Trop. Med., 30 (3), 205−212, September, 1988

Threshold Core Temperatures for Tail Vasodilation During General Warming in Spontaneously Hypertensive Rats (SHR) and Stroke-prone SHR (SHRSP)

Katsuhiko TSUCHIYA[1], Hisashi OHTA[2], Masayori OZAKI[2] and Mitsuo KOSAKA[1]

1 *Department of Environmental Physiology, Institute of Tropical Medicine, Nagasaki University, 12−4 Sakamoto-machi, Nagasaki 852, Japan*

2 *The 2nd Department of Pharmacology, Nagasaki University School of Medicine, 12−4 Sakamoto-machi, Nagasaki 852, Japan*

Abstracts: In order to study heat dissipation ability of spontaneously hypertensive rats, threshold core temperatures for occurrence of the tail vasodilation were compared among adult male spontaneously hypertensive rats (SHR), stroke-prone SHR (SHRSP) and Wistar-Kyoto rats (WKY). Mean age of month (M.) and mean systolic blood pressure were 8.4±0.5 M; 205±5 mmHg for SHR, 7.2±0.6 M; 240±8 mmHg for SHRSP and 7.6±1.1 M; 140±6 mmHg for WKY. For the measurement, each rat was placed into a small wire-mesh cage for a loose restraint. Rectal temperature, tail skin temperature and air temperature were simultaneously recorded by means of thermistor probes or copper-constantan thermocouples. Air temperature was gradually raised at a constant rate of 0.17℃/min. Stepwise changes in the tail skin temperature were observed during the gradual elavation of the air temperature. The beginning of the tail vasodilation was detected by the 1st increase in tail skin temperature. Mean threshold core temperature for the 1st vasodilation in SHR, SHRSP and WKY were, 38.9±0.1℃, 38.4±0.1℃ and 38.0±0.1℃, respectively. Threshold core temperatures for the 1st vasodilation in SHR and SHRSP were significantly high compared to that in WKY, while the threshold in SHRSP was significantly lower than SHR. Mean values of threshold Ta for the 1st tail vasodilation in SHR, SHRSP and WKY were 30.1±0.5℃, 29.9±0.6℃ and 29.7±0.5℃, respectively. There was no statistical significance among these values. These results are consistent with the fact that the core temperature in adult SHRSP is not always high as SHR, even though blood pressure of SHRSP is higher than SHR. And these facts also suggest that high systemic blood pressure itself may not cause developing high core temperature in these genetically hypertensive rats.

Key words: Spontaneously hypertensive rats (SHR), Stroke-prone SHR, Tail vasodilation, Core temperature

Received for Publication, August 2, 1988.

Contribution No. 2125 from the Institute of Tropical Medicine, Nagasaki University.

*This study was partially supported by a Grant-in-Aid for Scientific Research (No. 62570075) from the Ministry of Education, Science and Culture of Japan.

**A part of rats was reared in Laboratory Animal Center for Biomedical Research, Nagasaki University School of Medicine.

INTRODUCTION

It has been reported that a high core temperature and an increased susceptibility to thermal stress were observed in spontaneously hypertensive rats (SHR) (Wilson *et al.*, 1977; Wright *et al.*, 1977; Isobe *et al.*, 1980; O'Donnell and Volicer, 1981). Wilson *et al.* (1977) reported that there was no significant difference in metabolic rate between adult SHR and normotensive Wistar-Kyoto rats (WKY) in the basal condition. For the explanation for development of high core temperature in SHR, it was suggested that heat dissipation from the body surface might be impaired due to an increased resistance to peripheral blood flow by high activity of the sympathetic vasoconstrictors in SHR (Isobe *et al.* 1980; Iriuchijima, 1973 a, b), and Wilson *et al.* suggested that the thermoregulatory set point might shift upward in SHR (Wilson *et al.*, 1977; Wilson and Wilson, 1978). But it is not fully elucidated. And it is not clear whether high core temperature in SHR is due to effect of high systemic blood pressure on the thermoregulatory mechanisms or is due to an incidentally accompanied genetical characteristic (Collins *et al.*, 1987).

Okamoto *et al.* (1974) established stroke-prone SHR (SHRSP) which were severer hypertensive rats than SHR. It has been reported that the core temperature in adult SHRSP was not always high as in SHR, though systemic blood pressure of SHRSP measured by the tail cuff method was higher than SHR (Tsuchiya *et al.*, 1987, 1988). In order to confirm whether hypertention is an essential factor for development of high core temperature or not, threshold core temperatures for the tail vasodilation were compared among three kinds of strains, SHR, SHRSP and WKY, whose blood pressures were distinctly different.

MATERIALS AND METHODS

Adult male rats of three kinds of strains, spontaneously hypertensive rats (SHR, N=12), stroke-prone SHR (SHRSP, N=15) and normotensive Wistar-Kyoto rats (WKY, N=14) as a control, were used in this study. Mean age of months (M) and mean body weight were 8.4±0.5 M; 352±11 g for SHR, 7.2±0.6 M; 305±10 g for SHRSP and 7.6±1.1 M; 384±24 g for WKY. Two or three rats were housed in a cage in the room (24℃, 50%, r. h.) under 12−12 hr light and dark cycle (light on 8.00−20.00 hr) with food and water available *ad libitum*. Systolic blood pressure (BP) and heart rate (HR) were measured by the routine tail cuff method after previous general warming (38℃, 10 min) (PE-300, Narco, USA). During the experiment for the continuous recording the rectal temperature (Tre) and tail skin temperature (Ttail), each animal was placed in a loosely fitting small cage made of wire-mesh for the loose restraint (Amar and Sanyal, 1981). Tre was measured by the thermistor probe, of which the tip was coated by polyethylene (2 mm in diameter). The probe was inserted more than 5 cm from the anus. Ttail was measured by a small probe (less than 1 mm in tip diameter) of the thermistor or copper-

constantan thermocouples, attached on the tail surface at the mid-point of whole length of the tail, and loosely wrapped by the adhensive surgical tape. The small cage containing the rat was suspended in the air of the chamber of 255 ℓ. Air temperature (Ta) in the chamber was gradually raised by warming the perfusing water through coils of copper tubes as a heat exchanger. Change rate of air temperature was ranging from 0.1℃/min to 0.2℃/min (mean, 0.17℃/min). Ta was also monitored by the thermistor probe which was set near to the rat. Abrupt increases in the tail skin temperature were used as an index of occurrence of the tail vasodilation (Rand *et al.*, 1965; Johanson, 1962). All Parameters were recorded simultaneously on a paper of the UV oscillograph (NEC-Sanei, Japan). All data were given with arithmetical means±S.E.M. Significance of changes in parameters was determined by Mann Whitney U test.

RESULTS

After general warming, systolic BP and HR were measured by the routine tail cuff method. Mean BP (Mean±S. E.) was 205±5 mmHg for SHR (N=10), 240±8 mmHg for SHRSP (N=12) and 140±6 mmHg for WKY (N=11). BP in SHR was significantly high ($p<0.01$) compared to WKY, and BP in SHRSP was significantly high ($p<0.01$) compared to both WKY and SHR. Mean HR in SHR, SHRSP and WKY were 445±9 beats/min, 389±10 beats/min and 407±12 beats/min, respectively. HR in SHR was significantly high ($p<0.05$) compared to WKY, and HR in SHESP was low compared to SHR ($p<0.01$). These results are summarized in Table 1.

Rats were individually placed in the small cage and probes were attached for the measuring of the rectal (Tre) and tail skin temperatures (Ttail) at 24℃ of ambient temperature. At first, Ttail was near the ambient temperature (Ta), which showed the vasoconstriction in the tail. Air temperature was gradually raised from 24℃ to the level more than 33℃. When Ta attained a certain level of Ta during gradual warming, Ttail

Table 1. Mean systolic blood pressure (BP) and heart rate (HR) measured by the tail cuff method (Mean±S.E.)

Strain	N	BP (mmHg)	HR (beats/min)
WKY	11	140±6	407±12
SHR	10	205±5**(a)	445± 9*(a)
SHRSP	12	240±8**(a,b)	389±10**(b)

N: the number of animals
Symbols for statistical significance as follows:
* $p<0.05$, ** $p<0.01$,
(a): compered to WKY (WKY → SHR, SHRSP)
(b): compered to SHR (SHR → SHRSP)

began to increase stepwise. An example was shown in Fig. 1. A small increase in Ttail occurred and successively followed by risings in Ttail. A marked increase in Ttail and a slight but definite decrease in Tre were observed simultaneously. When the 1st, 2nd and 3rd tail vasodilations were triggered during the increasing in Ta, Ta and Tre corresponding to the vasodilations were picked up in each case. Mean thresholds for Ta to the 1st vasodilation in SHR, SHRSP and WKY were 30.1±0.5℃, 29.9±0.6℃ and 29.7±0.5℃, respectively. Mean Tre at the 1st tail vasodilation in SHR, SHRSP and WKY were

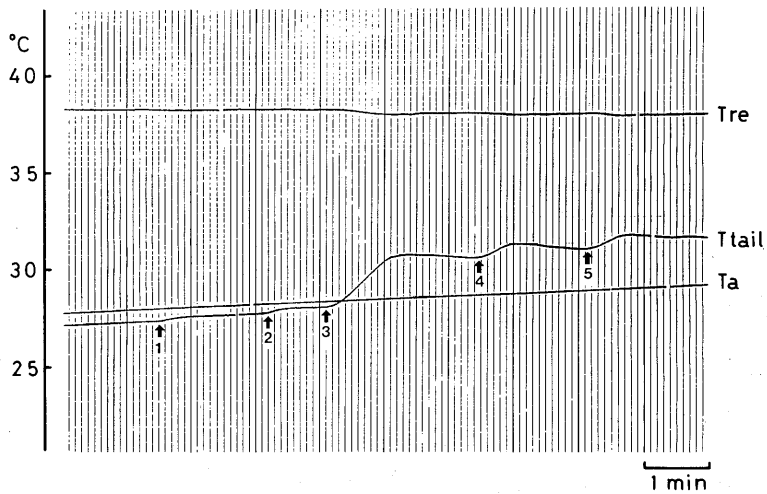

Fig. 1. An example of the tail vasodilations during gradual elevation of Ta. Symbols in the figure are as follows, Tre: rectal temperature, Ttail: tail skin temperature, Ta: air temperature in the experimental chamber. Solid arrows with the numbers indicate the beginning of abrupt increases of Ttail, which show the tail vasodilation.

Table 2. Mean threshold rectal temperature (Tre) and mean threshold air temperature (Ta) for the vasodilation in the tail during gradual warming. Threshold temperatures for the 1st vasodilation are demonstrated in A. Mean values of the threshold temperatures for the 1st, 2nd, 3rd vasodilations are shown in B

		A		B	
Strain	N	Tre(℃)	Ta(℃)	Tre(℃)	Ta(℃)
WKY	14	38.0±0.1	29.7±0.5	38.0±0.1	29.9±0.5
SHR	12	38.9±0.1**(a)	30.1±0.5	38.9±0.1**(a)	30.5±0.5
SHRSP	15	38.4±0.1 *(a), **(b)	29.9±0.6	38.3±0.1 *(a), **(b)	30.3±0.6

Symbols for statistical significance are the same as in Table 1 (Mean±S.E.).

38.9±0.1℃, 38.4±0.1℃ and 38.0±0.1 ℃, respectively. If mean threshold Ta and Tre for the 1st, 2nd and 3rd vasodilations in each case were calculated, almost the same results in the three strains were obtained. These results are summarized in Table 2. In both cases, mean threshold Tre for the tail vasodilation in SHR was significantly high compared to WKY ($p<0.01$), and mean threshold Tre in SHRSP was significantly high ($p<0.05$) compared to WKY but significantly low ($p<0.01$) compared to SHR. Mean threshold Ta for the occurrence of the tail vasodilation were not significantly different among the three strains (Table 2). The relationship between Ta and Tre at the occurrence of the tail vasodilation was illustrated in Fig. 2.

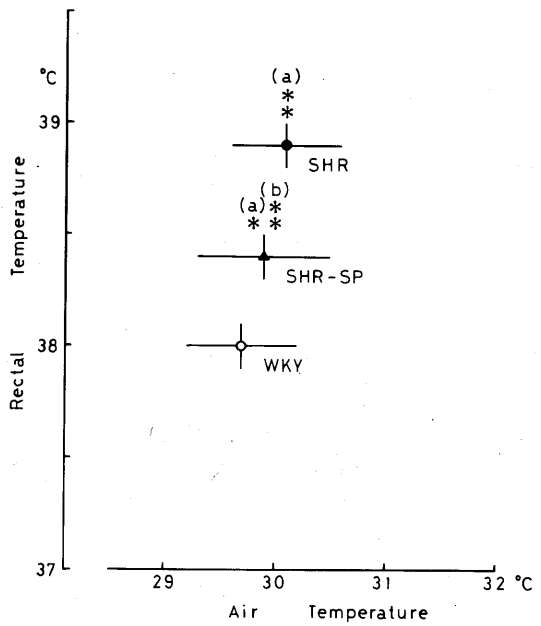

Fig. 2. Relationship between rectal temperature (Tre) and ambient air temperature (Ta) when the tail vasodilation occurred during gradual elevation of Ta. Mean values of threshold temperature in Tre and Ta for the 1st vasodilation in the tail are shown. Horizontal and vertical bars represent standard errors. Symbols for statistical significance are the same as in Table 1.

DISCUSSION

It has been reported that an elevated core temperature and an increased susceptibility to heat stress were observed in SHR (Wilson *et al.*, 1977; Isobe *et al.*, 1980; O'Donnell and Volicer, 1981). In this study, threshold temperature of Tre for occurrence of the tail vasodilation was compared among SHR, SHRSP and WKY. During gradual rising of Ta, Tre at the first occurrence of the tail vasodilation in SHRSP was lower than SHR but higher than WKY. During general warming, Ttail increased stepwise (Hellström, 1975). This suggests that total resistance for the tail blood flow might be decreased stepwise

during gradual rising of Ta. It is, however, still not known which changes stepwise, the magnitude of AVA vasodilation or the number of dilated AVA.

The rat tail is considered to be the important organ for heat dissipation. Though the tail surface amounts to about 10% of total surface area (Lyzak and Hunter, 1987), it is capable of dissipating as much as 17% of the total heat production (Rand, 1965). This phenomenon may be explained by the following fact that blood flow through the rat tail is effectively regulated by arteriovenous anastmoses (AVA) (Gemmell and Hales, 1977), which controlled by the sympathetic vasoconstrictor nerves (Folkow, 1955; Hales *et al.*, 1978; O'Leary *et al.*, 1985).

In this study, tail vasodilation was associated with a slight decrease in Tre as demonstrated in Fig. 1. Efferent discharge rate of the sympathetic nerve in SHR is higher than in WKY (Okamoto *et al.*, 1967; Iriuchijima 1973 b). It has been suggested that a heat dissipation from the body surface, mostly from the tail might be impared in SHR (Isobe *et al.*, 1980). Carlisle and Laudenslager (1979) reported that the threshold hypothalamic temperature for elicitation of tail vasodilation decreased systematically as ambient temperature increased when no behavioral option was available. Hensel (1981) discussed this hyperbolic relationship between peripheral and central (hypothalamic) temperatures for initiation thermal responses such as shivering and nonshivering thermogenesis as well as tachypnoea for heat dissipation. Because the tail vasodilations were elicited at similar Ta in this experiment, threshold core temperature for the vasodilation can be simply compared. Systemic blood pressure in SHRSP was the highest among the three strains in this study. If higher systemic blood pressure of SHRSP compared to SHR might be due to high sympathetic activity in the periphery, a high threshold temperature for the tail vasodilation might be expected. But threshold core temperature for the vasodilation in SHRSP was lower than in SHR. This suggests that there may be some functional differences for developing hypertension between SHR and SHRSP in this age.

Though it was reported that an increased oxygen consumption was obsereved especially in young (9−12 weeks of age) SHR (Tadepalli *et al.*, 1974) and in adult SHR (15−20 weeks of age) during heat stress (Wright *et al.*, 1978), Wilson *et al.* (1977) found no significant difference in oxygen consumption between adult SHR (15−20 weeks of age) and age-matched WKY at basal condition of 25℃. They suggested that the thermoregulatory set point might be upward shifted from the fact that SHR, relative to WKY, responded for more reinforcement during cold stress and but less reinforcement during heat stress in lever-pressing operant experiment. Detail mechanisms of the upward shift of the thermoregulatory set point, however, were not explained. If the high systemic blood pressure directly or indirectly contributes to the shift of thermoregulatory set point, it is expected that higher core temperature in SHRSP than in SHR might be observed. In this study, however, SHRSP showed lower threshold core temperature for the tail vasodilation. Yamori *et al.* (1985) recorded basal core temperature by a telemetry system. They reported that the rectal temperature was low in SHRSP which already developed a significant hypertension. It was also reported that core temperature of SHRSP (6−10 months

old) was lower than that of SHR, though systemic blood pressure measured by the tail cuff method in SHRSP was higher than in SHR (Tsuchiya *et al.*, 1987, 1988). On the other hand, O'Donell and Volicer (1981) normalized systemic blood pressure by antihypertensive therapy with chlonidine or hydraladine. But the difference in core temperature between SHR and WKY and the increased heat susceptibility of SHR remained. These facts eliminate the possibility of the direct or indirect effects, such as the reflex *via* the arterial baroceptors, of high systemic blood pressure itself on the thermoregulatory set point.

In this study, rats of three strains of 7−8 months old were mildly restrained by a loosely fitting cage for the temperature measuring. The effects of emotional stress by the restraint on thermoregulatory function must be taken acount of (Hajós and Engberg, 1986).

Acknowledgements

Authors would like to thank Mrs. N. Yamamoto and Mr. T. Maeda for a technical assistance during the blood pressure measurement of rats, and Miss J. Hayashima for preparing the manuscript.

References

1) Amar, A. & Sanyal, A. K. (1981): Immobilization stress in rats: Effect on rectal temperature and possible role of brain monoamines in hypothermia. Psycopharmacology, 73, 157−160.
2) Carlisle, H. J. & Laudenslager, M. L. (1979): Observations on the thermoregulatory effects of preoptic warming in rats. Physiol. Behav., 23, 723−732.
3) Collins, M. G., Hunter, W. S. & Blatteis, C. M. (1987): Factors producing elevated core temperature in spontaneously hypertensive rats. J. Appl. Physiol., 63, 740−745.
4) Folkow, B. (1955): Nervous control of the blood vessels. Physiol. Rev., 35, 629−663.
5) Gemmell, R. T. & Hales, J. R. S. (1977): Cutaneous arteriovenous anastomoses present in the tail but absent from the ear of the rat. J. Anat., 124, 355−358.
6) Hensel, H. (1981): Thermoreception and temperature regulation. Academic press, London, New York, Toronto, Sydney, San Francisco.
7) Hajós, M. & Engberg, G. (1986): Emotional hyperthermia in spontaneously hypertensive rats. Psychopharmacol., 90, 170−172.
8) Hales, J. R. S., Iriki, M., Tsuchiya, K. & Kozawa, E. (1978): Thermally-induced cutaneous sympathetic activity related to blood flow through capillaries and arteriovenous anastomoses. Pflügers Arch., 375, 17−24.
9) Hellstöm, B. (1975): Heat vasodilation of the rat tail. Can. J. Physiol. Pharmacol., 53, 202−206.
10) Iriuchijima, J. (1973a): Cardiac output and total peripheral resistance in spontaneously hypertensive rats. Jpn. Heart J., 3, 267−272.
11) Iriuchijima, J. (1973b): Sympathetic discharge rate in spontaneously hypertensive rats. Jpn. Heart J., 14, 350−356.

12) Isobe, Y., Ohara, K., Kosaka. M. & Aoki, K. (1980): Relationships between hypothalamic catecholamines, blood pressure and body temperature in spontaneously hypertensive rats. Jpn. J. Physiol., 30, 805−810.
13) Johansen, K. (1962): Heat exchange through the muskrat tail. Evidence for vasodilator nerves to the skin. Acta Physiol. Scand., 55, 160−169.
14) Lyzak, W. A. & Hunter, W. S. (1987): Regional surface areas of spontaneously hypertensive and Wistar-Kyoto rats. J. Appl. Physiol., 62, 752−755.
15) O'Donnell, A. & Volicer, L. (1981): Thermoregulation in spontaneously hypertensive rats: Effects of antihypertensive treatments. Clin. Exper. Hypertens., 3, 555−567.
16) Okamoto, K., Nosaka, S., Yamori, Y. & Matsumoto, M. (1967): Participation of neural factor in the pathogenesis of hypertension in the spontaneously hypertensive rat. Jpn. Heart J., 2, 168−180.
17) Okamoto, K., Yamori, Y. & Nagaoka, A. (1974): Establishment of the stroke-prone spontaneously hypertensive rat (SHR). Circ. Res. 34/35 Suppl. I, 143−153,
18) O'Leary, D. S., Johnson, J. M. & Taylor, W. F. (1985): Mode of neural control mediating rat tail vasodilation during heating. J. Appl. Physiol., 59, 1533−1538.
19) Rand, R. P., Burton, A. C. & Ing, T. (1965): The tail of the rat, in temperature regulation and acclimatization. Can. J. Physiol. Pharmacol., 43, 257−267.
20) Tadepalli, A. S., Walsh, G. M. & Tobia, A. J. (1974): Normal cardiac output in the conscious young spontaneously hypertensive rat: Evidence for higher oxygen utilization. Life Sci. 15, 1103−1114.
21) Tsuchiya, K., Kosaka, M., Ohta, H., Maeda, T. & Ozaki, M. (1988): Change in body temperature with age in spontaneously hypertensive rat (SHR) and stroke-prone SHR (SHRSP). Jpn. Heart J., 29, 550.
22) Tsuchiya, K., Kosaka, M., Ohata, H. & Ozaki, M. (1987): Autonomic nervous tones in spontaneously hypertensive rats (SHR) and stroke-prone SHR (SHRSP). Jpn. Heart J., 28, 626.
23) Wright, G. L., Knecht, E., Badger, D., Samueloff, S., Toraason, M. & Dukes-Dobos, F. (1978): Oxygen consumption in the spontaneously hypertensive rat. Proceed. Soc. Exp. Biol. Med., 159, 449−452.
24) Wright, G., Iams, S. & Knecht, E. (1977): Resistance to heat stress in the spontaneously hypertensive rat. Can. J. Physiol. Pharmacol., 55, 975−982.
25) Wilson, J. R., Wilson, L. M. & DiCara, L. V. (1977): Evidence for an elevation in thermoregulatory set-point in the SHR. Proc. 2nd Int. Sym. on SHR, DHEW Publ., No. (NIH), 77−1179, pp. 477−485.
26) Wilson, J. R. & Wilson, L. M. (1978): Spontaneously hypertensive rat (SHR): Possible elevation in thermoregulatory set-point. Psychophysiology., 15, 295−296.
27) Yamori, Y., Ikeda, K., Kulakowski, E. C., McCarty, R. & Lovenberg, W. (1985): Enhanced sympathetic-adrenal medullary response to cold exposure in spontaneously hypertensive rats. J. Hypertens., 3, 63−66.