Pyrogenic Response in Pika (Whistle Rabbit)*

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Abstract: Pikas's better heat conservation ability thought to be due to its higher metabolic rate, poor heat dissipation through weak panting and smaller ear surface area. Although it's very sensitive to narcotics, it responds poorly to intraperitoneal Lipopolysaccharide (LPS) pyrogen.

In this experiment 9 pikas (mean body weight: 262.2g) reared at 22℃ were subjected to intravenous LPS pyrogen (3.8ug/kg) in the environmental control chamber (temp 28℃ and 60% r.h.). Throughout the experiment the animals were unrestrained in cages with thermister probe *in situ* deep in rectum and fixed to the tail by adhesive plaster. 15 minutes prior to i.v. pyrogen injection, rectal temperature (Tre) and respiratory rate (RR) were recorded every 5 minutes, and thereafter every 10 minutes. The LPS pyrogen evoked a monophasic fever (mean peak Tre: 40.23℃, mean △Tre: 0.73℃±0.3℃) which persisted for 70 minutes after a mean latent period of 20 minutes. RR decreased from precontrol rate of 108c/min to 100c/min at the peak of fever to a low 92c/min at the end of the pyrexia. It was also observed that the pika developed piloerection and shivering during the rising phase of the fever. Occasionally they licked their body but mostly they had minimal movement during the pyrexic period. These observation show that Pika rabbits can elicit fever with i.v. LPS pyrogen but the heat loss mechanisms differ from those of albino rabbits.

Key words: Pika, LPS pyrogen, Intra−venous injection, Monophasic fever, Respiratory rate, Temperature regulation

INTRODUCTION

Many terrestrial animals have evolved from variable ecosystems and as such the remaining species we see today owe some or part of their physiological responses to those of their previous terrestrial habitant. It has been reported that temperature regulation in Pika rabbit differs substantially from other rabbits because of its evolution. And its general morphology and evolutionary characteristics dictate its thermoregulation (Kosaka

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*All Pikas were reared at the Animal Research Center for Infectious Tropical Diseases, The Institute of Tropical Medicine, Nagasaki University where a portion of this experiment was performed.

et al., 1985) and its response to LPS pyrogens (Kosaka *et al.*, 1987). However, there is at present no data on Pika rabbits response to intra-venous (i.v.) LPS pyrogen possibly due to difficulty in i.v. administration of pyrogen. Other investigators have reported that the Pika rabbit does not respond to intraperitoneal LPS pyrogen (Horiuchi *et al.*, 1983). Therefore, the aim of the present experiment was to determine the response of Pika rabbit to i.v. LPS pyrogen.

Materials and Methods

Nine pika rabbits (7 males, 2 females) average body weight 262.2g (range 195g-290 g) were used in these experiments. They had been reared at the Animal Research Center of the temperature at 22℃ and relative humidity about 60%. These were brought up in cages and had food and water ad libitum. They had not been subjected to any other experiment.

On the day of experiment the animal was removed from its cage into another similar one without food or water and transferred to the climatic chamber (temp. 28℃ and 60% r.h.) where the experiments were performed. A thermister was inserted deep into the rectum and fixed onto the tail. This thermister was then connected to a digital thermometer (Terumo). The animal was then left undisturbed for 30 minutes to attain a thermal equilibrium. After the 30 minutes respiratory rate (RR) (determined by observation) and rectal temperature (Tre) were recorded every five minutes for 10 minutes.

Freshly prepared LPS pyrogen 3.8μg/kg was administered through the marginal vein of the ear. The animal was left undisturbed in the cage and continuous recording of the RR and Tre was done every 10 minutes for 110 minutes. 9 experiments were performed, one for each animal.

Results

The i.v. LPS pyrogen evoked a monophasic fever. The pyrogenic responses in the 9 experiments are shown in Fig. 1.

The latent time was 20 minutes, reaching a mean peak of 40.23℃ (SE 0.09℃). This was a mean increase of 0.73±0.3℃. This pyrogenic response lasted for 70 minutes after which the mean rectal temperature was 39.34℃ (Table 1).

Respiratory pattern was observed to diminish from precontrol frequency of 108 cycles/min to a mean of 100 cycles/min at peak of fever and further down to 92 cycles/min at the end of the fever (Table 2).

The behavioral aspect of the Pika rabbits during the experiment were noteworthy. Before the LPS injection the animals moved from one place to another quite frequently. They were quite mobile. They would lie down and stand up and run around from time to time. After the LPS injection the aminals were more composed, less mobile and mostly preferred to lie down. During the rising phase of the fever, the animals shivered, and

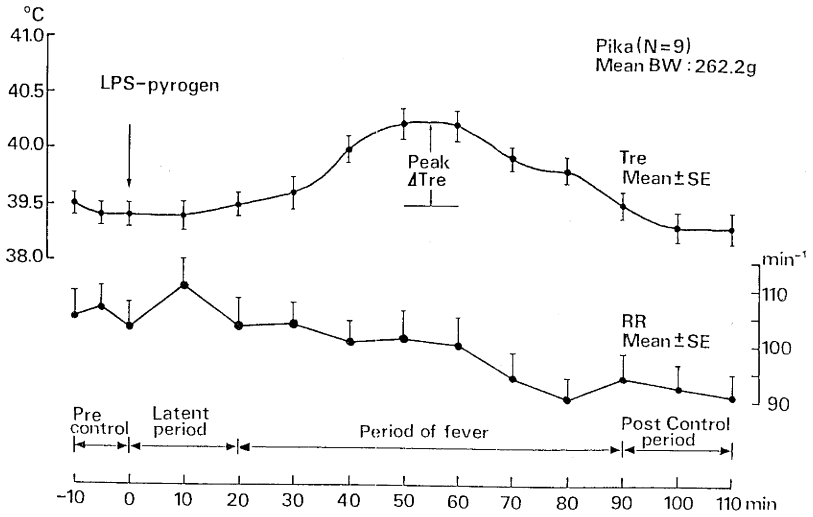

Fig. 1. The time course changes in core temperature and respiratory rate due to i.v. LPS pyrogen in Pika rabbits.

the fur elicited piloerection. Mostly the animals lied down on the abdomen with all limbs stretched out and licked their body and limbs. There was minimal movements especially at the peak of fever. During the declining phase of the fever, the animals persisted on licking the body and limbs and frequently standing up and strecting the body. As the fever subsided the animals became more active in the cage and more alert to the surroundings.

Table 1. Temperature pattern in i.v. LPS pyrogen induced fever in Pika rabbits (n=9)

	T (core)before LPS inj. (℃)	Latent time (minutes)	Peak temp △T (core) (℃)	Mean T (core) increase (℃)	Fever duration(minutes)	Post fever T (core) (℃)
Mean	39.34	20.0	40.21	0.73	70.0	39.3
SE	0.33	3.71	0.09	0.12	5.28	0.10

Table 2. Repiratory rate (RR) in i.v. LPS pyrogen induced fever in Pika rabbits (n=9)

	RR before LPS inj. (cycles/min)	RR during latent period (cycles/min)	RR at peak temp. (△Tcore)	Mean increase (cycles/min)	RR after fever (cycles/min)
Mean	108	107.7	100	−8	92
SE	4.54	4.12	3.99		4.88

DISCUSSION

In this experiment, it was found out that the Pika rabbits respond to i.v. LPS pyrogen by elicitation of a monophasic fever. Although the temperature of the environmental control chamber was higher (28℃) than the Animal Research Center chamber temperature (22℃), this did not interfere with the results because experiments on pyrogenicity should of necessity be performed in a warmer ambient temperature. The monophasic fever with a peak increase of 0.73℃±0.3℃ characterise the pyrogenicity of the LPS pyrogen at doses of 3.8μg/kg·body weight.

We can not in this experiment explain the monophasic characteristic in Pika rabbit which contrasts very much to pyrogenicity of i.v. LPS pyrogen in Albino rabbits (Fujiwara *et al.*, 1984). They found out that out of 24 Albino rabbits, 20 responded with biphasic type of fever on i.v. LPS pyrogen at closes of 0.2μg/kg·body wieght. This could be due to Pika rabbit peculiarity in response to LPS pyrogen and in particular to route of administration, dosage or pyrogen itself (exogenous(LPS), endogenous (IL−1, TNF) or even a final mediator like PGE_2) (Stitt, 1973; Morimoto *et al.*, 1984; Fujiwara *et al.*, 1984; Iwamoto 1986). The respiratory pattern of the Pika rabbits after i.v. LPS administration decreased with the rise in core temperature but before i.v. LPS injection the respiratory rate was lower than that previously reported by Kosaka et al. (1985) in which they found out that mean respiratory rate of Pika rabbits (n=20, mean Body weight: 80−90g) was 131 cycles/min at ambient temperature of 22℃. Our environmental control chamber temperature was higher (28℃, 60%) and the mean respiratory rate of 9 Pika rabbits (n=9, mean BW: 262g) was lower (108 cycles/min). Although there is difference in body weight and age between the former and the present study, this disparity needs further investigation. The decrease in respiratory rate by LPS pyrogen as well as by spinal cooling in Albino rabbits has been reported elsewhere (Kosaka *et al.*, 1969; Iwamoto *et al.*, 1985) although in their observation, RR of Albino rabbit was lower than in Pika rabbits even before i.v. LPS injection.

The behavioural aspect of fever response in Pika rabbit was characteristic of shivering thermogenesis, heat conservation (lower RR and piloerection) and during the decline of fever the animals displayed heat dissipation features (stretching on the abdomen with limb extension).

It is concluded therefore that Pika rabbits are able to respond to i.v. LPS pyrogen and that the behavioural aspect of heat dissipation differs substantially from Albino rabbits.

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ナキウサギ (Pika, Whistle Rabbit)の発熱反応

小坂光男，楊　果杰，Peter G. Riwa，松本孝朗，大渡　伸，范　育仁（長崎大学熱帯医学研究所疫学部門・環境生理）

ナキウサギ (pika)の体温が家ウサギより高い理由は，その高い熱産生能と低い熱放散能に起因するが，運動量・耳介の含む体表面積や行動性体温調節能などを統合して考えるべきである．ナキウサギは麻酔剤に高感受性を示す反面，腹腔内投与の外因性発熱物質 (LPS−pyrogen)に反応しないと報告されている．

今回，私共は細い耳介静脈注入の困難を克服して，22℃室内に飼育のナキウサギ（n＝9，平均体重：262.2 g）を人工気象室 (28℃，60% rh)に移し 3.8μg/kg の LPS−pyrogen を耳介静脈注入して発熱反応の有無を検索し，次の結果を得た．

（1）無麻酔，無拘束のナキウサギの平均直腸温 (39.34℃) は LPS−pyrogen 静注後，20分の潜時を経て上昇開始，最高直腸温 40.23℃ (ΔTre:0.73℃) を経て発熱持続時間70分の一峰性発熱曲線を示した．

（2）呼吸頻度 (RR)は LPS 静注前値 108c/min，発熱極期 100c/min，発熱終了時 92 c/min と変化し，これは家ウサギの RR 変化率より小さく，熱放散反応の不備を示唆している．

（3）発熱上昇期にはふるえ (shivering)熱産生，立毛反射や体動減少など，熱産生反応や熱保存反応には首尾一貫性がみられ，この結果からナキウサギが家ウサギに劣らない体温上昇能のみならず LPS−pyrogen による発熱特性を有することが明らかになった．

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