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Research progress of low temperature adaptation mechanism of tree shrew (*Tupaia belangeri*): A review

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ABSTRACT

Low temperature environment is an important ecological factor that affects the growth, development and reproduction of animals, which plays an important role in the morphology, physiology, behavior and distribution of animals. This review discusses *Tupaia belangeri's* body weight, fatness, digestive tract, skull morphology, resting metabolic rate, basal metabolic rate, feed intake, energy intake, white adipose tissue, brown adipose tissue, liver, uncouple protein-1, cytochrome coxidase, insulin, thyroid hormone, semi-arboreal behavior and feeding behavior in response to low temperature. This paper summarized the adaptive strategies of *T. belangeri* to low temperature environment, in order to provide a basic theoretical basis for the study of omics and intestinal microbiology of *T. belangeri* in low temperature environment.

Keywords: *Tupaia belangeri*; low temperature; adaptation mechanism; resting metabolic rate; adipose tissue

1. INTRODUCTION

Ambient temperature affects almost all levels of biological tissue, from the function of cells, tissues, and organs to their combined role in the whole organism (Guderleyet al., 2002). Environmental temperature is also an important factor affecting the growth, development and reproduction of animals, and plays an important role in regulating the morphology, physiology and behavior of animals (Zhanget al., 2012a, Thyrringet al.,2017). Studies have shown that animals can adapt to low temperature by adjusting phenotypic changes, Animals also adapt to low temperature by regulating physiological changes, Animals also adapt to low temperatures by regulating their metabolites. Low temperatures also cause animals to develop behavioral strategies (Hanya 2004). In addition, low temperature also has an important impact on energy metabolism. Low temperature will bring energy crisis to animals, and endotherms need more energy to maintain a constant body temperature (Boströmet al., 2012).

As an independent taxon, Scandentia's status in systematical classification is still controversial, however, most studies agree that *Tupaia belangeri* is closely related to primates (Janecka et al., 2007), and it is considered as a new experimental animal model due to its rapid reproduction rate, small size and easy reproduction (Xiao et al., 2017; Wang et al., 2021), for example, *T. belangeri* are widely used in biomedical and medical research (Feng et al., 2017). The only tree shrew distributed in China is the *T. belangeri*, also known as the Northern tree shrew, it belongs to the order Scandentia and the family Tupaiidae, it mainly distributes in Yunnan, Sichuan, Guizhou, Guangxi and Hainan Island, Therefore, where are may be the northern limit of the geographical distribution of *T. belangeri*. In addition, tree shrew is a diurnal animal, which feed on a wide range. The physiological and ecological studies of shrews can provide a theoretical basis for more biological and medical research in the future. In this paper, the research progress of low temperature adaptation mechanism of *T. belangeri* was summarized.

2. Morphologicaladaptive changes of *Tupaia belangeri* under low temperature

2.1 Adaptive changes of body weight and fatness of *Tupaia belangeri* under low temperature

Phenotypic plasticity of animals has long been considered as an energy adaptation strategy for animals to cold environment. Studies have shown that the weight of *T. belangeri* has obvious seasonal changes, the body length of did not change significantly in different seasons. Therefore, with the increase of body weight in winter, the relative body surface area decreased, heat conduction decreased, and energy loss was reduced to enhance their adaptation to low temperature. Animals in different distribution areas adopt different body weight regulation methods to adapt to the environment in low temperature environment. The fatness of animals can reflect the physiological and nutritional status of animals, and is used as an important indicator to measure the adaptation of animals to the habitat environment (Table 1). The fatness of *T. belangeri* showed a certain seasonal difference; when winter came, the weight of *T. belangeri* increased significantly, body length changed little, and fatness was the highest, reduce energy loss relative to body surface area to survive the low temperature. They have strong phenotypic plasticity, which is crucial in adapting to the low temperature environment (Zhanget al., 2017).

2.2 Changes of digestive tract of *Tupaia belangeri* under low temperature

Studies have shown that, the environmental temperature in the region where *T. belangeri* live decreases, and the morphology of their digestive tract is longer in winter than in summer with seasonal changes. In winter, the contents and contents of stomach, large intestine and small intestine are significantly increased, and the digestive tract volume increases to improve the utilization rate of food and compensate for the increase of energy consumption in cold environment (Table 2). The change of digestive tract morphology is closely related to energy demand and consumption, which is conducive to the intake of more food and can ensure that animals obtain enough energy (Munn et al., 2006).

2.3 Changes in skull morphology of *Tupaia belangeri* to adapt to low temperature environment

Compared with animals in high temperature regions, *T. belangeri* in low temperature regions have evolved nasal morphology that is more adapted to low temperature environment, and molar morphology that is more conducive to obtaining food in bad environment, which provides an important guarantee for their survival in cold environment. The morphological changes of the skulls of mammals can reflect the environmental conditions of their existence (Yom-Tov et al., 2004). Changes of the skulls of *T. belangeri* under different temperature were mainly concentrated in the nasal cavity and molar teeth, which evolved molar teeth that improve feeding efficiency.

Table1: Changes in body weight of *Tupaia belangeri* and other rodents in cold environment

Name of species	Body weight	References
Tupaia belangeri	increase	Zhanget al., 2017
Albino Rat	reduce	Zhuet al., 2012
Apodemus chevrieri	reduce	Zhuet al., 2012
Lasiopodomys brandtii	reduce	Li and Wang, 2005a
Microtus oeconomus	reduce	Wang et al., 2006a
Ochotona curzoniae	no significant change	Wang et al., 2006b
Phodopus sungorus	reduce	Mercer, 1998

Table2: Changes in alimentary size canal of *Tupaia belangeri* and other rodents in cold environment

Name of species	Alimentary size canal	References
Tupaia belangeri	increase	Zhanget al., 2017
Peromyscus leucopus	increase	Dertinget al., 1995
M.penns-ylvanicus	increase	Dertinget al., 1995
Albino Rat	increase	Zhuet al., 2012

3. Physiological adaptation of energy metabolism to low temperature in *Tupaia belangeri*

3.1 Changes in resting metabolic rate (RMR) or basal metabolic rate (BMR) of *Tupaia belangeri* under low temperature

The amount of heat energy released per unit time of animals is called metabolic rate. The change of metabolic rate of small mammals is one of the regulatory mechanisms for adapting to different environments, which is of great significance for adapting to different environments. It is generally believed that metabolic rate includes resting metabolic rate and basal metabolic rate.

Small mammals adopt different mechanisms to regulate energy metabolism in different seasons. RMR of *T. belangeri* increased in low temperature environment, but with the extension of cold exposure time, its proportion in basal heat production decreased, while BMR increased significantly. The change of metabolic rate provided the possibility for it to adapt to low temperature environment, and the proportion of metabolic rate to basal heat production decreased, which explained that the tree shrew could not adapt to lower temperature (Table 3).

3.2 Regulation of energy intake, digestible energy, assimilation rate and digestibility of *Tupaia belangeri* under low temperature environment

Endotherms need to expend more energy to maintain a constant body temperature in cold environments, and disposable energy is limited by the dynamic balance between energy intake and energy expenditure (Oliveira et al., 2019). In winter, *T. belangeri* obtain higher energy from poor food conditions by increasing their food intake, energy intake, digestible energy, assimilation rate, digestibility and metabolic rate, so as to make up for higher energy consumption in cold environment, maintain constant body temperature and survive the low temperature environment.

3.3 Liver energy metabolism of *Tupaia belangeri* under low temperature

During cold exposure, liver weight, relative weight of liver, total protein content of liver, mitochondrial protein content and mitochondrial oxidation capacity of *T. belangeri* were significantly increased (Zhang et al., 2012b), which led to the increase of BMR(or RMR) and the number of mitochondria in liver. Improving the ability of RMR of liver in *T. belangeri* was to resist low temperature. At the same time in the cold environment state of liver mitochondria Ⅲ respiration, liver mitochondrial state Ⅳ were increased significantly, because the original ATP levels cannot meet the demand of biochemical reaction of the body's normal energy, increase the efficiency of mitochondrial oxidative phosphorylation and mitochondrial ADP is used after the respiratory rate, to supplement the energy demand increases (Villarin et al., 2003). When faced with cold, the liver responds quickly, regulating its weight and mitochondrial content to regulate energy production efficiency and increase heat production.

3.4 Metabolism of white adipose tissue

Adipose tissue in *T. belangeri* mainly exists in the form of WAT and BAT (Cinti 2001). Under cold environment, WAT weight of *T. belangeri* significantly increases. WAT’s main function is to store excess energy in the form of triglyceride and secrete some complement proteins to regulate the energy metabolism of animals, such as adiponectin and leptin. When animals are stimulated by low temperature, WAT will turn brown and turn into beige adipose tissue in order to effectively resist cold, and NST will be increased to compensate for the lack of metabolic heat production. In cold environment, WAT increases and browns to beige adipose tissue, which helps increase disposable energy and survive the cold environment?

3.5 Metabolism of brown adipose tissue

BAT is a specialized thermogenic tissue, whose growth is mainly controlled by the sympathetic nervous system (Zafrir 2013). Its main function is to mediate NST and increase adaptive thermogenesis of animals in cold environment (Reynes et al., 2019). Low temperature can stimulate the increase of uncoupling protein 1 content (UCP1) in BAT mitochondrial intima, directly affecting animal NST. When *T. belangeri* adapt to cold environment, the weight of BAT, UCP1 content, and NST increased, leading to the enhancement of thermogenic activity to cope with low temperature stress.

Low temperature can stimulate sympathetic nerve excitation, release norepinephrine and activate cyclic adenosine monophosphate (cAMP) in BAT. Protein kinase A produces biochemical effects that activate UCP1 activity (Maurer et al., 2019). The increase of UCP1 activity directly promotes the increase of BAT-mediated NST, but with the extension of cold exposure time, the proportion of NST in the basic heat production will decrease, which may be the reason why *T. belangeri* cannot adapt to the colder environment.

3.6 Cytochrome Coxidase (COX)

Cytochromic C oxidaseox, as an important component in the respiratory chain, is a bridge for protons from the cytoplasm to enter the cell membrane to synthesize ATP (Zhang et al., 2017), involved in mitochondrial energy metabolism (Zhang et al., 2012a). Under the condition of cold domestication, the activity of cytochromic C oxidase in BAT, liver and muscle of *T. belangeri* was significantly increased, indicating that mitochondrial energy metabolism in BAT, liver and muscle was enhanced.

Table3: Changes in non shivering thermogenesis of *Tupaia belangeri* and other rodents in cold environment

Name of species	Nonshivering thermogenesis	References
Tupaia belangeri	increase	Zhanget al., 2017
Microtus oeconomus	increase	Wang et al., 2006a
Ochotona curzoniae	increase	Wang et al., 2006b
Lasiopodomys brandtii	increase	Li and Wang, 2005a
Meriones unguiculatus	increase	Li and Wang, 2005b

Table4: Changes in serum leptin levels of *Tupaia belangeri* and other rodents in cold environment

Name of species	Serum leptin levels	References
Tupaia belangeri	increase	Zhanget al., 2017
Microtus oeconomus	reduce	Wang et al., 2006a
Ochotona curzoniae	no significant change	Wang et al., 2006b
Lasiopodomys brandtii	reduce	Li and Wang, 2005a

4. Changes of hormone levels in *Tupaia belangeri* under low temperature

4.1 insulin

Insulin plays a crucial role in the regulation of blood glucose (Andrali et al., 2008). The relative stability of blood glucose level has an important impact on the health status of animals. Insulin level also affects the concentration of other substances. Low temperature when animals reduce glucose metabolism is mainly due to increase in blood sugar levels (Diwan et al., 1976), under the condition of cold acclimation, *T. belangeri* insulin levels compared with the control group decreased, content of insulin and leptin levels were positively correlated, with *T. belangeri* under cold acclimation weight gain, These results suggest that *T. belangeri* may resist the rise in blood glucose level caused by low temperature through increased energy intake during cold domestication .

4.2 Thyroid hormone

Thyroid hormone has a significant influence on metabolic rate in mammals and plays an important regulatory role in animal heat production. Thyroid hormones stimulate cell thermogenesis, and their varying levels reflect thermogenesis regulation in animals under cold conditions (Tomasi et al., 1994). In simulated winter environment, the serum Triiodothyronine (T_3) concentration increased significantly, the Thyroxine (T_4) concentration decreased significantly, and the T_3/T_4 ratio increased significantly, indicating that the *T. belangeri* used up a large amount of T_4 in blood to generate T_3 with stronger thermo generating activity. This results in the enhancement of heat production capacity.

4.3 Serum leptin

Leptin is a complement protein produced by WAT and has the function of regulating food intake, and plays an important role in the seasonal energy balance and thermogenesis regulation of animals (Krol and Speakman, 2007). The decrease of leptin content in *T. belangeri* in cold environment is conducive to their increased food intake to compensate for the increase in energy consumption under cold stress, which may be related to the role of leptin as a hunger signal during cold adaptation (Krol and Speakman 2007). Leptin regulates energy metabolism through the combination of blood circulation and hypothalamus, and feedback the negative energy balance state of the body to the central center, so as to increase the energy intake of animals to compensate for the energy expenditure for metabolic heat production. In cold conditions, *T. belangeri* regulate leptin content and further regulate food intake to obtain more energy to compensate for high energy expenditure at low temperatures (Table 4).

5. Behavioral adaptation to low temperature in *Tupaia belangeri*

5.1 Semi-arboreal habits of *Tupaia belangeri*

T. belangeri escape with developed four-legged hops, inhabit in bushes, middle and lower levels of trees, and fruit forests. They move on the ground and in bushes with extremely fast movement speed and frequent activities in the morning and dusk. *T. belangeri* dig holes in mounds and build nests in trees, which can help them survive low temperatures.

5.2 Food storage behavior of *Tupaia belangeri*

Animal food storage is mainly due to the uneven distribution of food resources in different seasons, and food storage behavior can help animals to survive the environment of food scarcity. Hoarding food in the wild environment is beneficial to prevent food competition from other animal species. As an omnivorous animal, *T. belangeri* like to eat insects, grains, fruits and leaves, as well as other animal foods such as insects, and their hoarding behavior can help them survive the cold environment of food scarcity (Peng et al., 2020).

6. Summary and Prospect

In a word, *T. belangeri* can adjust the configuration, energy metabolism, hormone level and behavior to adapt to low temperature environment, although the part have evolved to adapt to the low temperature, but its adaptation mechanisms of low temperature is not yet perfect, such as, tree shrew only increased NST and the heat production of UCP1 to a certain extent, indicating that it had a certain adaptability to low temperature, but it was not enough to resist the excessively low temperature to continue to spread northward. At present, the studies on the adaptation of *T. belangeri* to low temperature mainly focus on morphology, physiology and behavior, while the studies on omics and intestinal microflora need to be further studied. Global warming is a common climate problem faced by the whole world. Under the influence of greenhouse effect, global warming, melting of glaciers and rising sea level lead to the change of global temperature zone, which will eventually have an impact on the living environment of animals. With global temperature rising, whether the morphology, physiology and behavior of animals can adapt to new changes without being eliminated by natural selection is worth further study. Low temperature environment is the main factor limiting the northbound spread of *T. belangeri*. During the process of spreading from the tropics to the present habitat, although *T. belangeri* have evolved some ways to adapt to low temperature, there are still defects. Whether global climate change will affect the northern limit of *T. belangeri* remains to be studied.

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