Maternal-fetal in vivo transfer of $^{13}$C]docosahexaenoic and other fatty acids across the human placenta 12 h after maternal oral intake$^{1–4}$

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ABSTRACT

Background: Fetal growth and development require n–3 (omega-3) long-chain polyunsaturated fatty acids, but mechanisms for their placental transfer are not well understood.

Objective: We assessed distribution and human placental transfer of $^{13}$C-labeled fatty acids (FAs) 12 h after oral application.

Design: Eleven pregnant women received 0.5 mg $^{13}$C-palmitic acid ($^{13}$C-PA; 16:0), 0.5 mg $^{13}$C-oleic acid ($^{13}$C-OA; 18:1n–9), 0.5 mg $^{13}$C-linoleic acid ($^{13}$C-LA; 18:2n–6), and 0.1 mg $^{13}$C-docosahexaenoic acid ($^{13}$C-DHA; 22:6n–3) per kilogram of body weight orally 12 h before elective cesarean section. Maternal blood samples were collected before tracer intake (−12 h) and at −3, −2, −1, 0, and +1 h relative to the time of cesarean section. At birth, venous cord blood and placental tissue were collected, and FA concentrations in individual lipid fractions and their tracer content (atom percent excess values) were determined.

Results: Relatively stable tracer enrichment was achieved in maternal lipid fractions 12 h after tracer administration. In maternal plasma, most $^{13}$C-PA and $^{13}$C-OA were found in triglycerides, whereas $^{13}$C-LA and $^{13}$C-DHA were found mainly in plasma phospholipids and triglycerides. In placental tissue, $^{13}$C-FAs were mainly found in phospholipids, which comprise 80% of placental tissue lipids. Placenta-maternal plasma ratios and fetal-maternal plasma ratios for $^{13}$C-DHA were significantly higher than those for any other FA.

Conclusions: Twelve hours after oral application of $^{13}$C-labeled FAs, relatively stable tracer enrichment was achieved. We found a significantly higher ratio of $^{13}$C-DHA concentrations in cord plasma than in maternal plasma, which was higher than that for the other studied FAs. $^{13}$C-DHA is predominantly esterified into phospholipids and triglycerides in maternal plasma, which may facilitate its placental uptake and transfer. Am J Clin Nutr 2010;92:115–22.

INTRODUCTION

The potential of the early diet for child growth, health, and development is of considerable interest. Long-chain polyunsaturated fatty acids (LC-PUFAs), particularly docosahexaenoic acid (DHA; 22:6n–3), are found in high proportions in structural lipids of the central nervous system where they are important for an extensive array of membrane-associated functions (1–3). Fetal tissue deposition of LC-PUFAs depends on the quantity and composition of fatty acids (FAs) delivered via the placenta. However, the mechanisms involved in the placental transfer of FAs and the influence of maternal diet are not fully understood.

Placental lipoprotein lipase (LPL) hydrolyzes maternal plasma triglycerides into nonesterified FAs (NEFA) for placental uptake and transfer (4, 5). Endothelial lipase (EL) was recently shown in human placenta at term to have a higher mRNA expression than that of LPL (6). The high phospholipase activity of EL (7, 8) raises the question of the quantitative contribution that different lipid fractions provide for placental FA uptake and transfer to the fetus.

NEFA hydrolyzed from esterified lipids may enter placenta cells through passive diffusion or a saturable protein–mediated transfer mechanism involving plasma membrane FA binding protein (FABPpm/GOT2), FA translocase (FAT/CD36), FA transport proteins (FATP), and FA binding proteins (FABP) (4, 5, 9). Differences in the affinity of placental FA carriers toward individual FAs may contribute to their rates of maternal-fetal transfer. Whereas proportions of parental essential FAs with 18-carbon atoms are lower in lipids in cord than in maternal plasma, LC-PUFA percentages are higher in cord than in maternal plasma.


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2 This article does not necessarily reflect the views of the Commission of the European Communities and in no way anticipates future policy in this area.

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lips (10–12), which raised the hypothesis that LC-PUFAs may be preferentially transferred across the human placenta to support the rapid accretion of LC-PUFAs in nerve tissue during the period of brain growth spurt (2, 13), given that the fetal and placental synthesis of LC-PUFAs is considered to be rather limited (14, 15).

We previously reported a higher placental-maternal plasma lipid ratio for $^{13}$C-DHA relative to the studied saturated [palmitic acid (PA); 16:0], monounsaturated [oleic acid (OA); 18:1n−9], and essential [linoleic acid (LA) 18:2n−6] FAs 4 h after their maternal oral application, but we did not find a significant difference in cord-to-maternal plasma lipid ratio for $^{13}$C-DHA relative to other FAs (16). We also did not detect tracer incorporation into maternal phospholipids and cholesterol esters (CEs), and thus could not evaluate the role of these maternal plasma lipids in providing substrates for placental transfer.

With the aim of studying a possible contribution of maternal plasma phospholipid FAs as well as other slow turnover pools to placental transfer, we extended the time period between tracer administration and cesarean delivery in the current study. We applied an optimized study protocol for evaluation of placental transfer of FAs in healthy pregnant women by using a 12-h interval between tracer application and elective cesarean section. The different distribution of each labeled FA in maternal, placental, and fetal circulation may contribute to the understanding of mechanisms involved in placental FA transfer.

SUBJECTS AND METHODS

Subjects

Eleven pregnant women undergoing elective cesarean section were recruited for the study in the Service of Gynecology and Obstetrics, Hospital Virgen de la Arrixaca (Murcia, Spain). Recruitment of patients started in February 2006 and was completed in December 2007. Participants fulfilled the following inclusion criteria: singleton pregnancy with term delivery, age 18–40 y, nonsmoking, a body mass index (in kg/m$^2$) at the beginning of pregnancy <30, and a fetal Doppler scan within the normal reference range on the day before the cesarean delivery (17). All subjects habitually consumed an omnivorous diet, and none reported any health problems or pregnancy complications. Subjects consuming DHA-containing supplements during pregnancy were excluded. The study protocol was approved by the Virgen de la Arrixaca Hospital ethical committee, Murcia, Spain. Written informed consent was obtained from all participating women after careful explanation of the study.

Twelve hours before delivery, the subjects received one oral dose of uniformly $^{13}$C-labeled FAs (Martek Biosciences, Columbia, MD) with 0.5 mg $^{13}$C-PA/kg body weight, 0.5 mg $^{13}$C-OA/kg body weight, 0.5 mg $^{13}$C-LA/kg body weight, and 0.1 (99% $^{13}$C enrichment) or 0.01 (10% $^{13}$C enrichment) mg $^{13}$C-DHA/kg body weight. Tracers were supplied as free FAs on a sugar cube to the pregnant women. The women remained otherwise fasted until cesarean section.

Blood and placenta sampling

Blood samples were collected from the women before tracer intake (at −12 h) and at −3, −2, −1, 0, and +1 h relative to the time of cesarean section. Three-milliliter blood samples were collected by venipuncture and immediately transferred into tubes containing EDTA. Venous cord blood was sampled immediately after clamping the cord. Blood cells and plasma were separated within 1 h by centrifugation at 1000 × g for 5 min. An aliquot of ≥200 μL plasma was subsequently frozen at −80°C for later analysis.

The total placenta was weighed immediately after delivery. Samples of 1 × 1 × 1 cm of placental central cotyledons were cut with a sharp knife. Placenta samples were subjected to 3 washings with cold 0.9% NaCl solution until as much blood as possible was removed, and then the samples were frozen in liquid nitrogen. The samples were stored at −80°C until later analysis. Placental samples were processed within 10 min of delivery.

Analysis of plasma and placental FAs

FAs from plasma and placental tissue were extracted by using a modified Folch method (18). After addition of 100 μL internal standard [5 mg FA each of pentadecanoic acid, tri-pentadecanoin, phosphatidylcholine dipentadecanoyl, and cholesteryl pentadecanoate dissolved in 50 mL methanol/chloroform (1:1); Sigma, Deisenhofen, Germany] to 250 μL of plasma or internal standard to ≈0.3 g of placent tissue, total lipids were extracted into chloroform/methanol (2:1) (18). The lipid extract was dried under reduced pressure, and the residue was collected with 400 μL chloroform/methanol (1:1) and added to silicone gel plates (Merek, Darmstadt, Germany). Phospholipids, triglycerides, CE, and NEFA were isolated by development of the plates in N-heptane/disopropylether/glacial acetic acid (60:40:3, by vol) (19). From the individual fractions, FA methyl esters were synthesized in 3 mol methanolic HCl/L (Supelco, Bellfonte, PA) at 85°C for 45 min. Methyl esters were extracted into hexane and stored in hexane-containing butylated hydroxytoluene as antioxidant at −20°C until gas chromatographic analysis.

Gas chromatography was performed on a Hewlett-Packard 5890 series II gas chromatograph (Hewlett-Packard, Waldbronn, Germany), equipped with a BPX70 column (60 m in length × 0.32 mm in inner diameter; SGE, Weiterstadt, Germany). The $^{13}$C enrichment of individual FA methyl esters was measured by gas chromatography-combustion-isotope ratio mass spectrometry (gas chromatograph interfaced with a Finnigan MAT delta S mass spectrometer; Hewlett-Packard, Bremen, Germany) (20).

Expression of results

From the $^{13}$C/$^{12}$C ratio of the samples measured by gas chromatography-combustion-isotope ratio mass spectrometry, the $^{13}$C atom percent excess (APE), representing the $^{13}$C-enrichment (the percentage contribution of tracer $^{13}$C to total carbon), was calculated (21). Concentrations of labeled FAs (μmol $^{13}$C/L or nmol $^{13}$C/g) were calculated by multiplying absolute concentrations of FAs by their $^{13}$C APE. The enrichment (APE) values include the $^{13}$C/$^{12}$C (tracer-tracee) ratio in each FA in the samples, but for tracer concentration values the enrichment of $^{13}$C should be multiplied by the concentration of the corresponding FA in the sample.
The distribution of the tracer FAs between mother and fetus was estimated by calculating the percentage of tracer concentration (μmol $^{13}$C/L) in venous cord blood relative to the area under the tracer concentration curve (AUC; μmol $^{13}$C · h/L) in maternal plasma. AUC was derived by integrating the measured tracer concentration until delivery over time according to the trapezoidal rule. AUC tracer concentration instead of tracer concentration at the time of delivery was chosen because it is considered a better proxy of tracer availability for transfer than the concentration at a single time point, even though the limited sampling time points available may not fully reflect the true AUC. The ratio of distribution of $^{13}$C-tracers between placental tissue and AUC in maternal plasma was calculated as the percentage of the tracer concentration in placenta (nmol $^{13}$C/g) relative to the AUC tracer concentration (μmol $^{13}$C · h/L) in the maternal plasma until delivery.

Though 2 different doses of $^{13}$C-DHA were applied to subjects, we did not consider it necessary to apply respective mathematical corrections. All subjects uniformly received 99% $^{13}$C-enriched DHA tracer, but in 5 subjects it was diluted with 9 vol unlabeled DHA. Dilution resulted in lower APE values and $^{13}$C-DHA concentration in the aforementioned 5 subjects, and thus increased variance between subjects for these variables, but the ratios between tracer concentrations in the different compartments were unaffected. Because these ratios are the main outcome measure, no adjustments for different tracer doses were made.

**Statistical analysis**

Our results are expressed in means ± SEMs. Statistically significant differences according to time evolution of FA enrichment in maternal plasma were evaluated by using a general linear model of repeated measures. The comparison between ratios of distribution, FA lipid fractions, or proportions of different FAs was assessed by using analysis of variance followed by the post hoc Bonferroni procedure. The significance level was set at $P < 0.05$. All analyses were performed by using the statistical software SPSS, version 15.0 (SPSS, Chicago, IL).

**RESULTS**

The 11 participants undergoing elective cesarean section at a mean (±SD) of 279 ± 3 d of gestation were 33 ± 1 y old, had an average weight at delivery of 78 ± 8 kg, and a height of 161 ± 2 cm. Mean (±SD) prepregnancy weight and body mass index of the participants were 64 ± 6 kg and 25.0 ± 4.1, respectively. The time between tracer administration and birth was 12 h 17 min ± 4 min.

**FIGURE 1.** A–D: Mean (±SEM) time course of $^{13}$C enrichment [$^{13}$C-APE % (atom percent excess)] of fatty acids in maternal plasma lipid fractions during the time of study. Time 0 indicates the time of cesarean section ($n = 11$). General linear model of repeated measures was used. † Significant differences over time for a given fatty acid ($P < 0.05$). PA, palmitic acid; OA, oleic acid; LA, linoleic acid; DHA, docosahexaenoic acid.
13C-FA enrichment was detected in all lipid fractions (Figure 1); thus, contribution of all plasma lipid fractions to maternal-fetal FA transfer could be considered. At ≈12 h, there was a slightly decreasing trend for 13C enrichment in both NEFA and triglyceride-bound FAs, whereas in CE enrichments were still increasing and phospholipid enrichment hardly changed (Figure 1). However, the AUC for plasma concentrations of 13C-PA and 13C-OA (μmol 13C · h/L) was highest in triglycerides, whereas 13C-LA and 13C-DHA were mostly incorporated into both plasma phospholipids and triglycerides (Figure 2). More than 90% of placental FAs were found in phospholipids (Table 1). Accordingly, 13C-FAs in placental tissue were predominantly esterified into placental phospholipids, although appreciable amounts of 13C-PA were also found in placental NEFA (Figure 3). There was high 13C-FA enrichment (APE values) in placental triglycerides, whereas CE showed the lowest enrichment (results not shown), but these lipid fractions contribute only relatively small amounts to placental lipids. The ratio of the cord plasma tracer concentration and maternal plasma AUC of concentration was significantly higher for 13C-PA, [13C]palmitic acid; 13C-OA, [13C]oleic acid; 13C-LA, [13C]linoleic acid; 13C-DHA, [13C]docosahexaenoic acid; PL, phospholipids; NEFA, nonesterified fatty acids; TG, triglycerides; CE, cholesterol esters.

DISCUSSION

The methodology used in this study showed tracer enrichment in all studied maternal plasma lipid fractions as well as placental and cord blood lipids at the time of cesarean section 12 h after oral FA tracer application, which leads us to conclude that this methodologic approach is suitable for the assessment of human placental FA transfer in vivo. Under these conditions, a significantly higher proportion of 13C-DHA appeared in cord blood than all the other FAs investigated.

Frequent maternal blood sampling during the 12 h period before a scheduled cesarean delivery the next morning was not feasible in the clinical setting as it would have disturbed women during their nightly sleep and cord blood and placental tissue could only be sampled at the time of delivery, and therefore there were limitations for data analysis and interpretation. Kinetics of enriched FAs in the maternal plasma lipid pools during the first 9 h after tracer intake could not be determined, and the AUC for individual fractions and FAs could only be approximated on the basis of data obtained around delivery. For data analysis, we assumed that turnover was not different between the studied FAs and that the total AUC tracer concentration is proportional to the area calculated from the available data. These assumptions seem justified but preclude the determination of absolute transfer rates, and only comparisons between the studied FAs are possible. With respect to tracer appearance, on the fetal side, only the concentration at one time point was available, thus no kinetic data was obtained. Therefore, we focused data analysis on the tracer distribution at the time on delivery. Because FA influx and outflux in the fetal circulation was not quantitatively known, on the basis of the experimental data, we could not decide whether a higher tracer

![Figure 2](https://academic.oup.com/ajcn/article-abstract/92/1/115/4597213)

**FIGURE 2.** Mean (±SEM) area under the curve of tracer concentration (μmol 13C · h/L) in maternal plasma lipid fractions (n = 11). ANOVA followed by post hoc Bonferroni test were used to assess for each fatty acid difference between lipid fractions. Different letters indicate significant differences (P < 0.05). 13C-PA, [13C]palmitic acid; 13C-OA, [13C]oleic acid; 13C-LA, [13C]linoleic acid; 13C-DHA, [13C]docosahexaenoic acid; PL, phospholipids; NEFA, nonesterified fatty acids; TG, triglycerides; CE, cholesterol esters.
concentration was due to higher placental transfer or a lower elimination from fetal plasma and whether any inflow of the respective FAs from fetal tissues into fetal plasma had occurred. Our interpretation of the data was based on the assumption that elimination from fetal plasma and potential inflow from fetal tissues was similar for all the studied FAs. To our knowledge, there is currently no information available on tissue incorporation or oxidation of individual FAs from fetal plasma, but DHA is required in considerable amounts for the synthesis of fetal brain and nervous tissue; thus, an accumulation of DHA fetal plasma due to relatively low deposition or metabolization does not seem plausible (2, 13).

Previously, we reported a greater placental uptake of DHA relative to the uptake of other FAs in pregnant women who received labeled FAs 4 h before cesarean section (16). Whereas incorporation of tracer into maternal plasma and placental

### TABLE 1

<table>
<thead>
<tr>
<th></th>
<th>Maternal plasma</th>
<th>Cord plasma</th>
<th>Placental tissue</th>
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<tbody>
<tr>
<td><strong>Phospholipids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PA (% wt/wt)</td>
<td>31.18 ± 0.47a</td>
<td>29.6 ± 0.63b</td>
<td>25.45 ± 0.26c</td>
</tr>
<tr>
<td>OA (% wt/wt)</td>
<td>8.89 ± 0.39a</td>
<td>7.16 ± 0.29b</td>
<td>8.51 ± 0.22a</td>
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<tr>
<td>LA (% wt/wt)</td>
<td>19.82 ± 0.73a</td>
<td>7.02 ± 0.39b</td>
<td>9.62 ± 0.43a</td>
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<tr>
<td>DHA (% wt/wt)</td>
<td>4.91 ± 0.27</td>
<td>5.43 ± 0.43</td>
<td>5.57 ± 0.23</td>
</tr>
<tr>
<td>Total FA (mg/dL)²</td>
<td>168.17 ± 7.39a</td>
<td>58.42 ± 2.89</td>
<td>6.45 ± 0.28c</td>
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<tr>
<td><strong>Triglycerides</strong></td>
<td></td>
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<tr>
<td>PA (% wt/wt)</td>
<td>29.19 ± 0.59a</td>
<td>30.71 ± 0.98b</td>
<td>23.14 ± 1.39b</td>
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<tr>
<td>OA (% wt/wt)</td>
<td>36.0 ± 1.17a</td>
<td>26.01 ± 0.93b</td>
<td>16.44 ± 0.68b</td>
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<tr>
<td>LA (% wt/wt)</td>
<td>20.06 ± 1.61a</td>
<td>11.83 ± 0.87b</td>
<td>11.16 ± 0.72b</td>
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<tr>
<td>DHA (% wt/wt)</td>
<td>0.69 ± 0.09a</td>
<td>3.11 ± 0.51b</td>
<td>5.98 ± 0.84a</td>
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<tr>
<td>Total FAs (mg/dL)²</td>
<td>133.10 ± 9.13a</td>
<td>17.93 ± 3.23b</td>
<td>0.23 ± 0.08c</td>
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<tr>
<td><strong>CEs</strong></td>
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<tr>
<td>PA (% wt/wt)</td>
<td>12.49 ± 0.29a</td>
<td>21.48 ± 0.43b</td>
<td>16.47 ± 0.40b</td>
</tr>
<tr>
<td>OA (% wt/wt)</td>
<td>18.53 ± 0.86a</td>
<td>26.55 ± 1.14b</td>
<td>17.36 ± 0.59b</td>
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<td>LA (% wt/wt)</td>
<td>53.25 ± 1.52a</td>
<td>17.40 ± 0.97b</td>
<td>36.08 ± 1.76b</td>
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<td>DHA (% wt/wt)</td>
<td>0.81 ± 0.06a</td>
<td>1.19 ± 0.13b</td>
<td>2.09 ± 0.20a</td>
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<td>Total FAs (mg/dL)²</td>
<td>98.78 ± 6.45a</td>
<td>23.24 ± 1.66b</td>
<td>0.19 ± 0.02c</td>
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<td><strong>Nonesterified FAs</strong></td>
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<td>PA (% wt/wt)</td>
<td>26.92 ± 0.39a</td>
<td>37.99 ± 1.40a</td>
<td>24.77 ± 0.96b</td>
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<td>OA (% wt/wt)</td>
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<td>8.73 ± 0.88a</td>
<td>8.82 ± 0.37b</td>
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<tr>
<td>LA (% wt/wt)</td>
<td>15.84 ± 0.97a</td>
<td>5.70 ± 0.56b</td>
<td>8.25 ± 0.55b</td>
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<tr>
<td>DHA (% wt/wt)</td>
<td>0.73 ± 0.09a</td>
<td>1.07 ± 0.23b</td>
<td>4.02 ± 0.46b</td>
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<tr>
<td>Total FAs (mg/dL)²</td>
<td>19.74 ± 1.75a</td>
<td>5.93 ± 1.30a</td>
<td>0.60 ± 0.11b</td>
</tr>
</tbody>
</table>

1 PA, palmitic acid; OA, oleic acid; LA, linoleic acid; DHA, docosahexaenoic acid; CEs, cholesterol esters. ANOVA followed by the post hoc Bonferroni procedure was used to assess differences for each FA percentage between maternal plasma, fetal plasma, and placental tissue. Significant differences are indicated by different superscript letters (P < 0.05).

2 In placenta, total FAs are expressed in mg/g wet weight.

![FIGURE 3](https://academic.oup.com/ajcn/article-abstract/92/1/115/4597213)

**FIGURE 3.** Mean (±SEM) concentrations of tracer (nmol ¹³C/g) in placental tissue lipid fractions at the time of delivery (12 h after tracer administration; n = 11). ANOVA followed by the post hoc Bonferroni procedure were used to assess for each fatty acid difference between lipid fractions. Different letters indicate significant differences (P < 0.05). ¹³C-PA, [¹³C]palmitic acid; ¹³C-OA, [¹³C]oleic acid; ¹³C-LA, [¹³C]linoleic acid; ¹³C-DHA, [¹³C]docosahexaenoic acid; PL, phospholipids; NEFA, nonesterified fatty acids; TG, triglycerides; CE, cholesterol esters.
phospholipids and CE was not detected in that study, in the current study the administration of labeled FAs 12 h before cesarean section led to significant tracer incorporation into all lipid fractions.

Maternal plasma concentrations of FAs in specific lipid classes may have substantial effects on FA delivery to the fetus. Plasma concentration of labeled saturated FAs (\(^{13}\)C-PA) and mono-unsaturated FAs (\(^{13}\)C-OA) were higher in maternal triglycerides, whereas PUFAs (\(^{13}\)C-LA and \(^{13}\)C-DHA) were found mainly in phospholipids and triglycerides (Figure 2A). There was a trend of higher incorporation of \(^{13}\)C-DHA into maternal plasma phospholipids than \(^{13}\)C-LA. Human plasma triglycerides contain much lower concentrations of LC-PUFAs than phospholipids (22). Even though plasma triglyceride concentrations increase considerably during pregnancy (23), the concentration of LC-PUFAs is highest in maternal PL. The incorporation of dietary PUFAs into maternal plasma phospholipids could be important for PUFA placental uptake and transfer of FAs, which may involve placental EL activity.

Maternal plasma NEFA as well as NEFA released by LPL from maternal plasma triglycerides are often considered as the quantitatively most important sources of placental FA transfer (4, 5). However, another member of the triglyceride lipase gene family, EL, was found at both interfaces of human placenta and in vascular endothelial cells (24). EL is primarily an A1-phospholipase with a restricted ability to release sn-2 (FAs stereified in position 2)-bound FA from phospholipids (7). Saturated FAs are predominantly found in the sn-1 position of PL, whereas PUFAs are typically esterified to sn-2 (24). Therefore, EL activity may result in enhancing levels of maternal plasma lysophospholipids enriched in LC-PUFAs. These lyso-phospholipids could be an additional source of FAs for the placenta. This is supported by reports that lyso-phosphatidylcholine may represent a preferred physiologic carrier of DHA relative to NEFA for incorporation into the brain (25, 26). Similarly, lysophosphatidylcholines seem to deliver \(^{13}\)C-DHA more efficiently to erythrocytes than NEFA (27).

The higher enrichment of LC-PUFAs than essential precursor FAs in the placenta might be achieved by placental FA carriers (5, 9, 28) and/or the preferential release of lyso-phospholipids enriched in LC-PUFAs by EL. EL shows selectivity for the phospholipids species containing DHA at the sn-2 position (29). Gauster et al (7) proposed that the degree of unsaturation and the acyl chain length affect the cleavage efficiency of FAs by EL because the LC-PUFA 20:4\(^{\text{n-6}}\) was released by EL 4.5-fold lower from HDL\(_{3}\)-PC than the precursor essential FA LA 18:2\(^{\text{n-6}}\).

Placental EL activity might be important given that pregnant women with LPL deficiency still can allow for placental transfer of LC-PUFAs (and presumably other FAs) for apparently normal child development (30). A study in mice showed that EL can compensate for a lack of LPL in adipose tissue and mediates some of the NEFA taken up by the tissue (31). A higher placental EL expression was reported in LPL-deficient mice (32).

In our study the observed enrichments of all \(^{13}\)C-FAs in triglycerides and NEFAs in the maternal plasma are in agreement with the classical mechanism of FA placental transfer mediated by LPL in the placenta. Because the available information on LPL does not indicate discrimination among FAs, this pathway does not explain a higher placental uptake of DHA than of other FAs. On the other hand, we also found a significantly higher concentration of \(^{13}\)C-FAs in placental phospholipids than in other lipid fractions. Klingler et al (33) reported that phospholipids contributed the majority of lipids in placental tissue (87.5 ± 4.2%)
followed by NEFAs, triglycerides, and CEs. Lyso-phospholipids might also contribute to the generation of phospholipids in the placental membranes, as described, in gut mucosa (34).

When considering the affinity of tracer FAs with placental lipid fractions expressed by APE values, we found high enrichment of $^{13}$C-FA in triglycerides, similar to our previous results at 4 h after tracer application (16). Szabo et al (35) estimated that $\sim$20% of isotope-labeled palmitate was esterified in placental triglycerides after 2 h of incubation of human placental tissue. Crabtree et al (36), using human placental choriocarcinoma (BeWo) cells as an in vitro model, reported that almost 60% of the total amount of (H)DHA taken up by the cells was esterified into triglycerides, whereas 37% was found in phospholipids (36). Because the NEFA fraction in the placenta is very small, NEFAs that are later on released on the fetal side may well originate from A2-phospholipase and triglyceride hydrolyase activity of human placenta (4). The synthesis of apoprotein B in human placenta (37) and the identification of small amounts of lipoproteins very similar to LDL and VLDL in human term placentas suggest further mechanisms of exportation of esterified FAs to the fetal side. Both mechanisms of FA release to fetal circulation need time, which has to be considered in planning and interpreting in vivo studies of placental FA transfer. It appears that a tracer experiment with a 12-h interval between tracer application and birth reflects the transfer process more completely than a shorter interval of only 4 h.

Higher DHA percentages in both placenta and cord than in maternal blood might reflect a higher rate of placental transfer relative to other FAs to meet fetal DHA requirements (11, 38). Evidence on the role of the placental uptake in the LC-PUFA relative to other FAs to meet fetal DHA requirements (11, 38). Furthermore, our results suggest a contribution of arachidonic acid but not arachidonic acid influences central nervous system fatty acid status in baboon neonates. Prostaglandins Leukot Essent Fatty Acids 2009;81:105–10.


Thies F, Delachambre MC, Bentejac M, Lagarde M, Locorri J. Un saturated fatty acids esterified in 2-acyl-l-lysophosphatidylcholine bound to albumin are more efficiently taken up by the young rat brain than the unesterified form. J Neurochem 1992;59:1110–6.


