Plasma fatty acid composition is associated with the metabolic syndrome and low-grade inflammation in overweight adolescents

Carine Klein-Platat, Jocelyne Drai, Mohamed Oujaa, Jean-Louis Schlienger, and Chantal Simon

ABSTRACT

Background: Together with adiposity, plasma fatty acid (FA) composition can modulate the development of the metabolic syndrome (MS).

Objective: Our aim was to investigate the relations of FA composition in plasma phospholipids and cholesterol esters (CEs) with weight status, MS, and inflammation in adolescents.

Design: Plasma FA composition was measured by gas-liquid chromatography in 120 (60 normal-weight and 60 overweight) 12-y-old adolescents. We also measured the presence of MS, insulin resistance with the homeostasis model assessment, and interleukin 6 and C-reactive protein concentrations in the adolescents.

Results: MS was present in 25% of the overweight adolescents but in none of the normal-weight adolescents. Compared with overweight adolescents, normal-weight adolescents had lower saturated FAs (SFAs) in both phospholipids (P < 0.001) and CEs (P < 0.01) and higher docosahexaenoic acid in phospholipids (P < 0.001). In overweight subjects, FA composition was associated with MS features independent of body fat. The odds ratios of MS for a 0.1 increase in the ratio of polyunsaturated FAs (PUFA) to SFAs (PUFA:SFA) were 0.91 in phospholipids (P = 0.03) and 0.90 in CEs (P = 0.06). In phospholipids, PUFA:SFA and linoleic acid were associated positively with HDL cholesterol (P < 0.01 for both). Eicosapentaenoic acid in phospholipids and CEs were associated inversely with interleukin 6 (P < 0.05 for both). Eicosapentaenoic acid in phospholipids (P = 0.06) and CEs (P < 0.05) and linolenic acid in CEs (P < 0.05) were inversely related to C-reactive protein. These relations remained significant after adjustment for the waist-to-hip ratio. No significant relation between FA composition and the homestasis model assessment was observed.

Conclusions: Plasma FA composition is associated with weight status in healthy adolescents. High intake of long-chain PUFAs, especially n-3 PUFAs, may protect obese subjects against MS and low-grade inflammation as early as adolescence.


KEY WORDS Adolescents, plasma fatty acid composition, low-grade inflammation, metabolic syndrome, obesity

INTRODUCTION

Much evidence exists that the metabolic syndrome (MS), which affects adults but also affects a worrisome proportion of adolescents (1, 2), is closely connected to cardiovascular disease risk (3). MS is defined by the clustering of several metabolic abnormalities in the same person, mainly overweight status and more specifically abdominal adiposity, insulin resistance, dyslipidemia, and high blood pressure. Besides these factors, low-grade inflammation is increasingly viewed as a significant component of MS (4, 5). Different cytokines and chemical messengers, which induce their effects individually or in interaction with each other, constitute the main regulators of this inflammatory process. Among them, interleukin (IL) 6, a proinflammatory cytokine produced by different cells including adipose tissue, is overexpressed in adults with MS (6) and in obese adolescents (4, 7). These disorders are important because elevated IL-6 and C-reactive protein (CRP) concentrations are associated with a higher risk of developing type 2 diabetes and cardiovascular disease (8).

Although the association between adiposity and MS is well recognized, other factors, such as diet, are thought to be significant contributors. Epidemiologic and experimental studies conducted on adults have shown that dietary fat and plasma fatty acid (FA) composition, which is at least partly influenced by the diet ingested over the preceding several weeks (9, 10), are related to insulin sensitivity and several features of MS, such as blood pressure, plasma lipid profile (11, 12), and inflammation (13).

Studies of diet or plasma FA composition conducted in children, mostly in obese children (14–16), focused mainly on lipid variables; none has examined low-grade inflammation. The study of children or young adolescents may furnish new insight into the early mechanisms that underlie the development of MS, because they are not confounded by the consequences of advanced metabolic disorders or atheromatous disease. These young persons are also free of several lifestyle confounders, such as smoking and alcohol consumption.

In the present study, we investigate the cross-sectional relations between the FA composition in both plasma phospholipids and cholesterol esters (CEs) and different features of MS as well as 2 markers of low-grade inflammation (IL-6 and CRP) in 60

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normal-weight and 60 overweight adolescents who participated in the Intervention Centered on Adolescents’ Physical Activity and Sedentary Behavior Study (ICAPS). Our hypothesis was that plasma FA composition is associated with obesity and, more specifically, with MS. We also examined whether the contribution of plasma FA composition to components of MS is independent of adiposity and fat localization and whether it might modulate the relation between obesity and metabolic or inflammatory profiles.

SUBJECTS AND METHODS

Population

ICAPS is an ongoing randomized intervention study that began in 2002 and was aimed at encouraging physical activity in adolescents to reduce weight gain and cardiovascular disease risk (17). Briefly, 1048 adolescents aged 12 y from 8 public schools of the Department of the Bas-Rhin (eastern France) were eligible to participate. Of the eligible subjects, 91% participated and ≈66% agreed to provide a blood sample. The present study included a randomized subsample of 60 normal-weight (30 adolescent females and 30 adolescent males) and 60 overweight (30 adolescent females and 30 adolescent males) subjects. ICAPS was reviewed and approved by the local Ethics Committee and the schools’ governing bodies. Written consent to participate was obtained from all adolescents and their parents.

Anthropometric and medical measurements

An initial examination was conducted by trained professionals according to standardized methods (17). Height, weight, and waist and hip circumferences were measured, and the waist-to-hip ratio (WHR) was calculated. The percentage of body fat (BF) was evaluated by bioelectrical impedance (Tanita TBF-310, Tanita Corporation, Tokyo, Japan). Body mass index was calculated as weight (in kg)/height² (in m), and overweight was as was recently proposed (21). The cutoffs that were chosen to define the presence of the MS features were the following: >90th percentile for triacylglycerol concentrations, <5th percentile for HDL-cholesterol concentrations, >90th percentile for blood pressure measurements, >6.1 mmol/L for glucose concentrations, and >95th percentile for waist measurements. The percentiles for triacylglycerols, HDL cholesterol, and blood pressure were based on US age and sex reference curves (22, 23), and the percentiles for waist measurements were based on British reference curves (24).

Fatty acid composition of phospholipids

For FA analyses, lipids were extracted with a chloroform-methanol mix (1:1, by vol). The extract was washed with a saline solution to remove proteins. The chloroform phase was concentrated under a stream of nitrogen and redissolved in chloroform-methanol. The lipid classes were separated by thin-layer chromatography on silica gel plates (Merck KgaA, Darmstadt, Germany) with petroleum ether-ethylic ether-acetic acid (87:13:2) as the developing solvent. The plates were sprayed with bromphenol blue, and individual bands of phospholipids and CEs were scraped off into separate tubes. The phospholipid fraction was saponified and transmethylated with sodium methylate, and the CE fraction was methylated with sulfuric acid and dehydrated methanol. The methyl esters of each fraction were removed with hexane and analyzed by gas-liquid chromatography on a Fison GC-8000 gas chromatograph (Thermo Separation Products, Les Ulis, France) equipped with a CP-SIL fused silica capillary column (25 m, 0.25 mm internal diameter) coated with 100% cyanopropyl siloxane 88 phase 0.2 μm (Chrompack, Les Ulis, France) with helium as the carrier gas and a split ratio of 1:20.

The identity of each FA peak was ascertained by comparison of the peak’s retention time with the retention times of synthetic standards with known FA composition. The relative amount of each FA (% of total FA) was quantified by integrating the area under the peak and dividing the result by the total area for all fatty acids.
TABLE 1
Anthropometric and biochemical characteristics of the normal-weight and overweight adolescents

<table>
<thead>
<tr>
<th>Variables</th>
<th>Normal weight (n = 60)</th>
<th>Overweight (n = 60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>11.5 ± 0.1</td>
<td>11.6 ± 0.1</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>17.4 ± 0.3</td>
<td>23.3 ± 0.3</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>61.3 ± 0.7</td>
<td>74.2 ± 0.9</td>
</tr>
<tr>
<td>Hip circumference (cm)</td>
<td>76.0 ± 1.0</td>
<td>87.8 ± 0.9</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.81 ± 0.01</td>
<td>0.85 ± 0.01</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>15.5 ± 0.8</td>
<td>27.2 ± 0.8</td>
</tr>
<tr>
<td>Metabolic syndrome (%)</td>
<td>0</td>
<td>25</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>109.5 ± 1.6</td>
<td>113.5 ± 1.6</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>65.1 ± 1.4</td>
<td>67.3 ± 1.3</td>
</tr>
<tr>
<td>Insulin (pmol/L)</td>
<td>49.5 ± 3.8</td>
<td>82.2 ± 4.7</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>5.0 ± 0.1</td>
<td>5.2 ± 0.1</td>
</tr>
<tr>
<td>HOMA</td>
<td>1.62 ± 0.13</td>
<td>2.74 ± 0.16</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>0.80 ± 0.03</td>
<td>0.98 ± 0.05</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>1.30 ± 0.05</td>
<td>1.09 ± 0.10</td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>0.64 ± 0.07</td>
<td>0.84 ± 0.07</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>0.8 ± 0.2</td>
<td>1.5 ± 0.3</td>
</tr>
</tbody>
</table>

1 HOMA, homeostasis model assessment; IL, interleukin; CRP, C-reactive protein.
2 ± SEM (all such values).
3–6 Significantly different from normal-weight adolescents (ANOVA):
3 P < 0.0001; 4 P < 0.001; 5 P < 0.01; 6 P < 0.05.
7 Tested with log transformed values.

Acids. Concentrations of plasma saturated FAs (SFAs), monounsaturated FAs, and polyunsaturated FAs (PUFAs) were calculated by summing the respective FAs with 16–24 carbon atoms. The ratios of PUFA to SFA (PUFA:SFA) and of n–6 PUFA to n–3 PUFA (n–6 PUFA:n–3 PUFA) were also calculated.

Statistical analysis
Data are presented as means ± SEMs. Comparisons between the different groups were made with general linear models and post hoc Bonferroni tests. The relations between variables were analyzed by general linear regression models. Interactions between FA composition and the different adjustment variables were tested. Because no interaction was observed with sex, all the results are presented with both sexes pooled. Because of a modifying effect of weight status on the relation between FA composition and different MS features, the analyses were performed separately for the normal-weight and overweight groups. The analyses were made after adjustment for different sets of covariates: 1) sex, sexual maturity, and physical activity; 2) additional adjustment for BF; and 3) additional adjustment for WHR. A multiple logistic regression analysis was performed to estimate the independent associations of MS with FA composition. Because of their skewed distribution, HOMA, triacylglycerol concentrations, and CRP concentrations were log transformed before analysis. All statistical analyses were carried out with SAS software (version 8; SAS Institute Inc, Cary, NC).

RESULTS
Subjects’ characteristics
Anthropometric and biological characteristics of the adolescents are presented in Table 1 according to weight status. The mean (±SEM) age of the subjects was 11.5 ± 0.1 y. All the components of MS except blood pressure were significantly different between overweight and normal-weight subjects. MS was present in 25% of the overweight adolescents but in none of the normal-weight adolescents.

Fatty acid composition of plasma lipids according to weight and metabolic syndrome status
SFAs and PUFAs represented almost 50% and 37%, respectively, of FAs in the phospholipid fraction. As expected, the proportion of SFAs was lower in CEs than in phospholipids, whereas PUFA concentrations were roughly 60% of FAs in the CE fraction. FA compositions of plasma phospholipids and CEs are presented in Table 2 by weight and MS status, with adjustment for sex, sexual maturity, and physical activity. Compared with normal-weight adolescents, overweight adolescents without MS were characterized by higher SFA concentrations in both the CE and the phospholipid fractions. Overweight adolescents also had lower docosahexaenoic acid (22:6n–3) and total n–3 PUFA concentrations in phospholipids than did normal-weight subjects, which explained the marginally higher n–6 PUFA:n–3 PUFA (P = 0.07).

Overweight adolescents with MS had a lower PUFA:SFA in both lipid fractions than did overweight adolescents with no MS. The presence of MS was also associated with an increase in palmitoleic acid (16:1n–7) in phospholipids and in CEs and a reduction in linoleic acid (18:2n–6) in phospholipids.

After adjustment for sex, sexual maturity, and physical activity, the risk of preventing MS in overweight subjects was inversely related to the ratio of PUFAs to SFAs in both lipid fractions, although it was only marginally significant for CEs (P = 0.06). The odds ratio of MS for a 0.1 increase in PUFA:SFA was 0.91 in phospholipids (95% CI: 0.84, 0.99; P = 0.03) and 0.90 in CEs (95% CI: 0.90, 1.01; P = 0.06). The relation between PUFA:SFA in phospholipids and the risk of MS remained significant after additional adjustment for both BF and WHR (odds ratio: 0.92; 95% CI: 0.85, 0.99; P < 0.05).

Fatty acid composition of plasma lipids, components of the metabolic syndrome, and low-grade inflammation
Weight status had a modifying effect on the relation between FA composition and the different features of MS. Whereas no significant relation was observed between plasma FA composition and any of the components of MS in normal-weight subjects, significant relations were observed in overweight subjects.

The relation between plasma FA lipid composition and the components of MS in overweight adolescents with adjustment for sex, sexual maturity, physical activity, and BF are presented in Table 3. PUFA:SFA was associated positively with HDL-cholesterol concentrations in phospholipids and inversely with IL-6 in both the phospholipid (Figure 1) and the CE fractions. In phospholipids, but not in CEs, 18:2 n–6 PUFA was positively associated with HDL-cholesterol concentrations and tended to be inversely associated with triacylglycerol concentrations (P = 0.07). CRP concentrations were inversely related to linolenic acid (18:3n–3) in CEs and to eicosapentaenoic acid (20:5n–3) in CEs (P < 0.05) and marginally in phospholipids (P = 0.06). In contrast, insulin resistance, as measured by HOMA, was not significantly associated with FA composition. All the significant relations observed in overweight subjects remained significant after additional adjustment for WHR.
Our study confirms that the FA composition of plasma lipids, particularly SFA proportion, is associated with the weight status of otherwise healthy adolescents. It additionally indicates that the PUFA:SFA and the high long-chain PUFA concentrations are inversely related to MS and inflammation in overweight, but not in non-weight-adolescents, independent of body fat and fat distribution. More specifically, 18:2n–6 PUFA was positively associated with plasma HDL-cholesterol concentrations, whereas the PUFA:SFA and long-chain n–3 PUFA concentrations were inversely associated with IL–6 and CRP concentrations, 2 markers of low-grade inflammation. In contrast, no significant association was observed between FA composition and insulin resistance. The lower risk factor variances in

### TABLE 3
Relations between plasma fatty acid composition and metabolic syndrome features in overweight subjects

<table>
<thead>
<tr>
<th>Fatty acid type</th>
<th>HOMA&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Triacylglycerols&lt;sup&gt;2&lt;/sup&gt;</th>
<th>HDL cholesterol</th>
<th>Systolic blood pressure</th>
<th>IL–6</th>
<th>CRP&lt;sup&gt;2&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phospholipids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Total SFA</td>
<td>−0.01 ± 0.03</td>
<td>−0.01 ± 0.02</td>
<td>−0.02 ± 0.01</td>
<td>0.36 ± 0.72</td>
<td>0.07 ± 0.03&lt;sup&gt;†&lt;/sup&gt;</td>
<td>0.01 ± 0.06</td>
</tr>
<tr>
<td>PUFA:SFA</td>
<td>0.16 ± 0.66</td>
<td>−0.03 ± 0.55</td>
<td>0.82 ± 0.33&lt;sup&gt;‡&lt;/sup&gt;</td>
<td>−11.96 ± 17.33</td>
<td>−1.63 ± 0.71&lt;sup&gt;‡&lt;/sup&gt;</td>
<td>0.28 ± 1.42</td>
</tr>
<tr>
<td>18:2n–6</td>
<td>0.01 ± 0.02</td>
<td>−0.04 ± 0.02</td>
<td>0.04 ± 0.01&lt;sup&gt;‡&lt;/sup&gt;</td>
<td>−0.20 ± 0.62</td>
<td>−0.03 ± 0.03</td>
<td>0.07 ± 0.05</td>
</tr>
<tr>
<td>18:3n–3</td>
<td>0.43 ± 0.49</td>
<td>−0.24 ± 0.42</td>
<td>0.24 ± 0.25</td>
<td>−20.91 ± 12.63</td>
<td>0.19 ± 0.56</td>
<td>−0.54 ± 1.06</td>
</tr>
<tr>
<td>20:5n–3</td>
<td>−0.32 ± 0.49</td>
<td>−0.03 ± 0.42</td>
<td>−0.08 ± 0.26</td>
<td>6.06 ± 13.08</td>
<td>−0.03 ± 0.57</td>
<td>−1.95 ± 1.04</td>
</tr>
<tr>
<td>22:6n–3</td>
<td>−0.08 ± 0.17</td>
<td>0.16 ± 0.14</td>
<td>0.02 ± 0.09</td>
<td>0.56 ± 4.48</td>
<td>−0.14 ± 0.19</td>
<td>−0.23 ± 0.37</td>
</tr>
<tr>
<td><strong>Cholesterol esters</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total SFA</td>
<td>0.03 ± 0.05</td>
<td>−0.01 ± 0.04</td>
<td>−0.04 ± 0.03</td>
<td>1.00 ± 1.34</td>
<td>0.15 ± 0.05&lt;sup&gt;‡&lt;/sup&gt;</td>
<td>−0.01 ± 0.11</td>
</tr>
<tr>
<td>PUFA:SFA</td>
<td>−0.04 ± 0.11</td>
<td>−0.03 ± 0.09</td>
<td>0.09 ± 0.05</td>
<td>−2.69 ± 2.90</td>
<td>−0.27 ± 0.12&lt;sup&gt;‡&lt;/sup&gt;</td>
<td>0.04 ± 0.24</td>
</tr>
<tr>
<td>18:2n–6</td>
<td>0.0001 ± 0.010</td>
<td>−0.01 ± 0.01</td>
<td>0.01 ± 0.01</td>
<td>−0.39 ± 0.38</td>
<td>−0.01 ± 0.02</td>
<td>0.01 ± 0.03</td>
</tr>
<tr>
<td>18:3n–3</td>
<td>0.42 ± 0.52</td>
<td>−0.18 ± 0.45</td>
<td>0.17 ± 0.27</td>
<td>−7.74 ± 14.14</td>
<td>0.37 ± 0.58</td>
<td>−2.24 ± 1.10&lt;sup&gt;‡&lt;/sup&gt;</td>
</tr>
<tr>
<td>20:5n–3</td>
<td>−0.37 ± 0.75</td>
<td>−0.37 ± 0.63</td>
<td>−0.02 ± 0.390</td>
<td>3.20 ± 20.19</td>
<td>0.48 ± 0.83</td>
<td>−3.32 ± 1.57&lt;sup&gt;‡&lt;/sup&gt;</td>
</tr>
<tr>
<td>22:6n–3</td>
<td>0.65 ± 1.16</td>
<td>1.27 ± 0.96</td>
<td>−0.38 ± 0.60</td>
<td>35.10 ± 30.96</td>
<td>−2.16 ± 1.26</td>
<td>−0.63 ± 2.53</td>
</tr>
</tbody>
</table>

<sup>1</sup> All values are β ± SEMs. HOMA, homeostasis model assessment; IL, interleukin; CRP, C-reactive protein; SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.

<sup>2</sup> Tested with the log-transformed values.

<sup>3</sup> General linear regression models were used with adjustment for sex, sexual maturity, physical activity, and body fat: <sup>†</sup> P < 0.05, <sup>‡</sup> P < 0.01.
normal-weight than in overweight persons may partly explain why no significant relations were seen in the former. Our results may also indicate that overweight represents a necessary prereq-uisite that catalyzes the deleterious relations of FA composition, MS, and inflammation.

A positive association was reported between the dietary fat contribution to energy intake and the level of obesity. In accordance with previous studies in adults (25–27) and adolescents (14), higher SFA and lower n−3 PUFA concentrations were found in overweight subjects than in normal-weight adolescents in the present study. Although the increase in SFAs concerned mainly stearic acids (18:0) in our overweight adolescents with no MS, higher proportions of palmitic acids (16:0) were associated with higher palmitoleic acid (16:1n–7) concentrations (which reflect mostly endogenous desaturation of 16:0 FAs) in obese adults (26, 27) and in our adolescents with MS. Similarly, both n−3 PUFA and 18:2n−6 FA concentrations were low in obese adults (27) and in our overweight adolescents with MS, whereas n−3 PUFA concentrations, but not 18:2n−6 FA concentrations, were low in the overweight adolescents without MS. The finding of lower 22:6n−3 and total n−3 PUFA concentrations in our overweight subjects agree with the reduction in BF that was observed in healthy adults after substitution of visible fat with fish oil (28). Whether higher 16:0 and 16:1 FAs and lower 18:2n−6 PUFA are specifically associated with the risk of MS or only reflect a lower PUFA:SFA in overweight subjects with MS than in subjects without MS remains to be determined.

Significant relations have been reported between the type of dietary fat or plasma FA composition and several classic and nonclassic cardiovascular disease risk factors, which include components of inflammation in adults (11–13). In children, the FA profile of plasma lipids was related to the presence of MS in one study (14, 15). On the other hand, abdominal obesity has been shown to be a central component of MS and of the associated low-grade inflammation (29). Our results suggest that this excess in adipose tissue may be necessary to observe a synergistic influence of FA composition on MS and inflammation. We hypothesize an indirect amplifying effect via adipocyte products; conversely, because plasma FA composition is influenced not only by diet but also by de novo synthesis and transformation of exogenous FAs (12), one cannot exclude that the composition of plasma FAs is partly influenced by excess fat. Also, genetic determinants may interact with FA metabolism and contribute to both FA composition and some MS features (30, 31). However, in contrast with most of the studies conducted in adults, we ruled out that the relations observed here were the consequences of severe insulin resistance, evolutive atheromatous lesions, or chronic diseases. Because of the young age of our subjects, we can exclude the confounding effect of smoking or alcohol consumption. The relations were also independent of physical activity levels.

Our data showed no significant association between FA composition and insulin or HOMA. This contrasts with several studies in adults that related serum phospholipid SFAs to incident diabetes and to increased fasting and meal-induced insulinemia in healthy, obese, or diabetic adults (12, 32, 33). Insulin resistance has been attributed to changes in membrane composition and fluidity. A similar association with insulinemia has been found in obese children but was especially apparent postprandially (34). The relatively low concentrations and variability of insulin in our moderately obese subjects may explain why we did not see the same relations.

Different epidemiologic data have shown a weak negative relation between the proportions of dietary and plasma n−3 PUFA concentrations and plasma triacylglycerol concentrations, with a positive association with HDL-cholesterol concentrations (11, 12). Moreover, supplementation with long-chain n−3 PUFA has been shown to be associated with a decrease in triacylglycerol concentrations in hypertriglyceridemic persons and in persons with type 2 diabetes. Differences in the dietary fat content (12) and the absence of established dyslipidemia or insulin-resistance in our adolescents may partly explain why we did not find such a relation. The relations between n−6 PUFA and plasma lipids are less consistent among studies, possibly because of the FAs studied. Note that the beneficial association found here between plasma lipid concentrations and 18:2n−6 PUFA concentrations was found only for the phospholipid fraction.

Supplementation with 18:3n−3 PUFA has been shown to decrease CRP concentrations (35, 36) and also IL-6 concentrations in dyslipidemic patients (35). Moreover, supplementation with 20:5n−3 and 22:6n−3 PUFA resulted in a modulation of the phospholipid FA composition and reduced the production of tumor necrosis factor α and IL-6 by mononuclear cells, even at doses <1g/d. Conversely, palmitate (16:0) was shown to induce the expression of IL-6 in human myotubules (38). The
influence of n−6 PUFA s on inflammation is less consistent. Although arachidonic acid (20:4n−6 PUFA) is a potent proinflammatory factor (30), 18:2n−6 PUFA has been shown to inhibit the palmitate-induced IL-6 production (38). The present findings support a stimulation of IL-6 secretion by SFAs and an inhibition of low-grade inflammation by 18:2n−6 and n−3 PUFAs as early as adolescence. Because this relation was observed in overweight subjects only, we can speculate that this inhibition concerns, at least partly, the production and secretion of IL-6 by adipose tissue. It was shown that 10−35% of basal circulating human IL-6 derives from this tissue (39).

In conclusion, our findings suggest that plasma FA composition contributes to the heterogeneity that exists in the relations between BF and features of MS. A high ratio of PUFAs to SFAs, and more specifically a high intake of long-chain n−3 PUFAs, may protect obese persons against the development of metabolic complications as early as adolescence.

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CS designed and conducted the study. CK-P analyzed the data and wrote the manuscript in collaboration with CS. JD was responsible for the analyses of fatty acids. MO assisted with the statistical analyses. J-LS provided significant advice and consultation. None of the authors had any conflicts of interest.

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