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High dietary intake of medium-chain fatty acids during pregnancy in rats prevents later-life obesity in their offspring

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Abstract

We investigated the effects of dietary fatty acids of different chain lengths during pregnancy in the rat on the susceptibility of offspring to later-life obesity and the underlying mechanisms. Pregnant rats were fed three different diets: standard (STD), high medium-chain fatty acids (MCFA); and high long-chain fatty acids (LCFA). The male offspring were assigned to three groups: STD control, MCFA and LCFA according to the maternal diets and suckled by dams fed with STD during pregnancy and lactation. After weaning, the offspring were fed with STD from 3 to 8 weeks of age. At the age of 8 weeks, rats in three groups: high-fat diet (HFD) control, MCFA and LCFA were fed with HFD until 14 weeks of age in an attempt to induce obesity, and rats in the HFD control group were selected randomly from the STD control group. Body weight and body fat content were decreased in the MCFA group accompanied by down-regulated mRNA expression of fatty acid synthase and acetyl-coA carboxylase 1, and increased mRNA and protein expression of adenosine monophosphate (AMP)-activated protein kinase (AMPK), carnitine palmitoyltransferase 1 and uncoupling protein 3 compared with the corresponding controls at 3, 8 and 14 weeks of age. The results suggested that the MCFA diet during pregnancy prevented later-life obesity in the offspring when they were exposed to HFD in later life, which might be related to programming of the expression of genes involved in fatty acid metabolism.

Keywords: Medium-chain fatty acids; Metabolism programming; Offspring; Obesity; Fatty acid oxidation

1. Introduction

Obesity has become an important health problem in the 21st century [1] and nutrition is a critical influential factor of adult obesity. Earlier studies showed that the fetal nutritional environment was the key determinant of later-life obesity [2–5], which can be explained by "metabolism programming" [6–9].

Most conventional edible oils, including soybean (*Glycine max*), peanut (*Arachis hypogaea*), palm (*Elaeis guineensis*), corn (*Zea mays*), lard and butter, are composed primarily of long-chain triglycerides. There has been a great deal of research on the role of dietary medium-chain triglycerides [coconut oil (*Cocos nucifera*) and palm kernel oils contain a high proportion of medium-chain triglycerides] in weight control. Medium-chain triglycerides containing medium-chain fatty acids (MCFAs, 8–12 carbon atoms) can reduce body weight and body fat mass in animals and humans compared with long-chain triglycerides that contain long-chain fatty acids (LCFAs, ≥14 carbon atoms) [10,11]. In an animal study, Sprague-Dawley rats fed with medium-chain triglycerides for 6 weeks had lower body fat mass and gained less weight than those fed with long-chain triglycerides [10]. Tsuji et al. [11] found that overweight human subjects (with BMI ≥23 kg/m^2) fed with a diet containing medium-chain triglycerides had significantly lower body weight and body fat mass than overweight subjects fed with a long-chain triglyceride diet. Furthermore, earlier studies suggested that dietary medium-chain triglycerides would decrease the concentration of cholesterol in blood and liver, and the concentration of triglyceride (TG) in heart and skeletal muscle [12,13]. However, little research has been done to confirm whether dietary MCFA or LCFA during pregnancy can influence body weight, fat mass and change the serum lipid profile in the later life of the offspring. In this study, we asked whether dietary MCFA or LCFA fed to pregnant rats could affect body weight, fat mass and the serum lipid profile in the later life of the offspring. We also investigated the expression of genes involved in lipid metabolism.

2. Materials and methods

2.1. Experimental design and animal care

All procedures were approved by the Animal Experimentation Ethics Committee of Harbin Medical University. Rats were housed in a temperature-controlled room with a 12-h light/12-h dark cycle and water was available ad libitum.

Female (170±10 g body weight) and male (210±10 g body weight) Wistar rats were purchased from Shanghai SLAC Laboratory Animal (Shanghai, China). Female rats

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Table 1
Diet compositions

Ingredients	STD	MCFA	LCFA	HFD
g/100 g diet				
Casein	20.00	20.00	20.00	20.00
L-Cystine	0.30	0.30	0.30	0.30
L-Methionine	0.16	0.16	0.16	0.16
Carbohydrates	66.84	52.54	53.84	55.84
Fat	7.00[a]	21.30[b]	20.00[a]	18.00[c]
Cellulose	1.00	1.00	1.00	1.00
Vitamin mix, AIN-93G	1.00	1.00	1.00	1.00
Mineral mix, AIN-93G	3.50	3.50	3.50	3.50
Choline bitartrate (50% choline)	0.20	0.20	0.20	0.20
Sources of energy (%)				
Protein	20	17	17	17
Carbohydrates	65	45	45	48
Fat	15	38[d]	38	35

[a]Soybean oil; [b]coconut oil (17.8g) plus soybean oil (3.5g); [c]lard (14.0g) plus soybean oil (4.0g); [d]the energy yield of coconut oil is 8.3 kcal/g [36].

were mated overnight with male rats. The day of a sperm-positive vaginal smear was designated as day 0 of pregnancy. The pregnant rats were moved to individual cages and (n=30 for each diet) and fed with a purified American Institute of Nutrition (AIN-93G) diet as a standard diet (STD), an MCFA diet or an LCFA diet (Table 1). Food intake and body weight were measured every 3 days until the rats delivered on Day 21, which was considered as age 0 weeks for the offspring. A flowchart of the procedure is shown in Fig. 1.

Male offspring were selected and assigned to one of three groups, STD, MCFA or LCFA, according to the maternal diet. Then male offspring were standardized to 8 per litter within 6 hours of delivery and were suckled by dams fed STD during pregnancy and lactation. In order to further standardize the postnatal environment (from 3 to 8 weeks of age), male offspring were housed in individual cages and fed with STD ad libitum. At 8 weeks of age, 30 offspring were selected randomly from the STD control group to be the high-fat diet (HFD) control group. The other rats in the STD control group continued to be fed with STD. Rats in MCFA, LCFA and HFD control groups were fed HFD (Tables 1 and 2) until 14 weeks of age in an attempt to induce obesity.

Food intake was measured daily and body weight of the offspring was measured weekly. The weight-adjusted energy intake of mothers and offspring was calculated as:

kilocalorie intake × 100 / body weight

The obesity rate (n=30) at 14 weeks of age was calculated as:

(number of obese offspring rats) / (total number of offspring rats) × 100%

Table 2
Fatty acid composition of coconut oil, soybean oil and lard[a]

Fatty acid	Coconut oil	Soybean oil	Lard
% of total fatty acids			
C 8:0	4.3	–	–
C 10:0	5.0	–	–
C 12:0	39	–	–
C 14:0	18	Trace	2.3
C 16:0	11.3	11	26.3
C 16:1	1.0	0.4	2.9
C 18:0	3.2	3.8	15.1
C 18:1	8.9	22.2	41.2
C 18:2	8.5	54.2	7.2
C 18:3	-	7.7	0.5
Others	0.8	0.7	4.5

[a] All data are based on laboratory analysis.

Obesity was defined as: body weight>mean+2 S.D. Body fat content of the offspring was calculated as:

100(perirenal and epididymal fat pads) / body weight

To determine whether metabolism programming induced changes in the later life of the offspring, we chose dynamic observation points 0 (birth), 3 (weaning), 8 (near adulthood) and 14 (after 6 weeks obesity inducing) weeks of age. At these time points, 10 offspring were selected randomly from each group, fasted overnight and then anaesthetised with pentobarbital. Blood was collected by decapitation at 0 and 3 weeks and from the abdominal aorta at 8 and 14 weeks old. Liver and skeletal muscle were removed, weighed, snap-frozen in liquid nitrogen and stored at −80°C.

2.2. Fatty acid composition of oils

The fat in the diets was provided in the form of coconut and soybean oils (MCFA), soybean oil (LCFA), soybean oil (STD) and soybean and lard oils (HFD). The fatty acid composition of coconut, soybean and lard oils was analysed by gas chromatography coupled to an ion trap mass spectrometer (TRACE GC/PolarisQ MS; Thermo Finnigan, San Jose, CA, USA), and the results are given in Table 2.

2.3. Levels of serum TG, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C)

Serum was obtained by centrifugation and stored at –80 °C. Serum contents of TG, HDL-C and LDL-C were assayed by standard enzymatic colorimetric methods with

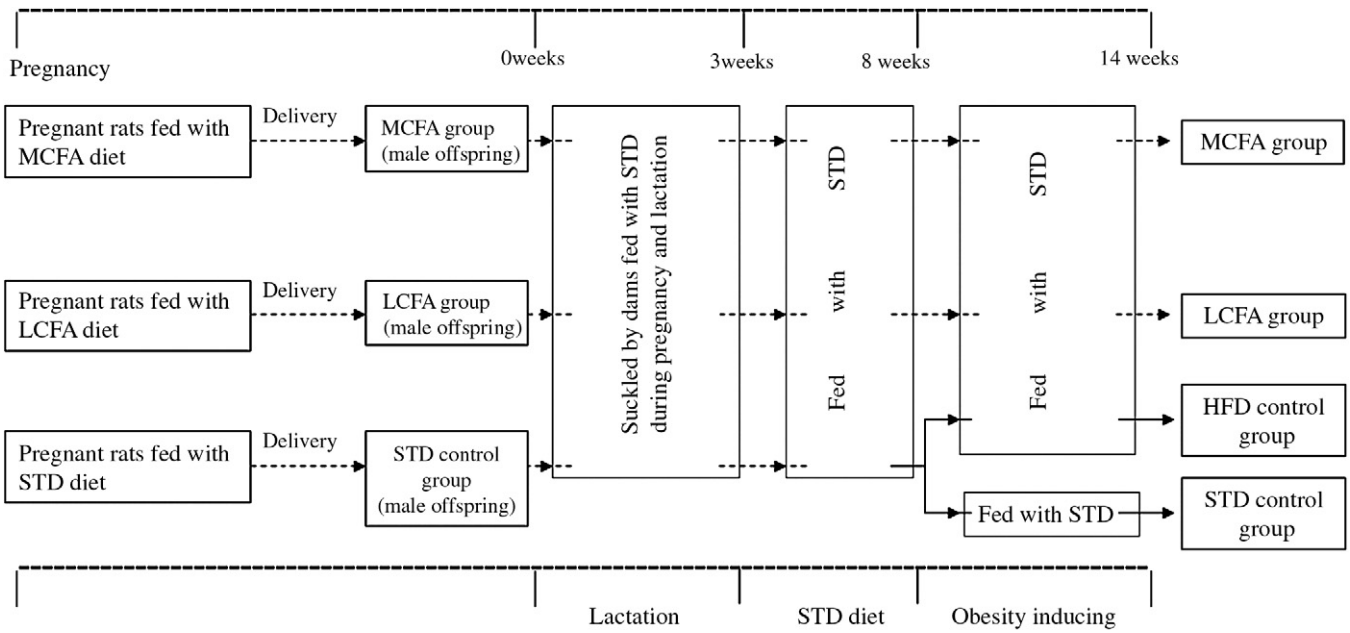

Fig. 1. The study design and the flow of treatment groups and times.