PLACENTAL TRANSFER OF FATTY ACIDS AND FETAL IMPLICATIONS

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FETAL PROGRAMMING

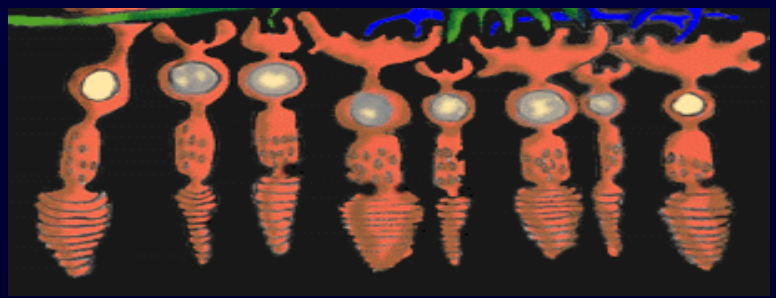
BRAIN

60% FAT (dry matter)

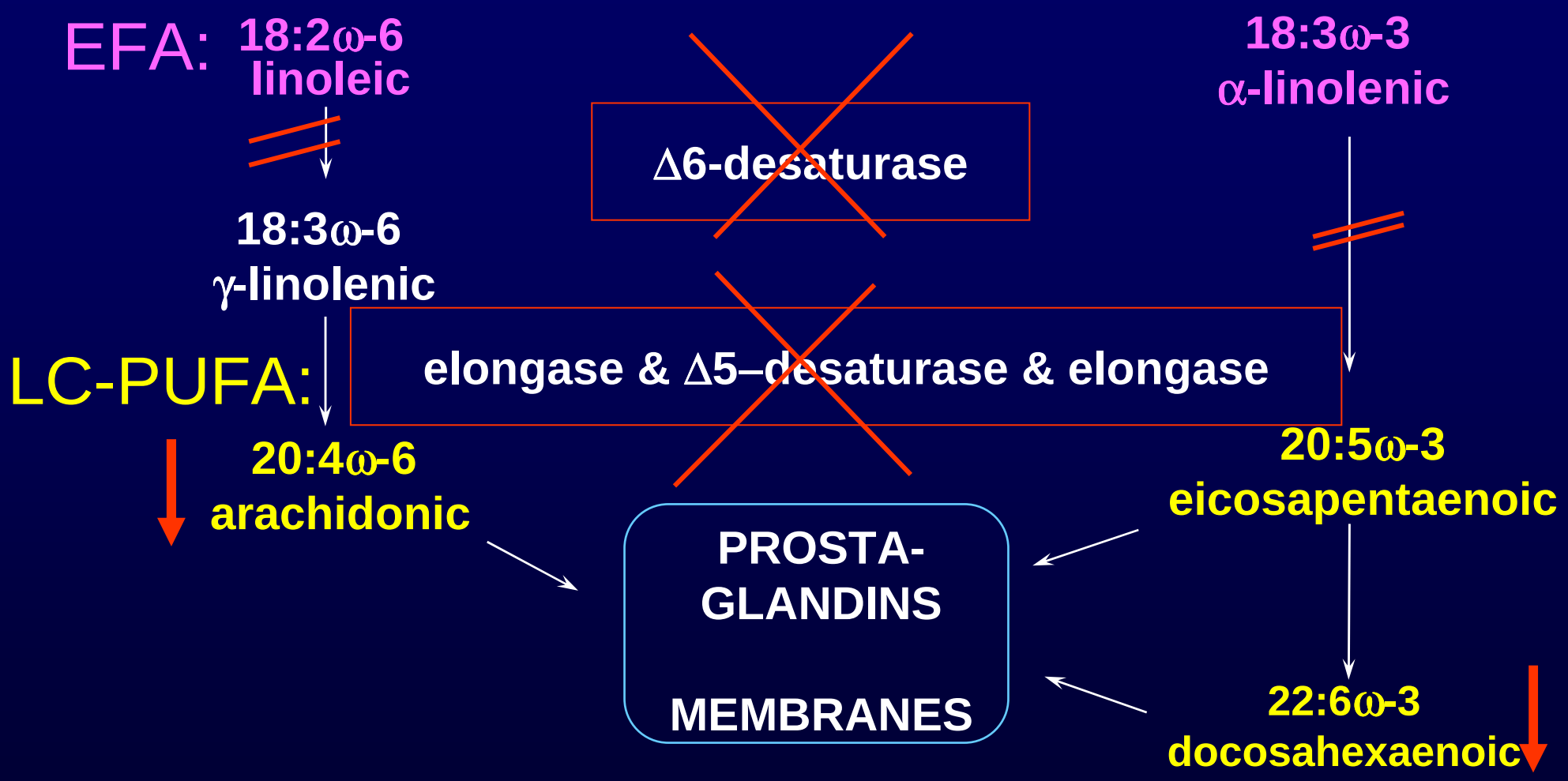
~ 40% LONG CHAIN POLYUNSATURATED FATTY ACIDS (LC-PUFA):

- 15% DOCOSAHEXAENOIC ACID (**DHA, 22:6 n-3**): **Neuronal development**

- 10% ARACHIDONIC ACID (**AA, 20:4 n-6**) : **Infantile Growth**

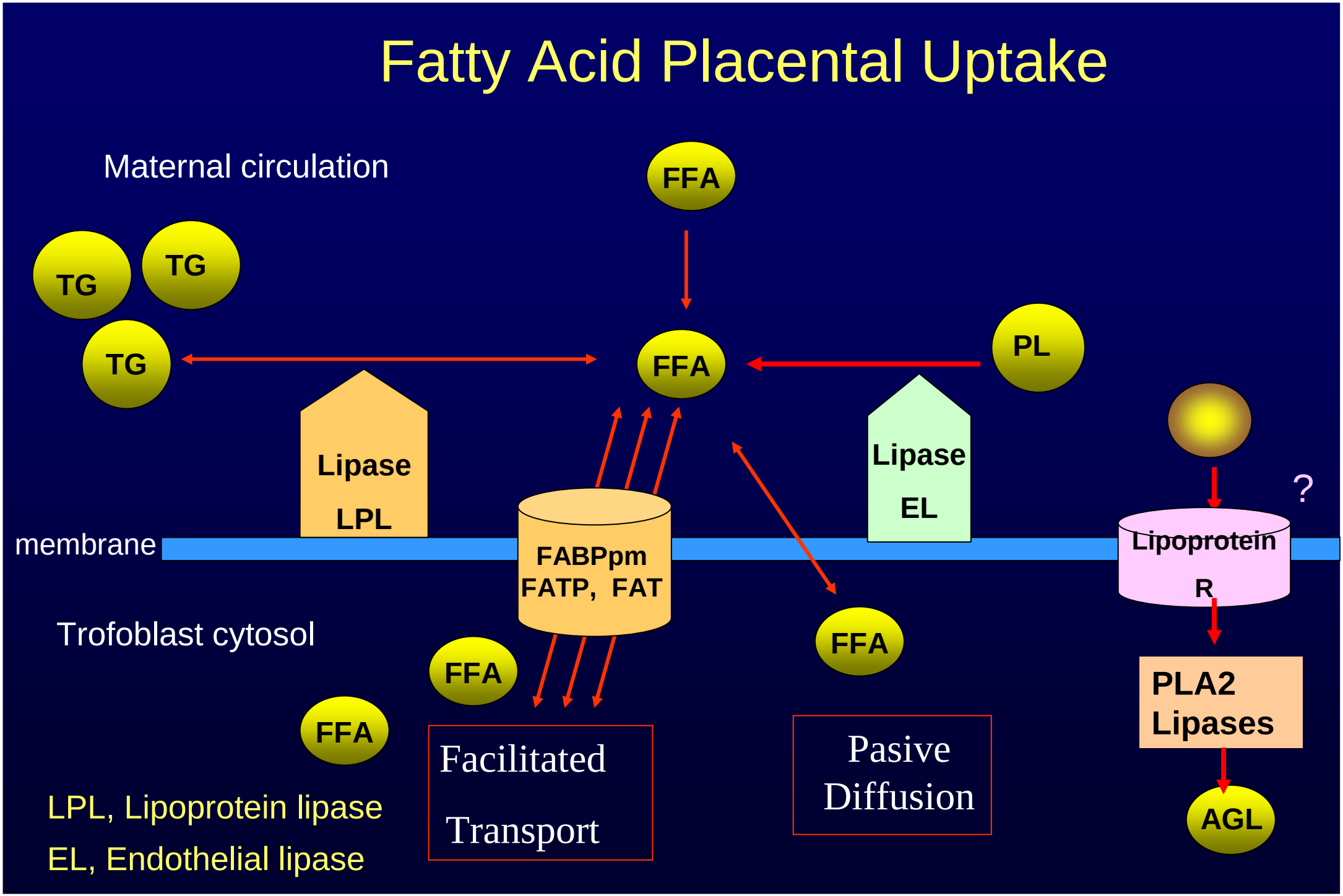


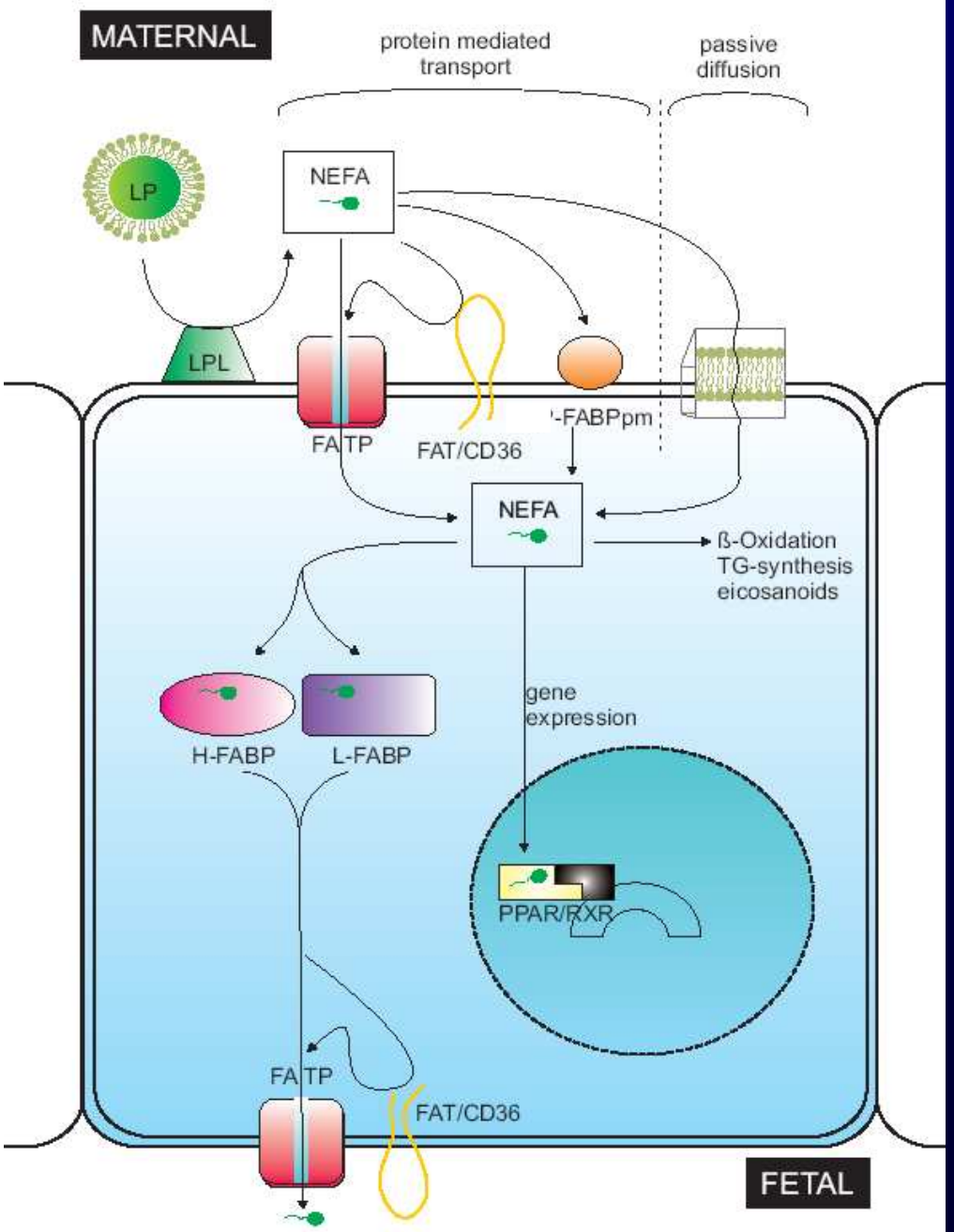
Polyunsaturated FA Synthesis



EFA and LC-PUFA PROVIDED BY PLACENTAL TRANSFER

Fatty Acid Placental Uptake





Fatty Acid Placental Transfer

- Placental transfer of fatty acids is a complex process that includes their binding to membrane and cytosolic protein carriers

p-FABPpm (placental plasma fatty acid binding protein) not sequenced??.

BIOMAGNIFICATION OF LC-PUFA

Fatty-Acid Percentages of Maternal and Cord Plasma Phospholipids [median (IQR)]

	maternal	cord
SAT	47.1 (2.5)	49.9 (1.7)
MUFA	14.9 (2.7)	13.4 (2.2)
18:2n-6 **(LA)**	21.0 (3.4)	7.4 (1.4)
18:3n-3 **(ALA)**	0.20 (0.10)	0.00 (0.03)
20:4n-6 **(AA)**	7.7 (1.9)	16.1 (2.5)
22:6n-3 **(DHA)**	2.9 (1.0)	4.8 (1.7)

Koletzko et al. Eur J Pediatr 1998

Stable Isotope Study on FA Placental Transfer

PERILIP PROJECT (FP6 EU)

Aim

In vivo evaluation of the placental transfer of fatty acids labeled with stable isotopes in humans

Material y methods

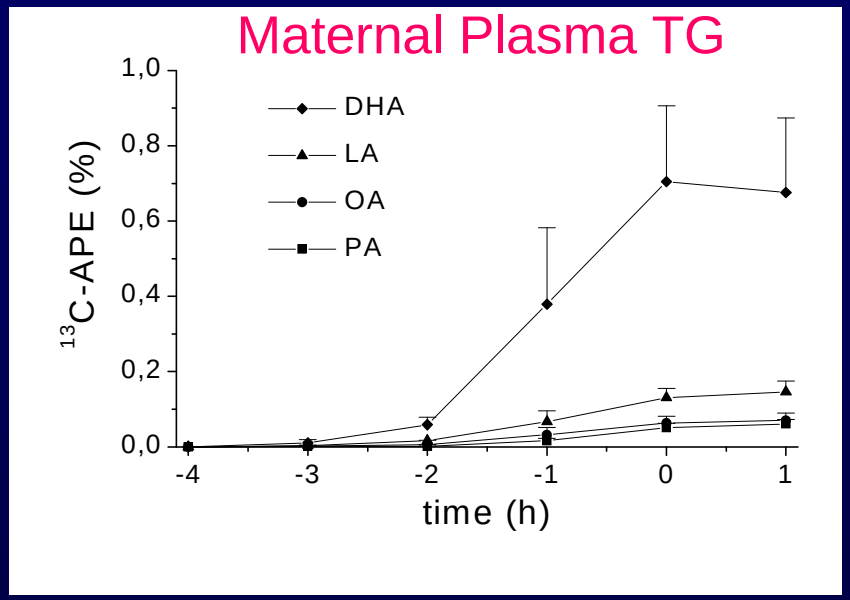
Single oral dose of stable isotope tracer in a sugar cube:

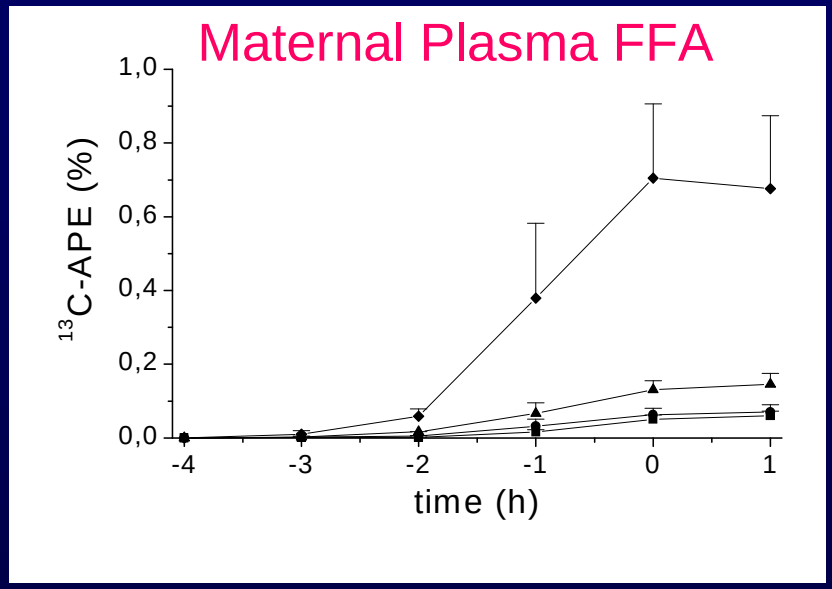
- ^{13}C-PA (Palmitic acid: saturated FA): 0.5 mg/Kg
- ^{13}C-OA (Oleic acid: monounsaturated FA): 0.5 mg/Kg
- ^{13}C-LA (Linoleic acid: essential FA): 0.5 mg/kg
- ^{13}C-DHA (Docosahexaenoic acid, LC-PUFA): 0.1 mg/kg

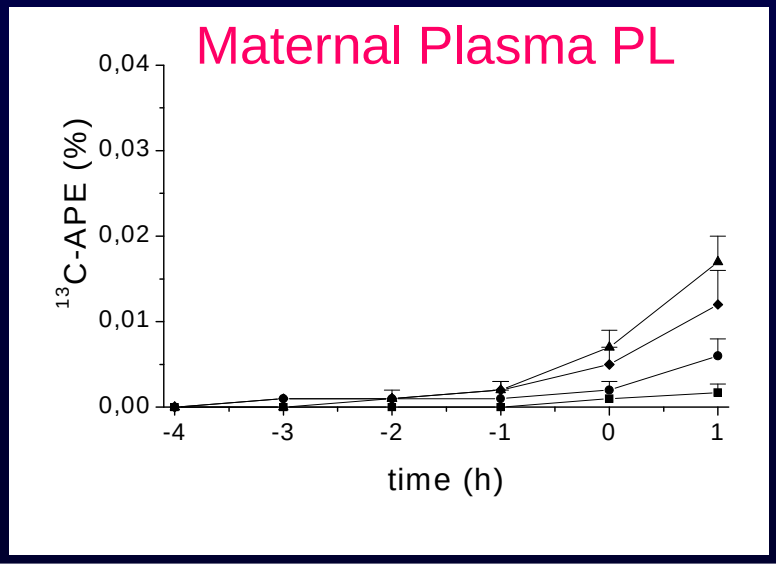
- Study 4 hours before cesarean section (n=4)
- Study 12 hours before cesarean section (n=11)

4h FA Tracer Study

Appearance of ^{13}C-FA enrichment in maternal plasma







No enrichment in Maternal Cholesterol Esters

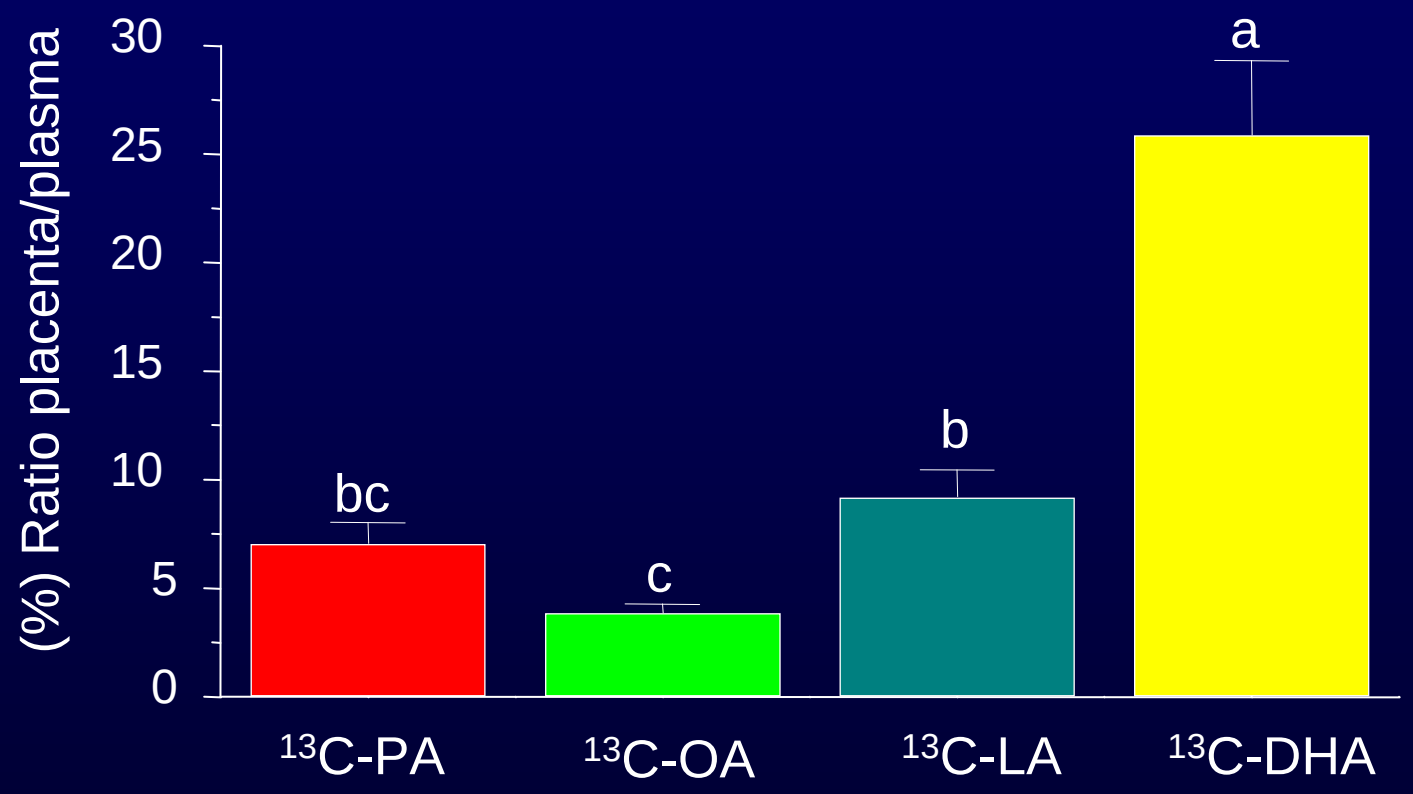
N=4

(Larqué et al. J. Lipid Res., 2003)

4h FA Tracer Study

Distribution of tracer between placenta and plasma (M ± SEM)

(Larqué et al. J. Lipid Res., 2003)



$$\text{(\%) Ratio Placenta/plasma} = \frac{\text{fatty acid concentration in placenta (µmol/g) * APE-placenta}}{\text{fatty acid concentration in plasma (µmol/ml) * APE-plasma}} \times 100$$

Design of 12h FA tracer Study

Subjects: 11 pregnant women, elective caesarian section

weight:	78 ± 8 kg	height:	161± 6 cm
age:	33 ± 4 years	gestation:	39.8 ± 1 wk

Tracer administration (12h before caesarean section)

Oral application of stable isotope tracer in a sugar cube:

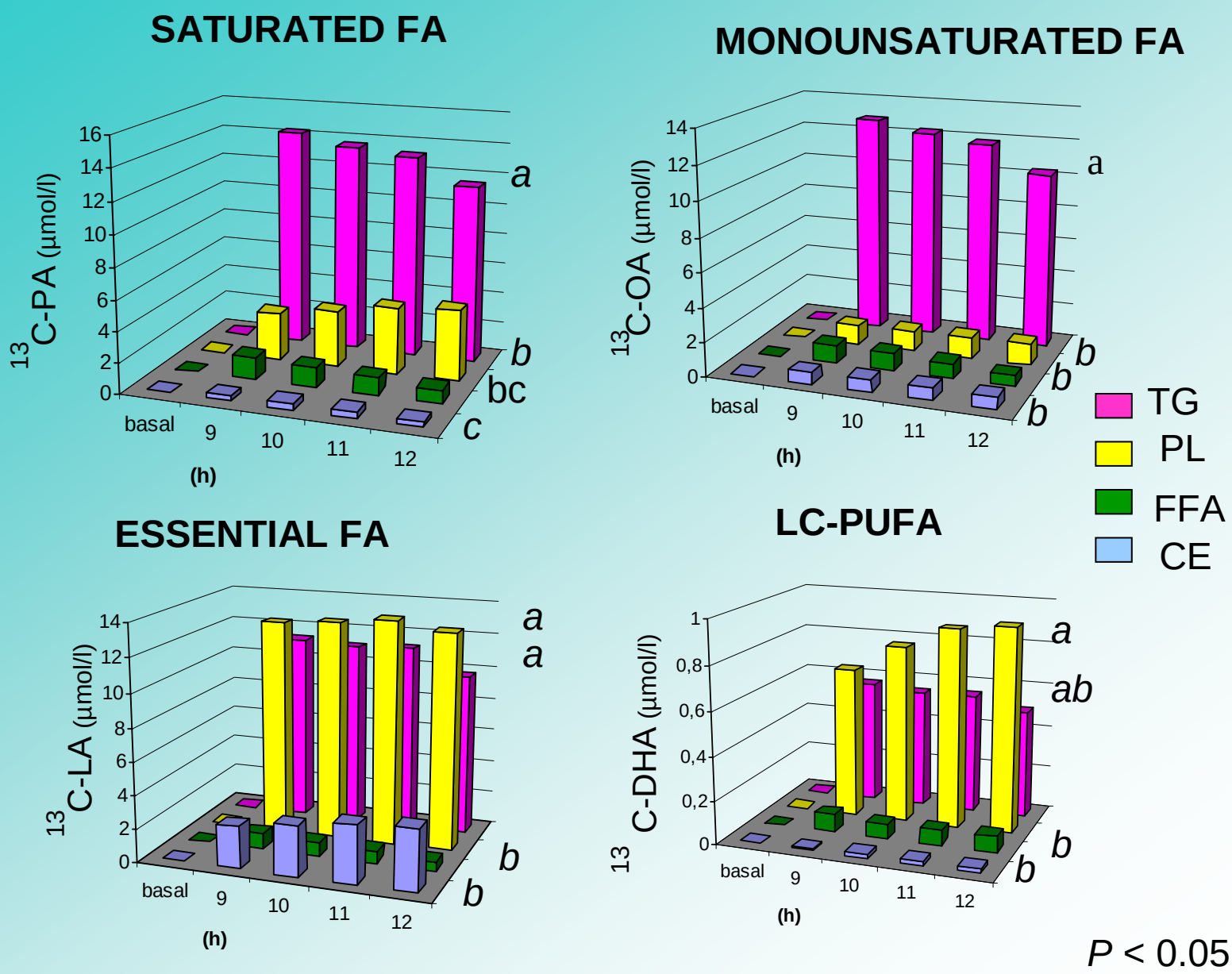
- palmitic acid (^{13}C-PA): 0.5 mg/kg
- oleic acid (^{13}C-OA): 0.5 mg/kg
- linoleic acid (^{13}C-LA): 0.5 mg/kg
- docosahexaenoic acid (^{13}C-DHA): 0.1 mg/kg

- Maternal blood: 0h, 9h, 10,11h, 12h (c-section), 13h
- Placenta collection and venous cord blood

^{13}C-enrichment of FA by gas chromatography combustion isotope ratio mass spectrometry (GC-C-IRMS)

13C-FA CONCENTRATION IN MATERNAL PLASMA

12h FA tracer study



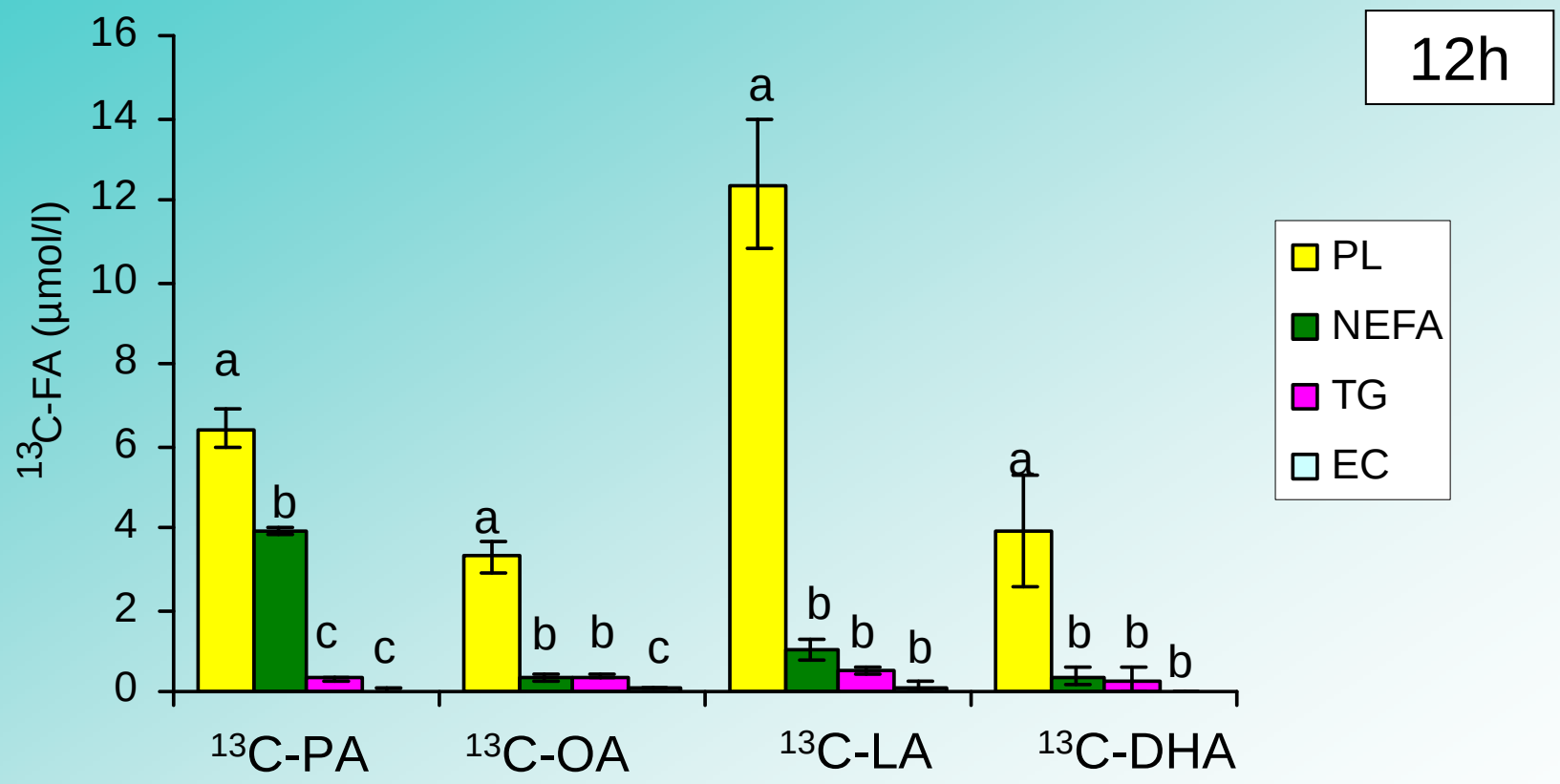
$P < 0.05$

13C-FA Concentration in Placenta

12h FA tracer study

^{13}C-FA enrichment in placental TG and NEFA tended to be high

Phospholipids constituted about 80-90% of FA in placenta

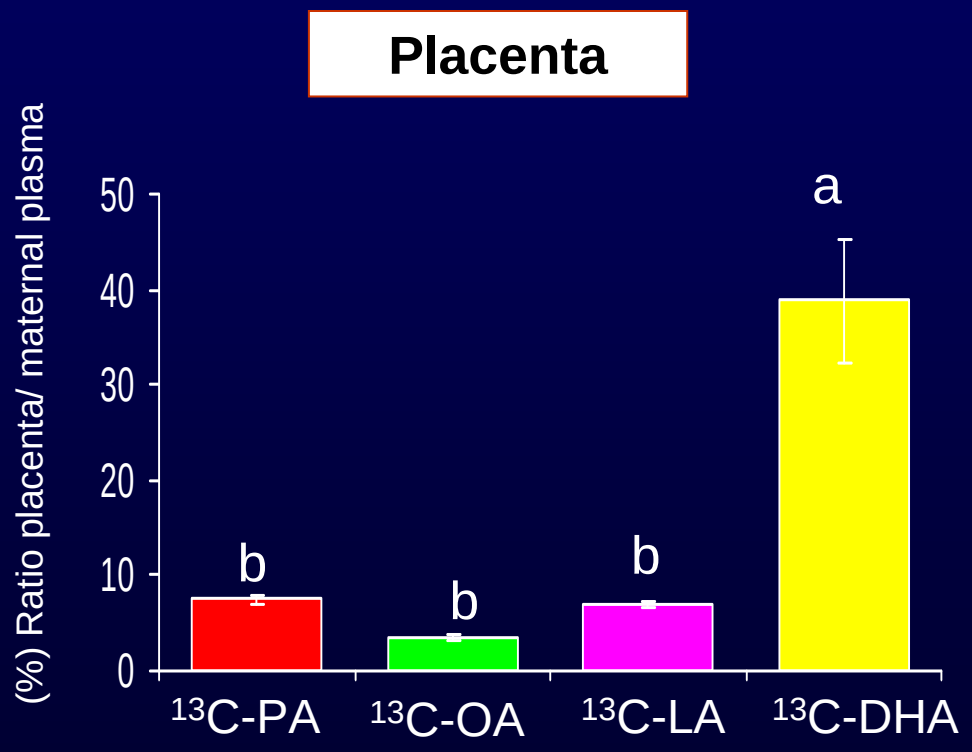


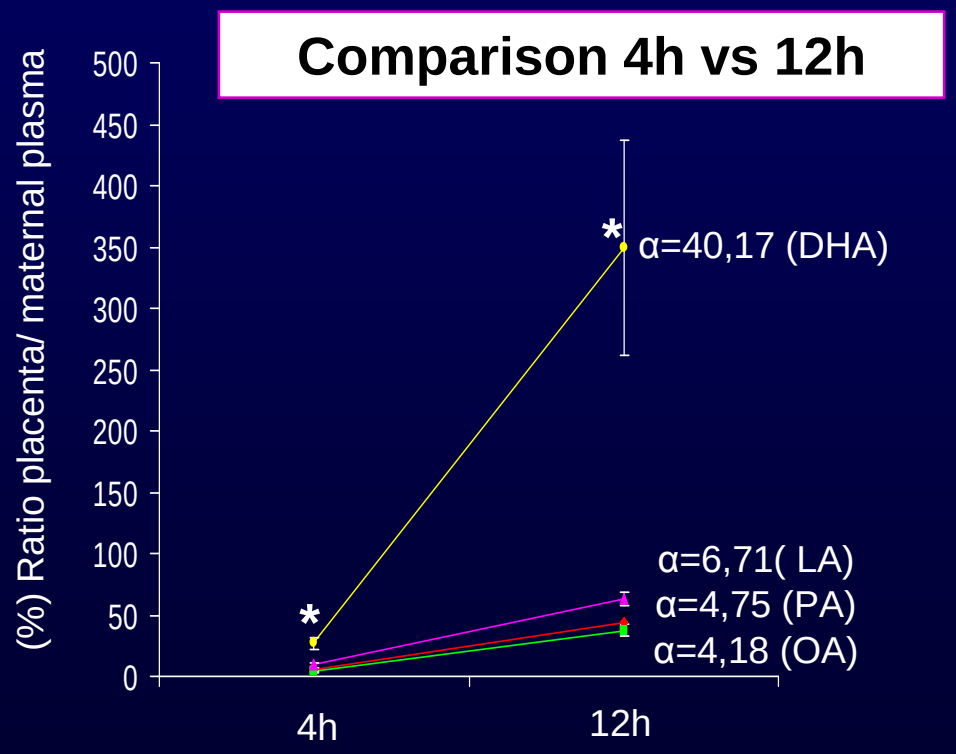
Mean ± SD, $P < 0.05$

12h FA tracer study

Distribution placenta/maternal plasma (M ± SEM)

(Gil-Sánchez, Larqué et al. Am. J. Clin. Nutr., 2010)





Different letters: P<0,05

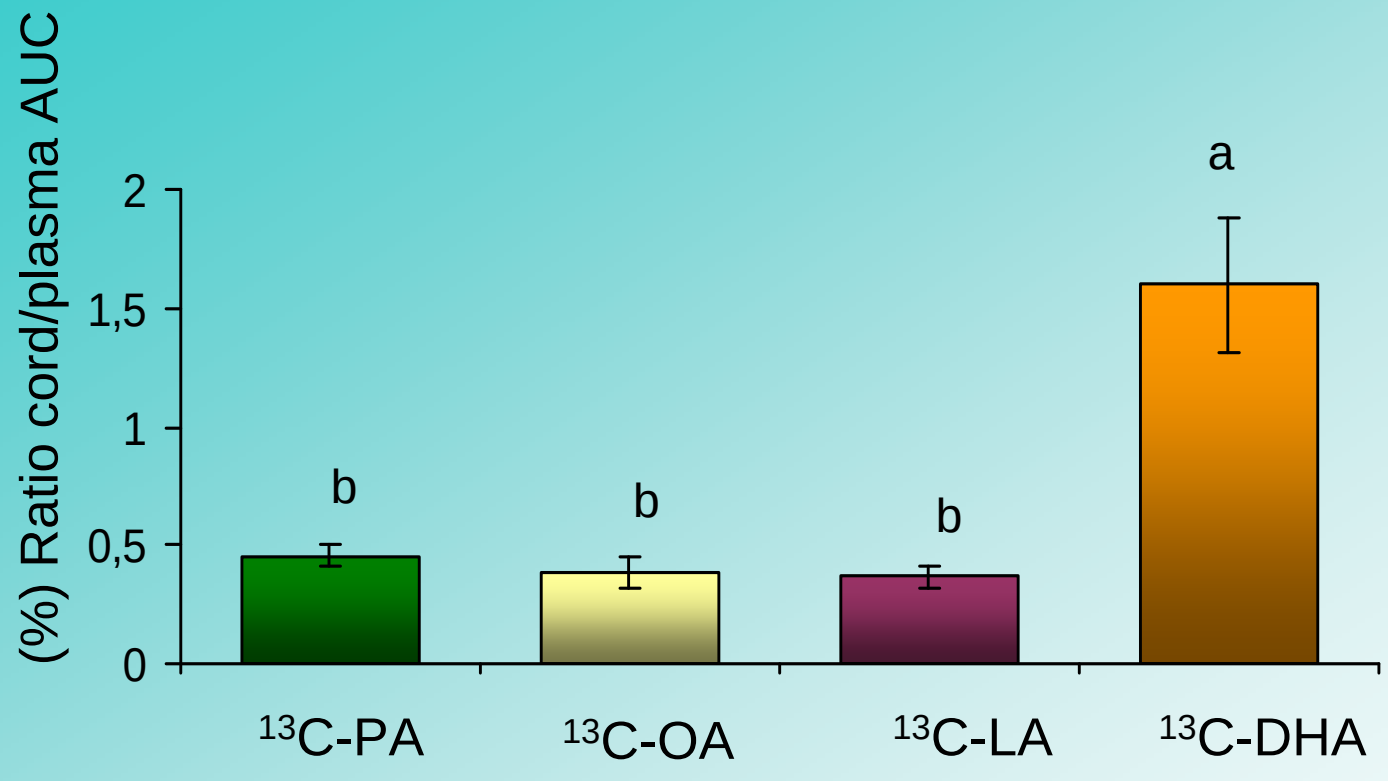
α = slope

* P<0,05

Distribution Cord/Maternal Plasma

12h FA tracer study

12h

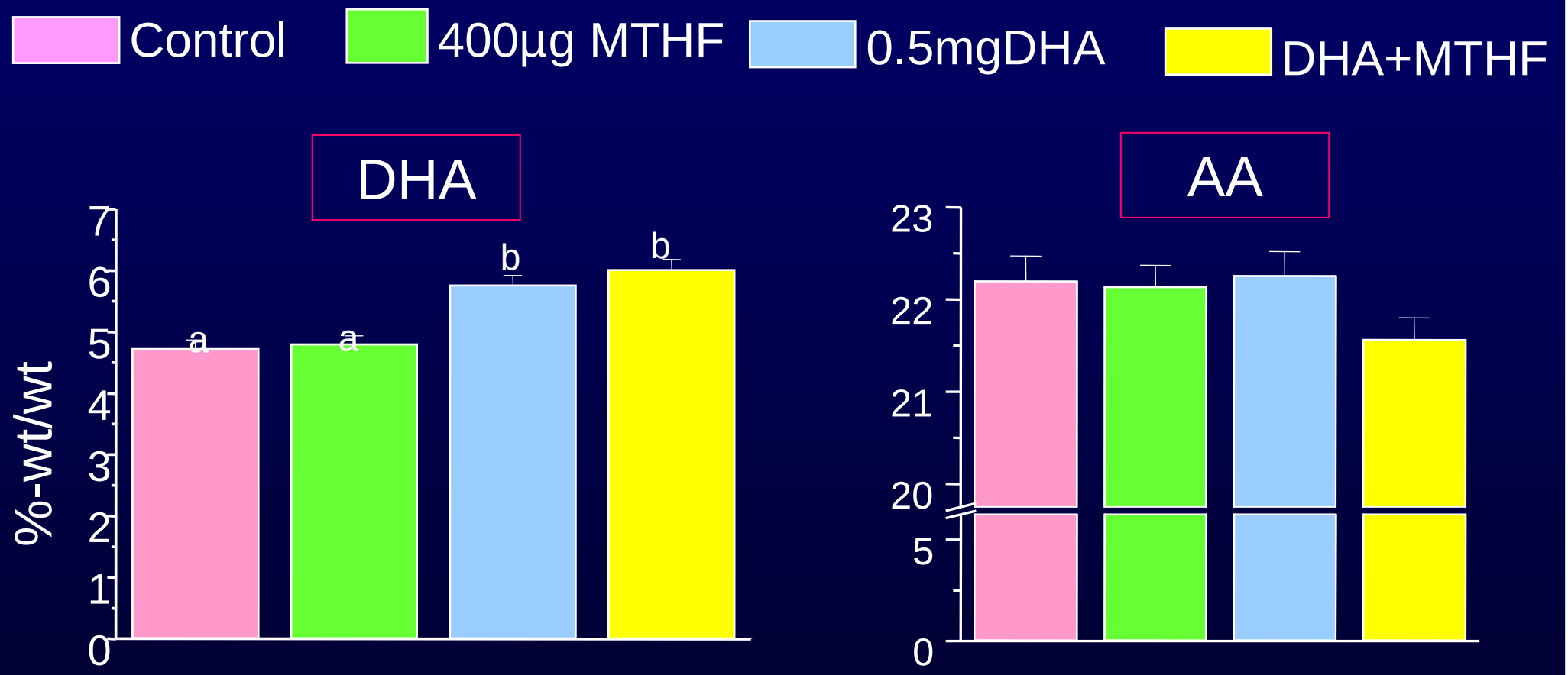


$$\text{(\%) Ratio Cord/plasma} = \frac{\text{FA concentration in cord (µmol/g) * APE-cord plasma}}{\text{AUC FA concentration in plasma (µmol/ml) * APE-mat. plasma}} \times 100$$

Mean ± SD, $P < 0.05$

PROYECTO NUHEAL: Placental PL

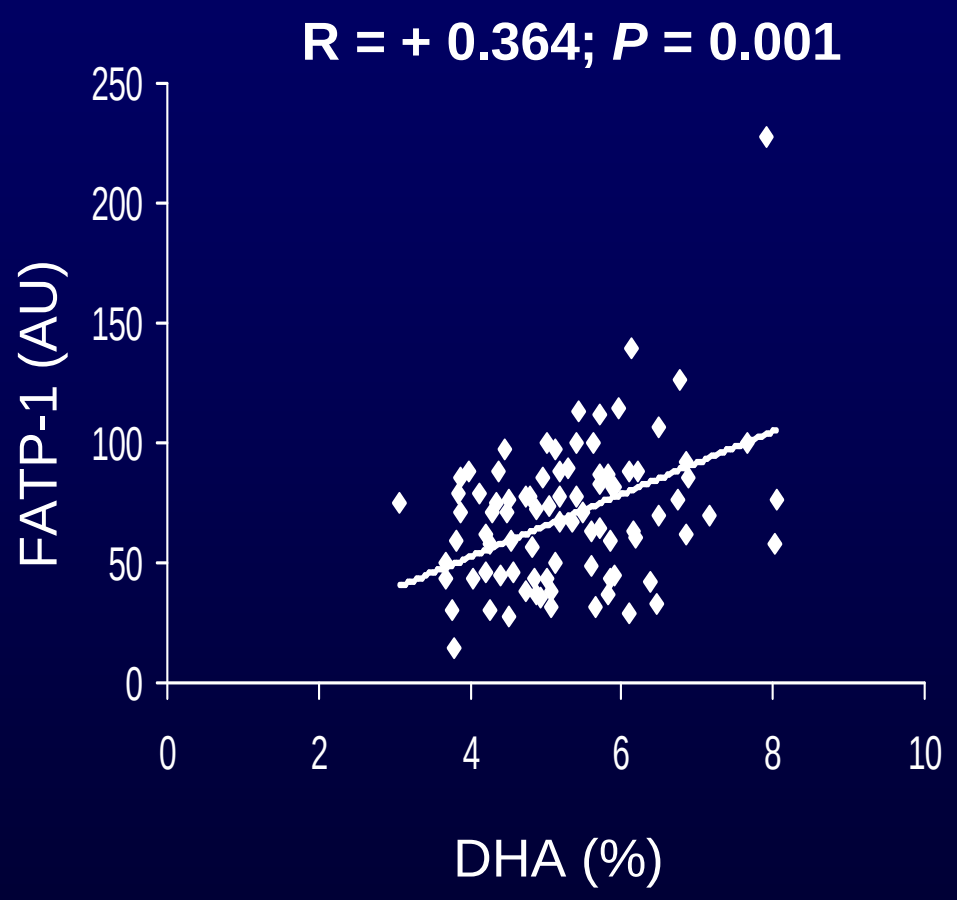
- Supplementation of 136 Spanish pregnant women from wk 20 to delivery

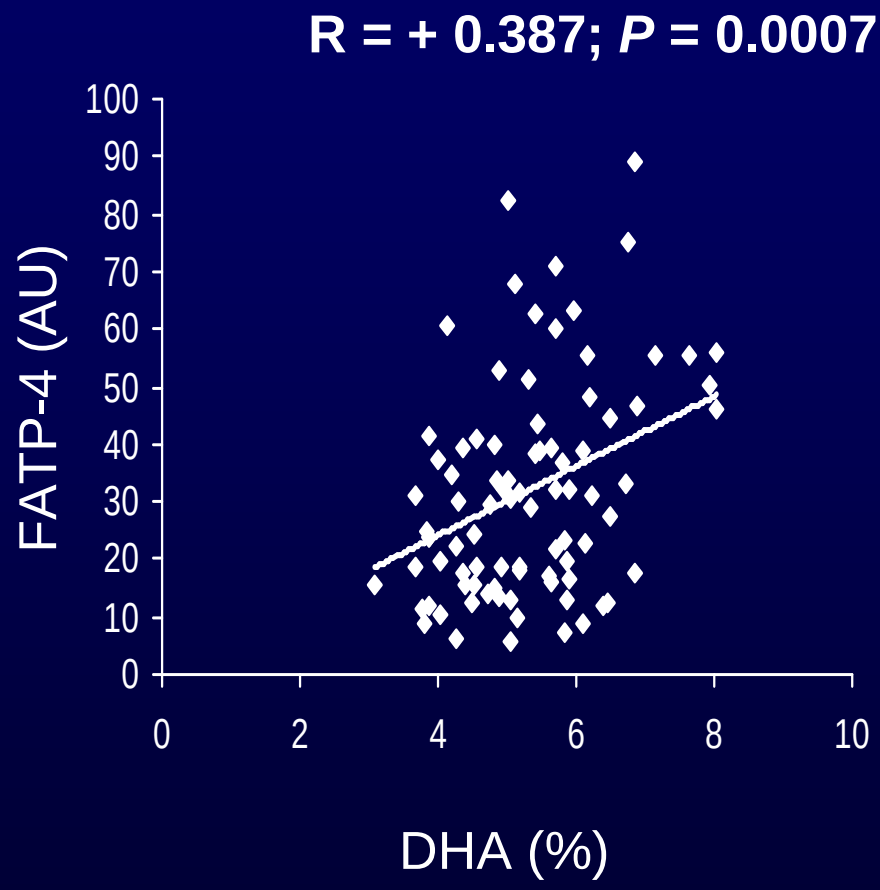


No significant changes in placental mRNA expression of FATP-1, FATP-4, FATP-6, FAT, FABPpm, H-FABP, B-FABP, A-FABP among the groups

NUHEAL: Correlations placental carriers-Placental PL

(Larqué et al. Am J Clin Nutr. 2006)

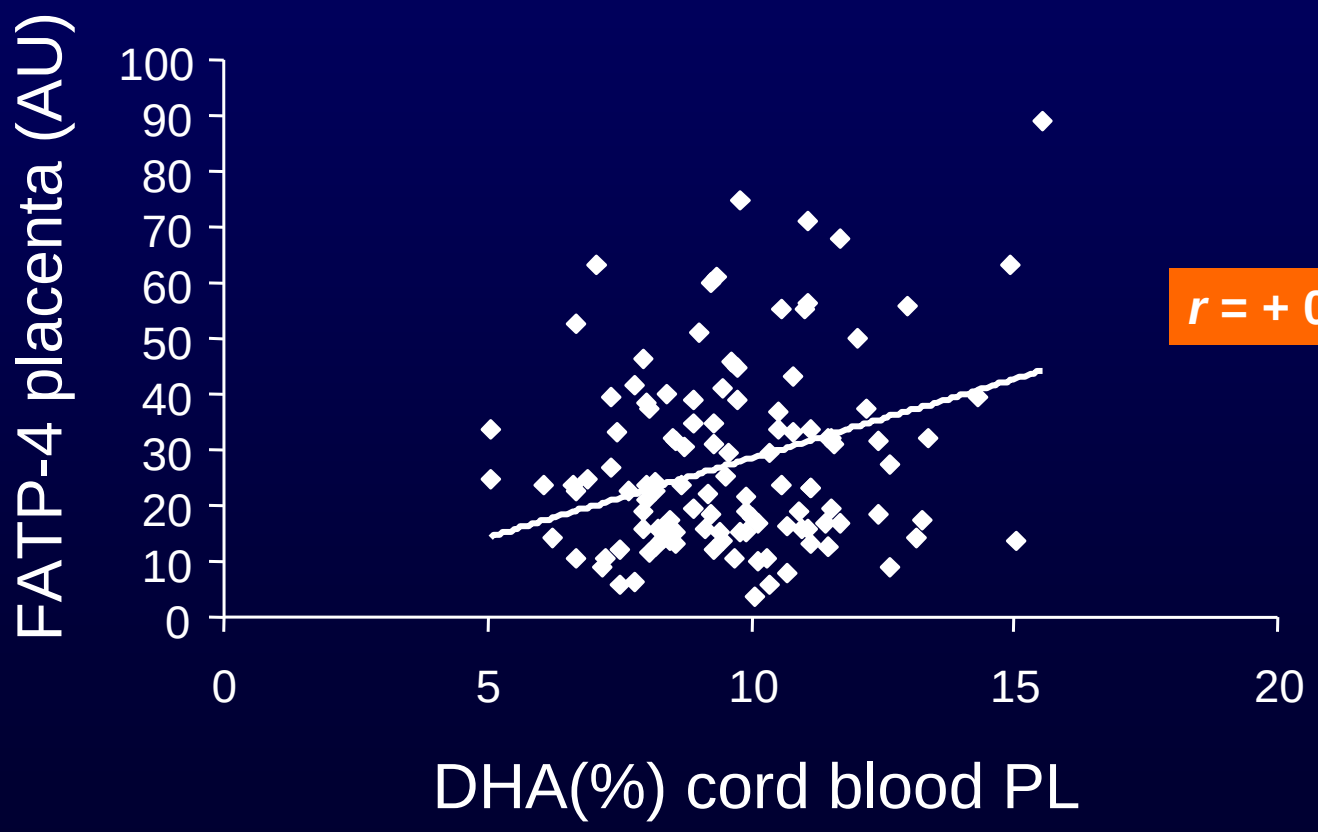




DHA (%) IN MATERNAL PLASMA PL CORRELATES WITH PLACENTAL PROTEINS FATP-1 (r=0.32, p=0.001) AND FATP-4 (r=0.23, p=0.012)

NUHEAL: Correlations placental FA carriers-Cord Plasma PL

(Larqué et al. Am J Clin Nutr. 2006)



r* = + 0.20; *P* = 0.032

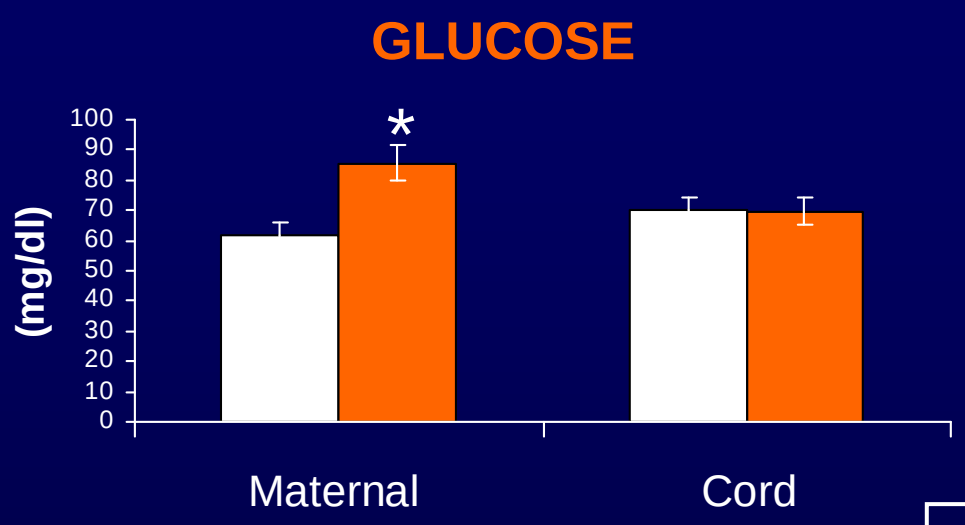
GESTATIONAL DIABETES MELLITUS

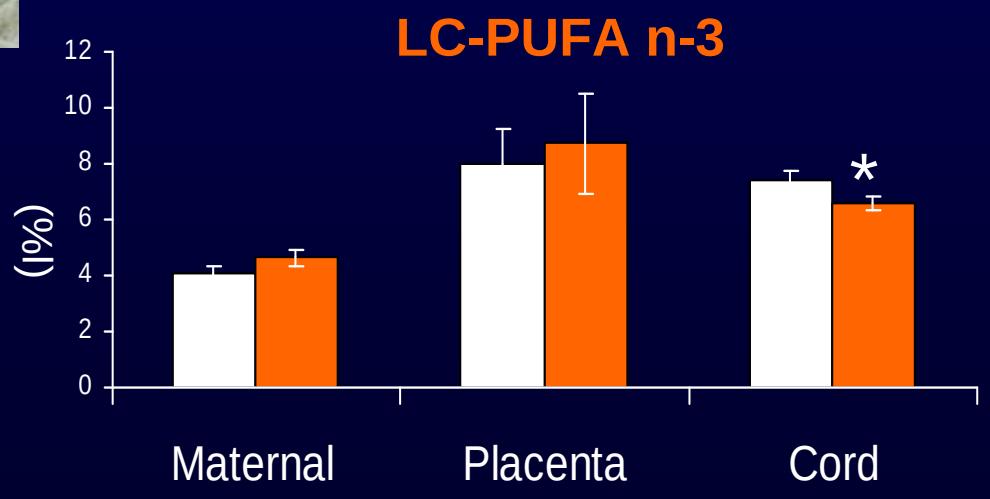
Normal plasma LC-PUFA in women with gestational diabetes mellitus, but low erytrocyte PL LC-PUFA in their babies (Wijendran et al. 2000)

Delayed brain maturity in these newborns compared to controls?

Pregestational or gestational diabetes mellitus was found to adversely affect attention span and motor functions of offspring at school age (Ornoy et al. 2001)

PREELIMINARY RESULTS



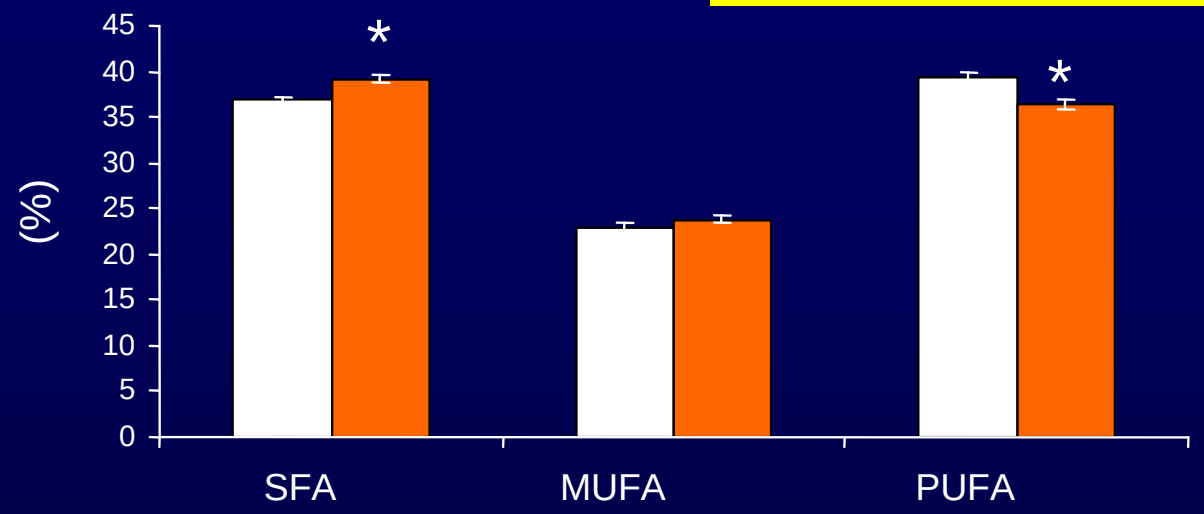


Control (n=22)

Gestational Diabetes (n=26)

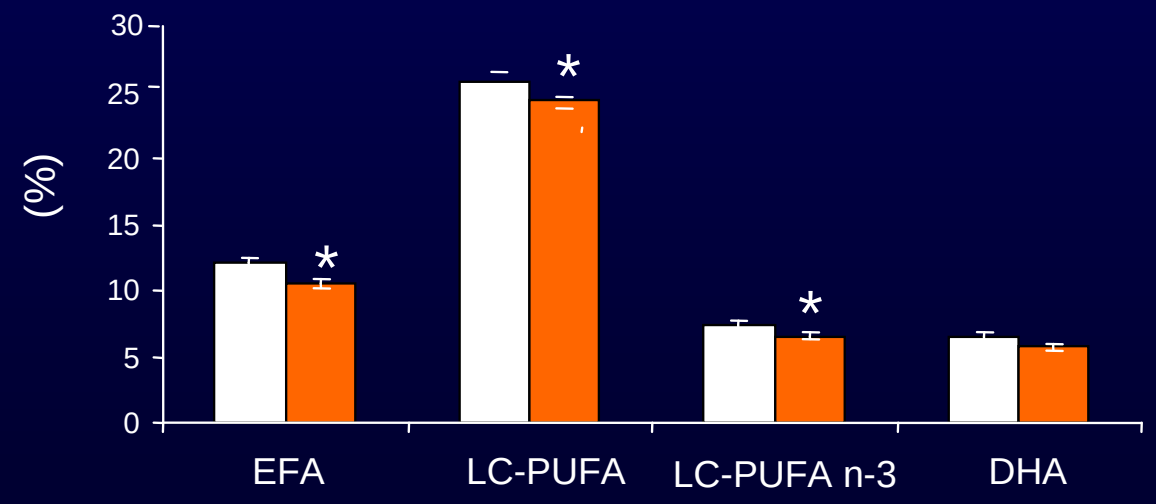
PREELIMINARY RESULTS

VENOUS CORD BLOOD



SATURATED (SFA)

EFA, LC-PUFA n-3



Control (n=22)

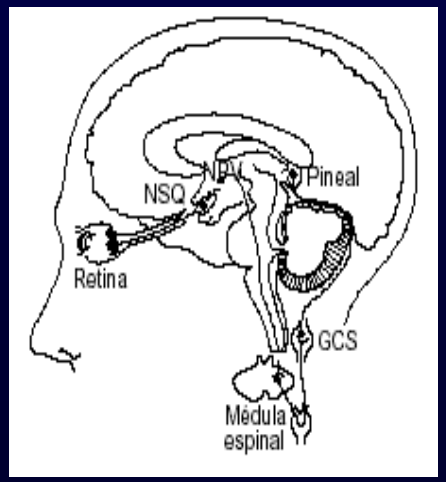
Gestational diabetes (n=26)

DHA *P* =0.062

PLACENTAL TRANSFER OF LABELED FA IN GESTATIONAL DIABETES ON GOING

NEURONAL DEVELOPMENT IN BABIES FROM GESTATIONAL DIABETES MOTHERS DURING THE 1º YEAR OF LIFE

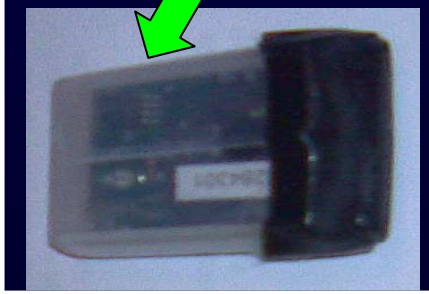
- Bayleys test (6 months and 12 months)
- Sleep/wake cycles by actigraphy methods
- Evaluation of circadian rhythms of temperature using temperature sensors.



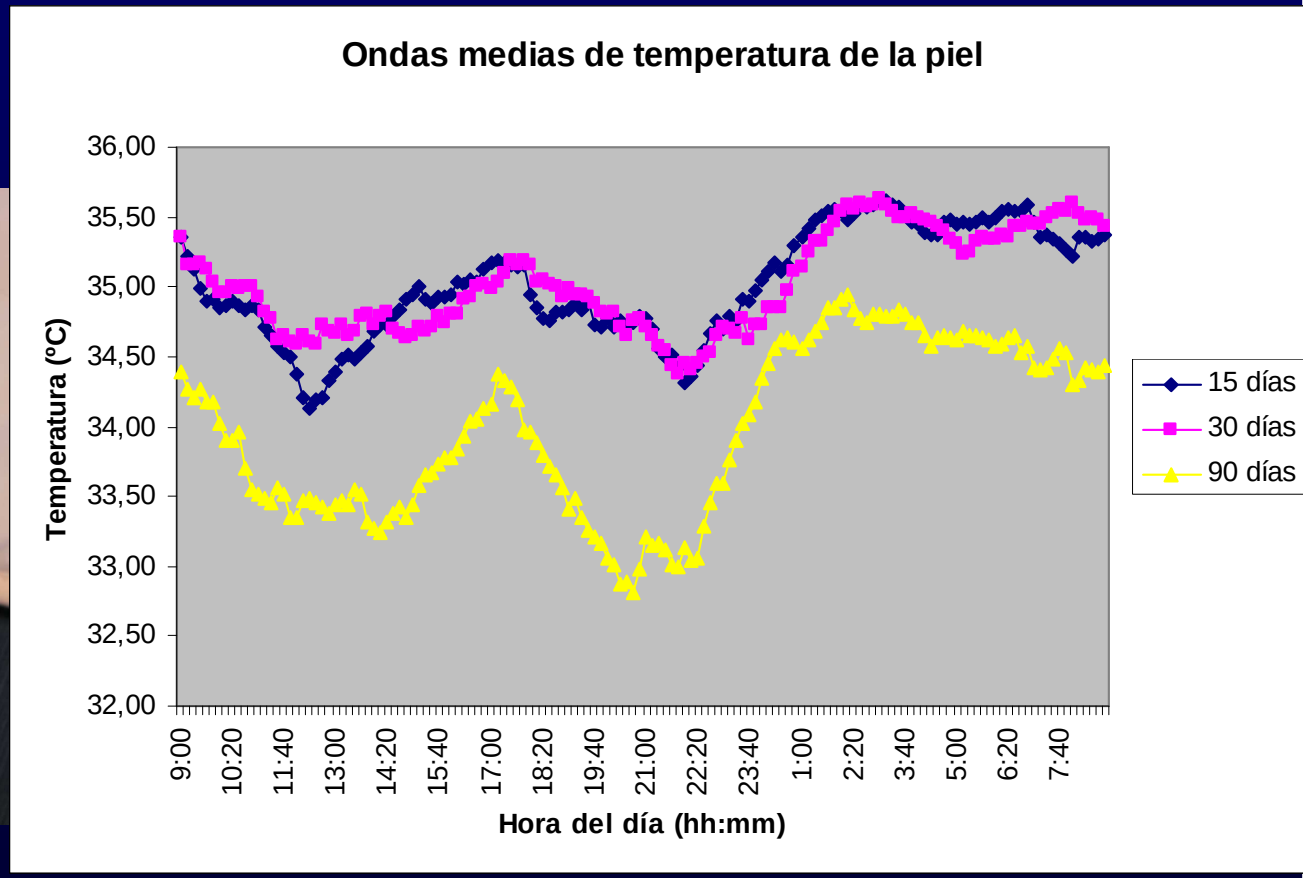
Institute for Infant Nutrition
Hero

EVOLUTION OF CHRONOBIOLOGICAL RHYTHMS

Temperature sensor



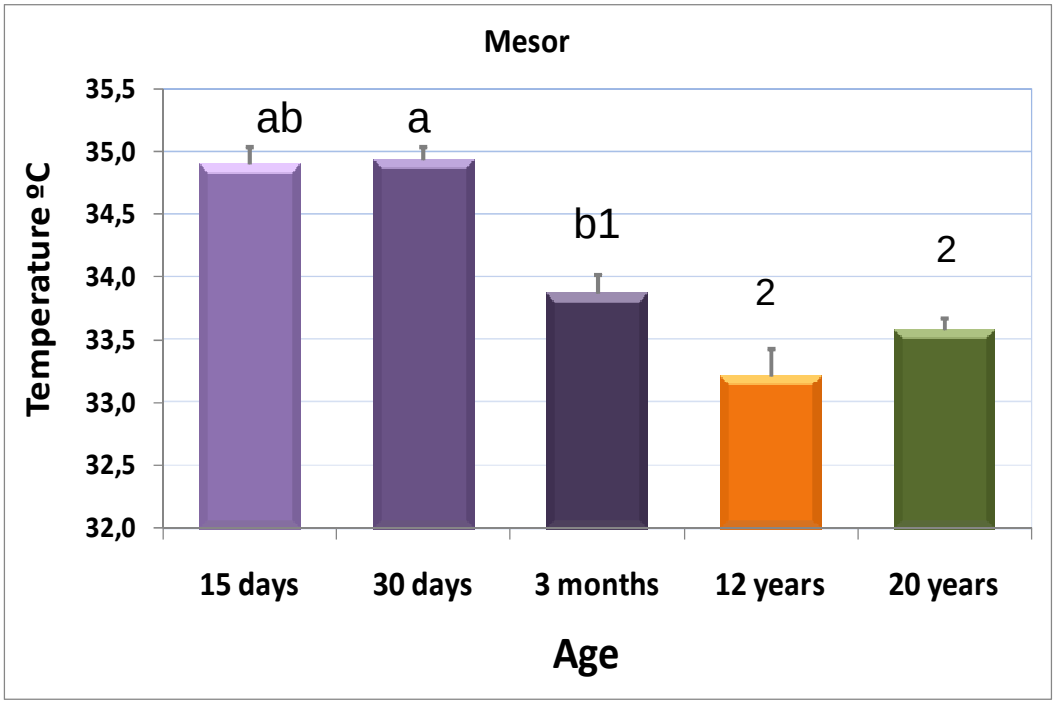
Actimeter



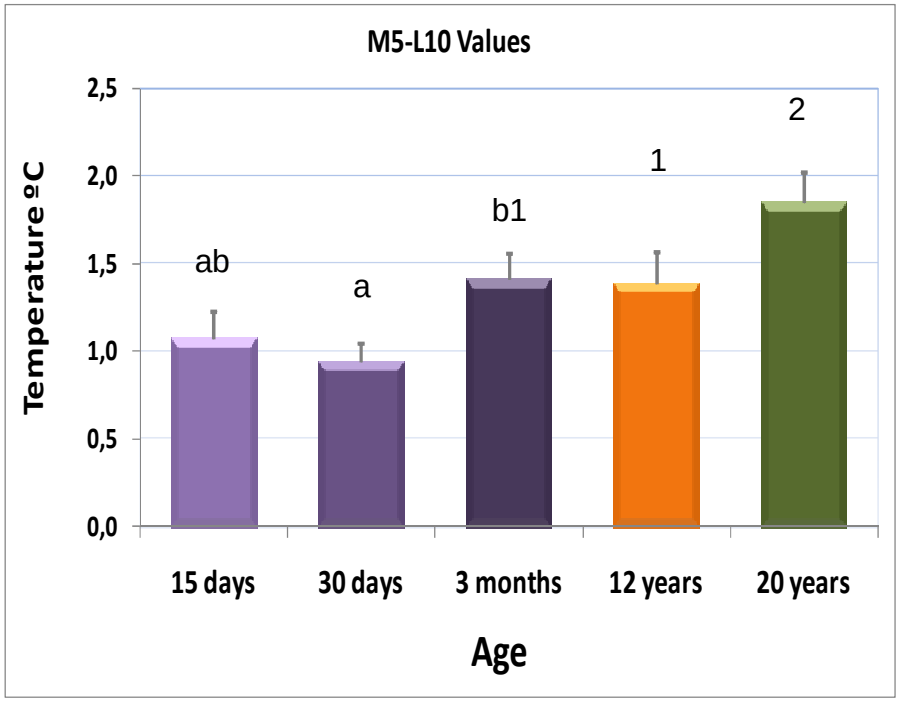
EVOLUTION OF CORE BODY TEMPERATURE

PREELIMINAR RESULTS

MEAN OF TEMPERATURE



AMPLITUD OF TEMPERATURE



Different letters indicate significant differences by repeated measures ANOVA (for 15 days, 30 days and 3 months comparisons). Different numbers indicate significant differences when comparing babies (3 months) with child and adult groups.

Sarabia et al. 2009. Acta Physiologica, 195 (667):101

Thank you for your kind attention!!!!

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THANK YOU !

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