A Maternal Low-Fiber Diet Predisposes Offspring to Improved Metabolic Phenotypes in Adulthood in an Herbivorous Rodent*

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ABSTRACT

The maternal or paternal dietary composition can have important effects on various aspects of their offspring's physiology. Studies from animal models and humans showed that a maternal high-fiber diet protected offspring against fat accumulation. However, little is known about how a maternal low-fiber diet modifies the metabolism of offspring in herbivorous rodents. We hypothesized that a maternal low-fiber diet would confer long-lasting beneficial effects on offspring metabolic phenotypes in herbivorous Brandt's vole (*Lasiopodomys brandtii*). Female voles were fed either a control (12.4% fiber) or a low-fiber (3.5% fiber) diet throughout pregnancy and lactation, and all offspring were fed the control diet after weaning till 14 wk old. Offspring were sampled from each litter at 18 d and 14 wk of age. Another subset of adult offspring at 15 wk of age was fed a high-fat diet for 8 wk. We found that there was no difference in litter size, litter mass, or pup mass before weaning between the two maternal diet groups. Offspring from the maternal low-fiber diet increased energy intake, body mass, and lean mass; suppressed fat accumulation; and improved glucose tolerance compared with those from the control diet. Moreover, the maternal low-fiber diet alleviated high-fat diet-induced obesity in the adult offspring. Serum leptin concentration and uncoupling protein 1 content in brown adipose tissue of offspring were not affected by a maternal low-fiber diet. We demonstrate that herbivorous females fed a low-fiber diet during pregnancy and lactation may predispose their offspring to accelerated growth of lean tissue, which may increase the opportunity for survival and reproduction in offspring.

Keywords: maternal low-fiber diet, energy intake, thermogenesis, leptin, offspring.

Introduction

The causal effect of parental environments or parental phenotypes on offspring's Darwinian fitness has become an interesting topic in ecology and evolution (Uller 2008; Uller and Pen 2011). The perinatal period is critical for determining an animal's fitness, since most life-history traits are developed during this period. Studies in animal models and humans indicate that maternal environments—such as maternal diet during pregnancy and/or lactation—modify offspring's metabolic phenotypes, immune function, and reproductive performance in a long-term manner (Levin 2006; Triggs and Knell 2012; Warner and Lovern 2014). Maternal malnutrition during pregnancy is associated with low pup mass at birth and sustained growth retardation until adulthood (Pennington et al. 2001); maternal food restriction during lactation results in increased sex ratio of females and stunted growth (Huck et al. 1986) and reduced reproductive capability of offspring (Liang and Zhang 2006; Liang et al. 2007). In contrast, maternal consumption of high-fat or high-protein diets leads to obesity and impaired glucose tolerance in offspring in mice, rats, and humans (Rattanatray et al. 2010; Hallam and Reimer 2013), whereas maternal high-fiber diets protect offspring against high-fat diet-induced obesity and mammary tumorigenesis (Yu et al. 2006; Han et al. 2015). Therefore, high dietary fiber intake has been recommended to reduce the risk of obesity and type 2 diabetes in humans.

According to the optimal foraging theory (Krebs et al. 1978), animals prefer food with high-protein but low-fiber content (Sinclair et al. 1982; Bozinovic 1997). Mammal herbivores have to consume plant material with low digestibility because of the separated trophic niche (Sinclair et al. 1982; Karasov 1989; Bozinovic 1997). These species evolved some physiological and behavioral adaptive strategies to compensate for the low-quality food. For example, species that exploit food with a high cost of digestion have low metabolic rates to reduce energy expenditure (Veloso and Bozinovic 1993). In response to a high-fiber diet, all of these small mammals increase food intake and energy efficiency by increasing turnover time of digesta (Bozinovic 1995; Pei et al. 2001) and practicing caecotrophy (Liu et al. 2007). Alternatively, small herbivores exhibit ultradian rhythm in locomotion and feeding to meet their energy demands (Liu et al. 2007). Although they have several compensatory mechanisms for high metabolic rate and

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low-quality food, the wild herbivorous rodents show seasonal variations in body mass in a year cycle (Li and Wang 2005; Wang et al. 2006).

Brandt's voles (*Lasiopodomys brandtii*) are the dominant herbivore species inhabiting the typical steppe in Inner Mongolia (China), Mongolia, and the Baikal region of Russia. They mainly feed on vegetable leaves and a small amount of roots, and their food selection shows obvious seasonal variations (Wang et al. 1992). The captive-bred voles, feeding on high-fiber diets with low energy content and digestibility, show average 3-h ultradian rhythms in feeding behaviors, and they compensate for 9% crude protein and 8% metabolizable energy (about 0.9 kJ/g) of dry matter mass by caecotrophy (Liu et al. 2007). The body (fat) mass of voles is highest during breeding seasons and lowest in winter (Li and Wang 2005; Zhang and Wang 2006; Zhao and Wang 2006; Wan et al. 2014). In the wild, more than 80% of voles die in winter, even if a family of about 21 voles hoards an average of 16.8 kg of wet grass in autumn (Shi and Hai 1997). The energy availability during reproduction would influence maternal metabolism and reproductive investment. A previous study reported that lactating females fed a low-fiber diet increased digestible energy intake (Lou et al. 2015*b*). Other studies also indicate that appropriate supplement of maternal nutrition and energy improves the metabolic phenotype and immunity of offspring (Zhang et al. 2011; Triggs and Knell 2012; Lou et al. 2015*a*). It has rarely been addressed whether changes in maternal dietary fiber affect reproductive outcomes and offspring metabolic phenotypes in herbivores. This study was to test the hypothesis that a maternal low-fiber diet would confer long-lasting beneficial effects on adult metabolic phenotypes of offspring in Brandt's voles. We predicted that reproductive output and metabolic phenotypes would be improved in offspring from a maternal low-fiber diet.

Material and Methods

Experimental Animals

Captive-bred Brandt's voles descended from populations in the grasslands of Inner Mongolia were housed with same-sex siblings after weaning in plastic cages (30 cm × 15 cm × 20 cm) with sawdust beddings. They were maintained at 23° ± 1°C on a 16L : 8D cycle (lights on at 0400 hours) with ad lib. access to commercial rabbit pellets (Beijing HFK Bioscience) and water. All animal procedures were approved by the Animal Care and Use Committee at the Institute of Zoology, Chinese Academy of Sciences.

Experimental Design

Experiment 1 was designed to detect the effects of maternal low-fiber diet on reproductive output and offspring's metabolic phenotypes. Weight-matched virgin female voles with ages between 120 and 150 d were housed individually for at least 2 wk and then fed either commercial rabbit pellets (control diet; gross energy of 17.5 kJ/g, digestible energy of 11.6 kJ/g) containing 17.6% protein, 2.7% fat, 12.4% fiber, and 47.0% carbohydrate or a low-fiber diet (gross energy of 17.4 kJ/g, digestible energy of 14.7 kJ/g) containing 17.0% protein, 3.0% fat, 3.5% fiber, and 55.9% carbohydrate. One female vole was mated with one male for 1 wk. The mothers with litter sizes of five to 10 were selected ($n = 9$ litters for each diet). At 18 d of age, one pup from each litter was sampled for later measurement, and the other pups were weaned and maintained with their littermates. All the offspring were fed with the control diet after weaning. At 28 d of age, one male and one female (at most two from a litter) were randomly chosen from each litter and housed individually until 14 wk of age. According to maternal diets, the offspring were divided into four groups: male offspring from the maternal control diet (ConM, $n = 12$) or low-fiber diet (LFM, $n = 10$) and female offspring from the maternal control diet (ConF, $n = 10$) or low-fiber diet (LFF, $n = 12$). Body mass was measured every 3 d in pups and every 2 wk after weaning. Energy intake was measured every 2 wk from 4 to 12 wk of age.

Experiment 2 was conducted to test whether the adult offspring from control and low-fiber diets showed diverse responses to a high-fat diet. Another subset of adult offspring (at 15 wk of age) from maternal control (ConM, $n = 9$; ConF, $n = 9$) and low-fiber diets (LFM, $n = 9$; LFF, $n = 10$) were all fed a high-fat diet (26% fat content) for 8 wk. Body mass and food intake were detected once a week.

Energy Intake

Food intake and energy values of dried food and feces were measured as previously described (Zhao and Wang 2009). Gross energy intake (GEI), digestible energy intake (DEI), and digestibility were calculated as follows: GEI (kJ/d) = dry food intake (g/d) × energy content of food (kJ/g); DEI (kJ/d) = GEI − dry mass of feces (g/d) × energy content of feces (kJ/g); digestibility (%) = DEI (kJ/d) × 100%/GEI.

Glucose Tolerance Test

At 11 wk of age, all subjects were fasted overnight, and then an intraperitoneal glucose tolerance test was conducted between 0800 and 1100 hours. Blood samples were taken by tail venipuncture, and glucose concentrations were measured at 0, 15, 30, 60 and 120 min after glucose was administered (2 g/kg body mass) with a FreeStyle blood meter (Abbott Diabetes Care, Alameda, CA). The linear trapezoidal rule was used for estimation of area under the curve (AUC).

Tissue Collection and Body Composition Analysis

At the end of experiment 1 (at 14 wk of age), all subjects were killed by CO_2 asphyxiation in the morning. Blood samples were collected, and the interscapular brown adipose tissue (BAT) was dissected, immediately frozen in liquid nitrogen, and then stored at −80°C. The heart, liver, spleen, lung, and kidneys were dissected and weighed. The digestive tract (including stomach, small intestine, cecum, and colon) was removed, rinsed with saline, and weighed (±1 mg). The fat pads (including mesenteric, epigonadal, retroperitoneal, and inguinal fat pads) were also dissected and weighed (±1 mg). The remaining carcass and all or-

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gans were dried in an oven at 60°C for a week and then weighed again to obtain the dry mass. Lean body mass was estimated by subtracting the measured fat mass from whole body mass.

Serum Leptin Assay

Serum leptin concentration was determined using a radioimmunoassay (multispecies kit XL-85K; Linco Research, St. Charles, MO), which was validated in Brandt's voles (Li and Wang 2005; Zhang and Wang 2006). The samples were run in duplicate, and the intra-assay coefficient of variation (CV) was 3.4%–6.5%. The inter-assay CV was not calculated for the present state but was <8.7% on the basis of the assay protocol of the manufacturer.

Quantification of Uncoupling Protein 1 (UCP1)

Protein content of UCP1 in BAT at weaning and in adults was measured by Western blot (Li and Wang 2005; Zhang and Wang 2006). Total BAT protein (80 μg per lane) was separated by gel electrophoresis (10% running gel and 4% stacking gel) and transferred to polyvinylidene difluoride membranes (IPVH00010; Millipore; 200 mA, 2 h). Using 5% nonfat dry milk in Tris-buffered saline-Tween, the membrane was blocked for 1 h at room temperature with gentle agitation. The membrane was incubated with the primary antibody of a polyclonal rabbit anti-hamster UCP1 (1∶5,000) overnight at 4°C and with the secondary antibody of horseradish peroxidase-conjugated goat anti-rabbit IgG (1∶5000; Yeasen) for 1 h at room temperature. Immunoreactive protein was detected by enhanced chemoluminescence (Yeasen) and scanned using Bio-Rad ChemiDoc MP Imaging System. Density of bands was quantified using Quantity One software (ver.4.4.0; BioRad). UCP1 content was expressed as relative units.

Statistical Analyses

All data were expressed as means ± SE and analyzed using SPSS 17.0 (SPSS, Chicago). Independent-samples *t*-test was used to determine group differences in mean pup mass, litter mass, litter size, sex ratio, serum leptin concentration, and UCP1 content at weaning. Body mass, digestibility, glucose concentration, and cumulative mass gain were analyzed by repeated-measures ANOVA and a two-way ANOVA (maternal diets and sex). GEI, DEI, and cumulative food intake were analyzed by repeated-measures ANCOVA and two-way ANCOVA, using body mass as the covariate. The data of body composition were analyzed by two-way ANCOVA, with body mass as the covariate.

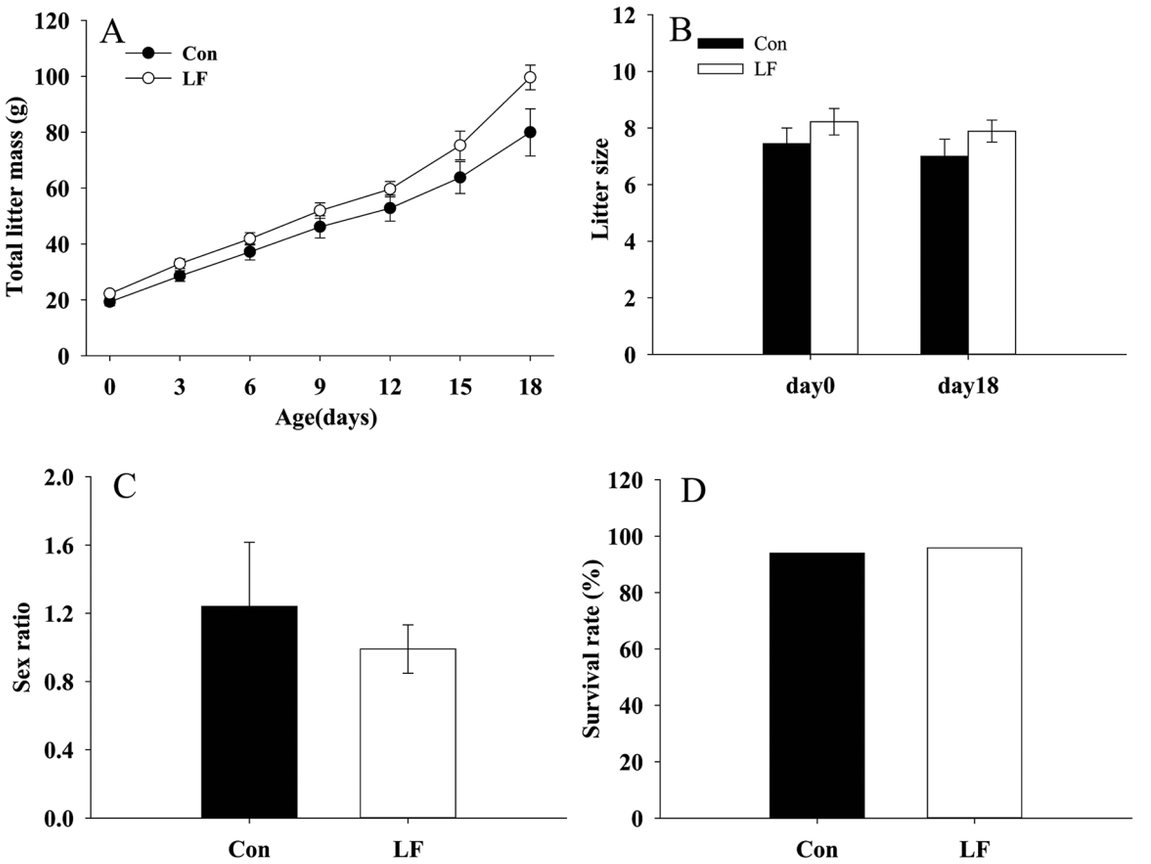

Figure 1. Effects of maternal low-fiber diet on total litter mass (*A*), litter size (*B*), sex ratio (male∶female; *C*), and survival rate (*D*). Con, maternal control diet; LF, maternal low-fiber diet.

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UCP1 content, serum leptin concentration in adults, and AUC were analyzed by two-way ANOVA. Pearson correlation analyses were used to detect possible associations of serum leptin with GEI. Statistical significance was assumed at $P < 0.05$.

Results

Reproductive Outcomes

Maternal low-fiber diet showed no effect on total litter mass, litter size, sex ratio, or survival rate of offspring during lactation ($P > 0.05$; fig. 1).

Body Mass and Energy Intake

There was no difference in body mass of offspring at 4 and 5 wk of age between males and females or between the two kinds of maternal diets ($P > 0.05$). But from week 6, body mass of males was higher than that of females ($F_{1,40} = 25.708$, $P < 0.001$; fig. 2*A*). From week 8, body mass was higher in offspring from the maternal low-fiber diet than those from the control diet ($F_{1,40} = 3.825$, $P < 0.05$). Body mass increased with time of development ($F_{10,400} = 242.477$, $P < 0.001$).

At week 4, there were no differences in GEI, DEI, or digestibility. Maternal low-fiber diet increased offspring energy intake from week 8 (GEI: $F_{1,39} = 9.026$, $P = 0.005$; DEI: $F_{1,39} = 7.489$, $P = 0.009$) to week 10 (GEI: $F_{1,39} = 5.800$, $P = 0.021$; DEI: $F_{1,39} = 4.693$, $P = 0.036$; fig. 2*B*, 2*C*). Male offspring have higher GEI and DEI than females during the whole development ($P < 0.05$). Digestibility increased significantly with time of development ($F_{4,160} = 151.147$, $P < 0.001$) but was not affected by sex ($P > 0.05$) or diet ($P > 0.05$), except at week 4 ($F_{1,40} = 8.094$, $P = 0.007$; fig. 2*D*). All the energetic parameters were not affected by the interaction of diets and sex.

Body Composition

The mass of most organs was not affected by maternal diet, but kidney, stomach, and small intestine mass increased in off-

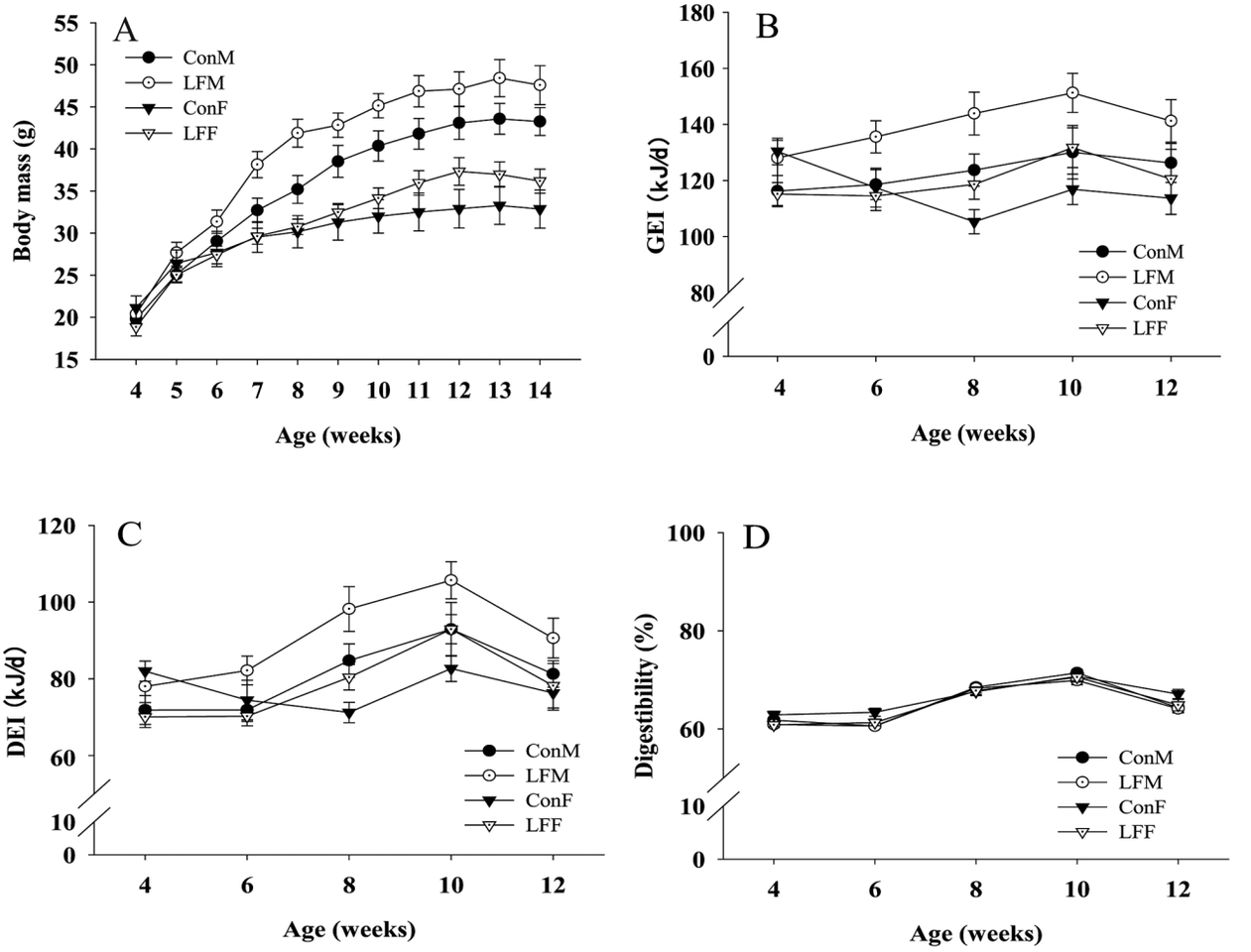

Figure 2. Effects of maternal low-fiber diet on offspring body mass (*A*), gross energy intake (GEI; *B*), digestible energy intake (DEI; *C*), and digestibility (*D*). ConM, male offspring from maternal control diet; LFM, male offspring from maternal low-fiber diet; ConF, female offspring from maternal control diet; LFF, female offspring from maternal low-fiber diet.

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Table 1: Effects of maternal low-fiber diet on offspring body composition (g) at 14 wk of age

	Male		Female		
Parameter	Control diet	Low-fiber diet	Control diet	Low-fiber diet	Statistical summary
Body	43.3 ± 1.6	47.6 ± 2.3	32.9 ± 2.2	36.2 ± 1.4	D,* S***
Dry organ:					
Heart	.045 ± .002	.052 ± .003	.039 ± .001	.042 ± .002	M***
Liver	.397 ± .018	.486 ± .027	.331 ± .018	.383 ± .018	M***
Spleen	.007 ± .001	.010 ± .002	.007 ± .000	.007 ± .001	M**
Lung	.064 ± .002^{A}	.079 ± .004^{B}	.062 ± .005^{B}	.064 ± .002^{AB}	M,*** S × D*
Kidneys	.111 ± .003	.128 ± .007	.087 ± .004	.096 ± .003	M,*** D,* S*
Stomach	.048 ± .002	.056 ± .002	.050 ± .002	.054 ± .003	M,* D,* S*
Small intestine	.060 ± .002	.048 ± .006	.051 ± .005	.047 ± .005	M,* D**
Cecum	.041 ± .002	.047 ± .005	.041 ± .004	.046 ± .004	M*
Colon	.046 ± .002^{A}	.040 ± .003^{B}	.043 ± .003^{AC}	.047 ± .003^{C}	S,** D × S*
White fat:					
Mesenteric	.255 ± .015	.232 ± .016	.239 ± .021	.250 ± .023	M,*** D,* S***
Epigonadal	.475 ± .040	.464 ± .043	.270 ± .092	.270 ± .052	M,*** D*
Retroperitoneal	.582 ± .064	.363 ± .041	.414 ± .143	.349 ± .070	M,*** D,*** S**
Inguinal	1.711 ± .154	1.158 ± .082	1.096 ± .232	.932 ± .127	M,*** D***
Total	3.021 ± .259	2.217 ± .145	2.019 ± .481	1.800 ± .254	M,*** D,*** S*
Dry carcass	11.898 ± .522	11.523 ± .501	9.544 ± .997	10.096 ± .587	M,*** D,*** S***
Water	16.805 ± .690	18.927 ± 1.079	12.132 ± .572	13.064 ± .451	M,*** S***
Lean body	40.229 ± 1.434	45.363 ± 2.266	30.840 ± 1.833	34.373 ± 1.259	M,*** D,*** S*

Note. Values are expressed as means ± SE (uncorrected). Different letters indicate a significant difference ($P < 0.05$). D, maternal diet; S, sex; M, body mass.
$^{*}P < 0.05$.
$^{**}P < 0.01$.
$^{***}P < 0.001$.

spring from the maternal low-fiber diet compared with those of the control diet. Offspring from the maternal low-fiber diet had less fat pad mass—including mesenteric, epigonadal, retroperitoneal, and inguinal fat pads—but more lean mass compared with control offspring (table 1). Female offspring had more fat pad (mesenteric and retroperitoneal fat pads) and carcass mass but less lean mass than males.

UCP1 Content in BAT

At weaning, offspring UCP1 content in BAT was not affected by maternal diet ($t = 0.092$, df = 11, $P > 0.05$; fig. 3*A*). In adulthood, it was still not affected by maternal diet ($F_{1,37} = 1.440$, $P > 0.05$), sex ($F_{1,37} = 3.532$, $P > 0.05$), or the interaction between diet and sex ($F_{1,37} = 0.033$, $P > 0.05$; fig. 3*B*).

Serum Leptin Concentrations

Serum leptin concentrations were not significantly affected by maternal diet at weaning ($t = 1.630$, df = 13, $P > 0.05$; fig. 4*A*) or in adulthood ($F_{1,37} = 0.909$, $P > 0.05$; fig. 4*B*). Serum leptin concentrations were also not affected by sex ($F_{1,37} = 3.070$, $P > 0.05$) or the interaction between diet and sex ($F_{1,37} = 1.595$, $P > 0.05$). There was no correlation between serum leptin concentration and energy intake in adults ($r = 0.082$, $P > 0.05$).

Glucose Tolerance Test

Glucose concentrations of offspring from the maternal low-fiber diet decreased significantly compared with those from the control diet, especially at 60 min after glucose injection ($F_{1,28} = 9.223$, $P < 0.01$). Males had lower glucose concentrations than females, especially at 15 and 30 min ($F_{1,28} = 5.836$, $P < 0.05$; fig. 5*A*). Data of the AUC also showed that glucose tolerance was affected by maternal diet ($F_{1,28} = 9.438$, $P < 0.01$) and sex ($F_{1,28} = 4.120$, $P < 0.05$) but not by the interaction between diet and sex ($F_{1,28} = 1.771$, $P > 0.05$; fig. 5*B*).

Cumulative Mass Gain and Food Intake after High-Fat Diet Feeding

Offspring from the maternal low-fiber diet had significantly lower cumulative mass gain after high-fat diet feeding as compared with those from the control diet ($P < 0.05$). There were no sex differences or interactive effects on body mass gain ($P > 0.05$; fig. 6*A*). Cumulative food intakes were not affected by maternal diet, sex, or their interaction ($P > 0.05$; fig. 6*B*).

Discussion

An emerging body of evidence suggests that nutritional experiences in early life determine long-term physiology and behaviors in mammals. Maternal malnutrition during pregnancy and/or

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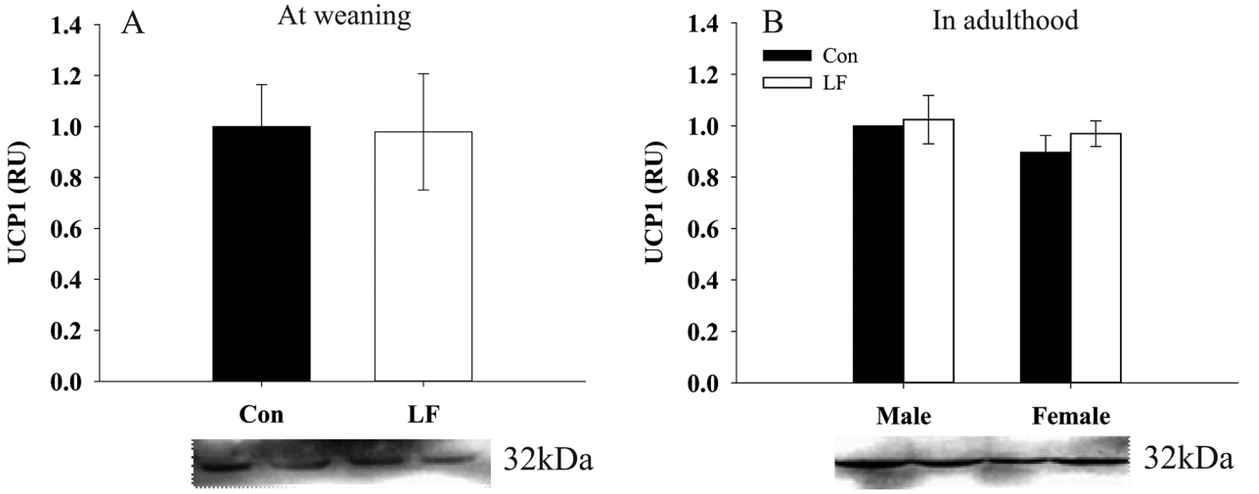

Figure 3. Effects of maternal low-fiber diet on offspring uncoupling protein 1 (UCP1) contents in brown adipose tissue at 18 d (at weaning; *A*) and 14 wk (in adulthood; *B*) of age. Con, maternal control diet; LF, maternal low-fiber diet; RU, relative unit.

lactation results in growth retardation and preference for a high-fat diet in young adult offspring (Pennington et al. 2001; Cagampang et al. 2009), while feeding on a high-fat diet during pregnancy and lactation also establishes a preference for a similar diet and a tendency to develop obesity in offspring (Purcell et al. 2011; Wright et al. 2011). However, maternal high-fiber diets protect offspring against high-fat diet-induced obesity in laboratory mice and rats (Hallam and Reimer 2013). Mammal herbivores suffer inadequate nutrition and energy intake because of low digestibility of a high-fiber diet (Sinclair et al. 1982; Karasov 1989; Bozinovic 1997). We demonstrated previously that supplementing energy in the diet (low-fiber diet) of mothers results in an increase in digestible energy intake (Lou et al. 2015*b*). In an attempt to explore whether a maternal low-fiber diet would confer long-term beneficial effects on the metabolism of offspring, we measured the reproductive outcomes and offspring metabolic phenotypes in herbivorous Brandt's voles.

Parental investment theory assumes that mothers—depending on their physical and nutritional conditions—must balance their current and future reproductive outcomes (Trivers 1974; Uller 2008). Previous studies have shown that milk composition and energy content are affected by maternal diet (Hacklander et al. 2002; Derrickson and Lowas 2007; Purcell et al. 2011; Priego et al. 2013; Hallam et al. 2014); thus, reproductive outcomes may be altered by maternal diet changes. Maternal high-fat or high-protein diet in rats does not affect litter size, male-female ratio, or birth weight but does increase pup growth (Purcell et al. 2011; Hallam and Reimer 2013). In our study, we found that litter size at birth

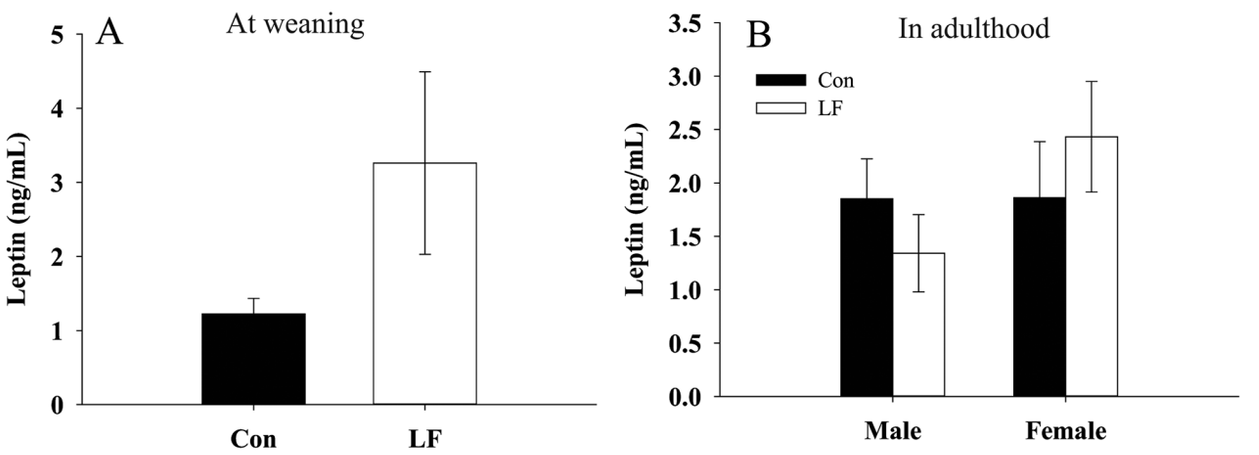

Figure 4. Effects of maternal low-fiber diet on offspring serum leptin concentration at 18 d (at weaning; *A*) and 14 wk (in adulthood; *B*) of age. Con, maternal control diet; LF, maternal low-fiber diet.

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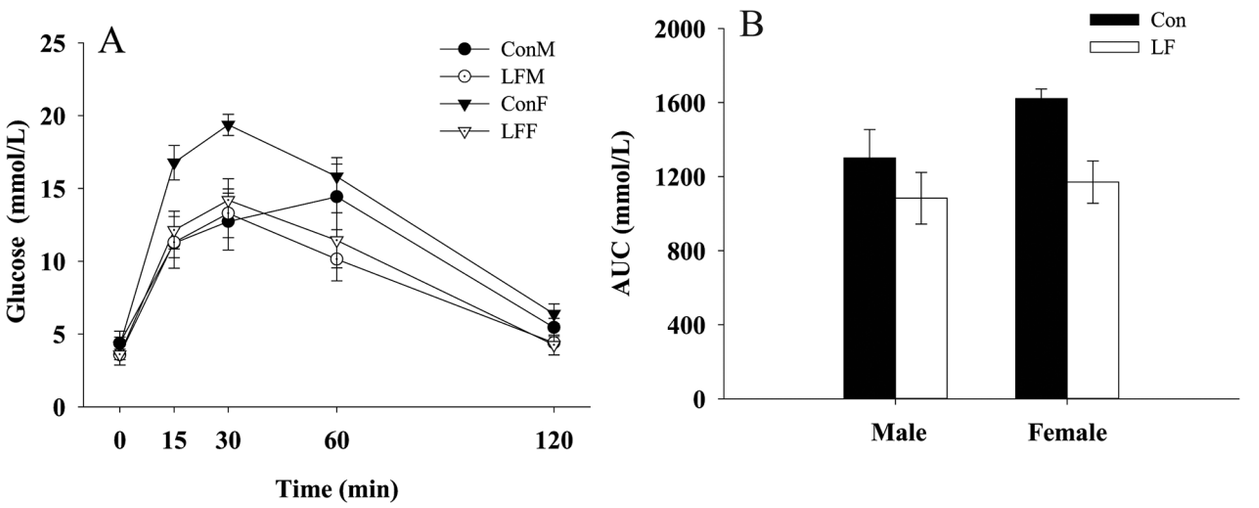

Figure 5. Effects of maternal low-fiber diet on offspring glucose tolerance. Blood glucose concentrations (*A*) and area under the curve (AUC; *B*) during the glucose tolerance test at 11 wk of age. ConM, male offspring from maternal control diet; LFM, male offspring from maternal low-fiber diet; ConF, female offspring from maternal control diet; LFF, female offspring from maternal low-fiber diet.

or at weaning, pup mass, total litter mass, sex ratio, and survival rate during lactation are not significantly affected by a maternal low-fiber diet. No change in reproductive outcome was also confirmed in the mothers of Brandt's voles, rats, and mice fed high-fiber or high-protein diets (Derrickson and Lowas 2007; Howie et al. 2009; Maurer and Reimer 2011; Lou et al. 2015*a*). These data indicate that the short-term effect of maternal diet alterations on reproductive outcomes may be diverse in different species and also depends on energy values of maternal diets.

Although reproductive outcomes were not altered, accelerated growth after weaning was identified in offspring from a maternal low-fiber diet. We also found that a maternal low-fiber diet resulted in increased energy intake in both male and female offspring until adulthood. Nonshivering thermogenesis indicated by UCP1 content in BAT at weaning and in adulthood was not altered by a maternal low-fiber diet in this study or by a maternal high-protein diet (Lou et al. 2015*a*), suggesting the same efficiency at retaining energy. The increase in mass of the stomach and small intestine could meet the need for increased energy intake in offspring from a maternal low-fiber diet. These results were consistent with studies in rats and monkeys, which showed that a maternal high-fiber diet promotes offspring mass loss (Fairbanks et al. 2010; Maurer et al. 2010). The change in body fat mass is usually in the same direction as the change in body mass. Interestingly, vole offspring from a maternal low-fiber diet accumulated less fat but gained more lean mass. The increased lean mass is probably the factor driving the rapid clearance of glucose in the low-fiber group. It also drives the higher basal metabolic rate, which may increase overwinter survival in wild small mammals (Jackson et al. 2001; Lardy et al. 2013). In addition, high body

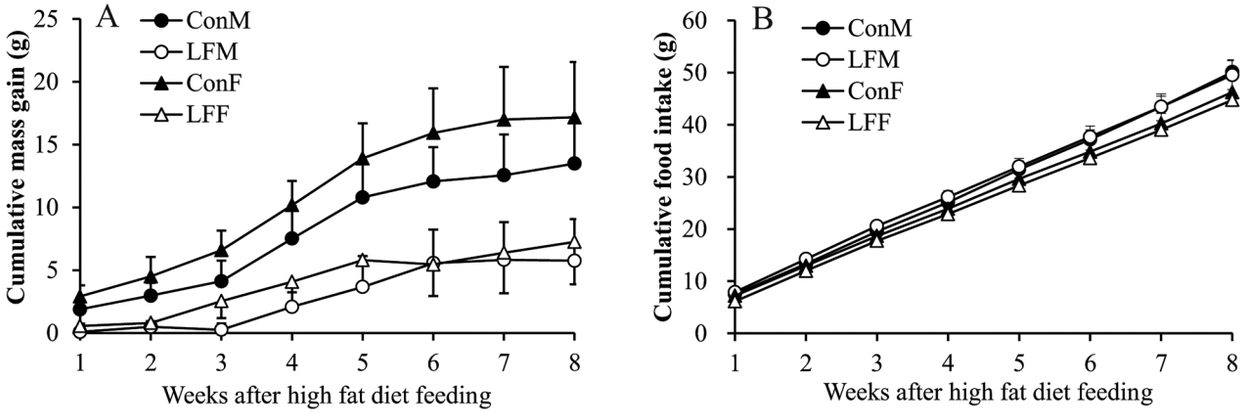

Figure 6. Effects of maternal low-fiber diet on offspring cumulative mass gain (*A*) and cumulative food intake (*B*) in response to high-fat diet in adults. ConM, male offspring from maternal control diet; LFM, male offspring from maternal low-fiber diet; ConF, female offspring from maternal control diet; LFF, female offspring from maternal low-fiber diet.

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mass is associated with high aggressive behavior and social rank, which may increase the opportunity for mating (Schorr et al. 2009). Our study also showed that offspring from a maternal low-fiber diet gained less body mass, with no decrease in food intake in response to a high-fat diet, implying that herbivores have the potential to protect against obesity in order to avoid predation. These data emphasize that herbivorous females feeding on diets with an appropriate low-fiber content during reproduction may allow their offspring to consume more energy and grow lean tissue faster, thus increasing fitness.

Energy balance is controlled partly by serum leptin concentration and its negative feedback circuit in the hypothalamus (Friedman and Halaas 1998). The premature leptin surge plays a critical role in programming metabolic disorders in adult (Itoh et al. 2005). Much evidence shows that a maternal high-fat diet or nutrition restriction eliminates the postnatal leptin surge (Leonhardt et al. 2003; Yura et al. 2005; Bautista et al. 2008; Delahaye et al. 2008; Long et al. 2011). Alteration in the serum leptin concentration during the early stage contributes to altered development in energy intake and energy expenditure in adults. Many previous studies have indicated that increased serum leptin at weaning is followed by increased energy intake during later development when mothers are exposed to high-fat or high-protein diets. We here found that there were no significant changes in serum leptin concentration at weaning or energy intake early after weaning between the two diets. These data validate the fact that serum leptin concentration during the early stage may program the development of appetites and metabolic phenotypes in later life.

In summary, it is clear that the reduced fiber content of maternal diet during reproduction has a lasting beneficial consequence on promoting the growth, glucose tolerance, and obesity resistance of offspring in herbivorous rodents. Offspring from a maternal low-fiber diet grew lean tissue faster, deposited less abdominal and visceral fat, and increased glucose tolerance in adulthood. Moreover, these adult offspring resisted high-fat diet-induced obesity. Our data validate the fact that herbivorous mothers consuming a low-fiber diet during reproduction could confer increased body mass (especially lean mass) on their offspring in adulthood to increase the opportunity for survival and reproduction. The mechanisms by which a maternal low-fiber diet improves offspring metabolic phenotypes in herbivores warrant further investigation.

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