Online Supplement

PREECLAMPSIA IS ASSOCIATED WITH COMPROMISED MATERNAL SYNTHESIS OF LONG CHAIN POLYUNSATURATED FATTY ACIDS LEADING TO OFFSPRING DEFICIENCY

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Short Title: PUFA status in healthy & complicated pregnancy

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Methods

Subjects

Blood pressure measurements were taken at all routine antenatal visits by a midwife using an automated sphygmomanometer (A&D digital BP machine) in the left arm in a seated position. Urinalysis was initially screened using a combiscreen dipstick (Analyticon Biotechnologies) and if abnormal on visual screening confirmed on dipstick reader (Combiscan 100, Analyticon Biotechnologies). For women recruited just prior to undergoing Caesarean section, pre-operative blood pressure was taken using a Dinamap® (GE Healthcare) in the left arm with women in a semi-recumbent position and repeat urinalysis was not performed if a recent measurement in clinic had been negative. In PE women, third trimester blood pressure measurements were taken in the left arm in semi-recumbent position using a Dinamap®. PE was defined according to the ISSHP criteria i.e. recruitment of a patient with PE required a reading of diastolic blood pressure >110 mmHg on one occasion, or >90 mmHg on repeated readings and being normotensive at booking. In addition, urinalysis on dipstick, using the method described above, was greater or equal to 2+ proteinuria on at least one occasion in the absence of renal disease or infection, with minimal or no proteinuria on previous urinalysis. Women were classified as having severe PE according to the Hypertension in Pregnancy NICE clinical guideline 107 i.e. a diastolic blood pressure of 110mmHg or greater, and/or a systolic blood pressure 160mmHg or greater. Twenty-one of the PE mothers were classified as having severe PE and samples were available from 9 babies from a severe PE pregnancy. IUGR was defined as an estimated fetal weight $<5^{th}$ percentile for gestation with associated oligohydramnios (amniotic fluid index <5) and/or abnormal umbilical artery blood flow on Doppler ultrasound. Four women with PE also had IUGR and were included in the PE group only. Multiparous pregnancies were excluded. None of the women had a medical history of metabolic disease or had suspected fetal anomalies likely to contribute to reduced fetal growth. Subject characteristics were recorded at time of sampling. Delivery details were recorded from patient notes. Deprivation category (DEPCAT score), a measure of socioeconomic status, was assigned using the Scottish Area Deprivation Index for Scottish postcode sectors, 1998[1]. Customised birth weight centiles were calculated using the Gestation Network Centile Calculator 5.4 (http://www.gestation.net/birthweight_centiles/centile_online.htm). Non-fasting venous blood was collected from non-labouring mothers. Plasma was harvested at 5°C by low speed centrifugation within 30 minutes of collection and plasma and erythrocytes stored at -80°C. Placental biopsies were collected at delivery. Subcutaneous adipose tissue was obtained at Caesarean section from under the skin on entry into the abdomen and visceral adipose tissue was obtained from the omentum following closure of the uterus and haemostasis. Biopsies were flash frozen in liquid nitrogen and stored at -80°C until analyzed.

Plasma metabolites

Plasma NEFA was quantitated by colorimetric assay (Wako, Alpha Laboratories, Eastleigh, UK). Insulin quantitation was performed by ELISA (Mercodia, Sweden) according to the manufacturer's instructions. HOMA was calculated as follows: [fasting insulin (mU/L) x fasting glucose (mmol/L)]/22.5. Plasma leptin, adiponectin, IL-6 and TNFα were assayed by ELISA (R&D Systems, Abingdon, UK).

Fatty acid compositions

Erythrocyte membranes were collected as described previously[2]. An 11μm thick cryosection of adipose tissue was extracted by washing with 1mL chloroform:methanol (2:1 vol/vol) and made up to a final volume of 5 ml. Fatty acid extracts were prepared by modified Folch extraction and derivatised[2, 3]. Methyl fatty acids were separated, identified and quantitated by gas chromatography[2, 4]. Identification of fatty acid methyl esters was made by comparison with authentic standard mixtures (Fatty acid methyl ester mixture #189-19, L9405, Sigma, Sweden). Inclusion of heneicosanoic acid or pentadecanoic acid (0.2mg/ml toluene) during extraction allowed quantitation of fatty acid absolute concentrations.

Messenger RNA expression

Total RNA was isolated from placental and adipose tissue using the ABI PRISM 6100 Nucleic Acid Prepstation following manufacturer's instructions (Applied Biosystems, Warrington, UK). cDNA was reverse transcribed from RNA using a High Capacity cDNA Reverse Transcriptase Kit (Applied Biosystems). Target gene expression was quantitated relative to a control gene (*TOP1* Hs00243257_m1 placenta[5] and *PPIA* Hs99999904_m1 adipose tissue[6]) using commercial primer probe sets (*FADS1* Hs00203685_m1, *FADS2* Hs00188654_m1, *SCD* Hs01682761_m1, *ELOVL2* Hs00214936_m1, *ELOVL6* Hs00225412_m1, *GOT2* Hs00905827_g1 and *FABP7* Hs00361426_m1 Applied Biosystems) in a final volume of 25ul on an 7900HT Sequence Detection System (Applied Biosystems). The expression of target assays were normalised by subtracting the C_T value of the endogenous control from the C_T value of the target assay. The fold increase relative to the control was calculated using the formula $2^{-\Delta CT}$ and expressed as a percentage. Fold increase data was square root or log transformed to achieve a normal distribution before statistical analysis.

Statistical analysis

Normality testing used the Ryan-Joiner test and, where necessary, data were transformed to log or square root values to achieve normality. *ELOVL2* expression was undetectable in the entire PE group and non-parametric analysis used. Chi squared test was used to test for differences among groups for categorical and ANOVA or Kruskal-Wallis for continuous variables. *Post hoc* comparison between groups was by Tukey-Kramer test or by comparison of proportions of detectable expression by Fisher's exact test. Multivariate analysis was carried out using the General Linear Model. Statistical analysis was carried out using Minitab (Vs 15.1) or JMP 7.

Abbreviations

12:0 lauric acid; 14:0 myristic acid, 16:0 palmitic acid; 18:0 stearic acid; 20:0 arachidic acid; 22:0 behenic acid; 24:0 lignoceric acid; 16:1n-7, palmitoleic acid; 18:1n-9 oleic acid; 20:1n-9 eicosenoic acid, 22:1n-9 erucic acid; 24:1n-9 nervonic acid; 18:2n-6 linoleic acid; 18:3n-6 gamma-linolenic acid; 20:3n-6 dihomo-gamma-linolenic acid; 20:4n-6 arachidonic acid; 22:4n-6 adrenic acid; 22:5n-6 docosapentaenoic acid; 18:3n-3 alpha-linolenic acid; 20:3n-3 eicosatrienoic acid; 20:5n-3 eicosapentaenoic acid; 22:5n-3 docosapentaenoic acid; 22:6n-3 docosahexaenoic acid (DHA); n-9 omega-9 monounsaturated fatty acids; n-7 omega-7 monounsaturated fatty acids; n-6 omega-6 polyunsaturated fatty acids; n-3 omega-3 polyunsaturated fatty acids; BMI body mass index; C20-22 fatty acids with carbon chain length of 20 to 22 carbons; CRP C reactive protein; DEPCAT Deprivation score which is a measure of socio-economic status; HDL high density lipoprotein; HOMA homeostasis model of assessment; ISSHP International Society for the Study of Hypertension in Pregnancy; IUGR intrauterine growth restriction; LC long chain; MUFA monounsaturated fatty acids; NEFA non-esterified fatty acids; PE preeclampsia; pFABPpm placental plasma membrane fatty acid binding protein; PUFA polyunsaturated fatty acid; SAFA saturated fatty acid; SCD stearyl CoA desaturase; SHBG steroid hormone binding globulin.

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Table S1. Maternal antenatal booking characteristics for Control, preeclampsia (PE) and intrauterine growth restriction (IUGR) mothers. Values are mean and standard deviation (SD) for continuous variables or number (%) for categorical variables. ANOVA* was used to test for differences among groups (†on log transformed data). Chi squared test was used to test for differences among groups for categorical variables. Different superscript letters indicate differences between individual groups using *post hoc* Tukey-Kramer test or subgroup chi-squared test. Significance level P<0.005.

Maternal Parameter	Control (n=164)	PE (n=62)	IUGR (n=23)	P*
Demographic data				
BMI† (kg/m^2)	27.8 (5.9)	27.8 (5.5)	24.5 (4.9)	0.021
Age (years)	29.6 (5.6)	29.1 (6.3)	29.4 (5.4)	0.83
DEPCAT Score	4.8 (1.8)	4.4 (1.8)	5.3 (1.8)	0.11
Primigravidae (n, %)	83 (50.3)	43 (69.4)	12 (52.2)	0.039
Smokers (n, %)	43 (26.1)[a]	6 (9.8)[b]	13 (56.5)[c]	<0.001
Sampling gestation (weeks)	37.4 (2.9)	36.3 (3.2)	36.1 (2.9)	0.028
Systolic BP† (mmHg)	120 (14)[a]	152 (19)[b]	107 (10)[a]	<0.001
Diastolic BP† (mmHg)	71 (9)[a]	95 (11)[b]	71 (7)[a]	<0.001
Gestation at delivery (weeks)	39.8 (1.4)[a]	36.7 (3.0)[b]	36.5 (3.1)[b]	<0.001
Birth weight (g)	3575 (552)[a]	2563 (799)[b]	2018 (565)[c]	<0.001
Birth weight centile	56.2 (31.6)[a]	24.1 (27.7)[b]	2.0 (3.2)[c]	<0.001

Table S2. Maternal third trimester plasma and cord plasma metabolic and inflammatory markers for Control, preeclampsia (PE) and intrauterine growth restriction (IUGR) pregnancies. Values are mean and standard deviation (SD) for continuous variables or number (%) for categorical variables. ANOVA* was used to test for differences among (†on log transformed or ‡ square root transformed data). Different superscript letters indicate differences between individual groups using *post hoc* Tukey-Kramer test or subgroup chi-squared test. Significance level P<0.005. ‡adjusted for maternal body mass index (BMI), parity, smoking status and gestational age at sampling (for mothers) or gestational age at delivery (for offspring).

Biochemical Parameter	Control	PE	IUGR	P*	§Adjusted P
Maternal plasma (n)	n=164	n=62	n=23		
Total cholesterol (mmol/L)	6.16 (1.08)	6.62 (1.17)	6.27 (1.01)	0.022	0.010
Triglyceride† (mmol/L)	2.78 (0.99)^{a}	3.36 (1.01)^{b}	2.63 (1.06)^{a}	<0.001	<0.001
HDL cholesterol† (mmol/L)	1.61 (0.38)	1.66 (0.46)	1.70 (0.45)	0.63	0.20
NEFA† (mmol/L)	0.34 (0.20)^{a}	0.51 (0.23)^{b}	0.52 (0.50)^{a,b}	<0.001	<0.001
Leptin† (mg/mL)	37 (26)^{a}	58 (33)^{b}	34 (27)^{a}	0.001	0.002
Adiponectin† (ug/mL)	8.3 (3.2)^{a}	10.7 (4.7)^{b}	8.5 (3.3)^{a,b}	0.002	<0.001
IL-6† (pg/mL)	2.6 (1.6)^{a}	4.7 (4.8)^{b}	2.7 (1.8)^{a}	0.001	<0.001
TNFα† (pg/mL)	1.96 (2.02)	1.71 (0.93)	3.44 (5.28)	0.11	0.62
CRP† (mg/L)	5.50 (4.81)	7.44 (11.28)	5.36 (3.89)	0.99	0.98
Cord blood (n)	n=85	n=21	n=13	P*	§Adjusted P
Total cholesterol† (mmol/L)	1.62 (0.47)^{a}	2.27 (0.68)^{b}	1.22 (0.32)^{c}	<0.001	<0.001
Triglyceride† (mmol/L)	0.45 (0.39)^{a}	0.58 (0.07)^{b}	0.59 (0.22)^{b}	0.004	0.003
HDL cholesterol† (mmol/L)	0.78 (0.25)^{a}	0.81 (0.30)^{a}	0.44 (0.17)^{b}	<0.001	<0.001
NEFA† (mmol/L)	0.13 (0.10)	0.14 (0.09)	0.15 (0.14)	0.36	0.37
Glucose† (mmol/L)	4.31 (1.23)	4.57 (0.97)	4.48 (1.28)	0.47	0.68
Insulin‡ (mU/L)	8.2 (12.3)	10.2 (15.7)	5.5 (9.3)	0.058	0.14
HOMA†	1.7 (3.7)	2.2 (3.5)	1.1 (1.7)	0.17	0.10
Leptin† (mg/mL)	13.1 (14.3)^{a}	7.1 (6.8)^{b}	4.2 (6.2)^{b}	<0.001	0.57
Adiponectin (ug/mL)	0.93 (0.41)^{a}	0.58 (0.59)^{b}	0.37 (0.44)^{b}	<0.001	0.23
IL-6† (pg/mL)	6.74 (8.44)	6.79 (5.86)	6.68 (5.68)	0.42	0.66
TNFα† (pg/mL)	2.31 (1.26)	1.90 (0.60)	2.57 (0.76)	0.063	0.15
CRP ‡ (mg/L)	0.27 (1.06)	0.11 (0.08)	0.05 (0.06)	0.14	0.26

Table S3. Maternal antenatal booking characteristics and third trimester plasma metabolic and inflammatory markers and maternal erythrocyte fatty acid concentrations (nmol/mL blood) for Control, mild preeclampsia (PE) and severe PE mothers. Values are mean and standard deviation (SD) for continuous variables or number (%) for categorical variables. ANOVA* was used to test for differences among groups (†on log transformed data). Chi squared test was used to test for differences among groups for categorical variables. Different superscript letters indicate differences between individual groups using *post hoc* Tukey-Kramer test or subgroup chi-squared test. Significance level P<0.005.

Maternal Parameter	Control (n=164)	Mild PE (n=38)	Severe PE (n=21)	P*
Demographic data				
BMI (kg/m^2)	27.8 (5.9)	28.0 (5.4)	27.4 (5.8)	0.89
Smokers (n, %)	43 (26.1)^{a}	2 (5.3)^{b}	4 (23.8)^{a,b}	0.004
Systolic BP† (mmHg)	120 (14)^{a}	142 (13)^{b}	171 (12)^{c}	<0.001
Diastolic BP† (mmHg)	71 (9)^{a}	91 (10)^{b}	103 (9)^{c}	<0.001
Gestation at delivery(weeks)	39.8 (1.4)^{a}	37.2 (2.9)^{b}	36.1 (3.2)^{b}	<0.001
Birth weight (g)	3575 (552)^{a}	2702 (816)^{b}	2377 (703)^{b}	<0.001
Birth weight centile	56.2 (31.6)^{a}	29.1 (32.1)^{b}	16.3 (15.2)^{b}	<0.001
Biochemical data				
Triglyceride† (mmol/L)	2.78 (0.99)^{a}	3.38 (1.00)^{b}	3.19 (0.88)^{a,b}	<0.001
NEFA† (mmol/L)	0.34 (0.20)^{a}	0.53 (0.26)^{b}	0.54 (0.19)^{b}	<0.001
Leptin† (mg/mL)	37 (26)^{a}	61 (33)^{b}	51 (32)^{a,b}	<0.001
Adiponectin† (ug/mL)	8.3 (3.2)^{a}	10.6 (4.9)^{b}	10.9 (4.6)^{b}	0.003
IL-6† (pg/mL)	2.6 (1.6)^{a}	3.9 (2.6)^{b}	5.5 (6.3)^{b}	0.002
Fatty Acid				
SAFA				
22:0	22 (14)^{a}	24 (14)^{a}	9 (15)^{b}	<0.001
PUFA n-6				
18:2n-6	171 (54)^{a}	141 (52)^{b}	110 (47)^{b}	<0.001
20:2n-6	4 (5)^{a}	2 (3)^{b}	2 (3)^{b}	<0.001
20:3n-6	32 (15)^{a}	25 (14)^{b}	18 (14)^{b}	<0.001
20:4n-6	225 (89)^{a}	161 (99)^{b}	102 (81)^{c}	<0.001
22:4n-6	43 (20)^{a}	31 (20)^{b}	18 (17)^{c}	<0.001
22:5n-6	10 (6)^{a}	6 (6)^{b}	3 (4)^{b}	<0.001
PUFA n-3				
22:5n-3	32 (14)^{a}	22 (15)^{b}	12 (10)^{c}	<0.001
22:6n-3	65 (30)^{a}	48 (38)^{b}	25 (25)^{c}	<0.001
Summary indices				
% SAFA	49 (7)^{a}	53 (9)^{b}	58 (7)^{c}	<0.001
% MUFA	21 (2)^{a}	23 (2)^{b}	23 (2)^{b}	<0.001
% PUFA	30 (7)^{a}	24 (9)^{b}	18 (8)^{c}	<0.001
% UNSAT	51 (7)^{a}	47 (9)^{b}	42 (7)^{c}	<0.001
UI	131 (29)^{a}	109 (35)^{b}	87 (29)^{c}	<0.001
Av CL	18.5 (0.3)^{a}	18.3 (0.3)^{b}	18.1 (0.3)^{c}	<0.001
C 20-22	26 (6)^{a}	22 (7)^{b}	17 (6)^{c}	<0.001

DHA deficiency index	0.20 (0.11)[a]	0.15 (0.15)[b]	0.09 (0.17)[b]	<0.001
EFA deficiency index	1.44 (0.39)[a]	1.06 (0.42)[b]	0.81 (0.39)[b]	<0.001

Table S4. Fatty acid composition (mol% of total fatty acids) and summary indices in subcutaneous adipose tissue from Control, preeclampsia (PE) and intrauterine growth restriction (IUGR) mothers biopsied at delivery.

All values are mean and standard deviation (SD). ANOVA* was used to test for differences among groups (†on log transformed where appropriate). Lipogenic index is represented by 18:2n-6/16:0.

Fatty acid	Control n=28	PE n=13	IUGR n=5	*P
Mol% of Total Fatty Acids				
SAFA				
12:0	0.58 (0.44)	0.45 (0.21)	0.66 (0.22)	0.45
14:0	2.98 (0.64)	2.89 (0.50)	3.00 (0.76)	0.88
16:0	24.0 (1.7)	23.7 (1.8)	23.3 (2.2)	0.67
18:0	3.63 (0.84)	3.18 (0.76)	3.71 (0.48)	0.21
20:0	0.12 (0.05)	0.13 (0.05)	0.16 (0.04)	0.27
MUFA				
14:1n-7	0.12 (0.14)	0.09 (0.09)	0.16 (0.14)	0.52
16:1n-7	5.21 (1.19)	5.56 (1.15)	5.60 (0.95)	0.61
18:1n-7	1.92 (0.50)	1.84 (0.27)	1.39 (0.71)	0.073
18:1n-9	47.2 (2.5)	47.9 (2.9)	48.1 (2.7)	0.65
20:1n-9	0.61(0.35)	0.60 (0.35)	0.78 (0.19)	0.56
PUFA n-6				
18:2n-6	12.1 (2.2)	12.2 (2.2)	11.8 (1.8)	0.93
18:3n-6	0.08 (0.04)	0.11 (0.03)	0.10 (0.03)	0.069
20:3n-6	0.18 (0.07)	0.20 (0.12)	0.10 (0.04)	0.093
20:4n-6	0.26 (0.06)	0.27 (0.10)	0.25 (0.05)	0.89
PUFA n-3				
18:3n-3	0.89 (0.28)	0.90 (0.22)	0.86 (0.11)	0.95
20:5n-3	0.01 (0.01)	0.01 (0.02)	0.02 (0.02)	0.45
22:5n-3	0.005 (0.017)	0.017 (0.040)	0.00 (0.00)	0.30
22:6n-3	0.01 (0.03)	0.02 (0.04)	0.03 (0.06)	0.54
Summary Indices				
% SAFA	31.3 (3.0)	30.3 (2.4)	30.9 (3.2)	0.56
% MUFA	55.1 (3.1)	56.0 (3.7)	56.0 (2.2)	0.65
% PUFA†	13.6 (2.3)	13.7 (2.4)	13.1 (1.9)	0.89
% UNSAT	68.7 (3.0)	69.7 (2.4)	69.1 (3.2)	0.56
% n-6 PUFA†	12.7 (2.2)	12.8 (2.3)	12.2 (1.9)	0.90
% n-3 PUFA	0.91 (0.28)	0.95 (0.23)	0.90 (0.10)	0.88
n-6/n-3 ratio	16.4 (12.9)	13.9 (2.9)	13.6 (1.8)	0.71
Lipogenic Index	0.51 (0.11)	0.52 (0.10)	0.51 (0.12)	0.98

Table S5. Fatty acid composition (mol% of total fatty acids) and summary indices in visceral adipose tissue from Control, preeclampsia (PE) and intrauterine growth restriction (IUGR) mothers biopsied at delivery.

All values are mean and standard deviation (SD). ANOVA* was used to test for differences among groups (†on log transformed where appropriate). Different superscript letters indicate differences between individual groups using *post hoc* Tukey-Kramer test. Lipogenic index is represented by 18:2n-6/16:0.

Fatty acid	Control n=26	PE n=13	IUGR n=5	*P
	Mol% of total fatty acids			
SAFA				
12:0	0.56 (0.13)[a]	0.52 (0.13)[a]	0.87 (0.38)[b]	0.001
14:0	3.22 (0.61)	2.99 (0.61)	3.49 (1.00)	0.34
16:0	23.1 (1.7)	22.7 (1.9)	24.2 (3.3)	0.37
18:0	4.46 (0.83)[a,b]	3.90 (0.95)[a]	5.07 (0.86)[b]	0.036
20:0	0.27 (0.06)	0.23 (0.07)	0.29 (0.06)	0.099
MUFA				
14:1n-7	0.22 (0.18)	0.25 (0.20)	0.11 (0.11)	0.34
16:1n-7	5.32 (1.01)	5.58 (1.24)	4.94 (0.71)	0.51
18:1n-7	0.75 (0.82)	0.99 (0.87)	0.71 (0.78)	0.50
18:1n-9	47.6 (3.4)	48.2 (34.0)	46.5 (3.8)	0.69
20:1n-9	0.81 (0.36)	0.83 (0.30)	0.84 (0.08)	0.98
PUFA n-6				
18:2n-6	12.3 (2.2)	12.3 (2.6)	11.9 (1.6)	0.91
18:3n-6	0.06 (0.03)	0.08 (0.03)	0.07 (0.02)	0.44
20:3n-6	0.12 (0.05)	0.16 (0.05)	0.11 (0.06)	0.047
20:4n-6	0.231 (0.07)	0.24 (0.12)	0.19 (0.06)	0.60
PUFA n-3				
18:3n-3	0.84 (0.25)	0.81 (0.23)	0.70 (0.20)	0.48
20:5n-3	0.04 (0.04)	0.04 (0.06)	0.04 (0.04)	0.57
22:5n-3	0.05 (0.05)	0.06 (0.07)	0.03 (0.06)	0.49
22:6n-3	0.02 (0.04)	0.02 (0.04)	0.03 (0.07)	0.82
Summary Indices				
% SAFA	31.6 (2.8)	30.4 (2.9)	33.9 (5.4)	0.11
% MUFA	55.1 (3.1)	55.9 (4.1)	53.1 (4.2)	0.37
% PUFA†	13.6 (2.2)	13.8 (2.7)	13.0 (1.7)	0.85
% UNSAT	68.4 (2.8)	69.6 (2.9)	66.1 (5.4)	0.11
% n-6 PUFA†	12.7 (2.1)	12.8 (2.6)	12.2 (1.7)	0.88
% n-3 PUFA	0.95 (0.27)	0.95 (0.19)	0.80 (0.25)	0.44
n-6/n-3 ratio	14.5 (5.0)	13.9 (3.5)	16.8 (6.0)	0.49
Lipogenic Index	0.54 (0.10)	0.55 (0.13)	0.50 (0.14)	0.78

Figure S1

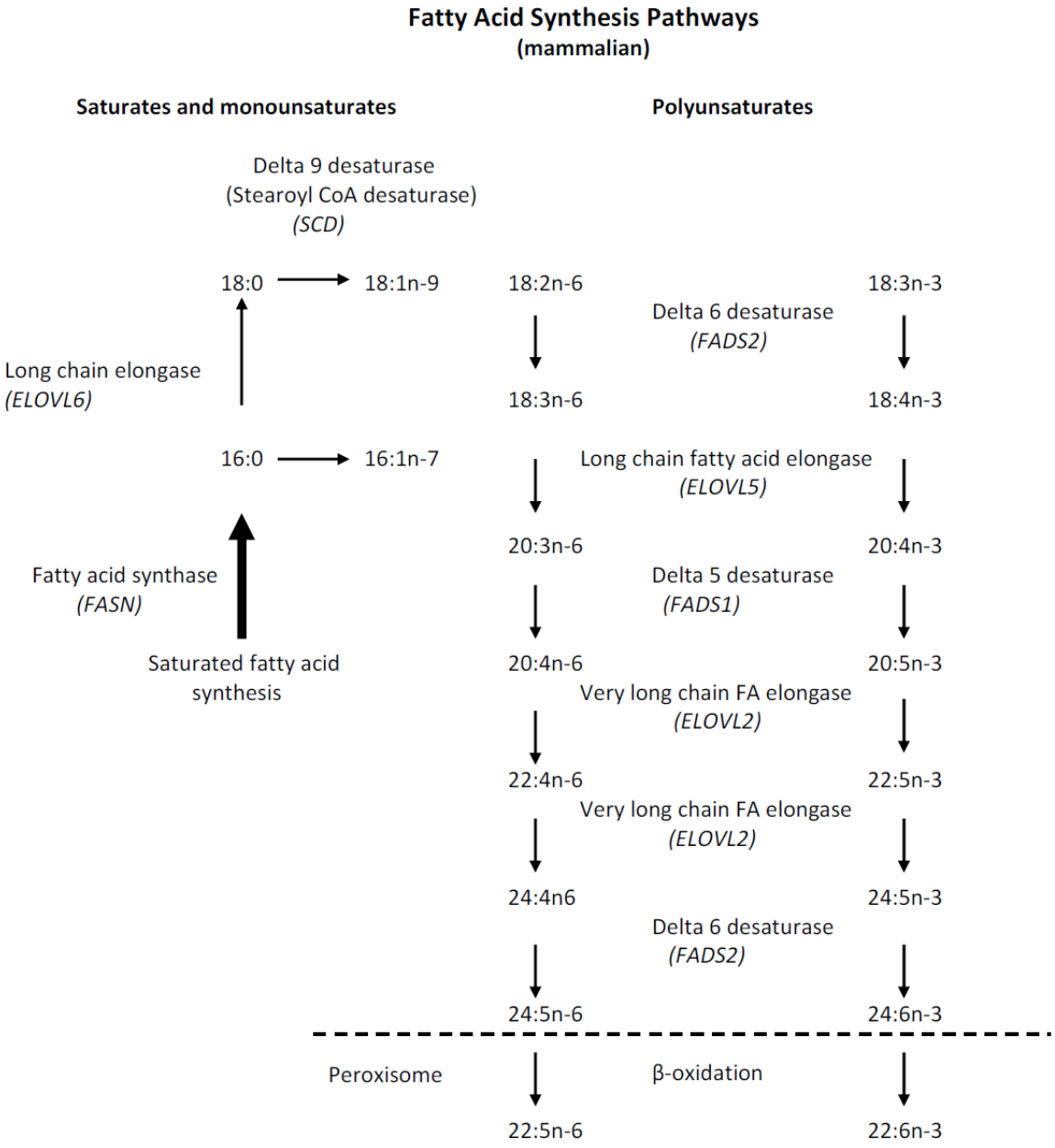

Figure S1. Mammalian fatty acid synthesis pathways. Mammalians can synthesize saturated and monounsaturated fatty acids. The substrates for long chain polyunsaturated fatty acid (LC PUFA) synthesis, 18:2n-6 and 18:3n-3 cannot be made by mammals and required to be derived from the diet. The n-6 LC PUFA and n-3 LC PUFA biosynthetic pathways are carried out in parallel and share the same elongase and desaturase enzymes.

Figure S2

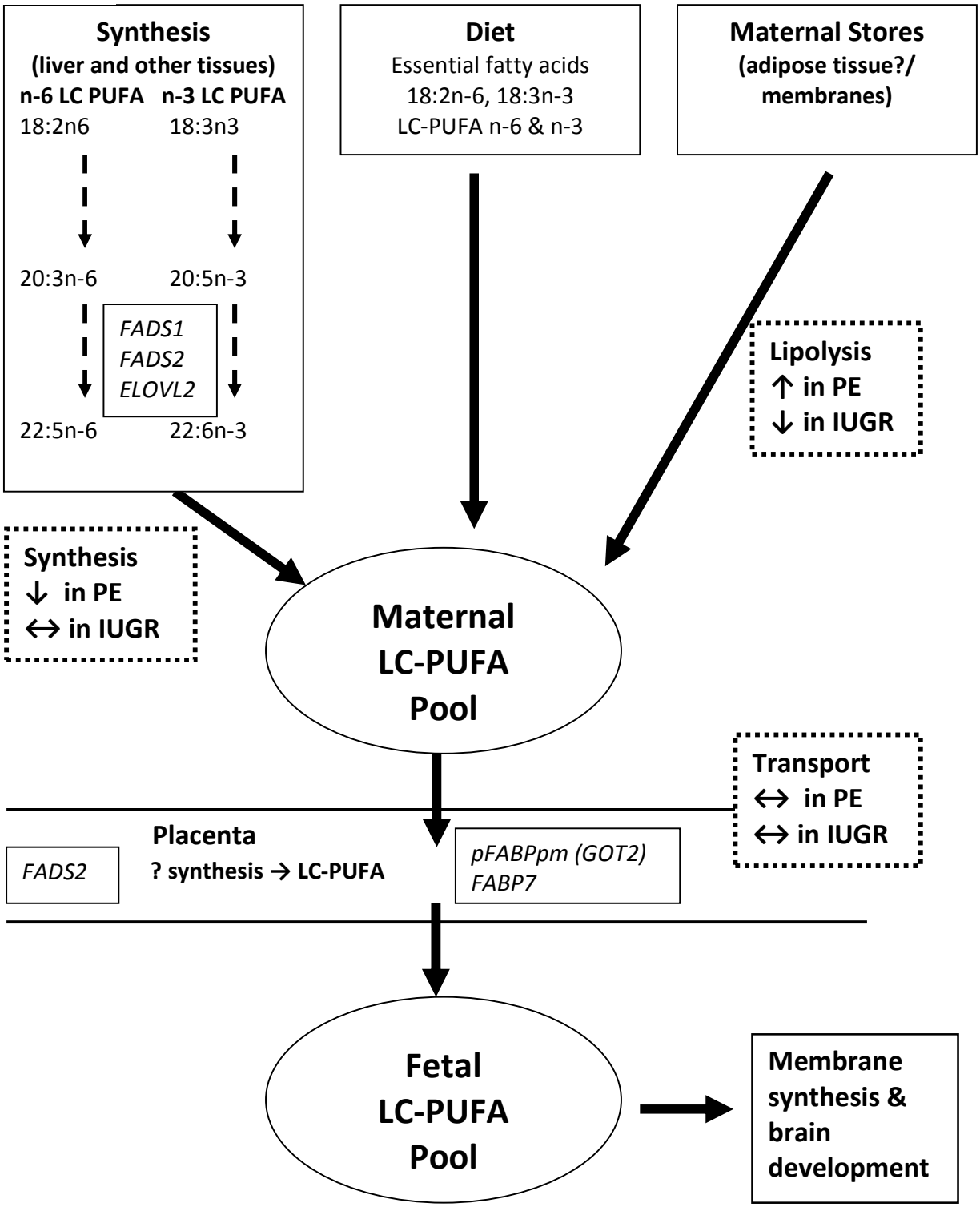
Synthesis
(liver and other tissues)
n-6 LC PUFA
n-3 LC PUFA
18:2n6
18:3n3
20:3n-6
20:5n-3
FADS1
FADS2
ELOVL2
22:5n-6
22:6n-3
Diet
Essential fatty acids
18:2n-6, 18:3n-3
LC-PUFA n-6 & n-3
Maternal Stores
(adipose tissue?/
membranes)
Lipolysis
↑ in PE
↓ in IUGR
Synthesis
↓ in PE
↔ in IUGR
Maternal
LC-PUFA
Pool
Transport
↔ in PE
↔ in IUGR
Placenta
FADS2
? synthesis → LC-PUFA
pFABPpm (GOT2)
FABP7
Fetal
LC-PUFA
Pool
Membrane
synthesis &
brain
development

Figure S2. Long chain polyunsaturated fatty acid metabolism (LC PUFA) metabolism in preeclampsia (PE) and intrauterine growth restriction (IUGR) pregnancy. Sources that contribute to the maternal circulating LC PUFA pool include *de novo* synthesis from shorter chain essential fatty acid precursors in the liver and other tissues, dietary intake and release from maternal stores via lipolysis. Others have shown that lipolysis is increased in PE and reduced in IUGR. We provide evidence that LC PUFA synthesis is decreased in PE via reduced *FADS1*, *FADS2* and *ELOVL2* expression. LC PUFA are transported across the placenta and together with LC PUFA that might be synthesised *de novo* in the placenta contribute to the fetal LC PUFA pool. We observed no difference in the mRNA expression of placental transport proteins specific for 22:6n3 between control and PE or IUGR pregnancies. The fetus requires LC PUFA for the synthesis of membranes and brain development.