ELSEVIER

Physiology & Behavior 87 (2006) 607–613

PHYSIOLOGY & BEHAVIOR

# Food restriction affects reproduction and survival of F1 and F2 offspring of Rat-like hamster (*Cricetulus triton*)

Hong Liang [a,b], Zhibin Zhang [a,*]

[a] *State Key Laboratory of Integrated Management of Pest Insects and Rodents in Agriculture, Institute of Zoology, Chinese Academy of Sciences, 25 Beisihuanxi Road, Haidian District, Beijing 100080, PR China*
[b] *Graduate School of the Chinese Academy of Sciences, Beijing 100039, PR China*

Received 4 June 2005; received in revised form 16 December 2005; accepted 16 December 2005

**Abstract**

Food restriction in parent may have long-term consequence on the reproductive capabilities of the offspring, and these consequences may, in turn, play an important role in population regulation. In this paper, we systematically examined the effect of maternal food restriction on reproduction and survival of maternal individuals, and F1 and F2 offspring of Rat-like hamsters (*Cricetulus triton*). Food restriction to 75% of that eaten by ad libitum-fed hamsters (75% FR) did not affect the reproductive organs and hormone concentration of maternal females, but 50% FR significantly reduced the size of ovarian organ and estradiol concentration of maternal females. 75% FR significantly reduced the testosterone concentration of maternal males; 50% FR significantly reduced both the size of epididymides and concentration of testosterone of maternal males. 70% FR in maternal females significantly reduced the sizes of reproductive organs and hormone concentrations of both their male and female F1 offspring. FR maternal females also produced significantly more male than female F1 offspring. The sizes of reproductive organs or hormone concentration of F2 males of maternal FR continued to significantly decline, but no such effect was observed in F2 females. However, the number of F2 offspring per F1 female of FR maternal females at birth became significantly smaller and with significantly more males than females. Survival to weaning of F1 and F2 offspring of FR maternal females became significantly smaller during the period from birth to weaning. Thus, the effects of maternal food restriction could be an important mechanism to explain the prolonged low population density that is commonly observed after the population crash of this species.


*Keywords:* Maternal effect; Food restriction; Reproduction; Litter size; Sex ratio; *Cricetulus triton*

## 1. Introduction

Food availability affects reproduction in many species [1]. It was hypothesized that females with restricted food availability would have lower sex gland mass and sex hormone levels [2]. In natural circumstance, maternal food restriction affects the reproductive success of both female and male offspring [3]. However, systematic investigations on the effects of maternal food restriction on the reproductive success of offspring are rare, and the current results are often controversial. It has been reported that maternal nutrition has negative impact on the reproductive success of FR offspring [3,4]. But Rogers et al. did not find intergenerational reproductive effects due to malnutrition in the female CD-1 mouse [5]. Food restriction may have long-term consequences on sex ratios of subsequent generations in mammals [6,7]. Previous studies with hamster and mice have demonstrated that mothers experiencing food restriction will skew the sex ratio of her offspring toward females and reduce litter size, suggesting that male fetuses are more susceptible than females to maternal under-nutrition [7,8]. But some studies reported that the sex ratio is not altered in rat or mice when deprived of adequate food [3,9,10], or even has a reverse result [6,11–13].

Population densities of rodents often fluctuate dramatically in nature. The senescence-maternal effect hypothesis has been suggested as an explanation for density lows of cyclic populations [14,15]. Pre- and postnatal stresses have been shown to have long-term, irreversible consequences on behavior and reproductive performance of the offspring [16–21]. Individuals that were born, raised or conceived during peak

* Corresponding author. Fax: +86 1062565689.
*E-mail address:* zhangzb@ioz.ac.cn (Z. Zhang).

0031-9384/$ - see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.physbeh.2005.12.006

and early decline phases will continue to exhibit physiological and behavioral responses to the stressful environment within which they were born [15,19,22]. During peak phases, rodents often experience food shortage [23–25], which may result in long-term effect on rodents in low phases. Most previous studies of food restriction in laboratory rodents were emphasized on health sciences [5,26,27]. There are few studies on the role of food restriction in population regulation of wild rodents.

The Rat-like hamster (*Cricetulus triton*) is one of the dominant rodent species in croplands of the Northern China Plain. They breed 1–3 times from March to August, with litter sizes ranging from 9 to 11. The population abundances of the species vary greatly among seasons, and among years. There was a prolonged low population density after the population crash of the Rat-like hamster [28]. Maternal food restriction was proposed to be an important causative factor in the population regulation of Rat-like hamsters [29]. We hypothesized that malnutrition in maternal hamsters would negatively affect reproductive success of offspring. In this paper, by manipulating food availability of adult males and females, we systematically examined the effect of maternal food restriction on the reproductive capabilities of maternal individuals, and the F1 and F2 offspring of Rat-like hamsters. Using the Rat-like hamster system, we investigate the effect of food restriction on maternal individuals and their F1 and F2 offspring.

## 2. Materials and methods

### *2.1. Experiment 1: effect of FR on maternal female and male reproduction*

#### *2.1.1. Animals and housing conditions*

Forty-five estrous female and 30 scrotal male individuals were used in this study. Each individual was around 3 months of age and the second descendants of Rat-like hamsters captured in farmland at the center of Hebei Province, North China Plain. Reproductive condition in females was defined by detection of vaginal secretions and their behavioral responses to males. The subjects were weighed and randomly assigned to one of three experimental diet groups for a 4-week trial. All animals were housed singly in plastic cages (40 cm × 25 cm × 15 cm) with wood shavings as bedding and maintained on a 16L/8D light cycle (lights on at 2100 h) at approximately 23 °C. Tap water was available ad libitum.

#### *2.1.2. Feeding regimens*

Animal models of malnutrition differ primarily in the severity and timing of the deficiency. The most common approach is to offer animals a reduced proportion of the usual diet. Control animals were allowed to continue to eat diet ad libitum. Food restricted animals were restricted to 75% and 50% of the mean food intake by control hamsters. The food intake of the ad lib group was recorded daily and used to assign the quantity of food to be consumed by the 75% and 50% FR groups. The animals were weighed daily prior to food allocation. FR animals were provided with food 1 h before the start of the dark phase of the light cycle.

#### *2.1.3. Blood sampling and tissue collections*

Four weeks later, the animals were sacrificed by decapitation, and trunk bloods were collected. Blood samples were allowed to clot at 4 °C for 1 h and, then, were centrifuged at 3500 rpm at 4 °C for 30 min. The samples were stored at −80 °C until the assay of sex hormone. Testes, uterine and ovarian were quickly removed, cleaned of connective tissue and weighed.

#### *2.1.4. Sex hormone radioimmunoassay*

Serum estradiol concentration of females and testosterone concentration of males were determined using $^{125}$I Radioimmunoassays kits provided by the Beimian Institute of Biotechnology (Beijing, China). For estradiol, the detectable range of the assay was 10–2000 pg/ml, the intra- and inter-assay coefficients of variation were 3.7–8.0% and 4.74–7.7%, respectively. For testosterone, the detectable range of the assay was 10–2000 ng/ml, the intra-assay and inter-assay coefficients of variation were <5% and <10% respectively.

### *2.2. Experiment 2: effect of maternal food restriction on the reproduction of F1 offspring*

Maternal individuals were captured in farmland at the center of Hebei Province, North China Plain. Forty-three females weighing 109–210 g (mean = 148.9 ± 24.3 g) were mated. The first day on which sperm was identified in vaginal smears was designated d1 of pregnancy. Pregnant females were housed individually. Tap water was available ad libitum. Previous experiments had shown that females receiving approximately 70% of the ad libitum intake of females could successfully reproduce. During pregnancy, the food-restricted animals ($n$ = 21) were presented with 70% of the mean daily intake of ad-lib-fed animals ($n$ = 22). Rat chow was provided as described by Liang et al. [29].

All animals delivered on day 18 of the pregnancy. On the day of parturition, designated d 1 of lactation, litters were counted and sexed as they were at 25 days (weaning). Food and tap water were provided ad libitum in both groups after parturition. F1 offspring were removed from their mothers at 25 days of age and were housed individually in new polycarbonate cages. Rat chow and water were available ad libitum within two groups. At the age of 60 days, 10 pups of every group were killed and anatomized, blood and tissue was sampled and sex hormone in serum was determined with the method described above.

### *2.3. Experiment 3: effect of maternal food restriction on reproduction of F2 offspring*

At 90 days old, 20 F1 daughters were selected randomly from the control and FR mother groups (all animals were within 1 week of age of each other). Each control and FR daughter was paired with a male chosen randomly from their own group (no sibling mate). On the day each litter was born, the litter (F2 offspring) was counted and sexed as they were at 25 days (weaning). The F2 offspring all received the normal diets throughout their development. At the age of 60 days, 10 pups of every group were killed and anatomized, blood and tissue was

Table 1
Effect of food restriction on sex hormone concentrations and relative reproductive organs of *C. triton*

| | Control group | 75% FR group | 50% FR group |
|---|---|---|---|
| Male | | | |
| Testis (mg/g) | 15.04±2.08[a] | 21.78±2.62[a] | 16.47±2.78[a] |
| Epididymides (mg/g) | 6.08±0.65[a] | 4.75±0.53[ab] | 3.61±0.78[b] |
| Testosterone (pg/ml) | 100.55±7.22[a] | 72.05±9.89[b] | 71.36±9.64[b] |
| Female | | | |
| Ovarian (mg/g) | 0.60±0.09[a] | 0.49±0.04[ab] | 0.37±0.03[b] |
| Uterine (mg/g) | 1.09±0.10[a] | 1.28±0.11[a] | 0.97±0.11[a] |
| Estradiol (pg/ml) | 31.17±4.3[a] | 31.73±3.81[a] | 19.33±1.74[b] |

Different letters indicate a significant difference at $P<0.05$.

sampled and sex hormone in serum was again determined using the method described in experiment 1.

### 2.3.1. Statistical analyses

All data are presented as the mean±S.E.M. Statistical analyses were performed using the SPSS statistical Package. Reproductive organ indices and hormone assay data were analyzed using a one-way analysis of variance (ANOVA). Pair-wise comparisons were examined by post-hoc tests, LSD were used where variances were homogeneous (homogeneity of variances tests, $P>0.05$), Games–Howell were used where the homogeneity of variance were violated (homogeneity of variances tests, $P<0.05$). Litter sizes were compared using Student's *t*-test. Sex ratio and survival to weaning rate were analyzed with Chi-square test. Results were considered significant if $P<0.05$.

## 3. Results

### 3.1. Influence of FR on reproduction of maternal Rat-like hamsters

#### 3.1.1. Reproductive organs indices and sex hormone concentrations of maternal Rat-like hamsters

Food restriction had no significant effect on testis indices of *C. triton*. Significant differences in epididymides indices were found between food regimes ($F_{2,\ 27}=3.529$, $P<0.05$), with the 50% FR group having significantly smaller epididymides than the control (LSD test, $P<0.05$). The 75% FR group did not differ significantly from the control and 50% FR group in epididymides size. The FR group displayed significantly lower serum testosterone concentrations than the control group ($F_{2,\ 27}=3.428$, $P<0.05$). The differences of serum testosterone concentrations between control and two FR groups were both significant (LSD test, $P<0.05$), whereas no differences were found in the serum testosterone concentration of the 75% and 50% FR groups.

Food restriction had no effect on uterine indices or ovarian indices. However, the 50% FR group had significantly lower ovarian indices than control group (Games–Howell test, $P<0.05$); the ovarian indices between the 75% group and the other two groups did not differ. The different feeding regimens resulted in a significant between-treatment difference in estradiol concentration ($F_{2,\ 27}=3.927$, $P<0.05$), which was significantly lower in 50% FR group (LSD test, $P<0.05$); The serum estradiol concentrations of the control and 75% FR groups did not differ (Table 1).

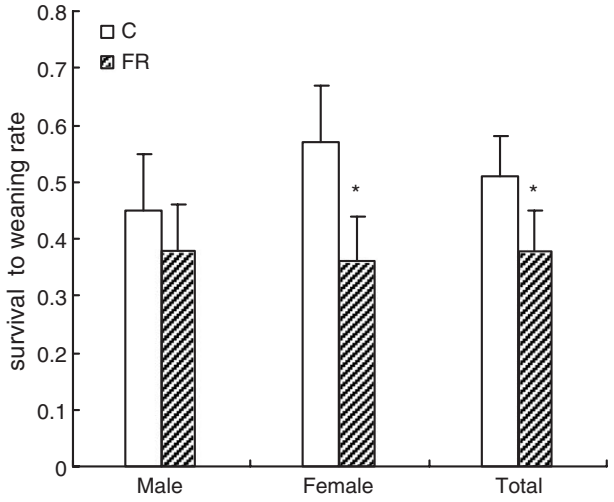


Fig. 2. Effect of maternal food restriction on survival to weaning rate of F1 offspring of *C. triton*. *, $P<0.05$.

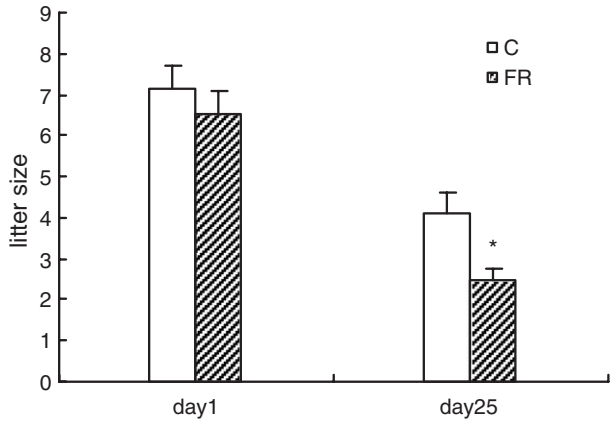


Fig. 1. Effect of maternal food restriction on number of F1 offspring per female of *C. triton*. *, $P<0.05$.

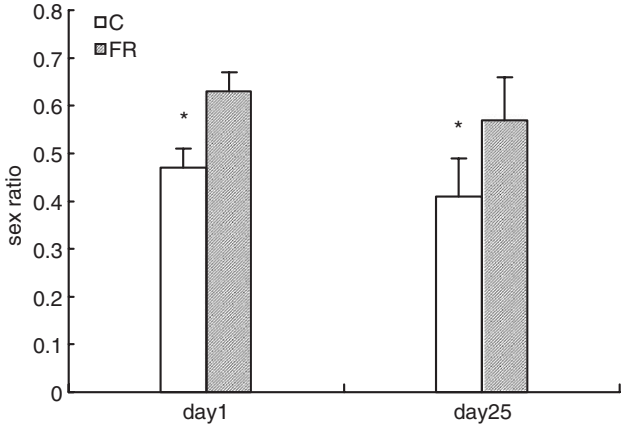


Fig. 3. Effect of maternal food restriction on sex ratio (proportion males) of F1 offspring of *C. triton*. *, $P<0.05$.

Table 2
Effect of maternal FR on sex hormone concentrations and relative reproductive organs of F1 offspring of *C. triton*

| | Control group | FR group |
|---|---|---|
| Male | | |
| Testis (mg/g) | 28.40±2.30 | 15.20±2.57* |
| Epididymides (mg/g) | 3.90±0.34 | 2.70±0.39* |
| Testosterone (pg/ml) | 90.29±11.53 | 37.67±18.05* |
| Female | | |
| Ovarian (mg/g) | 0.31±0.05 | 0.17±0.01* |
| Uterine (mg/g) | 1.18±0.12 | 1.07±0.11 |
| Estradiol (pg/ml) | 25.74±2.25 | 20.12±1.44* |

* $P<0.05$.

In general, the results in Table 1 indicate that 75% FR did not affect maternal female's reproductive organs and hormone, but 50% FR significantly reduced the size of ovarian organ and estradiol concentration of maternal females. Males seemed to be more vulnerable to food restriction. 75% FR significantly reduced the concentration of testosterone of maternal males, whilst 50% FR significantly reduced both the size of epididymides and concentration of testosterone of maternal males.

### 3.1.2. Number of F1 offspring per female and sex ratio at birth and weaning

There was no difference of litter size between control and FR maternal females of F1 at birth. However the number of F1 offspring per female at weaning of FR group was significantly lower than the control group ($t_{25}=2.591$, $P<0.05$) (Fig. 1), indicating the survival of FR F1 offspring between birth and weaning was significantly smaller than control group ($x^2=5.47$, $df=1$, $P<0.05$). The survival to weaning of FR female F1 offspring was significantly lower than the control group ($x^2=5.726$, $df=1$, $P<0.05$), whereas the survival to weaning of FR male F1 offspring did not differ significantly from the control group (Fig. 2). The percentages of FR F1 male offspring at parturition ($x^2=4.672$, $df=1$, $P<0.05$) and weaning ($x^2=4.459$, $df=1$, $P<0.05$) were both significantly greater than control group (Fig. 3), indicating FR resulted in significant male-biased offspring. In summary, FR maternal females produced more male than female F1 offspring. Survival of F1 offspring of FR maternal females became smaller from birth to weaning.

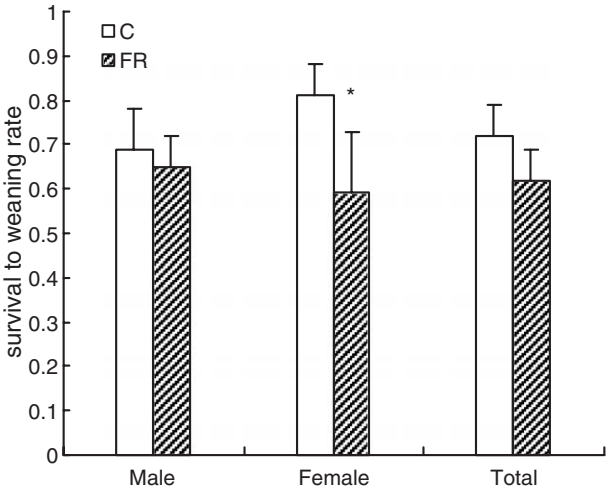


Fig. 5. Effect of maternal food restriction on survival to weaning rate of F2 offspring of *C. triton*.

### 3.2. Effect of maternal FR on reproduction and survival to weaning of F1 offspring

### 3.2.1. Reproductive organs indices and sex hormone concentrations of F1 offspring

Experimental group F1 males had significantly lower testosterone concentration ($t_{18}=2.457$, $P<0.05$), smaller testis ($t_{18}=3.834$, $P<0.01$), and smaller epididymides mass ($t_{18}=2.284$, $P<0.05$) than the control group (Table 2). Compared with the control group, the estradiol concentrations in serum were significantly lower in FR group females ($t_{18}=2.112$, $P<0.05$). The ovary indices of FR F1 females

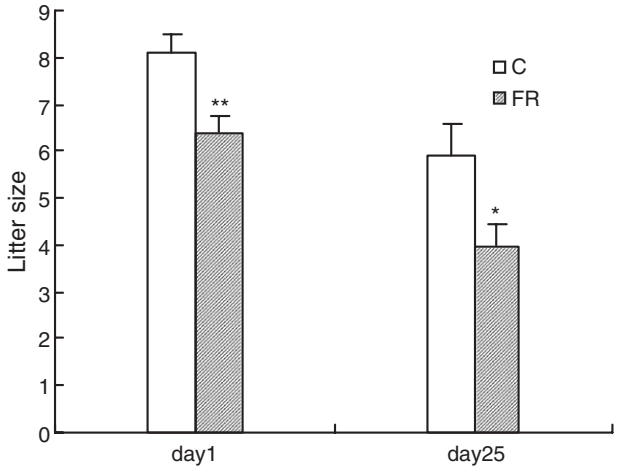


Fig. 4. Effect of maternal food restriction on number of F2 offspring per F1 female of *C. triton*. **, $P<0.01$; *, $P<0.05$.

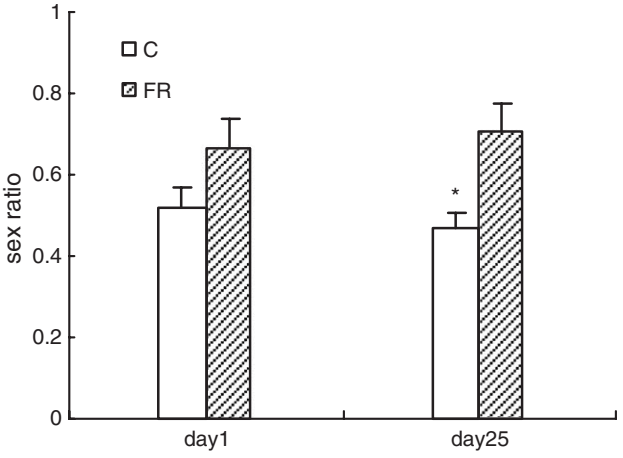


Fig. 6. Effect of maternal food restriction on sex ratio (proportion males) of F2 offspring of *C. triton*. *, $P<0.05$.

were also significantly smaller than control animals ($t_{18}$=2.440, $P$<0.05), whereas the uterine indices of FR group have no significant difference from the control group (Table 2).

*3.2.2. Number of F2 offspring per F1 female and sex ratio at birth and weaning*

The number of F2 offspring per F1 female in the FR group was significantly smaller than control group at both birth ($t_{18}$=3.561, $P$<0.01) and at weaning ($t_{18}$=2.273, $P$<0.05) (Fig. 4). There were no significant differences in the survival to weaning of male, and total F2 offspring from birth to weaning between the FR and control groups, but the survival to weaning of FR F2 females was significantly smaller than that of control group ($x^2$=3.832, $df$=1, $P$=0.05)(Fig. 5). Sex ratio (proportion of males) of F2 offspring at birth did not differ significantly from that of control litters, however there was a greater proportion of males of weaning in the FR group than the control group ($x^2$=4.543, $df$=1, $P$<0.05) (Fig. 6).

In summary, 70% FR in maternal females significantly reduced reproductive organ and hormone of both male and female F1 offspring. Furthermore, the number of F2 offspring per F1 female of FR maternal group at birth became significantly smaller, and with significantly more males. The survival to weaning of FR F2 females was significantly smaller than that of control group.

*3.3. Effect of maternal FR on reproduction and survival to weaning of F2 offspring*

F2 males of FR group had significantly lower serum testosterone concentrations ($t_{18}$=2.301, $P$<0.05) and smaller testis mass ($t_{18}$=2.127, $P$<0.05) than the control group. There was no significant difference of epididymides masses between the FR and control group; no significant difference of serum estradiol concentrations, ovarian indices and uterine indices between the FR and control group (Table 3). Thus, the reproductive organ or hormone of F2 males was still significantly inhibited by maternal FR, but no such effect was extended to the reproductive organ or hormone of F2 females.

Table 3
Effect of maternal FR on sex hormone concentrations and relative reproductive organs of F2 offspring of *C. triton*

| | Control group | FR group |
|---|---|---|
| Male | | |
| Testis (mg/g) | 29.72±5.11 | 15.80±4.09* |
| Epididymides (mg/g) | 10.30±2.71 | 4.84±1.12 |
| Testosterone (pg/ml) | 50.93±6.42 | 31.36±5.58* |
| Female | | |
| Ovarian (mg/g) | 0.48±0.07 | 0.44±0.04 |
| Uterine (mg/g) | 1.23±0.12 | 0.97±0.12 |
| Estradiol (pg/ml) | 19.16±1.74 | 22.97±1.84 |

* $P$<0.05.

## 4. Discussion

In this paper, we have shown that the reproductive organs and hormone concentration of male hamsters were more vulnerable to food restriction than those of females, but survival to weaning of FR F1 and F2 females were significantly smaller than that of males. Though 75% FR caused no obvious harm to the reproductive organs or hormone concentration of females, 70% FR during female pregnancy had a profound negative effect on the mass of reproductive organs and hormone concentrations in both male and female F1 offspring of the FR group. FR maternal females produced significantly more F1 males, and survival to weaning of F1 female offspring became significantly smaller. The negative effect of food restriction in maternal females on the mass of reproductive organs or hormone persisted in F2 males, but not to F2 females. F1 females of FR group produced significantly smaller F2 offspring and more male F2 offspring, and survival to weaning of FR F2 female offspring became significantly smaller. F2 males of FR group had significantly smaller reproductive organ masses, which may affect negatively the reproduction of F3 offspring. Therefore, the effects of maternal food restriction could be an important mechanism to explain the prolonged low population density that is commonly observed after the population crash of the Rat-like hamster in field.

The neural mechanisms by which food restriction affects reproductive development and maintenance are not well understood. The important anatomical locus of the effect of food restriction on reproductive function is likely to occur at the level of the hypothalamus, ultimately regulating GnRH release and subsequent LH and FSH release [2]. Changes in GnRH content and GnRH release have all been reported in various species in response to food restriction [30]. In this study, we found that estradiol or testosterone concentration significantly decreased with the degree of food restriction, the testis, epididymides and ovarian indices had the same changes with sex hormones, demonstrating that food restriction could damage the reproductive potential of adult male and female Rat-like hamsters.

Previous evidences indicated that if offspring experience malnutrition in utero through food deprivation of the mother during gestation, the reproductive success of male offspring may be most affected [3,7]. For example, Drickamer and Meikle found that depriving food of mothers during gestation had no effect on the timing of the first oestrus, body weight at weaning or sexual maturity for the female offspring of house mice (*Mus domesticus*) [31]. However, our study showed that food restriction during gestation equally affected male and female F1 offspring. In the F2 offspring, males were more vulnerable to the food restriction of grandmothers during gestation.

Adaptive sex-ratio theory predicts that parents should overproduce the more beneficial offspring sex. Kalmbach et al. reported such an effect in sexually dimorphic birds that overproduce the smaller sex under adverse conditions [32]. The local-resource-competition hypothesis predicts that in species with sex differences in natal philopatry the sex ratio of offspring should vary in response to the availability of resources for

philopatric offspring. For example, sex ratios would be biased towards the dispersing sex during low resource availability. In mammals, female offspring usually show natal philopatry whilst males disperse, so mammalian sex ratios are often male-biased [6,11]. The degree of sex ratio bias at the species level will be related to typical levels of resource competition [12]. In our study, the FR female hamsters and their daughters tend to bias the sex ratio towards the more dispersive, male offspring (see Ref. [28]). Thus, our results seemed to be consistent with local resource competition between mothers and daughters. An alternative explanation may be that more males mean lower capacity of population growth and may be a mechanism of response to food shortage.

Several hypotheses have been proposed to explain the physiological mechanisms of sex ratio skews in mammals [6]. Conditions within the reproductive tract, such as vaginal pH [33] or viscosity of cervical mucus [34], may favor Y-sperm over X-sperm, or vice versa, in terms of the fertilization potential. For example, Rosenfeld et al. showed that mothers on a more highly saturated fat diet produce a significantly higher fraction of male offspring and postulated that the diet may create a hormonal change affecting the reproductive tract of the female [35]. The developmental asynchrony hypothesis suggests that mothers adaptively alter sex ratios of offspring by influencing the relative time of insemination within the estrous cycle, or by altering reproductive hormone concentrations around the ovulation and early embryonic development periods [36]. The dynamics of reproductive hormones in response to implantation signals prepare the uterus during a specific part of the estrus cycle [37]. In mice, male blastocysts develop at higher rate than female blastocysts prior to implantation [38,39]. Hence, if uterine responsiveness is synchronized with male blastocysts development, male biases at birth would result, and vice versa. Adverse conditions for pre-implantation embryo development might result in death after implantation [40]. If females are developing more slowly than males, fetal death should predominantly affect female embryos. Sex ratio biases might result at birth if the dynamics of reproductive hormone concentrations shift the mean time of uterine responsiveness, its extent or symmetry. It is conceivable that changes in hormone concentrations can cause such asynchrony. Embryo transfer experiments have shown progesterone treatment can prevent the adverse effects of asynchrony in cows [41]. In humans, a slight dietary increase of fat can enhance the steroid hormone concentrations in serum [42]. Similarly, the results of this study demonstrated that food restriction significantly depressed the circulating concentrations of steroid hormones of parental, and F1 and F2 offspring in the Rat-like hamster. Such changes could provide the basis for the observed skew in the sex ratio in this species. Because FR female offspring had a higher mortality than that of FR males, we speculate that the mortality of female embryos might also be higher, resulting in the male offspring bias.

The effect of maternal malnutrition on litter sizes of rodents has been reported in a number of studies, where food restricted litters contain significantly fewer offspring than that of control litters [3,8,43]. For example, Meikle and Westberg showed that for the wild house mouse (*Mus musculus*) the mean number of pups weaned in the second litters by daughters of control females was greater than the number weaned by daughters of food-deprived females [3]. Conversely, other studies have reported that litter size in rats is not affected by maternal malnutrition [44]. Similarly no significant difference was found in the number of F2 offspring produced per F1 female at birth for CD-1 mouse mothers experiencing malnutrition during gestation. The undernourished females either carried full litters to term or completely reabsorb litters [5]. No significant difference in the number of F2 offspring per F1 were found for the female red-backed vole (*Clethrionomys gapperi*), but in the meadow vole (*Microtus pennsylvanicus*), the mean number of F2 offspring per F1 female malnourished as infants was greater than those of control [45]. These contrasting results could be explained by different degrees of food restriction or species-specific responses. Our study showed that FR mothers produced the same offspring as control mothers at birth, but daughters of FR group produced significantly less offspring than control daughters at birth. We also found that the survival of F1 and F2 female offspring of FR females became significantly smaller from birth to weaning, that effect not observed in males. This phenomenon has not been noted before.

In general, maternal food restriction has long-term consequences for both the reproduction and survival of offspring of Rat-like hamsters. Its role in the population regulation of Rat-like hamsters is worth exploring. Future experiments should examine if maternal food restriction in hamsters could extended to offspring beyond F2 offspring, and the mechanisms producing sex biases, as well as the poor survival of females.

## Acknowledgment

This work was supported by the Innovation Program of Chinese Academy of Sciences (KSCX2-SW-103), CAS Innovative Research International Partnership Project (CXTDS2005-4) and the Grant of National Natural Science Foundation of China (30370232). Mr. Fusheng Wang provided help in capturing wild hamsters. We are grateful to Dr. Greg McInerny, NERC Centre for Ecology and Hydrology, UK, for improving our English writing of the manuscript.

## References

[1] Bronson FH, Heideman PD. Seasonal regulation of reproduction in mammals. In: Knobil E, Neill JD, editors. The physiology of reproduction, 2nd ed., vol. 2. New York: Raven Press; 1994. p. 541–84.
[2] Wade GN, Schneider JE. Metabolic fuels and reproduction in female mammals. Neurosci Biobehav Rev 1992;16:235–72.
[3] Meikle D, Westberg M. Maternal nutrition and reproduction of daughters in wild house mice (*Mus musculus*). Reproduction 2001;122:437–42.
[4] Clutton-Brock TH. Reproductive success. In: Clutton-Brock TH, editor. Reproductive success. Chicago: University of Chicago Press; 1988. p. 472–85.
[5] Rogers EH, Hunter ES, Rosen MB, Rogers JM, Lau C, Hartig PC, et al. Lack of evidence for intergenerational reproductive effects due to prenatal and postnatal undernutrition in the female CD-1 mouse. Reprod Toxicol 2003;17:519–25.

[6] Clutton-Brock TH, Iason GR. Sex ratio variation in mammals. Rev Biol 1986;61(3):339–74.
[7] Meikle DB, Thornton MW. Premating and gestational effects of maternal nutrition on secondary sex ratio in house mice. J Reprod Fertil 1995;105 (2):193–6.
[8] Huck UW, Labov JB, Lisk RD. Food restricting young hamsters (*Mesocricetus auratus*) affects sex ratio and growth of subsequent offspring. Biol Reprod 1986;35:592–8.
[9] Pascalon A, Bertrand M. Effects of overall food restriction on embryo-fetal development in the rat. Ann Rech Vet 1987;18(4):379–88.
[10] Krackow S. Maternal investment, sex-differential prospects, and the sex ratio in wild house mice. Behav Ecol Sociobiol 1997;41:435–43.
[11] Cockburn A. Sex ratio variation in marsupials. Aust J Zool 1990;37:467–79.
[12] Johnson CN. Dispersal and the sex ratio at birth in primates. Nature 1988;332:726–8.
[13] Silk JB. Local resource competition and facultative adjustment of sex ratios in relation to competitive abilities. Am Nat 1983;121:56–66.
[14] Boonstra R. Population cycles in microtines: the senescence hypothesis. Evol Ecol 1994;8:196–219.
[15] Boonstra R, Krebs CJ, Stenseth NC. Population cycles in small mammals: the problem of explaining the low phase. Ecology 1998;79:1479–88.
[16] Drickamer LC, Mikesic DG. Urinary chemosignals, reproduction, and population size for house mice (*Mus domesticus*) living in field enclosures. J Chem Ecol 1990;16:2955–69.
[17] Hansson L. Tracking or delayed effects in microtine reproduction? Acta Theriol 1989;34:125–32.
[18] Henry C, Kabbaj M, Simon H, Moal ML, Maccari S. Prenatal stress increases the hypothalamo–pituitary–adrenal axis response in young and adult rats. J Neuroendocrinol 1994;6:341–5.
[19] Mihok S, Boonstra R. Breeding performance in captivity of meadow voles (*Microtus pennsylvanicus*) from decline- and increase-phase populations. Can J Zool 1992;70:1561–6.
[20] Polland I. Prenatal stress effects over two generations in rats. Endocrinology 1986;109:239–44.
[21] Ward IL, Read J. Prenatal stress and prepubertal social rearing conditions interact to determine sexual behavior in male rats. Behav Neurosci 1985;99:301–9.
[22] Newson J, Chitty D. Haemoglobin levels, growth and survival in two *Microtus* populations. Ecology 1962;43:733–8.
[23] Lack D. The natural regulation of animal numbers. Oxford, UK: University Press; 1954.
[24] Keith LB. Some features of population dynamics in mammals. In: Kjerner I, Bjurholm P, editors. XI International Congress of Game Biologists, Stockholm. Stockholm, Sweden: National Swedish Environment Protection Board; 1974. p. 17–58.
[25] Fox JF, Bryant JP. Instability of the snowshoe hare and woody plant interaction. Oecologia 1984;63:128–35.
[26] Lass A, Sohal BH, Weindruch R, Forster MJ, Sohal RS. Caloric restriction prevents age-associated accrual of oxidative damage to mouse skeletal muscle mitochondria. Free Radic Biol Med 1998;25(9):1089–97.
[27] Sakamoto S, Muto T, Yokota M, Ishimura N, Niwa Y, Harada N, et al. Comparison between short-term food restriction and exercise on whole body glucose disposal in high-fat fed rats. J Med Invest 2000;47:138–44.
[28] Zhang ZB, Yang HF, Wang SQ, Wang FS, Hao SS, Cao XP. The ecology and sustainable management of the Rat-like hamster. In: Zhang ZB, Wang ZW, editors. Ecology and management of rodent pests in agriculture. Beijing: Ocean Press; 1998. p. 1–19. [in Chinese].
[29] Liang H, Zhang JJ, Zhang ZB. Food restriction in pregnant Rat-like hamsters (*Cricetulus triton*) affects endocrine, immune function and odor attractiveness of male offspring. Physiol Behav 2004;82:453–8.
[30] Bergendahl M, Veldhuis JD. Altered pulsatile gonadortropin signaling in nutritional deficiency in the male. Trends Endocrinol Metab 1995;6:145–59.
[31] Drickamer LC, Meikle DB. Food deprivation affects reproduction in adult female mice (*Mus musculus*) and the age of puberty for their female progeny. Acta Biol Hung 1988;39:361–75.
[32] Kalmbach E, Nager RG, Griffiths R, Furness RW. Increased reproductive effort results in male-biased offspring sex ratio: an experimental study in a species with reversed sexual size dimorphism. Proc R Soc Lond B 2001;268:2175–9.
[33] Pratt NC, Huck UW, Lisk RD. Offspring sex ratio in hamsters is correlated with vaginal pH at certain times of mating. Behav Neural Biol 1987;48:310–6.
[34] Martin JF. Length of the follicular phase, time of insemination, coital rate and the sex of offspring. Hum Reprod 1997;12(3):611–6.
[35] Rosenfeld CS, Grimm KM, Livingston KA, Brokman AM, Lamberson WE, Roberts RM. Striking variation in the sex ratio of pups born to mice according to whether maternal diet is high in fat or carbohydrate. Proc Natl Acad Sci 2003;100(8):4628–32.
[36] Krackow S. Developmental asynchrony hypothesis for sex ratio manipulation. J Theor Biol 1995;176:273–80.
[37] Pope W. Uterine asynchrony: a cause of embryonic loss. Biol Reprod 1988;39:999–1003.
[38] Valdivia RPA, Kunieda T, Aauma S, Toyoda Y. PCR sexing and developmental rate differences in preimplantation mouse embryos fertilized and cultured in vitro. Reprod Dev 1993;35:121–6.
[39] Tsunoda Y, Tokunaga T, Sugie T. Altered sex ratio of live young after transfer of fast- and slow-developing mouse embryos. Gamete Res 1985;12:301–4.
[40] Ertzeid G, Storeng R. Adverse effects of gonadotropin treatment on pre- and postimplantation development in mice. J Reprod Fertil 1992;96:649–55.
[41] Geisert RD, Fox TC. Survival of bovine embryos transferred to progesterone-treated asynchronous recipients. J Reprod Fertil 1991;92:475–82.
[42] Dorgan J, Hunsberger S, McMahon R, Kwiterovich PJ, Lauer R, Van Horn L, et al. Diet and sex hormones in girls: findings from a randomized controlled clinical trial. J Natl Cancer Inst 2003;95:132–41.
[43] McGuire MK, Littleton AW, Schulze KJ, Rasmussen KM. Pre- and postweaning food restrictions interact to determine reproductive success and milk volume in rats. J Nutr 1995;125(9):2400–6.
[44] Woodall SM, Breier BH, Johnston BM, Gluckman PD. A model of intrauterine growth retardation caused by chronic maternal undernutrition in the rat: effects on the somatotrophic axis and postnatal growth. J Endocrinol 1996;150(2):231–42.
[45] Bondrup-Nielsen S, Foley PM. Long-term effects of malnutrition on reproduction: a laboratory study with measow voles, *Microtus pennsylvanicus* and red-backed voles, *Clethrionomys gapperi*. Can J Zool 1994;72:232–8.