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Effect of leptin resistance on body weight regulation in pregnant *Apodemus chevrieri*

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ABSTRACT

In order to clarify whether the *Apodemus chevrieri* has leptin resistance during pregnancy. The body weight, food intake, fat weight and serum leptin concentration of 12 adult female *A. chevrieri* were measured. The results showed that the body weight, food intake and serum leptin concentration of pregnant *A. chevrieri* were significantly higher than those of non-pregnant *A. chevrieri*. Serum leptin concentration was positively correlated with body weight and fat content. The results indicated that there might be leptin resistance in pregnant *A. chevrieri*, which allowed the body weight adjustment point to rise and adapt to the increase of energy demand during pregnancy.

Keywords: *Apodemus chevrieri; leptin resistance; serum leptin concentration; energy metabolism*

1. INTRODUCTION

Leptin is a kind of protein hormone secreted by white adipocytes, higher concentration of serum leptin can inhibit food intake, promote heat production and reduce body weight (Tang et al., 2019). The findings provide strong support for the hypothesis that "adiposity signal" hormone determines the maintenance of energy homeostasis in mammals, and the discovery of leptin resistance has provided a new understanding of animal energy homeostasis (Daniella et al., 2018). There are two main states of leptin resistance, one is pathological, such as food induced obesity; the other is adaptive response to allow changes in body weight adjustment point, such as mammalian pregnancy (Gonzalez-Bulnes et al., 2013). Generally, in order to adapt to the stress pressure caused by environmental changes, animals often produce new adaptive changes to the future environmental changes, including changing the body weight adjustment point to make the body weight level higher or lower than the "default value" level, so as to meet the challenges of environmental changes on the survival and adaptation of animals (Ladyman, 2010).

Pregnancy is not only the initial stage of mammalian reproduction, but also an important link. The metabolism, physiological and biochemical indexes of pregnant animals change, and their energy consumption mainly includes tissue growth of fetus, enlargement of uterus and placenta, development of mammary gland and energy consumption of maintaining these tissues (Hennin et al., 2019). Previously study found that the leptin level of pregnant animals increased significantly, body weight and food intake increased, which indicated that the body may not be sensitive to leptin during pregnancy, which may produce leptin resistance, increase food intake, allow the body weight setting point higher than the "missing value" level to adapt to the increase of energy demand during pregnancy (Henson and Castracane, 2006).

Apodemus chevrieri is a inherent species in Hengduan mountain region(Zhu et al. 2016). The breeding period is longer, in which June to September is the concentrated period. Previous studies had demonstrated the presence of a seasonal variation in body mass and serum leptin levels in non reproductive *A. chevrieri* (Zhu et al., 2012), and cold temperature reduced serum leptin levels but enhance thermogenic capacity (Zhu et al., 2011), whereas the short photoperiod also enhanced thermogenic capacity, (Zhu et al. 2013). All of the studies suggested that serum leptin plays a fat signaling role in the seasonal changes of energy homeostasis in *A. chevrieri.* On the basis of the above studies, the present paper studies whether there is leptin resistance during pregnancy and the role of leptin in the regulation of body weight, so as to provide a scientific basis for understanding the energetic changes of this species during pregnancy.

2. MATERIALS AND METHODS

2.1 Samples

A. chevrieri were captured in farmland (26°15´-26°45´N; 99°40´-99°55´E; altitude 2,590m) in Jianchuan County, Yunnan province. All animals were healthy female adults. *A. chevrieri* was housed individually in a wire cage (350×300×250mm3). Food and water were provided ad libitum. All animal procedures were licensed under the Animal Care and Use Committee of School of Life Sciences, Yunnan Normal University (Permit No.: 13-0901-011).

Six *A. chevrieri* in pregnancy and non pregnancy were selected. After the measurement of body mass, Food intake was calculated as the mass of food missing from the hopper, subtracting orts mixed in the bedding.

2.2 Measurement of fat mass

The entire gastrointestinal tract was removed, and the eviscerated carcass was dried to constant weight at 60°C for determination of dry body mass. Total body fat was extracted from the dried carcass by ether extraction in a Soxhlet apparatus (Li and Wang, 2005).

2.3 Measurement of serum leptin level

Serum leptin levels were determined by radioimmunoassay (RIA) with the 125I Multi-species Kit (Cat. No. XL-85K, Linco Research Inc.).The lowest level of leptin that can be detected by this assay was 1.0 ng/ml when using a 100-μl sample size. And the inter- and intra-assay variability for leptin RIA were <3.6% and 8.7%, respectively.

2.4 Statistical analysis

Data were analyzed using SPSS 15.0 software package. Prior to all statistical analyses, data were examined for assumptions of normality and homogeneity of variance, using Kolmogorov-Smirnov and Levene tests, respectively. Differences in body mass, food intake, fat mass and serum leptin levels between pregnancy and non pregnancy group were assessed by independent-samples t test. Pearson correlation analyses were used to detect possible associations of serum leptin levels with body mass, body fat mass, and food intake. Results were presented as mean ± SEM, and $P < 0.05$ was considered to be statistically significant.

3. RESULTS

The body weight, fat content, food intake and serum leptin concentration in pregnant group were significantly higher than those of non pregnant group (body weight: $T = -9.45$, $P < 0.01$; fat content: $T = -11.47$, $P < 0.01$; food intake: $T = -18.43$, $P < 0.01$; serum leptin concentration: $T = -7.12$, $P < 0.01$, Table 1).

Table 1: The changes of body mass, body fat content, food intake and serum leptin levels in pregnancy and non-reproductive *Apodemus chevrieri*

	Non pregnancy group	Pregnancy group	P value
Samples	6	6	
Body mass (g)	35.54±0.57	43.41±0.61	<0.01
Fat mass (g)	5.29±0.19	7.99±0.15	<0.01
Food intake (g)	5.73±0.01	9.17±0.16	<0.01
Leptin levels (ng/ml)	1.22±0.05	1.75±0.14	<0.01

Serum leptin concentration was positively correlated with body weight, fat weight and food intake (body weight: $r = 0.879$, $P < 0.01$, Fig. 1A; fat weight: $r = 0.874$, $P < 0.01$, Fig. 1B; food intake: $r = 0.866$, $P < 0.01$, Fig. 1C).

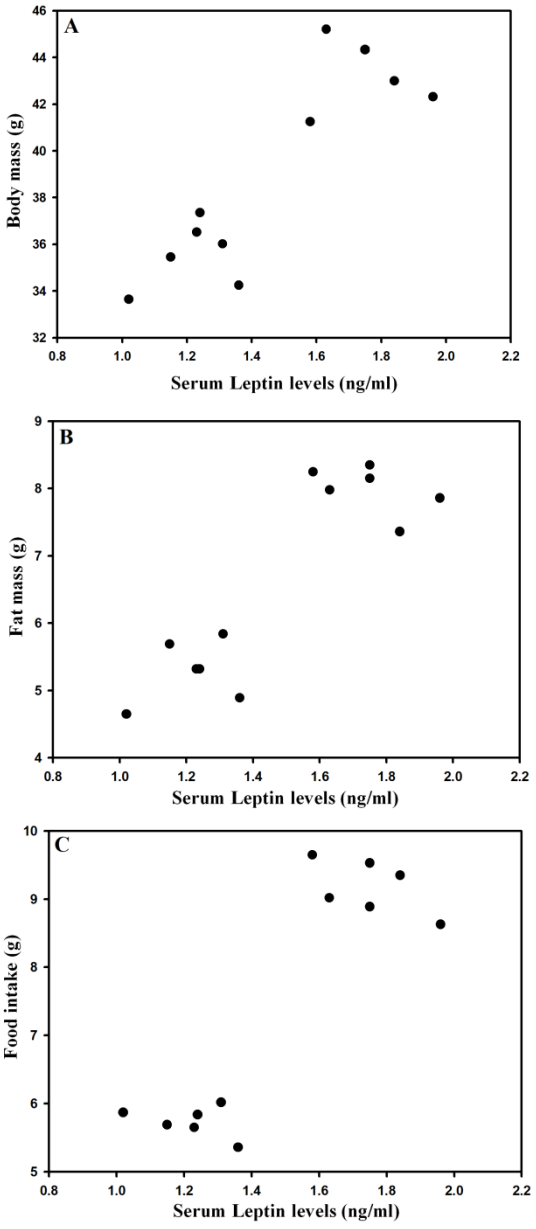

Figure 1 Relationship between serum leptin levels and body mass(A), fat mass (B) and food intake (C) in *Apodemus chevrieri*

4. DISSCUSSION

"Lipid homeostasis" suggests that animals can regulate energy homeostasis by sensing the change of total body fat weight, and leptin, as a "body fat signaling" hormone, plays an important role in animal weight regulation (Fu et al., 2012). Higher leptin concentration can inhibit food intake. In general, serum leptin concentration is positively correlated with body weight and fat content in small rodents. The serum leptin level of obese rodents is higher than that of normal individuals (Guo et al., 2013). Studies on serum leptin of wild type mice showed that higher concentration of leptin could reduce body weight by 12% and body fat by 11.5%, suggesting that leptin plays an important role in the regulation of energy homeostasis in wild type mice (Roth et al., 2008). In the present study, there was a significant positive correlation between serum leptin concentration and body weight and body fat content in *A. chevrieri*, which also indicated that serum leptin concentration played an important role in regulating body weight in maintaining energy homeostasis.

At present, studies on the regulation of energy homeostasis by leptin mainly focus on the molecular mechanism of leptin resistance (Daniella et al., 2018). For example, the molecular mechanism of leptin resistance in human under pathological conditions (obesity) was studied (Atilla, 2018). Leptin resistance plays an important role in the plasticity adaptation physiological response of animal energy homeostasis mechanism. It allows adaptive changes in body weight regulation points, such as mammalian pregnancy or seasonality. During pregnancy, the body weight, food intake and serum leptin concentration of the animals increase significantly (Tang et al., 2019). This may be due to the increase of energy demand during pregnancy. By increasing food intake, the body weight adjustment point can be changed to make the body weight higher than the "missing value" level, so as to meet the pressure of increased energy demand during pregnancy. The serum leptin level of pregnant animals increased, but the food intake and body weight did not decrease, indicating that the body may not be sensitive to leptin, that is leptin resistance (Dhillon et al., 2018). In our study, the serum leptin concentration, body weight and body fat content of the pregnant rats were higher than those of the non pregnant group, suggesting that the pregnant rats may have leptin resistance, and the higher concentration of serum leptin does not play a role in inhibiting food intake and reducing body weight. The results showed that leptin resistance occurred during pregnancy and the body weight setting point was higher than the "missing value", which may lead to a significant increase in food intake to cope with the cost of energy consumption during delivery, fetal growth and lactation during pregnancy and subsequent lactation.

5. CONCLUSION

In comclusion, pregnant *A. chevrieri* have leptin resistance, higher body weight and fat content are conducive to coping with the increase of energy demand during pregnancy, and preparing for lactation delivery, fetal growth and lactation. Leptin resistance in pregnant *A. chevrieri* may reflect the energy strategy and survival adaptation mechanism of small rodents in Hengduan Mountain region during pregnancy.

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7. ACKNOWLEDGEMENTS

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