionnaires following standard methodology [20]. At the 23-year follow-up evaluation (wave III), we collected self-reported information on weight and height using questionnaires. We excluded five implausible height/weight measurements above or below the age- and sex-specific mean ± 4 standard deviations. We also excluded children with only two growth measurements available so as to achieve sufficient stability of growth trajectory models and increase precision in our effect estimates [21]. After these exclusions, an average of 7 repeated measurements (inter-quartile range: 1 for males, and 2 for females) were available for both BMI, calculated as weight in kilograms divided by height in meters squared, and height per offspring (either male or female).

We analyzed untransformed growth measures, rather than age-standardized metrics (i.e. z-scores), because they yield estimates that are more precise and sensitive to factors altering change when modelling growth trajectories; z-scores represent cross-sectional deviations from norms, thereby, removing some of the longitudinal change in growth patterns within individuals [22,23].

2.2. Polyunsaturated fatty acid analysis

Blood samples from the umbilical vein of infants were collected immediately after delivery. Methods of fatty acid analysis and the phospholipid PUFAs identified in MEFAB have been described in detail elsewhere [17]. For the present analysis, our primary exposures of interest were the dietary essential n-3 PUFA precursor α-linolenic acid (ALA, C18:3 n-3), the sum of its major biologically active metabolic products eicosapentaenoic acid (EPA, C20:5 n-3) and docosahexaenoic acid (DHA, C22:6 n-3), and the sum of total n-3 fatty acids assayed; the dietary essential n-6 PUFA precursor, linoleic acid (LA, C18:2 n-6), its major metabolic product arachidonic acid (AA, C20:4 n-6), and the sum of total n-6 fatty acids assayed; and the total n-3: n-6 PUFA ratio.

Secondary exposures of interest were intermediate metabolic products in the biosynthetic pathway of PUFAs that have been previously associated with pregnancy outcomes and child growth including: the n-3 docosapentaenoic acid (DPA, C22:5 n-3), and the n-6 γ-linolenic acid (GLA, C18:3 n-6), dihomo-γ-linolenic acid (DGLA, C20:3 n-6), and osbond acid (C22:5 n-6) [18,19]. Individual fatty acid measurements were expressed as weight percentage of total fatty acids measured (wt%). To enable comparison with other studies, we constructed standardized values (z-scores) for PUFA concentrations.

2.3. Child growth measures

Data on length/height and weight were collected at 9 different time points from birth till young adulthood. Information on birth weight and length was obtained via medical records. At follow-up wave I, we collected data on length/height and weight measurements from 6 months up to 5 years with one-year interval from paediatrician records, which form part of standard child care in the Netherlands, and measured children’s weight and height at age 7 using standard procedures [19]. At age 12 (wave II), we measured adolescent weight and height following standard methodology [20]. At the 23-year follow-up evaluation (wave III), we collected self-reported information on weight and height using questionnaires. We excluded five implausible height/weight measurements above or below the age- and sex-specific mean ± 4 standard deviations. We also excluded children with only two growth measurements available so as to achieve sufficient stability of growth trajectory models and increase precision in our effect estimates [21]. After these exclusions, an average of 7 repeated measurements (inter-quartile range: 1 for males, and 2 for females) were available for both BMI, calculated as weight in kilograms divided by height in meters squared, and height per offspring (either male or female).

We analyzed untransformed growth measures, rather than age-standardized metrics (i.e. z-scores), because they yield estimates that are more precise and sensitive to factors altering change when modelling growth trajectories; z-scores represent cross-sectional deviations from norms, thereby, removing some of the longitudinal change in growth patterns within individuals [22,23].

2.4. Statistical analysis

We modelled height and BMI growth trajectories from birth through young adulthood using multi-level models (two levels: measurement occasion and individual) with fractional polynomials of age to identify the best-fitting curves. A description of the methodology followed is presented in the online Supplementary material. Given that males and females follow a different growth pattern and exhibit differences in fatty acid metabolism [24], all analyses were stratified by sex.

We examined associations between cord blood PUFA concentrations and growth measures with mixed linear regression models. We assessed possible non-linear relations by fitting and comparing linear and lowess curves. No severe departures from linearity were detected. Following a directed acyclic graph approach (Fig. S1), we selected...
Finally, we assessed associations with BMI measures available in young paired fetal growth (birth weight for gestational age < 10th percentile). We performed analyses with Stata version 13.0 (StataCorp). Statistical significance for all estimates was set at the 5% level. We also repeated analyses after excluding children with impaired fetal growth (birth weight for gestational age < 10th percentile). Finally, we assessed associations with BMI measures available in young adulthood following further adjustment for fish oil supplementation (yes, no), education level (primary, secondary, or tertiary) and alcohol consumption (glasses per week) measured at the age of outcome assessment. As a sensitivity analysis, we re-run our models for primary PUFAs exposures with further adjustment for gestational age (measured in weeks). We also repeated analyses after excluding children with impaired fetal growth (birth weight for gestational age < 10th percentile).

### 3. Results

#### 3.1. Participant’s characteristics

Basic characteristics of the study population are presented in Table 1. Participating mothers had a mean age (SD) of 30.2 (4.0) years at study entry, and more than half of the mothers did not breastfeed their infants. About 40% of parents had medium educational level. Mean (SD) cord blood levels of n-3 and n-6 PUFAs for boys were 6.79 (1.58) and 32.26 (1.67) wt%, respectively; the corresponding values for girls were 6.92 (1.65) and 32.03 (1.61) wt% (Table 2).

At the age of 6 months, mean (SD) length was 67.6 (2.6) cm for boys and 65.5 (3.0) cm for girls, while for BMI, boys had a mean (SD) of 17.0 (1.3) kg/m², and girls had a mean (SD) of 16.6 (1.3) kg/m² (Table S2). At 23 years, mean (SD) height for men and women was 182.2 (8.2) and 167.0 (8.0) cm, respectively; the corresponding values for BMI were 23.2 (3.8) and 23.3 (3.8) kg/m² (Table S2). Fig. 1 demonstrates the height and BMI trajectories from infancy up to young adulthood in our study sample. Repeated height and BMI measures throughout the study period were strongly correlated within individuals (Tables S3 & S4).

#### 3.2. Cord blood PUFAs and height

Among male participants, we found that both higher total n-3 PUFA levels and a higher n-3: n-6 ratio were associated with higher length at 6 months of age; $\beta = 0.44$ cm [95% CI: 0.07, 0.82] per SD increase in n-3 PUFAs and 0.40 cm [95% CI: 0.01, 0.78] per unit increase in the n-3: n-6 ratio (Table 3). When we examined individual PUFAs in males, we also found an association of n-3 EPA + DHA levels with higher infant length ($\beta = 0.44$ cm [95% CI: 0.06, 0.82] per SD increase) (Table 3). Among female participants, we observed that higher total n-6 PUFA concentrations were associated with lower length in infancy ($\beta = −0.69$ cm [95% CI: −1.08, −0.30] per SD increase), whereas a higher n-3: n-6 ratio was associated with higher infant length ($\beta = 0.42$ cm [95% CI: 0.05, 0.79] per unit increase). We also saw an inverse association of the n-6 LA with female length in infancy ($\beta = −0.73$ cm [95% CI: −1.23, −0.22] per SD increase) (Table 3). No other associations between cord blood PUFAs and height in mid-childhood and young adulthood were observed for both males and females.

#### 3.3. Cord blood PUFAs and BMI

Among males, we did not find any association of cord blood PUFAs with BMI from 6 months to 23 years of age (Table 4). In females, we also found no evidence for an association of PUA status with BMI at any time point examined (Table 4).
other relations were found for PUFAs from early childhood onwards in either sex (Table S5). No associations between secondary PUFAs of interest and BMI were found at any time point (Table S6).

When we included gestational age in the models of height, we saw that effect estimates for n-3 PUFAs and infant length were largely attenuated (Table S7). Associations between PUFAs and BMI measures remained of similar magnitude following additional adjustment for gestational age (Table S8). Removal of children with impaired fetal growth did not alter the results (data not shown). Additionally, effect estimates for BMI in young adulthood did not substantially change when we further adjusted for fish oil supplementation, educational level, and alcohol consumption assessed at the age of outcome assessment (Table S9).

4. Discussion and conclusions

In this analysis of the MEFAB cohort, we examined associations of cord blood PUFA levels with height and BMI measures from childhood to young adulthood. To our knowledge, this is the first study to examine child-to-adult growth in relation to early PUFA status. We measured cord blood phospholipid PUFA levels that constitute good surrogates of fetal exposure in late pregnancy, as they reflect maternal dietary intake of the last 2–4 weeks [29], and the efficiency of placental transfer [30]. We found that higher n-3 PUFA concentrations in cord blood were associated with increased infant length among males, while, for females, an association of the opposite direction was observed for n-6 PUFAs. A higher ratio of n-3 to n-6 PUFAs was associated with higher infant length in both sexes. The magnitude of these associations was small, corresponding to 0.4–0.7-cm changes per SD increase in PUFA concentrations. The associations with infant length seemed to be transient, as they not did not persist later in childhood and in young adulthood. No associations of cord blood PUFAs with BMI from infancy to young adulthood were observed in either sex.

4.1. Interpretation of main findings

We found sex-specific associations between PUFA levels at birth and infant height. Indeed, a systematic review has highlighted the

![Graph](image-url)

Fig. 1. Height (a) and BMI (b) trajectories from 6 months to 23 years of age in males (n=137) and females (n=113) from the MEFAB cohort.

3.4. Secondary and sensitivity analyses

Among males, higher n-3 DPA levels in cord blood were associated with a higher length at 6 months, while higher n-6 GLA concentrations were associated with lower length/height at 6 months and 2 years of age (Table S5). We also found an association of higher n-6 osbond acid levels with higher height among male adolescents at 12 years, but no

Table 3

<table>
<thead>
<tr>
<th>Height (cm)</th>
<th>6 months</th>
<th>2 years</th>
<th>4 years</th>
<th>7 years</th>
<th>12 years</th>
<th>23 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALA</td>
<td>−0.05 (−0.27, 0.16)</td>
<td>−0.13 (−0.39, 0.13)</td>
<td>−0.21 (−0.57, 0.14)</td>
<td>−0.34 (−0.67, 0.19)</td>
<td>−0.58 (−1.39, 0.22)</td>
<td>−1.43 (−3.28, 0.41)</td>
</tr>
<tr>
<td>EPA + DHA</td>
<td>0.44 (0.07, 0.82)</td>
<td>0.22 (−0.23, 0.66)</td>
<td>0.24 (−0.37, 0.85)</td>
<td>0.43 (−0.46, 1.32)</td>
<td>0.79 (−0.51, 2.09)</td>
<td>0.43 (−1.47, 2.32)</td>
</tr>
<tr>
<td>Total n−3 PUFAs</td>
<td>0.44 (0.07, 0.82)</td>
<td>0.19 (−0.26, 0.65)</td>
<td>0.19 (−0.42, 0.80)</td>
<td>0.36 (−0.53, 1.24)</td>
<td>0.69 (−0.61, 1.99)</td>
<td>0.37 (−1.51, 2.24)</td>
</tr>
<tr>
<td>LA</td>
<td>−0.32 (−0.73, 0.08)</td>
<td>−0.16 (−0.64, 0.33)</td>
<td>−0.33 (−0.99, 0.34)</td>
<td>−0.76 (−1.75, 0.22)</td>
<td>−1.39 (−2.85, 0.07)</td>
<td>−0.06 (−2.22, 2.10)</td>
</tr>
<tr>
<td>AA</td>
<td>0.21 (−0.20, 0.62)</td>
<td>0.39 (−0.10, 0.87)</td>
<td>0.48 (−0.17, 1.14)</td>
<td>0.51 (−0.44, 1.47)</td>
<td>0.37 (−1.04, 1.77)</td>
<td>0.09 (−2.85, 0.96)</td>
</tr>
<tr>
<td>Total n−6 PUFAs</td>
<td>0.05 (−0.32, 0.42)</td>
<td>0.26 (−0.19, 0.71)</td>
<td>0.17 (−0.45, 0.78)</td>
<td>−0.19 (−1.09, 0.71)</td>
<td>−0.84 (−2.16, 0.49)</td>
<td>−0.87 (−2.86, 1.11)</td>
</tr>
<tr>
<td>Total n:3−n:6 ratio</td>
<td>0.40 (0.01, 0.78)</td>
<td>0.12 (−0.33, 0.58)</td>
<td>0.13 (−0.48, 0.74)</td>
<td>0.35 (−0.55, 1.24)</td>
<td>0.77 (−0.54, 2.07)</td>
<td>0.46 (−1.46, 2.39)</td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALA</td>
<td>−0.16 (−0.68, 0.36)</td>
<td>−0.49 (−1.19, 0.22)</td>
<td>−0.64 (−1.64, 0.37)</td>
<td>−0.66 (−2.14, 0.83)</td>
<td>−0.37 (−2.53, 1.79)</td>
<td>1.54 (−0.79, 3.88)</td>
</tr>
<tr>
<td>EPA + DHA</td>
<td>0.35 (−0.03, 0.72)</td>
<td>0.10 (−0.41, 0.61)</td>
<td>0.15 (−0.87, 0.58)</td>
<td>0.44 (−1.51, 0.63)</td>
<td>0.70 (−2.25, 0.85)</td>
<td>0.81 (−1.64, 2.05)</td>
</tr>
<tr>
<td>Total n−3 PUFAs</td>
<td>0.33 (−0.04, 0.70)</td>
<td>0.08 (−0.42, 0.59)</td>
<td>0.16 (−0.88, 0.56)</td>
<td>0.42 (−1.48, 0.64)</td>
<td>0.62 (−2.16, 0.91)</td>
<td>0.43 (−1.41, 2.26)</td>
</tr>
<tr>
<td>LA</td>
<td>−0.73 (−1.23, −0.22)</td>
<td>−0.64 (−1.34, 0.07)</td>
<td>−0.44 (−1.45, 0.56)</td>
<td>−0.14 (−1.64, 1.35)</td>
<td>0.22 (−1.95, 2.38)</td>
<td>0.43 (−2.93, 2.07)</td>
</tr>
<tr>
<td>AA</td>
<td>−0.24 (−0.67, 0.19)</td>
<td>−0.27 (−0.85, 0.30)</td>
<td>−0.41 (−1.22, 0.41)</td>
<td>−0.66 (−1.86, 0.55)</td>
<td>−1.01 (−2.76, 0.75)</td>
<td>−0.79 (−2.90, 1.13)</td>
</tr>
<tr>
<td>Total n−6 PUFAs</td>
<td>−0.69 (−1.08, −0.30)</td>
<td>−0.53 (−1.08, 0.01)</td>
<td>−0.41 (−1.20, 0.38)</td>
<td>−0.30 (−1.48, 0.88)</td>
<td>−0.27 (−1.99, 1.46)</td>
<td>−1.02 (−2.92, 0.88)</td>
</tr>
<tr>
<td>Total n:3−n:6 ratio</td>
<td>0.42 (0.05, 0.79)</td>
<td>0.18 (−0.33, 0.68)</td>
<td>−0.06 (−0.78, 0.67)</td>
<td>−0.31 (−1.37, 0.67)</td>
<td>−0.49 (−2.03, 1.06)</td>
<td>0.62 (−1.23, 2.48)</td>
</tr>
</tbody>
</table>

β coefficients and their 95% CIs were calculated using mixed effects linear regression models adjusted for child age terms (age², age³), maternal age at birth, maternal BMI at study entry, gestational weight gain, maternal alcohol intake in pregnancy, maternal smoking in pregnancy, parity, parental education, breastfeeding status, and cross-products of each PUFA exposure with the child age terms. Effect estimates correspond to a standard deviation score (SDS) increase in PUFAs and to a unit increase in the total n-3:n-6 ratio. AA, arachidonic acid (C20:4 n-6); ALA, α-linolenic acid (C18:3 n-3); DHA, docosahexaenoic acid (C22:6 n-3); EPA, eicosapentaenoic acid (C20:5 n-3); LA, linoleic acid (C18:2 n-6); PUFA, polyunsaturated fatty acid; total n-3 (n=6) PUFAs, the sum of n-3 (n=6) PUFAs present in the chromatogram.

* p < 0.05.

** p < 0.01.
The placenta tissue carrying the fetal genome and sex appears as a promising candidate to be involved in mediating sex-specific effects [32]. A human study has recently demonstrated that placentas show sexually dimorphic gene expression and responsiveness to maternal n-3 long-chain PUFAs intervention in mid- and late pregnancy [33]. Genes located on sex chromosomes can contribute to differential gene expression between male and female somatic tissues, and sex steroid hormones are thought to provide the initiation of this sex-specific responsiveness [33].

A number of studies have previously assessed the effect of prenatal PUFAs exposure on later height. An analysis of the Southampton Women’s Survey reported a trend towards a positive relationship between maternal n-3 PUFA concentration in pregnancy and childhood height at 4 and 6 years [34]. In a Mexican trial, offspring of primiparous women supplemented with DHA in pregnancy were taller at 18 months compared to those in the placebo group [8]. In contrast, three small trials found no effect of n-3 long-chain PUFAs supplementation in pregnancy on child height up to 2.5 years of age [9-11]. Heterogeneity in previous findings may at least partly be explained by differences in the timing and definition of exposure, sample sizes and statistical analysis. Moreover, none of the previous studies stratified by sex. In our study, we found that higher levels of total n-3 PUFAs, EPA+DHA and DPA, and lower levels of n-6 GLA at birth were associated with a small increase in infant height in males. We also observed an association of n-6 eicosanoids with higher height in male adolescents, but no associations were found for other PUFAs from early childhood onwards. Hence, we treat the partitioning process, and increasing the activity of eicosanoids with myometrial relaxant properties [35,36]. n-6 PUFAs are generally considered as pro-inflammatory, and in high amounts, they might adversely influence the intrauterine environment and lead to suboptimal fetal development [37], which in turn may translate to altered height growth [38]. Another plausible explanation for the observed associations of PUFAs with height might relate to their effects on bone per se; n-6 PUFAs have been suggested to decrease osteoblastogenesis and inhibit bone formation, while n-3 PUFAs seem to have an opposite effect [7,39]. Such effects may lead to altered bone growth, and thus, impact height. In line with our findings for strongest associations of fetal PUFAs exposure with length in infancy, twin studies suggest that infancy is the most sensitive period regarding environmental influences on height variation [40].

BMI is a widely-used surrogate measure of adiposity status [41]. In our study, we did not find any association of cord blood PUFAs levels with BMI from infancy through young adulthood. These findings are in line with those of trials showing no effect of maternal n-3 long-chain PUFAs supplementation on offspring BMI up to 21 years of age [15,42]. Previous results from cohort studies with shorter follow-up periods in Europe and the US have also provided little evidence to substantiate that a modification of prenatal PUFAs status can affect later adiposity [12-14].

**4.2. Methodological considerations**

Strengths of our study include the population-based prospective design, detailed information on PUFAs levels, and repeated growth measures over a large time period that provide more definitive evaluation of within-person change across time and increase statistical power [43].

A limitation of this study is attrition raising the likelihood of selection bias. Our study population had somewhat lower maternal BMI values at study entry compared to those lost to follow-up. Assuming that children of mothers with a higher BMI are more likely to be overweight, our estimates may be underestimated. Nevertheless, our study sample and those excluded did not substantially differ in many baseline variables including parental educational level and socioeconomic status, as well as exposure levels. Although we controlled for a range of lifestyle and demographic characteristics that are associated...
with growth, we acknowledge that residual confounding from unmeasured covariates such as diet and physical activity patterns is still possible. Information on growth measures in young adulthood was self-reported, which might have led to misclassification. However, this potential misclassification is likely to be non-differential (i.e., not to relate to cord blood PUFAs). Moreover, self-reported growth measures in young adulthood were significantly positively correlated with those in childhood. We assessed many PUFAs exposures and child outcomes, raising concern about multiple testing. To our opinion, a correction for multiple comparisons is inappropriate, as our analysis was based on a pre-specified research hypothesis with biological rationale from experimental models [44,45]. Moreover, given the high correlation among the exposures and among the outcomes of interest, an application of correction for multiple comparisons such as the Bonferroni correction would result in overly conservative estimates and increased chance of conducting type II error [44,46]. Finally, we studied a population of relatively healthy participants from a high-income country. We cannot exclude the possibility that the small effect estimates for infant length and the lack of associations with growth outcomes at the other developmental ages cannot at least be partly explained by the fact that our study sample exhibited in general a healthy growth, thus having low variation in growth patterns, especially for height.

4.3. Conclusions

In the Dutch population-based MEFAB cohort, we found small sex-specific associations of cord blood PUFAs concentrations with length in infancy, corresponding to a 0.4–0.7-cm change per SD increase in PUFA levels. The associations with infant length seemed to be transient, as they did not persist later in childhood and in young adulthood. No associations of cord blood PUFAs with BMI from infancy till young adulthood were observed in either sex. Further studies, especially in low-income populations, are needed to disentangle the role of prenatal PUFAs in postnatal growth.

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Declaration of conflict of interest

None.

Authorship

N. S., M. G., and M. P. Z. conceived the study; all authors were involved in the design and planning of the study, and the data collection; N. S. and K. M. analyzed data; N. S., and M. G. wrote the paper; and all authors critically reviewed and approved the final manuscript.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.jplefa.2017.09.004.

References
