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Energy metabolism, thermogenesis and body mass regulation in Brandt's voles (*Lasiopodomys brandtii*) during cold acclimation and rewarming

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Abstract

Environmental cues play important roles in the regulation of an animal's physiology and behavior. The purpose of the present study was to test the hypothesis that ambient temperature was a cue to induce adjustments in body mass, energy intake and thermogenic capacity, associated with changes in serum leptin levels in Brandt's voles (*Lasiopodomys brandtii*). We found that Brandt's voles increased resting metabolic rate (RMR) and energy intake and kept body mass stable when exposed to the cold while showed a significant increase in body mass after rewarming. The increase in body mass after rewarming was associated with the higher energy intake compared with control. Uncoupling protein 1 (UCP1) content in brown adipose tissue (BAT) increased in the cold and reversed after rewarming. Serum leptin levels decreased in the cold while increased after rewarming, associated with the opposite changes in energy intake. Further, serum leptin levels were positively correlated with body mass and body fat mass. Together, these data supported our hypothesis that ambient temperature was a cue to induce changes in body mass and metabolism. Serum leptin, as a starvation signal in the cold and satiety signal in rewarming, was involved in the processes of thermogenesis and body mass regulation in Brandt's voles.

Keywords: Cold acclimation; Energy intake; Leptin; Rewarming; Resting metabolic rate (RMR); Uncoupling protein 1 (UCP1)

Introduction

In endothermic small mammals, ability to survive in cold environment requires proper strategies and efficient thermoregulatory mechanisms (McNab, 2002). Small mammals usually show seasonal changes in physiology and behavior (Bartness et al., 2002; Concannon et al., 2001; Klingenspor et al., 1996). To cope with winter or cold conditions, some small mammals will reduce their overall body mass and body fat and enhance nonshivering thermogenesis (NST) (Bartness et al., 2002; Concannon et al., 2001; Li and Wang, 2005a,b). The decline in body mass is an adaptive mechanism to reduce the energy requirements when food availability is limited and cold stress occurs (Wunder et al., 1977). An increase in NST could be attributed to the increased expression of uncoupling protein 1 (UCP1), which is the unique thermogenic protein found in the inner membrane of mitochondria in brown adipose tissue (BAT). UCP1 uncouples the oxidation of fuel from adenosine triphosphate (ATP) production and transforms electrochemical energy into heat (Cannon and Nedergaard, 2004; Himms-Hagen, 1985; Nicholls and Locke, 1984). The increased energy expenditure for thermogenesis in the cold may be compensated by hyperphagia in small mammals (Kenagy et al., 1989).

It has been indicated that circulating leptin, primarily synthesized and secreted from adipose tissue, acts with the long-form OB-Rb receptors in the hypothalamic arcuate nulceus to regulate food intake and body mass (Friedman and Halaas, 1998). Bing et al. (1998) found that decreased plasma leptin was accompanied by hyperphagia in cold-exposed rats. Exogenous leptin treatments could decrease food intake and increase energy utilization, thus resulting in the decline in body mass (Abelenda et al., 2003; Pelleymounter et al., 1995). Furthermore, leptin administration stimulated sympathetic nerve activity and

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increased animal's body temperature, basal metabolic rate (BMR), NST, and UCP1 mRNA expression in BAT, indicating a potential involvement in the regulation of thermogenesis (Haynes et al., 1997; Scarpace and Metheny, 1998). However, contradictory results have been reported. In the cold-exposed rats, low serum leptin levels were accompanied by an increase in UCP1 gene expression (Bing et al., 1998), and leptin administration reduced BAT thermogenesis (Abelenda et al., 2003). Thus, the role of leptin in regulating energy intake and expenditure is complex.

Brandt's voles (*Lasiopodomys brandtii*) are nonhibernating herbivores that mainly inhabit the grasslands of Inner Mongolia of China, Mongolia, and the region of Beigaer in Russia, where winter lasts for more than 5 months (Li and Wang, 2005a; Zhao and Wang, 2005). It has been reported that Brandt's voles showed seasonal changes in NST, energy intake, and body mass, indicating potential roles for photoperiod and temperature in the regulation of energy balance and body mass (Li and Wang, 2005a; Wang et al., 2003). Zhao and Wang (2005) have confirmed that short photoperiod, independent of ambient temperature and food availability, decreased body mass in Brandt's voles. It is well known that cold exposure increased BMR, NST, and energy intake in small mammals (Li et al., 2001), whereas available data of the rewarming effects on energy metabolism and body mass were limited. The present study was designed to investigate the role of cold acclimation and rewarming on the energy metabolism and body mass regulation in Brandt's voles. We hypothesized that ambient temperature was an important cue to influence body mass, and leptin was involved in the regulation of energy metabolism and body mass. We can predict that cold acclimation decreases body mass, while rewarming can increase body mass. Leptin will be decreased as a hungry signal to increase the energy intake in the cold while increased as a satiety signal to inhibit energy intake in the warm conditions.

Materials and methods

Animals and experimental designs

All animal procedures were licensed under the Animal Care and Use Committee of Institute of Zoology, the Chinese Academy of Sciences. Studies were carried out in adult male Brandt's voles. They were the offspring of Brandt's voles trapped in Inner Mongolian grasslands in May 1999 and raised in Institute of Zoology, the Chinese Academy of Sciences in Beijing (Li and Wang, 2005a; Zhao and Wang, 2005). Subjects were housed in groups (3–4) in plastic cages (30 × 15 × 20 cm^3) with sawdust bedding after being weaned, and were maintained at the room temperature of 23 ± 1°C, under a photoperiod of 12L:12D (with lights on at 0800). Subjects were fed with commercial rabbit pellets (Beijing KeAo Feed Co.) and water ad libitum.

Experiment 1

In order to test the effects of ambient temperature on body mass, sixteen weight-matched male voles were moved into individual cages and kept for at least 2 weeks and then were randomly assigned into two groups. One group (the treated group: Cold + warm) was transferred to cold (5 ± 1°C) and maintained for 4 weeks and then returned to 23 ± 1°C for further 4 weeks, the other group (Control) remained at 23 ± 1°C throughout the test. Photoperiod was kept at 12L:12D throughout the study. Body mass, RMR, and energy intake during the course of the experiment were measured.

Experiment 2

We further tested the response of leptin to the cold and its role in regulating energy intake, energy expenditure, and body mass in Brandt's voles. This experiment was carried out with another 50 male individuals. They were exposed to 5 ± 1°C for 28 days and then returned to 23 ± 1°C for further 28 days. On days 0, 1, 7, 28, 29, 35, and 56, different individuals were sacrificed and these 7 groups were named C0, C1, C7, C28, RW1, RW7, and RW28, respectively (C, cold; RW, rewarming). The experimental design was shown in Fig. 1. The voles were sacrificed between 0900 and 1100 by puncture of the posterior vena cava. Blood was centrifuged at 4000 rpm for 30 min, and serum was sampled and stored at −20°C for later measurement. The interscapular BAT was surgically removed and immediately frozen in liquid nitrogen and stored at −80°C for determining BAT cytochrome *c* oxidase (COX) activity and UCP1 contents.

Metabolic trials

Resting metabolic rate (RMR) was measured by using an established closed-circuit respirometer at 30 ± 0.5°C (within their thermal neutral zone) as described previously (Li and Wang, 2005a; Wang et al., 2003; Zhao and Wang, 2005). Briefly, the metabolic chamber volume was 3.6 l, and the temperature inside the chamber was maintained by a water bath. KOH and silica gel were used to absorb carbon dioxide and water respectively in the metabolic chamber. The voles were weighed before and after each test. After 60-min stabilization in the chamber, oxygen consumption was recorded for another 60 min at 5-min intervals. Two stable consecutive lowest readings were taken to calculate RMR and corrected to standard temperature and pressure (STP) (Li and Wang, 2005a; Zhao and Wang, 2005). All metabolic measurements were taken between 0900 and 1700 to minimize any effects of circadian rhythms.

Gross energy intake

Food intake was measured for 3 days once a week as described previously (Li and Wang, 2005a; Song and Wang, 2003). During each test, voles were housed individually in stainless steel mesh metabolic cage (24 × 24 × 24 cm^3), in which food and water were provided ad libitum. Uneaten food and feces were collected after the 3-day test, oven dried at 60°C and separated manually. The caloric values of food and feces were determined by Parr1281 oxygen bomb calorimeter (Parr Instrument, USA). Gross energy intake was calculated by the equation: Gross energy intake (kJ/day) = Dry food intake (g/day) × caloric value (kJ/g) of dry food (Li and Wang, 2005a,b; Song and Wang, 2003).

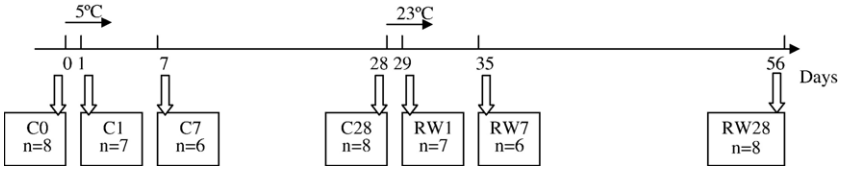

Fig. 1. The design of Experiment 2. The experiment started with 50 male Brandt's voles, raised at 23 ± 1°C and under a photoperiod of 12L:12D. They were exposed to 5 ± 1°C for 28 days and then returned to 23 ± 1°C. On days 0, 1, 7, 28, 29, 35, and 56, different individuals were killed and named as C0, C1, C7, C28, RW1, RW7, and RW28 respectively (C0 = before cold acclimation; C1, C7, and C28 = days of cold acclimation; RW1, RW7, and RW28 = days after rewarming).