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Journal
Lipids, 50(6)

ISSN
0024-4201

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Publication Date
2015-06-01

DOI
10.1007/s11745-015-4018-8

Peer reviewed

HHS Public Access

Author manuscript

Lipids. Author manuscript; available in PMC 2016 June 01.

Published in final edited form as:

Lipids. 2015 June ; 50(6): 565–573. doi:10.1007/s11745-015-4018-8.

Maternal High-Fat-Diet Programs Rat Offspring Liver Fatty Acid Metabolism

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Abstract

In offspring exposed *in utero* to a maternal diet high in fat (HF), we have previously demonstrated that despite similar birth weights, HF adult offspring at 6 months of age had significantly higher body weights, greater adiposity, and increased triacylglycerol (TAG) levels as compared to controls. We hypothesized that a maternal HF diet predisposes to offspring adiposity via a programmed increase in the synthesis of monounsaturated fatty acids in the liver and hence increased substrate availability for liver TAG synthesis. We further hypothesized that programmed changes in offspring liver fatty acid metabolism are associated with increased liver expression of the lipogenic enzyme stearoyl-CoA desaturase-1 (SCD-1). Female rats were maintained on a HF diet rich in monounsaturated fatty acids (MUFA) prior to and throughout pregnancy and lactation. After birth, newborns were nursed by the same dam, and all offspring were weaned to control diet. Plasma and liver fatty acid compositions were determined using gas chromatography/mass spectrometry. Fatty acid C16 desaturation indices of palmitoleic/palmitic and (vaccenic + palmitoleic)/palmitic and the C18 desaturation index of oleic/stearic were calculated. Liver protein abundance of SCD-1 was analyzed in newborns and adult offspring. Plasma and liver C16 desaturation indices were decreased in HF newborns, but increased in the adult offspring. Liver SCD-1 expression was increased in the HF adult offspring. These data show that the maternal HF diet during pregnancy and lactation increases offspring liver SCD-1 protein abundance and alters the liver C16 desaturase pathway.

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Conflict of interest The authors report no conflict of interest.

Keywords

Obesity; Monounsaturated fatty acid; Saturated fatty acid; Triglyceride; Stearoyl-CoA desaturase-1; Rat

Introduction

Obesity is a public health problem that affects more than one-third (35.8 %) of women [1]. Furthermore, obesity in pregnancy is an increasingly prevalent condition seen in one in five women [2]. The risk of pregnancy complications, including gestational diabetes, hypertension, preeclampsia, and cesarean delivery, is increased in obese women [3]. Moreover, obesity in the first trimester of pregnancy more than doubles the risk of childhood obesity [4].

The notion that the *in utero* environment programs obesity and obesity-associated disorders is supported by data from human and animal studies [5]. Initial experimental studies of fetal programming demonstrated that offspring exposed to maternal undernutrition during pregnancy are predisposed to developing adult obesity and metabolic syndrome, despite being born small-for-gestational age [6, 7]. Maternal over-nutrition, however, is perhaps more clinically relevant in today's Western society. Fetal exposure to various indicators of maternal overnutrition, such as the increased pre- or early pregnancy body mass index, gestational weight gain, or gestational diabetes, increases the risk of offspring obesity and metabolic syndrome in humans and animals [8–12].

Mechanisms for programmed obesity likely involve perturbations in fatty acid metabolism that promote fatty acid availability and TAG synthesis for fat storage. Specifically, monounsaturated fatty acids (MUFA), which are the preferred substrate for TAG synthesis, are a product of endogenous (*de novo*) synthesis from saturated fatty acid (SFA) precursors [13, 14]. The conversion of SFA to MUFA is catalyzed by the lipogenic enzyme, stearoyl-CoA desaturase enzyme-1 (SCD-1), which introduces a double bond at the Δ9 position [15, 16]. The product-to-precursor ratio of MUFA to SFA is the desaturation index (DI) and directly reflects SCD-1 expression/activity [17]. Highly abundant SFA are 16:0 (palmitic) and 18:0 (stearic), which when desaturated produce MUFA 16:1(n-7) (palmitoleic) and 18:1(n-9) (oleic), respectively. Additionally, direct elongation of palmitoleic acid results in the MUFA 18:1(n-7) (vaccenic acid). Hence, the DI of palmitoleic/palmitic and (vaccenic + palmitoleic)/palmitic represent activity of the 16-carbon (C16) desaturation pathway, whereas oleic/stearic represents activity of the 18-carbon (C18) desaturation pathway. Notably, both the DI and SCD-1 activity correlate with measures of adiposity [18–21].

We established a model of maternal obesity by feeding dams a high-fat diet prior to and during pregnancy, which results in normal-birth-weight newborns that become obese with increased body weights and body fat content both during and following nursing [10, 11]. We hypothesized that a maternal HF diet results in offspring with increased plasma and liver DI indicative of increased liver synthesis of MUFA substrates for TAG synthesis. We further hypothesized that a maternal HF diet is associated with upregulated liver SCD-1 enzyme activity in the offspring.

Materials and Methods

The study was approved by the Animal Care Committee at the Los Angeles Biomedical Research Institute at Harbor-University of California, Los Angeles, and was conducted in accordance with guidelines provided by the American Accreditation Association of Laboratory Care and the Public Health Service Policy on Humane Care and Use of Laboratory Animals. The rat model of a maternal HF diet used in the current study has been previously described [10, 11]. In brief, 3-week-old female Sprague-Dawley rats (Charles River Laboratories, Hollister, CA) were housed in a facility with constant temperature and humidity and a controlled 12:12 h light/dark cycle. The rats were randomly assigned to either a diet high in fat (HF 60 % kcal fat, 20 % kcal protein, 20 % kcal carbohydrate, purified diet 58Y1, New Brunswick, NJ, USA; $n = 5–6$) to induce obesity or a normal control diet (control 10 % kcal fat, 20 % kcal protein, 70 % kcal carbohydrate, purified diet 58Y2; $n = 5–6$). The specific fatty acid composition of each diet is given in Table 1. At 11 weeks of age, rats were mated and continued on their respective diets during pregnancy and lactation.

Male Offspring

After birth at 1 day of age (P1), litters were culled to 8 pups (4 males and 4 females) per dam to standardize nursing. All pups were nursed by their respective HF or control dams until 3 weeks age (P21). At the end of this lactation period, offspring from both groups were weaned to the control diet. We elected to study male offspring only because females would have required estrus assessment, since estrogen is known to affect adiposity and lipid metabolism [22]. Body weights were recorded at P1 (newborns) and at 6 months of age (adults). In addition, at 6 months of age, noninvasive body composition measurements were obtained using a dual-energy X-ray absorptiometry scan system with a software program for small animals, and the percentage of body fat was determined (QDR 4500A; Hologic, Bedford, MA).

Blood and Tissue Collection

Maternal blood was obtained at term (gestational age E20) via tail bleed, after removal of food 1 h prior. Excess P1 male pups during litter culling were euthanized by decapitation and blood pooled per litter. Male offspring at 6 months age were anesthetized by 5 % isoflurane/2 % oxygen by mask and blood collected via cardiac puncture. Following this, animals were euthanized by an overdose of pentobarbital (200 mg/kg i.p.), liver tissue collected, snap-frozen in liquid nitrogen and stored at −80 °C until analysis.

Gas Chromatography/Mass Spectrometry (GC/MS)

The extraction of total fatty acids (including those from phospholipids, TAG, cholesterol esters, and free fatty acids) from plasma and liver tissue was performed, as previously described [21]. Tissue samples (~15 mg liver) or plasma samples (30 μl) were saponified overnight in equal volumes (100 μl) of 200-proof ethanol and 30 % KOH (w/v) on a 70 °C heating block. HCl was subsequently added to acidify the samples, followed by extraction of fatty acids three times with petroleum ether and air drying. Samples are stored under a vacuum until derivatization. Fatty acids were then derivatized as methyl esters with 0.5 N

methanolic HCl and dried under a nitrogen stream. Reconstitution of the extract with hexane allowed for analysis using GC/MS. Heptadecanoic acid-d3 (tri-deuterated) was added as an internal standard to each sample.

GC/MS analysis was run on a Hewlett-Packard model 5973 selective mass detector connected to a model 6890 GC. SFAs (palmitic, stearic), MUFAs (palmitoleic, oleic, vaccenic), and polyunsaturated fatty acids (PUFAs; linoleic, α-linolenic, arachidonic, eicosapentaenoic, docosahexaenoic) were separated on the GC with a Bpx70 column (30 m length, 250 μm diameter, 0.25 μm film thickness, from SGE, Inc., Austin, TX). GC conditions were as follows: helium flow rate, 1 ml/min; initial oven temperature, 150 °C, which was programmed to increase at 3 °C/min to a final temperature of 221 °C. Under such conditions, expected retention times (by comparison to known standards) for palmitic, palmitoleic, stearic, oleic, and vaccenic acids were 6.1, 6.6, 8.9, 9.4, and 9.5 min, respectively. Mass spectra of fatty acids were acquired to confirm compound identity using electron impact ionization in linear mode.

If a peak was too low for integration or the mass spectrum of a peak at the expected retention time did not show characteristic ions, then the fatty acid was considered undetectable. All samples were run in triplicate, and the relative proportion of any given fatty acid was presented as a molar percent of select fatty acids that are related to or may influence *de novo* synthesis and desaturation (myristic, palmitic, palmitoleic, stearic, oleic, vaccenic, linoleic, and arachidonic acids). α-Linolenic, eicosapentaenoic, and docosahexaenoic acids were not detected in nearly all the samples, and, if present, each comprised <0.2 % of the total abundance and was therefore not included.

Desaturation Index (DI)

After determination of the relative proportions of fatty acids through the integrated areas under the gas chromatogram peaks, the DI was determined by calculating the ratio of MUFA to the corresponding SFA: palmitoleic/palmitic, (vaccenic + palmitoleic)/palmitic, or oleic/stearic.

Protein Extraction and Western Blotting

Liver protein was extracted in radioimmunoprecipitation assay buffer (1×) containing protease inhibitors (HALT cocktail; Pierce, Rockford, IL), and the total protein concentration in the supernatant was determined using a bicinchoninic acid assay (BCA kit; Pierce, Rockford, IL). Western blotting was performed as previously described [23], using an antibody against stearoyl-CoA desaturase-1 (SCD-1; sc-14720 Santa Cruz Biotechnology, TX, USA), primary antibody 1:500, and secondary antibody 1:2000. The depicted bands had the expected molecular weight.

Statistical Analysis

For all offspring studies, six males were studied per group (one male from each of six litters), with the exception of newborn plasma where blood was pooled from all excess male pups in each litter. Differences between the HF and control diet groups were compared using

unpaired Student's *t* test. *P* values ≤0.05 were considered significant, and values are expressed as mean ± standard error (SE).

Results

Triacylglycerol Levels

At E20, HF dams had comparable plasma TAG levels to the control dams. However, plasma TAG levels in HF newborns were significantly lower than in controls, whereas in HF adult males they were significantly higher (Fig. 1).

Plasma 16-Carbon Pathway Fatty Acids

HF dams had significantly lower proportions of palmitic and palmitoleic fatty acids. HF dams also demonstrated lower vaccenic acid, which is made by chain elongation of palmitoleic acid [24]. Unlike the HF dams, the HF newborns at 1 day of age showed no change in plasma palmitic acid. Similar to the HF dams, the HF newborns exhibited reduced proportions of plasma MUFA (palmitoleic and vaccenic acids) as compared to control newborns (Table 2). In contrast to HF dams and male newborns, the adult offspring had significantly higher plasma abundance of MUFA (palmitoleic and vaccenic acids) than controls (Table 2).

Plasma 18-Carbon Pathway Fatty Acids

In HF dams, male newborns, and adult offspring, the abundance of SFA (stearic) and MUFA (oleic acid) was comparable to their respective controls (Table 2).

Plasma Desaturation Index

Consistent with their C16 and C18 fatty acid profiles, both HF dams and HF newborns had lower C16-related plasma DI (palmitoleic/palmitic; vaccenic + palmitoleic/palmitic ratios) as compared to controls. However, the C18-related plasma DI (oleic/stearic) was similar for both groups. In contrast, adult HF males exhibited increased C16- and C18-related DI (Fig. 2).

Liver 16-Carbon Pathway Fatty Acids

The HF newborns had lower liver palmitoleic and vaccenic acid levels, although proportions of SFA palmitic were unchanged compared to controls. The HF adult male offspring showed increased proportions of vaccenic acid only compared to controls (Table 3).

Liver 18-Carbon Pathway Fatty Acids

The HF newborns and HF adults showed no changes compared with controls (Table 3).

Liver Desaturation Index

The changes in liver DI were similar to the changes in plasma DI in the HF male offspring. In HF newborns, liver C16-related DI were lower (palmitoleic/palmitic and vaccenic + palmitoleic/palmitic) than in controls, although there was no difference in the C18-related

DI (oleic/stearic). In HF adult males, liver C16-related DI was higher than in controls, and again no changes were seen in C18-related DI (Fig. 3).

Liver Protein Abundance of SCD-1

Compared with control newborns, HF newborns exhibited a trend toward decreased protein abundance of liver SCD-1. However, HF adult male offspring demonstrated significantly higher liver SCD-1 expression than controls (Fig. 4).

Discussion

The current study demonstrates that exposure to a maternal HF diet rich in MUFA programs male offspring fatty acid metabolism. We have previously published data that showed that at the end of the nursing period, offspring of the obese dams used in the current study exhibited increased adiposity and developed metabolic syndrome [10]. Specifically, the HF dams were significantly heavier prior to mating (29 %), at E20 (14 %) and at the end of lactation (12 %) as compared to controls [10, 11]. Despite increased maternal body weight, the HF newborns had similar birth weight as the controls (7.3 ± 0.1 *vs.* 7.4 ± 0.2 g). However, with continued nursing by HF dams, the HF male offspring began showing accelerated growth, and, importantly, when weaned to a normal diet, the HF male offspring continued to show a significant weight increment. As adults, the HF males were markedly heavier (823 ± 40 *vs.* 627 ± 20 g, $P < 0.05$) with greater adiposity (21 %) than controls [10, 11]. Consistent with this phenotype, the principal findings of the present study demonstrate altered fatty acid metabolism, including specific changes in C16-related DI in plasma/liver of the same group of HF dams and their male newborn and adult offspring. Namely, (1) HF obese dams have decreased plasma DI, (2) HF male newborns exhibit parallel changes to obese dams with lower plasma and liver DI, despite normal birth weight, and, most importantly, (3) obese HF adult male offspring demonstrate increased plasma and liver DI with upregulated liver SCD-1 protein abundance.

The mechanism accounting for the paradoxically reduced plasma DI in obese dams and their newborn male offspring is unknown, but may, at least in part, result from the composition of the maternal HF diet. High-fat diets are usually low in carbohydrates. Carbohydrates are potent stimulators of *de novo* fatty acid synthesis, which in turn provides substrates to promote SCD-1 desaturation [25]. Therefore, animals exposed to low carbohydrates in our study may conversely demonstrate decreased desaturation indices. Also noteworthy is the fact that the HF diet is highest in palmitic acid and MUFA; however, the maternal plasma abundances of palmitic and oleic acids are proportionally lower or unchanged, suggesting that contributions from endogenous fatty acid synthesis and modification impact the overall composition. Therefore, the plasma fatty acid profile is not only a reflection of dietary intake. Future studies may be done to determine whether the fatty acid profiles observed in this study are specific to a diet high in MUFA and SFA versus other types of fats (e.g., predominantly SFA or polyunsaturated fatty acids).

Despite the increased dietary supply of both SFA (substrates for SCD-1) and MUFA (products of SCD-1), the maternal HF diet selectively affected the liver C16 desaturase pathway in the HF dams and their newborn male offspring. Since the C16 DI is a good index

of liver SCD-1 activity [17], these data may reflect a specific effect of maternal HF diet on *de novo* lipogenesis, since the majority of C16 MUFA (palmitoleic) is obtained via *de novo* lipogenesis, whereas C18 MUFA (oleic) is abundant in dietary sources [18, 26]. The greater amount of SFA and MUFA in the HF diet compared with the control diet in the present study may have affected the desaturase activity, since increased proportions of C18 MUFA (oleic) have been shown to decrease C16 and increase C18 DI in healthy humans [18]. Along with decreased liver DI in HF newborns, there was a corresponding trend ($P = 0.07$) toward decreased liver SCD-1 expression. However, the effect of an HF diet during pregnancy on maternal liver SCD-1 expression is unknown, as we were unable to sacrifice the dam at the end of pregnancy.

Notably, not only were the DI profiles of HF newborns similar to those of the HF obese dams, but the plasma DI profiles in HF newborns also mirrored their liver profiles, consistent with previous studies indicating that plasma fatty acid composition reflects liver fatty acid composition [17, 27]. Further studies are required to determine whether plasma DI profiles may provide useful clinical information as biomarkers for altered liver newborn fatty acid metabolism. In contrast, the present results suggest that birth weight is neither a good indicator of underlying metabolic alterations nor a good predictor of future adiposity in male offspring exposed to an HF diet *in utero* [10, 28].

Several studies have confirmed that exposure to a maternal HF diet during pregnancy may program adult offspring obesity, high TAG levels and insulin resistance [10, 28–30]. However, few mechanistic studies have addressed the role of altered fatty acid metabolism in the underlying mechanism of programmed obesity. In adults, fatty acid DI and SCD-1 activity have been shown to positively correlate with lipogenesis and adiposity [16, 21, 31, 32]. In the current study, despite being weaned to the control diet and having a suppressed C16 desaturase pathway at birth, the HF male offspring developed increased plasma and liver DI, increased liver SCD-1 expression, and obesity as adults. Studies in SCD-1-deficient mice suggest that *de novo* production of MUFA from SFA is necessary for the production of liver TAG, which are subsequently directed for use in adipose lipid storage [13, 31, 33]. Although we did not measure liver TAG in our study, other studies of maternal high-fat diets have shown increased liver TAGs in the offspring as early as ages day 1 and day 10 [34, 35]. Hence, increased *de novo* production fatty acids and their storage as TAG may contribute to the development of obesity in this model of programming by maternal HF diet [16, 21, 31, 32]. Dietary fat content and composition affect the composition of lipids secreted in rats' milk [36–38], which may contribute to the programmed offspring phenotype [10, 11]. We have previously shown increased adiposity and high TAG levels in 24-week-old rats that were exposed to a maternal HF diet regardless of whether the exposure to an HF diet occurred during pregnancy, during lactation, or both [10]. Whether offspring fatty acid metabolism is affected by the dams' milk composition in the current study is unknown.

In HF adult male offspring, the proportions of C16-related MUFA, their plasma and liver DI (palmitoleic/palmitic and vaccenic + palmitoleic/palmitic), and notably liver SCD-1 expression were all higher than in controls. These data are consistent with previous studies that demonstrated developmental programming of offspring fatty acid metabolism by altered

maternal nutrition during pregnancy [32, 39]. Maternal obesity is now the most common pregnancy comorbidity encountered in the clinical setting. The present study demonstrates that exposure to a maternal diet high in fat during pregnancy and nursing programs increased liver SCD-1 activity and increased plasma and liver C16 desaturase pathway in the adult male offspring, providing increased MUFA for TAG synthesis. Furthermore, perturbations in fatty acid metabolism were evident prior to the onset of obesity in our model. Further studies are required to determine whether plasma fatty acid DI may be used as an early marker of altered liver fatty acid metabolism to assist in the identification of offspring that may be at risk of increased adiposity in adulthood, offering the potential for both obesity intervention and prevention.

Acknowledgments

We thank Stacy Behare for her assistance in animal husbandry and tissue retrieval. We are grateful to Dr. Wai-Nang Paul Lee for his support and guidance with fatty acid analysis. This work was supported by the National Institutes of Health Grants R01DK081756 and R01HD054751. Fatty acid analyses were performed at the Biomedical Mass Spectrometry Facility, supported by UCLA CTSI Grant UL1TR000124, at the Los Angeles Biomedical Research Institute at Harbor-UCLA.

Abbreviations

SCD-1	Stearoyl-CoA desaturase-1
HF	High fat
SFA	Saturated fatty acid
MUFA	Monounsaturated fatty acids
PUFA	Polyunsaturated fatty acids
DI	Desaturation index
E20	Embryonic day 20
P1	1 Day of postnatal age
P21	3 Weeks postnatal age
GC/MS	Gas chromatography/mass spectrometry
KOH	Potassium hydroxide
HCl	Hydrochloric acid
SE	Standard error

References

1. Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999–2010. JAMA. 2012; 307(5):491–497. [PubMed: 22253363]
2. Fisher SC, Kim SY, Sharma AJ, Rochat R, Morrow B. Is obesity still increasing among pregnant women? Pre pregnancy obesity trends in 20 states, 2003–2009. Prev Med. 2013; 56(6):372–378. [PubMed: 23454595]

3. Baeten JM, Bukusi EA, Lambe M. Pregnancy complications and outcomes among overweight and obese nulliparous women. Am J Public Health. 2001; 91(3):436–440. [PubMed: 11236410]
4. Whitaker RC. Predicting preschooler obesity at birth: the role of maternal obesity in early pregnancy. Pediatrics. 2004; 114(1):e29–e36. [PubMed: 15231970]
5. McMillen IC, Robinson JS. Developmental origins of the metabolic syndrome: prediction, plasticity, and programming. Physiol Rev. 2005; 85(2):571–633. [PubMed: 15788706]
6. Hales CN, Desai M, Ozanne SE. The 35 phenotype hypothesis: how does it look after 5 years? Diabet Med. 1997; 14(3):189–195. [PubMed: 9088766]
7. Dulloo AG, Jacquet J, Seydoux J, Montani JP. The thrifty 'catch-up fat' phenotype: its impact on insulin sensitivity during growth trajectories to obesity and metabolic syndrome. Int J Obes (Lond). 2006; 30(Suppl 4):S23–S35. [PubMed: 17133232]
8. Hull HR, Thornton JC, Ji Y, Paley C, Rosenn B, Mathews P, Navder K, Yu A, Dorsey K, Gallagher D. Higher infant body fat with excessive gestational weight gain in overweight women. Am J Obstet Gynecol. 2011; 205(3):211. [PubMed: 21621185]
9. Boney CM, Verma A, Tucker R, Vohr BR. Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. Pediatrics. 2005; 115(3):e290–e296. [PubMed: 15741354]
10. Desai M, Jellyman JK, Han G, Beall M, Lane RH, Ross MG. Rat maternal obesity and high-fat diet program offspring metabolic syndrome. Am J Obstet Gynecol. 2014; 211(3):237e1. [PubMed: 24631702]
11. Guberman C, Jellyman JK, Han G, Ross MG, Desai M. Maternal high-fat diet programs rat offspring hypertension and activates the adipose renin-angiotensin system. Am J Obstet Gynecol. 2013; 209(3):262. [PubMed: 23743273]
12. Schack-Nielsen L, Michaelsen KF, Gamborg M, Mortensen EL, Sørensen TI. Gestational weight gain in relation to offspring body mass index and obesity from infancy through adulthood. Int J Obes (Lond). 2010; 34(1):67–74. [PubMed: 19918246]
13. Miyazaki M, Kim YC, Ntambi JM. A lipogenic diet in mice with a disruption of the stearoyl-CoA desaturase 1 gene reveals a stringent requirement of endogenous monounsaturated fatty acids for triglyceride synthesis. J Lipid Res. 2001; 42(7):1018–1024. [PubMed: 11441127]
14. Yee JK, Mao CS, Hummel HS, Lim S, Sugano S, Rehan VK, Xiao G, Lee WN. Compartmentalization of stearoyl-coenzyme A desaturase 1 activity in HepG2 cells. J Lipid Res. 2008; 49(10):2124–2134. [PubMed: 18599738]
15. Enoch HG, Catalá A, Strittmatter P. Mechanism of rat liver microsomal stearyl-CoA desaturase. Studies of the substrate specificity, enzyme-substrate interactions, and the function of lipid. J Biol Chem. 1976; 251(16):5095–5103. [PubMed: 8453]
16. Jeyakumar SM, Lopamudra P, Padmini S, Balakrishna N, Giridharan NV, Vajreswari A. Fatty acid desaturation index correlates with body mass and adiposity indices of obesity in Wistar NIN obese mutant rat strains WNIN/Ob and WNIN/GR-Ob. Nutr Metab (Lond). 2009; 6:27. [PubMed: 19519902]
17. Peter A, Cegan A, Wagner S, Lehmann R, Stefan N, Königsrainer A, Königsrainer I, Häring HU, Schleicher E. Hepatic lipid composition and stearoyl-coenzyme A desaturase 1 mRNA expression can be estimated from plasma VLDL fatty acid ratios. Clin Chem. 2009; 55(12):2113–2120. [PubMed: 19850634]
18. Vessby B, Gustafsson IB, Tengblad S, Berglund L. Indices of fatty acid desaturase activity in healthy human subjects: effects of different types of dietary fat. Br J Nutr. 2013; 110(5):871–879. [PubMed: 23414551]
19. Warensjö E, Rosell M, Hellenius ML, Vessby B, De Faire U, Risérus U. Associations between estimated fatty acid desaturase activities in serum lipids and adipose tissue in humans: links to obesity and insulin resistance. Lipids Health Dis. 2009; 8:37. [PubMed: 19712485]
20. Sjögren P, Sierra-Johnson J, Gertow K, Rosell M, Vessby B, de Faire U, Hamsten A, Hellenius ML, Fisher RM. Fatty acid desaturases in human adipose tissue: relationships between gene expression, desaturation indexes and insulin resistance. Diabetologia. 2008; 51(2):328–335. [PubMed: 18030445]

21. Yee JK, Mao CS, Ross MG, Lee WN, Desai M, Toda A, Kjos SL, Hicks RA, Patterson ME. High oleic/stearic fatty-acid desaturation index in cord plasma from infants of mothers with gestational diabetes. J Perinatol. 2014; 34(5):357–363. [PubMed: 24577432]
22. Cooke PS, Naaz A. Role of estrogens in adipocyte development and function. Exp Biol Med (Maywood). 2004; 229(11):1127–1135. [PubMed: 15564439]
23. Desai M, Han Guang, Ferelli M, Kallichanda N, Lane RH. Programmed upregulation of adipogenic transcription factors in intrauterine growth-restricted offspring. Reprod Sci. 2008; 15(8):785–796. [PubMed: 19017816]
24. Sardesai, V. Introduction to clinical nutrition. 3rd edn.. Florida: Taylor and Francis Group; 2011.
25. Chong MF, Hodson L, Bickerton AS, Roberts R, Neville M, Karpe F, Frayn KN, Fielding BA. Parallel activation of de novo lipogenesis and stearoyl-CoA desaturase activity after 3 days of high-carbohydrate feeding. Am J Clin Nutr. 2008; 87(4):817–823. [PubMed: 18400702]
26. Yee JK, Lee WN, Han G, Ross MG, Desai M. Organ-specific alterations in fatty acid de novo synthesis and desaturation in a rat model of programmed obesity. Lipids Health Dis. 2011; 10:72. [PubMed: 21569358]
27. Benkalfat NB, Merzouk H, Bouanane S, Merzouk SA, Bellenger J, Gresti J, Tessier C, Narce M. Altered adipose tissue metabolism in offspring of dietary obese rat dams. Clin Sci (Lond). 2011; 121(1):19–28. [PubMed: 21288203]
28. Hodson L, Fielding BA. Stearoyl-CoA desaturase: rogue or innocent bystander? Prog Lipid Res. 2013; 52(1):15–42. [PubMed: 23000367]
29. Guo F, Jen KL. High-fat feeding during pregnancy and lactation affects offspring metabolism in rats. Physiol Behav. 1995; 57(4):681–686. [PubMed: 7777603]
30. Srinivasan M, Katewa SD, Palaniyappan A, Pandya JD, Patel MS. Maternal high-fat diet consumption results in fetal mal programming predisposing to the onset of metabolic syndrome-like phenotype in adulthood. Am J Physiol Endocrinol Metab. 2006; 291(4):E792–E799. [PubMed: 16720630]
31. Ntambi JM, Miyazaki M, Stoehr JP, Lan H, Kendziorski CM, Yandell BS, Song Y, Cohen P, Friedman JM, Attie AD. Loss of stearoyl-CoA desaturase-1 function protects mice against adiposity. Proc Natl Acad Sci USA. 2002; 99(17):11482–11486. [PubMed: 12177411]
32. Kotronen A, Seppänen-Laakso T, Westerbacka J, Kiviluoto T, Arola J, Ruskeepää AL, Yki-Järvinen H, Oresic M. Comparison of lipid and fatty acid composition of the liver, subcutaneous and intra-abdominal adipose tissue, and serum. Obesity (Silver Spring). 2010; 18(5):937–944. [PubMed: 19798063]
33. Chu K, Miyazaki M, Man WC, Ntambi JM. Stearoyl-coenzyme A desaturase 1 deficiency protects against hyper-triglyceridemia and increases plasma high-density lipoprotein cholesterol induced by liver X receptor activation. Mol Cell Biol. 2006; 26(18):6786–6798. [PubMed: 16943421]
34. Guéant JL, Elakoum R, Ziegler O, Coelho D, Feigerlova E, Daval JL, Guéant-Rodriguez RM. Nutritional models of foetal programming and nutrigenomic and epigenomic dysregulations of fatty acid metabolism in the liver and heart. Pflugers Arch. 2014; 466(5):833–850. [PubMed: 23999818]
35. Bringhenti I, Ornellas F, Martins MA, Mandarim-de-Lacerda CA, Aguila MB. Early hepatic insult in the offspring of obese maternal mice. Nutr Res. 2015; 35(2):136–145. [PubMed: 25582085]
36. Brandorff NP. The effect of dietary fat on the fatty acid composition of lipids secreted in rats milk. Lipids. 1980; 15(4):276–278. [PubMed: 7374383]
37. Rodríguez-Cruz M, Sánchez R, Bernabe-Garcia R, Maldonado J, Del Prado M, López-Alarcón M. Effect of dietary levels of corn oil on maternal arachidonic acid synthesis and fatty acid composition in lactating rats. Nutrition. 2009; 25(2):209–215. [PubMed: 18849148]
38. Purcell RH, Sun B, Pass LL, Power ML, Moran TH, Tamashiro KL. Maternal stress and high-fat diet effect on maternal behavior, milk composition, and pup ingestive behavior. Physiol Behav. 2011; 104(3):474–479. [PubMed: 21605577]
39. Mingrone G, Manco M, Mora ME, Guidone C, Iaconelli A, Gniuli D, Leccesi L, Chiellini C, Ghirlanda G. Influence of maternal obesity on insulin sensitivity and secretion in offspring. Diabetes Care. 2008; 31(9):1872–1876. [PubMed: 18535193]

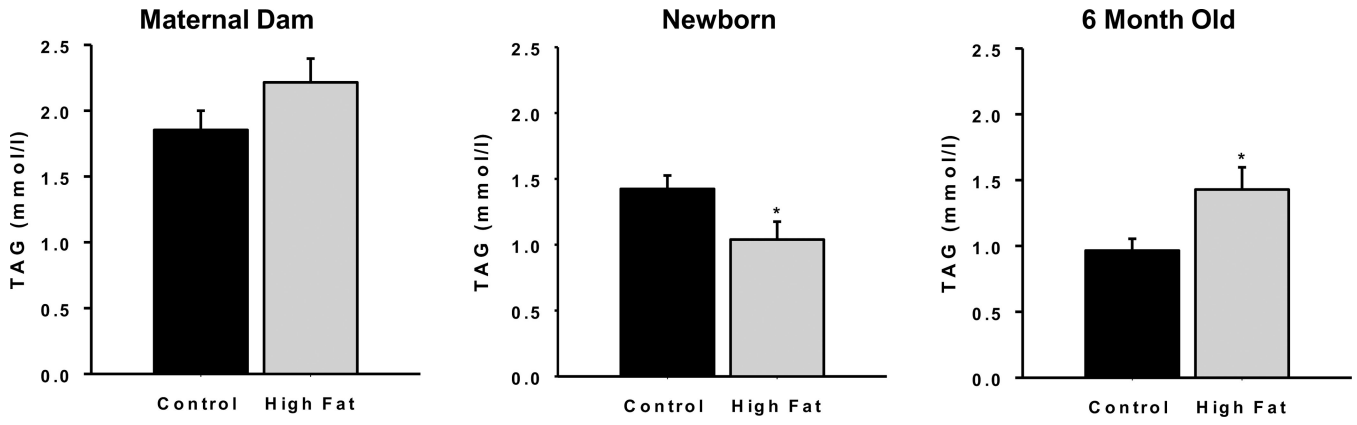

Fig. 1.

Maternal and offspring plasma triacylglycerol concentrations. Plasma TAG levels in high-fat (HF) newborns were significantly lower than in controls, whereas in HF adult offspring they were significantly higher. Values are mean ± SE of six males from six litters for control and HF offspring. $P \leq 0.05$ *vs.* control

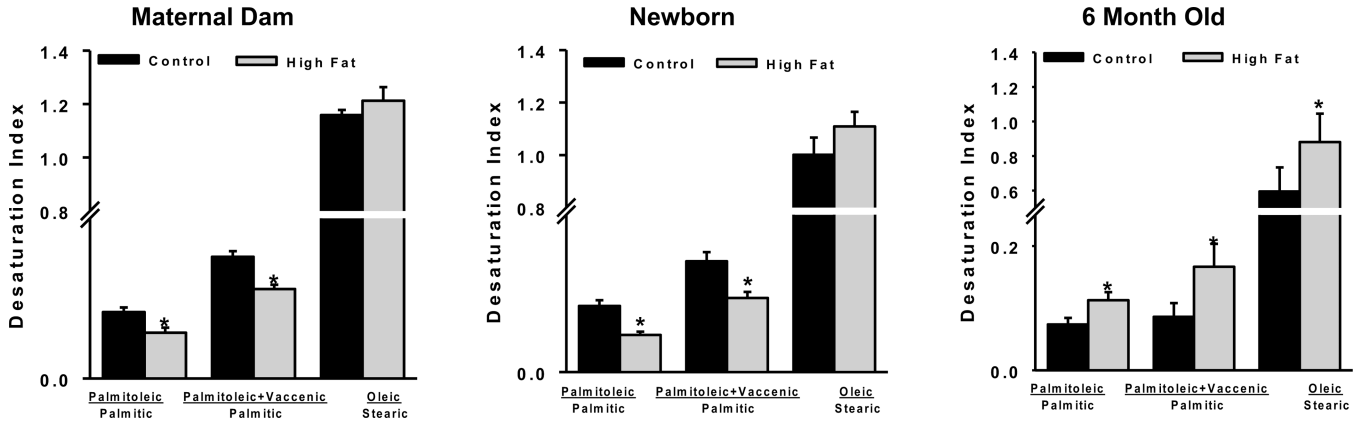

Fig. 2.

Maternal and offspring plasma desaturation indicies (DI). High-fat (HF) dams and HF newborns had lower C16-related plasma DI compared with controls; however, the C18-related plasma DI was similar for both groups. Adult HF offspring exhibited increased C16- and C18-related DI. Values are mean ± SE of six males from six litters for control (*black bars*) and HF (*gray bars*) offspring. In newborns, plasma was pooled per litter because of the small blood volume at this age. $P \leq 0.05$ *vs.* control

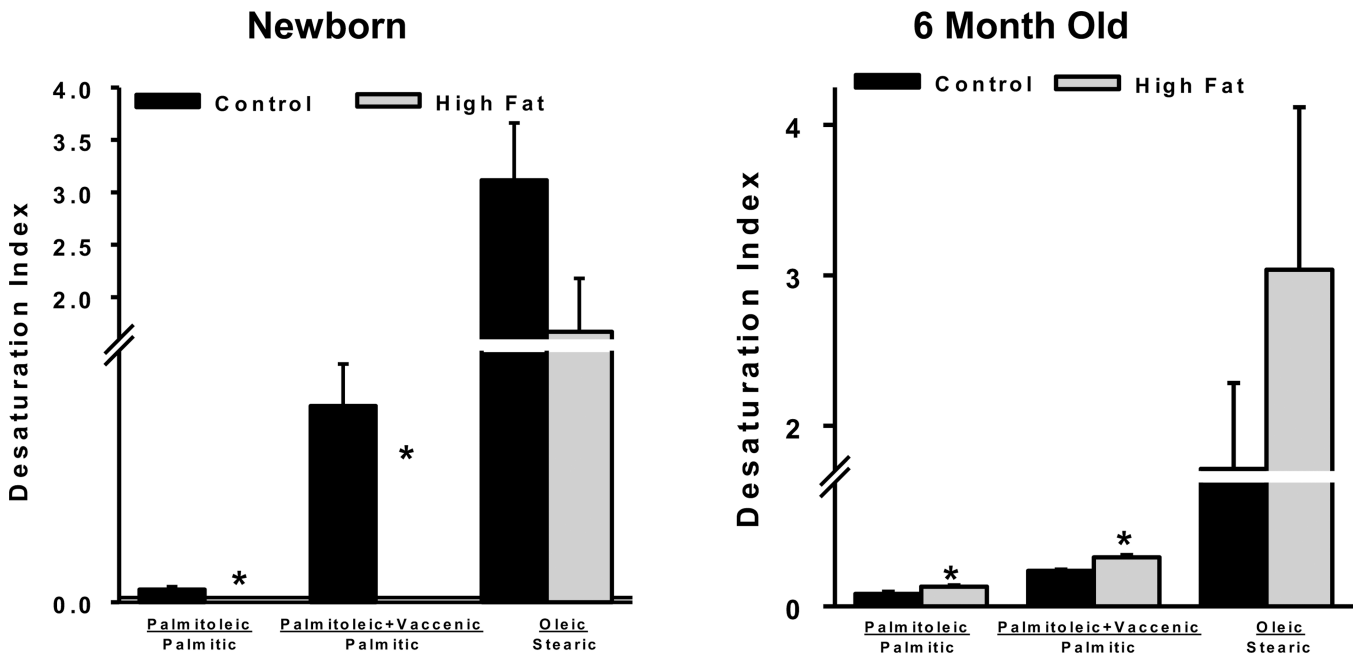

Fig. 3.

Offspring liver desaturation indicies (DI). In High-fat (HF) newborns, liver C16-related DI were lower than in controls, and there was no difference in the C18-related DI. In HF adult offspring, the liver C16-related, but not C18-related DI was higher than in controls. Values are mean ± SE of six males from six litters for control (*black bars*) and HF (*gray bars*) offspring. $P \leq 0.05$ *vs.* control

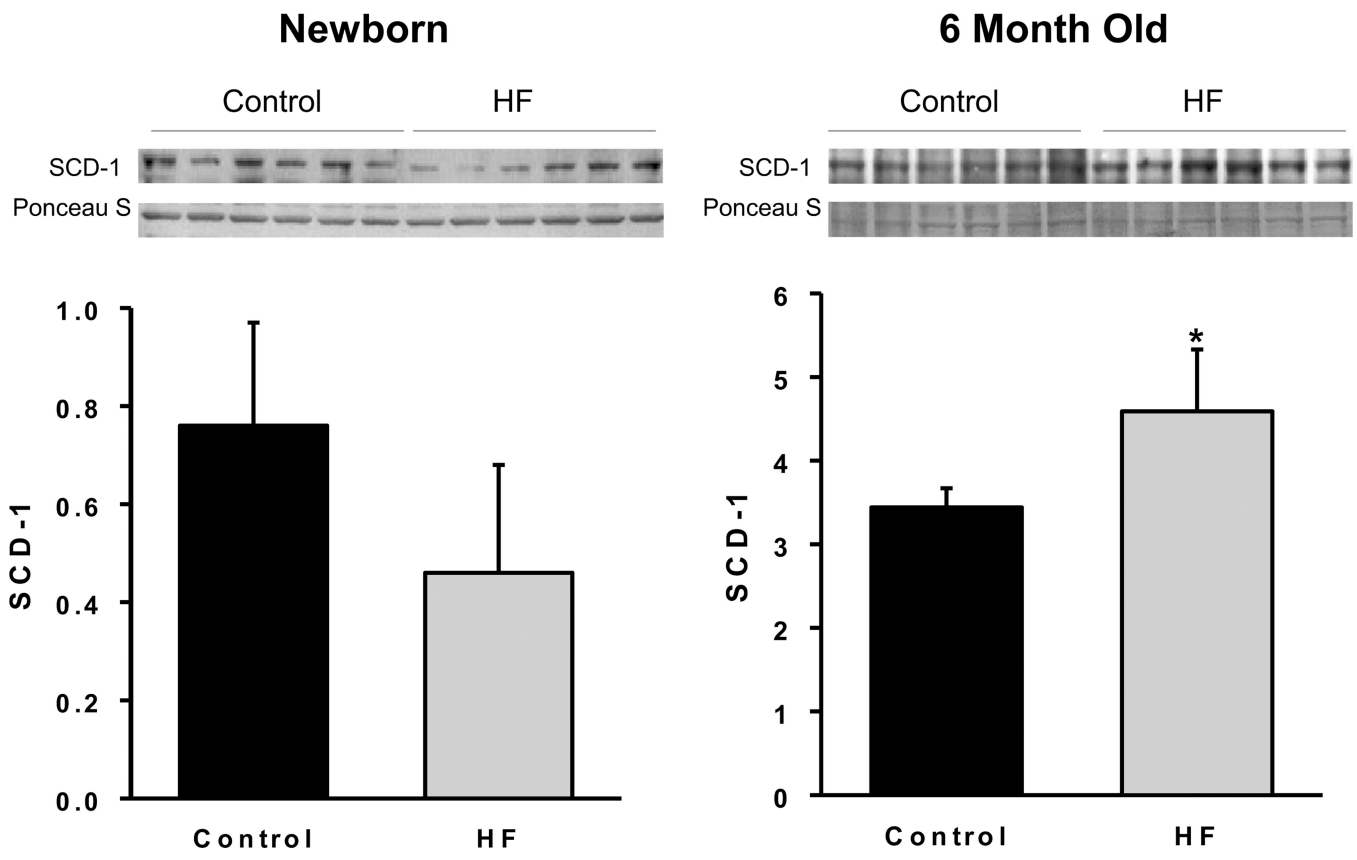

Fig. 4.

Offspring liver stearoyl-CoA desaturase-1 (SCD-1) protein abundance. High-fat (HF) newborns exhibited a trend toward decreased protein abundance of liver SCD-1, whereas liver SCD-1 expression was significantly higher in HF adult offspring than in controls. Values are mean ± SE of six males from six litters for control and HF offspring. $P \leq 0.05$ *vs.* control

Table 1

Fatty acid composition of control and high-fat diets

Fatty acid	Control diet (g/1000 kcal)	HF diet (g/1000 kcal)
14:0, myristic	0.05	0.54
14:1(n-5), myristoleic	0.02	0.30
16:0, palmitic	1.77	14.47
16:1 (n-7), palmitoleic	0.20	2.29
18:0, stearic	0.89	8.26
18:1 (n-9), oleic	3.52	26.32
18:2, linoleic	3.72	8.48
18:3, α-linolenic	0.54	1.08
20:4, arachidonic	0.07	1.04

High-fat (HF 60 % kcal fat, purified diet 58Y1) and control diet (10 % kcal fat, purified diet 58Y2) from New Brunswick, NJ, USA

Table 2

Profile of plasma fatty acids of interest for maternal dam, newborn, and 6-month-old offspring

Fatty acid (mol%)	Maternal dam		Newborn		6 Month old	
	Control	HF	Control	HF	Control	HF
14:0, myristic	2.0 ± 0.2	1.9 ± 0.5	4.1 ± 1.1	3.1 ± 0.7	0.8 ± 0.1	0.6 ± 0.1
16:0, palmitic	30.0 ± 0.6	27.3 ± 0.6*	29.8 ± 0.6	30.1 ± 1.3	27.4 ± 0.9	27.5 ± 0.3
16:1(n-7), palmitoleic	1.7 ± 0.2	1.1 ± 0.2*	1.9 ± 0.3	1.1 ± 0.2*	2.1 ± 0.3	3.1 ± 0.4*
18:0, stearic	21.4 ± 0.7	22.7 ± 0.8	26.0 ± 1.0	27.3 ± 0.9	29.8 ± 3.6	19.9 ± 2.0*
18:1(n-9), oleic	24.8 ± 0.3	27.4 ± 1.4	25.9 ± 2.0	29.4 ± 1.6	17.1 ± 1.9	18.3 ± 1.3
18:1(n-7), vaccenic	2.4 ± 0.1	1.7 ± 0.2*	2.9 ± 0.3	1.9 ± 0.2*	2.4 ± 0.2	3.4 ± 0.4*
18:2(n-6), linoleic	11.1 ± 1.1	12.0 ± 1.1	6.0 ± 0.4	5.6 ± 0.7	8.3 ± 1.4	10.6 ± 1.4
20:4(n-6), arachidonic	6.9 ± 0.4	5.7 ± 0.7	2.1 ± 0.2	1.1 ± 0.3*	9.9 ± 2.8	12.9 ± 2.2

Fatty acids of interest, each expressed as mol% of a select pool of plasma fatty acids (myristic, palmitic, palmitoleic, stearic, oleic, vaccenic, linoleic, and arachidonic)

Values are of mean ± SE

HF high-fat-diet group

* $P < 0.05$ *vs.* control

Table 3

Profile of liver fatty acids of interest for newborn and 6-month-old offspring

Fatty acid (mol%)	Newborn		6-month-old	
	Control	HF	Control	HF
14:0, myristic	1.4 ± 0.1	0.5 ± 0.1*	0.4 ± 0.1	0.6 ± 0.1
16:0, palmitic	43.0 ± 1.0	43.6 ± 1.3	37.5 ± 2.0	39.2 ± 1.6
16:1(n-7), palmitoleic	1.4 ± 0.1	0.5 ± 0.1*	2.4 ± 0.5	3.9 ± 0.7
18:0, stearic	11.3 ± 1.2	12.7 ± 1.0	21.5 ± 4.2	14.1 ± 2.7
18:1(n-9), oleic	28.0 ± 2.0	29.9 ± 0.5	25.6 ± 3.4	28.7 ± 2.6
18:1(n-7), vaccenic	3.5 ± 0.2	2.5 ± 0.1*	3.7 ± 0.2	5.0 ± 0.2*
18:2(n-6), linoleic	10.8 ± 0.4	10.1 ± 0.7	4.6 ± 0.9	5.3 ± 1.3
20:4(n-6), arachidonic	0.9 ± 0.3	0.3 ± 0.1	4.2 ± 0.8	3.3 ± 0.8

Fatty acids of interest, each expressed as mol% of a select pool of liver fatty acids (myristic, palmitic, palmitoleic, stearic, oleic, vaccenic, linoleic, and arachidonic)

Values are of mean ± SE

HF high-fat-diet group

* $P < 0.05$ *vs.* control